Supplementary Online Content

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eAppendix 1. Centers for Disease Control and Prevention, Guideline for the Prevention of Surgical Site Infection 2017 –Background, Methods and Evidence Summaries

eAppendix 2. Centers for Disease Control and Prevention Guideline for the Prevention of Surgical Site Infection, 2017: Supplemental Tables

This supplementary material has been provided by the authors to give readers additional information about their work.

eAppendix 1. Centers for Disease Control and Prevention, Guideline for the Prevention of Surgical Site Infection 2017: Background, Methods and Evidence Summaries

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1. BACKGROUND

In 2006, approximately 80 million surgical procedures were performed in the United States at inpatient hospitals (46 million)[1] and ambulatory hospital-affiliated or free-standing (32 million) settings.[2] Between 2006 and 2009, surgical site infections (SSIs) complicated approximately 1.9% of surgical procedures in the U.S.[3] However, the number of SSIs is likely to be underestimated for several reasons including poor case ascertainment after hospital discharge (given that approximately 50% of SSIs become evident after discharge) and exclusion of some high-risk procedures from estimates (e.g., non-closed incisions).[4]National approaches to SSI surveillance have produced varied estimates of risk in the scientific literature,[5] which in combination with inconsistencies in coding and a lack of standardization of post-discharge surveillance, has made it challenging to evaluate or compare interventions and track SSIs over time.[6]

Multiple patient co-morbidities and risk factors, in addition to procedure-related risk factors, can impact the risk of SSI.[6] SSIs result in increased morbidity and mortality. Direct and indirect costs from SSIs include increased hospital length of stay, readmissions for treatment including repeat surgical procedures, outpatient and emergency care visits, use of ancillary services, additional medications (including prolonged antimicrobial therapy), lost productivity, and temporary or permanent disability.[7] Actual attributable costs of SSIs are difficult to determine. Cost estimates are commonly restricted to hospital charges and vary according to surgical procedure, depth of infection, facility, region, country, publication year, study design, and accounting method.[7-9] Estimated average attributable costs of SSIs range from $10,443 to $25,546 per infection (2005 and 2002 dollars, respectively).[10-13] *Staphylococcus aureus* and coagulase negative staphylococci are the organisms most commonly associated with SSIs, but pathogens can vary by procedure.[5] Costs can exceed $90,000 per infection when the SSI involves a prosthetic joint implant[14,15] or antimicrobial resistant organism.[16] Approximately 55% of SSIs are deemed preventable by application of evidence-based strategies.[13]

In 2002, the Centers for Disease Control and Prevention (CDC) and Centers for Medicare & Medicaid Services (CMS) instituted the Surgical Infection Prevention (SIP) project with the goal of reducing SSIs and developing effective prevention programs.[17] In 2006, SIP became the Surgical Care Improvement Program (SCIP) and expanded to include patient hair removal at the surgical site, glycemic control, and normothermia process measures.[18] With the Deficit Reduction Act of 2005, the U.S. Congress set forth a mandate for hospital reporting of process, outcome, and other quality improvement measures, and for making this information available to the public and CMS.[19] This act required CMS to adjust payments downward for healthcare-associated infections that could have been prevented through the application of evidence-based strategies. In 2009, the U.S. Department of Health and Human Services' (HHS) *National Action Plan to Prevent Health Care-Associated Infections: Road Map to Elimination* set a 5-year target goal of a 25% reduction in SSIs detected on admission and readmission, or a 0.75 Standardized Infection Ratio (SIR).[20] Since January of 2012, CMS's Hospital Inpatient Quality Reporting Program has required facilities to report SSI outcome data through CDC's National Healthcare Safety Network (NHSN).[21] These data provide some national estimates of SSI prevention progress (http://www.cdc.gov/hai/surveillance/progress-reports).[22]

1.1. Prosthetic Joint Arthroplasty

Prevention efforts should target all surgical procedures, but especially those in which both the human and financial burden is greatest. In 2011, primary total knee arthroplasty (TKA) accounted for over half of the 1.2 million prosthetic joint arthroplasty procedures (primary and revision) performed in the U.S., followed by total hip arthroplasty (THA), and hip hemi-arthroplasty.[23] Primary shoulder, elbow, and ankle arthroplasties are much less common. By 2030, prosthetic joint arthroplasties are projected to increase to 3.8 million procedures per year.[24-26]

Infection is the most common indication for revision in TKA[27] and the third most common indication in THA,[28] following instability/dislocation and mechanical loosening, *S. aureus* and coagulase negative staphylococci are the most common pathogens associated with orthopaedic SSIs.[5] Between 2001 and 2009, there was a significant increase in the risk of infection following hip and knee arthroplasties (from 1.99% to 2.18% and from 2.05% to 2.18%, respectively).[15] By 2030 the infection risk for hip and knee arthroplasty is expected to increase to 6.5% and 6.8%, respectively.[29] Owing to both increasing risk and the number of individuals undergoing prosthetic joint arthroplasty procedures, by 2020 the total number of hip and knee prosthetic joint infection (PJI) cases is projected to increase to 70,000 (from 25,000 in 2010) and up to 221,500 cases per year by 2030.[15,29] Treatment of PJI commonly involves a 2-stage procedure, with 4-to-8 weeks of parenteral antimicrobial therapy between stages. When eradication of the infection is not possible, treatment can include arthrodesis or even amputation.[30] In 2009, the average hospital cost for the revision of an infected hip or knee arthroplasty was $93,600 and $24,200, respectively.[15] Between 2001 and 2009, estimated total hospital costs for treating PJI increased from $320 million to $566 million; costs reached $1 billion in 2014 and are projected to reach $1.62 billion by 2020.[15]

Any indwelling medical device or prosthetic implant has the potential to become colonized by organisms and embedded in biofilm.[31,32] In the U.S., as many as 13 million people experience a biofilm-related infection every year.[33] Biofilm is defined as "a microbially derived sessile community characterized by cells that are irreversibly attached to a substratum or interface or to each other, are embedded in a matrix of extracellular polymeric substances that they have produced, and exhibit an altered phenotype with respect to growth rate and gene transcription."[32] Biofilm embedded organisms exhibit significant resistance to antimicrobial agents (10 to 1,000 times the minimum inhibitory concentration [MIC]) as compared with their free floating, planktonic counterparts.[32] Between 7% and 39% of PJIs are culture negative,[34,35] which is often attributed to previous antimicrobial therapy[36] or the presence of difficult-to-culture biofilm embedded organisms, making diagnosis, treatment, and the identification of prevention measures difficult to assess.

Evidence-based guidelines have provided recommendations for the diagnosis of PJI using conventional testing techniques including serologic and synovial fluid markers, tissue histopathology, traditional culture-based techniques, and imaging studies.[37] Recently published studies further support or add to these recommendations.[35,36,38-40] Potential future strategies for the diagnosis of PJI include the use of novel serologic[41-45] and synovial fluid[46] markers. In addition, novel strategies to improve the recovery of biofilm organisms may enhance detection of organisms present in lower numbers or species present as a minority.[31] Sonication of the explanted prosthesis[35,47-50] or cement spacer[49] produces a diluent of released biofilm sonicate. Culture of sonicate effluent may have improved culture sensitivity as compared with standard synovial fluid or tissue culture techniques. Different growth media[35,51] and microscopic[35,51-55] techniques to better grow and characterize biofilm and the embedded organisms are also being explored. Adjunct molecular techniques hold the potential to improve the sensitivity and specificity of traditional culture-based techniques.[51-53,55-61] However, only culture-based techniques provide information on antimicrobial susceptibility, which drives PJI treatment. Therefore exploring ways to enhance culturing techniques continues to be important.[62] Multidisciplinary work to standardize the clinical diagnosis of PJI is ongoing. [63]

2. SCOPE AND PURPOSE

The *Centers for Disease Control and Prevention Guideline for the Prevention of Surgical Site Infections, 2017* provides updated and new recommendations for the prevention of surgical site infection (SSI). This Guideline does not provide comprehensive infection control recommendations for prevention of SSIs; the exceptions are mentioned below. In 2014, the Healthcare Infection Control Practices Advisory Committee (HICPAC), a federal advisory committee of the Centers for Disease Control and Prevention (CDC), reviewed the strong recommendations found in the *Guideline for Prevention of Surgical Site Infection, 1999.*[64] HICPAC determined many of the 1999 recommendations to be accepted practices for the prevention of SSI. HICPAC recommended to CDC that these recommendations be considered core surgical infection prevention practices. These recommendations are located in Section 5 of this Guideline. The 1999 recommendations not updated in this Guideline are considered archived.

The specific areas of focus for the 2017 Guideline were informed by feedback received from clinical experts and input from HICPAC. As in the *Guideline for Prevention of Surgical Site Infection, 1999*,[64] the 2017 Guideline does not address SSI prevention issues unique to: burns; trauma; surgical incisions allowed to heal by secondary intention; transplant procedures; transmission of bloodborne pathogens from healthcare personnel to the patient; pediatric surgical practice; minimally invasive procedures; procedures performed outside of the operating room (e.g., endoscopic procedures); non-surgical invasive procedures (e.g., cardiac catheterization, interventional radiology); and other procedures or conditions not specifically mentioned.[64] In general, SSI prevention measures deemed effective in adults are also indicated in the pediatric surgical population, and those effective in the operating room can be adapted or modified for other settings. In addition, this update does not address SSI surveillance or public reporting.[65] Recommendations on infection control in healthcare personnel,[4,66] environmental infection control,[67] and disinfection and sterilization of medical devices[68] in healthcare settings are addressed by other guidelines.

To evaluate the evidence on SSI prevention, questions addressing 13 intervention categories were examined. The Core Section of the 2017 Guideline encompasses literature across all surgical procedures and is comprised of 6 topics: parenteral antimicrobial prophylaxis, non-parenteral antimicrobial prophylaxis, glycemic control, normothermia, oxygenation, and antiseptic prophylaxis. The literature for 7 topics related specifically to prosthetic joint arthroplasty procedures was evaluated in the Prosthetic Joint Arthroplasty section of the Guideline. These 7 topics include: blood transfusions, systemic immunosuppressive therapy, intra-articular corticosteroid injections, anticoagulation, orthopaedic surgical space suit, postoperative antimicrobial prophylaxis, and biofilm.

The 2017 Guideline is intended for use by surgeons; physician assistants; perioperative nurses and other allied perioperative assistive personnel; anesthesia providers; postoperative inpatient and clinic nurses; infection prevention staff; healthcare epidemiologists; healthcare administrators; other healthcare providers; and persons responsible for developing, implementing, delivering, and evaluating infection prevention and control programs for surgical procedures performed in an operating room (inpatient or ambulatory setting). The Guideline can also be used as a resource for professional societies or organizations that wish to develop more detailed implementation guidance or to identify future research priorities where there are evidence gaps for the prevention of SSI.

3. METHODS

The 2017 Guideline was based on a targeted systematic review of the best available evidence on SSI prevention. An adapted approach to the Grading of Recommendations Assessment, Development and Evaluation (GRADE) was used to assess the quality of the available evidence and the strength of the resulting recommendations, and to provide explicit links between them.[69-72] The Guideline development process has been previously described.[73] Methods and details that were unique to this Guideline are included below.

3.1Guideline Questions

A preliminary list of questions was developed from a review of the 1999 CDC SSI Guideline.[64] The current guideline does not re-evaluate several strong recommendations (Section 5) offered by the 1999 CDC SSI guideline which are now considered to be accepted

practice for the prevention of SSI. Content experts were surveyed to provide feedback on the questions and to identify additional topics of interest. Guideline questions were put in final form after they were vetted by the co-authors and HICPAC.

3.1A. Core Section Guideline Questions

Parenteral Antimicrobial Prophylaxis (AMP)

Q1. What are the most effective strategies for administering parenteral AMP to reduce the risk of SSI?
- What is the optimal timing of preoperative AMP?
- What is the optimal timing of AMP in cesarean section: prior to skin incision or at cord clamping?
- How safe and effective is weight-adjusted AMP dosing?
- How safe and effective is intraoperative redosing of AMP?
- How safe and effective is postoperative AMP and what is the optimal duration?

Non-Parenteral Antimicrobial Prophylaxis

Q2. What are the most effective strategies for administering non-parenteral antimicrobial prophylaxis at the surgical incision to reduce the risk of SSI?
- A. How safe and effective is antimicrobial irrigation?
- B. How safe and effective are antimicrobial agents applied to the surgical incision?
- C. How safe and effective are antimicrobial-coated sutures; when and how should they be used?
- D. How safe and effective are antimicrobial dressings applied to surgical incisions following primary closure in the operating room?

Glycemic Control

Q3. How do perioperative blood glucose and hemoglobin A1c levels impact the risk of SSI, and what are their optimal perioperative target levels in diabetic and non-diabetic patients?

Normothermia

Q4. How safe and effective is the maintenance of perioperative normothermia in reducing the risk of SSI?

Q5. What are the most effective strategies for achieving and maintaining perioperative normothermia?

Oxygenation

Q6. In patients with normal pulmonary function, how safe and effective is the perioperative use of increased fraction of inspired oxygen (FiO_2) in reducing the risk of SSI?

Q7. What is the optimal target FiO_2 to reduce the risk of SSI; how and when should it be administered?

Antiseptic Prophylaxis

Q8. What are the most effective strategies for preparing the patient's skin prior to surgery to reduce the risk of SSI?
- A. How safe and effective is preoperative antiseptic bathing or showering?
- B. How safe and effective are antiseptic skin preparation agents individually and in combination?
- C. How safe and effective is the application of a microbial sealant immediately following skin preparation?
- D. How safe and effective are plastic adhesive drapes?

Q9. How safe and effective is antiseptic irrigation prior to closing the surgical incision?

Q10. How safe and effective is repeat application of an antiseptic skin preparation agent to the surgical site immediately prior to closing the surgical incision?

3.1B. Prosthetic Joint Arthroplasty Section Guideline Questions

Blood Transfusion

Q11. How do perioperative blood transfusions impact the risk of SSI in prosthetic joint arthroplasty patients?
- A. Are specific blood products associated with a risk of SSI?
- B. If the risk of SSI is increased, can this effect be isolated from the risk associated with more complex cases?
- C. How does the volume of transfused blood product impact the risk of SSI?
- D. How safe and effective is withholding blood transfusion to reduce the risk of SSI?

Systemic Immunosuppressive Therapy

Q12. How does systemic corticosteroid or other immunosuppressive therapy impact the risk of SSI in prosthetic joint arthroplasty patients?
- A. Does the type of agent impact the risk of SSI?
- B. Does the preoperative duration of the therapy impact the risk of SSI?
- C. Does the agent dose impact the risk of SSI?

Q13. What are the most effective strategies in managing systemic corticosteroid or other immunosuppressive therapy perioperatively to reduce the risk of SSI in prosthetic joint arthroplasty patients?

A. How safe and effective is the discontinuation of these agents preoperatively, and when should they be resumed?
B. Should the agent dose be adjusted, and if so, for how long?

Q14. What is the optimal duration of postoperative AMP to reduce the risk of SSI in prosthetic joint arthroplasty patients who are on systemic corticosteroid or other immunosuppressive therapy?

Intra-articular Corticosteroid Injections

Q15. How do preoperative intra-articular corticosteroid injections impact the risk of SSI in prosthetic joint arthroplasty patients?

Q16. What are the most effective strategies for managing the preoperative use of intra-articular corticosteroid injections to reduce the risk of SSI in prosthetic joint arthroplasty patients?

A. Does the length of time between intra-articular corticosteroid injection and prosthetic joint arthroplasty impact the risk of SSI?
B. Does the corticosteroid injection dose impact the risk of SSI?

Anticoagulation

Q17. What are the most effective strategies for managing perioperative venous thromboembolism (VTE) prophylaxis to reduce the risk of SSI?

A. Does the risk of SSI differ by individual VTE prophylaxis agent?
B. What is the optimal timing and duration of perioperative VTE prophylaxis that also reduces the risk of SSI?
C. How safe and effective is modifying the dose of the perioperative VTE prophylaxis agent to reduce the risk of SSI?

Orthopaedic Space Suit

Q18. How safe and effective are orthopaedic space suits in reducing the risk of SSI in prosthetic joint arthroplasty patients, and which healthcare personnel should wear them?

Antimicrobial Prophylaxis Duration with Drain Use

Q19. What is the optimal duration of postoperative AMP to reduce the risk of SSI in prosthetic joint arthroplasty in the presence of a drain?

Biofilm

Q20. What are the most effective strategies to reduce the risk of biofilm formation and SSI in prosthetic joint arthroplasty patients?

A. How effective are cement modifications (i.e., antimicrobial and nanoparticle loading)?
B. How effective are prosthesis surface modifications (i.e., antimicrobial coating, galvanic couples, “printing” technologies, and nanotechnology)?
C. How effective are vaccines?
D. How effective are other biofilm control agents (e.g., biofilm dispersants, quorum-sensing inhibitors, novel antimicrobial agents)?

3.2. Literature Search

Following the development of Guideline questions, search terms were developed for identifying literature most relevant to those questions. For the purposes of quality assurance, these terms were compared to those used in relevant seminal studies and guidelines. These search terms were then incorporated into search strategies for the relevant databases. Searches were performed in MEDLINE, EMBASE, CINAHL, and the Cochrane Library. All databases were searched from 1998, when the previous guideline searches ended, through April 2014 for the Core Section and December 2011 for the Prosthetic Joint Arthroplasty Section. Literature published since these dates could affect one or more of the recommendations in this Guideline. References were imported into a reference manager where duplicates were resolved. The detailed search strategy and results for the Core Section and the Prosthetic Joint Arthroplasty Section can be found in eAppendix 2 of this Supplement.

Initial searches were designed to identify systematic reviews (SRs) and randomized controlled trials (RCTs). SRs that included non-randomized trials and observational studies (OBS) were eligible for inclusion. Three factors influenced the decision to limit literature searches to RCTs and SRs:

1. RCTs control for confounding more effectively than OBS and thus provide higher quality evidence on the efficacy of therapies;
2. the broad scope of the Guideline; and
3. the value of providing updated recommendations in a timely manner.

When Guideline questions in the Prosthetic Joint Arthroplasty Section were not adequately addressed in the studies identified by the initial searches, additional searches were performed. The additional searches used keywords that were more specific to each relevant question and were not limited to SRs and RCTs.

3.3. Study Selection

Titles and abstracts were screened by one independent reviewer (S.I.B.T., D.B., R.R.K., or C.E.R.). A random sample of 10% of titles and abstracts had a second independent review to ensure consistency in screening. Kappa scores, used to measure agreement between the two independent reviewers beyond chance, ranged from 0.4–0.5, indicating "moderate agreement" between reviewers.[74] Full text articles were retrieved if they were:

1. relevant to one or more Guideline questions;
2. clinical practice guidelines, SRs, or primary study designs meeting the inclusion criteria (RCT for the Core and Prosthetic Joint Arthroplasty sections and OBS for the Prosthetic Joint Arthroplasty section);
3. written in English; and
4. available as full text studies (meeting abstracts were excluded). Animal studies and in vitro basic science studies were excluded from all topics except biofilm. Pediatric patient studies were included. Although the literature databases were searched from 1998 to 2014, studies published earlier than 1998 were eligible for inclusion (e.g., studies suggested by the expert panel, included in the 1999 guideline, or identified in published SRs).

Full-text articles were screened by two independent reviewers (S.I.B.T and R.R.K.; S.I.B.T. and C.E.R.; S.I.B.T and D.B., or D.B and E.C.S.) and disagreements were resolved by discussion. Full-text articles were excluded if:

1. SSI was not reported as an outcome;
2. all patients included had "dirty" surgical procedures (except for Q2 addressing the use of aqueous iodophor irrigation);
3. the study only included oral or dental health procedures;
4. the surgical procedures did not include primary closure of the incision in the operating room (e.g., orthopedic pin sites, thoracotomies, or percutaneous endoscopic gastrostomy [PEG] procedures, or wounds healing by secondary intention);
5. the study evaluated wound protectors used post-incision.

In the Core Section for Q1, parenteral antimicrobial prophylaxis studies comparing the efficacy of antimicrobial prophylaxis to no prophylaxis (placebo-controlled studies) and studies comparing the efficacy of different prophylactic antimicrobial agents were excluded. Also for Q2, non-parenteral antimicrobial prophylaxis, use of gentamicin collagen sponge studies were excluded because they are not approved by the U.S. Food and Drug Administration (FDA). For Q8-10 antiseptic prophylaxis, studies evaluating vaginal antisepsis in combination with abdominal antisepsis were excluded. In addition, studies using electrolyzed ionized solution (not approved by the FDA for intraoperative irrigation of the surgical site) and dry povidone iodine powder spray studies were excluded.

For the Prosthetic Joint Arthroplasty section, studies were excluded if they did not specifically examine prosthetic joint arthroplasties. Questions from 4 topics in the Prosthetic Joint Arthroplasty section were excluded from a targeted search when both:

1. the initial broad search identified very few or no RCTs or SRs that fit the inclusion criteria, and
2. the content experts excluded them as lower-priority topics for guideline questions (i.e., surgical attire [specifically gloves], surgical techniques, anesthesia, and environmental factors).

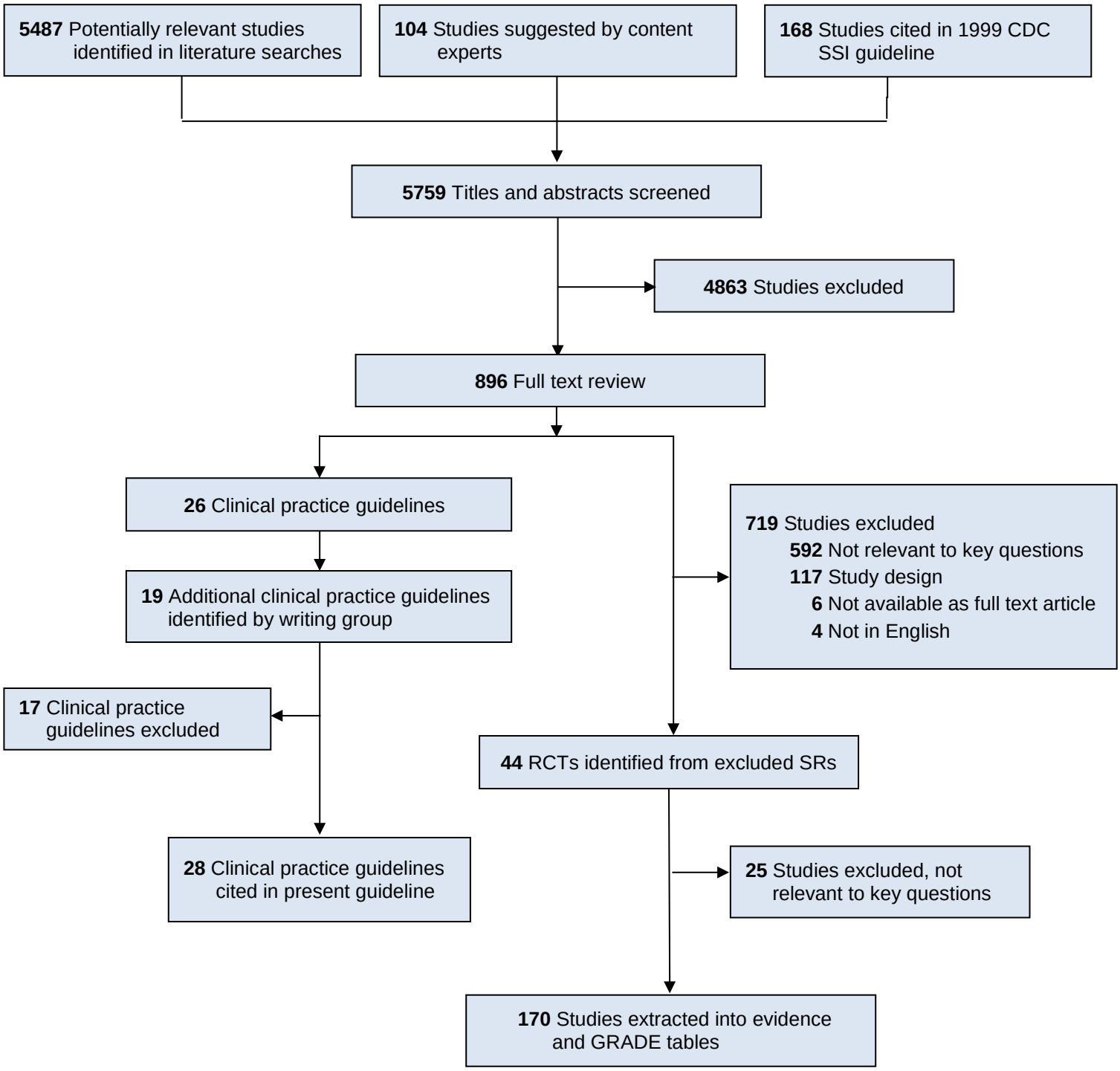
Also, questions and related studies addressing diagnosis of periprosthetic joint infection (PJI) or biofilm were excluded because they did not address SSI prevention. eTable 74 provides a list of inclusion and exclusion criteria used by reviewers.

eTABLE A. Inclusion and Exclusion Criteria for Study Selection

General Exclusion Criteria	Section 1 (all key questions)	Section 2 (all key questions)
Not relevant to key questions	✓	✓
Not RCT or SR	✓	
Not in English	✓	✓
Not available as full text article	✓	✓
Surgical site infection not included as outcome	✓	✓
Oral medicine / dental health procedures	✓	✓
Not primary closure	✓	✓
Wound protector used post incision	✓	✓
Animal studies	✓	
Basic science studies	✓	
Not a prosthetic joint arthroplasty		✓
Specific Exclusion Criteria	Topic	
Placebo-controlled studies	Antimicrobial prophylaxis	
Comparison of different antibiotics	Antimicrobial prophylaxis	
Vaginal antisepsis	Skin Preparation	
Epoeitin administration	Blood transfusion	
Specific Inclusion Criteria	Topic	
"Dirty" procedures	Antimicrobial prophylaxis	
Timing of AMP in high-risk Cesarean sections	Antimicrobial prophylaxis	
Non-AMP irrigation / topical application prior to wound closure (povidone iodine, electrolyzed/ionized solutions)	Antimicrobial prophylaxis	
Platelet gel prior to skin closure	Skin preparation	

A draft bibliography was shared with a panel of content experts, and the additional suggested references then progressed through title and abstract screening and full text review as described above. Results of the entire study selection process are depicted in *eFigure 1*.

eFIGURE 1. Results of the Study Selection Process



3.4. Data Extraction and Synthesis

For studies meeting the inclusion criteria, data on the study author, year, design, risk of bias, objective, population, setting, sample size, interventions, and results of clinically relevant outcomes were extracted into standardized evidence tables. From these, evidence tables were developed for each clinical topic represented by the questions. Studies were extracted into the most relevant evidence table. Studies were organized by individual questions and subquestions. Data were extracted by a single author (S.I.B.T., E.C.S., B.L., or R.A.) and cross-checked by another author (S.I.B.T. or E.C.S.). Disagreements were resolved by the remaining authors. Data and analyses were extracted as originally presented in the included studies. Meta-analyses were performed only where their use was deemed critical to a recommendation and only in circumstances in which multiple studies with sufficiently homogenous populations, interventions, and outcomes could be analyzed.

SRs were included if the individual studies fit the inclusion criteria. To avoid duplication of data, primary studies identified by the search were excluded if they were also included in a SR captured in the search, unless:

1. the primary study also addressed a relevant question that was outside the scope of the included SRs, or
2. it was one of a select number of studies in the SR that fit the inclusion criteria and was used to perform a new meta-analysis. SRs of primary studies that were fully captured in a more recent SR were excluded. The only exception was older SRs that addressed a question relevant to the Guideline that was outside the scope of the newer SR.[75]

Statistical analyses were performed using Review Manager 5.1. For the purposes of this review, statistical significance was defined as $p \leq 0.05$.

The risk of bias associated with each study was assessed using scales developed by the ECRI Institute Penn Medicine Center for Evidence-based Practice, and scores were recorded in the evidence tables. eAppendix 2 of this Supplement includes the questions used to assess the risk of bias of the included SRs, RCTs, and OBS. When the risk of bias was rated as “High” for >50% of studies making up the evidence base for a given outcome, one point was deducted for Study Quality in the GRADE tables.

Heterogeneity was assessed using the I^2 statistic and by evaluation of forest plots. When the I^2 value exceeded 50%, and the source of heterogeneity could not be explained by characteristics of the included studies, subgroup analysis, or examination of the forest plots, one point was deducted for consistency in the GRADE tables.

Publication bias was evaluated for questions that addressed commercial products if there was a reasonable expectation that bias in the publication of studies or the reporting of outcomes might be influenced by the sources of study funding. Additionally, funnel plots were examined for patterns suggestive of publication bias. Disclosures of study authors’ reported conflicts of interest were also reviewed, and relevant information is included in the evidence tables. When these analyses indicated the likely presence of publication or reporting bias, 1 point was deducted for publication bias in the GRADE tables. All GRADE Tables, Evidence Tables, and Risk of Bias Tables can be found in eAppendix 2 of the Supplement.

Evidence-based recommendations were cross-checked with those from other guidelines identified in an initial systematic search.

For all other methods, please refer to the Guideline Methods supplement.[73]

3.5. Formulating Recommendations

Recommendations were formulated based on current evidence that addressed Guideline questions at the time the literature searches were conducted. Explicit associations between the evidence and recommendations are mentioned in the Evidence Review of the Guideline (eAppendix 1 of the Supplement) as well as in the evidence tables and GRADE tables (eAppendix 2 of the Supplement). Evidence-based recommendations were cross-checked with those from other guidelines identified in an initial systematic search.

Category I (levels A, B, and C) recommendations are ALL considered strong and should be equally implemented; only the *quality* of the evidence underlying the recommendation(s) distinguishes levels A and B. Category IC recommendations are required by state or federal regulation without regard to level of supporting evidence. Category II recommendations are considered weak recommendations to be implemented at the discretion of individual institutions as supplementary procedures -- never in place of Category I recommendations -- and are not intended to be systematically and routinely enforced. The categorization scheme used in this Guideline is presented in eTable 2.

eTABLE B. CDC and HICPAC Categorization Scheme for Recommendations [73,76]

Recommendation Category	Category Description
Category IA	A strong recommendation supported by high-to-moderate quality evidence suggesting net clinical benefits or harms.
Category IB	A strong recommendation supported by low-quality evidence suggesting net clinical benefits or harms, or an accepted practice (e.g., aseptic technique) supported by low-to-very low-quality evidence.
Category IC	A strong recommendation required by state or federal regulation.
Category II	A weak recommendation supported by any quality evidence suggesting a tradeoff between clinical benefits and harms.
No recommendation/ unresolved issue	An unresolved issue for which there is either low-to-very low-quality evidence with uncertain tradeoffs between benefits and harms or no published evidence on outcomes deemed critical to weighing the risks and benefits of a given intervention.

The wording of each recommendation reflects the recommendation's strength. Active voice is used for Category I recommendations - the strong recommendations. For example, phrases such as “do” or “do not” are used to convey certainty. Passive voice is used for Category II recommendations - the weak recommendations. Words such as "consider” or “is not necessary” are used to reflect lesser certainty about an intervention. Additionally, some interventions described in this guideline may have clinical utility beyond the prevention of SSIs, but these other uses were not evaluated and are outside the scope of this guideline. To recognize the possibility that other uses may exist, these recommendations specified “for the prevention of SSI.”

Readers who wish to examine the evidence underlying the recommendations are referred to the Evidence Review in eAppendix 1 of the Supplement and the evidence tables and GRADE tables in eAppendix 2 of the Supplement. The Evidence Review includes narrative summaries of the data presented in the evidence tables and GRADE tables. The evidence tables include all study-level data used in the Guideline, and the GRADE tables assess the overall quality of the evidence for each question and outcome examined.

4. EVIDENCE REVIEW

4.1. Core Section Evidence Review

4.1A. PARENTERAL ANTIMICROBIAL PROPHYLAXIS (AMP)

Q1. What are the most effective strategies for administering parenteral AMP to reduce the risk of SSI?

Q1A. What is the optimal timing of preoperative AMP?

The search did not identify RCTs or SRs that evaluated different timings of preoperative AMP administration and its impact on the risk of SSI. The search only identified RCTs that evaluated timing of preoperative AMP administration in surgeries involving tourniquets.

The available data on the optimal timing of antimicrobial prophylactic agent administration in surgeries involving tourniquets examined AMP administered either before or after tourniquet inflation. For this comparison, deep SSI was the critical outcome in decision-making. Length of stay and antimicrobial resistance were also evaluated. The evidence for this comparison consists of 2 RCTs.[77,78] The findings of the evidence review and the grades for all important outcomes are shown in eAppendix 2 of the Supplement: GRADE Table Q1 and Evidence Table Q1A.

Low-quality evidence suggested a benefit of AMP administration 1 minute after tourniquet inflation as compared with 5 minutes before limb exsanguination and tourniquet inflation in elective lower limb musculoskeletal procedures. This was based on 1 small RCT[77] (N=106, high risk of bias) suggesting significantly fewer deep infections in the post-tourniquet inflation group. Patients had a preoperative admission time of up to 5 days, and limbs were exsanguinated prior to tourniquet inflation. Tourniquet time was longer in the pre-inflation AMP study group, but this difference was not significant.

Moderate-quality evidence suggested no difference in SSI rates based on AMP administration 10 minutes before tourniquet release vs. 10-30 minutes before tourniquet inflation, in total knee arthroplasties. This was based on no difference in deep SSI in 1 large, single-institution RCT[78] with 908 total knee arthroplasties and a moderate risk of bias. There were no differences in length of stay and antimicrobial resistance between groups.

Other guidelines

The *1999 CDC Guideline for Prevention of Surgical Site Infection* and other clinical practice guidelines, based on a review of the evidence and expert opinion, recommend administering by the intravenous route a single dose of prophylactic antimicrobial agent only when indicated. For most prophylactic agents, the 1999 CDC guideline recommended preoperative administration be timed such that a bactericidal concentration of the drug is established in the serum and tissues when the incision is made, and other clinical practice guidelines recommend that administration should be within 60 minutes prior to incision (vancomycin and fluoroquinolones within 60-120 minutes prior to incision).[17,64,79-85] This is considered accepted practice. None of the recommendations address whether it is necessary to administer a complete or a partial infusion of the parenteral AMP dose prior to surgical incision.

Q1B. What is the optimal timing of AMP in cesarean section: prior to skin incision or at cord clamping?

The available data on optimal timing of antimicrobial prophylactic agent administration in cesarean section examined AMP administered prior to skin incision versus at cord clamping.

For this comparison, post-partum endometritis was the critical outcome in decision-making. Other outcomes were also evaluated, including incisional SSI, neonatal sepsis, neonatal sepsis workup, neonatal antimicrobial resistance, and neonate admission to higher level of care. In general, endometritis was defined as fever > 100.4°F (38°C) on 2 occasions with uterine tenderness, purulent lochia, tachycardia or leukocytosis. The findings of the evidence review and the grades for all important outcomes are shown in eAppendix 2 of the Supplement: GRADE Table Q1 and Evidence Table Q1B.

High-quality evidence suggested a benefit of AMP administration prior to skin incision as compared with administration immediately after the umbilical cord is clamped in cesarean sections. This was based on a meta-analysis (N=2493) of 7 RCTs[86-92] suggesting a 43% reduction in the risk of developing post-partum endometritis and no difference in the odds of developing incisional SSI. High-quality evidence from a meta-analysis (N=1080) of 3 RCTs[86,87,92] showed no difference in neonatal sepsis. Moderate-quality evidence consisting of 2 RCTs[86,91] evaluating neonatal antimicrobial resistance in cases of sepsis found either no difference in neonatal antimicrobial resistance between groups, or no cases of antimicrobial resistance, respectively. In addition, high-quality evidence from a meta-analysis (N=1604) of 5 RCTs[86-88,91,92] suggested no difference in neonatal sepsis workups. Lastly, high-quality evidence from a meta-analysis (N=1694 neonates) of 5 studies[86,87,89,91,92] suggested no difference in admissions to higher level of care. One of these studies[89] reported being funded by a pharmaceutical company.

Other guidelines

Clinical practice guidelines based on a review of the evidence and expert opinion recommend administration of a single preoperative prophylactic antimicrobial agent by the intravenous route, based on the agent pharmacokinetics, commonly beginning within 60

minutes prior to skin incision in both elective and emergency cesarean section.[79-81,83] Administration of AMP after cord clamping is no longer recommended.[64]

Q1C. How safe and effective is weight-adjusted AMP dosing?
Searches of published studies did not identify RCTs or SRs that evaluated weight-adjusted AMP dosing and its impact on the risk of SSI.

Other guidelines
Clinical practice guidelines based on a review of the evidence and expert opinion recommend increasing the single preoperative prophylactic antimicrobial agent dose for select prophylactic antimicrobial agents in obese and morbidly obese patients.[79-84] For cefazolin, recommendations are to administer 2.0 g[80-82,84] for patients weighing >60-80 kg and 3.0 g[81,84] if >120 kg. For aminoglycosides, dosing is calculated using the patient's ideal body weight plus 40% of the difference between the actual and ideal body weight.[81,84,93] Vancomycin should be dosed at 15 mg/kg.[80-82,84]

Q1D. How safe and effective is intraoperative redosing of AMP?
The available data examining intraoperative redosing of AMP compared 1 preoperative dose versus 1 preoperative dose plus an additional dose at 2 hours intraoperatively.

For this comparison, abdominal and perineal wound SSI and intra-abdominal abscess were the critical outcomes in decision-making. Antimicrobial resistance was also evaluated as an outcome of interest. The evidence for this question consists of 1 RCT at moderate risk of bias in elective colorectal surgery.[94] The findings of the evidence review and the grades for all important outcomes are shown in eAppendix 2 of the Supplement: GRADE Table Q1 and Evidence Table Q1D.

Moderate-quality evidence suggested no benefit of intraoperative AMP redosing. This was based on no difference in abdominal or perineal wound infection, intra-abdominal abscess, or antimicrobial resistance in 1 elective colorectal surgery study from 1991.[94] However, procedures with durations >3 hours had a significantly higher risk of SSI and 22% of patients with procedure durations ≥2 hours were not redosed. Fecal contamination almost doubled the SSI rate at every level of contamination (of note, patients underwent mechanical bowel prep). Procedure duration and fecal contamination were not reported by study group. Limited power of the study could result in a false negative finding.

Other guidelines
Clinical practice guidelines based on a review of the evidence and expert opinion recommend prophylactic antimicrobial agent redosing in cases of prolonged procedures (when the procedure exceeds the half-life of the prophylactic antimicrobial agent or is longer than 3-4 hours) and in patients with major blood loss (>1,500 ml) or extensive burns.[80-84,95] Redosing should also be performed at intervals of 1-2 times the prophylactic antimicrobial agent half-life, starting at the beginning of the preoperative dose.[80-84,95] No recommendations are provided for optimal prophylactic antimicrobial agent dosing in obese and morbidly obese patients when redosing.

Q1E. How safe and effective is postoperative AMP and what is the optimal duration?
Administration of postoperative AMP was evaluated, both with all surgical procedures combined and by select surgical specialties. Analysis focused on studies that used the same prophylactic antimicrobial agent in both arms. Studies that compared different prophylactic antimicrobial agents or those administering only oral AMP were excluded. Postoperative AMP was defined as any parenteral prophylactic antimicrobial agent administered after intraoperative closure of the surgical incision. Therefore, postoperative AMP (in hours or days) does not include any AMP administered as a single preoperative dose and/or any intraoperative redosing.

The available data examined the following comparisons for different postoperative AMP durations:

1. All surgeries—No post-op AMP vs. ≤24 hours
2. Cardiac
    a. No post-op AMP vs. ≤24 hours
    b. No post-op AMP vs. <96 hours
    c. No post-op AMP vs. 72–96 hours
    d. ≤24 vs. 72 hours
3. Thoracic—No post-op AMP vs. 2 days
4. Vascular
    a. No post-op AMP vs. ≤24 hours
    b. <24 hours vs. 3–5 days
    c. No post-op AMP vs. 5 days
5. Ear, nose, and throat - ≤24 hours vs. 3–5 days
6. Gynecologic
    a. No post-op AMP vs. ≤24 hours

    b. b. <24 hours vs. <2.5 days
7. Orthopaedic
    a. Fracture—No post-op AMP vs. ≤24 hours
    b. Prosthetic Joint Arthroplasty—No post-op AMP vs. ≤24 hours
8. Colorectal: Bowel preparation with oral antimicrobials
    a. No post-op AMP vs. 3 days
    b. ≤24 hours vs. 5 days
9. Colorectal: Bowel preparation only
    a. No post-op AMP vs. ≤24 hours
    b. b. No post-op AMP vs. <2-3 days
10. Colorectal: Bowel preparation not reported
    a. No post-op AMP vs. ≤24 hours
    b. ≤24 hours vs. 2–3 days
11. Colorectal: No bowel preparation
    a. No post-op AMP vs. ≤24 hours
    b. No post-op AMP vs. <2–3 days
12. Appendectomy
    a. No post-op AMP vs. ≤24 hours
    b. No post-op AMP vs. 2 days
13. Rectal surgery—No post-op AMP vs. ≤24 hours
14. Gastric surgery
    a. No post-op AMP vs. ≤24 hours
    b. No post-op AMP vs. 2 days
    c. None vs. 4 days
15. Hepatectomy—2 days vs. 5 days

For all comparisons, SSI (superficial, deep incisional, and organ/space) and trocar wound infection were the critical outcomes for decision-making. Antimicrobial resistance, adverse events, length of stay, mortality, and other outcomes were also evaluated. The evidence for this question consists of 45 RCTs in cardiac;[96-100] thoracic;[101] vascular; [102-104] ear, nose and throat;[105,106] gynecologic;[107-112] orthopaedic;[113-118] and general surgical[119-140] procedures. Twenty-eight (62%) studies were published between 1972 and 1998; 17 (38%) studies were published between 2003 and 2013. The findings of the evidence review and the grades for all important outcomes are shown in eAppendix 2 of the Supplement: GRADE Table Q1 and Evidence Table Q1E.

Q1E.1. All surgeries - none vs. ≤24 hours

High-quality evidence suggested no benefit of continuing AMP after intraoperative closure of the surgical incisions. This was based on no difference in SSI in 1 large meta-analysis (N=14,285) of 21 RCTs in cardiac; thoracic; vascular; ear, nose and throat; gynecologic; orthopaedic; and general surgical procedures.[99,102,108-120,122-124,128,133,137] Fourteen (67%) studies were published between 1984 and 1995; 7 were published between 2005 and 2013. Thirteen studies[97,98,108,111,115,118,120-122,125,127-129] reported funding of the study and/or receipt of study supplies from pharmaceutical companies.

Moderate-quality evidence suggested no benefit of continuing AMP after intraoperative closure of the surgical incision in cardiac surgery. This is based on a meta-analysis (N=1746) of sternal organ/space infections in cardiac surgeries in 3 RCTs.[97-99] Two studies[97,98] reported the authors received funding from pharmaceutical companies.

Results by select surgical specialties or procedures and individual comparators are available in eAppendix 2 of the Supplement: GRADE Table Q1.

Q1. Recommendations

1A. Administer preoperative antimicrobial agent(s) only when indicated, based on published clinical practice guidelines and timed such that a bactericidal concentration of the agent(s) is established in the serum and tissues when the incision is made. **(Category IB – strong recommendation; accepted practice)** [64] (Guideline Question 1A)

1A1. No further refinement of timing can be made for preoperative antimicrobial agents based on clinical outcomes. **(No recommendation/unresolved issue)** [77,78] (Guideline Question 1A)

1B. Administer the appropriate parenteral prophylactic antimicrobial agent(s) prior to skin incision in all cesarean section procedures. **(Category IA – strong recommendation; high-quality evidence)** [86-92] (Guideline Question 1B)

1C. The search did not identify randomized controlled trials evaluating the harms and benefits of weight-adjusted AMP dosing and its affect on the risk of SSI. Other organizations have made recommendations based on observational and pharmacokinetic data and a summary of these recommendations can be found in the Other guidelines section of the narrative summary for this question**. (No recommendation/unresolved issue)** (Guideline Question 1C)

1D. The search did not identify sufficient randomized controlled trial evidence to evaluate the harms and benefits of intraoperative redosing of parenteral prophylactic antimicrobial agents for the prevention of SSI. Other organizations have made recommendations based on observational data and a summary of these recommendations can be found in the Other guidelines section of the narrative summary for this question**. (No recommendation/unresolved issue)** [94] (Guideline Question 1D)

1E. In clean and clean-contaminated procedures, do not administer additional prophylactic antimicrobial agent doses after the surgical incision is closed in the operating room, even in the presence of a drain. **(Category IA – strong recommendation; high-quality evidence)** [96-140] (Guideline Question 1E)

4.1B. NON-PARENTERAL ANTIMICROBIAL PROPHYLAXIS

Q2. What are the most effective strategies for administering non-parenteral antimicrobial prophylaxis at the surgical incision to reduce the risk of SSI?

Q2A. How safe and effective is antimicrobial irrigation?

The search identified 2 RCTs examining the impact of antimicrobial irrigation on SSI. For this comparison, SSI was the critical outcome for decision-making. Product-related adverse events and antimicrobial resistance were also evaluated.

In elective colorectal surgeries, moderate-quality evidence suggests a reduction in SSI with intraperitoneal lavage using clindamycin-gentamicin solution that is allowed to rest in the abdominal cavity for 3 minutes. This was based on 1 small RCT[141] at low risk of bias in 103 surgeries. In this study, both groups received preoperative AMP followed by an intraoperative bolus at 4 hours if the surgery exceeded this time. Post-irrigation microbiologic samples were only taken from the group irrigated with clindamycin-gentamicin solution. Post-irrigation cultures were positive in 2 patients (4%) in this group and both the *Klebsiella spp.* and *Streptococcus salivarius* recovered were resistant to clindamycin and gentamicin. Product-related adverse events were not assessed.

In acute appendectomies, low-quality evidence suggested a reduction in SSI with wound irrigation using ampicillin solution when compared with normal saline irrigation. This was based on 1 RCT[142] (N=249) at moderate risk of bias in adult and pediatric patients undergoing appendectomies for suspected acute appendicitis. Both groups received AMP, which was continued for 5 days postoperatively if the appendix was found to be gangrenous or perforated. Almost all *Streptococcus* and *Enterococcus* isolates cultured from intraoperative peritoneal and wound swabs were sensitive to ampicillin except for 30% of *E. coli* isolates. Postoperative complications were infrequent and not associated with the intervention.

The search did not identify RCTs or SRs that evaluated the safety and effectiveness of soaking of surgical implants (e.g., meshes, neurosurgical ventricular shunts) in antimicrobial solution prior to insertion (in combination with parenteral AMP) and its impact on SSI.

Other guidelines

Two clinical practice guidelines, based on a review of the evidence, recommend against antimicrobial wound irrigation or intra-cavity lavage to reduce the risk of SSI.[85,95]

Q2B. How safe and effective are antimicrobial agents applied to the surgical incision?
The available data examined the following comparisons:

1. Ampicillin solution vs. no topical antimicrobial agent
2. Ampicillin powder vs. no topical antimicrobial agent
3. Chloramphenicol vs. no topical antimicrobial agent
4. Rifampin vs. no topical antimicrobial agent
5. Vancomycin powder in hemostatic paste vs. hemostatic paste
6. Autologous platelet-rich plasma (APRP) (spray or gel) vs. no APRP

For all comparisons, SSI was the critical outcome for decision-making. Wound dehiscence, wound closure, and product-related adverse event outcomes were also evaluated. The evidence for the pharmacologic antimicrobial prophylactic agent comparators consists of 6 RCTs,[143-148] and for the APRP comparator the evidence consists of 4 RCTs.[149-152] APRP provides a platelet concentrate commonly used to enhance both wound hemostasis (formation of a fibrin clot) and wound healing (clot provides a matrix for the migration of tissue-forming cells and endothelial cells involved in angiogenesis and thus the remodeling of the clot into repair tissue).[153,154] These characteristics have led to a significant increase in the use of APRP therapies for the treatment of chronic wounds and multiple orthopaedic conditions including bone repair, tendon, and soft tissue injuries.[155,156] In addition, in vitro studies have demonstrated that APRP holds strong bactericidal activity and suggest its potential value as an adjunct topical antimicrobial prophylactic agent for use at the time of surgical incision closure.[157,158] In all studies, both groups received parenteral AMP. The findings of the evidence review and grades for all important outcomes are shown in eAppendix 2 of the Supplement: GRADE Table Q2 and Evidence Table Q2B.

Q2B.1. Ampicillin solution vs. no topical antimicrobial agent
In elective colorectal surgeries, low-quality evidence suggests no benefit to application of ampicillin solution to the subcutaneous and subfascial layers when combined with bowel prep and AMP for 3 days postoperatively. This was based on 1 RCT[145] (N=203) at moderate risk of bias. This RCT included patients with previously known infections, including 1 patient with Fournier's Gangrene. This study noted no adverse events associated with the intervention.

In acute appendectomies, moderate-quality evidence suggested a benefit to cleaning the subcutaneous tissues with ampicillin solution-soaked gauze. This was based on 1 RCT[146] (N=246) at moderate risk of bias. This reduction in SSI was not present in the simple, acute appendicitis cases, but was significant in the perforated and gangrenous appendicitis cases. Both groups received preoperative intramuscular AMP.

Q2B.2. Ampicillin powder vs. no topical antimicrobial agent
In elective colorectal surgeries, moderate-quality evidence suggested no benefit to ampicillin powder applied to the subfascial and subcutaneous layers when compared with no topical antimicrobial. This is based on 1 RCT[147] in (N=170) at moderate risk of bias. AMP was administered preoperatively and was continued postoperatively for 2 doses over 12 hours for both groups.

Q2B.3. Chloramphenicol vs. no topical antimicrobial agent
Moderate-quality evidence suggested no benefit of topical chloramphenicol ointment in combination with parenteral AMP. This was based on no difference in SSI in 1 small study at low risk of bias in 92 hemi-arthroplasty or dynamic hip screw fixation procedures for hip fractures.[143]

Q2B.4. Rifampin vs. no topical antimicrobial agent
Low-quality evidence suggested a benefit of topical rifampin in combination with parenteral AMP. This was based on a reduced risk of wound leakage, fewer local signs of inflammation, and reduced risk of wound dehiscence at the umbilical port site in 1 very small (N=48) laparoscopic cholecystectomy study at moderate risk of bias.[144] Umbilical port-site infection was defined as "purulent wound leakage." Based on results reported in a histogram, at 12 hours postoperatively, 71% of patients had purulent wound leakage including almost half of the rifampin and all of the control groups. By 24 hours, the entire control group remained infected; a week later, only 2 infections remained. It is not clear if any of these were true infections.

Q2B.5. Vancomycin powder in hemostatic paste vs. hemostatic paste alone
Low-quality evidence suggested a benefit to applying vancomycin powder mixed with hemostatic paste to the cut sternal edges during heart surgery. This was based on 1 RCT[148] (N=416) at high risk of bias evaluating the effectiveness of vancomycin powder mixed with hemostatic paste for the prevention of mediastinal/sternal SSI. This study showed a reduction in mediastinal/sternal SSI when vancomycin powder was mixed with hemostatic paste and applied to cut sternal edges versus hemostatic paste alone applied to cut sternal edges.

Other guidelines
Clinical practice guidelines based on a review of the evidence and expert opinion have recommendations both for[82] and against[95] the use of non-parenteral antimicrobials in the prevention of SSI. There are also strong recommendations against the use of antimicrobial

ointments or creams on umbilical catheter insertion sites and other insertion sites, because of their potential to promote fungal infections and antimicrobial resistance.[159] These recommendations exclude dialysis catheters.

Q2B.6. Autologous platelet-rich plasma (spray or gel) vs. nothing

Moderate-quality evidence suggested no benefit of APRP spray or gel in combination with parenteral AMP. This was based on no difference in SSI in a meta-analysis (N=452) of 4 small RCTs: 3 studies in cardiac procedures (low[149], moderate[151] and high[152] risk of bias) and 1 study in total knee arthroplasty (TKA) procedures[150] (low risk of bias). Each individual study found no difference. The cardiac studies applied APRP spray[149,152] or gel[151] (produced using the same type of commercial platelet concentrate system) to the saphenous vein harvest site[149,151] and/or the sternum.[151,152] The TKA study[150] applied APRP spray (produced using a different platelet concentrate system than the cardiac studies) to the femoral and tibial cut bone surfaces and joint capsule followed by platelet poor plasma sprayed on the subcutaneous tissue. Moderate-quality evidence from this latter study[150] suggested significantly increased risk of delayed total wound closure at 2 weeks postoperatively. Three of the 4 RCTs[150-152] reported either industry support of the study or receiving study supplies from the manufacturer.

Q2C. How safe and effective are antimicrobial-coated sutures, when and how should they be used?

The available data examined triclosan-coated sutures (absorbable) versus sutures without triclosan (absorbable) for the prevention of SSI. The evidence for this question consists of 14 RCTs.[160-173] For this comparison, overall SSI and deep SSI were the critical outcomes for decision-making. Organ/space SSI, superficial SSI, ASEPSIS score[174] (where points are given for Additional treatment, the presence of Serous discharge, Erythema, Purulent exudate, Separation of the deep tissues, the Isolation of bacteria, and the duration of inpatient Stay), antimicrobial resistance, wound dehiscence, and product-related adverse event outcomes were also evaluated.

Moderate-quality evidence suggested tradeoffs in the use of triclosan-coated sutures to reduce overall SSI rates. A meta-analysis (N=5388) of 14 RCTs[160-173] in colorectal, abdominal, lower limb revascularization, cardiac, breast, cerebrospinal fluid shunt, and mixed surgeries provided high-quality evidence for the reduction in the incidence of "overall SSI" with the use of triclosan-coated sutures. However, a meta-analysis of 2 RCTs[161,163] (N=1285) reporting on the outcome of "deep SSI" provided moderate-quality evidence suggesting no benefit to using triclosan-coated sutures to prevent deep SSI. Given that all 14 RCTs utilized triclosan-coated sutures in the deep and/or fascial layer, it was considered important to identify a benefit in the layer in which they are used. Unfortunately, most of the 14 RCTs evaluating triclosan sutures only examined "overall SSI" and did not stratify analyses by SSI type. Only the 2 aforementioned RCTs actually reported on "deep SSI." The tradeoff between benefit in "overall SSI" and no benefit in "deep SSI" (the layer most important to the evaluation of these deep antimicrobial sutures) results in a Category II recommendation to consider their use, rather than a Category I recommendation to always use these sutures.

In addition, low-quality evidence based on a meta-analysis of 4 RCTs[161,162,165,168] (N=1081) in appendectomies and coronary artery bypass grafts (CABG), elective colorectal, and pediatric cerebrospinal fluid shunt surgeries, with heterogeneous patients and closure types, suggested no difference in organ/space SSI rates when triclosan-coated sutures were used primarily in the deep layer. Moreover, high-quality evidence suggested no benefit to using triclosan-coated sutures for the reduction of superficial SSI when this outcome was specifically reported. This is based on a meta-analysis of 4 RCTs[161,163,165,171] (N=1922) in appendectomies and CABG, open abdominal, and breast cancer surgeries, where triclosan-coated sutures were used in deep closure in all 4 RCTs. Only 1 of the 4 RCTs[171] with superficial SSI as an outcome utilized triclosan-coated sutures in cutaneous closure.

Moderate-quality evidence suggested no difference in SSI in colorectal surgeries where absorbable triclosan-coated sutures were used to close the deep abdominal and fascial layers. This was based on a meta-analysis (N=1912) of 5 RCTs. [163,167-170,175] Administration of bowel prep, length of postoperative AMP, suture type, length of follow-up, SSI definition, and method of closure were not uniform across studies.

High-quality evidence suggested a benefit to using absorbable triclosan-coated sutures to close the abdominal and fascial layers in abdominal surgeries, laparotomies and appendectomies (excluding colorectal surgeries). This was based on a meta-analysis (N=1208) of 3 RCTs.[161,163,167] Administration of postoperative AMP, suture type, length of follow up, SSI definition, and method of closure were not uniform across studies.

High-quality evidence suggested a benefit to using absorbable triclosan-coated sutures in a subgroup of all surgery types excluding colorectal and abdominal surgeries. This was based on a meta-analysis (N=2183) of 8 RCTs.[160,162,164-166,171-173] Surgical populations included CABG, lower limb revascularization, breast cancer surgery, pediatric cerebrospinal fluid shunt, and mixed pediatric and adult surgeries. Length of postoperative AMP, suture type, length of follow up, SSI definition, and method of closure were not uniform across studies.

In terms of harms, low-quality evidence suggested no difference between groups in antimicrobial resistance. Eight RCTs[161,162,165,167-169,172,173] reported no difference in cultured antimicrobial resistant bacteria between groups. However, none of the studies evaluated triclosan resistance. This evaluation is limited by the absence of standardized methods for determining triclosan-resistance. Low-quality evidence also suggested no difference in wound dehiscence between groups. This is based on a meta-analysis of 3

RCTs[163,166,170] (N=1582) in elective colorectal, CABG, and open abdominal surgeries. Moreover, moderate-quality evidence consisting of 2 RCTs[166,171] suggested no difference in ASEPSIS scores in breast cancer surgeries and CABG open vein harvesting. Lastly, low-quality evidence suggested no difference in product-related adverse events, based on 4 RCTs[160-163] which reported no product-related adverse events for either suture type. The authors of 5 of the 14 RCTs reported receiving funds from and/or being employed by the manufacturer of triclosan-coated sutures.[162,163,166,167,171]

The findings of the evidence review, results by surgical procedures, and grades for all important outcomes are shown in eAppendix 2 of the Supplement: GRADE Table Q2 and Evidence Table Q2C.

Q2D. How safe and effective are antimicrobial dressings applied to surgical incisions following primary closure in the operating room?

The available data examined silver-impregnated dressings versus standard dressing or standard gauze and tape for the prevention of SSI. This data consisted of 2 RCTs. The evidence for this question consists of 1 RCT[176] at moderate risk of bias and 1 RCT[177] at low risk of bias, both in elective colorectal surgeries. For this comparison, all SSI outcomes were critical outcomes for decision-making. The duration of inpatient stay and product-related adverse event outcomes were also evaluated.

Moderate-quality evidence suggested no benefit to silver impregnated dressings. This was based on no difference in overall, organ/space, deep, or superficial SSI in 1 small RCT[177] (N=112). Dressings were removed on the seventh postoperative day in the intervention group and "as necessary" in the control group. Patients received mechanical bowel prep in accordance with predefined protocols. No adverse events related to the study were noted. An additional small RCT[176] (N=109) suggested a reduction in superficial SSI related to silver impregnated dressings; however, the SSI definition used in this study included antibiotic treatment for any questionable infection. There was no difference in deep infections in this study. In both studies, authors reported receiving funds from the dressing manufacturer.

The findings of the evidence review and the grades for all important outcomes are shown in eAppendix 2 of the Supplement: GRADE Table Q2 and Evidence Table Q2D.

The search did not identify RCTs or SRs that evaluated the safety and effectiveness of other antimicrobial dressings (e.g., iodine or other antimicrobial ointment-impregnated dressing) applied to surgical incisions closed primarily in the operating room (i.e., the skin edges are re-approximated at the end of the procedure) and their impact on the risk of SSI.[64] The search identified a SR of 16 RCTs evaluating various non-antimicrobial dressings.[178] This SR found no evidence to suggest that either covering the wound was effective or that any one non-antimicrobial dressing was more effective than another in reducing the risk of SSI in surgical incisions that were closed primarily in the operating room. This Guideline does not address prevention of SSI in trauma-related procedures, in surgical incisions left open to heal by secondary intention (i.e., left open in the operating room to be closed later, left open to heal by granulation, or which break open postoperatively), or burns.

Q2. Recommendations

2A.1. Randomized controlled trial evidence suggests uncertain tradeoffs between the benefits and harms regarding intraoperative antimicrobial irrigation (e.g., intra-abdominal, deep or subcutaneous tissues) for the prevention of SSI. Other organizations have made recommendations based on the existing evidence and a summary of these recommendations can be found in the Other Guideline section of the narrative summary for this question**. (No recommendation/unresolved issue)** [141,142] (Guideline Question 2A)

2A.2. The search did not identify randomized controlled trials evaluating soaking prosthetic devices in antimicrobial solutions prior to implantation for the prevention of SSI. **(No recommendation/unresolved issue)** (Guideline Question 2A)

2B.1. Do not apply antimicrobial agents (i.e., ointments, solutions, or powders) to the surgical incision for the prevention of SSI. **(Category IB – strong recommendation; low-quality evidence)** [143-148] (Guideline Question 2B)

2B.2. Application of autologous platelet-rich plasma is not necessary for the prevention of SSI. **(Category II – weak recommendation; moderate-quality evidence suggesting a trade-off between clinical benefits and harms)** [149-152] (Guideline Question 2B)

2C. Consider the use of triclosan-coated sutures for the prevention of SSI. **(Category II – weak recommendation; moderate-quality evidence suggesting a trade-off between clinical benefits and harms)** [160-173,175] (Guideline Question 2C)

2D. Randomized controlled trial evidence suggests uncertain tradeoffs between the benefits and harms regarding antimicrobial dressings applied to surgical incisions following primary closure in the operating room for the prevention of SSI. **(No recommendation/unresolved issue)**[176,177] (Guideline Question 2D)

4.1C. GLYCEMIC CONTROL

Q3. How do perioperative blood glucose and hemoglobin A1c levels impact the risk of SSI, and what are their optimal perioperative target levels in diabetic and non-diabetic patients?

To answer this question, analysis focused on:

A) Blood glucose
B) Hemoglobin A1c
C) Optimal perioperative target levels
D) Risk of SSI

Q3A. Blood glucose and optimal perioperative target levels

The available data examined strict versus standard blood glucose control in the prevention of SSI.

For this comparison, SSI and hypoglycemia were considered the critical outcomes for decision-making. Each study reported a primary composite outcome variable that included SSI. Mortality, length of hospital stay, and surgical intensive care unit (SICU) stays were also evaluated in weighing the risks and benefits of perioperative glycemic control. The evidence for this question consists of 2 RCTs in cardiac surgery patients with glycemic control protocols (intravenous, intensive insulin therapy) instituted intraoperatively and continued in the SICU for 24-36 hours.[179,180] In both of these studies, 70-80% of patients were non-diabetics, highlighting the importance of glycemic control in both diabetic and non-diabetic surgical populations. The findings of the evidence review and the grades for all important outcomes are shown in eAppendix 2 of the Supplement: GRADE Table Q3 and Evidence Table Q3.

Moderate-quality evidence suggested no benefit of strict (80–100 mg/dL[180] or 80–130 mg/dL[179]) as compared with standard blood glucose target levels (<200 mg/dL[180] or 160–200 mg/dL[179]) in diabetic and non-diabetic cardiac patients. This was based on no differences between groups for both the composite outcome variable and SSI in both studies. In Gandhi et al.[180] (N=371), the composite outcome variable included: death, sternal wound infections, prolonged pulmonary ventilation, cardiac arrhythmias, heart block requiring pacemaker or cardiac arrest, stroke or acute renal failure within 30 days postoperatively. In Chan et al.[179] (N=109), the composite infection outcome included pneumonia, urinary tract infection, sepsis, septic shock, wound infection, bloodstream infection, and "catheter" infection (did not specify if venous or urinary).

High-quality evidence suggested no increased risk of hypoglycemia with strict blood glucose target levels. This was based on no differences between groups for the number of hypoglycemic episodes in the SICU[180] or the ratio of hypoglycemic episodes per number of glucose measurements.[179] Hypoglycemia definitions differed among studies: <60 mg/dL in Gandhi and <50 mg/dL in Chan. While there was no difference between groups for the number of hypoglycemic episodes in the SICU, in Chan et al., both groups reported a higher proportion of hypoglycemia postoperatively as compared with intraoperatively, suggesting the importance of continued close monitoring of glucose levels and the risk of hypoglycemic episodes in the postoperative period, even with standard glycemic control. No clinical complications resulting from hypoglycemia were reported at 30 days of follow-up. In 1 study, authors reported receiving funds from an insulin manufacturing company. [180]

Other guidelines

While previous CDC guideline recommendations did not specify a perioperative blood glucose target level, they reported that in diabetics "increased glucose levels (>200 mg/dL) in the immediate postoperative period (≤48 hours) were associated with increased risk of SSI."[64] Blood glucose target level of <200 mg/dL became standard clinical practice. Both studies reviewed in this guideline used <200 mg/dL as the upper blood glucose target level.[179,180] Recently published professional society guidelines have recommended a slightly lower absolute serum blood glucose target level of <180 mg/dL in diabetic[84,181,182] and non-diabetic,[84,181] non-critically ill patients. In critically ill patients, blood glucose target levels <150–180 mg/dL[183] and 140–200 mg/dL[184] have been recommended. For terminally ill patients, those with limited life expectancy, or those at high risk for hypoglycemia, a blood glucose target level of 200 mg/dL has been recommended.[182] Intensive insulin therapy (blood glucose target levels of 80–110 mg/dl) to normalize blood glucose in the intensive care unit setting (surgical and medical) is not recommended in either diabetic or non-diabetic patients.[84,184]

Q3B. Perioperative hemoglobin A1C and optimal target levels

The search did not identify RCTs or SRs examining the association between hemoglobin A1c levels and risk of SSI.

Q3. Recommendations

3A.1. Implement perioperative glycemic control and use blood glucose target levels <200 mg/dL in diabetic and non-diabetic patients. **(Category IA – strong recommendation; high to moderate-quality evidence)** [179,180] (Guideline Question 3)

3A.2. The search did not identify randomized controlled trials evaluating lower (<200 mg/dL) or narrower blood glucose target levels than recommended in this guideline, nor the optimal timing, duration, or delivery method of perioperative glycemic control for the prevention of SSI. Other organizations have made recommendations based on the existing evidence and a summary of these recommendations can be found in the Other guidelines section of the narrative summary for this question**. (No recommendation/unresolved issue)** (Guideline Question 3)

3B. The search did not identify randomized controlled trials evaluating the optimal hemoglobin A1c target levels for the prevention of SSI in diabetic and non-diabetic patients. **(No recommendation/unresolved issue)** (Guideline Question 3)

4.1D. NORMOTHERMIA

Q4. How safe and effective is the maintenance of perioperative normothermia in reducing the risk of SSI?

The available data examined the following comparisons:

1. Warming vs. no warming
2. Warming: perioperative vs. intraoperative only

For all comparisons, SSI was the critical outcome for decision-making. ASEPSIS score, mortality, blood loss, core temperature, length of hospital stay, and duration of surgery outcomes were also evaluated. The evidence for this question consists of 3 RCTs.[185-187] The lower limit of normothermia has been inconsistently defined, ranging from a core temperature of 95.9°F to 96.8°F (35.5°C-36°C). The findings of the evidence review and the grades for all important outcomes are shown in eAppendix 2 of the Supplement: GRADE Table Q4-5 and Evidence Table Q4.

Q4A.1. Warming vs. no warming

High-quality evidence suggested a benefit of patient warming over no warming. This was based on a reduced risk of SSI in a meta-analysis (N=616) of 2 RCTs with warming and maintenance of normothermia using various warming techniques in patients undergoing elective hernia repair, varicose vein surgery, and breast surgery (preoperative warming)[186] and elective colorectal surgery (intraoperative warming).[185] Normothermia was also associated with reduced risk of ASEPSIS scores >20, lower mean units of blood transfused per patient, fewer patients transfused, and reduced hospital length of stay.[185] No difference in mortality was observed.[185] Both of these studies reported receiving funds from a warming equipment manufacturer.

Q4A.2. Warming: perioperative vs. intraoperative only
Moderate-quality evidence suggested a benefit of perioperative warming. This was based on reduced incidence of SSI with perioperative warming in 1 RCT of 103 patients undergoing elective major abdominal surgery.[187]

Q4. Recommendation
4. Maintain perioperative normothermia. **(Category IA – strong recommendation; high to moderate- quality evidence)** [185-187] (Guideline Question 4)

Q5. What are the most effective strategies for achieving and maintaining perioperative normothermia?
The search did not identify RCTs or SRs that evaluated the most effective strategies for achieving and maintaining perioperative normothermia and their impact on the risk of SSI.

Other guidelines
Evidence-based clinical practice guidelines provide recommendations on perioperative management of normothermia including risk factor assessment, temperature monitoring tools, and the safety and effectiveness of warming devices.[188-191] Recently published professional society guidelines have recommended a minimum temperature of 95.9°F (35.5°C) during the perioperative period.[84]

Q5. Recommendation
5. The search did not identify randomized controlled trials evaluating strategies to achieve and maintain normothermia, the lower limit of normothermia, or the optimal timing and duration of normothermia for the prevention of SSI. Other organizations have made recommendations based on observational data and a summary of these recommendations can be found in the Other guidelines section of the narrative summary for this question**. (No recommendation/unresolved issue)** (Guideline Question 5)

4.1E. OXYGENATION

Q6. In patients with normal pulmonary function, how safe and effective is the perioperative use of increased fraction of inspired oxygen (FiO_2) in reducing the risk of SSI?
To answer this question, 3 settings of oxygen delivery were analyzed:

A) General anesthesia: intraoperative endotracheal intubation and postoperative non-rebreathing mask;
B) Neuraxial anesthesia: intraoperative and postoperative non-rebreathing mask; and
C) Post-operative only: facemask and/or nasal cannula.

Q6A. General anesthesia: intra-operative only endotracheal intubation, 80% oxygen vs. 30% oxygen – both without nitrous oxide
For all comparisons, SSI was the critical outcome for decision-making. Adverse events were also evaluated.

Moderate-quality evidence suggested no benefit to supplemental 80% FiO_2 compared with 30% FiO_2 administered via endotracheal intubation during the intraoperative period only. In 1 study[192] at low risk of bias, 434 patients underwent general anesthesia for abdominal, gynecologic and breast surgeries. Administration of FiO_2 commenced after intubation and ended at extubation. In cases where extubation was delayed beyond the end of the surgery, the FiO_2 was maintained at the programmed level and oxygen was administered during the postoperative period at the physician's discretion. There were significantly more protocol deviations in the control group; the reasons for these deviations included desaturation and/or bradycardia. No difference was seen between groups in adverse events, including nausea and vomiting, hypotension, and sternal pain. The authors of this study reported receiving study funding from a medical oxygen supply company.

The findings of the evidence review and the grades for all important outcomes are shown in eAppendix 2 of the Supplement: GRADE Table Q6-7 and Evidence Table Q6.

Q6B. General anesthesia: intra-operative endotracheal intubation and postoperative non-rebreathing mask
The available data examined the following comparisons:

1. 80% oxygen vs. 30% oxygen—both without nitrous oxide

2. 80% oxygen/20% nitrous oxide vs. 35% oxygen/65% nitrous oxide—both with nitrous oxide started 30 minutes after surgical incision

For all comparisons, SSI was the critical outcome for decision-making. ASEPSIS scores, mortality, respiratory failure, atelectasis, tissue oxygenation, and length of stay were also evaluated. The evidence for this question consists of 7 RCTs.[193-199] One study[198] represents a subanalysis of a larger study;[196] therefore results in the GRADE table reflect solely those of the larger study. The findings of the evidence review and the grades for all important outcomes are shown in eAppendix 2 of the Supplement: GRADE Table Q6-7 and Evidence Table Q6. The authors of 1 of these studies[193] reported receiving study funding from a medical oxygen supply company.

Q6B.1. 80% oxygen vs. 30% oxygen—both without nitrous oxide

Moderate-quality evidence suggested a benefit of supplemental 80% FiO_2 administered via endotracheal intubation intraoperatively and non-rebreathing mask for 2–6 hours postoperatively in patients under general anesthesia. This was based on a meta-analysis (N=2622) of 5 RCTs[193-196,198,199] at low risk of bias (2 in 791 elective colorectal surgeries,[193,195] 1 in 235 open reduction and internal fixation procedures,[199] 1 in 210 elective open appendectomy[194] procedures, and in 1 multicenter, mixed surgical population[196,198]). There was no significant difference in adverse events.[196,198]

The 3 studies reporting a significant SSI reduction all optimized perioperative tissue oxygen delivery by maintaining normothermia and avoiding hypo or hypervolemia.[193-195] Greif et al.,[195] the larger colorectal study (N=500), confirmed optimized tissue oxygen delivery, measuring significantly higher intraoperative and postoperative subcutaneous tissue oxygen tension and higher muscle oxygen tension using 80% oxygen.

Meyhoff et al., [196,198] the large (N=1386), multicenter, mixed population study of emergency or elective laparotomy for a variety of general and gynecologic surgical conditions, found no difference in overall, organ/space, deep, or superficial SSI. However, due to a number of factors, the study failed to optimize tissue oxygen delivery. While the target core temperatures were 96.8°F to 98.6°F (36°C -37°C), the minimum reported temperatures were 95.0°F and 95.2°F (35.0°C and 35.1°C) in each group, respectively. More importantly, fluid replacement was intentionally restricted, limiting postoperative weight gain to less than 1 kg. Mortality at 14–30 days was rare, there was no difference between groups, and it was not associated with use of increased oxygenation.[193,195] In a recent follow-up study (median 2.3 years, range 1.3–3.4), administration of 80% oxygen was associated with significantly increased long-term mortality only in patients undergoing cancer surgery. The only gynecologic patients included in this study were those with ovarian cancer.[200] It is not clear what other cancer patients were included. One study[199] of elective open reduction and internal fixations of 235 tibial fractures in 217 patients also showed no difference. Optimized tissue oxygen delivery, normothermia, and normovolemia were not described. This study identified no treatment-associated adverse events.

Q6B.2. 80% oxygen/20% nitrous oxide vs. 35% oxygen/65% nitrous oxide—both groups started nitrous oxide 30 minutes after incision

Moderate-quality evidence suggested no benefit of supplemental 80% FiO_2 (20% nitrous oxide added 30 minutes after incision) administered via endotracheal intubation intraoperatively and non-rebreathing mask for 2–6 hours postoperatively in patients under general anesthesia. This was based on increased risk of SSI (all combined) in 1 small (N=160), mixed surgical population study.[197] Several factors may account for the increased incidence of total SSIs in the intervention group. Patients in the 80% FiO_2 group had significantly increased body mass index (BMI), higher blood loss, and were more crystalloid infused. On multivariate logistic regression analysis, 80% oxygen and remaining intubated postoperatively remained predictive of SSI. Mortality was rare in either group and unrelated to increased supplemental oxygenation.

Q6C. Neuraxial anesthesia: Intraoperative and postoperative non-rebreathing mask

The available data on the impact of different levels of supplemental increased FiO_2 on SSI in patients under regional anesthesia examined 80% oxygen versus 30% oxygen.

For this comparison, SSI was the critical outcome for decision-making. Length of stay was also evaluated. The evidence for this question consists of 3 RCTs.[201-203] The findings of the evidence review and the grades for all important outcomes are shown in eAppendix 2 of the Supplement: GRADE Table Q6-7 and Evidence Table Q6.

Moderate-quality evidence suggested no benefit of supplemental 80% FiO_2 administered via non-rebreathing mask intra and postoperatively in patients under neuraxial anesthesia. This was based on no difference in risk of SSI in a meta-analysis of 3 studies[201-203] (N=1559) in cesarean sections. Two studies[201,203] (N=728) did not note any protocol used during the study to optimize tissue oxygenation. The largest study[202] (N=831) ensured adequate volume replacement and normothermia.

Q6D. Postoperative only: Facemask and/or nasal cannula

The data available on the impact of different levels of supplemental increased FiO_2used in the postoperative period only examined 28–30% oxygen versus room air.

For this comparison, SSI was the critical outcome for decision-making. SSI type (organ/space, superficial and deep SSI), ASEPSIS scores, mortality, adverse events, tissue oxygenation, and length of stay were also evaluated. The evidence for this question consists of 2 RCTs.[204,205] The findings of the evidence review and the grades for all important outcomes are shown in eAppendix 2 of the Supplement: GRADE Table Q6-7 and Evidence Table Q6.

Moderate-quality evidence suggested no benefit of supplemental 28–30% FiO_2 administered via facemask and/or nasal cannula solely in the postoperative period. This was based on no difference in SSIs from 2 studies.[204,205] Turtiainen et al., [204] a lower limb vascular surgery study (N=274) at low risk of bias, used 30% oxygen via facemask in the recovery room and on the first postoperative day on the ward, followed by constant oxygen flow of 5 L/min via nasal cannula during the second postoperative day. A significant reduction in SSI was seen only in isolated groin incisions. Subcutaneous tissue oxygen tension (measured hourly for the first 4 hours, then at 18 and 36 hours) was significantly higher in the supplemental oxygenation group. Whitney et al.,[205] a second, smaller study at high risk of bias in 24 cervical spine procedures reported no wound complications in either group (supplemental 28% oxygen administered at 2L/min via nasal cannula for 36 hours after discharge from the post-anesthesia care unit as compared with room air). Mortality[204] and adverse events[204,205] were rare, did not differ between groups, and were unrelated to use of supplemental oxygenation.

Q6. Recommendations

6A. Randomized controlled trial evidence suggests uncertain tradeoffs between the benefits and harms regarding the administration of increased fraction of inspired oxygen (FiO_2) via endotracheal intubation during only the intraoperative period in patients with normal pulmonary function undergoing general anesthesia for the prevention of SSI. **(No recommendation/unresolved issue)** [192] (Guideline Question 6)

6B. For patients with normal pulmonary function undergoing general anesthesia with endotracheal intubation, administer increased FiO_2 intraoperatively and post-extubation in the immediate postoperative period. To optimize tissue oxygen delivery, maintain perioperative normothermia and adequate volume replacement. **(Category IA – strong recommendation; moderate quality evidence)** [193-199] (Guideline Question 6)

6C. Randomized controlled trial evidence suggests uncertain tradeoffs between the benefits and harms regarding the administration of increased FiO_2 via facemask during the perioperative period in patients with normal pulmonary function undergoing general anesthesia without endotracheal intubation or neuraxial anesthesia (i.e., spinal, epidural, or local nerve blocks) for the prevention of SSI. **(No recommendation/unresolved issue)** [201-203] (Guideline Question 6)

6D. Randomized controlled trial evidence suggests uncertain tradeoffs between the benefits and harms regarding the administration of increased FiO_2 via facemask or nasal cannula during only the postoperative period in patients with normal pulmonary function for the prevention of SSI. **(No recommendation/unresolved issue)** [204,205] (Guideline Question 6)

Q7. What is the optimal target FiO_2 to reduce the risk of SSI; how and when should it be administered?

The search did not identify RCTs or SRs that evaluated both the optimal FiO_2 and how and when it should be administered, and included SSI as an outcome. All studies evaluating the use of supplemental increased oxygenation both intraoperatively and postoperatively used 80% FiO_2 as the target level.

Other guidelines

Evidence-based clinical practice guidelines recommend maintaining patient homeostasis by optimizing oxygenation during major surgery and in the recovery period (maintaining a >95% hemoglobin saturation) in concert with maintaining both patient temperature to avoid hypothermia, and adequate perfusion during surgery.[84,95]

Q7. Recommendation

7. The search did not identify randomized controlled trials evaluating the optimal target level, duration, and delivery method of FiO_2 for the prevention of SSI. Other organizations have made recommendations based on observational data and a summary of these recommendations can be found in the Other guidelines section of the narrative summary for this question**. (No recommendation/ unresolved issue)** (Question 7)

4.1F. ANTISEPTIC PROPHYLAXIS

Q8. What are the most effective strategies for preparing the patient's skin prior to surgery to reduce the risk of SSI?
To answer this question, 4 subquestions were asked:

A) How safe and effective is preoperative antiseptic bathing or showering?
B) How safe and effective are antiseptic skin preparation agents individually and in combination?
C) How safe and effective is the application of a microbial sealant immediately following intraoperative skin preparation?
D) How safe and effective are plastic adhesive drapes? *It should be noted that while the recommendations in this section apply to patients known to be colonized with S. aureus, they do not separately address the different antiseptic skin preparations that may be suggested for these patients.*

Q8A. How safe and effective is preoperative antiseptic bathing or showering?
The available data examined the following comparisons:

1. Chlorhexidine gluconate (CHG) solution vs. placebo solution
2. CHG solution vs. un-medicated bar soap
3. CHG solution vs. no wash
4. CHG whole body wash vs. partial body wash
5. Aqueous iodophor solution vs. control ("routine personal hygiene")
6. CHG washcloth vs. un-medicated bar soap

For all comparisons, SSI was the critical outcome for decision-making. Product-related adverse reactions were also evaluated. The evidence for this question consists of 1 SR[206] (7 RCTs[207-213]) evaluating CHG solution and 1 RCT[214] evaluating povidone iodine solution. The RCTs span a 26-year period, with 6 published between 1983 and 1992, and 2 between 2008[214] and 2009.[212] The search did not identify RCTs or SRs that evaluated optimal preoperative timing, number of showers/baths, or number of product applications at each shower/bathing episode, and their impact on the risk of SSI. The findings of the evidence review and grades for all important outcomes are shown in eAppendix 2 of the Supplement: GRADE Table Q8-10 and Evidence Table Q8A.

Q8A.1. CHG solution vs. placebo solution
High-quality evidence suggested no benefit of preoperative bathing or showering with 4% CHG solution as compared with placebo. This was based on no difference in SSI in both a meta-analysis (N=7791) of 4 RCTs[206,207,209,211,212] and a meta-analysis (N=6302) restricted to only the 2 higher-quality studies.[206,207,211] Each individual trial found no difference. Five months into 1 large study, the placebo solution was found to have antimicrobial properties and was changed; however, the study did not stratify by or exclude that data.[209] Procedures included in the studies were elective or potentially contaminated surgery,[207] elective inpatient surgery,[209] elective clean surgical procedures including thyroidectomy, inguinal herniorrhaphy, hip and knee surgery, laminectomy, mastectomy, vascular surgery,[211] and elective plastic surgery of the trunk.[212] Number of preoperative showers/baths, amount of antiseptic used per bath, bathing instructions to each group, intraoperative antiseptic skin preparation agent, use of AMP, and follow-up varied among studies. Three studies instructed patients to shower[207,211,212] and 1 instructed them to shower or bathe.[209] Product-related adverse reactions (irritation, itching, reddening of the skin) were rare and did not differ between groups.[206,207,211,212]

Q8A.2. CHG solution vs. un-medicated bar soap
High-quality evidence suggested no benefit of preoperative bathing or showering with 4% CHG solution as compared with un-medicated bar soap. This was based on no difference in SSI in a meta-analysis (N=1443) of 3 RCTs.[206,208-210] Heterogeneity for this comparison was high. Only the largest study (N=1315) reported a reduction in SSI with 4% CHG; however, no special showering/bathing instructions were given to the un-medicated bar soap group, whereas "great care was taken to ensure that the patients using [CHG]…complied with the instructions."[209] Of the 2 smaller, lesser-quality studies, one[208] suggested a higher rate of SSI with CHG, while the other[210] suggested no difference. Number of preoperative baths, bathing instructions, intraoperative antiseptic skin preparation agent, AMP use, procedures, and follow up varied among studies. One study instructed patients to bathe,[208] 1 to shower,[210] and 1 to shower or bathe.[209]

Q8A.3. CHG solution vs. no wash
Moderate-quality evidence suggested no benefit of preoperative showering with 4% CHG solution as compared with no wash. This was based on no difference in a meta-analysis (N=1142) of 3 RCTs.[206,210,212,213] Despite instructions not to shower, it is unclear whether the "no wash" groups showered. The largest study[213] favored 4% CHG, while the other 2[210,212] suggested no difference. Heterogeneity for this comparison was significant. Studies included outpatient and inpatient procedures, patients undergoing vasectomy,[210] plastic surgery of the trunk,[212] and elective, clean biliary tract, inguinal hernia, or breast cancer[213] procedures. There were also differences in SSI definitions among studies.

Q8A.4. CHG whole body vs. partial body wash
Moderate-quality evidence suggested a benefit of a CHG shower (i.e., a whole body wash including the scalp) as compared with a partial body wash (restricted to the proposed surgical site). This was based on reduced risk of SSI with whole body washing (1 time, 2

applications on the afternoon before surgery) in 1 large RCT (N=1093) of elective clean biliary tract, inguinal hernia, and breast cancer procedures.[206,213]

Q8A.5. Aqueous iodophor solution vs. control ("routine personal hygiene")
Very low-quality evidence suggested no benefit of preoperative shower with 10% aqueous iodophor solution as compared with routine personal hygiene. This was based on no infections reported in either group in 1 small RCT (N=114) in elective, clean plastic surgical procedures (thorax or abdomen) designed to evaluate the product's efficacy in reducing skin contamination, not SSI.[214]

Q8A.6. CHG washcloth vs. un-medicated bar soap
Moderate-quality evidence suggested no benefit of 2 full body wipes with 2% chlorhexidine washcloths the night before and morning of surgery as compared with a shower with un-medicated bar soap the morning of surgery. This was based on no infections reported in either group in 1 small RCT[215] (N=100) in elective, shoulder surgeries designed to evaluate the product's efficacy in reducing skin contamination, not SSI. In this study, authors reported receiving funds from the CHG washcloth manufacturer.

Other guidelines
Clinical practice guidelines recommend that patients shower or bathe with an antiseptic agent or soap on at least the night before surgery.[64,85,95] This is considered accepted practice. They do not favor the use of one antiseptic agent over another. There may be contraindications for specific antiseptic-agent use in some patients or surgical procedures.

Q8B. How safe and effective are antiseptic skin preparation agents individually and in combination?
The available data examined the following comparisons:

1. Aqueous iodophor: 1-step vs. 2-step
2. Aqueous iodophor (1- or 2-step) vs. iodophor in alcohol (1-step with or without adhesive drape)
3. CHG-alcohol (1- or 2-step) vs. aqueous iodophor (1- or 2-step)
4. CHG-alcohol (1- or 2-step) vs. iodophor-alcohol (1- or 2-step)
   a. CHG-alcohol (2-step) vs. iodophor-alcohol (2-step)
   b. CHG-alcohol (1-step) vs. iodophor-alcohol (1-step)

For all comparisons, SSI was the critical outcome for decision-making. Product-related adverse event outcomes were also evaluated. The evidence for this question consists of 14 RCTs.[216-229] The findings of the evidence review and the grades for all important outcomes are shown in eAppendix 2 of the Supplement: GRADE Table Q8-10 and Evidence Table Q8B.

Q8B.1. Aqueous iodophor: 1-step vs. 2-step
High-quality evidence suggested no benefit of using 2-step as compared with 1-step aqueous iodophor for skin preparation of the surgical site. This was based on no difference in SSI in 2 RCTs at moderate risk of bias.[220,227] One study in 234 clean (30%) and clean-contaminated (70%) oncologic, non-laparoscopic abdominal procedures compared povidone iodine paint (1% iodine) to a 5-minute povidone iodine scrub (0.75% iodine) followed by povidone iodine paint (1% iodine).[220] Another study in 108 CABG procedures did not report the product concentration or scrub duration.[227] In the latter study, patients were also instructed to take antimicrobial showers (unspecified product) the evening before and the morning of surgery.

Q8B.2. Aqueous iodophor (1- or 2-step) vs. iodophor in alcohol (1-step with or without adhesive drape)
Low-quality evidence suggested no benefit of iodophor in alcohol as compared with aqueous iodophor. This was based on no difference in SSI in a meta-analysis (N=626) of 5 RCTs including 4 RCTs at moderate risk[221,222,226,227] and 1 at low risk[225] of bias. Only 1 study at moderate risk of bias in CABG procedures showed a reduced risk of sternal SSI with iodophor in alcohol (with or without plastic adhesive drape).[227] A second study (low risk of bias) in CABG procedures using iodophor impregnated plastic adhesive drape at the sternal site showed no difference between groups.[225] The remaining studies, at moderate risk of bias, reported no infections in THA and TKA,[221] shoulder,[226] and foot and ankle[222] procedures. However, each was designed to evaluate the products' efficacy in reducing skin contamination, not SSI.

Q8B.3. CHG-alcohol (1- or 2-step) vs. aqueous iodophor (1- or 2-step)
High-quality evidence suggested a benefit of CHG-alcohol as compared with aqueous iodophor. This was based on a reduced risk of SSI in a meta-analysis (N=1976) of 5 RCTs (2 low risk,[219,228] 1 moderate risk,[226] and 2 high risk[217,224] of bias) and no difference in product-related adverse events. Only 1 large study showed a reduced risk of SSI in multiple mixed clean-contaminated abdominal and non-abdominal (thoracic, gynecologic, and urologic) procedures.[219] CHG-alcohol was specifically associated with reduced risk of superficial and deep incisional SSI, but not organ/space SSI or sepsis. The study in clean hernia repairs (herniotomy, herniorrhaphy, or hernioplasty) showed no difference between groups.[228] In both of these studies, authors reported receiving funds from and/or being employed by the manufacturer of the CHG-alcohol product. Of the 3 studies at moderate or high risk of bias, 1 in clean, clean-contaminated or contaminated general surgery[224] procedures showed no difference, and the studies in clean elective shoulder[226] and foot and ankle[217] procedures reported no infections; however, each was designed to evaluate the products' efficacy in reducing skin contamination, not SSI.

High-quality evidence from 2 studies suggested no difference in product-related adverse events, including skin irritation or pruritus or erythema around the wound.[219,224]

Q8B.4. CHG-alcohol (1- or 2-step) vs. iodophor-alcohol (1- or 2-step)

High-quality evidence suggested no benefit of CHG-alcohol (1- or 2-step) as compared with iodophor alcohol (1-or 2-step). This was based on no difference in SSI in a meta-analysis (N=1323) of 6 RCTs.[216,218,223,226,229,230] Three studies (1 at low risk,[216] 1 at moderate risk,[218] and 1 at high risk[229] of bias) compared 2-step application, and 3 studies[223,226,230] at moderate risk of bias compared 1-step product application. There was no difference in SSI in individual meta-analyses of "2-step" or "1-step" product application. Details are available under the individual comparators below.

Q8B.4.a. CHG-alcohol (2-step) vs. iodophor-alcohol (2-step)

High-quality evidence suggested no benefit of 2-step CHG-alcohol as compared with 2-step iodophor-alcohol. This was based on no difference in SSI in 3 studies that compared 0.5% chlorhexidine gluconate and alcohol with 10% povidone-iodine (1% available iodine) and 23% isopropyl alcohol.[216,218,229] No preoperative antiseptic shower protocol was reported in the studies. The large, moderate risk of bias study in a mixed general surgery population reported no difference.[216] CHG-alcohol was associated with a significant reduction in SSI in biliary and "other clean procedures." One study (at high risk of bias) in elective, clean, plastic surgery breast procedures reported no difference between groups.[229] The smallest study (at moderate risk of bias) in foot procedures reported no infections in either group.[218] However, the study was designed to evaluate the products' efficacy in reducing skin contamination, not SSI.

Q8B.4.b. CHG-alcohol (1-step) vs. iodophor-alcohol (1-step)

High-quality evidence suggested no benefit of 1-step CHG-alcohol as compared with 1-step iodophor-alcohol. This was based on no difference in SSI in 3 studies at moderate risk of bias that compared 2% chlorhexidine gluconate with 70% alcohol (water insoluble film) to 0.7% iodine with 74% alcohol (water insoluble film).[223,226,230] One study in shoulder procedures (96 arthroscopies and 4 arthroplasties) reported no infections in either group.[226] Patients were instructed to shower the evening prior to surgery (product not reported). Iodophor-impregnated plastic adhesive drapes were applied to the shoulder arthroplasties' operative site. The second study reported only 1 wound infection following 80 foot and ankle procedures.[223] Patients were not instructed to take an antiseptic shower prior to surgery. The third study[230] of 100 patients undergoing elective lumbar spine surgery reported no deep or superficial SSI in either group at 6 months follow-up. Patients were instructed to adhere to routine bathing practices. All 3 studies were designed to evaluate the products' efficacy in reducing skin contamination, not SSI, and all received funding by one or both product manufacturers.

Other guidelines

Clinical practice guidelines recommend skin preparation with an antiseptic agent, but do not favor one antiseptic agent over another.[64,95,231] Recently published professional society guidelines have recommended skin preparation with alcohol-containing preoperative skin preparatory agents.[84] There may be contraindications to the use of specific antiseptic skin preparation agents for specific patients.

Q8C. How safe and effective is the application of a microbial sealant immediately following intraoperative skin preparation?

The available data examined the application of a cyanoacrylate-based microbial skin sealant immediately after skin preparation as compared to no sealant.

For this comparison considered SSI was the critical outcome for decision-making. Product-related adverse events were also evaluated. The evidence for this question consists of 4 RCTs.[232-235] The findings of the evidence review and the grades for all important outcomes are shown in eAppendix 2 of the Supplement: GRADE Table Q8-10 and Evidence Table Q8C.

Low-quality evidence suggested no benefit of cyanoacrylate-based microbial skin sealant applied immediately following skin preparation. This was based on no difference in SSI in a meta-analysis (N=609) of 4 RCTs evaluating surgical site skin preparation with povidone iodine alcohol[232,234,235] or aqueous povidone iodine [233,234] solution followed by application of cyanoacrylate-based skin sealant before skin incision (1 CABG sternal and/or venous harvest site,[234] 1 CABG leg saphenous vein harvest site,[232] 1 open inguinal hernia repair[233], and 1 pediatric scoliosis correction[235]). The 2 CABG studies also followed skin sealant application with plastic adhesive drape application. One study at moderate risk of bias[235] and 2 studies at low risk of bias[232,233] suggested no difference between groups. However, due to the low number of events in the latter study, superiority could not be established and study enrollment ceased once the cyanoacrylate sealant was granted regulatory approval by the FDA (based on porcine data on skin contamination).[233] All studies were funded by and/or authors had a financial relationship with the skin sealant manufacturer. Only 1 small study[232] (low risk of bias) suggested a reduced risk of SSI; however, the authors acknowledged that the apparent increased risk of SSI in the control legs could be explained by their use of a grading system[236] whose stringent criteria included minimal erythema or discharge as SSI. High-quality evidence suggested no significant product-related sensitivity or other adverse events.[232-234] In the inguinal hernia repair study, surgeons reported difficulty incising through the clear film (4/166 patients) and 1 reported visible "flaking" of the film at the time of procedure (no report of plastic adhesive drape use).[233]

Q8D. How safe and effective are plastic adhesive drapes?
The available data examined the following comparisons:

1. Non-iodophor impregnated adhesive drape vs. no drape
2. Iodophor-impregnated adhesive drape vs. no drape

For all comparisons, SSI was the critical outcome for decision-making. The evidence for this question consists of 6 RCTs.[227,237-241] The findings of the evidence review and the grades for all important outcomes are shown in eAppendix 2 of the Supplement: GRADE Table Q8-10 and Evidence Table Q8D.

Q8D.1. Non-iodophor impregnated drape vs. no drape
Moderate-quality evidence suggested no benefit of non-iodophor impregnated plastic adhesive drapes in addition to skin preparation as compared with skin preparation alone. This was based on no difference in SSI in a meta-analysis (N=1742) of 4 RCTs spanning a 30-year period (1971–2001), each reporting no difference.[237,239-241] The 2 most recent studies[237,241] used polyurethane adhesive drapes; drape material information was not reported in the older[239,240] studies. The surgical skin preparation agent applied prior to the application of the adhesive drapes varied among studies and may have impacted drape adhesion. Studies included general surgery,[239,240] cesarean section,[241] and hip fracture[237] surgery.

Q8D.2. Iodophor-impregnated drape vs. no drape
High-quality evidence suggested no benefit of iodophor-impregnated plastic adhesive drapes in addition to skin preparation as compared with skin preparation alone. This was based on no difference in SSI in a meta-analysis (N=1113) of 2 RCTs spanning a 15-year period (1987-2002), each reporting no difference.[227,238] Both studies used povidone iodine alcohol skin preparation (2-step application in the study at low risk of bias in abdominal procedures[238] and 1-step application in the study at moderate risk of bias in CABG[227] procedures).

Other guidelines
Other evidence-based clinical practice guidelines recommend against the routine use of non-iodophor impregnated plastic adhesive drapes and recommend that if a plastic adhesive drape is required, then an iodophor-impregnated one should be used (unless the patient has an iodine allergy).[84,95,242]

Q8. Recommendations

8A. Advise patients to shower or bathe (full body) with soap (antimicrobial or non-antimicrobial) or an antiseptic agent on at least the night before the operative day. **(Category IB – strong recommendation; accepted practice)** [206-214] (Guideline Question 8A)

8A.1. Randomized controlled trial evidence suggests uncertain tradeoffs between the benefits and harms regarding the optimal timing of the preoperative shower or bath, the total number of soap or antiseptic agent applications, or the use of chlorhexidine gluconate washcloths for the prevention of SSI. **(No recommendation/unresolved issue)** [215] (Guideline Question 8A.1)

8B. Perform intraoperative skin preparation with an alcohol-based antiseptic agent, unless contraindicated. **(Category IA – strong recommendation; high-quality evidence)** [216-230] (Guideline Question 8B)

8C. Application of a microbial sealant immediately following intraoperative skin preparation is not necessary for the prevention of SSI. **(Category II – weak recommendation; low-quality evidence suggesting a trade-off between clinical benefits and harms)** [232-235] (Guideline Question 8C)

8D. The use of plastic adhesive drapes with or without antimicrobial properties, is not necessary for the prevention of SSI. **(Category II – weak recommendation; high to moderate-quality evidence suggesting a trade-off between clinical benefits and harms)** [227,237-241] (Guideline Question 8D)

Q9. How safe and effective is antiseptic irrigation prior to closing the surgical incision?
The available data examined aqueous iodophor irrigation versus normal saline for the prevention of SSI.

For this comparison, superficial and deep SSIs and organ/space abscess were the critical outcomes for decision-making. Product-related adverse events including wound healing and iodine toxicity outcomes were also evaluated. The evidence for this question consists of 7 RCTs.[243-249] In all studies, both groups received parenteral AMP, but the specific protocol was not necessarily described.

The findings of the evidence review and the grades for all important outcomes are shown in eAppendix 2 of the Supplement: GRADE Table Q8-10 and Evidence Table Q9.

Moderate-quality evidence suggested no benefit of aqueous iodophor peritoneal lavage in contaminated and dirty general surgical abdominal cases. This was based on no difference in organ/space abscess formation in meta-analysis (N=268) of 3 RCTs.[246,247,249] Aqueous iodophor solution amount, concentration, application, and perioperative AMP regimen varied among studies.

Moderate-quality evidence suggested a benefit of intraoperative aqueous iodophor irrigation of the deep incision, in combination with parenteral AMP, for clean spine procedures. This was based on moderate-quality evidence from a meta-analysis (N=660) of 2 RCTs suggesting a reduced risk of deep SSI when the deep tissues were irrigated and allowed to soak for 3 minutes with 0.35% povidone iodine solution, then irrigated with an additional 2 L of normal saline prior to bone grafting and spinal instrumentation.[243,244] All procedures in both studies were performed by the same surgeon. Perioperative AMP included preoperative parenteral dose, postoperative parenteral dosing for 2 days followed by oral prophylaxis for an additional 3 days. Over 80% of the SSIs were caused by Methicillin-resistant *Staphylococcus aureus* (MRSA).

High-quality evidence suggested a benefit of aqueous iodophor irrigation of the subcutaneous tissue in combination with parenteral AMP for clean-contaminated, contaminated, and dirty open abdominal procedures. This was based on reduced risk of superficial SSI on meta-analysis (N=329) of 2 RCTS that performed 60 seconds of subcutaneous tissue irrigation with 10% aqueous iodophor solution prior to wound closure.[245,248] The larger [248] study administered parenteral AMP preoperatively and for 48 hours postoperatively, while the smaller[245] study only reported administering perioperative parenteral AMP. Individual meta-analyses of clean-contaminated (N=149) and dirty (N=90) procedures both showed reduced risk of superficial SSI.

High-quality evidence from 3 studies suggested no increased risk of product-related adverse events[244,245,247] or iodine toxicity.[245-247] Moderate-quality evidence from 2 studies suggested no wound healing problems.[243,245]

The search did not identify RCTs or SRs that evaluated the safety and effectiveness of soaking surgical implants (e.g., meshes, neurosurgical ventricular shunts) in antiseptic solution prior to insertion (in combination with parenteral AMP) and its impact on SSI.

Q9. Recommendation

9A. Consider intraoperative irrigation of deep or subcutaneous tissues with aqueous iodophor solution for the prevention of SSI. Intra-peritoneal lavage with aqueous iodophor solution in contaminated or dirty abdominal procedures is not necessary. **(Category II – weak recommendation; moderate-quality evidence suggesting a trade-off between clinical benefits and harms)** [243-249] (Guideline Question 9)

9B. The search did not identify randomized controlled trials evaluating the soaking of prosthetic devices in antiseptic solutions prior to implantation for the prevention of SSI. **(No recommendation/unresolved issue)** (Guideline Question 9)

Q10. How safe and effective is repeat application of an antiseptic skin preparation agent to the surgical site immediately prior to closing the surgical incision?

The available data examined the repeat application of aqueous iodophor solution to the patient's skin immediately prior to closing the surgical incision versus no additional application of topical antiseptic agent for the prevention of SSI. For this comparison, SSI was considered the critical outcome for decision-making.

Low-quality evidence suggested no benefit of repeat application of aqueous iodophor solution to the patient's skin immediately prior to closing the surgical incision, in combination with parenteral AMP. This was based on no difference in SSI (combined or individual incisional or organ/space SSI) in a small study at high risk of bias, in 107 gastric and colorectal procedures.[250]

The search did not identify RCTs or SRs that evaluated repeat application of chlorhexidine, chlorhexidine-alcohol, iodophor alcohol or topical antiseptic agents other than aqueous iodophor solution. The findings of the evidence review and the grades for all important outcomes are shown in eAppendix 2 of the Supplement: GRADE Table Q8-10 and Evidence Table Q10.

Q10. Recommendation

10. RCT evidence is insufficient to evaluate the tradeoffs between the benefits and harms of repeat application of antiseptic agents to the patient's skin immediately prior to closing the surgical incision for the prevention of SSI. (No recommendation/unresolved issue) [250] (Guideline Question 10)

4.2. Prosthetic Joint Arthroplasty Section Evidence Review

4.2A. BLOOD TRANSFUSION

Q11. How do perioperative blood transfusions impact the risk of SSI in prosthetic joint arthroplasty patients?

For the general question of risk of any blood transfusion on SSI, SSI was the critical outcome for decision-making. The evidence for this question consists of 2 RCTs[251,252] and 4 OBS.[253-256] All of the studies reflect European transfusion practices between 1999 and 2007. Studies were published between 2001 and 2008; however, only 2 report the study periods (1998–2000).[255,256] All studies were at low risk of bias.

When reported, hemoglobin thresholds for blood transfusion ranged between 8 and 11g/dL. The findings of the evidence review and the grades for all important outcomes are shown in eAppendix 2 of the Supplement: GRADE Table Q11 and Evidence Table Q11.

High-quality evidence suggested blood transfusions increased the risk of SSI. This was based on increased risk of SSI in a meta-analysis (N=8493) of 6 studies, 2 RCTs[251,252] and 4 OBS,[253-256] and a separate meta-analysis (N=7484) of the 4 OBS. Analysis combined allogeneic, autologous, and autologous plus allogeneic blood transfusion data. Data in both of these meta-analyses may be driven by 2 OBS with a large number of patients who received allogeneic-only blood transfusion and the possibility of selection bias inherent in OBS.[254,256] In contrast, meta-analysis of the 2 RCTs (N=1009) does not suggest an increased risk of SSI with autologous and autologous plus additional allogeneic blood transfusions.

Q11A. Are specific blood products associated with a risk of SSI?

The available data examined the following comparisons:

1. Allogeneic blood (any) vs. no transfusion
   a. Allogeneic not WBC depleted vs. no transfusion
   b. Allogeneic WBC depleted vs. no transfusion
   c. Allogeneic "buffy coat depleted" vs. no transfusion
   d. Allogeneic WBC filtered vs. no transfusion
   e. Allogeneic "lower WBC content" vs. allogeneic "higher WBC content"
2. Autologous blood (any) vs. no transfusion
   a. Autologous ±WBC filtration vs. no transfusion
   b. Autologous whole blood vs. no transfusion
   c. Autologous "not WBC depleted" vs. no transfusion
   d. Autologous buffy coat depleted vs. no transfusion
   e. Autologous "lower WBC content" vs. autologous "higher WBC content"
   f. Post-operative salvage only vs. autologous donated blood
3. Allogeneic blood (any) vs. autologous blood (any)
   a. Allogeneic WBC± WBC depleted vs. autologous not WBC depleted
   b. Allogeneic WBC filtered vs. autologous buffy coat depleted.
4. Combined autologous and allogeneic (any) vs. no transfusion
   a. Combined autologous and allogeneic vs. autologous only

For all comparisons, SSI, PJI, or reoperation due to wound infection were the critical outcomes for decision-making. Wound disturbance was also evaluated. The evidence for this question consists of 2 RCTs[251,252] and 7 OBS[253-259] studies. There were differences among studies, including: surgical procedures; definition of SSI; blood product white blood cell (WBC) content; length of blood product storage; hemoglobin transfusion trigger levels and other criteria for transfusion; as well as follow-up. In several studies, missing data resulted in discrepancies in the numbers. The findings of the evidence review and the grades for all important outcomes are shown in eAppendix 2 of the Supplement: GRADE Table Q11 and Evidence Table 11A.

Q11A.1. Allogeneic blood (any) vs. no transfusion

Low-quality evidence suggested that allogeneic blood transfusions increased the risk of SSI. This was based on increased risk of SSI in a meta-analysis (N=5737) of 4 OBS[253-256] studies in primary and revision THA and TKA and no difference in reoperation due to wound infection in another OBS.[259] See individual comparators in eAppendix 2 of the Supplement: GRADE Table 11 for specific study findings.

Q11A.2 Autologous blood (any) vs. no transfusion
Moderate-quality evidence suggested that autologous blood transfusions did not increase the risk of SSI. This was based on no difference in a meta-analysis (N=970) of 2 RCTs.[251,252] One large RCT in THA suggested no difference at 90 days of follow-up.[251] The second small RCT in THA reported no infections in either group; however, this study was designed to evaluate transfusion induced immunomodulation, not SSI, and follow-up was limited to 7 days.[252] In contrast, 1 large[254] (N=912) prospective OBS in primary and revision THA and TKA suggested reduced risk of SSI and a smaller[253] study in primary THA and TKA reported only 1 infection in the transfused group. One RCT reported receiving study supplies from a blood bag manufacturer.[251] See individual comparators in eAppendix 2 of the Supplement: GRADE Table 11 for specific study findings.

Q11A.3. Allogeneic blood (any) vs. autologous blood (any)
Moderate-quality evidence suggested that allogeneic blood transfusions increased the risk of SSI when compared with autologous transfusions. This was based on a greater than 4-fold increase in risk in a meta-analysis (N=2592) of 3 OBS.[253,254,258] Allogeneic blood products included whole blood, WBC depleted, WBC filtered and not filtered; autologous products included whole blood, buffy coat depleted, and perioperative cell salvage-washed blood. See individual comparators in eAppendix 2 of the Supplement: GRADE Table Q11 for specific study findings.

Q11A.4. Combined autologous and allogeneic blood (any) vs. no transfusion
Moderate-quality evidence suggested that combined autologous and additional allogeneic blood transfusions did not increase the risk of SSI. This was based on no difference in subanalysis in 1 RCT[251] (N=470) and 2 OBS[253,254] (N=1632). In each study, patients received allogeneic blood transfusion only after all (2–3 units) of the autologous donated blood (with or without additional salvage blood) had been transfused. Autologous blood products included autologous whole blood, packed red blood cells, salvage blood,[254] "buffy coat depleted,"[253] or "WBC filtered."[251] Allogeneic blood products included "WBC depleted or not depleted"[254] or "WBC filtered (WBCF)."[253,256] Transfusion triggers included: hemoglobin levels of 8-9 g/dL,[251,254] <11g/dL for autologous transfusions and <6 g/dL for allogeneic transfusions or <10 g/dL in patients with cardiovascular or cerebrovascular disease, or symptomatic anemia in another[257] study. See individual comparators in eAppendix 2 of the Supplement: GRADE Table Q11 for specific study findings.

Other guidelines
Recent blood transfusion practice guidelines recommend more restrictive transfusion strategies than those used in these studies.[260] In hemodynamically stable postoperative surgical patients, transfusion is recommended for hemoglobin levels of 8 g/dL or less for those with symptoms (e.g., chest pain, orthostatic hypotension or tachycardia unresponsive to fluid resuscitation, or congestive heart failure). In adult and pediatric intensive care unit patients, the recommended hemoglobin level for transfusion is 7 g/dL or less.

Q11B. If the risk of SSI is increased, can this effect be isolated from the risk associated with more complex cases?
The search did not identify data that directly evaluated the association between increasing blood transfusion requirements, more complex cases, and the risk of SSI in prosthetic joint arthroplasty patients. However, data from 3 OBS[254,256,257] stratified blood transfusion requirements and 1 OBS[254] reported blood loss, both by procedure type. See individual comparators in eAppendix 2 of the Supplement: GRADE Table Q11 for specific study findings.

Q11C. How does the volume of transfused blood product impact the risk of SSI?
The search did not identify data that evaluated differences in the volume of transfused blood product and their impact on the risk of SSI in prosthetic joint arthroplasty patients.

Q11D. How safe and effective is withholding blood transfusions to reduce the risk of SSI?
The search did not identify data that both evaluated the safety and effectiveness of withholding blood transfusions and its impact on the risk of SSI in prosthetic joint arthroplasty patients.

Other guidelines
Clinical practice guidelines recommend against withholding transfusion of necessary blood products from surgical patients as a means to prevent SSI.[64] This is considered accepted practice.

Q11. Recommendation

11A. Available evidence suggests uncertain tradeoffs between the benefits and harms of blood transfusions on the risk of SSI in prosthetic joint arthroplasty. Other organizations have made recommendations on this topic and a summary of these recommendations can be found in the Other guidelines section of the narrative summary for this question**. (No recommendation/unresolved issue)** [251-259] (Guideline Question 11A-C)

11B. Do not withhold transfusion of necessary blood products from surgical patients as a means to prevent SSI. **(Category IB –strong recommendation; accepted practice)** [64] (Guideline Question 11D)

4.2B. SYSTEMIC IMMUNOSUPPRESSIVE THERAPY

Q12. How does systemic corticosteroid or other immunosuppressive therapy impact the risk of SSI in prosthetic joint arthroplasty patients?

Immunosuppressive therapies used to treat rheumatoid arthritis (RA) are divided into disease-modifying antirheumatic drugs (DMARDs) and biologic agents. The most common DMARD is methotrexate, but these drugs can also include hydroxychloriquine, leflunomide, minocycline, sulfasazaline, azathioprine, cyclosporine and gold. DMARD combination therapy includes 2 or 3 drugs, most of which are methotrexate-based. Biologic agents are commonly divided into "non-tumor necrosis factor (TNF)" agents (e.g., anakinra, abatacept, rituximab, and tocilizumab) and "anti-TNF" agents (e.g., adalimumab, etanercept, infliximab, certolizumab pegol, and golimumab). Systemic corticosteroids most commonly refer to oral prednisone use.

To answer this question, the following subquestions were asked:

A) Does the type of agent impact the risk of SSI?
B) Does the preoperative duration of therapy impact the risk of SSI? and
C) Does the agent dose impact the risk of SSI?

Q12A. Does the type of agent impact the risk of SSI?

The available data examined the following comparisons:

1. Biologic agents (non-TNF and anti-TNF) vs. DMARDs
2. DMARDs: methotrexate vs. no DMARD therapy

For all comparisons, SSI, PJI, superficial SSI, deep wound abscess, and infected hematoma were the critical outcomes for decision-making. Drug-related adverse events, as well as the adverse events of a surgical wound necrotic eschar, and serous drainage were also evaluated. "Adverse events of surgical wound" was a composite variable that included: wound dehiscence (not completely healed 14 days after surgery or needs secondary closure), continued discharge, and culture-positive infection. The evidence for this question consists of 4 OBS in RA patients.[261-264] All studies were at low risk of bias. The authors in 2 of these studies reported receiving funds from pharmaceutical companies.[261,262] The findings of the evidence review and the grades for all important outcomes are shown in eAppendix 2 of the Supplement: GRADE Table Q12-16 and Evidence Table Q12-16.

Q12.A.1. Biologic agents (non-TNF and anti-TNF) vs. DMARDs

Very low-quality evidence suggested biologic agent therapy (non-TNF and anti-TNF) increased the risk of SSI. This was based on greater than 5-fold increase in risk of SSI and superficial SSI, but no difference in PJI in 3 separate meta-analyses (N=528) of 2 OBS.[261,262] Multivariate logistic regression analyses in both studies identified biologic agents as a significant risk factor for infection, and in 1 study[261] they were also a risk factor for deep venous thrombosis (DVT). Very-low quality evidence also suggested no difference in other adverse events of the surgical wound.[263] For superficial SSI, the large[262] study in primary or revision THA or TKA RA patients (superficial SSI rate 18.8%) reported a significantly increased risk with biologic agents, while the smaller[261] study (superficial SSI rate of 7.4%) reported no difference. The large and small studies each reported no difference in PJI; however, the number of events in both groups (n=3 and 1, respectively) and the number of arthroplasty procedures in the smaller study (N=108) limited the power of the analyses.

Biologic agents included anti-TNFs (etanercept, infliximab, adalimumab) and non-TNFs (anakinra, abatacept and rituximab). In each study, patients had established RA (on average > 10 years). All patients on biologic agent therapy also received prednisone 3-5 mg/day, and the majority also received methotrexate (88%[261] to 92%[263]) and/or another DMARD[261] (13%). DMARD patients in all 3 studies were on single or multiple DMARD therapy in addition to daily prednisone (average, 3 mg/day). The most common DMARD was methotrexate, but none of the studies reported average weekly doses, and only 1 reported the DMARD perioperative administration protocol (it was administered continuously).[262]

Q12.A.2. DMARDs: methotrexate vs. no DMARD therapy
Very low-quality evidence suggested methotrexate therapy did not increase the risk of SSI. This was based on no difference in PJI, deep wound abscess, infected hematoma, necrotic eschar, or serous drainage at 6 months of follow-up in 1 OBS.[264] For each outcome, both the study size and the total number of events were limited. This 1991 study utilized data collected between 1978 and 1987 with patients on a mean weekly methotrexate dose of 8.7 mg (range: 7.5–12.5 mg) and could be considered sub-therapeutic in current clinical practice.[265] The methotrexate group included both patients who had continued and patients who had stopped methotrexate within 4 weeks of surgery. While patients in the no therapy group had never taken methotrexate, some were on daily prednisone (the study does not report how many).

Q12B. Does the preoperative duration of the therapy impact the risk of SSI?
The search did not identify data that directly evaluated the length of time that immunosuppressive therapy was used preoperatively and the impact this therapy had on the risk of SSI in prosthetic joint arthroplasty patients. Thus, disease duration was evaluated as a proxy. SSI was the critical outcome for decision-making. The evidence for this question consists of 2 OBS.[261,262] The search did not reveal data that evaluated patients with early RA (<6 months). The findings of the evidence review and the grades for all important outcomes are shown in eAppendix 2 of the Supplement: GRADE Table 12-16 and Evidence Table Q12.

Low-quality evidence suggested that in patients with established RA (>6 months), years of disease duration was a risk factor for SSI. This was based on increased risk in 2 OBS that performed multivariate logistic regression analyses comparing infected to non-infected patients on biologic (anti-TNF) agents and DMARDs.[261,262]

Q12C. Does the agent dose impact the risk of SSI?
The search did not identify data that directly evaluated different doses of biologic agents or DMARDs and their impact on the risk of SSI in arthroplasty patients. The available data examined doses of prednisone and risk of SSI in patients on biologic agents (anti-TNF) as compared with those on DMARDs.

For this comparison, SSI was the critical outcome for decision-making. The evidence for this question consists of 2 OBS in RA patients.[261,262] The findings of the evidence review and the grades for all important outcomes are shown in eAppendix 2 of the Supplement: GRADE Table Q12-16 and Evidence Table Q12.

Very low-quality evidence suggested higher prednisone dose increased the risk of SSI. This was based on increased risk of SSI on multivariate logistic regression analyses comparing infected and non-infected patients in 2 OBS.[261,262] The small study, with the majority of patients on combination biologic/DMARD or dual DMARD therapy, suggested that increasing prednisone dose was a risk factor for SSI.[261] Patients in the biologic agent group were on significantly higher daily prednisone doses (5 mg/day; range 2–7) than those in the DMARD group (3 mg/day; range 0–5). The larger study, where none of the patients were on combination biologic and DMARD therapy, suggested prednisone dose was not a risk factor for SSI. Patients in both groups were on an average prednisone dose of 3 mg/day (range, 0–5).[262] Results were not stratified by immunosuppressive therapy agent.

Q13. What are the most effective strategies in managing systemic corticosteroids or other immunosuppressive therapy perioperatively to reduce the risk of SSI in prosthetic joint arthroplasty patients?
Q13A. How safe and effective is the discontinuation of these agents preoperatively and when should they be resumed?
The available data examined the following comparisons:

1. DMARDs: methotrexate stopped vs. continued perioperatively
2. Biologic agents: anti-TNF stopped vs. continued perioperatively

The evidence for this question consists of 4 OBS examining DMARDs[264,266-268] and 1 OBS examining biologic agents[266] in RA patients. All studies were at low risk of bias. For all comparisons PJI was the critical outcome for decision-making. RA flares, infected hematomas, necrotic eschar, and non-communicating serous drainage outcomes were also evaluated. The findings of the evidence review and the grades for all important outcomes are shown in eAppendix 2 of the Supplement: GRADE Table Q12-16 and Evidence Table Q12-13.

Q13A.1. DMARDs: methotrexate stopped vs. continued perioperatively
Low-quality evidence suggested no increased risk of PJI with methotrexate continued throughout the perioperative period. This was based on no difference in PJI in a meta-analysis of 3 small OBS[264,267,268] and a separate OBS[266] . In the meta-analysis, both the number of procedures (N=180) and events (n=7) were small. The studies were performed between 1991 and 1996, and the methotrexate doses could be considered subtherapeutic in current practice.[265] Procedures followed, and length of time during which therapy was stopped varied. In a larger study, stopping DMARD therapy at the time of surgery (not defined) reduced the incidence of subsequent PJI.[266] The authors of this larger study reported receiving funds from multiple pharmaceutical companies.

Q13A.2. Biologic agents: anti-TNF stopped vs. continued perioperatively

Very low-quality evidence suggested no difference in risk of PJI with continuation of biologic (anti-TNF) therapy perioperatively. This was based on no difference in risk of PJI in a small subanalysis in 1 OBS in THA and TKA patients. [266] Both the number of patients (N=50) and events (n=3), all in the group continuing biologic agent therapy perioperatively, were very small.

Q13B. Should the agent dose be adjusted, and if so, for how long?

The search did not identify data that evaluated perioperative immunosuppressive therapy dose adjustment and its impact on the risk of SSI in prosthetic joint arthroplasty patients.

Other guidelines

Clinical practice guidelines provide conflicting recommendations regarding the perioperative management of immunosuppressive therapy. In 2008, the American College of Rheumatology (ACR) provided no recommendation for the perioperative management of DMARDs due to the "absence of consistent evidence".[269] The following year, a multinational guideline suggested that methotrexate could be safely continued in the perioperative period in RA patients undergoing elective orthopaedic surgery.[265] Their recommendation was based on studies with low methotrexate dosing (4–13 mg/week). For biologic agents, the British Society for Rheumatology recommended in 2005 that treatment with anti-TNF agents be withheld for 2–4 weeks prior to major surgical procedures and restarted postoperatively if there was no evidence of infection and wound healing was satisfactory.[270] Recommendations were based solely on information provided by pharmaceutical companies. In 2008, ACR recommended that biologic agents not be used for at least 1 week prior to and 1 week following surgery (based on the pharmacokinetic properties of a given agent).[269] The 2012 ACR update does not address perioperative management of immunosuppressive therapy.[271]

Q12 and Q13. Recommendation

12 and 13. Available evidence suggests uncertain tradeoffs between the benefits and harms of systemic corticosteroid or other immunosuppressive therapy on the risk of SSI in prosthetic joint arthroplasty. Other organizations have made recommendations based on the existing evidence and a summary of these recommendations can be found in the Other guidelines section of the narrative summary for this question**. (No recommendation/unresolved issue)** [261-264,266-268] (Guideline Questions 12 and 13)

Q14. What is the optimal duration of postoperative AMP to reduce the risk of SSI in prosthetic joint arthroplasty patients who are on systemic corticosteroid or other immunosuppressive therapy?

The search did not identify data that specifically evaluated differences in duration of postoperative AMP in prosthetic joint arthroplasty patients who were on systemic corticosteroids or other immunosuppressive agents and its impact on the risk of SSI. However, multiple procedures examined in the Core Section, Q1.E: Postoperative AMP duration that included patients on immunosuppressive therapy showed no benefit of continuing AMP after closing the surgical incision in the operating room. Therefore, the broader recommendation for duration of postoperative AMP should be applied to prosthetic joint arthroplasty procedures irrespective of use of systemic corticosteroid or other immunosuppressive therapies.

Q14. Recommendation

14. For prosthetic joint arthroplasty patients on systemic corticosteroid or other immunosuppressive therapy, Recommendation 1E applies: In clean and clean-contaminated procedures, do not administer additional prophylactic antimicrobial agent doses after the surgical incision is closed in the operating room, even in the presence of a drain. **(Category IA – strong recommendation; high- quality evidence)** [96-140] (Guideline Question 14)

4.2C. INTRA-ARTICULAR CORTICOSTEROID INJECTIONS

Q15. How do preoperative intra-articular corticosteroid injections impact the risk of SSI in prosthetic joint arthroplasty patients?

The available data examined the following comparisons:

1. History of corticosteroid injection vs. no injection
   a. TKA: injection vs. no injection
   b. THA: injection vs. no injection

For all comparisons, any SSI, PJI, and superficial SSI were the critical outcomes for decision-making. The evidence for this question consists of 2 OBS in TKA[272,273] and 3 OBS in THA[274-276] patients. All studies were at low risk of bias. The findings of the evidence review and the grades for all important outcomes are shown in eAppendix 2 of the Supplement: GRADE Table Q12-16 and Evidence Table Q15.

Low-quality evidence suggested that preoperative intra-articular corticosteroid injection did not increase the risk of SSI following total joint arthroplasty. This was based on no difference in a meta-analysis (N=1146) of 5 OBS in TKA[272,273] and THA.[274-276] See individual comparators below and in eAppendix 2 of the Supplement: GRADE Table Q12-16 for individual TKA and THA findings.

Q15.1.a. TKA: injection vs. no injection

Very low-quality evidence suggested that preoperative intra-articular corticosteroid injection did not increase the risk of SSI following TKA. This was based on no difference in SSI, PJI, or superficial SSI in meta-analyses (N=414) of 2 OBS.[272,273] Both the total number of patients and events were small. One study in 144 patients[273] suggested that a history of preoperative intra-articular injection was significantly associated with PJI after TKA (3 infections, all in the injection group) while another study in 270 TKAs[272] reported no PJIs in either group. Both studies had 1 year of follow-up. The majority of infections were superficial SSIs, and no difference was reported at 30 days of follow-up. In the smaller study, patients received injections in the orthopaedic clinic, rheumatology clinic, or general practice setting, while those in the larger study all received their injections in the operating room using strict aseptic technique. Patients had been injected within 11[273] and 12[272] months of surgery.

Q15.1.b. THA: injection vs. no Injection

Very low-quality evidence suggested that a preoperative intra-articular corticosteroid injection did not increase the risk of infection following THA. This was based on no difference in SSI, PJI, or superficial SSI on separate meta-analyses of 3 OBS.[274-276] No difference in PJI or superficial SSI was reported in each individual study. In 2 studies, both the number of patients and events was small.[274,276] Corticosteroid doses and follow-up periods varied. In each study, corticosteroid injection was administered in a radiology suite using standard protocols for aseptic technique, and 1 study also indicated that the radiologists wore sterile masks and gowns.[274]

Q16. What are the most effective strategies for managing the preoperative use of intra-articular corticosteroid injections to reduce the risk of SSI in prosthetic joint arthroplasty patients?

The search did not identify data that evaluated different intra-articular corticosteroid injection agents and their impact on risk of SSI. To answer this question, 2 subquestions were asked:

A) Does the length of time between corticosteroid injection and prosthetic joint arthroplasty impact the risk of SSI?
B) Does the corticosteroid injection dose impact the risk of SSI?

Q16A. Does the length of time between intra-articular corticosteroid injection and prosthetic joint arthroplasty impact the risk of SSI?

The available data evaluated different lengths of time between preoperative intra-articular corticosteroid injection and prosthetic joint arthroplasty and the impact on the risk of SSI in THA only, not TKA.

For all comparisons, SSI was the critical outcome for decision-making. The evidence for this question consists of 2 OBS.[274,275] The findings of the evidence review and the grades for all important outcomes are shown in eAppendix 2 of the Supplement: GRADE Table Q12-16 and Evidence Table Q16.

Low-quality evidence suggested no association between the length of time between intra-articular corticosteroid injection and THA and the development of SSI. This was based on no difference in the length of time between injection and surgery and the development of SSI in 2 OBS.[274,275] The smaller, underpowered study also reported no association between the number of injections and SSI.[274] In the larger study, while there was no difference in PJI or superficial SSI (mean time between injection and THA was 112 days), the mean time from injection to surgery for those diagnosed with PJI was less than half as long as those diagnosed with superficial SSI (44 vs. 112 days).[275]

Q16B. Does the corticosteroid injection dose impact the risk of SSI?

The search did not identify data that evaluated different doses of preoperative intra-articular corticosteroid injections and their impact on the risk of SSI.

Other guidelines

While clinical practice guidelines include intra-articular corticosteroid injections among their pharmacologic recommendations for the initial management of knee and hip osteoarthritis, they do not provide recommendations on management strategies with regard to SSI prevention.[277] Safe injection practices apply to the administration of intra-articular corticosteroid injections.[278]

Q15 and Q16. Recommendation

15 & 16. Available evidence suggests uncertain tradeoffs between the benefits and harms of preoperative intra-articular corticosteroid injection on the incidence of SSI in prosthetic joint arthroplasty. Other organizations have made recommendations based on observational data and a summary of these recommendations can be found in the Other guidelines section of the narrative summary for this question**. (No recommendation/unresolved issue)**[272-276] (Guideline Questions 15 and 16)

4.2D. ANTICOAGULATION

Q17. What are the most effective strategies for managing perioperative venous thromboembolism (VTE) prophylaxis to reduce the risk of SSI in prosthetic joint arthroplasty patients?

To answer this question 3 subquestions were asked:

A) Does the risk of SSI differ by individual VTE prophylaxis agent?
B) What is the optimal timing and duration of perioperative VTE prophylaxis for the reduction of SSI in prosthetic joint arthroplasty patients?
C) How safe and effective is modifying the dose of the perioperative VTE prophylaxis agent to reduce the risk of SSI?

Q17A. Does the risk of SSI differ by individual VTE prophylaxis agent?

The available data examined the following comparisons between different anticoagulation agents:

1. Enoxaparin vs. fondaparinux
2. Enoxaparin vs. rivaroxaban
3. Enoxaparin vs. aspirin (acetylsalicylic acid [ASA]) and mechanical prophylaxis
4. Enoxaparin vs. bemiparin vs. fraxiparin vs. fondaparinux
5. Low molecular weight heparin (LMWHs) or fondaparinux vs. ASA
6. Warfarin vs. no pharmacologic or mechanical prophylaxis
7. Warfarin vs. ASA ± mechanical prophylaxis
8. Higher vs. lower mean International Normalized Ratio (INR)

For all comparisons, SSI and PJI were the critical outcomes in decision-making. Hemorrhagic wound complications, time until wound was dry or persistent wound drainage, drug-related adverse events, and wound hematoma outcomes were also evaluated. The evidence for this question consists of 1 SR,[279] 4 RCTs,[280-283] and 5 OBS[28,284-287] in primary and revision, unilateral, THA, TKA, and hip fracture procedures. Injectable agents included LMWHs (Factor Xa and some thrombin inhibition), most commonly enoxaparin or the indirect Factor Xa inhibitor fondaparinux. Oral agents included rivaroxaban (direct Factor Xa inhibitor), warfarin (Vitamin K antagonist, Factors II, VII, IX, X inhibitors), and ASA (cyclooxygenase inhibitor). No reversing agents currently exist for fondaparinux or rivaroxaban. The search did not identify studies that evaluated warfarin as compared to enoxaparin or the impact of unfractionated heparin or clopidogrel on the risk of SSI. The findings of the evidence review and the grades for all important outcomes are shown in eAppendix 2 of the Supplement: GRADE Table Q17 and Evidence Table Q17A-B.

Q17A.1. Enoxaparin vs. fondaparinux

Low-quality evidence suggested no difference between perioperative injectable VTE prophylaxis with enoxaparin or fondaparinux and risk of SSI. This was based on no difference in SSI and no drug-related adverse events at the end of VTE prophylaxis (11 days) in a large meta-analysis (N=7237) of 4 RCTs (in primary and revision THA, TKA, and hip fracture procedures (osteosynthesis and hemi-arthroplasties).[279,288-291] The studies were large, international, multi-center studies evaluating the safety and effectiveness of these agents in reducing the risk of postoperative VTE, not SSI. While fondaparinux administration was standardized (2.5 mg once a day starting postoperatively, except in hip fractures where it was started preoperatively if the case was delayed for >24 hours), enoxaparin dose and timing of administration varied among studies (30 mg twice a day starting postoperatively[288,291] or 40 mg once a day starting preoperatively[289,290]). In all 4 studies, prophylaxis was scheduled to last 5-9 days postoperatively. SSI was a secondary outcome and follow-up was limited (up to 11 days postoperatively). The 4 individual RCTs and the SR meta-analysis were all sponsored by the manufacturer of fondaparinux and authored by the same investigators, in which the lead, senior, and multiple co-authors reported serving as scientific consultants to the manufacturers of both agents evaluated in the studies. Turpie et al., indicated that the sponsor was responsible for data collection and final statistical analysis.[291]

Q17A.2. Enoxaparin vs. rivaroxaban

High-quality evidence suggested no difference between injectable enoxaparin and oral rivaroxaban and risk of SSI. This was based on no difference in SSI in a large meta-analysis (N=12,383) of 4 RCTs in elective primary or revision THA or TKA, and no difference in hemorrhagic wound complications or drug-related adverse events.[280-283] These studies were large, international, multi-center studies at

low risk of bias, evaluating the safety and effectiveness of once daily dosing with enoxaparin or rivaroxaban in reducing the risk of postoperative VTE, not SSI. Eriksson et al.,[280] and Kakkar et al.,[282] compared enoxaparin 40 mg once-a-day started preoperatively to rivaroxaban 10 mg once-a-day started postoperatively in elective unilateral primary (95%) or revision THA. Rivaroxaban was administered for 35 days in both studies; enoxaparin was administered for 35 days in one[280] and 10-14 days in the other.[282] Follow up was approximately 2 months. Two other studies evaluated these agents in elective unilateral primary (97%) or revision TKA, administered over 10-14 days.[281,283] While rivaroxaban administration was standardized (10 mg once-a-day, started preoperatively), enoxaparin dose and timing varied among studies (40 mg once-a-day, started preoperatively[283] or 30 mg twice a day started postoperatively). SSI was a secondary outcome, and follow-up was approximately 6 weeks. All studies were sponsored by the manufacturer of rivaroxaban and authored by investigators who were employees of the manufacturer or who served as scientific consultants to the manufacturers of both agents evaluated in the studies.

Q17A.3 Enoxaparin vs. ASA and mechanical prophylaxis

Very low-quality evidence suggested no difference between injectable enoxaparin and combined oral ASA and mechanical prophylaxis and risk of SSI. This was based on no increased risk of SSI on logistic regression analysis in 1 large study in primary THA or TKA.[286] Enoxaparin was associated with a longer time until wound was dry in THA, but not TKA. Enoxaparin was started 12-24 hours postoperatively. ASA 325 mg along with pneumatic compression devices was started on the morning after surgery. Analysis was limited to patients with a closed suction drain and normal coagulation profile. Duration of VTE prophylaxis and follow-up period were not reported.

Q17A.4. Enoxaparin vs. bemiparin vs. fraxiparin vs. fondaparinux

Very low-quality evidence suggested no difference between perioperative injectable LMWHs, ultra LMWH and fondaparinux, and risk of SSI. This was based on no difference in PJI at 6 months of follow-up in a small, nested, case-control study within a larger European multicenter prospective study investigating the independent effects of VTE prophylaxis timing on the risk of PJI in TKA (low risk of bias).[284] Of note, logistic regression analysis suggested that hematoma formation increased the risk of PJI 4-fold.

Q17A.5. Enoxaparin, dalterparin, tinzaparin or fondaparinux vs. ASA ± mechanical prophylaxis

Very low-quality evidence suggested no difference between perioperative injectable LMWH, fondaparinux, and combined oral ASA (with or without mechanical VTE prophylaxis), and risk of SSI. This was based on no difference in SSI in a subanalysis (n=41,917) of a very large retrospective OBS (low risk of bias) using administrative data from a national sample of primary TKAs.[28] Data were collected from 307 facilities over a 2-year period and compared the risk of VTE, bleeding, SSI, and mortality in primary TKA patients, 4,719 (5.0%) of whom were on ASA, 51,923 (55.3%) on oral warfarin, and 37,198 (39.6%) on injectable agents (LMWHs and fondaparinux were combined in the analysis). Pneumatic compression devices were used on the day of surgery or on the first postoperative day in 1,795 (38%), 28,757 (55%), and 17,756 (48%) of the populations, respectively. Patients on ASA had fewer baseline comorbidities, lower baseline risk of VTE, and received care in hospitals with shorter average length of stay that more commonly discharged to the patient's home after surgery. The study included SSIs detected at the time of admission or upon readmission to the hospital within 30 days of the index procedure using International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) wound infection codes. Authors indicated that subtherapeutic dosing and/or inappropriate dose timing of the LMWHs or synthetic Factor Xa inhibitor may have impacted the results.

Q17A.6. Warfarin vs. no pharmacologic or mechanical prophylaxis

Very low-quality evidence suggested no difference between oral warfarin VTE prophylaxis and no pharmacologic or mechanical prophylaxis, and risk of SSI. This was based on no difference in SSI (deep or superficial) in 1 large retrospective OBS in primary unilateral TKA at 3 months of follow-up (low risk of bias).[287] History of anticoagulation prophylaxis for cardiac (arrhythmia or prosthetic valve) or thromboembolic event was not associated with increased risk of SSI or gastrointestinal bleed in patients on 6 weeks of postoperative warfarin VTE prophylaxis. INR levels (target INR: 1.6–2.2) were monitored and medication adjusted twice weekly. Standardized postoperative protocols in both groups included continuous passive motion, physical therapy, weight bearing, and similar pain and nausea medications.

Q17A.7. Warfarin vs. ASA ± mechanical prophylaxis

Low-quality evidence suggested no difference between perioperative oral warfarin and ASA (with or without mechanical VTE prophylaxis), and risk of SSI. This was based on no difference in SSI in 2 large retrospective studies at low risk of bias.[28,286] In 1 large single institution study, logistic regression analysis suggested that in THA and TKA, warfarin (target INR=2) started on the day of surgery was not associated with an increased risk of SSI or longer time until wound was dry, as compared with ASA 325 mg with pneumatic compression devices started on the morning after surgery.[286] Duration of VTE prophylaxis and follow-up period were not reported. Analysis was limited to patients with a closed suction drain and normal coagulation profile. A second, large study using administrative data collected from 307 facilities over a 2-year period, suggested no difference in SSI in primary TKAs.[28] Target INR was not reported. Pneumatic compression devices were used on the day of surgery or on the first postoperative day in 55% of patients on warfarin and 38% of patients on ASA. SSIs were detected on admission or readmission to the hospital within 30 days of the index procedure using ICD-9-CM wound infection codes. Authors indicated that subtherapeutic dosing or inappropriate timing may have impacted results.

Q17A.8. Higher vs. lower INR

Very low-quality evidence suggested no difference between higher and lower oral warfarin INRs and risk of SSI. This was based on no difference in PJI in a small (N=154) 1:2 case control study in primary and revision THA and TKAs (low risk of bias).[285] Low dose

warfarin (target INR=1.5) was administered on the day of surgery and continued for 6 weeks. Thirteen patients on anticoagulation therapy preoperatively for a chronic condition were heparinized postoperatively until fully anticoagulated on warfarin with a higher target INR=2–3. All of these patients were in the infected cohort. The INR was also significantly higher in patients with wound-related problems who later developed infection. In addition, infected patients and those with wound complications were more likely to have INR > 1.5 at the time of hospital discharge. Infected patients also had a significantly higher incidence of wound hematomas. On multivariate logistic regression analysis, wound hematomas and persistent wound drainage were significant risk factors for PJI. Nine (69%) of the heparinized patients developed wound complications, including: hematomas, persistent wound drainage, or delayed wound healing.

Q17B. What is the optimal timing and duration of perioperative VTE prophylaxis that also reduces the risk of SSI?
The available data examined VTE prophylaxis started preoperatively as compared with postoperatively in patients receiving injectable LMWHs (enoxaparin, bemiparin, or fraxiparin) or fondaparinux.

For this comparison, PJI was the critical outcome in decision-making. The evidence for this question consists of 1 OBS in TKA, at low risk of bias.[284] The search did not identify data that evaluated optimal timing in THA or in patients taking oral agents. The search did not identify data that evaluated optimal duration of perioperative anticoagulation prophylaxis and its impact on SSI. The findings of the evidence review and the grades for all important outcomes are shown in eAppendix 2 of the Supplement: GRADE Table Q17 and Evidence Table Q17A-B.

Very low-quality evidence suggested that close perioperative administration of injectable LMWHs or fondaparinux VTE prophylaxis agents did not increase the risk of PJI. This was based on no difference in PJI at 6 months of follow-up, in a small, nested, multicenter, case control study in TKAs.[284]

Other guidelines
Clinical practice guidelines on prevention of VTE in patients undergoing THA, TKA, or hip fracture procedures provide recommendations on choice, timing, and duration of VTE prophylaxis.[292,293]

Q17C. How safe and effective is modifying the dose of perioperative VTE prophylaxis agent to reduce the risk of SSI?
The search did not identify data that evaluated the safety and effectiveness of modifying the dose of perioperative VTE prophylaxis agent and its impact on the risk of SSI.

Q17. Recommendation

17. Available evidence suggests uncertain tradeoffs between the benefits and harms of venous thromboembolism prophylaxis on the incidence of SSI in prosthetic joint arthroplasty. Other organizations have made recommendations based on the existing evidence and these references can be found in the Other guidelines section of the narrative summary for this question**. (No recommendation/unresolved issue)**[28,279-288,290,291] (Guideline Question 17)

4.2E. ORTHOPAEDIC SURGICAL SPACE SUIT

Q18. How safe and effective are orthopaedic surgical space suits in reducing the risk of SSI in prosthetic joint arthroplasty patients, and which healthcare personnel should wear them?
The available data evaluated the use of a space suit as compared with no space suit.

For this comparison, deep SSI requiring reoperation, deep SSI requiring revision, and deep SSI were the critical outcomes in decision-making. Superficial SSI outcome was also evaluated. The evidence for this question consists of 3 OBS at low risk of bias.[294-296] The findings of the evidence review and the grades for all important outcomes are shown in eAppendix 2 of the Supplement: GRADE Table Q18 and Evidence Table Q18.

Very-low quality evidence suggested no benefit to using an orthopaedic space suit to reduce the risk of SSI. This was based on no difference in deep SSI requiring reoperation,[295] deep SSI requiring revision surgery,[294] or deep or superficial SSI[296] in 3 OBS. The number of events for each of these studies was low. The largest national joint registry study with multiple subgroup analyses suggested that use of a space suit was associated with an increased number of deep SSIs requiring revision surgery within 6 months of THA or TKA, but this evidence was limited in size.[294] Results did not differ based on the presence or absence of laminar flow. A large multicenter study using administrative data from patients undergoing TKA suggested no difference in deep SSIs requiring reoperation within 90 days.[295] Reoperations included incision and drainage and implant removal. The definition of deep SSI in this study may have included PJI. Space suit and laminar flow use varied between groups. A third small study in THA and hip hemiarthroplasties reported only 1 deep SSI in the space suit group and 1 superficial SSI in each group at 24 months of follow-up.[296] High-efficiency particulate air (HEPA)/mixed turbulent filtration was used in both groups.

The search did not identify data that quantified potential complications associated with the use of space suits. In 1 large national joint registry study (N=88,311), comments by surgeons completing a questionnaire (n=35) included "limited spatial awareness and ease of contamination due to an apparent false sense of security" with the use of a space suit.[294] The efficacy of the space suit as personal protective equipment was not evaluated.

Also, the search did not identify data that evaluated the association between specific health care personnel wearing a space suit and SSI. One retrospective controlled study included a surgeon questionnaire reporting that the surgeon, assistant, and scrub nurse were the team members wearing a full space suit.[294] One prospective controlled study reported those same team members wearing the space suit in the intervention group.[296]

Q18. Recommendation

18. Available evidence suggests uncertain tradeoffs between the benefits and harms of orthopaedic surgical space suits or the health care personnel who should wear them for the prevention of SSI in prosthetic joint arthroplasty. **(No recommendation/unresolved issue)** [294-296] (Guideline Question 18)

4.2F. POSTOPERATIVE AMP DURATION IN PROSTHETIC JOINT ARTHROPLASTY WITH THE USE OF A DRAIN

Q19. What is the optimal duration of postoperative AMP to reduce the risk of SSI in prosthetic joint arthroplasty in the presence of a drain?

The search did not identify data that directly evaluated optimal postoperative AMP duration in the presence of a drain and its impact on the risk of SSI in prosthetic joint arthroplasty patients. However, multiple procedures examined in the Core Section, Q1.E: Postoperative AMP duration that included use of a drain (including prosthetic joint arthroplasty procedures) showed no benefit of continuing AMP after closing the incision in the operating room. Therefore, the broader recommendation for postoperative AMP duration should be applied to prosthetic joint arthroplasty procedures irrespective of drain use.

Q19. Recommendation

19. In prosthetic joint arthroplasty, Recommendation 1E applies: In clean and clean-contaminated procedures, do not administer additional prophylactic antimicrobial agent doses after the surgical incision is closed in the operating room, even in the presence of a drain. **(Category IA – - strong recommendation; high-quality evidence)** [96-140] (Guideline Question 19)

4.2G. BIOFILM

Q20. What are the most effective strategies to reduce the risk of biofilm formation and SSI in prosthetic joint arthroplasty patients?

To answer this question 4 subquestions were asked:

A) How effective are cement modifications (i.e., antimicrobial and nanoparticle loading)?
B) How effective are prosthesis modifications (i.e., antimicrobial coating, galvanic couples, "printing" technologies, and nanotechnology)?
C) How effective are vaccines?
D) How effective are other biofilm control agents (e.g., biofilm dispersants, quorum-sensing inhibitors, novel antimicrobial agents)?

Q20A. How effective are cement modifications (i.e., antimicrobial and nanoparticle loading)?

The search did not identify data that evaluated the safety and effectiveness of cement modifications in THA and the risk of SSI. In vitro studies and studies that evaluated antimicrobial loaded cement in the absence of perioperative parenteral AMP were excluded from the analysis. The available data examined cefuroxime loaded cement vs. plain cement in primary TKA patient receiving perioperative AMP.

For this comparison, deep SSI was the critical outcome in decision-making. In these studies, deep SSI likely refers to or includes PJI. The evidence for this question consists of 2 RCTs.[297,298] The findings of the evidence review and the grades for all important outcomes are shown in eAppendix 2 of the Supplement: GRADE Table Q20 and Evidence Table Q20.

Moderate-quality evidence suggested a benefit of cefuroxime loaded cement. This was based on a reduced risk of deep SSI in a meta-analysis (N=428) of 2 RCTs: 1 large study in non-diabetic[297] patients and 1 small study (N=78) in diabetic [298] patients. Both studies were at moderate risk of bias. There were no deep SSIs in the cefuroxime loaded cement groups at an average 49 months of follow-up. A single surgeon performed all TKAs in an operating room without ultraviolet lights, laminar flow, or use of an orthopaedic surgical space suit. Only the tibial and patellar components were cemented. Cefuroxime 2 g in 40 g polymethyl methacrylate cement was used

in the study groups. AMP included parenteral cefazolin and gentamicin preoperatively then every 6 and 12 hours, respectively, postoperatively for 36 hours followed by cefazolin orally for 7 more days. Data on organisms isolated from the SSIs and antimicrobial resistance were not reported.

Q20B. How effective are prosthesis surface modifications (i.e., antimicrobial coating, galvanic couples, "printing" technologies, and nanotechnology)?

The search did not identify in vivo studies that evaluated the safety and effectiveness of prosthesis modifications and their impact on biofilm formation and the risk of SSI.

Q20C. How effective are vaccines?

The search did not identify in vivo studies that evaluated the safety and effectiveness of vaccines and their impact on biofilm formation and the risk of SSI.

Q20D. How effective are other biofilm control agents (e.g., biofilm dispersants, quorum-sensing inhibitors, novel antimicrobial agents)?

The search did not identify in vivo studies that evaluated the safety and effectiveness of other biofilm control agents and their impact on biofilm formation and the risk of SSI

Q20. Recommendations

20A. Available evidence suggests uncertain tradeoffs between the benefits and harms regarding cement modifications and the prevention of biofilm formation or SSI in prosthetic joint arthroplasty. **(No recommendation/unresolved issue**) [297,298] (Guideline Question 20A)

20B. The search did not identify studies evaluating prosthesis modifications for the prevention of biofilm formation or SSI in prosthetic joint arthroplasty. **(No recommendation/unresolved issue)** (Guideline Question 20B)

20C. The search did not identify studies evaluating vaccines for the prevention of biofilm formation or SSI in prosthetic joint arthroplasty. **(No recommendation/unresolved issue)** (Guideline Question 20C)

20D. The search did not identify studies evaluating biofilm control agents such as biofilm dispersants, quorum-sensing inhibitors, or novel antimicrobial agents for the prevention of biofilm formation or SSI in prosthetic joint arthroplasty. **(No recommendation/unresolved issue)** (Guideline Question 20D)

5. RE-EMPHASIS OF SELECT 1999 CDC AND HICPAC RECOMMENDATIONS FOR PREVENTION OF SURGICAL SITE INFECTIONS

The Centers for Disease control and Prevention (CDC), Guideline for Prevention of Surgical Site Infection 2017 addresses new and updated strategies for the prevention of Surgical Site Infections (SSIs) in healthcare settings. The 2017 Guideline focuses on a few select areas, and not all of the recommendations that were made in 1999 were reviewed as a part of the guideline development process. However, CDC and the Healthcare Infection Control Practices Advisory Committee (HICPAC) recognized that many of the recommendations remain important and have become infection control standards for surgical infection prevention.

In 2014, HICPAC reviewed the 1999 strong recommendations for which the evidence was not re-assessed as part of the development of the 2017 Guideline. This was to reaffirm them as accepted practices (e.g., standard of care). At the July 2014 HICPAC meeting, HICPAC reviewed and recommended to CDC that many of the 1999 strong recommendations should be re-emphasized as accepted practice for preventing surgical site infections.[299] CDC and HICPAC recommend that facilities should continue to follow the recommendations outlined below.

5.1. Recommendations

1. **PREPARATION OF THE PATIENT**
   - **a.** Whenever possible, identify and treat all infections remote to the surgical site before elective operations and postpone elective operations on patients with remote site infections until the infection has resolved.
   - **b.** Do not remove hair preoperatively unless the hair at or around the incision site will interfere with the operation. If hair removal is necessary, remove immediately before the operation, with clippers.
   - **c.** Encourage tobacco cessation for a minimum of at least 30 days before elective operations.
   - **d.** Ensure skin around the incision site is free of gross contamination before performing antiseptic skin preparation.

2. **HAND/FOREARM ANTISEPSIS FOR SURGICAL TEAM**
   - **a.** Perform preoperative surgical hand/forearm antisepsis according to manufacturer's recommendations for the product being used.
   - **b.** See 2002 Guidelines for Hand Hygiene in Healthcare Settings for additional surgical hand antisepsis recommendations.[300]

3. **OPERATING ROOM VENTILATION**
   - **a.** Maintain positive pressure ventilation in the operating room and adjoining spaces. Maintain the number of air exchanges, airflow patterns, temperature, humidity, location of vents, and use of filters in accordance with recommendations from the most recent version of the Facilities Guidelines Institute – Guidelines for Design and Construction of Hospitals and Outpatient Facilities (current version – 2014).[301]

4. **CLEANING AND DISINFECTION OF ENVIRONMENTAL SURFACES**
   - **a.** Do not perform special cleaning or closing of operating rooms after contaminated or dirty operations.

5. **REPROCESSING OF SURGICAL INSTRUMENTS**
   - **a.** Sterilize all surgical instruments according to published guidelines and manufacturer's recommendations.
   - **b.** Immediate-use steam sterilization should never be used for reasons of convenience, as an alternative to purchasing additional instrument sets, or to save time. This practice should be reserved only for patient care items that will be used immediately in emergency situations when no other options are available.
   - **c.** Refer to CDC and HICPAC Guideline for Disinfection and Sterilization in Healthcare Facilities, 2008 for additional recommendations.[68]

6. **SURGICAL ATTIRE AND DRAPES**
   - **a.** Wear a surgical mask that fully covers the mouth and nose when entering the operating room if an operation is about to begin or already under way, or if sterile instruments are exposed. Wear the mask throughout the operation.
   - **b.** Wear a new, disposable, or hospital laundered head covering for each case, when entering the operating room. Ensure it fully covers all hair on the head and all facial hair not covered by the surgical mask.
   - **c.** Wear sterile gloves if serving as a member of the scrubbed surgical team. Put on sterile gloves after donning a sterile gown.
   - **d.** Use surgical gowns and drapes that are effective barriers when wet (i.e., materials that resist liquid penetration).
   - **e.** Change scrub suits that are visibly soiled, contaminated, and/or penetrated by blood or other potentially infectious materials.

7. STERILE AND SURGICAL TECHNIQUE

a. Adhere to principles of sterile technique when performing all invasive surgical procedures.

b. If drainage is necessary, use a closed suction drain. Place a drain through a separate incision distant from the operative incision. Remove the drain as soon as possible.

8. POST-OP INCISION CARE

a. Protect primarily closed incisions with a sterile dressing for 24-48 hours postoperatively**.**

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eAppendix 2. Centers for Disease Control and Prevention, Guideline for the Prevention of Surgical Site Infection 2017: Supplemental Tables

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1. GUIDELINE SEARCH STRATEGIES

1.1. Core Section Search Strategies

1.1A. CORE SECTION GENERAL SEARCHES

eTABLE 1. MEDLINE Search: Core Section

#	Search History	Results
1	exp Surgical Wound Infection/	25,893
2	"surgical site infection*".af.	2,130
3	1 or 2	26,382
4	limit 3 to English language	19,318
5	limit 4 to yr="1998 -Current"	8,709
6	limit 5 to guideline	19
7	limit 5 to systematic reviews	429
8	limit 5 to practice guideline	27
9	limit 5 to meta analysis	161
10	limit 5 to "reviews (maximizes specificity)"	262
11	6 or 7 or 8 or 9 or 10	469
12	limit 5 to randomized controlled trial	715
13	11 or 12	1,170

eTABLE 2. EMBASE Search: Core Section

#	Search History	Results
1	'surgical infection'/exp or 'surgical site infection' or 'surgical wound infection'	19,658
2	limit 1 to English language	13,666
3	limit 2 to 'randomized controlled trial'/de	749
4	limit 3 [1998-2012]/py	566
5	limit 2 to [review]	1,580
6	limit 2 to ('meta analysis'/de OR 'practice guideline'/de)	639
7	'systematic review'/exp	43,081
8	5 and 7	82

#	Search History	Results
9	6 or 8	679
10	limit 9 to [1998-2012]/py	654
11	4 or 10	1,220

1.2. Prosthetic Joint Arthroplasty Section Search Strategies

1.2A. PROSTHETIC JOINT ARTHROPLASTY SECTION GENERAL SEARCHES

eTABLE 3. MEDLINE Search: Ortho Section

#	Search History	Results
1	(arthroplast* or replac* or replant* or joint* or implant* or reconstruct* or prosthe*).af.	1,052,637
2	exp Arthroplasty, Replacement/ or exp Arthroplasty/	29,697
3	exp Orthopedic Procedures/	176,717
4	exp Joints/su [Surgery]	42,769
5	1 or 2 or 3 or 4	1,135,596
6	exp Wound Infection/	34,108
7	"surgical site infection*".af.	2,130
8	exp Prosthesis-Related Infections/	6,283
9	exp Bone Diseases, Infectious/	29,730
10	exp Soft Tissue Infections/	1,876
11	exp Skin Diseases, Infectious/	90,359
12	6 or 7 or 8 or 9 or 10 or 11	158,415
13	5 and 12	24,509
14	exp Surgical Procedures, Operative/	2,113,349
15	(surgical* or surgery* or operati*).af.	2,629,634
16	14 or 15	3,467,669
17	(arthro* or orthop*).af.	316,829
18	16 and 17	206,698
19	12 and 18	9,513
20	13 or 19	26,888
21	limit 20 to (english language and yr="1998 - Current")	11,604
22	limit 21 to systematic reviews	262
23	limit 21 to meta analysis	50

#	Search History	Results
24	limit 21 to guideline	14
25	limit 21 to practice guideline	22
26	limit 21 to "reviews (maximizes specificity)"	137
27	limit 21 to randomized controlled trial	294
28	22 or 23 or 24 or 25 or 26 or 27	595

eTABLE 4. EMBASE Search: Ortho Section

#	Search History	Results
1	'wound infection'/exp or 'surgical infection'/exp or 'prosthesis infection'/exp or 'bone infection'/exp or 'soft tissue infection'/exp or 'skin infection'/exp or 'surgical site infection'; limit to English language, EMBASE, and [1998-2012]/py	69,175
2	'arthroplasty'/exp or 'arthroplasty replacement'/exp or 'orthopedic surgery'/exp or ('joint'/exp and surg*) or arthroplast* or replac* or replant* or (joint* and' surgery'/exp) or implant* or reconstruct* or prosthe* or (('surgery'/exp or surgical* or operativ* and (arthro* or orthop*)) and [1998-2012]/py	856,609
3	1 and 2	14,117
4	'meta-analysis'/exp	57,212
5	3 and 4	121
6	limit 3 to 'systematic review'/de	234
7	limit 3 to 'practice guideline '/de	383
8	limit 3 to 'randomized controlled trial'/de	430
9	5 or 6 or 7 or 8	1,059

1.2B. PROSTHETIC JOINT ARTHROPLASTY SECTION TARGETED SEARCHES: TRANSFUSION

eTABLE 5. MEDLINE Targeted Search: Transfusion

#	Search History	Results
1	(exp "prostheses and implants"/ or prosthe*.af. or implant*.af. or orthoped*.af. or orthopaed*.af.) and (exp joints/ or joint*.af.)	101,924
2	exp Joints/su [Surgery]	44,456
3	exp Arthroplasty, Replacement/ or exp Arthroplasty/	32,010
4	arthroplast*.af.	42,928
5	exp "Orthopedic Procedures"/ and exp "Joints"/	39,956
6	or/1-5	141,563
7	exp Infection/ or infection*.af. or infecting.af. or infected.af. or exp "Prosthesis-Related Infections"/	1,533,905
8	exp Blood Transfusion/ or (blood and transfus*).af.	114,443
9	exp Blood Platelets/ or platelet*.af. or "blood product*".af.	195,879
10	8 or 9	292,467
11	exp Random Allocation/	73,596
12	exp Randomized Controlled Trials as Topic/ or exp Randomized Controlled Trial/	394,924
13	exp Double-Blind Method/	113,512
14	exp Single-Blind Method/	15,853
15	exp Clinical Trial/	667,767
16	exp Clinical Trials as Topic/	251,205
17	clinical trial.pt.	467,170
18	clinical trial, phase i.pt.	11,868
19	(clinical trial, phase ii or clinical trial, phase iii or clinical trial, phase iv or controlled clinical trial or randomized controlled trial or multicenter study or clinical trial).pt.	665,448
20	or/11-19	895,443
21	(clinical adj trial$).tw.	164,609
22	((singl$ or doubl$ or treb$ or tripl$) adj (blind$3 or mask$3)).tw.	111,059
23	placebo$.tw.	133,778
24	randomly allocated.tw.	13,342

#	Search History	Results
25	(allocated adj2 random$).tw.	15,627
26	exp Placebos/	30,626
27	or/20-26	996,307
28	case report.tw.	164,158
29	letter/	735,581
30	historical article/	280,723
31	exp Editorial/	291,753
32	or/28-31	1,454,788
33	27 not 32	956,341
34	exp "Sensitivity and Specificity"/	350,527
35	(sensitivity or specificity).tw.	590,136
36	((pre-test or pretest) adj probability).tw.	980
37	post-test probability.tw.	268
38	predictive value$.tw.	54,259
39	likelihood ratio$.tw.	6,512
40	exp "Predictive Value of Tests"/	117,980
41	or/33-40	1,740,790
42	exp Meta-Analysis as Topic/	11,873
43	(meta analy$ or metaanaly$).tw. or exp Meta-analysis/	48,899
44	(systematic adj (review$1 or overview$1)).tw.	29,904
45	exp Review Literature as Topic/	6,079
46	or/41-45	1,784,999
47	(embase or cochrane or psyclit* or psychlit* or psycinfo or psychinfo).tw.	27,796
48	(cinahl or cinhal).ab.	5,997
49	(science citation index or bids or cancerlit).ab.	2,135
50	or/46-49	1,792,516

#	Search History	Results
51	(reference list$ or bibliograph$ or hand-search$ or relevant journals or manual search$).ab.	18,484
52	(selection criteria or data extraction).ab.	20,349
53	exp Review/	1,675,847
54	52 and 53	14,038
55	50 or 51 or 54	1,800,552
56	exp Comment/ or exp Editorial/ or exp Letter/	1,108,385
57	55 not 56	1,770,101
58	exp Epidemiologic studies/ or exp case control studies/ or exp cohort studies/ or Case control.tw. or (cohort adj (study or studies)).tw. or cohort analy$.tw. or (Follow up adj (study or studies)).tw. or (observational adj (study or studies)).tw. or Longitudinal.tw. or Retrospective.tw. or Cross sectional.tw. or exp Cross-sectional studies/	1,553,551
59	57 or 58	2,972,690
60	6 and 7 and 10 and 59	150
61	limit 60 to english language	136
62	limit 61 to yr="1998 -Current"	103

eTABLE 6. EMBASE Targeted Search: Transfusion

#	Search History	Results
1	'blood transfusion'/exp or ('blood'/exp and (transfusion'/exp or transfused)) or 'thrombocyte'/exp or 'blood'/exp or platelet* or 'blood product'/exp or 'blood products' and [english]/lim and [embse]/lim and [1998-2012]/py	627,207
2	'prostheses and orthoses'/exp or prosthe$ or implant$ or orthoped$ or orthopaed$	399,873
3	'joint'/exp or joint$ or 'joint surgery'/exp or 'arthroplasty'/exp or arthroplasty or arthroplasties or 'arthroplasty replacement' or ('orthopedic surgery'/exp and 'joint'/exp)	603,883
4	2 and 3	69,054
5	'infection'/exp	2,328,600
6	infection$ or infecting or infected	2,654,665
7	'prosthesis related' and infections	95
8	'prosthesis-related infections'/exp	2,328,600
9	5 or 6 or 7 or 8	2,660,483

#	Search History	Results
10	1 and 4 and 9	353
11	‘clinical study’/exp or ‘case control study’/exp or ‘family study’/exp or ‘longitudinal study’/exp or ‘retrospective study’/exp	5,942,135
12	‘prospective study’/exp	189,505
13	‘randomized controlled trial’/exp	307,692
14	12 not 13	165,671
15	‘cohort analysis’/exp or (cohort and adj and (study or studies)) or (case and control and adj and (study or studies)) or (follow and up and adj and (study or studies)) or (observational and adj and (study or studies)) or (epidemiologic$ and adj and (study or studies)) or (cross and sectional and adj and (study or studies))	115,089
16	11 or 12 or 14 or 15	5,986,679
17	‘meta analysis’/exp or (meta and adj and analy$) or metaanaly$ or (systematic and adj and (review$ or overview$))	61,427
18	cancerlit or cochrane or ‘embase’/exp or psychlit’/exp or ‘psyclit’/ or ‘science citation index’/exp or bids or scopus	44,494
19	‘reference lists’ or bibliograph$ or ‘hand search$’ or ‘manual search$’ or ‘relevant journals’ or ‘data extraction’/exp or ‘selection criteria’	28,035
20	review.pt.	4
21	‘review’/exp	1,831,423
22	20 or 21	1,831,427
23	19 and 22	15,584
24	letter.pt. or editorial.pt.	3
25	‘letter’/exp or ‘editorial’/exp	1,179,933
26	24 or 25	1,179,934
27	17 or 18 or 23	98,049
28	27 not 26	93,355
29	‘sensitivity and specificity/exp or sensitivity or specificity or (‘pre test’ or pretest and adj and ‘probability’/exp) or ‘post-test probability’ or predictive and value$ or likelihood and ratio$ or ‘predictive value’/exp or ‘diagnostic accuracy ‘/exp and [english]/lim and [embase]/lim and [1998-2012]/py	144,775
30	‘clinical trial’/exp or ‘randomized controlled trial’/exp or ‘randomization’/exp or ‘single blind procedure’/exp or ‘double blind procedure’/exp or ‘crossover procedure’/exp or ‘placebo’/exp or randomi?ed and controlled and trial$ or rct$ or ‘random allocation’ or ‘randomly allocated’ or ‘allocated randomly’ or allocated and adj2 and random$ or single and blind$ or double and blind$ or (treble or triple and adj and blind$) or placebo$ or ‘prospective study’/exp	541,923

#	Search History	Results
31	'case study'/exp or 'case study' or 'case report'/exp or 'case report' or 'abstract report'/exp or 'abstract report' or 'letter'/exp or letter and [1998-2012]/py	1,237,206
32	30 not 31	529,538
33	16 or 28 or 29 or 32	6,160,948
34	10 and 33	232

eTABLE 7. Cochrane Database of Systematic Reviews Targeted Search: Transfusion

#	Search History	Results
1	(transfus* or platelet* or "blood product*") and (surgery or surgical* or operat*) and (joint* or arthroplast* or prosthe* or implant***)** in Title, Abstract or Keywords	6

1.2C. PROSTHETIC JOINT ARTHROPLASTY SECTION TARGETED SEARCHES: IMMUNOSUPPRESSIVE THERAPY

eTABLE 8. MEDLINE Targeted Search: Immunosuppressive Therapy

#	Search History	Results
1	(exp "prostheses and implants"/ or prosthe*.af. or implant*.af. or orthoped*.af. or orthopaed*.af.) and (exp joints/ or joint*.af.)	102,099
2	exp Joints/su [Surgery]	44,522
3	exp Arthroplasty, Replacement/ or exp Arthroplasty/	32,116
4	arthroplasty*.af.	43,040
5	exp “Orthopedic Procedures”/and exp “Joints”/	40,017
6	or/1-5	141,821
7	exp Infection/ or infection*.af. or infecting.af. or infected.af. or exp "Prosthesis-Related Infections"/	1,540,242
8	exp Random Allocation/	73,745
9	exp Randomized Controlled Trials as Topic/ or exp Randomized Controlled Trial/	397,784
10	exp Double-Blind Method/	113,903
11	exp Single-Blind Method/	15,934
12	exp Clinical Trial/	670,938
13	exp Clinical Trials as Topic/	253,167
14	clinical trial.pt.	467,996
15	clinical trial, phase i.pt.	11,949
16	(clinical trial, phase ii or clinical trial, phase iii or clinical trial, phase iv or controlled clinical trial or randomized controlled trial or multicenter study or clinical trial).pt.	668,584
17	or/8-16	900,674
18	(clinical adj trial$).tw.	165,764
19	((singl$ or doubl$ or treb$ or tripl$) adj (blind$3 or mask$3)).tw.	111,446
20	placebo$.tw.	134,478
21	randomly allocated.tw.	13,417
22	(allocated adj2 random$).tw.	15,704
23	exp Placebos/	30,699
24	or/17-23	1,002,057

#	Search History	Results
25	case report.tw.	164,536
26	letter/	742,239
27	historical article/	281,301
28	exp Editorial/	295,205
29	or/25-28	1,465,799
30	24 not 29	961,541
31	exp “Sensitivity and Specificity”/	351,908
32	(sensitivity or specificity).tw.	592,438
33	((pre-test or pretest) adj probability).tw.	988
34	post-test probability.tw.	272
35	predictive value$.tw.	54,458
36	likelihood ratio$.tw.	6,573
37	exp "Predictive Value of Tests"/	118,435
38	or/30-37	1,748,938
39	exp Meta-Analysis as Topic/	12,009
40	(meta analy$ or metaanaly$).tw. or exp Meta-analysis/	49,740
41	(systematic adj (review$1 or overview$1)).tw.	30,487
42	exp Review Literature as Topic/	6,208
43	or/38-42	1,793,694
44	(embase or cochrane or psyclit* or psychlit* or psycinfo or psychinfo).tw.	28,506
45	(cinahl or cinhal).ab.	6,190
46	(science citation index or bids or cancerlit).ab.	2,196
47	or/43-46	1,801,291
48	(reference list$ or bibliograph$ or hand-search$ or relevant journals or manual search$).ab.	18,852
49	(selection criteria or data extraction).ab.	20,813
50	exp Review/	1,682,836

#	Search History	Results
51	49 and 50	14,472
52	47 or 48 or 51	1,809,350
53	exp Comment/ or exp Editorial/ or exp Letter/	1,119,204
54	52 not 53	1,778,639
55	exp Epidemiologic studies/ or exp case control studies/ or exp cohort studies/ or Case control.tw. or (cohort adj (study or studies)).tw. or cohort analy$.tw. or (Follow up adj (study or studies)).tw. or (observational adj (study or studies)).tw. or Longitudinal.tw. or Retrospective.tw. or Cross sectional.tw. or exp Cross-sectional studies/	1,560,697
56	54 or 55	2,986,243
57	exp Immunosuppressive Agents/	229,191
58	exp Immunosuppression/	46,654
59	"immunosuppressive therapy".af.	10,624
60	immune*.af.	408,428
61	immunolog*.af.	56
62	exp Adrenal Cortex Hormones/	315,501
63	exp Steroids/	657,932
64	exp methotrexate/ or exp cyclophosphamide/	67,761
65	exp Tumor Necrosis Factor-alpha/	83,932
66	"systemic corticosteroids".af.	2,228
67	steroid*.af.	244,914
68	“tumor necrosis factor*”.af.	116,734
69	(cyclophosphamide or cytoxan or methotrexate).af.	83,530
70	tnf.af.	90,322
71	exp Injections, Intra-articular/ or intra-articular*.af.	11,059
72	or/57-71	1,544,611
73	6 and 7 and 56 and 72	360
74	limit 73 to english language	312
75	limit 74 to yr="1998 -Current"	250

eTABLE 9. EMBASE Targeted Search: Immunosuppressive Therapy

#	Search History	Results
1	'prostheses and orthoses'/exp or prosthe$ or implant$ or orthoped$ or orthopaed$	399,873
2	'joint'/exp or joint$ or 'joint surgery'/exp or 'arthroplasty'/exp or arthroplasty or arthroplasties or 'arthroplasty replacement' or ('orthopedic surgery'/exp and 'joint'/exp)	603,893
3	1 and 2	69,054
4	'infection'/exp	2,328,600
5	infection$ or infecting or infected	2,654,665
6	'prosthesis related' and infections	95
7	'prosthesis-related infections'/exp	2,328,600
8	4 or 5 or 6 or 7	2,660,483
9	'clinical study'/exp or 'case control study'/exp or 'family study'/exp or 'longitudinal study'/exp or 'retrospective study'/exp	5,942,135
10	'prospective study'/exp	188,505
11	'randomized controlled trial'/exp	307,692
12	10 not 11	165,671
13	'cohort analysis'/exp or (cohort and adj and (study or studies)) or (case and control and adj and (study or studies)) or (follow and up and adj and (study or studies)) or (observational and adj and (study or studies)) or (epidemiologic$ and adj and (study or studies)) or (cross and sectional and adj and (study or studies))	115,089
14	9 or 10 or 12 or 13	5,986,679
15	'meta analysis'/exp or (meta and adj and analy$) or metaanaly$ or (systematic and adj and (review$ or overview$))	61,427
16	cancerlit or cochrane or 'embase'/exp or psychlit'/exp or 'psyclit'/ or 'science citation index'/exp or bids or scopus	44,495
17	'reference lists' or bibliograph$ or 'hand search$' or 'manual search$' or 'relevant journals' or 'data extraction'/exp or 'selection criteria'	28,035
18	review.pt.	4
19	'review'/exp	1,831,423
20	18 or 19	1,831,427
21	17 and 20	15,584
22	letter.pt. or editorial.pt.	3

#	Search History	Results
23	'letter'/exp or 'editorial'/exp	1,179,933
24	22 or 23	1,179,934
25	15 or 16 or 21	98,049
26	25 not 24	93,355
27	'sensitivity and specificity/exp or sensitivity or specificity or ('pre test' or pretest and adj and 'probability'/exp) or 'post-test probability' or predictive and value$ or likelihood and ratio$ or 'predictive value'/exp or 'diagnostic accuracy '/exp and [english]/lim and [embase]/lim and [1998-2012]/py	144,775
28	'clinical trial'/exp or 'randomized controlled trial'/exp or 'randomization'/exp or 'single blind procedure'/exp or 'double blind procedure'/exp or 'crossover procedure'/exp or 'placebo'/exp or randomi?ed and controlled and trial$ or rct$ or 'random allocation' or 'randomly allocated' or 'allocated randomly' or allocated and adj2 and random$ or single and blind$ or double and blind$ or (treble or triple and adj and blind$) or placebo$ or 'prospective study'/exp	539,487
29	'case study'/exp or 'case study' or 'case report'/exp or 'case report' or 'abstract report'/exp or 'abstract report' or 'letter'/exp or letter and [1998-2012]/py	1,237,206
30	28 not 29	529,538
31	14 or 26 or 27 or 30	6,160,948
32	'immunosuppressive agent'/exp or 'immunosuppressive treatment'/exp or 'immunosuppressive therapy' or 'immunosuppressive agents' or immunolog* or methotrexate or cyclophosphamide or 'adrenal cortex hormones' or 'systemic corticosteroids' or 'tumor necrosis factor' or cytoxan or tnf or 'intra articular' or 'tumor necrosis factor'/exp or 'intraarticular drug administration'/exp or 'steroid'/exp or 'corticosteroid'/exp or 'methotrexate'/exp or 'cyclophosphamide'/exp and [1998-2012]/py	1,749,571
33	3 and 8 and 32	697
34	31 and 33	398

eTABLE 10. Cochrane Database of Systematic Reviews Targeted Search: Immunosuppressive Therapy

#	Search History	Results
1	**"**(immuno* or immunolog* or steroid* or corticosteroid* or "adrenal cortex hormone*" or methotrexate or cyclophosphamide or cytoxan or tnf or "tumor necrosis factor*" or (intra-articular" and inject*)) and (surgery or surgical* or operat*) and (joint* or arthroplast* or prosthe* or implant*) in Title, Abstract or Keywords	21

1.2D. PROSTHETIC JOINT ARTHROPLASTY SECTION TARGETED SEARCHES: ANTICOAGULATION

eTABLE 11. MEDLINE Targeted Search: Anticoagulation

#	Search History	Results
1	(exp "prostheses and implants"/ or prosthe*.af. or implant*.af. or orthoped*.af. or orthopaed*.af.) and (exp joints/ or joint*.af.)	101,924
2	exp Joints/su [Surgery]	44,456
3	exp Arthroplasty, Replacement/ or exp Arthroplasty/	32,010
4	arthroplasty*.af.	42,928
5	exp “Orthopedic Procedures”/and exp “Joints”/	39,956
6	or/1-5	141,563
7	exp Infection/ or infection*.af. or infecting.af. or infected.af. or exp "Prosthesis-Related Infections"/	1,533,905
8	exp Random Allocation/	73,596
9	exp Randomized Controlled Trials as Topic/ or exp Randomized Controlled Trial/	394,924
10	exp Double-Blind Method/	113,512
11	exp Single-Blind Method/	15,853
12	exp Clinical Trial/	667,767
13	exp Clinical Trials as Topic/	251,205
14	clinical trial.pt.	467,170
15	clinical trial, phase i.pt.	11,868
16	(clinical trial, phase ii or clinical trial, phase iii or clinical trial, phase iv or controlled clinical trial or randomized controlled trial or multicenter study or clinical trial).pt.	665,448
17	or/8-16	895,443
18	(clinical adj trial$).tw.	164,609
19	((singl$ or doubl$ or treb$ or tripl$) adj (blind$3 or mask$3)).tw.	111,059
20	placebo$.tw.	133,778
21	randomly allocated.tw.	13,342
22	(allocated adj2 random$).tw.	15,627
23	exp Placebos/	30,626
24	or/17-23	996,307

#	Search History	Results
25	case report.tw.	164,158
26	letter/	735,581
27	historical article/	280,723
28	exp Editorial/	291,753
29	or/25-28	1,454,788
30	24 not 29	956,341
31	exp “Sensitivity and Specificity”/	350,527
32	(sensitivity or specificity).tw.	590,136
33	((pre-test or pretest) adj probability).tw.	980
34	post-test probability.tw.	268
35	predictive value$.tw.	54,259
36	likelihood ratio$.tw.	6,512
37	exp "Predictive Value of Tests"/	117,980
38	or/30-37	1,740,790
39	exp Meta-Analysis as Topic/	11,873
40	(meta analy$ or metaanaly$).tw. or exp Meta-analysis/	48,899
41	(systematic adj (review$1 or overview$1)).tw.	29,904
42	exp Review Literature as Topic/	6,079
43	or/38-42	1,784,999
44	(embase or cochrane or psyclit* or psychlit* or psycinfo or psychinfo).tw.	27,796
45	(cinahl or cinhal).ab.	5,997
46	(science citation index or bids or cancerlit).ab.	2,135
47	or/43-46	1,792,516
48	(reference list$ or bibliograph$ or hand-search$ or relevant journals or manual search$).ab.	18,484
49	(selection criteria or data extraction).ab.	20,349
50	exp Review/	1,675,847

#	Search History	Results
51	49 and 50	14,038
52	47 or 48 or 51	1,800,552
53	exp Comment/ or exp Editorial/ or exp Letter/	1,108,385
54	52 not 53	1,770,101
55	exp Epidemiologic studies/ or exp case control studies/ or exp cohort studies/ or Case control.tw. or (cohort adj (study or studies)).tw. or cohort analy$.tw. or (Follow up adj (study or studies)).tw. or (observational adj (study or studies)).tw. or Longitudinal.tw. or Retrospective.tw. or Cross sectional.tw. or exp Cross-sectional studies/	1,553,551
56	54 or 55	2,972,690
57	exp Heparin/	53,476
58	exp warfarin/	12,695
59	exp aspirin/	35,444
60	exp Anticoagulants/ or anticoagul*.af.	191,442
61	"low-dose unfractionated".af.	111
62	(clopidogrel or plavix).af.	6,385
63	(warfarin* or aspirin* or heparin*).af.	136,516
64	exp Platelet Aggregation Inhibitors/	84,124
65	anti-platelet*.af.	2,453
66	or/57-65	299,002
67	6 and 7 and 56 and 66	52
68	limit 67 to english language	45
69	limit 68 to yr-“1998-Current”	28

eTABLE 12. EMBASE Targeted Search: Anticoagulation

#	Search History	Results
1	‘infection’/exp	2,328,600
2	Infection$ or infecting or infected	2,654,665
3	‘prosthesis related’ and infections	95

#	Search History	Results
4	‘prosthesis-related infections’/exp	2,328,600
5	1 or 2 or 3 or 4	2,660,483
6	‘prostheses and orthoses’/exp or prosthe$ or implant$ or orthoped$ or orthopaed$	399,873
7	‘joint’/exp or joint$ or ‘joint surgery’/exp or ‘arthroplasty’/exp or arthroplasty or arthroplasties or ‘arthroplasty replacement’ or (‘orthopedic surgery’/exp and ‘joint’/exp)	603,883
8	6 and 7	69,054
9	‘heparin’/exp or ‘warfarin’/exp or ‘acetylsalicylic acid’/exp or ‘anticoagulant agent’/exp or ‘antithrombotic agent’/exp or anticoagul* or ‘low-dose unfractionated’ or clopidogrel or plavix or warfarin* or heparin* or aspirin or ‘anti platelet’	481,497
10	5 and 8 and 9	374
11	‘meta analysis’/exp or (meta and adj and analy$) or metaanaly$ or (systematic and adj and (review$ or overview$))	61,427
12	cancerlit or cochrane or ‘embase’/exp or psychlit’/exp or ‘psyclit’/ or ‘science citation index’/exp or bids or scopus	44,495
13	‘reference lists’ or bibliograph$ or ‘hand search$’ or ‘manual search$’ or ‘relevant journals’ or ‘data extraction’/exp or ‘selection criteria’	28,035
14	review.pt.	4
15	‘review’/exp	1,831,423
16	14 or 15	1,831,427
17	13 and 16	15,584
18	letter.pt. or editorial.pt.	3
19	‘letter’/exp or ‘editorial’/exp	1,179,933
20	18 or 19	1,174,934
21	11 or 12 or 17	98,049
22	21 not 20	93,355
23	‘clinical trial’/exp or ‘randomized controlled trial’/exp or ‘randomization’/exp or ‘single blind procedure’/exp or ‘double blind procedure’/exp or ‘crossover procedure’/exp or ‘placebo’/exp or randomi?ed and controlled and trial$ or rct$ or ‘random allocation’ or ‘randomly allocated’ or ‘allocated randomly’ or allocated and adj2 and random$ or single and blind$ or double and blind$ or (treble or triple and adj and blind$) or placebo$ or ‘prospective study’/exp	541,923
24	‘case study’/exp or ‘case study’ or ‘case report’/exp or ‘case report’ or ‘abstract report’/exp or ‘abstract report’ or ‘letter’/exp or letter and [1998-2012]/py	1,237,206
25	23 not 24	529,538

#	Search History	Results
26	'clinical study'/exp or 'case control study'/exp or 'family study'/exp or 'longitudinal study'/exp or 'retrospective study'/exp	5,942,135
27	'prospective study'/exp	189,505
28	'randomized controlled trial'/exp	307,692
29	27 not 28	165,671
30	'cohort analysis'/exp or (cohort and adj and (study or studies)) or (case and control and adj and (study or studies)) or (follow and up and adj and (study or studies)) or (observational and adj and (study or studies)) or (epidemiologic$ and adj and (study or studies)) or (cross and sectional and adj and (study or studies))	115,089
31	26 or 27 or 29 or 30	5,986,679
32	'sensitivity and specificity/exp or sensitivity or specificity or ('pre test' or pretest and adj and 'probability'/exp) or 'post-test probability' or predictive and value$ or likelihood and ratio$ or 'predictive value'/exp or 'diagnostic accuracy '/exp and english]/lim and [embase]/lim and [1998-2012]/py	144,775
33	22 or 25 or 31 or 32	6,160,948
34	10 and 33 and [english]/lim and [embase]/lim and [1998-2012]/py	221

eTABLE 13. Cochrane Database of Systematic Reviews Targeted Search: Anticoagulation

#	Search History	Results
1	("low molecular weight" or "low-molecular-weight" or anticoag* or heparin or warfarin or aspirin or clopidogrel or plavix or "Platelet Aggregation Inhibit*" or anti platelet*) and (surgery or surgical* or operat*) and (joint* or arthroplast* or prosthe* or implant*) in Title, Abstract or Keywords	8

1.2E. PROSTHETIC JOINT ARTHROPLASTY SECTION TARGETED SEARCHES: ORTHOPAEDIC SPACE SUIT

eTABLE 14. MEDLINE Targeted Search: Orthopaedic Space Suit

#	Search History	Results
1	(exp “prostheses and implants”/ or prosthe*.af. or implant*.af. or orthoped*.af. or orthpaed*.af.) and (exp joints/ or joint*.af.)	102,254
2	exp Joints/su [Surgery]	44,595
3	exp Arthroplasty, Replacement/ or exp Arthroplasty/	32,203
4	arthroplasty*.af.	43,132
5	exp “Orthopedic Procedures”/ and exp “Joints”/	40,095
6	or/ 1-5	142,045
7	exp Infection/ or infection*.af. or infecting.af. or infected.af. or exp “Prosthesis-Related Infections”/	1,541,705
8	exp Random Allocation/	73,817
9	exp Randomized Controlled Trials as Topic/ or exp Randomized Controlled Trial/	398,286
10	exp Double-Blind Method/	114,004
11	exp Single-Blind Method/	15,965
12	exp Clinical Trial/	671,638
13	exp Clinical Trials as Topic/	253,375
14	clinical trial.pt.	468,127
15	clinical trial, phase i.pt.	11,960
16	(clinical trial, phase ii or clinical trial, phase iii or clinical trial, phase iv or controlled clinical trial or randomized controlled trial or multicenter study or clinical trial).pt.	669,278
17	or /8-16	901,656
18	(clinical adj trial$).tw.	166,027
19	((singl$ or doubl$ or treb$ or tripl$) adj (blind$3 or mask$3)).tw.	111,543
20	placebo$.tw.	134,617
21	randomly allocated.tw.	13,439
22	(allocated adj2 random$).tw.	15,726
23	exp Placebos/	30,724
24	or/17-23	1,003,206

#	Search History	Results
25	case report.tw.	164,737
26	letter/	742,890
27	historical article/	281,494
28	exp Editorial/	295,617
29	or/25-28	1,467,233
30	24 not 29	962,656
31	exp “Sensitivity and Specifity”/	352,539
32	(sensitivity or specifity).tw.	593,131
33	((pre-test or pretest) adj probability).tw.	988
34	post-test probability.tw.	273
35	predictive value$.tw.	54,533
36	likelihood ratio$.tw.	6,584
37	exp “Predictive Value of Tests”/	118,653
38	or/30-27	1,751,101
39	exp Meta-Analysis as Topic/	12,014
40	(meta analy$ or metaanaly$).tw. or exp Meta-analysis/	49,880
41	(systematic adj (review$1 or overview$1)).tw.	30,599
42	exp Review Literature as Topic/	6,214
43	or/38-42	1,795,992
44	(embase or Cochrane or psyclit* or psychlit* or psycinfo or psychinfo).tw.	28,587
45	(cinahl or cinhal).ab.	6,206
46	(science citation index or bids or cancerlit).ab.	2,197
47	or/43-46	1,803,599
48	(reference list$ or bibliograph$ or hand-search$ or relevant journals or manual search$).ab.	18,879
49	(selection criteria or data extraction).ab.	20,833
50	exp Review/	1,684,812

#	Search History	Results
51	49 and 50	14,483
52	47 or 48 or 51	1,811,665
53	exp Comment/ or exp Editorial/ or exp Letter/	1,120,430
54	52 not 53	1,780,921
55	exp Epidemiologic studies/ or exp case control studies/ or exp cohort studies/ or Case control.tw. or (cohort adj (study or studies)).tw. or cohort analy$.tw. or (Follow up adj (study or studies)).tw. or (observational adj (study or studies)).tw. or Longitudinal.tw. or Retrospective.tw. or Cross sectional.tw. or exp Cross-sectional studies/	1,563,211
56	54 or 55	2,990,436
57	exp Protective Clothing/ or exp Space Suits/	9,233
58	(exhaust* or 'exhaust suit*").af.	27,803
59	("body exhaust suit*" or "body-exhaust suit*" or "space suit*").af.	254
60	57 or 58 or 59	36,996
61	6 and 7 and 56 and 60	37
62	limit 61 to english language	35
63	limit 62 to yr="1998-Current"	21

eTABLE 15. EMBASE Targeted Search: Orthopaedic Space Suit

#	Search History	Results
1	'meta analysis'/exp or (meta and adj and analy$) or metaanaly$ or (systematic and adj and (review$ or overview$))	61,427
2	cancerlit or cochrane or 'embase'/exp or psychlit'/exp or 'psyclit'/ or 'science citation index'/exp or bids or scopus	44,494
3	'reference lists' or bibliograph$ or 'hand search$' or 'manual search$' or 'relevant journals' or 'data extraction'/exp or 'selection criteria'	28,035
4	review.pt.	4
5	'review'/exp	1,831,422
6	4 or 5	1,831,427
7	3 and 6	15,584
8	letter.pt. or editorial.pt.	3
9	'letter'/exp or 'editorial'/exp	1,179,933

#	Search History	Results
10	8 or 9	1,179,934
11	1 or 2 or 7	98,049
12	11 not 10	93,355
13	‘clinical trial’/exp or ‘randomized controlled trial’/exp or ‘randomization’/exp or ‘single blind procedure’/exp or ‘double blind procedure’/exp or ‘crossover procedure’/exp or ‘placebo’/exp or randomi?ed and controlled and trial$ or rct$ or ‘random allocation’ or ‘randomly allocated’ or ‘allocated randomly’ or allocated and adj2 and random$ or single and blind$ or double and blind$ or (treble or triple and adj and blind$) or placebo$ or ‘prospective study’/exp	541,923
14	‘case study’/exp or ‘case study’ or ‘case report’/exp or ‘case report’ or ‘abstract report’/exp or ‘abstract report’ or ‘letter’/exp or letter and [1998-2012]/py	1,237,206
15	13 not 14	529,538
16	‘clinical study’/exp or ‘case control study’/exp or ‘family study’/exp or ‘longitudinal study’/exp or ‘retrospective study’/exp	5,942,135
17	‘prospective study’/exp	189,505
18	‘randomized controlled trial’/exp	307,692
19	17 not 18	165,671
20	‘cohort analysis’/exp or (cohort and adj and (study or studies)) or (case and control and adj and (study or studies)) or (follow and up and adj and (study or studies)) or (observational and adj and (study or studies)) or (epidemiologic$ and adj and (study or studies)) or (cross and sectional and adj and (study or studies))	115,089
21	16 or 19 or 20	5,986,679
22	‘sensitivity and specificity/exp or sensitivity or specificity or (‘pre test’ or pretest and adj and ‘probability’/exp) or ‘post-test probability’ or predictive and value$ or likelihood and ratio$ or ‘predictive value’/exp or ‘diagnostic accuracy ‘/exp and english]/lim and [embase]/lim and [1998-2012]/py	144,775
23	12 or 15 or 21 or 22	6,160,948
24	‘infection’/exp	2,328,600
25	Infection$ or infecting or infected	2,654,665
26	‘prosthesis related’ and infections	95
27	‘prosthesis-related infections’/exp	2,328,600
28	24 or 25 or 26 or 27	2,660,483
29	‘prostheses and orthoses’/exp or prosthe$ or implant$ or orthoped$ or orthopaed$	399,873
30	‘joint’/exp or joint$ or ‘joint surgery’/exp or ‘arthroplasty’/exp or arthroplasty or arthroplasties or ‘arthroplasty replacement’ or (‘orthopedic surgery’/exp and ‘joint’/exp)	603,883

#	Search History	Results
31	29 and 30	69,054
32	‘surgical attire’/exp or ‘surgical attire’ or ‘protective clothing’/exp or ‘space suit’ or ‘exhaust suit’ or ‘body exhaust suit’ or ‘body-exhaust suit’	12,127
33	23 and 28 and 31 and 32 and [english]/lim and [embase]/lim and [1998-2012]/py	7

eTABLE 16. Cochrane Database of Systematic Reviews Targeted Search: Orthopaedic Space Suit

#	Search History	Results
1	(suit* or clothing) and (surgery or surgical* or operat*) and (joint* or arthroplast* or prosthe* or implant*) in Title, Abstract or Keywords	8

eTABLE 17. CINAHL Targeted Search: Orthopaedic Space Suit

#	Search History	Results
1	(MH “Protective Clothing+”)	3,434
2	“exhaust suit*”	4
3	“space suit*”	3
4	1 or 2 or 3	3,438
5	(MH “Arthoplasty+”) or (MH “Arthroplasty, Replacement+”)	10,000
6	(MH “Prostheses and Implants+”)	34,039
7	(MH “Joints/SU”)	111
8	(MH “Surgery, Operative+”)	197,035
9	(MH “Surgery, Operative+”) and orthopedic* or orthopaedic* or joint*	20,595
10	((prosthe* or implant* or orthopaed* or orthoped*)) and MW joints	196
11	arthroplasty or arthroplasties	10,691
12	5 or 6 or 7 or 10 or 11	62,799
13	11 and 12	22
14	13 and 4	21
15	(MH “Infection+”)	62,911

#	Search History	Results
16	(MH “Prosthesis-Related Infections”)	610
17	infection* or infected or infecting	129,848
18	15 or 16 or 17	129,848
19	14 and 18	14
20	(MH “Operating Rooms”)	4,940
21	“operating room*”	8,369
22	20 or 21	8,369
23	19 and 22	7

1.2F. PROSTHETIC JOINT ARTHROPLASTY SECTION TARGETED SEARCH: ANTIMICROBIAL PROPHYLAXIS WITH A DRAIN

eTABLE 18. MEDLINE Targeted Search: Antimicrobial Prophylaxis with a Drain

#	Search History	Results
1	exp Anti-Infective Agents/	1,155,786
2	exp Antibiotic Prophylaxis/	7,457
3	(antimicrobial or ("anti-infective" and agents) or “anti-infective agents”).af.	139,832
4	1 or 2 or 3	1,181,549
5	exp Time/ or exp Time Factors/ or timing.af. or time.af. or timed.af. or duration.af.	2,675,015
6	exp Drainage/	41,403
7	drain*.af.	93,852
8	6 or 7	102,200
9	4 and 5 and 8	1,930
10	(exp "prostheses and implants"/ or prosthe*.af. or implant*.af. or orthoped*.af. or orthopaed*.af.) and (exp joints/ or joint*.af.)	102,254
11	exp Joints/su [Surgery]	44,595
12	exp Arthroplasty, Replacement/ or exp Arthroplasty/	32,203
13	arthroplasty*.af.	43,132
14	exp “Orthopedic Procedures”/and exp “Joints”/	40,095
15	or/10-14	142,045
16	exp Infection/ or infection*.af. or infecting.af. or infected.af. or exp "Prosthesis-Related Infections"/	1,541,705
17	exp Random Allocation/	73,817
18	exp Randomized Controlled Trials as Topic/ or exp Randomized Controlled Trial/	398,286
19	exp Double-Blind Method/	114,001
20	exp Single-Blind Method/	15,965
21	exp Clinical Trial/	671,638
22	exp Clinical Trials as Topic/	253,375
23	clinical trial.pt.	468,127
24	clinical trial, phase i.pt.	11,960
25	(clinical trial, phase ii or clinical trial, phase iii or clinical trial, phase iv or controlled clinical trial or randomized controlled trial or	669,278

#	Search History	Results
	multicenter study or clinical trial).pt.	
26	or/17-25	901,656
27	(clinical adj trial$).tw.	166,027
28	((singl$ or doubl$ or treb$ or tripl$) adj (blind$3 or mask$3)).tw.	111,543
29	placebo$.tw.	134,617
30	randomly allocated.tw.	13,439
31	(allocated adj2 random$).tw.	15,726
32	exp Placebos/	30,724
33	or/26-32	1,003,206
34	case report.tw.	164,737
35	letter/	742,890
36	historical article/	281,494
37	exp Editorial/	295,617
38	or/34-37	1,467,233
39	33 not 38	962,656
40	exp “Sensitivity and Specificity”/	352,539
41	(sensitivity or specificity).tw.	593,131
42	((pre-test or pretest) adj probability).tw.	988
43	post-test probability.tw.	273
44	predictive value$.tw.	54,533
45	likelihood ratio$.tw.	6,584
46	exp "Predictive Value of Tests"/	118,653
47	or/39-46	1,751,101
48	exp Meta-Analysis as Topic/	12,014
49	(meta analy$ or metaanaly$).tw. or exp Meta-analysis/	49,880
50	(systematic adj (review$1 or overview$1)).tw.	30,599

#	Search History	Results
51	exp Review Literature as Topic/	6,214
52	or/47-51	1,795,992
53	(embase or cochrane or psyclit* or psychlit* or psycinfo or psychinfo).tw.	28,587
54	(cinahl or cinhal).ab.	6,206
55	(science citation index or bids or cancerlit).ab.	2,197
56	or/52-55	1,803,599
57	(reference list$ or bibliograph$ or hand-search$ or relevant journals or manual search$).ab.	18,879
58	(selection criteria or data extraction).ab.	20,833
59	exp Review/	1,684,812
60	58 and 59	14,483
61	56 or 57 or 60	1,811,665
62	exp Comment/ or exp Editorial/ or exp Letter/	1,120,430
63	61 not 62	1,780,921
64	exp Epidemiologic studies/ or exp case control studies/ or exp cohort studies/ or Case control.tw. or (cohort adj (study or studies)).tw. or cohort analy$.tw. or (Follow up adj (study or studies)).tw. or (observational adj (study or studies)).tw. or Longitudinal.tw. or Retrospective.tw. or Cross sectional.tw. or exp Cross-sectional studies/	1,563,211
65	63 or 64	2,990,436
66	9 and 15 and 16	79
67	65 and 66	46
68	limit 67 to english language	38
69	limit 68 to yr=”1998-Current”	24

eTABLE 19. EMBASE Targeted Search: Antimicrobial Prophylaxis with a Drain

#	Search History	Results
1	‘antiinfective agent’/exp or ‘antibiotic prophylaxis’/exp or ‘antimicrobial’/exp or ‘anti infective’ or ‘anti-infective agents’/exp and [english]/lim and [embase]/lim and [1998-2012]/py	909,070
2	‘meta analysis’/exp or (meta and adj and analy$) or metaanaly$ or (systematic and adj and (review$ or overview$))	61,427
3	cancerlit or cochrane or ‘embase’/exp or psychlit’/exp or ‘psyclit’/ or ‘science citation index’/exp or bids or scopus	44,494

#	Search History	Results
4	'reference lists' or bibliograph$ or 'hand search$' or 'manual search$' or 'relevant journals' or 'data extraction'/exp or 'selection criteria'	28,035
5	review.pt.	4
6	'review'/exp	1,831,423
7	5 or 6	1,831,427
8	4 and 7	15,584
9	letter.pt. or editorial.pt.	3
10	'letter'/exp or 'editorial'/exp	1,179,933
11	9 or 10	1,179,934
12	2 or 3 or 8	98,049
13	12 not 11	93,355
14	'clinical trial'/exp or 'randomized controlled trial'/exp or 'randomization'/exp or 'single blind procedure'/exp or 'double blind procedure'/exp or 'crossover procedure'/exp or 'placebo'/exp or randomi?ed and controlled and trial$ or rct$ or 'random allocation' or 'randomly allocated' or 'allocated randomly' or allocated and adj2 and random$ or single and blind$ or double and blind$ or (treble or triple and adj and blind$) or placebo$ or 'prospective study'/exp	541,923
15	'case study'/exp or 'case study' or 'case report'/exp or 'case report' or 'abstract report'/exp or 'abstract report' or 'letter'/exp or letter and [1998-2012]/py	1,237,206
16	14 not 15	529,538
17	'clinical study'/exp or 'case control study'/exp or 'family study'/exp or 'longitudinal study'/exp or 'retrospective study'/exp	5,942,135
18	'prospective study'/exp	189,505
19	'randomized controlled trial'/exp	307,692
20	18 not 19	165,671
21	'cohort analysis'/exp or (cohort and adj and (study or studies)) or (case and control and adj and (study or studies)) or (follow and up and adj and (study or studies)) or (observational and adj and (study or studies)) or (epidemiologic$ and adj and (study or studies)) or (cross and sectional and adj and (study or studies))	115,089
22	17 or 20 or 21	5,987,932
23	'sensitivity and specificity/exp or sensitivity or specificity or ('pre test' or pretest and adj and 'probability'/exp) or 'post-test probability' or predictive and value$ or likelihood and ratio$ or 'predictive value'/exp or 'diagnostic accuracy '/exp and english]/lim and [embase]/lim and [1998-2012]/py	144,775
24	13 or 16 or 22 or 23	6,162,421

#	Search History	Results
25	'infection'/exp	2,328,600
26	Infection$ or infecting or infected	2,654,665
27	'prosthesis related' and infections	95
28	'prosthesis-related infections'/exp	2,328,600
29	25 or 26 or 27 or 28	2,660,841
30	'prostheses and orthoses'/exp or prosthe$ or implant$ or orthoped$ or orthopaed$	399,873
31	'joint'/exp or joint$ or 'joint surgery'/exp or 'arthroplasty'/exp or arthroplasty or arthroplasties or 'arthroplasty replacement' or ('orthopedic surgery'/exp and 'joint'/exp)	603,883
32	30 and 31	69,062
33	1 and 24 and 29 and 32 and [english]/lim and [embase]/lim and [1998-2012]/lim	1,364
34	'drain'/exp or drain*	138,118
35	33 and 34	115

eTABLE 20. Cochrane Database of Systematic Reviews Targeted Search: Antimicrobial Prophylaxis with a Drain

#	Search History	Results
1	(antisept* or antibiotic* or antimicrobial* or anti-infect*) and (surgery or surgical* or operat*) and (joint* or arthroplast* or prosthe* or implant*) in Title, Abstract or Keywords	12

1.2G. PROSTHETIC JOINT ARTHROPLASTY SECTION TARGETED SEARCH: BIOFILM

eTABLE 21. MEDLINE Targeted Search: Biofilm

#	Search History	Results
1	(exp "prostheses and implants"/ or prosthe*.af. or implant*.af. or orthoped*.af. or orthopaed*.af.) and (exp joints/ or joint*.af.)	100,195
2	exp Joints/su [Surgery]	43,624
3	exp Arthroplasty, Replacement/ or exp Arthroplasty/	30,982
4	arthroplast*.af.	41,886
5	exp "Orthopedic Procedures"/ and exp "Joints"/	39,075
6	or/1-5	139,184
7	exp Infection/ or infection*.af. or infecting.af. or infected.af. or exp "Prosthesis-Related Infections"/	1,511,311
8	(adhesin* or biofilm*).af.	22,728
9	exp Adhesins, Bacterial/	5,227
10	"adhesin, staphylococcus aureus".af.	93
11	("bacterial adhesin receptor" or "polysaccharide intercellular adhesin" or "adhesin, Pseudomonas" or "Bap protein, Staphylococcus aureus").af.	322
12	exp Biofilms/	11,763
13	exp Staphylococcus aureus/	42,676
14	or/8-13	64,215
15	6 and 7 and 14	515
16	limit 15 to english language	472
17	limit 16 to yr="1998 -Current"	382
18	exp Random Allocation/	72,622
19	exp Randomized Controlled Trials as Topic/ or exp Randomized Controlled Trial/	386,853
20	exp Double-Blind Method/	111,942
21	exp Single-Blind Method/	15,496
22	exp Clinical Trial/	656,004
23	exp Clinical Trials as Topic/	247,358
24	clinical trial.pt.	464,810

#	Search History	Results
25	clinical trial, phase i.pt.	11,518
26	(clinical trial, phase ii or clinical trial, phase iii or clinical trial, phase iv or controlled clinical trial or randomized controlled trial or multicenter study or clinical trial).pt.	653,827
27	or/18-26	878,988
28	(clinical adj trial$).tw.	160,316
29	((singl$ or doubl$ or treb$ or tripl$) adj (blind$3 or mask$3)).tw.	109,518
30	placebo$.tw.	131,568
31	randomly allocated.tw.	13,041
32	(allocated adj2 random$).tw.	15,306
33	exp Placebos/	30,269
34	or/28-33	977,370
35	case report.tw.	161,905
36	letter/	726,601
37	historical article/	278,462
38	exp Editorial/	285,735
39	or/35-38	1,435,636
40	34 not 39	937,867
41	exp "Sensitivity and Specificity"/	342,804
42	(sensitivity or specificity).tw.	578,788
43	((pre-test or pretest) adj probability).tw.	953
44	post-test probability.tw.	260
45	predictive value$.tw.	53,070
46	likelihood ratio$.tw.	6,322
47	exp "Predictive Value of Tests"/	114,791
48	or/41-47	833,451
49	exp Meta-Analysis as Topic/	11,663
50	(meta analy$ or metaanaly$).tw. or exp Meta-analysis/	46,882

#	Search History	Results
51	(systematic adj (review$1 or overview$1)).tw.	28,388
52	exp Review Literature as Topic/	5,925
53	or/49-52	74,728
54	(embase or cochrane or psyclit* or psychlit* or psycinfo or psychinfo).tw.	26,489
55	(cinahl or cinhal).ab.	5,754
56	(science citation index or bids or cancerlit).ab.	2,076
57	or/54-56	28,166
58	(reference list$ or bibliograph$ or hand-search$ or relevant journals or manual search$).ab.	18,009
59	(selection criteria or data extraction).ab.	19,848
60	exp Review/	1,647,360
61	59 and 60	13,695
62	53 or 57 or 58 or 61	96,348
63	exp Comment/ or exp Editorial/ or exp Letter/	1,090,861
64	62 not 63	90,596
65	exp Epidemiologic studies/ or exp case control studies/ or exp cohort studies/ or Case control.tw. or (cohort adj (study or studies)).tw. or cohort analy$.tw. or (Follow up adj (study or studies)).tw. or (observational adj (study or studies)).tw. or Longitudinal.tw. or Retrospective.tw. or Cross sectional.tw. or exp Cross-sectional studies/	1,518,084
66	17 and 40	14
67	17 and 48	23
68	17 and 64	2
69	17 and 65	88
70	66 or 67 or 68 or 69	107

eTABLE 22. EMBASE Targeted Search: Biofilm

#	Search History	Results
1	'biofilm'/exp or 'adhesin'/exp or biofilm* or adhesion* and [english]/lim and [1998-2012]/py	23,287
2	'arthroplasty'/exp and [english]/lim and [1998-2012]/py	37,286

#	Search History	Results
3	1 and 2	104
4	3 and (‘case control study’/de or ‘clinical protocol’/de or ‘clinical study’/de or ‘clinical trial’/de or ‘consensus development’/de or ‘controlled clinical trial’/de or ‘controlled study’/de or ‘culture technique’/de or ‘human’/de or ‘in vitro study’/de or ‘major clinical study’/de or ‘practice guideline’/ de or ‘prospective study’/de)	94
5	‘infection’/exp and [english]/lim and [1998-2012]/py	1,005,608
6	4 and 5	82
7	4 and [embase]/lim and [1998-2012]/py	83

eTABLE 23. Cochrane Database of Systematic Reviews Targeted Search: Biofilm

#	Search History	Results
1	(biofilm* or adhesin*) in Title, Abstract or Keywords	8

2. EVIDENCE, GRADE and RISK OF BIAS ASSESSMENT TABLES

2.1. Core Section GRADE, Evidence, and Risk of Bias Assessment Tables

2.1A. Q1 PARENTERAL ANTIMICROBIAL PROPHYLAXIS (AMP)

2.1A1. GRADE TABLE: Q1 PARENTERAL AMP

eTABLE 24. GRADE Table for Q1 Parenteral AMP

Comparis-on	Outcom-e	Quantity and Type of Evidence	Findings	Starting GRADE	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcom-e	Overall GRADE of Evidenc-e Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Confounders		
Q1. What are the most effective strategies for administering parenteral AMP to reduce the risk of SSI? Q1A. What is the optimal timing of preoperative AMP?														
Elective Lower Limb Musculoskeletal Procedures (majority fracture repairs with some soft tissue surgeries)														
AMP 1 minute after vs. 5 minutes prior to tourniquet inflation	Deep SSI*	1 RCT [1]	• In 1 RCT (N=106) of a mixture of implant surgeries with soft tissue operations, where limbs were exsanguinated prior to tourniquet inflation, Patients in the group who received intravenous antibiotics after tourniquet inflation had significantly fewer deep infections: 2/52 (3.9%) vs. 8/54 (14.8%); p=0.03, at 12 month follow up.	High	-1	0	0	-1	0	0	0	0	Low	Low
Primary Total Knee Arthroplasty														
AMP 10 minutes before tourniquet release vs. 10-30 minutes before tourniquet inflation	Deep SSI*	1 RCT [2]	• In 1 RCT (N=908) of primary knee arthroplasties, patients who received intravenous antibiotics after tourniquet inflation had fewer deep SSI at 12 months follow up: 12/466 (2.6%) vs. 16/442 (3.6%); p=0.44 but this difference was not significant.	High	0	0	0	-1	0	0	0	0	Moderate	Moderate
	Length of Stay	1 RCT [2]	• There was no difference in the mean length of stay between groups: 6.4±1.6 vs. 6.5±2.1 days; p=0.58	High	0	0	0	-1	0	0	0	0	Moderate	
	Antimicr-obial Resista-nce	1 RCT [2]	• 19/ 31 organisms isolated from 28 SSI were *Staphylococcus.* • MRSA: 1/12 (8.3%) vs. 1/16 (6.25%) • Methicillin Resistant-Coagulase Negative	High	0	0	0	-1	0	0	0	0	Moderate	

Comparis-on	Outcom-e	Quantity and Type of Evidence	Findings	Starting GRADE	Decrease GRADE					Increase GRADE			GRADE of Evidenc e for Outcom-e	Overall GRADE of Evidenc-e Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Confounders		
			Staphylococcus aureus: 4/12 (25.0%) vs. 2/16 (12.5%)											
Q1B. What is the optimal timing of AMP in cesarean section: prior to skin incision or at cord clamping?														
Cesarean section AMP timing: Prior to skin incision vs. at cord clamping	SSI-Endome-tritis*	7 RCTs [3-9]	• N=2493 Mothers from 7 RCTs all undergoing Cesarean section overall OR: 0.57 (0.34-0.94); p=0.03; I^2=0 indicating a reduction in the odds of developing endometritis with administration of AMP prior to skin incision	High	0	0	0	0	0	0	0	0	High	High
	SSI Incisional	7 RCTs [3-9]	• N=2493 Mothers from 7 RCTs all undergoing cesarean section, overall OR: 0.82 (0.52 – 1.31); p=0.41; I^2=0; indicating no difference	High	0	0	0	0	0	0	0	0	High	
	Neonatal Sepsis	3 RCTs [6-8]	• N=1080 Neonates from 3 RCTs all delivered by Cesarean section, administration of AMP to the mother prior to skin incision did not significantly affect proven neonatal sepsis-OR: 0.81 (0.45 – 1.44); p=0.47; I^2=0 • 1 RCT[5] stated that there was no significant difference in the rate of neonatal sepsis between groups but data was not shown.	High	0	0	0	0	0	0	0	0	High	
	Neonatal Sepsis Workup	5 RCTs [4,6-9]	• N=1604 Neonates delivered by cesarean section from 5 RCTs, administration of AMP to the mother prior to skin incision did not significantly affect suspected sepsis that required workup: OR: 0.92 (0.68 – 1.24); p=0.58; I^2=0	High	0	0	0	0	0	0	0	0	High	
	Neonatal Antimicr-obial Resista-nce	2 RCTs [4,8]	• In 1 RCT [8], 13 cases of sepsis among 357 neonates did not show increased antimicrobial resistance 2/6 vs. 3/7 • In 1 RCT[4], with 38 cases of suspected sepsis there were no cases of antibiotic resistance in the neonates	High	0	0	0	-1	0	0	0	0	Moderate	

Comparis-on	Outcom-e	Quantity and Type of Evidence	Findings	Starting GRADE	Decrease GRADE					Increase GRADE			GRADE of Evidenc e for Outcom-e	Overall GRADE of Evidenc-e Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Confounders		
	Neonate Admissi-on to Higher Level Care	5 RCTs [3,4,6-8]	• N=1694 Neonates from 5 RCTs all delivered by Cesarean section, administration to the mother prior to skin incision did not significantly affect admission of neonate to an increased infant care unit. OR: 0.92 (0.64 – 1.32); p=0.64; I^2=0	High	0	0	0	0	0	0	0	0	High	
Q1C. How safe and effective is weight-adjusted AMP dosing? Our search did not identify RCTs or SRs that evaluated weight-adjusted AMP dosing and its impact on the risk of SSI.														
Q1D. How safe and effective is intraoperative redosing of AMP?														
1 Preoperati-ve dose vs. 1 preoperati-ve dose plus additional dose at 2h intraoperat-ively	SSI* (Abdomi-nal)	1 RCT [10]	• In 1 RCT (N=278) in elective colorectal surgery, 271 patients completed 30 day follow up. No difference: 10/143 (7%) vs. 7/128 (5%); p>0.05 • Patients with procedure duration >3h had a significantly higher probability of infection (5/37 (14%)) as compared to those with 2-3hr (5/127 (4%)) or <2h duration 7/107 (7%); p<0.05. Of note, 36/164 (22%) of patients with procedure durations ≥2h were not redosed intraoperatively (antimicrobial half-life was 68 min). Study does not report these infections by single dose versus redosed. • Increasing fecal contamination almost doubled the infection rate at every level from 2/67 (3%) in those with no contamination, to 10/162 (6%) in those with moderate, and 5/38 (13%) in those with gross contamination, p<0.05 (contamination unknown in 4). Study does not report these infections by single dose versus redosed.	High	0	0	0	-1	0	0	0	0	Moderate	Moderate
	Intra-Abdomi-nal Abscess*	1 RCT [10]	• No difference: 8/146 (5%) vs. 10/132 (8%)	High	0	0	0	-1	0	0	0	0	Moderate	

Comparis-on	Outcom-e	Quantity and Type of Evidence	Findings	Starting GRADE	Decrease GRADE					Increase GRADE			GRADE of Evidenc e for Outcom-e	Overall GRADE of Evidenc-e Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Confounders		
	Perineal Wound Infection*	1 RCT [10]	• No difference: 4/9 vs. 4/9	High	0	0	0	-1	0	0	0	0	Moderate	
	Antimicr-obial resistan-ce	1 RCT [10]	• No difference: 1 minor SSI in each group culture positive for MRSA as the sole organism	High	0	0	0	-1	0	0	0	0	Moderate	
Q1E. How safe and effective is postoperative AMP and what is the optimal duration?														
All Surgeries														
None vs. ≤24h	SSI*	21 RCT [11-31]	• In a meta-analysis of 21 RCTs, (N=14,285) no benefit of continuing AMP after the wound is closed in the operating room: OR: 1.19 (0.94 – 1.50); p=0.15; I^2=25%	High	0	0	0	0	0	0	0	0	High	High
Cardiac Surgery														
None vs. ≤96h	Organ-Space Sternal SSI*	3 RCT [12,32,33]	• In a meta-analysis of 3 RCTs[12,32,33] (N=1746), there was no benefit of continuing AMP after the wound was closed in the operating room: OR: 1.84 (0.82 – 4.14); p= 0.14; I^2=0	High	0	0	0	-1	0	0	0	0	Moderate	Moderate
None vs. ≤24h	SSI*	1 RCT [12]	• ≤24h AMP duration reduced the risk of SSI at 12 month follow up in 1 large RCT with N=838 patients undergoing CABG with or without valve replacement: 30 /419 (7.2%) vs. 15/419 (3.6%); p=0.02. Overall rate of SSI was 5.9%. • Patients received their first dose of AMP 20-30 min after induction of anesthesia, and those whose procedures lasted >3h were redosed intraoperatively. • The "no postoperative AMP" group also had statistically higher proportion of patients on intraaortic balloon pump postoperatively (0.03) and received more blood transfusions (0.01).Patients who presented with both osteomyelitis and mediastinitis were reported	High	0	0	0	-1	0	0	0	0	Moderate	Moderate

Comparis-on	Outcom-e	Quantity and Type of Evidence	Findings	Starting GRADE	Decrease GRADE					Increase GRADE			GRADE of Evidenc e for Outcom-e	Overall GRADE of Evidenc-e Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Confounders		
			as both an organ/space and a deep incisional SSI. Between 1 and 3 of 5 deep SSI patients in the "no postoperative AMP group" may have had both. Since the study did not stratify those results, deep SSI data were excluded from this analysis. • No *S. aureus* decolonization was performed.											
	Organ/ Space Sternal SSI	1 RCT [12]	• No difference: 14/419 (3.3%) vs. 8/419 (1.9%); p=0.19 at 12 month follow up. • No statistically significant differences between groups for osteomyelitis, mediastinitis, or endocarditis individually.	High	0	0	0	-1	0	0	0	0	Moderate	
	Superfic-ial SSI	1 RCT [12]	• ≤24 AMP reduced the risk of superficial incisional SSI:16 (3.8%) vs. 7 (1.7%); p=0.04 • However, it is not clear if incisional SSIs included both sternal and donor site wounds.	High	0	0	0	-1	0	0	0	0	Moderate	
	Mortality	1 RCT [12]	• No difference at 30d, 90d and 365d (P=0.12, 0.18, and 0.34, respectively)	High	0	0	0	-1	0	0	0	0	Moderate	
	Length of Stay	1 RCT [12]	• No differences: (14.75±15.8 vs. 12.2±14.2); p=0.25. • Of note, patients in both groups were hospitalized for approximately 10 days before surgery and had long mean ICU stays: 10.3±10.9 vs. 9.1±8.7; p=0.09.	High	0	0	0	-1	0	0	0	0	Moderate	
	Antimicr-obial Resista-nce	1 RCT [12]	• The most frequently isolated organisms were Staphylococcus epidermis and Staphylococcus aureus (p≥0.05) and the majority of SSIs were polymicrobial: 57.1% vs. 60.0%. • MRSA: 4/35 (11.4%) vs. 9/15 (60%); p<0.01	High	0	0	0	-1	0	0	0	0	Moderate	

Comparis-on	Outcom-e	Quantity and Type of Evidence	Findings	Starting GRADE	Decrease GRADE					Increase GRADE			GRADE of Evidenc e for Outcom-e	Overall GRADE of Evidenc-e Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Confounders		
None vs. 72-96h	Organ/ Space SSI* Sternal	2 RCT [32,33]	• No difference in meta-analysis (N=908) of 2 RCTs, OR: 4.28 (0.47 – 39.24); p=0.20; I^2=0	High	0	0	0	-1	0	0	0	0	Moderate	Moderate
	Superfic-ial Sternal SSI*`	3 RCT [32-34]	• No difference in meta-analysis (N=993) of 3 RCTs: OR: 1.23 (0.44 – 3.45); p=0.69; I^2=0	High	0	0	0	-1	0	0	0	0	Moderate	
	SSI* Leg Graft Donor Site	1 RCT [33]	• No difference in 1 large RCT where 766 (91%) of 844 CABG patients underwent leg vein harvest. 23/377 (6.1%) vs. 20/389 (5.1%); 7 day follow up. Overall donor site SSI rate 5.6% (43/766)	High	0	0	0	-1	0	0	0	0	Moderate	
	Leg Graft Donor Site Wound Dehisce-nce	1 RCT [33]	• No difference: 18 reports of wound dehiscence in each group (7-day follow up). The authors included donor site wound dehiscence in their calculation of the overall infection rate.	High	0	0	0	-1	0	0	0	0	Moderate	
	Superfic-ial Leg Graft Donor Site SSI*	1 RCT [33]	• No difference: 5/377 (1.3%) vs. 2/389 (0.5%); p=0.26 (7 day follow up)	High	0	0	0	-1	0	0	0	0	Moderate	
	Length of Stay	1 RCT [34]	• Significantly shorter length of stay with postoperative AMP in one small (N=85) RCT with data collected 35 years ago: 12.03±4.2 versus 14.6±7.5 days; P<0.05	High	-1	0	0	-1	0	0	0	0	Low	
	Antimicr-obial Resista-nce	2 RCT [32,34]	• One study [34] both incisional SSIs were Staphylococcus aureus • One study [32] incisional SSI: The “no	High	-1	0	0	-1	0	0	0	0	Low	

Comparis-on	Outcom-e	Quantity and Type of Evidence	Findings	Starting GRADE	Decrease GRADE					Increase GRADE			GRADE of Evidenc-e for Outcom-e	Overall GRADE of Evidenc-e Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Confounders		
			postoperative AMP group" had 1 Staphylococcus aureus and 1 Staphylococcus epidermis infection as compared to 1 *Serratia marcescens* and 1 Enterococcus infection in those with postoperative AMP. The one case of endocarditis in the group with "no postoperative AMP" was a Staphylococcus epidermis.											
≤24h vs. 72h	Sternal SSI*	1 RCT [35]	• No difference in 30 day SSI (N=231) 13/120 (10.8%) vs. 9/111 (8.1%); p=0.48	High	-1	0	0	-1	0	0	0	0	Low	Low
	Deep Sternal SSI*	1 RCT [35]	• No difference in deep sternal SSI (N=231) 3/120 (2.5%) vs. 1/111 (0.9%); p=0.62	High	-1	0	0	-1	0	0	0	0	Low	
	Superfic-ial Sternal SSI*	1 RCT [35]	• No difference in superficial sternal SSI (N=231) 3/120 (2.5%) vs. 2/111 (1.8%); p=1.00	High	-1	0	0	-1	0	0	0	0	Low	
	Harvest Site SSI*	1 RCT [35]	• No difference in harvest site SSI (N=231) at 30 days 73/120 (5.8%) vs. 6/111 (5.4%); p=0.89	High	-1	0	0	-1	0	0	0	0	Low	
	Total Length of Stay	1 RCT [35]	• No difference in length of stay: 15.1±5.2 days versus 16.7±9.1 days; p=0.10	High	-1	0	0	-1	0	0	0	0	Low	
	Antimicr-obial Resista-nce	1 RCT [35]	• No difference in rates of MSSA: 3/120 (2.5%) vs. 3/111 (2.7%); p=1.00; or MRSA: 2/120 (1.7%) vs. 3/111 (2.7%); p=0.67 • Although not significant, nasal swab screen results prior to surgery were higher in 1-day	High	-1	0	0	-1	0	0	0	0	Low	

Comparis-on	Outcom-e	Quantity and Type of Evidence	Findings	Starting GRADE	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcom-e	Overall GRADE of Evidenc-e Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Confounders		
			group for both MSSA: 8/120 (7.3%) vs. 16/111 (15.5%); p=0.06; and MRSA: 6/120 (5.5%) vs. 4/111 (3.9%); p=0.75.											
Thoracic Surgery														
None vs. 2 days	SSI*	1 RCT [36]	• No difference in 1 RCT (N=203) of patients undergoing thoracic surgery (thoracotomy with lung resection): 7/102 (7%) vs. 2/101 (2%); p=0.11. • Overall SSI rate was 4.4%.	High	0	0	0	-1	0	0	0	0	Moderate	Moderate
	Organ/ Space SSI (empye-ma)	1 RCT [36]	• Significantly more empyema in group without postoperative AMP: 6/102 (6%) vs. 1/101 (1%); p=0.03. • Both groups received AMP at induction of anesthesia and were redosed intraoperatively (2h).	High	0	0	0	-1	0	0	0	0	Moderate	
	Incisional SSI	1 RCT [36]	• No difference: 1/102 (1%) vs. 1/101 (1%); p=0.9.	High	0	0	0	-1	0	0	0	0	Moderate	
	Mortality	1 RCT [36]	• 4 (2%) postoperative deaths; none related to AMP or SSI.	High	0	0	0	-1	0	0	0	0	Moderate	
	Length of Stay	1 RCT [36]	• No differences: 15±1.6 days versus 13±1 days.	High	0	0	0	-1	0	0	0	0	Moderate	
	Adverse Events	1 RCT [36]	• No side effects of the antimicrobial prophylaxis were noted.	High	0	0	0	-1	0	0	0	0	Moderate	
Vascular Surgery														

Comparis-on	Outcom-e	Quantity and Type of Evidence	Findings	Starting GRADE	Decrease GRADE					Increase GRADE			GRADE of Evidenc e for Outcom-e	Overall GRADE of Evidenc-e Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Confounders		
None vs. <24 hours	SSI*	1 RCT [16]	• No difference in 1 RCT subanalysis (N=169) of clean, clean-contaminated, and contaminated elective and emergency vascular surgery procedures: 2/89 (3.8%) vs. 3/80 (2.3%), p>0.05 (1 month follow up).	High	0	0	0	-1	0	0	0	0	Moderate	Moderate
<24h vs. 3 days	SSI*	1 RCT [37]	• No difference in 1 RCT, of patients undergoing acute femoral embolectomy or thrombectomy, subanalysis (N=121): 2/52 (3.8%) vs. (3/69) 4.3%; p=0.89 (30 day follow up).	High	0	0	0	-1	0	0	0	0	Moderate	Moderate
None vs. 5 days	SSI*	1 RCT [38]	• Reduced risk of SSI with postoperative AMP in 1 RCT of emergency and elective open arterial reconstructions (N=302): 28/153 (18%) vs. 15/149 (10%); OR: 2.00 (1.02 – 3.92); p=0.04 (42 day follow up). • Overall SSI rate: 14.2% (43/302). • Patients received first dose of AMP (over 30 minutes) after induction of anesthesia. Patients tended to be “elderly and debilitated”, with a higher proportion of those in the “no postoperative AMP” being current smokers and insulin dependent diabetics.	High	0	0	0	-1	0	0	0	0	Moderate	Moderate
	Organ/ Space SSI	1 RCT [38]	• No difference: 1 graft infection in each group.	High	0	0	0	-1	0	0	0	0	Moderate	
Ear, nose, and throat (ENT) procedures														
≤24h vs. 3-5 days	SSI*	2 RCT [39,40]	• No difference on meta-analysis of 2 small RCTs (N=127): OR: 1.54 (0.59 – 4.05); p=0.38 ; I^2=0 • 1 RCT [39] of 53 patients undergoing head and neck procedures including myocutaneous flap reconstruction reported an overall wound infection rate of 24.5% (13/53) at 30 day	High	0	0	0	-1	0	0	0	0	Moderate	Moderate

Comparis-on	Outcom-e	Quantity and Type of Evidence	Findings	Starting GRADE	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcom-e	Overall GRADE of Evidenc-e Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Confounders		
			follow up and no difference between groups: 8/26 (30.7%) vs. 5/27 (18.5%); p=0.47. • 1 RCT [40] in 74 patients undergoing head and neck procedures including immediate flap reconstruction reported an overall wound infection rate of 10.8% (8/74) at 7 day follow up and no difference between groups 4/35 (11%) vs. 4/39 (10%); p=0.99											
	Length of Stay	1 RCT [39]	• No difference: 25±18 vs. 22±15 days; p=0.627.	High	0	0	0	-1	0	0	0	0	Moderate	
	Pharyng-ocutane-ous Fistula	1 RCT [40]	• No difference: 3/35 (9%) vs. 3/39 (8%) (7 day follow up). • Overall pharyngocutaneous fistula rate: 6/74 (8%).	High	0	0	0	-1	0	0	0	0	Moderate	
Gynecologic Procedures														
None vs. ≤24h	SSI*	5 RCT [13,27-30]	• No difference in SSI in a meta-analysis (N=1917) of 5 RCTs: OR: 0.92 (0.51 – 1.65); p=0.77; I^2=0 • In 1 RCT [13] (N=531) of patients undergoing laparoscopic-assisted vaginal hysterectomy (LAVH) or ovarian cystectomy (LAOC), total abdominal or vaginal hysterectomies (TAH or TVH), 1 trocar site infection was reported in each group at 90 day follow up: 1/267 vs. 1/264. • In 1 RCT [27] (N=66) of patients undergoing radical gynecologic pelvic surgery for malignancy, 1 abdominal wound infection was reported in each group at 8 day follow up: 1/37 vs. 1/29. • In 1 RCT [29] with a subpopulation of 608 patients undergoing unspecified gynecologic	High	-1	0	0	-1	0	0	0	0	Low	Low

Comparis-on	Outcom-e	Quantity and Type of Evidence	Findings	Starting GRADE	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcom-e	Overall GRADE of Evidenc-e Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Confounders		
			procedures, no difference in SSI at minimum 7 day follow up: 12/385 vs.4/223; p=0.53 • In 1 RCT [28] of 112 patients undergoing vaginal hysterectomy, no difference in SSI at 3-6 week follow up: 1/58 vs. 2/54 • In 1 RCT[30] of 500 women undergoing cesarean section, No difference in SSI at 30 day follow-up: 12/250 (4.8%) vs. 16/250 (6.4%).											
	Organ/ space SSI	1 RCT [13]	• In 1 RCT (N=531) among the 478 who had laparoscopic-assisted vaginal hysterectomy (LAVH), total abdominal or vaginal hysterectomies (TAH or TVH), only 1 vaginal cuff infection with pelvic abscess was reported in a patient who underwent LAVH in the 24 hour group: 0/237 vs. 1/241 (0.41%) at 90 day follow up.	High	-1	0	0	-1	0	0	0	0	Low	
	Trocar Wound Infection	1 RCT [13]	• In 1 RCT (N=531), among the 455 (86%) patients who had a laparoscopic-assisted vaginal hysterectomy (LAVH) or ovarian cystectomy (LAOC), only 1 trocar wound infection was reported in a patient who underwent LAOC in the no postoperative AMP group: 1/226 (0.44%) vs. 0/229. (90 day follow up).	High	-1	0	0	-1	0	0	0	0	Low	
	Length of Stay	3 RCT [13,27,28]	• One RCT [13] no difference: 4.02 ±1.51 vs. 3.97±1.27. • One RCT [27] no difference: 18 days (range 12-23) vs. 19 days (range, 12-23 days). • One RCT [28] no difference : days ±SD: 4.4±1.1 vs. 4.7±1.2 days.	High	-1	0	0	0	0	0	0	0	Moderate	

Comparis-on	Outcom-e	Quantity and Type of Evidence	Findings	Starting GRADE	Decrease GRADE					Increase GRADE			GRADE of Evidenc e for Outcom-e	Overall GRADE of Evidenc-e Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Confounders		
<24h vs. <2.5 days	SSI*	1 RCT [41]	• No difference: 1 RCT (N=156) in patients undergoing a laparoscopic-assisted vaginal hysterectomy (LAVH) no difference: 2/74 (2.7%) vs. 3/82 (3.6%) (7 day follow up) • Overall SSI rate: 3.2% (5/156)	High	0	0	0	-1	0	0	0	0	Moderate	Moderate
	Organ/ Space SSI	1 RCT [41]	• No difference 1 vaginal cuff abscess in each group. (7 day follow up).	High	0	0	0	-1	0	0	0	0	Moderate	
	Trocar wound infection	1 RCT [41]	• No difference: 1/74 (1.4%) vs. 3/82 (3.7%); p=0.38. (7 day follow up)	High	0	0	0	-1	0	0	0	0	Moderate	
Orthopaedic Surgery – Fracture Surgery														
None vs. ≤24h	SSI*	4 RCT [14,17-19]	• No difference on meta-analysis of 4 RCTs (N=1722): OR: 1.87 (0.70 – 4.94); p=0.21 ; I^2=44% • 3 RCTs [14, 17, 19] reported no difference between groups for all SSIs combined. • One RCT [14] (N=191) in hip fracture patients reported a total of 4 (2.1%) infections and no difference between groups at 6w follow up: 2/83 (2.4%) vs. 2/108 (1.9%); p=0.79. Both were superficial SSI. Postop dosing group received AMP for another 24h. • 1 RCT [17] (N=200) in a mix of clean orthopaedic fracture surgeries reported a total of 14(7%) infections, and no difference between groups at 28day follow up: 8% vs. 6%; p=0.27 Postop dosing group received AMP for another 24h. • 1 RCT [19] (N=614) in orthopaedic fracture fixation and arthroplasty patients, no difference: 2/301 (0.66%) vs. 3/313 (1.27%);	High	-1	0	0	-1	0	0	0	0	Low	Low

Comparis-on	Outcom-e	Quantity and Type of Evidence	Findings	Starting GRADE	Decrease GRADE					Increase GRADE			GRADE of Evidenc e for Outcom-e	Overall GRADE of Evidenc-e Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Confounders		
			p=0.45 (10 day follow up); overall SSI rate 0.98%. • 1 RCT [18] (N=717) in a mix of orthopaedic fracture surgeries, reported a total of 23 (3.2%) infections (follow up period not reported) with a significantly higher risk of SSI among the no postoperative AMP group : 20/382 (5.3%) vs. 3/335 (0.89%); p<0.01 This significance was seen for both hemiarthroplasties: 5/76 (6.5%) vs. 0/74 (0%); p=0.03 and all other procedures combined: 15/306 (5%) vs. 3/261 (1%); p<0.01. Postoperative dosing group received AMP for another 20h postop. Patients in both groups were hospitalized for approximately 5 days before surgery.										
	Deep SSI	2 RCT [14,17]	• No difference on meta-analysis of 2 RCTs (N=391): OR: 0.33 (0.03 – 3.19); p=0.34. • One RCT [14] (N=191) in hip fracture patients reported no deep infections in either group (0/83 vs. 0/108) at 6 week follow up. • 1 RCT [17] (N=200) in a mix of clean orthopedic fracture surgeries reported a total of 4 (2%) deep infections and no difference between groups at 28 day follow up: 1% vs. 3%; p=0.34.	High	-1	0	0	-1	0	0	0	0	Low	
	Superfic-ial SSI	2 RCT [14,17]	• No difference in meta-analysis of 2 RCT (N=391), no difference between groups OR: 1.99 (0.64 – 6.17); p=0.24; I^2=0%. • 1 RCT [14] (N=191) in hip fracture patients reported a total of 4 (2.1%) infections and no difference: 2/83 (2.4%) vs. 2/108 (1.9%); p=0.79 (6 week follow up). • 1 RCT [17] (N=200) in a mix of clean	High	-1	0	0	0	0	0	0	0	Moderate	

Comparis-on	Outcom-e	Quantity and Type of Evidence	Findings	Starting GRADE	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcom-e	Overall GRADE of Evidenc-e Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Confounders		
			orthopaedic fracture surgeries reported a total of 10 (5%) superficial SSIs and no difference: 7% vs. 3%; p=0.21 (28 days follow up).											
	Mortality	2 RCT [14,18]	• In 1 RCT [14] (N=191), there were 7 (3.4%) deaths. There were no significant differences in mortality between groups 3/121 (2.4%) vs. 4/83 (4.81%) and no deaths resulted from infections. • In 1 RCT [18] (N=717) there were 30 deaths (4%); 1 patient had an uncontrolled wound infection but the cause of death was a stroke.	High	0	0	0	0	0	0	0	0	High	
	Adverse Events	1 RCT [14]	• In 1 RCT (N=191), there were no anaphylactic reactions, allergies, or renal toxicity related to antimicrobial prophylaxis administration.	High	0	0	0	-1	0	0	0	0	Moderate	
	Antimicr-obial Resista-nce	3 RCT [14,17,18]	• In 1 RCT [14] (N=191), Staphylococcus aureus isolated from all SSIs. No gram negative organisms isolated. No mention of antimicrobial resistance. • In 1 RCT [17] (N=200) Staphylococcus aureus was the commonest organism isolated, followed by E. coli. Eight of the 14 SSIs had a negative wound culture (7 superficial, 1 deep). No mention of resistance. • In 1 RCT [18] (N=717) 31 organisms isolated from 23 wound infections: 9 Staphylococcus aureus, 4 S. epidermis, and 4 E. coli all sensitive to the AMP. In addition, 4 Pseudomonas aeruginosa, and 3 Streptococcus faecalis all resistant to the AMP and 7 strains of other gram negative bacilli, 2 of them resistant to the AMP.	High	0	0	0	0	0	0	0	0	High	
Orthopaedic Surgery - Prosthetic Joint Arthroplasty														

Comparis-on	Outcom-e	Quantity and Type of Evidence	Findings	Starting GRADE	Decrease GRADE					Increase GRADE			GRADE of Evidenc e for Outcom-e	Overall GRADE of Evidenc-e Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Confounders		
None vs. ≤ 24h	SSI*	2 RCT [20,21]	• No difference in a meta-analysis of 2 RCT, (N=2,847) no difference between groups OR: 1.84 (0.68 – 4.98); p=0.23. • In the larger RCT [20] (N=2651) in THA, TKA, and hemiarthroplasty patients, no difference in PJI between groups at 13 month follow up: 11/1327 (0.83%) vs. 6/1324 (0.45%); p=0.17; RR: 1.83, (0.68-4.93). • In the second smaller study [21] (N=196), in unilateral or bilateral THA or TKA patients no infections (including deep wound infections) were reported in either group at 12 month follow up.	High	0	0	0	0	0	0	0	0	High	High
Colorectal Surgery														
BOWEL PREPARATION INCLUDED ORAL ANTIMICROBIALS PREOPERATIVELY														
None vs. 3 days	SSI* Incisional	1 RCT [42]	• No difference in 1 RCT (N=360) in patients undergoing elective laparotomy for colorectal malignancy: 15/179 (8.4%) vs. 13/181 (7.2%); p=0.67 (30 day follow up).	High	0	0	0	-1	0	0	0	0	Moderate	Moderate
	SSI* Organ/ Space	1 RCT [42]	• No difference: 1/179 (0.6%) vs. 2/181 (1.1%); p=0.58 (30 day follow up). • All 3 caused by anastomotic leak.	High	0	0	0	-1	0	0	0	0	Moderate	
	Antimicr-obial resistan-ce	1 RCT [42]	• Culture isolates available for 23/28 patients with incisional SSI: Pseudomonas aeruginosa most commonly isolated in both groups followed by Enterococcus faecalis. MRSA isolated from 3 patients all in the groups without postoperative administration of AMP (in 2 as part of polymicrobial SSI).	High	0	0	0	-1	0	0	0	0	Moderate	
	Adverse events	1 RCT [42]	• No *Clostridium difficile* in either group.	High	0	0	0	-1	0	0	0	0	Moderate	

Comparis-on	Outcom-e	Quantity and Type of Evidence	Findings	Starting GRADE	Decrease GRADE					Increase GRADE			GRADE of Evidenc e for Outcom-e	Overall GRADE of Evidenc-e Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Confounders		
≤24h vs. 5 days	SSI*	1 RCT [43]	• 1 RCT (N=40) in patients with chronic ulcerative colitis, familial polyposis, or Gardner's syndrome undergoing colectomy, mucosal proctectomy with ileal pouch-anal anastomosis reported no wound or intra-abdominal infections in either group at 1yr follow up: 0/22 vs. 0/18.	High	0	0	0	-2	0	0	0	0	Low	Low
	Length of stay	1 RCT [43]	• No difference: (mean±SD) 8.7±0.4 days vs. 8.4±0.2 days.	High	0	0	0	-1	0	0	0	0	Moderate	
BOWEL PREPARATION ONLY														
None vs. ≤24h	SSI*	4 RCT [15,22-24]	• No difference in a meta-analysis of 4 RCTs (N=894), no difference between groups OR: 1.58 (0.76 – 3.28); p=0.22; I^2=57%. • 1 RCT [15] (N=377) in elective open and laparoscopic colorectal procedures for colon cancer postoperative AMP was associated with reduced risk of SSI at 30 day follow up: 27/190(14.2%) vs. 8/187(4.3%); p<0.01. On multivariate analysis antimicrobial dose was the only significant factor associated with incisional SSI (p<0.01). • 1 RCT [22] 1 subgroup analysis 1 (N=138) in patients undergoing elective colorectal procedures suggests no difference: 12/138 (8.7%); 5/71 (7.0%) vs. 7/67 (10.4%); p =0.48 (28-41 day follow up). • 1 RCT [22] subgroup analysis 2 (N=135) in patients undergoing elective colorectal procedures suggests no difference: 16/135 (11.9%); 8/65 (12.3%) vs. 8/70 (11.4%); p=0.87 (28-41 day follow up).	High	-1	-1	0	0	0	0	0	0	Low	Low

Comparis-on	Outcom-e	Quantity and Type of Evidence	Findings	Starting GRADE	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcom-e	Overall GRADE of Evidenc-e Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Confounders		
			• 1 RCT [24] (N=154) in elective colorectal procedures suggests no difference: 40/77 (5.2%) vs. 40/77 (5.2%); Follow up NR. • 1 RCT [23] (N= 90) in elective colorectal procedures, excluding inflammatory bowel disease, suggests no difference for abdominal wounds: 18/90 (20%): 7/22 (31%) vs. 11/68 (16%); p=0.12; or perineal wounds: 1/3 (33.3%) vs. 7/13 (53.8%); p=0.53. (6 week follow up).										
	Organ/ space SSI	2 RCT [15,24]	• No difference in a meta-analysis (N=531) of 2 RCTs OR: 0.73 (0.30 – 1.77); p=0.49; I^2=0%. • 1 RCT [15] no difference: 5/190 (2.6%) vs. 9/187 (4.8%); p=0.26. (30 day follow up). • 1 RCT [24] no difference for intra-abdominal abscess 2/77 (2.6%) vs. 1/77 (1.3%); p=0.57 or peritonitis 2/77 (2.6%) vs. 2/77 (2.6%); Follow up NR.	High	-1	0	0	0	0	0	0	0	Moderate	
None vs. <2 – 3 days	All SSI*	3 RCT [44-46]	• No difference in a meta-analysis of 3 RCTs: OR 1.35 (0.70 – 2.61); p=0.37; I^2=0%. • 1 RCT[44] with subanalysis in elective colorectal procedures (n=207) suggests no difference between groups at 35 day follow up: 11/102(10.7%) vs. 6/105 (5.6%); p=0.19. • 1 RCT [45] (N=443) in elective colorectal procedures for cancer, inflammatory bowel disease (10%), and other (10%), suggests no difference between groups for deep wound infections: 17/294 (5.8%); 9/149 (6%) vs. 8/145 (6%) or for intra-abdominal abscess: 3/294 (1.0%); 1/149 (1%) vs. 2/145 (1%) at 30 day follow up. • 1 RCT [46] (N=100) in elective colorectal procedures for cancer or diverticulitis	High	0	0	0	0	0	0	0	0	High	Moderate

Comparis-on	Outcom-e	Quantity and Type of Evidence	Findings	Starting GRADE	Decrease GRADE					Increase GRADE			GRADE of Evidenc e for Outcom-e	Overall GRADE of Evidenc-e Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Confounders		
			suggests no difference between groups: 3/100 (3.0%); 2/54 (3.7%) vs. 1/46 (2.1%); p=0.66 (Follow up NR).											
	Organ/ Space*	1 RCT [45]	• No difference: 1/149 (1%) vs. 2/145 (1%). • Overall Organ/Space SSI rate: 3/294 (1.0%).	High	0	0	0	-1	0	0	0	0	Moderate	
	Antimicr-obial Resista-nce	2 RCT [45,46]	• No difference in bacterial isolates and no report of antimicrobial resistance.	High	-1	0	0	-1	0	0	0	0	Low	
BOWEL PREPARATION NOT REPORTED														
None vs. ≤24h	SSI*	1 RCT [25]	• No difference for colorectal cases in 1 RCT (N=224) in at-risk abdominal surgery: 40/224 (17.9%); 23/113(20.4%) vs. 17/111 (15.3%); p>0.2 (30 day follow up).	High	0	0	0	-1	0	0	0	0	Moderate	Moderate
≤24h vs. 2-3 days	SSI*	4 RCT [47-50]	• No difference in a meta-analysis of 4 RCTs, (N=802) no difference between groups OR: 1.13; (0.75 – 1.70); p=0.57; I^2=12%. • 1 RCT [47] (N=87) colorectal surgery suggests no difference: 20/87 (23.0%); 13/45 (28.9%) vs. 7/42 (16.7%); p=0.18 (28 day follow up). • 1 RCT [48] with subanalysis (n=428) in high-risk colorectal procedures suggests no difference: 45/428 (11%); 22/209 (11%) vs. 23/219 (11%); p=0.99 (30 day follow up). • 1 RCT [49] (N=60) in elective colon surgery no difference: 6/30 (20%) vs. 10/30 (33.3%); p=0.25. • 1 RCT [50] in elective colorectal surgery subanalysis (n=227) no difference in abdominal wound: 23/113 (19.5%) vs. 22/114 (19.3); p=0.84; perineal wound: 7/113 (6.2%) vs. 3/114 (2.6%);p=0.20.	High	0	0	0	0	0	0	0	0	High	High

Comparis-on	Outcom-e	Quantity and Type of Evidence	Findings	Starting GRADE	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcom-e	Overall GRADE of Evidenc-e Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Confounders		
	Organ/ Space	3 RCTs [48-50]	• No difference in a meta-analysis (N=715) of 3 RCTs: OR: 0.77 (0.37 – 1.63); p=0.50; I^2=0%. • 1RCT [48] Intra-abdominal abscess. No difference: 14/428 (3%) total; 6/209 (3%) vs. 8/219 (4%); p=0.65 (30 day follow up). • 1RCT [49] Intra-abdominal abscess no difference: 2/30 (7%) vs. 2/30 (7%); Peritonitis no difference: 1/30 (3%) vs. 3/30 (10%); p=0.32 (follow up NR). • 1 RCT [50] Intrapelvic abscess no difference: 2/113 (1.8%) vs. 2/114 (1.8%); Intra-abdominal abscess no difference: 2/113 (1.8%) vs. 1/114 (0.9%); p=0.56; Peritonitis no difference: 0/113 vs. 1/114 (0.9%).	High	0	0	0	0	0	0	0	0	High	
	Adverse Events	1 RCT [50]	• Adverse events possibly related to antimicrobial agent included 2 patients with phlebitis in the group receiving <24 AMP and in the group receiving longer AMP, 2 cases of hypotension, 1 phlebitis, 1 erythema, and 1 rash.	High	0	0	0	-1	0	0	0	0	Moderate	
NO BOWEL PREPARATION														
None vs. ≤24h	SSI*	1 RCT [22]	• No difference in 1 RCT subpopulation (n=46) of emergency colorectal procedures: 6/46 (13.0%); 4/21 (19.0%) vs. 2/25 (8.0%); p=0.28 (28-42 day follow up).	High	0	0	0	-1	0	0	0	0	Moderate	Moderate
None vs. <2 – 3 days	SSI*	1 RCT [44]	• No difference in 1 RCT subpopulation (n=38) of emergency colorectal procedures: 1/17 (5.8%) vs. 4/21 (20.0%); p=0.26 (35 day follow up).	High	0	0	0	-1	0	0	0	0	Moderate	Moderate
General Surgery - OTHER														
Appendectomy														

Comparis-on	Outcom-e	Quantity and Type of Evidence	Findings	Starting GRADE	Decrease GRADE					Increase GRADE			GRADE of Evidenc e for Outcom-e	Overall GRADE of Evidenc-e Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Confounders		
None vs. ≤24h	SSI*	4 RCT [11,22,25,31]	• No difference in a meta-analysis of 4 RCTs (N=1039), OR: 0.85 (0.52 – 1.41); p=0.54; I^2=0. • 1 RCT[11] of emergency non-perforated open appendectomies reported no difference in incisional wound infections between groups: 6/92 (6.5%) vs. 6/94 (6.4%) at 30 day follow. No deep incisional or organ/space infections were reported in either group. • 1 RCT [31](N=377) of emergency open appendectomies suggested no difference: 9/195 (4.6%) vs. 8/182 (4.3%); p=0.92. • 1 RCT [25] with subpopulation of appendectomies (n=247): 11/114 (9.6%) vs. 21/133 (15.8%); p=0.16. • Drug regimen 1 [22]: n=112: 4/54 vs. 4/58. • Drug regimen 2 [22]: n=117 2/63 vs. 0/54.	High	0	0	0	0	0	0	0	0	High	High
None vs. 2 days	SSI*	1 RCT [44]	• Increased risk of SSI with 2 days postoperative AMP: 1 RCT subpopulation of appendectomies (n=246): 3/127 (2.3%) vs. 10/119 (8.4%); p<0.05.	High	0	0	0	-1	0	0	0	0	Moderate	Moderate
Rectal surgery														
None vs. ≤24h	SSI*	1 RCT [26]	• No difference in 1 RCT subanalysis of 48 elective rectal surgery patients: 2/19 (10.5%) vs. 1/29 (3.4%); p=0.35. (1 month follow up). • Number of events is small.	High	0	0	0	-1	0	0	0	0	Moderate	Moderate
Gastric Surgery														
None vs. ≤24h	Organ/ space*	1 RCT [26]	• No difference in 1 RCT with subanalysis gastric procedures (n=64) including gastrectomy (n=8), gastric banding (n=35) and other gastric (n=21) reported deep surgical sepsis: 1/24 (4%) vs. 4/40 (10%); p=0.41.	High	0	0	0	-1	0	0	0	0	Moderate	Moderate

Comparis-on	Outcom-e	Quantity and Type of Evidence	Findings	Starting GRADE	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcom-e	Overall GRADE of Evidenc-e Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Confounders		
None vs. 2 days	SSI*	2 RCT [51,52]	• No difference in meta-analysis of 2 RCTs (N=683) of elective gastric cancer surgeries both with 30 day follow up and intraoperative AMP bolus administered every 3 hours of surgery. OR: 0.87 (0.28 – 2.65); p=0.80; I^2=71% • 1 RCT[52] (N=325) 15/164 (9.1%) vs. 10/161 (6.2%); there was a higher incidence of transfusion in the multiple dose group. • 1 RCT[51] (N=355) suggested no difference 8/176 (5%) vs. 16/179 (9%); p=0.138; there was a higher incidence of transfusion in the multiple dose group: 0/176 vs. 4/176 (2.2%).	High	-1	-2	0	0	0	0	0	0	Very Low	Very Low
	Organ/ Space SSI	2 RCT [51,52]	• No difference in metaanalysis of two RCTs. (N=683); OR: 1.08 (0.37 – 3.17); P=0.89; I^2=75%. • In 1 RCT[52] (N=325) there were fewer SSI in the multiple dose group but this difference was not significant: 11/164 (6.7%) vs. 6/164 (3.7%); p=NS (Note: 9/164 (5.5%) vs. 3/161 (0.9%) patients manifested both organ/space and incisional infections). • 1 RCT[51] (N=355) suggested fewer SSI in the single dose group but this was not significant 7/176 (4%) vs. 11/179 (6%); p=0.47.	High	-1	-2	0	0	0	0	0	0	Very Low	
	Incisional SSI	2 RCT [51,52]	• No difference in metaanalysis of two RCTs. (N=683); 0.79 (0.08 – 7.87); 0.84; I^2=75%. • In 1 RCT[52] (N=325) there were fewer SSI in the multiple dose group but this difference was not significant: 14/164 (8.5%) vs. 7/164 (4.3%) (Note: 9/164 (5.5%) vs. 3/161 (19%) patients manifested both organ/space and incisional infections). • 1 RCT[51] (N=355) suggested higher SSI in the	High	-1	-2	0	0	0	0	0	0	Very low	

Comparis-on	Outcom-e	Quantity and Type of Evidence	Findings	Starting GRADE	Decrease GRADE					Increase GRADE			GRADE of Evidenc-e for Outcom-e	Overall GRADE of Evidenc-e Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Confounders		
			multiple dose group but this difference was not significant: 1/176 (<1%) vs. 5/179 (3%); p=0.215.											
	Antimicr-obial Resista-nce	1 RCT [52]	• No difference in antimicrobial resistance between groups: 2/15 vs. 0/10.	High	-1	0	0	-1	0	0	0	0	Low	
None vs. 4 days	SSI*	1 RCT [53]	• No difference in 1 RCT of elective gastric surgery for gastric cancer (excluded colorectal surgery): 23/243 (9.5%) vs. 21/243 (8.6%) p=NS. (30 day follow up) • Overall SSI rate of 9.1% (44/486)	High	0	0	0	-1	0	0	0	0	Moderate	Moderate
	Organ/ Space SSI	1 RCT[53]	• No difference: 12/243(4.9%). Vs. 10/243(4.1%) p=NS	High	0	0	0	-1	0	0	0	0	Moderate	
	Incisional SSI	1 RCT [53]	• No difference: 14/243 (5.8%) vs. 11/243 (4.5%); p=NS	High	0	0	0	-1	0	0	0	0	Moderate	
	Antimicr-obial Resista-nce	1 RCT [53]	• No difference in isolate resistance patterns.	High	0	0	0	-1	0	0	0	0	Moderate	
Hepatectomy														
None vs. 3 days	SSI*	1 RCT [54]	• No difference in 1 RCT (N=188) in hepatectomies: 7/94 (7.5%) vs. 13/94 (13.8%); 14 day follow up; p=0.24. • Overall SSI rate: 10.6% (20/188).	High	0	0	0	-1	0	0	0	0	Moderate	Moderate
	Organ/ Space SSI	1 RCT[54]	• No difference: 4/94 (4.3%) vs. 11/91 (11.7%); p=0.10	High	0	0	0	-1	0	0	0	0	Moderate	

Comparis-on	Outcom-e	Quantity and Type of Evidence	Findings	Starting GRADE	Decrease GRADE					Increase GRADE			GRADE of Evidenc e for Outcom-e	Overall GRADE of Evidenc-e Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Confounders		
	Incisional SSI	1 RCT [54]	• No difference: 3/94 (3.2%) vs. 3/94 (3.2%); p=1.00	High	0	0	0	-1	0	0	0	0	Moderate	
	Length of Stay	1 RCT [54]	• There was a significantly longer length of stay in the multiple dose group: 12 (4-91) days vs. 14 (5-265) days; p=0.03	High	0	0	0	-1	0	0	0	0	Moderate	
2 days vs. 5 days	SSI*	1 RCT [55]	• No difference in 1 RCT (N=180) in hepatectomies: 4/89 (4.5%) vs. 4/91 (4.4%); 14 day follow up • Overall SSI rate: 4.4% (8/180)	High	0	0	0	-1	0	0	0	0	Moderate	Moderate
	Organ/ Space SSI	1 RCT [55]	• No difference: 2/89 (2.2%) vs. 3/91 (3.3%); p=0.67	High	0	0	0	-1	0	0	0	0	Moderate	
	Incisional SSI	1 RCT [55]	• No difference: 2/89 (2.2%) vs. 1/91 (1.1%); p=0.56	High	0	0	0	-1	0	0	0	0	Moderate	

*Critical outcome; OR: Odds Ratio; RR: Risk Ratio; CI: Confidence Interval

2.1A2. EVIDENCE TABLES: Q1 PARENTERAL AMP

Q1. What are the most effective strategies for administering parenteral AMP to reduce the risk of SSI?

Q1A. What is the optimal timing of preoperative AMP? Our search did not identify RCTs or SRs that evaluated different timings of preoperative AMP administration and its impact on the risk of SSI.

eTABLE 25. Evidence Table Q1A. Q1A. What is the optimal timing of preoperative AMP in surgeries involving tourniquet inflation?

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
Akinyoo-la 2011 [1] (ES)	**RCT** 1, 2	To compare the clinical outcomes in patients administered prophylactic antibiotics 5 minutes before exsanguination and inflation of the tourniquet (Intervention) and those administered prophylactic antibiotics 1 minute after inflation of the tourniquet (control) in elective lower limb orthopedic operations.	**Number of patients: N=106** **Patient Characteristics** ·Age, y: mean±SD Intervention: 25.6±2 SD (17.5) Control: 31.2±2 SD (20.6) p=0.687 ·Gender: 76/106 (71.7%) were male but not reported which group ·Obesity: NR ·Comorbidities: NR **Procedures:** Open reduction internal fixation 76/106 (71.7%)) Intervention: 40/52 (74.1%) Control: 36/54 (69.2%) Soft tissue release: 23/106 (21.7%) Intervention: 11/52 (20.4%) Control: 12/54 (23.1%) Triple arthrodesis 5/106 (4.7%) Intervention: 2/52 (3.7%)	**Intervention group:** n=52 Intravenous cefuroxime at a dose appropriate to the patient's age and body weight was administered 1 minute after tourniquet inflation followed by 3 doses at 8 hour intervals during the initial postoperative period. **Timing of intervention:** intraoperative **Duration of intervention:** NA **Device/agent:** cefuroxime **Monitoring intervention:** NA **Control group**: n=54 Intravenous cefuroxime at a dose appropriate to the patient's age and body weight was administered 5 minutes before tourniquet inflation followed by 3 doses at 8 hour intervals during the initial postoperative period. **Standard preventive measures:**	**SSI** Postoperative wound infection Intervention: 2/52 (3.9%) Control: 8/54 (14.8%) P=0.031 **Other infections:** NR **Topic-specific outcomes** Interval to wound healing, weeks: mean±SD Intervention: 3.0±0.5 Control: 4.0 ±2.3 P=0.002 **Reoperations:** NR **Length of stay:** NR **Mortality:** NR **Adverse events:** NR	**Definitions:** Wound infections: spontaneous drainage of pus after suture removal or in association with overt wound dehiscence. If a wound infection was identified in the postoperative period, a swab specimen of exudate was sent for microscopy, culture and sensitivity testing to guide subsequent antibiotic therapy. Wound healing: a well coated non-tender wound with a linear scar and no sign of infection. **Perioperative care** Anesthesia: all patients

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			Control: 3/54 (5.8%) Keller's operation 2/106 (1.7%) Intervention: 1/52 (1.9%) Control: 1/54 (1.9%) **Indications:** Tibial fracture 54/106 (50.9%) Intervention: 26/52 (50%) Control: 28/54 (51.9%) Ankle fracture/ dislocation 22/106 (20.8%) Intervention: 10/52 (19.2%) Control: 12/54 (22.2%) Hallux valgus 2/106 (1.9%)) Intervention: 1/52 (1.9%) Control: 1/54 (1.9%) Clubfoot 28/106 (26.4%) Intervention: 15/52 (28.9%) Control: 13/54 (24.1%) **Setting:** 1 university hospital **Location:** Nigeria **Dates:** February 2005 – January 2006 **Inclusion Criteria:** Patients who underwent clean, elective orthopedic	All operations were performed within 5 days of admission Tourniquet time (min) mean±SD Intervention: 69.8±32.8 Control: 75.3 ±30.8 P=0.396		underwent general anesthesia except for 2 who had spinal anesthesia Eparch bandage was used for exsanguination and the tourniquet was applied to the thigh in all cases **Other notes:** Underpowered to measure infection rates **Follow-up:** 12 months postop **Funding Source Conflicts:** Authors: NR Institution: NR Study: NR Supplies: NR

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			operations on the lower limbs with the use of a tourniquet hemostasis. **Exclusion Criteria:** NR			
Soriano 2008 [2] (ES)	**RCT** 1, 3, 4, 5, 10	To evaluate the importance of a "tourniquet-release" dose, with a randomized, double-blind study of primary total knee arthroplasty performed during ischemia.	**Number of patients: N=908** **Patient Characteristics:** no differences in characteristics between groups ·Age, y: mean±SD Intervention: 70.9±7.2 Control: 71.2±7.6 ·Gender: female% Intervention: 73.6% Control: 76.5% ·Obesity: Intervention: 37.8% Control: 35.5% ·Comorbidities Diabetes mellitus Intervention: 14.6% Control: 18.3% **Procedures:** Total knee arthroplasty **Indications:** Arthritis Intervention: 98.8% Control: 98.7% Rheumatoid arthritis Intervention: 1.2% Control: 1.3% **Setting:** Single center **Location:** Spain	**Intervention group:** n=466 Placebo administered 10-30 minutes before inflation of the tourniquet and 1.5g of cefuroxime was administered 10 min before release of the tourniquet. A postoperative dose of 1.5g cefuroxime administered at 6h after the end of the procedure. **Timing of intervention:** intraoperative **Duration of intervention:** NR **Device/agent:** 1.5g cefuroxime **Monitoring intervention** **Control group:** n=442 1.5g cefuroxime administered 10-30 minutes before inflation of the tourniquet and placebo was administered 10 min before release of the tourniquet. A postoperative dose of	**SSI** **NOTE**: when an infection was suspected, the patient underwent open debridement Total Deep SSI at 3 months = 24/908 (2.64%) Intervention: 9/466 (1.9%) Control: 15/442 (3.4%) P=0.21 Total cumulative Deep SSI at 12 months = 28/908 (3.08%) Intervention: 12/466 (2.6%) Control: 16/442 (3.6%) P=0.44 **Other infections:** NR **Topic-specific outcomes:** MSSA SSI at 3 months = 9/24 (37.5%) Intervention: 3/9 (33.3%) Control: 6/15 (40%) MSSA SSI between 4-12 months = 4/4 (100%) Intervention: 3/3 (100%) Control: 1/1 (100%)	**Definitions:** Deep tissue infection rate: CDC SSI Guideline Criteria **Perioperative care:** Anesthesia: spinal **Other notes:** Sample size calculated from a previous deep tissue infection rate (4%) in the institution. **Follow-up:** 12 months post discharge **Funding Source Conflicts:** Authors: None Institution: NR Study: NR Supplies: NR

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			Dates: September 2004 – December 2005. **Inclusion Criteria:** Patients undergoing a primary total knee arthroplasty who signed the informed consent. **Exclusion Criteria:** Patients allergic to penicillin	1.5g cefuroxime administered at 6h after the end of the procedure. **Standard preventive measures:** Laminar Air Flow: not used Skin Prep: leg washed with soap then with 10% povidone iodine solution. Cement – All prostheses cemented and none used antimicrobial impregnated cement. Drains: 1 profound and 1 superficial drain tube left after closing the wound were removed within the first 48 hours after the surgical procedures Transfusion: during the surgical procedure and the first 6h after the procedure, an RBC transfusion was given when the hemoglobin level was <9g/dL. After this period, the threshold for RBC transfusion was <8g/dL Mean no of transfusions ±SD Intervention: 0.9±1.3 Control: 0.8±1.3 Duration of ischemia: (mean±SD, min)	MRSA SSI at 3 months = 6/24 (25%) Intervention: 1/9 (11.1%) Control: 1/15 (6.67%) MSSA SSI between 4-12 months = 0/4 Intervention: 0/3 Control: 0/1 COPD with/without deep tissue infection at 12 months Uninfected (n=880): 9.5% Infected (n=28): 21.4% P=0.05 ASA Score 3-4 at 12 months Uninfected (n=880): 129 (14.8%) Infected (n=28): 12 (42.9%) P<0.001 Low 4th day hematocrit infection rate at 12 months Uninfected (n=880): 28.3±3.8 Infected (n=28): 26.5±4.1 P=0.02 **Reoperations:** NR All deep prosthetic joint infections included an open debridement and ≥3 deep cultures of synovial fluid samples and periprosthetic	

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
				Intervention: 54.1±17.9 Control: 53.9±18.3	tissue samples from different sites. **Length of stay,** days**:** mean±SD Intervention: 6.4±1.6 Control: 6.5±2.1 **Mortality:** NR **Adverse events:** NR	

eTABLE 26. Evidence Table for Q1B. What is the optimal timing of AMP in cesarean section: prior to skin incision or at cord clamping?

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
Osman 2013 [3] (ES)	**RCT** 1, 2, 3, 4, 10	To investigate the timing of prophylactic ceftizoxime for elective cesarean delivery at the study hospital.	**Number of patients: N=180** **Patient Characteristics** ·Age, y, mean (SD) Intervention: 30.5 (7.4) Control: 32.2 (5.2) P=0.08 ·Gender: all female ·Obesity: BMI, mean Calculated by extractor from mean height & mean weight in study Intervention: 30.9 Control: 31.2 P=0.1 ·Comorbidities: NR	**Intervention group:** n=90 Patients who received a single intravenous injection of 1g ceftizoxime 40 minutes pre-incision **Timing of intervention:** preoperative **Duration of intervention:** NA **Device/agent:** 1g ceftizoxime **Monitoring intervention:** NA **Control group:** n=90 Patients who received a single intravenous injection of 1g	**SSI:** Endometritis Intervention: 0/90 Control: 0/90 Superficial wound infection: Intervention: 8/90 (6.7%) Control: 3/90 (3.3%) P=0.2 (all incidences occurred post-discharge) **Other infections:** NR **Topic-specific outcomes:** **Neonatal outcomes** Admission to the nursery: Intervention: 15/90	**Definitions:** Post-operative febrile morbidity: an oral temperature of ≥38^{0}C on two occasions at least 4 hours apart, excluding the first 24h. Postoperative infection Endometritis: fever, uterine tenderness, and abnormal lochia Wound infection: fever, cellulitis &

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			Gestational age, weeks: mean (SD) Intervention: 38.2 (1.1) Control: 38.3 (0.9) P=0.7 Gravidity: mean (SD) Intervention: 3.5 (1.6) Control: 36.9 (0.4) P=0.5 **Procedures:** elective cesarean section **Indications:** Repeated cesarean delivery: Intervention: 55/90 (61.1%) Control: 61/90 (67.8%) P=0.1 Breech presentation: Intervention: 10/90 (11.1%) Control: 8/90 (8.9%) P=0.6 Hypertensive disorder Intervention: 2/90 (2.2%) Control: 1/90 (1.1%) P=0.5 Bad obstetrics events Intervention: 7/90 (7.8%) Control: 11/90 (12.2%) P=0.3 Others Intervention: 16/90 (17.8%) Control: 9/90 (10%) P=0.1	ceftizoxime post cord clamping **Standard preventive measures :** NR	(16.7%) Control: 15/90 (16.7%) P=0.1 Jaundice Intervention: 5/90 (5.5%) Control: 4/90 (4.4%) P=1.0 **Reoperations:** NR **Length of stay:** NR **Mortality:** NR **Adverse events:** Skin rash Intervention: 0/90 (0) Control: 1/90 (1.1%) P=1.0	exudates Peritonitis: elevated temperature, tachycardia, abdominal distension and pain with guarding and rigidity aggravated by moving and breathing with absent bowel sounds at the onset of paralytic ileus. **Perioperative care:** NR **Other notes:** study was underpowered **Follow-up:** 6 weeks post op at clinic visit. **Funding Source Conflicts:** Authors: None Institution: NR Study: Industry Supplies: NR

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			Setting: 1 university hospital **Location:** Sudan **Dates:** May 2011 – August 2011 **Inclusion Criteria:** Patients who were planned for elective cesarean delivery (e.g. repeated scars, breech and low lying placenta) **Exclusion Criteria:** Severe anemia, twins, diabetes mellitus, impaired glucose test, received antibiotics within 2 weeks prior to the operation, if they had any visible infection at any site or elevated temperature at the time of the operation; if they were allergic to drug used; or refusal to participate in study			

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
Witt 2011 [5] (ES)	**RCT** 1, 2, 3, 4, 5, 6, 7, 8, 9	To compare the effectiveness of cefazolin, a first-generation cephalosporin, administered before skin incision vs. after umbilical cord clamping vs. placebo in a 3-arm randomized trial of women undergoing elective cesarean delivery.	**Number of patients: N=741** **Patient Characteristics** ·Age, y: mean (SD) Intervention: 31.3 (6.3) Control: 32.2 (5.8) ·Gender: all female ·Obesity: BMI (kg/m^2), mean (SD) Intervention: 28.3 (5.4) Control: 28.3 (5.4) ·Comorbidities: Gestational diabetes mellitus, Intervention: 39/370 (10.5%) Control: 33/371 (8.9%) History of allergy Intervention: 27/370 (17.3%) Control: 30/371 (8.1%) Immunosuppression, Intervention: 4/370 (1.1%) Control: 2/371 (0.5%) Anticoagulation: Intervention: 9/370 (2.4%) Control: 12/371 (3.2%) **Procedures:** elective cesarean delivery. **Indications:** NR **Setting:** 1 university hospital **Location:** Austria **Dates:** March 1, 2004 – January 31, 2010	**Intervention group:** n=370 2g of cefazolin mixed with 100mL saline administered 20-30 minutes before skin incision **Timing of intervention:** preoperative **Duration of intervention:** NA **Device/agent:** 2g cefazolin in 100mL saline **Monitoring intervention:** NA **Control group:** n=371 2g cefazolin in 100mL saline administered at cord clamping **Standard preventive measures:** NR	**SSI:** Local Wound Infection (LWI), Intervention: 9/370 (2.4%) Control: 9/371 (2.4%) Risk difference: 1.1%, 95%CI (-1.8%-4.0%); P=0.60 LWI during hospital stay Intervention: 6/370 (1.6%) Control: 8/371 (2.2%) LWI at 3 weeks postpartum Intervention: 3/370 (0.8%) Control: 1/371 (0.3%) Endometritis: Intervention: 1/370 (0.3%) Control: 1/371 (0.3%) Endometritis during hospital stay Intervention: 0/370 Control: 1/371 (0.3%) Endometritis at 3 weeks postpartum Intervention: 1/370 (0.3%) Control: 0/371 **Other infections:** Urinary tract infection (UTI), Intervention: 8/370 (2.2%)	**Definitions:** Wound infection: purulent discharge or erythema (>1cm in diameter) and induration of the incision site. Urinary tract infection: if there were clinical symptoms (i.e. polyuria and dysuria) and a positive urine dipstick nitrite test result. **Perioperative care:** delivery performed by resident under the supervision of fully trained attending physicians using a modified Misgav Ladach technique. **Other notes:** power calculation demonstrated a sample size of 360 per arm for a power of 90% to detect an absolute reduction of 5% in primary

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			Inclusion Criteria: women undergoing cesarean delivery with a gestational age of at least 37 weeks and reassuring fetal heart traces. Women who experienced rupture of membranes and labor contractions were also included **Exclusion Criteria:** fever >38°C, cephalosporin allergy, age <18 years, and exposure to any antibiotic agent within 1 week before delivery.		Control: 4/371 (1.1%) UTI during hospital stay Intervention: 5/370 (1.4%) Control: 4/371 (1.1%) UTI at 3 weeks postpartum Intervention: 3/370 (0.8%) Control: 0/371 **Topic-specific outcomes:** Pelvic Abscesses Intervention: 1/370 (0.3%) Control: 1/371 (0.3%) **Neonatal Outcomes:** showed no statistically significant difference between groups (data not shown) **Reoperations:** NR **Length of stay** days**:** mean (SD), Intervention: 5.5 (1.6) Control: 5.5 (1.9) **Mortality:** NR **Adverse events:** NR	outcome at α=0.05 **Follow-up:** 30 days postop via telephone survey. If patients reported any of the signs & symptoms of an outcome measure, they were asked to report to the clinic for confirmation **Funding Source Conflicts:** Authors: NR Institution: NR Study: NR Supplies: NR
Macones 2011 [4] (ES)	**RCT** 1, 2, 3, 4, 5, 6, 9	To compare maternal and neonatal outcomes in women who receive prophylactic antibiotics	**Number of patients: N=434** **Patient Characteristics:** both groups were similar with respect to baseline demographics	**Intervention group:** n=217 1 g Cefazolin given <30 minutes prior to skin incision. **Timing of intervention:** preop **Duration of intervention:**	**NOTE: study reported percentages only. Numerators were calculated by extractor:** **SSI:** Wound infection:	**Definitions:** Maternal infectious morbidities: (1) postoperative fever (defined as oral temp >38°C on two separate occasions more

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
		prior to skin incision with those who receive antibiotics at cord clamping	·Age, y: mean Intervention: 28.9 Control: 28.3 P=0.27 ·Gender: all females ·Obesity: Not reported but cited as similar at baseline ·Comorbidities: NR African American race: Intervention: 65.3% (142/217) Control: 64.7 (140/217) P=0.99 Gravidity: mean Intervention: 3.5 Control: 3.3 P=0.17 Gestational Age, weeks: mean Intervention: 38.7 Control: 38.9 P=0.70 **Procedures:** Scheduled cesarean Intervention: 73.4% (159/217) Control: 71.4% (155/217) P=0.62 Low transverse cesarean Intervention: 95.4% (207/217) Control: 95.4% (207/217) P=1.00	NA **Device/agent:** 1 g cefazolin **Monitoring intervention:** NA **Control group**: n=217 1g Cefazolin given at cord clamping **Standard preventive measures:** Antimicrobial prophylaxis: patients received 1g cefazolin. If allergic to penicillin, they received 900mg clindamycin. Cefazolin: Intervention: 90.2% (196/217) Control: 92.1% (200/217) P=0.71	Intervention: 0.5% (1/217) Control: 1.4% (3/217) RR: 2.8 (0.7-4.2), P=0.37 Endometritis Intervention: 2.8% (6/217) Control: 2.8% (6/217) RR: 1.0 (0.7-1.3), P=1.00 **Other infections:** Urinary Tract Infection: Intervention: 0.9% (2/217) Control: 0.9% (2/217) RR: 1.0 (0.3-4.0), P=1.00 **Topic-specific outcomes:** Fever: Intervention: 2.3% (5/217) Control: 3.7% (8/217) RR: 1.6 (0.8-2.2), P=0.42 **Neonatal outcomes:** NICU Admission Intervention: 3.5% (8/217) Control: 4.0% (9/217) RR: 1.1 (0.7-1.8) Suspected sepsis Intervention: 8.9% (19/217) Control: 8.9% (19/217) RR: 1.0 (0.7-1.3)	than 6h apart, after the initial 24h postop period); (2) wound infection (defined as purulent discharge from the incision); (3) endomyometritis (defined as fundal tenderness and fever); (4) urinary tract infection (defined as fever, positive urine culture). **Perioperative care:** Patients were managed in the postpartum period at the discretion of treating physicians. Regional Anesthesia Intervention: 92.1% (200/217) Control: 90.6% (197/217) P=0.88 **Other notes:** 217 subjects per arm

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			Indications **Setting:** 2 university hospitals **Location:** USA **Dates:** NR **Inclusion Criteria:** those undergoing nonemergency cesarean surgery at 36 weeks' gestation or greater. (Pregnancies were dated by best obstetric estimate using standard criteria.) **Exclusion Criteria:** known fetal anomaly, exposure to antibiotics within 7 days of admission (including intrapartum Group B *Streptococcus* prophylaxis), need for emergency cesarean delivery (i.e. for category III electronic fetal monitoring, maternal distress, obstetric hemorrhage), rupture of membranes >18h, and overt maternal intrapartum infection requiring antibiotics.		**Reoperations:** NR **Length of stay:** NR **Mortality:** NR **Adverse events:** NR	was calculated to see a decrease in the composite maternal infectious morbidity rate of 10% in the cord clamp group (based on pilot data), with type I error of 0.05, type II error of 0.20. **Follow-up:** in the hospital and postpartum stay. **Funding Source Conflicts:** Authors: NR Institution: NR Study: NR Supplies: NR

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
Yildirim 2009 [6] (ES)	**RCT** 1, 7, 8, 9	The aim was to determine whether the timing of prophylactic antibiotics at cesarean delivery influences maternal and neonatal infectious morbidity.	**Number of patients: N=389** Patient Characteristics: no significant differences in demographics between groups ·Age, y: mean ± SD Intervention: 28.25±4.87 Control: 27.53±5.02 P=0.15 ·Gender: all female ·Obesity: BMI (kg/m^2): mean ±SD Intervention: 31.98±2.89 Control: 31.96±2.29 P=0.93 ·Comorbidities Gravidity: mean±SD Intervention: 2.57±1.05 Control: 2.45±1.05 P=0.25 Parity: mean±SD Intervention: 1.14±0.67 Control: 1.11±0.68 P=0.59 Gestational Age at delivery: mean±SD, weeks Intervention: 38.32±0.94 Control: 38.24±0.69 P=0.31 **Procedures:** elective	**Intervention group:** n=194 1g cefazolin sodium administered 10-45min prior to skin incision. **Timing of intervention:** preop **Duration of intervention:** NA **Device/agent:** 1g cefazolin sodium **Monitoring intervention:** NA **Control group:** n=195 1g cefazolin sodium was administered after clamping of the umbilical cord. **Standard preventive measures** Antibiotic prophylaxis: 1 g of cefazolin sodium was used for antibiotic prophylaxis. No other antimicrobial prophylaxis was administered unless a postoperative infection was diagnosed. Catheter: a foley catheter was inserted pre-cesarean section and removed postop. Skin prep – the abdomen was cleaned with a povidone iodine solution. Incision: Pfannistiel	**SSI:** Wound infection: Intervention: 6/194 (3.1%) Control: 8 (4.1%) P = 0.59 RR: 1.34, 95%CI (0.45-3.93) Endometritis: Intervention: 5/194 (2.6%) Control: 7/195 (3.6%) P = 0.56 RR: 1.40, 95%CI (0.43-4.51) **Other infections:** Urinary Tract Infections: Intervention: 3/194 (1.5%) Control: 5/195 (2.6%) P = 0.47 RR: 1.67, 95%CI (0.39-7.11) **Topic-specific outcomes:** Postoperative hematocrit level, %: mean±SD, Intervention: 30.17±0.97 Control: 30.04±0.92 P=0.18 Postoperative hemoglobin level, (g/l): mean±SD Intervention: 9.91±0.50 Control: 9.78±0.59 P=0.02 Estimated blood loss, (ml): mean±SD	**Definitions :** Elective cesarean section: Cesarean section performed before the presence of labor Wound infection: signs of erythema, swelling, discharge or tenderness Urinary tract infection: clinical signs were checked and a urinalysis was performed. Neonatal sepsis: suspected if tachycardia and/or tachypnea as well as an increased white count with bands was present and was confirmed by positive culture. **Perioperative care:** NR **Other notes:** Prior to this study, the institution had a 20%

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			cesarean section **Indications:** indications for cesarean section were similar when the two groups were compared Previous cesarean, Intervention: 168 (86.6%) Control: 173 (88.7%) Multiple pregnancy Intervention: 5 (2.6%) Control: 5 (2.6%) Fetal macrosomia (>4500g) Intervention: 8 (4.1%) Control: 6 (3.1%) Breech and malpresentation, Intervention: 13 (6.7%) Control: 10 (5.1%) Placenta previa Intervention: 0 Control: 1 (0.5%) **Setting:** 1 tertiary care hospital **Location:** Turkey **Dates:** June 2007 – December 2007 **Inclusion Criteria:** Women undergoing elective cesarean section at the hospital without exclusion criteria **Exclusion Criteria:** use of antibiotics	incisions were done on all patients, followed by transverse lower uterine segment incision and delivery of the fetus and placenta. Closure: suturing of the uterine incision was performed without exteriorization of the uterus. The abdominal wall was closed in two layers then skin incisions were closed.	Intervention: 656.29±190.54 Control: 668.92±203.57 P=0.52 Operative time, (min): mean±SD Intervention: 36.63±2.66 Control: 37.12±3.89 P=0.14 **Neonatal outcomes:** Intervention: n=201 Control: n=198 Birth weight, (g): mean±SD Intervention: 3263.75±505.86 Control: 3232.92±500.26 P=0.53 5-minute Apgar score: mean±SD Intervention: 9.08±0.71 Control: 9.06±0.78 P=0.79 Neonatal Sepsis: Intervention: 9/201 (4.4%) Control: 13/198 (6.3%) P = 0.38 RR: 1.47 (0.61-3.53) NICU Admission Intervention: 4/201 (2%) Control: 7/198 (3.4%) P = 0.35 RR: 1.77 (0.51-6.16) Sepsis workup: Intervention: 23/201 (11.2%) Control: 30/198 (14.6%)	postcesarean endometritis rate. Study power. A sample size of 197 was calculated to provide 80% power to detect a 50% difference in postoperative infections, with α=0.05 **Follow-up:** 6 weeks postop **Funding Source Conflicts:** Authors: None Institution: None Study: None Supplies: None

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			during the last 24h, pathology that should be treated with antibiotics, pre-existing maternal diseases (such as diabetes, collagen vascular disease, immune system problems), chorioamnionitis, fever on admission, need of transfusion before or during the cesarean section, ruptured membranes, emergency cesarean section, and pre-term cesarean section.		P = 0.30 RR: 1.35 (0.75-2.42) NICU Length of Stay, days: mean±SD Intervention: 8.25±2.62 Control: 5.66±2.58 P=0.16 **Reoperations:** NR **Length of stay,** days**:** mean±SD Intervention: 2.30±1.09 Control: 2.39±1.18 p=0.46 **Mortality:** NR **Adverse events:** There were no serious side effects related to the use of cefazolin.	
Sullivan 2007 [8] (ES)	**RCT** 1, 2, 3, 4, 5, 6, 7, 8, 9, 10	To conduct a prospective, double-blind, randomized clinical trial to determine whether antibiotic prophylaxis administered preoperatively is more effective in preventing infectious morbidity following cesarean	**Number of patients: N=357** **Patient Characteristics:** No significant differences found between groups. ·Age, y: mean Intervention: 28.3±6.1 Control: 28.3±6.0 ·Gender: All Female ·Obesity (Maternal Weight) mean ±SD Intervention: 225.3±144.5 Control: 228.1±152.9 ·Comorbidities:	**Intervention group:** n=175 Received 1gm cefazolin mixed with 50 cc normal saline 15-60 minutes prior to incision. Placebo (50 cc normal saline) administered at cord clamp **Timing of intervention:** Pre and Intraoperative **Duration of intervention:** preoperative (Intervention) and Intraoperative (Control) **Device/agent:** Cefazolin **Monitoring intervention:**	**SSI: (Follow up 6 weeks)** Wound Infections Intervention: 5/175 (3%) Control: 10/182 (5%) Relative Risk (95% CI) 0.52 (0.18-1.5) P>0.05 Adjusted OR (95% CI) 0.4 (0.1-1.3) Endomyometritis Intervention: 2/175 (1%) Control: 10/182 (5%) Relative Risk (95% CI) 0.2 (0.2-0.94) P<0.05 Adjusted Odds Ratio (95% CI) 0.22 (0.05-0.9)	**Definitions:** Endomyometritis: maternal fever greater than 100.4°F on 2 separate occasions along with uterine fundal tenderness, tachycardia or leukocytosis. Wound Infection: purulent discharge, erythema, and induration of the incision site.

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
		delivery than administration following cord clamp.	Diabetes Intervention: 17/175 (10%) Control: 29/182 (16%) Preeclampsia Intervention: 18/175 (10.3%) Control: 25/182 (13.7%) Operative Time, min: mean ±SD Intervention: 43.5±13.6 Control: 48±14.9 Parity: mean Intervention: 1.4 Control: 1.2 Premature delivery (<37wks): Intervention: 30/175 (17%) Control: 46/182 (25%) **Procedures:** Cesarean Section Delivery; Performed by resident physicians as primary surgeons which resulted in increased average surgery time **Indications:** Arrest disorders Intervention: 50/175 (28.6%) Control: 53/182 (29.1%)	NR **Control group:** n=182 Received placebo (50 cc normal saline) 15-60 min prior to incision. 1gm cefazolin mixed with 50 cc normal saline administered at the time of cord clamping. **Standard preventive measures:** NR	<u>Total Infectious Morbidity</u> Intervention: 8/175 (4.5%) Control: 21/182 (11.5%) Relative Risk (95% CI) 0.4 (0.18-0.87) Statistically significant Adjusted OR (95% CI) 0.35 (0.14-0.82) **Other infections:** Pyelonephritis: 1 case in intervention group. Pneumonia: 1 case in control group **Topic-specific outcomes:** <u>Neonatal outcomes</u> Sepsis Intervention: 6/185 (3%) Control: 7/194 (3.6%) Suspected sepsis Intervention: 35/185 (19%) Control: 36/194 (18.5%) No difference in causative organisms or increased incidence of antibiotic resistant organisms. NICU Admission Intervention: 25/175 (14.3%) Control: 33/182 (18.3%) P=0.40 NICU Days: mean±SD Intervention: 14.2±15.8 Control: 19.7±24.9 P=0.01 No statistical difference in	<u>Hematomas, seromas, or wound breakdowns</u>: in the absence of previously discussed signs were not considered wound infections. <u>Neonatal Sepsis</u>: diagnosed by a positive blood culture. **Perioperative care:** NR **Other notes:** Weakness of this study is the high-risk nature of the study population. They were more obese, more likely to have diabetes, preterm delivery, multiple gestation and be of minority ethnicity than the general population. The location of the trial was in a tertiary care center. **Follow-up:**

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			Non-reassuring fetal status Intervention: 36/175 (20.6%) Control: 39/182 (21.4%) Not laboring Intervention: 51/175 (29.1%) Control: 44/182 (23.8%) Other Intervention: 38/175 (21.7%) Control: 45/182 (24.7%) **Setting:** 1 Tertiary Care Hospital **Location:** USA **Dates:** NR (26 months total) **Inclusion Criteria:** Women whose pregnancies were older than 24 weeks estimated gestational age and required cesarean delivery **Exclusion Criteria:** cephalosporin allergy, gestational age less than 18 weeks, exposure to any antibiotic agent within 1 week of delivery, or the need for emergent cesarean delivery.		terms of birth weight, gestational age, septic workup, intermediate admission, NICU admission, length of stay or pH<7.1 **Reoperations:** NA **Length of stay:** NR (NICU, see above) **Mortality:** NR **Adverse events:** No cases of maternal anaphylaxis or other adverse events related to cefazolin use reported during the trial. Hematomas & Seromas that did not meet criteria for wound infections: 7 cases total	Through their hospital course and up to the 6-week postpartum visit. **Funding Source Conflicts:** Authors: None Institution: None Study: None Supplies: None

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
Thigpen 2005 [7] (ES)	**RCT** 1, 2, 3, 4, 5, 6, 7, 8, 9	To determine if the administration of prophylactic antibiotics for cesarean section at the time of cord clamping, as opposed to immediately before the skin incision, influences the incidence of maternal infectious morbidity and/ or negatively impacts upon the neonatal course.	**Number of patients: N=302** **Patient Characteristics:** No significant statistical difference existed in baseline characteristics between groups ·Age, y: mean±SD Intervention: 23.5±5.7 Control: 24.3±5.9 ·Gender: 100% Female ·Obesity: NR ·Comorbidities: NR Time after ruptured membranes, h: mean±SD Intervention: 7.2±5.8 Control: 8.6±6.4 P=0.045 Gestational age at delivery, nulliparity and history of previous cesarean delivery, need for cervical ripening, induction, cervical exam on admission, cervical dilatation was similar. **Procedures:** Cesarean section delivery **Indications:** Arrest disorder Intervention: 86/153 (56.2%) Control: 91/149 (61.1%)	**Intervention group:** n=153. Received 2g cefazolin in fluid just before skin incision and placebo at cord clamping **Timing of intervention:** pre and intraoperatively **Duration of intervention:** preoperative (intervention) and intraoperative (at clamping) **Device/agent:** Cefazolin **Monitoring intervention:** NR **Control group:** n=149 Received placebo just before skin incision and 2g cefazolin in fluid at cord clamping **Standard preventive measures:** ABX: Group B Streptococcal ABX Intervention: 27/153 (17.6%) Control: 40/ 149 (26.8%) RR (95% CI): 0.74 (0.55-1.03) No other antibiotics were given unless a postoperative infection was diagnosed.	**SSI: (follow up 6 weeks)** Wound Infection: Intervention: 6/153 (3.9%) Control: 8/149 (5.4%) RR (95% CI): 0.84 (0.45-1.55) Not statistically significant Endometritis Intervention: 12/153 (7.8%) Control: 22/149 (14.8%) RR (95% CI): 0.67 (0.42-1.07) Not statistically significant ITT Analysis Maternal infection: RR (95% CI): 0.81 (0.52-1.40) **Other infections:** No cases of maternal Pneumonia or Pyelonephritis. **Topic-specific outcomes:** Neonatal morbidity No statistically significant difference between the two groups (birth weight, Apgars, UaPh, NICU admissions, sepsis or sepsis workup, or maternal comorbidities or contributing factors.	**Definitions:** Endometritis: Maternal temperature ≥100.4°F on 2 separate occasions 6 hours apart exclusive of the first 12 hours following surgery, accompanied by uterine tenderness and/ or purulent or foul smelling lochia. Wound infection: with or without an elevated maternal temperature, accompanied by tenderness with wound dehiscence, breakdown of the surgical edges, and/ or purulent drainage Urinary tract infection: Maternal temperature ≥100.4°F on 2 separate occasions 6

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			Fetal Distress Intervention: 17/153 (11.1%) Control: 18/149 (12.1%) Other Intervention: 50/153 (32.7%) Control: 40/149 (26.8%) P=.541 **Setting:** 1 Regional Medical center **Location:** USA **Dates:** NR (30 month period) **Inclusion Criteria:** Singleton pregnancies if the patient had labored and required cesarean surgery. Group B Strep prophylaxis (aqueous penicillin) was allowed. **Exclusion Criteria:** Multiple pregnancies, acute chorioamnionitis, allergy to penicillin or cephalosporins, cesarean section without labor, or the administration of systemic antibiotics within the past 2 weeks.		Infection: Intervention: 20/153 (13.1%) Control: 21/149 (14.1%) RR (95% CI): 0.96 (0.68-1.34) Sepsis Intervention: 7/153 (4.6%) Control: 7/149 (4.7%) RR (95% CI): 0.96 (0.58-1.69) Suspected sepsis Intervention: 11/153 (7.2%) Control: 14/149 (9.4%) RR (95% CI): 0.76 (0.47-1.22) Pneumonia Intervention: 1/153 (0.7%) Viral Syndrome Intervention: 1/153 (0.7%) Pyelonephritis: none NICU Admission Intervention: 14/153 (9.2%) Control: 8/149 (5.4%) RR: 1.28, 95%CI (0.91-1.79) **Reoperations:** NA **Length of stay:** NR **Mortality:** NR **Adverse events:** NR	hours apart exclusive of the first 12 hours following surgery, with a positive urine culture, abnormal urinalysis, and flank pain. Pneumonia: hyperpyrexia, as well as x-ray and physical examination findings consistent with lung consolidation. Neonatal Sepsis: Suspected if tachycardia and/ or tachypnea, as well as an increased white count with bands, was present and was confirmed by positive blood cultures. **Perioperative care:** Most women had regional anesthesia. General Anesthesia Intervention: 16/153 (10.5%)

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
						Control: 17/ 149 (11.4%) RR (95% CI): 0.95 (0.66-1.38) **Other notes:** Prospective power analysis performed for risk of endometritis and wound infection determined that 270 women in each arm were sufficient (power 0.80) to detect 10% difference. (Based on projected 10% risk of infection in post-cesarean population). An interim analysis was planned for the power analysis because the investigation was not concluded near the completion (4 months) of the fellowship of the senior author. The interim power analysis indicated that with the rate of infection being

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
						50% more than expected for the 2 groups, there was an 80% power to detect a difference with a total of 300 randomized women. **Follow-up:** For 6 weeks postpartum. **Funding Source Conflicts:** Authors: NR Institution: NR Study: NR Supplies: NR
Wax 1997 [9] (ES)	**RCT** 1, 2, 3, 4, 5, 6, 7, 8, 9, 10	To test the hypothesis that a single 1 g dose of cefazolin administered preoperatively is no more effective than one administered after cord clamping in preventing post-cesarean infections	**Number of patients: N=90** **Patient Characteristics:** Patients were similar between groups with regards to: · Maternal Age, y: mean±SD Intervention: 24.7±4.5 Control: 25.2±4.8 ·Gender: 100% Female ·Obesity: Weight: mean±SD Intervention: 191±26 lb. Control: 189±32 lb. ·Comorbidities: NR Duration of labor mean±SD Intervention: 13.0±7.2	**Intervention group:** n=49 1g cefazolin in 50 ml 0.9% saline administered within 5 min of deciding to proceed with cesarean delivery. The placebo of 50 ml 0.9% saline was administered over 5 minutes at cord clamping **Timing of intervention:** Pre and intraoperatively **Duration of intervention:** Intra and postoperatively **Device/agent:** Cefazolin **Monitoring intervention:** NR **Control group:** n=41 50 ml 0.9% saline was administered within 5	**SSI (follow up 2 & 6 weeks)** Wound infection: Intervention: 1/49 (2%) Control: 2/41 (4.9%) P=0.35 Endometritis: Intervention: 1/49 (2%) Control: 1/41 (2.4%) 1 subject in Intervention group experienced both endometritis and wound infection. **Other infections:** No secondary infections were seen in either group **Topic-specific outcomes:** Neonatal Morbidity: Pneumonia:	**Definitions:** Endometritis: Fever to 100.4°F on 2 occasions at least 6h apart or a single fever ≥101°F outside the first 24h following delivery associated with uterine or parametrial tenderness, malodorous or purulent lochia, or leukocytosis Wound infection: Incisional erythema, tenderness,

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			h Control: 9.9±7.3 h P=0.03 Duration of internal monitors mean±SD Intervention: 11.1±4.2 h Control: 9.3±4.7 h P=0.04 Newborn 1 and 5 minute Apgar scores<7, umbilical arterial cord pH<7.20 and NICU admissions similar between two groups **Procedures:** (not statistically significant between groups) Primary: 61/90 (67.8%) Primary w/ tubal ligation: 5/90 (5.6%) Repeat: 18/90 (20%) Repeat with tubal ligation: 6/90 (6.7%) All procedures were performed by surgical residents under the supervision of attending physicians. **Indications:** Arrest of dilation or descent: Intervention: 30/49 (61.2%) Control: 20/41 (48.8%) Fetal Distress	minutes of deciding to proceed with cesarean delivery. The 1.g of cephazolin in 50 ml 0.9% saline was administered over 5 minutes at cord clamping. **Standard preventive measures:** AMP: Time from first infusion to incision (min) mean ±SD Intervention: 35±31 Control: 36±26 Skin prep: All patients received identical skin prep of iodophor and isopropyl alcohol. Surgical Drape: Occlusive adhesive surgical drapes were used for each case. **Nonstandard preventive measures:** Technique: Intraoperative technique was determined by surgeon	Intervention: 2/49 (4.1%) Control: 0/41 Febrile illness readmissions Intervention: 2/49 (4.1%) Control: 0/41 No source of infection was identified in either neonate Treatment: Both discharged after receiving 72h of antibiotics and no further sequelae Suspected Sepsis workup: Intervention: 6/49 (12.2%) Control: 2/41 (4.9%) P=0.28 Workup was negative in all Meningitis: none Delayed onset or partially treated infections 2weeks: 84 infants : none 6 weeks: 76 infants: none **Reoperations:** NA **Length of stay:** NR **Mortality:** NR **Adverse events:** None reported for mothers or infants.	warmth, with or without purulent drainage. Intra-abdominal abscesses, septic pelvic thrombophlebitis, or symptomatic urinary tract infection: ND Neonatal Outcomes: Sepsis screen, sepsis, pneumonia (based on clinical and radiographic findings), and meningitis: ND **Perioperative care:** Indwelling catheter: placed preoperatively for bladder drainage. **Other notes:** None **Follow-up:** Mothers were counseled verbally and given written instructions describing signs of infection before leaving the hospital and scheduling

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			Intervention: 3/49 (6.1%) Control: 9/41 (22.0%) P=0.03 Malpresentation Intervention: 4/49 (8.2%) Control: 6/41 (14.6%) Repeat in labor Intervention: 4/49 (8.2%) Control: 5/41 (12.2%) Other Intervention: 8/49 (16.3%) Control: 1/41 (2.4%) P=0.03 **Setting:** 1 Military Hospital **Location:** USA **Dates:** NR (12 month period) **Inclusion Criteria:** Singleton subjects undergoing cesarean delivery at ≥37 week gestation. **Exclusion Criteria:** Penicillin or cephalosporin allergy, antibiotic use within 2 weeks of delivery, temperature ≥37.8^{o}C in labor, administration of group B streptococcal or sub-acute bacterial			follow-up. Mothers were contacted by phone or seen in clinic at 2weeks (n=83/90; 11 by phone and 72 in clinic) and 6 weeks (n=76/90; 5 by phone and 71 in clinic_ after delivery. Infants were examined by a pediatrician 2 weeks post-partum. Mothers were interviewed and infant charts reviewed at 6 weeks of life. **Funding Source Conflicts:** Authors: None Institution: None Study: None Supplies: None

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			endocarditis prophylaxis during labor, insulin-dependent diabetes mellitus, human immunodeficiency virus infection, chronic glucocorticoid use, or multiple gestation.			

Q1C. How safe and effective is weight-adjusted AMP dosing? Our search did not identify RCTs or SRs that evaluated weight-adjusted AMP dosing and its impact on the risk of SSI.

eTABLE 27. Evidence Table for Q1D. How safe and effective is intraoperative redosing of AMP?

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
Cuthbert-son 1991 [10] (ES)	**RCT** 1, 2, 4, 7	To determine whether a double dose of intravenous Timentin provides superior prophylaxis with respect to postoperative wound infection compared with a single dose, they performed a controlled clinical trial in patients undergoing elective colorectal surgery.	**Number of patients N=278** **Patient Characteristics:** there were no statistically significant differences between groups. Age: NR Gender: NR Obesity: NR Comorbidities: NR **Procedures:** Abdominal operations where the bowel was opened. **Setting:** 11 hospitals **Location:** Australia **Dates:** NR **Inclusion Criteria:** patients undergoing elective abdominal operations in which the bowel was opened. **Exclusion Criteria:** Patients known to be allergic to penicillin or who had received antimicrobials in the 72 hours before their planned operation. Patients were excluded if the large bowel was not opened at operation,	**Intervention group: n=132** Patients who received 2 doses of 3.1g of timentin. 1 intravenously just before incision the other, 2 hours after the beginning of the operation. **Timing of intervention:** pre and intra/post op **Duration of intervention:** 2h after the beginning of the operation. **Device/agent:** Timentin 3.1g **Control group: n=146** Patients received a single dose of timentin of 3.1g intravenously just before incision. **Standard preventive measures:** The bowel was mechanically cleansed preoperatively and no oral antimicrobials were administered.	**SSI:** **Intra-abdominal abscess:** 2doses: 10/132(8%) 1dose: 8/146 (5%) vs. **Perineal wound infection:** 2doses: 4/9 1dose: 4/9 **Antimicrobial Resistance:** No difference: 1 minor SSI in each group culture positive for MRSA as the sole organism	**Definitions:** Wound infection: if there was a purulent discharge from the suture line or if there was a non-purulent discharge that contained pathogenic bacteria. **Perioperative care:** NR **Other notes:** None **Follow-up:** 30 days **Funding Source Conflicts:** Authors: NR Institution: NR Study: NR Supplies: NR

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			if intra-abdominal pus was found at operation, if a stoma or mucous fistula was brought out through the main abdominal wound and/or if the main abdominal wound was not closed primarily.			

eTABLE 28. Evidence Table for Q1E. How safe and effective is postoperative AMP and what is the optimal duration?

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
Hirokawa 2013 [54] (ES)	**RCT** 1, 2, 6, 7, 8, 9, 10	To evaluate the necessity of postoperative antibiotic prophylaxis after liver resection without reconstruction of the intestine or biliary tract.	**Number of patients: N=190** **Patient Characteristics:** the two groups were matched for characteristics ·Age, y: median (range) Intervention: 68 (35-82) Control: 68 (22-88) ·Gender: m:f Intervention: 64:30 Control: 30:34 ·Obesity ·Comorbidities: Virus infection: Intervention: 42/94 (44.7%) Control: 29/94 (30.9%) **Procedures:** Liver resection Primary hepatectomy: Intervention: 9/94 (9.6%) Control: 17/94 (22.1%) P-0.14 Hemiheptaectomy: Intervention: 28/94 (29.8%) Control: 24/94 (25.5%) Segmentectomy: Intervention: 27/94 (28.7%) Control: 22/94 (23.4%) Limited resection: Intervention: 39/94	**Intervention group:** n=94 Flomoxef sodium (FMOX) 1.0g was given 30 minutes before the operation and every 3 hours during the operation. **Timing of intervention:** Preoperative **Duration of intervention:** NA **Device/agent:** 1.0g flomoxef sodium administered intravenously **Monitoring intervention:** NA **Control group:** n=94 Flomoxef sodium (FMOX) 1.0g was given 30 minutes before the operation and every 3 hours during the operation then every 12 hours for 3 days after the operation. **Standard preventive measures:** Surgery: performed according to standard techniques: Cavity Irrigation: abdominal cavity was irrigated 4L of warm saline. Drains: not inserted Blood transfusion: carried out when surgical	**SSI:** SSI: Intervention: 7/94 (7.5%) Control: 13/94 (13.8%) P=0.24 Superficial/deep incisional Intervention: 3/94 (3.2%) Control: 3/94 (3.2%) P=1.000 Organ/space Intervention: 4/94 (4.3%) Control: 11/94 (11.7%) P=0.10 **Other infections** Remote site infections Intervention: 2/94 (2.1%) Control: 8/94 (8.5%) P=0.10 **Topic-specific outcomes:** NA **Reoperations:** NR **Length of stay:** Postoperative hospital stay, days: median (range) Intervention: 12 (4-91 Control: 14 (5-265) P=0.034 **Mortality:** Intervention: 1/94 (1.1%) Control: 1/94 (1.1%) **Adverse events:** NR	**Definitions:** Combined SSI and remote infection. SS (secondary outcome): a condition in which purulent discharge was observed from any incision or space that was manipulated during operation <30 days after surgery with or without microbiologic evidence, per the guidelines issued by the CDC. Remote site infection: a condition in which fever and leukocytosis were present with bacteria in sputum, urine, catheter tip, blood, or bile juice or according to the physician's judgment regardless of microbiologic evidence.

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			(41.5%) Control: 48/94 (51.1%) **Indications:** Hepatocellular Carcinoma: Intervention: 44/94 (46.8%) Control: 44/94 (46.8%) Cholangiocellular carcinoma: Intervention: 3/94 (3.2%) Control: 4/94 (4.3%) Colorectal metastasis: Intervention: 42/94 (44.7%) Control: 37/94 (39.4%) Living-donor liver transplantation: Intervention: 1/94 (1.2%) Control: 4/94 (4.3%) **Setting:** 1 University Medical Hospital **Location:** Japan **Dates:** April 2008 – June 2011 **Inclusion Criteria:** patients from 18-90 years and adequate organ functional reserve of important organ systems (heart, lungs, kidneys, and liver [Child-Pugh class A or B])	bleeding >1000m and hemoglobin level decreased to <8.0 g/dL		Signs of infection (Primary Outcome): postoperative status with ≥1 of the following inflammatory findings after postoperative day (POD) 4: (1) body temperature ≥38^{o}C; (2) white blood cell count ≥12,000/mm^{3}; and (3) additional increase (>20% increase from the previous value) in white blood cell count and/or C-reactive protein. **Perioperative care:** NR **Other notes:** None **Follow-up:** NR **Funding Source Conflicts:** Authors: None Institution: None Study: None Supplies: None

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			Exclusion Criteria: (1) severe comorbidities, such as preoperative infection, hemodialysis, myocardial infarction, or respiratory disorders requiring oxygen inhalation; (2) concomitant operations on other organs, including biliary or digestive tract anastomosis; (3) proven mental illness; and (4) absences of informed consent.			
Lyimo 2013 [30] (ES)	**RCT** 1, 4, 7, 8, 9, 10	To determine the equivalence of intravenous single dose of gentamicin (3mg/kg) plus metronidazole (500mg) given 30 – 60 min before incision and multiple doses of gentamicin (3mg/kg) and metronidazole (500mg) given both 30-60 min before	**Number of patients: N=500** **Patient Characteristics:** patients in both groups were similar at baseline. ·Age ≤20 y: Intervention: 38/250 (15.2%) Control: 42/250 (16.8%) 21-30 y: Intervention: 146/250 (28.4%) Control: 135/250 (54.0%) >30 y:	**Intervention group:** n=250 Patients received a single intravenous dose of gentamicin(3mg/Kg) plus metronidazole (500mg) 30 – 60 minutes before operation **Timing of intervention:** preoperative **Duration of intervention:** NA **Device/agent:** Gentamicin (3mg/Kg) plus metronidazole (500mg): **Monitoring intervention:** NA **Control group:** n=250	**SSI:** Total Surgical Site Infection: Intervention: 12/250 (4.8%) [95%CI 2.2-7.4] Control: 16/250 (6.4%) Absolute difference (95%CI): 1.6% (-2.4-5.6%) [95%CI 3.4-9.4] Incidence rates of post cesarean infections Intervention: 1.7/ 1000 person days Control: 2.3 / 1000 person days Incidence rate ratio = 0.74 995%CI 0.32-1.65), p=0.2146 **Other infections:** NR	**Definitions:** Infection: presence of fever (temp >38^{o}C at least 4 hours apart on two or more occasions, excluding the first 24h post cesarean.)and signs and symptoms of abdominal wound infection or endometritis Abdominal wound infection: partial or total dehiscence,

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
		incision and followed by gentamicin (3mg/kg) once a day and metronidazole (500mg) every 8 hours for 24 hours after emergency cesarean surgery	Intervention: 66/250 (26.4%) Control: 73/250 (29.3%) ·Gender: 100% female ·Obesity: Intervention: 83/250 (33.2%) Control: 63/250 (25.2%) ·Comorbidities Gravidity: Multigravida: Intervention: 173/250 (69.2%) Control: 167/250 (66.8%) Presence of cesarean scar, yes Intervention: 98/250 (39.2%) Control: 87/250 (34.8%) Ruptured amniotic membrane Intervention: 129/250 (51.6%) Control: 158/250 (63.2%) P=0.01 Duration of operation (>60 min) Intervention: 99/250 (39.6%) Control: 110/250 (44.0%) **Procedures:** emergency cesarean section	3 doses - Patients received a dose of gentamicin (3mg/Kg) plus metronidazole (500mg) 30 – 60 minutes before operation followed by gentamicin (3mg/Kg) once a day and metronidazole (500mg) every 8 hours for 24h postoperatively **Standard preventive measures:** Wound dressing: wound was left open.	**Topic-specific outcomes:** NR **Reoperations:** NR **Length of stay:** NR **Mortality:** NR **Adverse events:** NR	presences of purulent or serous discharge form the wound with indurations, warmth and tenderness. Endometritis: the presence of fever (38^{o}C or above) in association with one or more of the following: uterine tenderness or foul smelling lochia. **Perioperative care:** Bladder catheter was removed after 48h **Other notes:** Sample size was calculated to be 490 based on alpha = 0.05 and beta = 0.20 **Follow-up:** 30 days postop. Patients who could not attend their follow up appointments were contacted via phone or by communicating

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			Indications: NR **Setting:** Single teaching hospital **Location:** Tanzania **Dates:** October 2011 – May 2012 **Inclusion Criteria:** pregnant women admitted to the institution's labor ward that needed or had indication for emergency cesarean section (under spinal anesthesia) during the study dates that had consented to the study. **Exclusion Criteria:** Pregnant women with fever (temp ≥38^{o}C), prolonged obstructed labor, and prolonged and premature rupture of membranes (rupture of membrane >12 hours). Pregnant women presenting with features of chorioamnionitis (i.e., foul smelling lochia, uterine tenderness associated with fever) allergies to the antibiotic used in the study, or those who had used the			with a ten cell leader via physical address. **Funding Source Conflicts:** Authors: None Institution: None Study: None Supplies: None

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			antibiotics in the 24 hours preceding the operation or unconscious patients who could not provide consent.			
Haga 2012 [52] (ES)	**RCT** 1, 6	To confirm the validity of single-dose antimicrobial prophylaxis for the prevention of SSI and examined independent risk factors influencing the development of surgical site infections following elective gastric cancer surgery.	**Number of patients: N=325** **Patient Characteristics** ·Age, y: mean (range) Intervention: 68 (33-90) Control: 68 (39-91) ·Gender: male:female Intervention: 118:46 Control: 117:44 ·Obesity: BMI mean (range), kg/m^2 Intervention: 21.7 (15.2-31.6) Control: 21.9 (15.4-31.6) ·Comorbidities: Diabetes mellitus: Intervention: 38/164 (23.2%) Control: 36/161 (22.4%) **Procedures:** elective gastric surgery Total gastrectomy: proximal/distal gastrectomy: Intervention: 66:98 Control: 66:95 Combined resection:	**Intervention group:** n=164 A single dose of 1g cefazolin administered intravenously. An additional dose administered when surgery duration >3h. **Timing of intervention:** preop **Duration of intervention:** preop **Device/agent:** 1g cefazolin **Monitoring intervention:** NA **Control group:** n=161 6 doses - 1g cefazolin administered intravenously. An additional dose administered when surgery duration >3h. An additional 5 doses were given every 12h postop **Standard preventive measures:** Wound covering: surgical towels for conventional gastrectomy, wound protectors for laparoscopic or	**SSI:** Overall SSI: Intervention: 15/164 (9.1%) Control: 10/161 (6.2%) Difference (95%CI): -2.9% (-5.9-0.00) Superficial/ Incisional Infections Intervention: 14/164 (8.5%) Control: 7/161 (4.3%) Difference (95%CI): -4.2 (-6.9- -1.5) Organ/space infections Intervention: 11/164 (6.7%) Control: 6/161 (3.7%) Difference (95%CI): -3.0 (-5.5- -0.6) Organ/space infections related to anastomic dehiscence or pancreatic fistula Intervention: 10/164 (6.1%) Control: 6/161 (3.7%) Both Superficial & Organ/Space Intervention: 9/164	**Definitions:** SSI – Incision site infection and organ/space infection were CDC SSI Guideline definitions Anastomotic dehiscence: confirmed by clinical and/or x-ray examination Remote infection: an infection occurring at a site other than the surgical site, such as pneumonia, urinary tract infection, enteritis, or bloodstream (catheter-related) infection. **Perioperative care:** **Other notes:** power calculation based on

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			Intervention: 37/164 Control: 36/161 Gallbladder: Intervention: 15/164 Control: 13/161 Spleen: Intervention: 23/164 Control: 20/161 Pancreas: Intervention: 3/164 Control: 2/161 Liver: Intervention: 2/164 Control: 2/161 Small intestine: Intervention: 0/164 Control: 1/161 **Indications:** gastric cancer Pathologic stage: 1/II:III/IV Intervention: 54:110 Control: 65:96 P=0.16 **Setting:** one university medical center **Location:** Japan **Dates:** February 2007 – November 2010 **Inclusion Criteria:** Patients undergoing elective surgery for gastric cancer **Exclusion Criteria:** Patients <20 years old, those with a known allergy to	laparoscopic-assisted surgeries. Anastomoses = stapled. Rinsing abdominal cavity-copiously rinsing with 2-3L saline before closure Closure – approximated by staples Drains – closed suction drains were placed sub-hepatically and/or subphrenically according to the type of gastrectomy, brought out through separate stab wounds. Drains were removed after 7 days. Dressing – sterile dressing was removed within 48h Blood Transfusion: Intervention: 10/164 (6.1%) Control: 21/161 (13.0%) P=0.03	(5.5%) Control: 3/161 (1.9%) **Other infections:** All remote infections: Intervention: 6/164 (3.7%) Control: 5/161 (3.1%) P=0.78 Pneumonia: Intervention: 3/164 (1.8%) Control: 2/161 (1.2%) Enterocolitis: Intervention: 1/164 (0.6%) Control: 2/161 (1.2%) Urinary Tract Infection: Intervention: 1/164 (0.6%) Control: 0/161 Bloodstream infection: Intervention: 1/164 (0.6%) Control: 1/161 (0.6%) **Topic-specific outcomes:** Multivariate regression analysis Blood Loss (every 100mL) OR (95%CI): 1.13 (1.05-1.23), p<0.01 BMI (≥25 kg/m^2): OR (95%CI): 2.76 (1.10-6.90), P=0.03 Age (every 10 years increment:	detecting an 8% difference in the incidence of SSIs with a CI of 95% and a power of 80% resulted in sample size of 159 in each arm. **Follow-up:** 30 days postop via inspection at outpatient clinic. **Funding Source Conflicts:** Authors: NR Institution: NR Study: NR Supplies: NR

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			cephalosporins, those with any infection within the prior 2 weeks, those with synchronous cancer at any sites other than the stomach, and those needing colon resection because of tumor involvement.		OR (95%CI): 1.65 (1.01-2.70), P=0.046 **Reoperations:** NR **Length of stay:** **Mortality:** NR **Adverse events:** NR	
Hussain 2012 [31] (ES)	**RCT** 1, 6, 7, 8, 10	To determine the role of postoperative antibiotics in reducing the surgical site infections (SSIs) and intra-abdominal abscess formation after open appendectomy in patients with non-perforated appendicitis (NPA), and to define the uniform guidelines in the management of these patients in our institution.	**Number of patients: N=377** **Patient Characteristics:** statistically there was no difference between group characteristics. ·Age, y: mean±SD, Intervention: 32.78±10.62 Control: 31.70±9.96 ·Gender: ratio of m:f Intervention: 1.15:1 Control: 1.16:1 ·Obesity: NR ·Comorbidities: NR Exclusionary criteria **Procedures:** emergency open appendectomy **Indications:** acute appendicitis **Setting:** 1 tertiary care hospital **Location:** Saudi Arabia **Dates:** January 2010 – July 2011	**Intervention group:** n=195 A single preoperative dose of cefuroxime sodium and metronidazole half an hour before surgery. **Timing of intervention:** Preoperative **Duration of intervention:** NA **Device/agent:** cefuroxime sodium **Monitoring intervention:** NA **Control group:** n=182 A preoperative dose of cefuroxime sodium and metronidazole half an hour before surgery plus an additional dose of cefuroxime sodium and metronidazole at 8h postop **Standard preventive measures** Technique: performed through right lower quadrant incision.	**SSI** Surgical site infection Intervention: 9/195 (4.6%) Control: 8/182 (4.3%) **Other infections:** NR **Topic-specific outcomes:** No Intraabdominal collection of fluid reported **Reoperations:** NR **Length of stay,** days**:** Intervention: 2.29±0.82 Control: 2.35±0.48 **Mortality:** no perioperative mortality **Adverse events:** NR	**Definitions :** SSI: pus discharge from wound that necessitated wound opening and drainage. Intra-abdominal collection: fluid collection inside the peritoneal cavity confirmed by ultrasound or computed tomography and requiring drainage. **Perioperative care:** NR **Other notes:** NR **Follow-up:** 30 days **Funding Source Conflicts:** Authors: NR Institution: NR Study: NR Supplies: NR

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			Inclusion Criteria: Patients admitted with the clinical diagnosis of acute appendicitis undergoing emergency open appendectomy. **Exclusion Criteria:** Patients who had received antibiotics within 72 hours of admission or who were diabetics, immunocompromised, or pregnant. Also, those who were found to have complicated appendicitis (gangrenous, perforated, appendicular mass or abscess) or normal appendix per-operatively were excluded as well.	Wound closure: primarily in all patients following washing with normal saline.		
Imamura 2012 [51] (ES)	**RCT** 1, 2, 4, 10	To assess non-inferiority of the omission of postoperative antimicrobial prophylaxis in patients with gastric cancer	**Number of patients: N=355** **Patient Characteristics:** patient characteristics were balanced between groups. ·Age: y, median (range) Intervention: 66 (36-84) Control: 65 (35-84)	**Intervention group:** n=176 1g Cefazolin 30 min after anesthesia and before the surgical incision plus every 3h intraoperatively. **Timing of intervention:** preoperative **Duration of intervention:** NA **Device/agent:** 1g	**SSI** Total: Intervention: 8/176 (5%) Control: 16/179 (9%) RR (95%CI) – 0.51 (0.22-1.16) P=0.138 OR for SSI with intraoperative antimicrobial prophylaxis: Patients with BMI<25 0.31 (0.099-0.998),	**Definitions:** Superficial, Deep incisional & organ/space infections were diagnosed by CDC NNIS infection definitions. **Perioperative care:** NR **Other notes:**

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			·Gender; Male: female Intervention: 115:61 Control: 120:59 ·Obesity: BMI (kg/m^2) Intervention: 22.3 (16.3-33.0) Control: 22.5 (12.4-32.9) ·Comorbidities: Blood loss, median (range) mL Intervention: 200 (1-880) Control: 210 (1-1700) **Procedures:** distal gastrectomies and lymphadenectomies. Two patients underwent a total gastrectomy because they had a positive resection margin, and one had palliative bypass surgery with gastrointestinal anastomosis. **Indications:** gastric cancer **Setting:** Seven hospitals (4 tertiary care & 3 university hospitals) **Location:** Japan **Dates:** June 2, 2005 – December 6, 2007 **Inclusion Criteria:** patients who had histologically proven	cefazolin **Monitoring intervention:** NA **Control group:** n=179 1 g cefazolin before the surgical incision, every 3h intraoperatively plus 1g cefazolin on postoperative day 0 (at night) and every 12h until postoperative day 2 (2g/ day for 2 postoperative days) **Standard preventive measures:** Drainage Tube: Intervention: 157/176 (89.2%) Control: 153/179 (85.5%) Transfusion: Intervention: 0/176 Control: 4/175 (2.3%) Care before and after surgery and wound management were done according to respective institutional standards.	p=0.050 Patients who with BMI≥25 1.09 (0.25-4.72), P=0.91 All 24 SSI in patients who underwent distal gastrectomy without protocol violation. Superficial incisional: Intervention: 1/176 (<1%) Control: 45/179 (3%) P=0.215 Deep Incisional: Intervention: 0/176 Control: 0/179 Organ/space Intervention: 7/176 (4%) Control: 11/179 (6%) P=0.469 O/S With anastomotic leakage Intervention: 1/176 (0.6%) Control: 4/179 (2.3%) O/S without anastomotic leakage Intervention: 6/176 Control: 7/179 (2.3%) **Other infections:** Remote site infections: Overall: Intervention: 5% (CI 2-10) Control: 3% (CI 1-7) Pneumonia or bronchitis:2 patients (unclear which group) UTI	power calculation was conducted for composite SSI. **Follow-up:** 30 days postop **Funding Source Conflicts:** Authors: None Institution: None Study: None Supplies: None

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			gastric adenocarcinoma that was deemed curable with a distal gastrectomy. Patients with an ASA score of 1 or 2 **Exclusion Criteria:** If patients had an active or uncontrolled infection, received neoadjuvant chemotherapy, or had been given steroids.		Intervention: 10/176 (0.6%) Control: 1/179 (0.6%) **Topic-specific outcomes:** NR **Reoperations :** NR **Length of stay:** Intervention: 12 (7-114) Control: 12 (7-87) P=0.742 **Mortality:** NR **Adverse events:** no severe reaction to antimicrobial prophylaxis occurred in either group.	
Lin 2011 [35] (ES)	**RCT** 1	To elucidate the effect of the duration of prophylactic antibiotics, a prospective, randomized control study was conducted to compare the effectiveness of preventing SSI after Coronary Artery Bypass Graft (CABG) using1-day or 3-day antibiotic prophylaxis.	**Number of patients: N=231** **Patient Characteristics:** baseline characteristics were similar in each group. ·Age, y: mean±SD Intervention: 64.4±9.6 Control: 65.5±11.5 P=0.45 ·Gender: male, Intervention: 94/120 (78.3%) Control: 90/111 (81.1%) P=0.60 ·Obesity: BMI (kg/^{m2}), mean±SD Intervention: 25.0±2.8 Control: 25.1±2.9	**Intervention group:** n=120 Patients received 1g of cefazolin within 1 hour prior to incision, and an additional dose was allowed if it was a prolonged operation (1 additional dose for every 3-4 hours of surgery). Then 1g cefazolin every 8 hours for 3 doses after the operation. **Timing of intervention:** pre and postoperatively **Duration of intervention;** Na **Device/agent:** Cefazolin **Monitoring intervention:** NA **Control group:** n=111	**SSI (30 days):** Sternal Wound infection Intervention: 13/120 (10.8%) Control: 9/111 (8.0%) P=0.48 Deep infections Intervention: 3/120 (2.5%) Control: 1/111 (0.9%) P=0.62 Superficial Intervention: 3/120 (2.5%) Control: 2/111 (1.8%) P=1.00 Harvest Site Infection Intervention: 7/120 (5.8%) Control: 6/111 (5.4%) P=0.89	**Definitions:** SSI – CDC 1999 Guideline Definitions **Perioperative care:** NR **Other notes:** None **Follow-up:** 1 month postop **Funding Source Conflicts:** Authors: NR Institution: NR Study: NR Supplies: NR

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			P=0.84 ·Comorbidities Hypertension: Intervention: 80/120 (66.7%) Control: 75/111 (67.6%) P=0.88 Diabetes Mellitus Intervention: 52/120 (43.3%) Control: 43/111 (38.7%) P=0.48 Smoking Intervention: 46/120 (38.3%) Control: 34/111 (30.6%) P=0.22 COPD Intervention: 3/120 (2.5%) Control: 0/111 P=0.60 Nasal Swab Screening *S. aureus* positive Intervention: 14/120 (12.7%) Control: 20/111 (19.4%) P=0.18 MSSA carrier Intervention: 8/120 (7.3%) Control: 16/111 (15.5%) P=0.06	Patients received 1g of cefazolin within 1 hour prior to incision, and an additional dose was allowed if it was a prolonged operation (1 additional dose for every 3-4 hours of surgery). Then 1g cefazolin every 8 hours for 9 doses after the operation. **Standard preventive measures:** MRSA Swab – screening for MRSA carriage was conducted 1 day preop. No decolonizing agents were used.	**Other infections:** NR **Topic-specific outcomes:** Time to SSI, d: Intervention: 12.8±3.3 Control: 18.9±5.3 P=0.004 **Reoperations:** NR **Length of stay:** Postop ICU Stay, d mean±SD Intervention: 2.2±0.9 Control: 2.6±1.6 P=0.05 Postop LOS, d mean±SD Intervention: 12.1±3.6 Control: 16.7±9.1 P=0.10 **Mortality:** 3 patients died immediately after surgery but were excluded. **Adverse events:** NR	

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			MRSA carrier Intervention: 6/120 (5.5%) Control: 4/111 (3.9%) P=0.75 **Procedures:** Coronary Artery Bypass Graft (CABG) Emergency Intervention: 26/120 (21.7%) Control: 30/111 (27.0%) P=0.34 **Indications** **Setting:** 1 university hospital **Location:** Taiwan **Dates:** June 2002 – April 2004 **Inclusion Criteria:** Patients who underwent non-emergency CABG surgery and were ≥18 years old. **Exclusion Criteria:** Patients with existing preoperative infections; those undergoing treatment with antibiotics; hypersensitivity to cefazolin; renal dysfunction (serum creatinine level			

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			>2mg/dL or creatinine clearance <35mL/min, or under hemodialysis treatment); left ventricular ejection fraction <30%; obesity (body mass index >31kg/m^2); chronic obstructive pulmonary disease (COPD); undergoing combined surgery other than CABG; neutropenia (leukocyte count <1000/cm^3); pregnancy or undertaking breastfeeding; or refusal of consent			
Suzuki 2011 [42] (ES)	**RCT** 1, 2, 7, 8, 9	To establish the optimal duration of perioperative antimicrobial administration of an oxacephem antimicrobial in patients undergoing elective colon cancer surgery, by determining the incidence of SSIs with the use of	**Number of patients: N=360** **Patient Characteristics:** No significant difference was observed in baseline patient characteristics between groups. ·Age, y, mean±SD Intervention 65±11 Control: 66±9. ·Gender m/f Intervention: 101/84 Control: 101/84 ·Obesity: NR ·Comorbidities: Diabetes	**Intervention group:** n=179 A single dose of oxacephem (1g) antimicrobial prophylaxis was administered intravenously before surgery. The antimicrobial was given from 1 hour before the incision was made. When the operative time exceeded 3 hours, an addition al gram of antimicrobial was administered **Timing of intervention:**	**SSI: (follow up 4 weeks)** Incisional SSI Intervention: 15/179 (8.4%) 11/15: No fever and were improved by removal of some sutures and abscess drainage 2/15: Developed fever and were treated by antimicrobials & abscess drainage Control: 13/181 (7.2%) 13/13: No fever and were improved by removal of some sutures and abscess	**Definitions:** Postoperative infection: an infection occurring within 30 days after surgery. SSI: diagnosed by ≥2 physicians Incisional SSI: macroscopic abscess or purulent discharge observed on the operative wound Organ/ space SSI: An infection in

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
		mechanical preparation and chemical preparation together with oral antimicrobial administration.	Intervention: 17/185 (9.2%) Control: 14/185 (7.6%) **Procedures:** Elective laparotomy for colon cancer **Indications:** colon cancer T Category Tis, T1/ T2-T4 Intervention: 21/164 Control: 29/156 TNM Classification: not significant; **Setting:** 1 university hospital **Location:** Japan **Dates:** August 2002-October 2007 **Inclusion Criteria:** Patients undergoing elective laparotomy for colon cancer **Exclusion Criteria:** Patients with stoma, those who could not undergo the normal mechanical preparation owing to stenosis or obstruction, and those with a preoperative diagnosis of stage IV and American Society of Anesthesiologists score of ≥3.	Pre and intraoperatively (based on procedure duration) **Duration of intervention:** Pre and intraoperatively (vs. up to 4 days in controls) **Device/agent**: oxacephem 1g IV antimicrobial **Monitoring intervention:** NR (Cultures of drainage or purulence were made) **Control group:** n=181 Oxacephem (1g) antimicrobial was administered intravenously twice daily for 4 days from the day of surgery until post-op day 3. The antimicrobial was given from 1 hour before the incision was made. When the operative time exceeded 3 hours, an addition al gram of antimicrobial prophylaxis was administered **Standard preventive measures:** Bowel Prep: All patients underwent mechanical and chemical preparation of the bowel. 1. Mechanical: 10 ml of sodium picosulfate was	drainage P=0.0008 (*Δ=0.10*) Organ/ space SSI Intervention: 1/179 (0.6%) Control: 2/181 (1.1%) P<0.001 (*Δ=0.10*) 3/3: anastomic leakage **Other infections:** Remote Infection Intervention: 8/179 (4.5%) 6/8: Catheter infection Detected Post-OP day 3 or later & resolved with catheternremoval & antimicrobial administration 1/8: Jugular vein phlebitis 1/8: Pneumonia Control: 6/181 (3.3 %) 4/6: Catheter infection Detected Post-OP n day 5 or later & resolved with catheter removal & abx 1/6: Urinary Tract Infection 1/6: Pneumonia P<0.0001 (*Δ=0.10*) *C. difficile* Colitis Intervention: 0/179 Control: 0/181 **Topic-specific outcomes:** NA **Reoperations:**	the organ subjected to surgery. Remote infection: Evaluated by chest plain films, sputum, urine, blood, or catheter culture after surgery. **Perioperative care:** NR **Other notes:** Non-inferiority margin is 10% (*Δ=0.10*). Based on this, there were no differences in incidence of SSIs, organ/space or remote infections between groups (single dose vs. postop dosing X up to 4 days) **Follow-up:** 4 weeks post-discharge at a hospital visit. **Funding Source Conflicts:** Authors: NR Institution: NR Study: NR Supplies: NR

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
				orally administered 2 days before surgery and 2,000 ml of polyethylene glycol-electrolyte sodium was orally administered in the morning of the day before surgery 2. Chemical: 0.5g of kanamycin sulfate and 0.5g of metronidazole were orally administered at 1, 2 and 11pm on the day before the operation.	3/3 Organ/ space SSI developed fever and required reoperation **Length of stay:** Mean Length of stay for patients with colon cancer: 15±4 days (facility data) **Mortality:** NR **Adverse events:** <u>Small Bowel Obstruction</u> Intervention: 5/179 (2.8%) Control: 8/181 (4.4 %) P<0.0001 (*Δ=0.10*) <u>Other</u> Intervention: 2/179 (1.1%) 1/2: Venous thrombosis of the lower extremities 1/2: Duodenal Stenosis Control: 2/181 (1.1 %) 1/2: Postoperative hemorrhage 1/2: Duodenal Stenosis	
Tamayo 2008 [12] (ES)	**RCT** 1, 2, 4, 7, 8, 9	To test the hypothesis that single doses of cefazolin are as effective as a 24-hour regimen of cefazolin in preventing SSIs in adults	**Number of patients: N=838** **Patient Characteristics:** Both groups were homogeneous and comparable in as far as their demographic profiles and clinical characteristics were concerned except for	**Intervention group:** n=419 A single dose of 2g cefazolin was administered intravenously between 20-30 minutes <u>after</u> the induction of anesthesia. . For all procedures lasting more than 3 hours, a new dose of 1g	**SSI: (Follow up at least 1 year)** <u>Total SSIs:</u> 50/838 (5.9%) Intervention: 30/419 (8.3%) Control: 15/419 (3.6%) P=0.004 <u>Total Incisional SSI</u> Intervention: 21 (5.0%) Control: 7 (1.7%) P=0.007	**Definitions:** CDC definitions were used throughout. <u>Superficial SSI</u> – The infection covers the skin and subcutaneous cellular tissue and is

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
		undergoing cardiac procedures	transfusions (below). ·Age, y: mean±SD Intervention: 67.5±10.5 Control: 68.2±10.5 ·Gender: m/f Intervention: 272/147 Control: 247/172 P=0.07 ·Obesity: NR ·Comorbidities Diabetes: Intervention: 111/419 (26.5%) Control: 125/419 (29.8%) Peripheral Vascular Disease Intervention: 25/419 (5.9%) Control: 38/419 (9%) P=0.08 ·Intraoperative values not statistically significant except for Intraoperative values: Hematocrit after CPB, mean±SD: Interventions:27.07±4.20 Control: 26.48±4.07 P=0.05 ·Postoperative values Intra-aortic balloon pump Intervention: 5/419 (1.1%) Control: 14/419	of cefazolin was administered intraoperatively. **Timing of intervention:** Single dose preoperatively (re-dosed intraoperatively depending on procedure duration)**Duration of intervention:** Pre and intraop vs. extended dosing X 24hrs postop in controls **Device/agent:** Cefazolin 2g IV **Monitoring intervention:** Wound cultures **Control group:** n=419 Administered 2g of cefazolin intravenously between 20-30 minutes <u>after</u> the induction of anesthesia, followed by 1g every 8 hours. For all procedures lasting more than 3 hours, a new dose of 1g of cefazolin was administered intraoperatively. **Standard preventive measures:** NR	<u>Superficial Incisional SSI</u> Intervention: 16 (3.8%) Control: 7 (1.7%) P=0.04 <u>Deep Incisional SSI</u> Intervention: 5 (1.2%) Control: 0 P=0.03 <u>Organ/Space SSI</u> Intervention: 14 (3.3%) Mediastinitis and endocarditis were documented simultaneously in 2 patients Control: 8 (1.9%) P=0.19 <u>Osteomyelitis</u> Intervention: 3 (0.7%) Control: 2 (0.5%) P=0.5 <u>Mediastinitis</u> Intervention: 8 (1.9%) Control: 5 (1.2%) P=0.28 <u>Endocarditis</u> Intervention: 5 (1.2%) Control: 1 (0.2%) P=0.10 **Other infections:** <u>Sepsis</u> Intervention: 17 (4.0%) Control: 18 (4.2%) P=0.50 **Topic-specific outcomes:** Antimicrobial resistance: Pathogens isolated were similar distribution	accompanied by one of the following: purulent drainage through the incision, positive results of the incisional culture, and classic inflammatory signs that allow the wound to be opened by the surgeon except in cases in which the incisional culture was negative. <u>Deep incisional SSI</u> – Infection involves the deep soft tissues of the incision with at least 1 of the following: purulent drainage, a deep incision that spontaneously dehisced or was deliberately opened by the surgeon when patient had a fever (temp ≥38^{o}C), or localized pain or

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			(3.3%) P=0.03 Red cell transfusion patients Intervention: 261/419 (62.3%) Control: 216/419 (51.5%) P=0.01 **Procedures:** Elective Coronary artery bypass grafting (CABG) or valve operations or both **Indications:** NR **Setting:** 1 tertiary-level hospital **Location:** Spain **Dates:** September 2003 – January 2007 **Inclusion Criteria:** Adult patients (>18 years of age) undergoing elective coronary artery bypass grafting (CABG), valve operations or both by means of sternotomy. **Exclusion Criteria:** Presence of active infection, the administration of antimicrobial therapy in the 48 hours before surgical intervention,		in both groups (P≥0.05). 43/50 (86%) of SSIs were gram positive cocci (S. epidermis (SE) most common, followed by S. aureus (SA). SE-MRSE Intervention: 12/20 SE and 12/35 (34.3%) SSI Control: 5/9 SE and 5/15 (33%) SSI SE-MSSE Intervention: 8/20 SE and 8/35 (22.8%) SSI Control: 4/9 se and 4/15 (26.6%) SSI SA-MRSA Intervention : 4/11 SA and 4/35 (11.4)% SSI Control: 1/5 SA and 1/15 SSI (6.6%) SA-MSSA: Intervention 7/11 SA and 7/35 (20.0%) SSI Control: 4/5 SA and 4/15 (26.6%) SSI Gram negative bacilli in 12/50 (24%) ; polymicrobial SSI rates similar between groups **Reoperations:** NR **Length of stay:** Preoperative hospitalization d, mean±SD Intervention: 9.7±7.9	tenderness (unless the results of an incisional culture were negative), or evidence of deep incision infection found in a direct examination or second operation Mediastinitis – Organ/space SSI characterized by 1 of the following: positive results of a culture obtained from mediastinal tissue or fluid during a surgical operation, patient fever (temp ≥38^{o}C), sternal pain or instability, mediastinal involvement suggested by a computed tomographic scan, or organisms cultured form the mediastinal area Sternal

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			emergency surgical intervention, or allergy to betalactams. Also, patients with transplants or who did not wish to participate in the study.		Control: 10.8±10.3 P=0.11 Mean ICU Stay d, mean±SD Intervention: 10.3±10.9 Control: 9.1±8.7 P=0.09 Duration of hospitalization after operation d, mean±SD Intervention: 14.75±15.8 Control: 12.2±14.2 P=0.25 **Mortality:** 30 day: Intervention: 22 (5.2%) Control: 31 (7.4%) P=0.12 90 day: Intervention: 29 (6.9%) Control: 37 (8.8%) P=0.18 365 day Intervention: 43 (10.3%) Control: 48 (11.5%) P=0.34 **Adverse events:** Intra-aortic balloon pump Intervention: 5 (1.1%) Control: 14 (3.3%) P=0.03 Red cell transfusion patients Intervention: 261 (62.3%) Control: 216 (51.5%) P=0.01	osteomyelitis – An organ/space SSI indicated by persistent purulent drainage from the sternotomy & confirmed by microbiologic and histopathologic findings. Endocarditis – Organ/space SSI characterized by Duke's criteria (Durack 1994) **Perioperative care:** NR **Other notes:** SSI Risk Stratification: NNIS Statistical Analysis: Study powered to detect reduction in SSI rate of <5% with a=0.20 and β=0.05 (n=419 in each arm) **Follow-up:** Patients were examined daily while in the hospital. Cardiac surgeons personally

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
					Arterial Fibrillation Intervention: 17 (4.0%) Control: 21 (5.0%) P=0.30 Respiratory Failure Intervention: 28 (6.6%) Control: 23 (5.4%) P=0.28 Acute Renal Failure Intervention: 21 (5.0%) Control: 27 (6.4%) P=0.22 Renal replacement treatment Intervention: 12 (2.8%) Control: 13 (3.1%) P=0.50	followed up with patients in the cardiac outpatient clinic for at least 1 year after discharge from the hospital **Funding Source Conflicts:** Authors: NR Institution: NR Study: NR Supplies: NR
Liu 2008 [39] (ES)	**RCT** 1, 2, 3, 4, 6, 7, 8, 10	To investigate the impact of the duration of prophylactic antimicrobials on post-operative wound infection in patients undergoing major head and neck neoplasm operations and to determine associated factors in post-operative wound infection.	**Number of patients: n=53** **Patient Characteristics:** There were no significant differences between groups according to basic data and laboratory studies. ·Age, y: mean±SD Intervention:56.4±12.3 Control: 56.5±11.1 ·Gender: m/f Intervention: 23/4 Control:21/5 ·Obesity: BMI, kg/m^2, average Intervention: 23.6 Control: 23.6	**Intervention group: n=27** Received one dose of preoperative prophylactic antimicrobial (intravascular clindamycin 300mg) one hour before incision and then at 6 hour intervals over a period of 72 hours. **Timing of intervention:** Pre and postoperatively **Duration of intervention:** 1 hour before incision to 24 or 72 hours after surgery **Device/agent:** clindamycin **Monitoring intervention:** NR **Control group: n=26**	**SSI: (follow up 30 days)** Surgical wound infection: Total: 13 (24.5%) Intervention: 5 (18.5%) Control: 8 (30.7%) P=0.473 Bivariate analysis of population based on infections Bivariate analysis of population based on infections Infected n=14 / Uninfected n=40 Tumor size, cm: mean±SD Infected: 3.2±1.3 Uninfected: 2.2±1.1 P=0.005 Tracheostomy Infected: 13 (100%) Uninfected: 14 (50%) P<0.001	**Definitions:** Surgical wound infection: Purulent discharge either spontaneously or by incision and drainage within 30 days after the operation. **Perioperative care:** NR **Other notes:** Operative procedures were all performed by one surgeon and all post-operative wound conditions were evaluated by

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			·Comorbidities Previous radiotherapy: Intervention: 2/27 (14.8%) Control: 8/26 (30.8%) Perioperative data: Surgical reconstruction Intervention: 4/27 (14.8%) Control: 10/26 (38.5%) Perioperative blood loss Intervention: 239±110 Control: 262±136 Perioperative blood transfusion: YES Intervention: 4/27 (14.8%) Control: 7/26 (26.9%) **Procedures:** Head and neck surgical procedures Reconstruction with free flaps or pectoralis major myocutaneous flaps: 14/53 (26.4%) Intervention: 4/27 (14.8%) Control: 10/26 (38.5%) Laryngectomies accounted for small portion of cases **Indications:** Tumor Sites Oral cavity/Oropharynx/ Larynx/	Received one dose of preoperative prophylactic antimicrobial (intravascular clindamycin 300mg) one hour before incision and then at 6 hour intervals over a period of 24 hours. **Standard preventive measures:** NR	Duration of antimicrobials 24 hours (Control) Infected: 8 (61.5%) Uninfected: 18 (45%) P<0.001 72 hours (Intervention) Infected: 5 (38.5%) Uninfected: 22 (55%) P<0.001 Previous radiotherapy Infected: 8 (61.5%) Uninfected: 4 (10.0%) P<0.001 Previous chemotherapy Infected: 9 (69.2%) Uninfected: 4 (10.0%) P<0.001 Surgical reconstruction Infected: 10 (76.9%) Uninfected: 4 (10%) P<0.001 Serum Albumin: g/dl±SD Infected: 3.5±0.7 Uninfected: 4.1±0.4 P=0.013 Hemoglobin: g/dl±SD Infected: 10.8±1.9 Uninfected: 13.4±1.8 P<0.001 Perioperative blood loss: ml±SD Infected: 380±113 Uninfected: 208 ±93 P<0.001 Perioperative blood transfusion Infected: 7 (53.8%) Uninfected: 4 (10.0%) P<0.001	another doctor (Statistical analysis: sample size not large enough and statistic power unsatisfied **Follow-up:** 30 days postoperatively **Funding Source Conflicts:** Authors: None Institution: None Study: None Supplies: None

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			Hypopharynx/ Others Intervention: 18/2/1/2/4 Control: 1/7/2/13/3 **Setting:** 1 Veterans Hospital **Location:** Taiwan **Dates:** January 2004-December 2004 **Inclusion Criteria:** Patients scheduled to receive head and neck surgical procedures that would enter the upper aerodigestive tract. **Exclusion Criteria:** Those under antimicrobial treatment, allergic to clindamycin, with diabetes mellitus, or reluctant to join this protocol.		Logistic regression identified preop hemoglobin ≤10.5g/dL (p=0.025) and surgical reconstruction (P=0.036) as independent risk factors **Other infections:** NR **Topic-specific outcomes:** Antimicrobial Resistance: NR 13/53 (24.5%) total SSIs 6/13 (46.1%) polymicrobial P. aeruginosa (9/13, 69.2%) E. faecalis (4/13, 30.0%) K. pneumonia (4/13, 30.8%) C. koseri (1/13, 7.7%) A. baumannii (1/13, 7.7%) **Reoperations:** NR **Length of stay, d:** Intervention: 22±15 Control: 25±18 P=0.627 **Mortality:** NR **Adverse events:** One patient developed an allergic reaction after treatment and was forced to drop out.	

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
Fujita 2007 [15] (ES)	**RCT** 1, 2, 7, 8, 9, 10	To determine the efficacy of a single-dose regimen of second-generation cephalosporin cefmetazole without metronidazole and oral antimicrobials with regards to reduction in incidences of surgical site infections and all other infectious complications following elective colorectal surgery.	**Number of patients: N=377** **Patient Characteristics:** Although patient age was significantly higher in the control group, other patient characteristics were identical. ·Age, y: mean±SD Intervention: 59.4±11.1 Control: 62.1±9.8 P=0.01 ·Gender: m/f Intervention: 126/64 Control: 107/80 ·Obesity: NR ·Comorbidities: NR **Procedures: Colorectal Surgery** <u>Conventional:</u> Intervention: 129/190 (67.9%) Control: 133/187 (71.1%) <u>Colectomy/ anterior resection/ abdominoperineal resection</u> Intervention: 73/56/0 Control: 77/53/3 <u>Laparoscopic:</u> Intervention: 61/190 (32.1%) Control: 54/187 (28.9%) <u>Colectomy/ Anterior</u>	**Intervention group:** n=190 Single Dose Group Received 1 g cefmetazole just before skin incision. Though additional doses are recommended every 3-4 hours during extended surgery, none were given **Timing of intervention:** Preoperatively **Duration of intervention:** Preoperatively or preoperatively and up to 16 hours postoperatively in controls. **Device/agent: c**efmetazole 1g **Monitoring intervention:** NA **Control group:** n=187 3-Dose Group Received 1 g cefmetazole just before skin incision plus 2 postoperative 1g doses at 8 and 16 hours after the first administration. Though additional doses are recommended every 3-4 hours during extended surgery, none were given **Standard preventive measures:**	**SSI: (follow up NR)** <u>Total SSI</u> Intervention: 32/190 (16.8%) High infection rate Control: 17/187 (9.1%) <u>Incisional SSI</u> Intervention: 27/190 (14.2%) Control: 8/187 (4.3%) P=0.009 <u>Organ or Space SSI</u> Intervention: 5 (2.6%) Control: 9 (4.8%) P=0.26 Because only incidence of incisional SSIs differed significantly between groups, subset analysis performed: Multivariate analysis revealed antimicrobial dose was the only significant factor associated with incisional SSI (P=0.002). This result is confusing unless they meant to say antimicrobial duration. The incidence of incisional SSI in the control was lower even in patients whose surgery lasted 3hrs or less than in the intervention group.	**Definitions:** ND **Perioperative care:** To ensure that the trial results were applicable generally, specific instructions on surgical techniques and on postoperative care were not included **Other notes:** Trial was designed as non-inferiority test to detect 5% difference in incidence of incisional SSI with CI 95%, power 90% assuming incidence of infection of 5%. Sample size of 238 required in both arm. After 1yr interim analysis revealed significant difference between groups and enrollment was stopped. Significance at <0.05

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			resection Intervention: 49/12 Control: 42/12 No gastric or hepatic resections included) **Indications:** Colon cancer: 241/377 (63.9%) Rectal cancer: 136/377 (36.1%) **Setting:** 7 major hospitals **Location:** Japan **Dates:** May 6, 2004 – April 25, 2005 **Inclusion Criteria:** Patients aged 20-80 years scheduled to undergo elective colorectal surgery. **Exclusion Criteria:** Emergency operations, obstruction of the small bowel, stomal surgery or bypass surgery, preoperative infectious diseases, penicillin or cephalosporin allergy, antimicrobial administration before hospitalization, inflammatory bowel diseases, angina or myocardial infarction, mild or severe renal	Bowel Prep: Patients underwent mechanical bowel prep with 2L polyethylene glycol-electrolyte solution 1 day before surgery. No oral AMP was administered as part of the bowel prep	The incidence of incisional SSI associated with laparoscopic surgery was lower than in conventional although not statistically significant **Other infections:** Urinary tract infections, pneumonia, septicemia, infective diarrhea and line sepsis. Other Intervention: 12/190 (6.3%) Control: 9/187 (4.8%) P=0.52 Total Infections: (SSI plus other) Intervention: 44/190 (23.1%) Control: 26/187 (13.9%) P=0.03 *C. difficile* Colitis: Intervention: 0 Control: 2/187 (1.1%) **Topic-specific outcomes:** NR **Reoperations:** NR **Length of stay, d: mean±SD** Intervention: 12.5±7.4 Control: 12.2±5.6 P=0.66 With incisional SSI: n=35 14.6±9.3 Without incisional SSI: n=342 12.1±6.2 P=0.03	**Follow-up:** Wounds were checked daily until discharge and at the first postoperative hospital visit (when? NR) **Funding Source Conflicts:** Authors: None Institution: None Study: None Supplies: None

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			dysfunction, mild or severe diabetes mellitus, and steroid administration before surgery		**Mortality:** NR **Adverse events:** Postoperative Complications [Mainly Small Bowel Obstruction] Intervention: 18/190 (9.5%) Control: 18/187 (9.6%) P= 0.96	
Mohri 2007 [53] (ES)	**RCT** 1, 4, 6, 7, 8, 9	To compare the efficacy of single- and multiple-dose antimicrobial prophylaxis for the prevention of surgical-site infection in patients undergoing elective gastric cancer surgery.	**Number of patients: N= 486** **Patient Characteristics:** Baseline characteristics were similar between groups. ·Age, y: mean (range) Intervention: 68 (22-91) Control: 68 (23-90) ·Gender: no male (%) Intervention: 174 (71.6%) Control: 164 (67.5%) ·Obesity, BMI, kg/m^2, Mean(range) Intervention: 21.6 (13.4-31.6) Control: 21.4 (13.6-34.0) ·Comorbidities Diabetes Mellitus (no Intervention: 17/243 (7.0%) Control: 19/243 (7.8%) Gastric Cancer: T1/ T2-	**Intervention group:** n=243 Single does prophylaxis Cefazolin 1 g IV: n=122 (50.2%) Ampicillin-Sulbactam 1.5g: n=121 (49.8%) 30 minutes prior to surgery, patients received either 1g cefazolin or 1.5 g ampicillin-sulbactam by slow intravenous infusion over 15 minutes. An additional dose was administered if the operation was prolonged beyond 3h. **Timing of intervention:** Preop and intraop if procedure lasted >3hrs **Duration of intervention:** Preop and intraop if procedure lasted >3hrs vs. perioperative in controls for total 7 AMP doses (at 12hr intervals) **Device/agent:** cefazolin	**SSI: (follow up 6 weeks)** Overall: 44 (9.1%) Intervention: 23 (9.5%) Control: 21 (8.6%) Difference %: 0.9 (-4.3, 5.9) 3 patients in the intervention group had an infection that involved both the incisional and deep or organ/space sites Incisional Intervention: 14 (5.8%) Control: 11 (4.5%) Difference %: 1.3 (-2.7, 5.2) Organ/Space Intervention: 12 (4.9%) Control: 10 (4.1%) Difference %: 0.8 (-2.9, 4.5) **Other infections:** NR **Topic-specific outcomes:** Antimicrobial Resistance: 33/47 (70.2%) SSIs had purulent discharge and were cultured.	**Definitions: CDC:** Incisional SSI: Infection occurring within 30 days after operation and involving skin, subcutaneous tissue or deep soft tissue (e.g. fascial and muscle layers) of the incision site, and at least one of the following • Purulent drainage, with or without laboratory confirmation, from the incision • Organisms isolated from an aseptically obtained culture of fluid or soft tissue from the incision • At least one of the following signs or symptoms of

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			4 Intervention: 94/149 Control: 108/135 Operative details: Blood loss: mean (range) Intervention: 338 (10-2811) Control: 405.7 (10-2917) P=0.028 Extent of Lymph node resection D0 or D1 Intervention: 92/243 (37.9%) Control: 112/243 (46.1%) D2 Intervention 151/243 (62.1%) Control: 131/243 (53.9%) **Procedures:** Elective gastric cancer surgery <u>Total or proximal gastrectomy/ distal gastrectomy/ wedge resection/ gastrojejunostomy</u> Intervention: 78/147/2/16 Control: 94/141/1/7 **Indications:** gastric cancer **Setting:** 10 centers	1g IV or ampicillin-sulbactam 1.5g (V **Monitoring intervention:** **Control group:** n=243 <u>Multiple dose prophylaxis</u> <u>Cefazolin: n=121 (49.8%)</u> <u>Ampicillin-sulbactam: n=122(50.2%)</u> 30 minutes prior to surgery, patients received either 1g cefazolin or 1.5 g ampicillin-sulbactam by slow intravenous infusion over 15 minutes. An additional dose was administered if the operation was prolonged beyond 3h. The same dose of antibiotics was given at 12 hour intervals postoperatively to achieve a total of 7 antibiotic doses. **Standard preventive measures:** Hair removal: Hair was "shaved" using electric clippers after induction of general anesthesia Skin prep: surgical site was wiped with 10% povidone-iodine solution before surgery and draped with a disposable towel. Closure: Absorbable synthetic sutures were	13/33 (39.3%) were culture positive S. aureus: 3 Intervention; 2 control MRSA: 2 intervention 2 control E. faecium 1 control Streptococcus spp. 1 control E. coli 1 intervention S. marcescens 1 intervention Enterobacter spp 1 intervention There were no appreciable differences between groups in the resistance pattern of isolates. **Reoperations:** NR **Length of stay:** NR **Mortality:** NR **Adverse events:** AMP was not associated with any major side effects	infection: pain or tenderness, localized swelling, redness, heat or fever (38^{o}C) • Spontaneous wound dehiscence • Abscess or other evidence of infection involving the fascia or muscle layer found on direct examination, during reoperation, or by histopathological or radiological examination. <u>Organ/space SSI</u>: Infection occurring within 30 days after operation and involving the intra-abdominal cavity and at least one of the following: • Purulent discharge from a drain placed through a stab wound into the intra-abdominal cavity • Organisms isolated form an aseptically obtained culture of fluid or tissue in

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			Location: Japan **Dates:** May 2001 – December 2004 **Inclusion Criteria:** Patients undergoing elective gastric cancer surgery in one of ten centers. **Exclusion Criteria:** Aged<20 years, pregnant, allergic to penicillins or cephalosporins, had received antimicrobial treatment in the past 2 weeks, had an infection at the time of surgery, had malignant disease of another organ, or had colorectal resection at the time of surgery. Also, moderate or severe liver disease (alkaline phosphatase, alanine aminotransferase, aspartate aminotransferase or total bilirubin more than 5 times the upper limit of normal) and sever renal impairment (serum creatinine level above 2.0	used for closure of the fascia and peritoneum. Skin was closed using stainless steel staples and the wound then wiped with normal saline. Staples were removed after 7 days. Drains: Intra-abdominal drainage tubes were passed through a stab incision separate from the wound. They were removed within 48h of surgery Local antimicrobial Irrigation: None Adhesive dressing: site kept covered with an adhesive dressing until removal of the staples. **Non-standard preventive measures:** Antimicrobial prophylaxis choice: choice of cefazolin or ampicillin-sulbactam was left to the operating surgeon who was blinded to treatment schedule.		the intra-abdominal cavity • Abscess or other evidence of infection involving the intra-abdominal cavity found on direct examination, during reoperation, or by histopathological or radiographic examination. **Perioperative care:** See standard preventive measures **Other notes:** None **Follow-up:** Patients assessed daily until discharge with postoperative follow-up at 6 weeks by an independent investigator at each institution. **Funding Source Conflicts:** Authors: NR Institution: NR Study: NR Supplies: NR

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			mg/dl.)			
Togo 2007 [55] (ES)	**RCT** 1, 2, 6, 7, 8, 9, 10	To investigate two different postoperative durations of antimicrobial prophylaxis administration (fluorometholone) after elective hepatectomy and their respective impact on the incidence of SSI and Systemic inflammatory response syndrome (SIRS). Specifically, 2-day versus 5-day postoperative regimens.	**Number of patients: N=180** **Patient Characteristics:** There were no significant differences in any category between groups. ·Age, y: mean ±SD Intervention: 62.8±11.2 Control: 61.6±10.7 ·Gender: m/f Intervention: 55/34 Control: 61/30 ·Obesity: NR ·Comorbidities Diabetes Mellitus (-/±/+) Intervention: 70/5/14 Control: 68/5/18 Operative findings: No significant difference between groups in terms of resection rates, number of liver segments resected, prognostic score, operation time,	**Intervention group:** n= 89 1g fluorometholone was administered 30 minutes before surgery, followed by 1g every 3 hours during surgery, 1g 2 hours after completion of surgery, and then 1g every 12 hours)for 2 days postoperatively **Timing of intervention:** Pre-, intra-, and postoperatively **Duration of intervention:** Beginning 30 minutes before surgery and continued for 2 days vs. 5 days in controls **Device/agent:** fluorometholone 1g IV **Monitoring intervention:** Hematological and biochemical tests were performed before surgery, immediately after surgery, and additional tests were	**SSI: (follow up 30 days)** Total SSI Intervention: 4/89 (4.5%) Control: 4/91 (4.4%) P=0.033 Intra-abdominal infection (infection at cut surface of liver= Organ/Space) Intervention: 2/89 (2.2%) Control: 3/91 (3.3%) Wound infection (Incisional) Intervention: 2/89 (2.2%) Control: 1/91 (1.1%) Statistically Significant Postoperative infection Risk Factors Infected n=13 Non-infected: n=167 Duration of operation, min: mean±SD Infected: 494±106 Non-infected: 352±107 P<0.001 Bile Fistula (+/-) Infected: 4/9 Non-infected: 4/163 P<0.001	**Definitions:** SSI: CDC Guideline definitions for Prevention of Surgical Site Infection were used. Inflammatory findings (fever and flare, drainage of pus from incision, or drain, detection of a pathogen by culture of fluid or tissue sample and fluid retention on imaging indicating presence of pus in a deep region. Cases judged as SSI by physician included even if pus drainage and culture negative.

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			blood loss or blood transfusion **Procedures:** Elective Hepatectomy without the reconstruction of the biliary or intestinal tract **Indications:** <u>Hepatocellular carcinoma/ liver metastasis/ donor/ other</u> Intervention: 33/43/4/9 Control: 33/45/5/8 **Setting:** 1 University Hospital **Location:** Japan **Dates:** April 2003 – March 2006 **Inclusion Criteria:** Patients who underwent elective liver resection for hepatic lesions. **Exclusion Criteria:** Patients who were concomitantly treated with the resection of other organs – resection and anastomosis of the bile duct; drainage and resection and anastomosis of the digestive tract and patients In whom apparent infection was noted at the	performed as needed. **Control group: n=91** 1g fluorometholone was administered 30 minutes before surgery, followed by 1g every 3 hours during surgery, 1g 2 hours after completion of surgery, and then 1g every 12 hours for 5 days postoperatively **Standard preventive measures:** ABX prophylaxis: No patient received pre-operative administration of oral antimicrobial agents.	**Other infections:** <u>Remote Infections</u> Intervention: 3/89 (3.4%) Control: 2/91 (2.2%) P=0.242 <u>Catheter Infection</u> Intervention: 2/89 (2.2%) Control: 2/91 (2.2%) <u>Pneumonia</u> Intervention: 1/89 (1.1%) Control: 0/91 <u>Postoperative infections total (SSI + RI)</u> Intervention: 7/89 (7.9%) Control: 6/91 (6.6%) P=0.049 <u>SIRS Positive Rate</u> <u>At Postop day 2</u> Intervention: 26/89 (31.7%) Control: 12/91 (14.1%) P=0.007 <u>At Postop day 3</u> Intervention: 12/89 (14.6%) Control: 4/91 (4.7%) P=0.029 <u>After Postop day 3</u> Intervention: 6/89 (7.3%) Control: 5/91 (5.9%) P=0.709 <u>SIRS Duration all (mean)</u> Intervention: 1.34 days Control: 0.95 days P=0.065 **Topic-specific outcomes:** Treatment: when post-	<u>Systemic Inflammatory Response Syndrome (SIRS)</u>: the consensus criteria established by the American Thoracic Society and the Society of Critical Care Medicine were used. When 2/ 4 of the following criteria were present: • Body temperature of ≤ 36°C and ≥38°C • A pulse rate of ≥90/min • A respiratory rate of ≥ 20/min or $PaCO_2$> 32 torr • White blood cell counts of ≥12,000/mm^3 and ≤4,000/mm^3 or ≥10% immature cells <u>Biliary Complications:</u> • Drainage of bile from the abdominal wound and drain, showing a total bilirubin level of >5mg/mL

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			time of surgery. Also, patients with a past medical history of allergic reaction to β-lactams, a pre-operative serum creatinine level of ≥1.5 mg/dL, diabetes mellitus under insulin control, treatment with antimicrobials within 1 week before surgery, judged ineligible by the attending physician, and non-consent to the study.		operative infection was diagnosed during the study, the treatment was changed to therapeutic antimicrobial agents. Diarrhea: Intervention: 2/89 (2.2%) Control: 0/91 P=0.150 No cases of *C. difficile* detected. **Reoperations:** NR **Length of stay:** Intervention: 15.24±6.84 days Control: 15.11±6.07 days P=0.896 **Mortality:** None during the admission period in either group **Adverse events:** No severe complications observed.	or 3 times the serum level in the discharge fluid. • An intra-abdominal accumulation of bile confirmed by percutaneous drainage • Cholangiographic evidence of bile leakage. Post-operative complications: conditions in which the admission period after surgery exceeded 22 das (mean±SD), **Perioperative care:** NR **Other notes:** None **Follow-up:** 30 days after surgery **Funding Source Conflicts:** Authors: None Institution: None Study: None Supplies: None
Ali 2006 [17] (ES)	**RCT** 4, 5	To compare the proportion of early postoperative infection	**Number of patients: N=200** **Patient Characteristics:**·Age, y: NR	**Intervention group: n=100** 1dose: 1 dose of 2g ceftazidime intravenously 30	**SSI** All SSI 1dose: 8/100 (8%) Multi: 6/100 (6%)	**Definitions:** Wound evaluation: done using the prescribed proforma for

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
		cases in clean orthopedic surgery after a single dose of prophylactic antimicrobial and multiple doses of prophylactic antimicrobial	·Gender: NR ·Obesity: NR ·Comorbidities: NR **Procedures:** mix of clean orthopedic fracture surgeries **Setting:** 1 public hospital **Location:** Pakistan **Dates:** April 2004 – March 2005 **Inclusion Criteria:** Any age and either gender undergoing clean orthopedic surgery and available for complete follow-up. **Exclusion Criteria:** Patients with any generalized debilitating disease, diabetes mellitus, any infective focus in the body, poor quality of the skin at the incision site, allergy to cephalosporin, open fracture, revision surgery within last 6 weeks, use of antimicrobials within the last 7 days and duration of surgery >3h.	minutes before the initial operative incision and 2 placebo doses after 12h each. **Timing of intervention:** pre and postop. **Duration of intervention:** preop up to 24h postop. **Device/agent:** ceftazidime. **Control group: n=100** 3dose: 1 dose of 2g ceftazidime intravenously 30 minutes before the initial operative incision and 2 doses after 12h each. **Standard preventive measures:** Weight adjusted dosing: in patients under 12y, the antimicrobial prophylaxis dose adjusted for weight.	<u>Deep SSI</u> Total: 4/200 (2%) 1 dose: 1% Multi: 3%; p=0.34 <u>Superficial SSI</u> Total of 10 (5%) superficial SSIs and no difference:: 1dose: 7% Multi: 3%; p=0.21 **Antimicrobial resistance:** Staphylococcus aureus was the commonest organism isolated, followed by E. coli. Eight of the 14 SSIs had a negative wound culture (7 superficial, 1 deep). No mention of resistance	postoperative fever developing or persisting 48hours after the surgery, discharge from the wound, and overlying skin inflammation. Wound infection was noted to be superficial or deep. **Other notes:** None **Follow-up:** 28 days **Funding Source Conflicts:** Authors: NR Institution: NR Study: NR Supplies: NR

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
Mui 2005 [11] (ES)	**RCT** 1, 6, 7, 8, 9	To investigate the infective complications rate after open appendectomy for non-perforated appendicitis (NPA)receiving different durations of prophylactic antimicrobials cefuroxime and metronidazole perioperative regimens: 1) single dose preoperative, 2) 1 preop and 2 postop (three-dose/1-day) and 3) preop and 5-days postop	**Number of patients: N=269** **Patient Characteristics**: All baseline characteristics were comparable ·Age, y: mean (SD) Intervention1: 36.3 (15.6) Intervention2: 32.1 (13.2) Control: 35.1 (13.4) P=0.12 ·Gender: m/f Intervention1: 65/27 Intervention2: 66/28 Control: 54/29 P=0.68 ·Obesity: NR ·Comorbidities: NR **Procedures:** Emergency open appendectomy through right lower quadrant incision using muscle splitting approach and appendices were removed in the standard fashion **Indications:** acute non-perforated appendicitis **Setting:** 1 university hospital **Location:** China **Dates:** July 1995 – December 2000	**Intervention1 group:** n= 92 Intravenous cefuroxime (1.5g) and metronidazole (500mg) were given at induction of general anesthesia. **Intervention2 group:** n= 94 Intravenous cefuroxime (1.5g) and metronidazole (500mg) were given at induction of general anesthesia followed by two more doses of IV antimicrobials. **Timing of intervention:** Pre operatively **Duration of intervention:** Single dose at induction of anesthesia vs. up to 5 days postoperatively for controls **Device/agent:** Intravenous cefuroxime 1.5g, and metronidazole 500mg. **Monitoring intervention:** NR **Control group:** n= 83 Intravenous cefuroxime (1.5g) and metronidazole (500mg) given at induction of general anesthesia followed by a 5-day course of antimicrobials. IV Antimicrobials were administered until	**SSI: (follow up 30 days)** Wound infections Intervention1: 6/92 (6.5%) Odds Ratio (95% CI): 1 Intervention2: 6/94 (6.4%) Odds Ratio (95% CI): 1.01 (0.34-3.26) Control: 3/83 (3.6%) Odds Ratio (95% CI): 0.89 (0.46-7.79) P I1&I2=0.97 P I1orI2 & C= 0.5 All required local wound exploration with daily dressing All infected wounds healed by 30-days postoperative follow up. Intra-abdominal Infections/abscesses No patients developed intra-abdominal collection or abscesses. **Other infections:** NR **Topic-specific outcomes:** The incidence of AMP-related complications was significantly higher in the control group (5d) as compared with Intervention 1 (single dose): OR, (95% CI) 1.05(1.001-1.1);	**Definitions:** Wound infection: discharge of pus that required surgical drainage before discharge Intra-abdominal collection or abscess: a fluid collection diagnosed at ultrasound or computed tomography which required drainage *C. difficile* enterocolitis-diagnosed by positive fecal clostridium toxin **Perioperative care:** Discharge: when fully mobilized, could tolerate a normal oral diet with evidence of bowel activity (normal bowel sounds and passing flatus or stool), apyrexial for 12h (<37^{o}C tympanic), and had adequate pain control on oral analgesics.

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			Inclusion Criteria: Patients aged 15-70 with the clinical diagnosis of acute, non-perforated appendicitis undergoing emergency open appendectomy **Exclusion Criteria:** Patients who had a history of preadmission antimicrobials, diabetes mellitus, steroid therapy, known drug allergy to the study antimicrobials, ruptured appendicitis and appendicular mass or abscess formation. Also, pregnant women and patients who refused consent.	patients could tolerate a semi-solid or solid diet when IV antimicrobials were substituted by oral formula: 250mg cefuroxime 2x/day and 400mg metronidazole 3X/day **Standard preventive measures:** Closure: The peritoneum, oblique muscles and the Scarpa's fascia closed with 3/O polyglycolic sutures and the skin was closed with interrupted vertical mattress with 3/O monofilament sutures in a standardized manner. Peritoneal lavage: none Wound Lavage: none Local antimicrobials: none	P=0.048 *C. difficile* enterocolitis Intervention1 (single dose): 0/92 Odds Ratio (95% CI): 1 Intervention2 (3d): 1/94 (1.1%) Odds Ratio (95% CI): 1.01 (0.99-1.03) Control (5d): 4/83 (4.8%) Odds Ratio I1 vs. C (95% CI): 1.05 (1.001-1.1) P I1&I2=1.0 P I1 & C= 0.048 via Fisher's exact test All cases of C. diff enterocolitis recovered uneventfully after 7d course of oral vancomycin **Reoperations:** By definition (see next column) all wound infections (15/15) required surgical drainage All infections were treated by laying open the wound site, and packing with normal saline ribbon gauze twice per day to allow healing by secondary intention. All infected wounds were healed at 30d f/u **Length of stay, d:** mean	**Other notes:** Study is underpowered Patients were randomized after open appendectomy determined NPA **Follow-up:** After discharge all patients were followed up at 10 days postoperatively for wound assessment and stitches removal and the second follow up was conducted for wound problems occurring at 30 days postoperatively **Funding Source Conflicts:** Authors: NR Institution: NR Study: NR Supplies: NR

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
					(SD) Intervention1: 4.3 (1.3) Intervention2: 4.6 (1.2) Control: 4.8 (2.3) P=0.13 **Mortality:** No perioperative mortality **Adverse events:** See topic specific events for AMP adverse events	
Chang 2005 [41] (ES)	**RCT (pilot study)** 1, 2, 9, 10	To investigate whether a short course of antimicrobials (<24 hours between the first and final doses) is as efficacious as longer courses (30-60 hours) in laparoscopically assisted vaginal hysterectomy (LAVH).	**Number of patients: N=156** **Patient Characteristics:** No differences in patient or operative characteristics between groups. ·Age, y: mean ±SD Intervention: 41.1±5.8 Control: 42.3±7.1 ·Gender: 100% Female ·Obesity: NR ·Comorbidities: NR **Procedures:** Laparoscopically assisted vaginal hysterectomy (LAVH) **Indications:** Myoma uterus: 70 Intervention: 37 Adenomyosis: 53 Intervention: 28 Cervical carcinoma in situ: 17 Intervention:10 Cervical carcinoma Ia1:	**Intervention group:** n=74 Intravenous push stat of 2g cephalothin followed by a 1g injection every 6 hours. Gentamycin began with an 80mg IV drip followed by a 60-80mg injection every 8 hours. The first dose was administered within 1 hour prior to the incision and continued for <24 hours **Timing of intervention:** Pre and postoperatively **Duration of intervention:** From 1 hour prior to incision to either <24 hours or 30-60hours **Device/agent:** Cephalothin 2g IV and gentamycin 80mg IV **Monitoring intervention:** NR **Control group:** n=82 Intravenous push stat of 2g cephalothin followed by a 1g every 6 hours. Gentamycin began with	**SSI: (follow up within 7 days of discharge)** Operative Site Infection Intervention: 2/74 (2.7%) 1/2: Trocar site wound infection 1/2: 1 cuff abscess Control: 3/82 (3.6%) 1/3: infection 1/3: cellulitis 1/3: trocar site wound infection during hospitalization (instead of within 7 days of discharge) P=0.735 **Other infections:** Urinary Tract Infection: Intervention: 2 (2.7%) 1/2: during hospitalization 1/2: w/in 7 days of discharge Control: 2 (2.4%) 2/2: w/in 7 days of discharge P=0.917	**Definitions:** Operative site infection: includes pelvic cellulitis, vaginal cuff abscess, pelvic abscess, and wound infection (Sharpiro 1982) Urinary tract infection (UTI): diagnosed from patients' symptoms and signs and to whether there was a positive urinalysis **Perioperative care:** NR **Other notes:** Pilot study with low power to determine statistically significant differences in the rate of

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			9 Intervention:3 Other: 7 **Setting:** 1 medical center **Location:** Taiwan **Dates:** June 2001-July 2002 **Inclusion Criteria:** Patients undergoing LAVH. Preop serum hemoglobin level>9g/dL and normal renal function tests (serum BUN/Creatinine) **Exclusion Criteria:** LAVH cases with complications and those patients who required therapeutic antimicrobials and other associated surgical procedures were excluded from the study	an 80mg IV drip followed by a 60-80mg injection every 8 hours. The first dose was injected within 1 hour prior to the incision and continued for 24 hours **Standard preventive measures:** NR	**Topic-specific outcomes:** NA **Reoperations:** NR **Length of stay,** d:mean±SD Intervention: 4.3±1.1 Control: 4.2±1.3 P=0.89 **Mortality:** NR **Adverse events:** NR	operation site infection and UTI between the 2 groups. To achieve power of 0.80, 3,800-5,200 cases in both groups would be necessary **Follow-up:** Within 7 days of discharge collected from patients' charts **Funding Source Conflicts:** Authors: None Institution: None Study: None Supplies: None
Su 2005 [13] (ES)	**RCT** 1, 2	To compare the efficacy of a single-dose versus a 1-day course of prophylactic antimicrobials for postoperative wound infection outcomes and cost-	**Number of patients: N=531** **Patient Characteristics:** (N=548 before 17 patients excluded due to loss to f/u) There were no differences between groups regarding general status ·Age, y: mean±SD Intervention:	**Intervention group:** n= 267 One dose of 1g cefazolin intravenously before surgery upon induction of anesthesia by the anesthesiologist within 30 minutes before surgery. If the surgery duration was greater than 4h, and additional dose of 1.g cefazolin administered	**SSI: (follow up 90 days)** Serious infectious morbidity Intervention: 1/267 (0.37%) 1/1: Trocar wound infection at postop day 27 from LAOC surgery Control: 1/264 (0.37%) 1/1: vaginal cuff infection with pelvic abscess at postop day 7 from LAVH surgery	**Definitions:** Infectious morbidity: If body temperature was greater than 38.5°C, the patient was assessed for signs and symptoms of infection including one or more of the

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
		effectiveness in gynecologic operations.	45.77±9.74 Control:45.18±9.31 ·Gender: 100% Female ·Obesity: BMI, kg/m^2, mean±SD Intervention: 23.21±1.13 Control:23.32±1.05 ·Comorbidities: NR Wound classification: Clean: LAOC Clean contaminated: TVH, TAH, LAVH Operative characteristics: Duration of surgery, min: mean±SD Intervention: 98.14±35.54 Control: 98.87±35.48 **Procedures:** Total vaginal hysterectomy (TVH) Total abdominal hysterectomy (TAH) Laparoscopic-assisted vaginal hysterectomy (LAVH) Laparoscopic assisted ovarian cystectomy (LAOC) LAOC/LAVH/TAH/TVH Intervention: 36/190/27/20 Control:34/195/25/21 **Indications:** NR **Setting:** 1 hospital	intravenously. **Timing of intervention:** Pre, intra and postoperatively **Duration of intervention:** Either preoperatively, or Preoperatively through 24 hours postoperatively. **Device/agent:** Cefazolin 1g IV **Monitoring intervention:** NR **Control group:** n= 264 One dose of 1g cefazolin intravenously before surgery upon induction of anesthesia by the anesthesiologist within 30 minutes before surgery followed by another three doses of 1g cefazolin every 6hr after surgery X1 day. If the surgery duration was greater than 4h, and additional dose of 1.g cefazolin was administered intravenously. **Standard preventive measures:** There were no differences between groups regarding preoperative examination and preparation, skin disinfection, postoperative	**Other infections:** Fever (≥38.5°C on two occasions 4 or more hours apart excluding the night of surgery) Intervention: 112/267(41.9%) 67/112 had blood drawn for cultures but none had septicemia Control: 120/264 (45.4%) 74/112 had blood drawn for cultures but none had septicemia **Topic-specific outcomes:** Timing of AMP before incision, min: mean±SD Intervention: 21.07±9.96 Control:22.70±13.22 Antimicrobial resistance: none reported. Intervention trocar wound culture: P. aeruginosa Control vaginal cuff cultures: E coli, B. fragilis **Reoperations:** Intervention: Infection required debridement of trocar wound and drainage with pen-rose drain. Readmission stay was 8 days Control: Infection & abscess required	following: • An abdominal wound infection or trocar wound infection (including wound discharge or abscess) • Pelvic Abscess or tubo-ovarian abscess • Vaginal cuff abscess • Postoperative septicemia **Perioperative care:** Anesthesia Genera/spinal Intervention n=273: 257/16 Control n=275:260/15 **Other notes:** NNIS SSI risk stratification. **Follow-up:** During hospitalization, abdominal and perineal exams were performed daily by gynecological staff to assess for infection. If signs/symptoms developed,

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			Location: Taiwan **Dates:** June 1, 2001 – January 31, 2003 **Inclusion Criteria:** Women ≥18 years old scheduled to undergo elective vaginal or abdominal hysterectomy (total vaginal hysterectomy (TVH) and total abdominal hysterectomy (TAH), laparoscopic-assisted vaginal hysterectomy or ovarian cystectomy (LAVH or LAOC) for nonmalignant disease. **Exclusion Criteria:** Women who had major surgery in the month before elective gynecologic surgery, had known or suspected hypersensitivity or intolerance to cephalosporin, or had any coexisting disease that would require antimicrobial therapy during the study. Also, patients who had taken antimicrobials the week before surgery	intravenous fluid therapy (for 36h only), and indwelling urethral catheterization (for 24h only). Skin Prep: The surgical site was prepared by swabbing with povidone-iodine or alcohol—iodine for about 5 min and Hair removal-trimming/ shaving of the surgical area according to the "standard practice" in our hospital (did not specify how many in each).	drainage with pen-rose drain and readmission stay was 4 days. **Length of stay,** days, mean±SD Intervention: 3.97±1.27 Control:4.02±1.51 **Mortality:** NR **Adverse events:** NR	examiner collected samples from pelvic cavity and wound site for culture before initiating antimicrobial therapy. After discharge: 90 days postoperatively at the first, second and third months after surgery, vital signs, physical examination, and pelvic sonography were performed when patient returned to the clinic for evaluation. **Funding Source Conflicts:** Authors: None Institution: None Study: None Supplies: None

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
Carroll 2003 [40] (ES)	**RCT** 1, 4, 8, 9, 10	To clearly address the duration of antimicrobial prophylaxis (either 3 doses [1 day] or 15 doses [3 days]) in patients with head and neck cancer requiring free-flap reconstruction of cancer defects.	**Number of patients: N=74** **Patient Characteristics:** No statistically significant difference existed between study groups or between patients with and without complications (data listed below is for entire population (N). ·Age, y: mean±SD61.6±12.5 range 21-88 years ·Gender (m/f): 46/28 ·Obesity: NR ·Comorbidities: NR Previous radiotherapy: 24/74 (32%) Flap Type: Fibula/jejunum/radial forearm/rectus: 9/19/31/15 Tumor site: Buccal/floor of mouth/hypopharynx/ larynx/maxilla/ oropharynx/roof of mouth/ tongue: 5/15/14/7/11/8/10/4 **Procedures:** Surgical ablation of head and neck malignancies with immediate free-flap reconstruction including: radial forearm, jejunum,	**Intervention group:** n= 35 Short course (1 day): 900mg Clindamycin intravenously initiated immediately preoperatively to total 3 doses every 8 hours. **Timing of intervention:** Pre and postoperatively **Duration of intervention:** From preoperatively to 16-56 hours postoperatively. **Device/agent:** Clindamycin **Monitoring intervention:** NR **Control group:** n= 39 Long Course (3 days) 900mg Clindamycin intravenously initiated preoperatively to total 15 doses every 8 hours. **Standard preventive measures:** NR	**SSI: (follow up: discharge or 7days postop)** <u>Wound infection</u> Intervention: 4/35 (11%) Control: 4/39 (10%) P=0.99 **Other infections:** Women were more likely than men to develop Remote Infections (specifically UTI) 25% vs. 2%; P=0.004 <u>Other/ remote infections (including UTI & enterocolitis)</u> Intervention: 4/35 (11%) Control: 4/39 (10%) P=0.99 **Topic-specific outcomes:** C. difficile enterocolitis: 1/74 (1%) they don't specify in which group **Reoperations:** NR **Length of stay:** NR **Mortality:** Intervention: 1/35 (3%) Control: 1/39 (3%) P=0.99 **Adverse events:** <u>Pharyngocutaneous Fistula</u> Intervention: 3/35 (9%) Control: 3/39 (8%)	**Definitions:** Head and neck wound and donor site evaluated for: <u>Wound color</u> 1: normal 2: pink 3: red or swollen <u>Drainage</u> 1: none 2: serious 3: purulent <u>Wound infection</u> A wound was considered infected when the color became red or the wound was swollen. A pink wound that developed purulent drainage was also considered infected. **Perioperative care:** NR **Other notes:** Accrual of patients for the study was stopped when annual review of the data disclosed that differences

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			rectus and fibula by descending order of frequency. **Indications: (n)** Stage II/III/IV: 7/21/46 (91% stage III or IV) **Setting:** 1 center **Location:** USA **Dates:** January 1, 1998- April 30, 2001 **Inclusion Criteria:** Patients scheduled to undergo surgical ablation of head and neck malignancies with immediate free-flap reconstruction **Exclusion Criteria:** Patients undergoing secondary reconstruction and those whose tumor did not involve the mucous membranes of the upper aerodigestive tract		P=0.99 Postoperative fistula was more common in men but P=0.08 <u>Flap Necrosis</u> Intervention: 0/35 Control: 1/39 (3%) P=0.99 <u>Vascular Compromise of flap</u> Intervention: 2/35 (6%) Control: 1/39 (3%) P=0.99	between the study groups were much lower than those projected in initial sample size determinations. A difference of 1%, recalculated estimate of sample size for 2 sided significance level of 0,005 with 80% power would require more than 10,000 subjects in each treatment arm. **Follow-up:** Wounds were evaluated daily for 7 days postoperatively (or until discharge) by a blinded faculty head and neck surgeon. **Funding Source Conflicts:** Authors: None Institution: None Study: None Supplies: None

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
Hall 1998 [38] (ES)	**RCT** 1, 2, 6, 7, 8, 9	To compare the incidence of wound infection after emergency elective vascular surgery following the administration of the same agent as either short-term prophylaxis or a multiple dose regimen.	**Number of patients: N=302** **Patient Characteristics:** Both groups were comparable with respect to putative risk factors for a wound infection at baseline and during the perioperative period. ·Age, y: median (range) Intervention: 70 (64-75) Control: 69 (64-76) ·Gender: m/f Intervention: 116/37 Control: 103/46 ·Obesity, BMI, kg/m^2, mean (range) Intervention: 25 (22-27) Control: 24 (22-27) ·Comorbidities IDDM: Intervention: 3/153 (2%) Control: 3/149 (2%) NIDDM: Intervention: 31/153 (20%) Control: 16/149 (11%) Current Smoker Intervention: 53/153 (35%) Control: 39/149 (26%) Previous myocardial infarction	**Intervention group:** n= 153 Single Dose 3g ticarcillin/ 0.1g clavulanate by slow intravenous infusion (over 30 minutes) immediately after the induction of anesthesia. Patients received an additional dose if the surgery was prolonged beyond 3 hours. **Timing of intervention:** Pre, intra and postoperatively **Duration of intervention:** From immediately after the induction of anesthesia to vs. five days in controls. **Device/agent:** 3g ticarcillin/ 0.1g clavulanate **Monitoring intervention:** NR **Control group:** n= 149 Multiple Dose 3g ticarcillin/ 0.1g clavulanate by slow intravenous infusion (over 30 minutes) immediately after the induction of anesthesia. Patients received an additional dose if the surgery was prolonged beyond 3 hours. After the initial dose, patients	**SSI: (follow up 42 days postop)** Overall rate of wound morbidity: (wound + minor wound): 101/302 (34%) Wound infection: 43/302 (14%) Intervention: 28/153 (18%) Control: 15/149 (10%) P=0.041 Relative risk estimate (95%CI) = 2.00 (-1.02-3.92) Median time to presentation of wound infection: 13 days (range: 2-43 days) Minor wound infections: 58/302 (19%) Intervention: 35/153 (23%) Control: 23/149 (15%) Graft infection: 2/302 (<1%) Intervention: 1/153 (<1%) Control: 1/149 (<1%) Patients undergoing lower limb surgery had greatest risk of wound infection (24/95 or 25%) **Other infections:** NR **Topic-specific outcomes:** No major side effects associated with the parenteral	**Definitions:** Wound infections: discharge of pus or a serous discharge that contains pathogenic organisms Graft infection: an overt clinical event characterized by the need for aggressive interventions and confirmed by microbiology. Minor wound infections: Local abscess or serous discharge not meeting their established criteria for wound infection Vascular surgery: All open arterial procedures. Shock: (Dellinger 1985) clinical signs of reduced peripheral perfusion plus any two of the following: • Systolic blood pressure (BP) <80

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			Intervention: 38/153 (25%) Control: 37/149 (25%) Previous stroke Intervention: 20/153 (13%) Control: 16/149 (11%) Previous ischemic attack Intervention: 15 (10%) Control: 9 (6%) Previous cardiovascular surgery Intervention: 62/153 (41%) Control: 65/149 (44%) Comparable with regards to operation type, duration, intraoperative shock, wound closure technique, total length of wounds and duration of drainage in days. Intervention vs. Control Use of Cell saver: 47 (31%) vs. 51(34%) Peri-op blood transfusion 32 (21%) vs. 40 (27%) Number of wounds per patient: 1: 86 (56%) vs. 83 (56%) 2: 34 (22%) vs. 41 (28%) 3: 31 (20%) vs. 22	received 3g ticarcillin/ 0.1g clavulanate intravenously at 6 hourly intervals for a maximum total of 20 doses (i.e., until the lines are removed but<5 days) **Standard preventive measures:** Skin prep: preoperative chlorhexidine skin wash. Wound closure & Drains: there was uniform wound closure and drain tubes did not exit through wounds. ABX irrigation: No local irrigation of tissues with antibiotic solutions. Diarrhea: Patients with postop diarrhea had stools evaluated for enteropathogens.	administration of AMP Diarrhea with *C. difficile* Intervention: 2/153 (1.3%) Control: 1/149 (0.7%) Antimicrobial resistance: Authors state that they did not detect any appreciable difference in the resistance patterns of the isolates between groups (statistical significance not tested) Among several isolates from 25 patients are the following: S. aureus Intervention: 5/15 (33%) Control: 4/10 (40%) MRSA Intervention: 1/5 SA (20%) or 1/15 isolates (7%) Control: 2/4 SA (50%) or 2/10 isolates (20%) S epidermis (SE) Intervention: 1/15 (7%) Control: 3/15 (20%) Resistance not reported for SE **Reoperations:** Intervention: 16 (10%) 8/16 Amputation/ debridement of tissue 5/16 Revision of graft 2/16 Hemostasis	mm HG for 1 hour • Pulse rate >120bmp (sinus minute rhythmia) for more than 1 hour • Urine output less than 80ml for any 4 hour period • Use of pressors to maintain the blood pressure for at least 1 hour. Obesity: Body mass index (BMI) weight/ the square of the height. Insulin dependent diabetes mellitus (IDDM): an episode of ketoacidosis or dependence on insulin Non-Insulin dependent diabetes mellitus (NIDDM): indicated by a requirement for oral hypoglycemic medication Length of stay = number of postoperative days in hospital **Perioperative care:** Nosocomial

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			(15%) 4: 2 (1%) vs. 3 (2%) **Procedures:** Emergency or Elective: Abdominal aortic aneurysm: 86/ 302 (28.5%) Groin-distal bypass: 73/302 (24.2%) Aorto-groin bypass: 49/302 (16.2%) Carotid endarterectomy: 37/302 (12.3%) Miscellaneous lower limb: 28/302 (9.3%) Groin procedures: 22/302 (7.3%) Other: 7/302 (2.3%) **Indications:** NR **Setting:** 1 hospital **Location:** Australia **Dates:** January 1993 – October 1995 **Inclusion Criteria:** All adults undergoing Vascular surgery (all open arterial procedures.) **Exclusion Criteria:** Patients undergoing endovascular procedures, administration of antimicrobial agents within 48 hours of surgery, a history of hypersensitivity to		0/16 CABG 1/16 Intestinal Adhesions Control: 17 (11%) 7/17 Amputation/ debridement of tissue 3/17 Revision of graft 4/17 Hemostasis 2/17 CABG 1/17 Intestinal Adhesions **Length of stay: median (range)** Intervention: 9/153 (6-13 Control: 9/149 (7-13%) 86% of patients admitted to ICU were discharged w/in 48 hours. **Mortality:** Intervention: 8/153 (5%) Control: 5/149 (3%) No patient died as a result of a wound or graft infection. **Adverse events:** <u>Administration of antimicrobials</u> Intervention: 37/153 (24%) Control: 27/149 (18%) <u>Requirement of wound dressing</u> Intervention: 23/153 (15%) Control: 22/149 (15%)	infections were managed in accordance with the institutional antimicrobial guidelines. **Other notes:** As might be expected, the patients tended to be elderly and debilitated. More intervention patients were smokers, NIDDM and had severe cardiac disease. **Follow-up:** 42 days after surgery **Funding Source Conflicts:** Authors: NR Institution: NR Study: Industry Supplies: NR

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			penicillin, and profound comorbidity.			
Kow 1995 [22] (ES)	**RCT** 1, 2, 6	To evaluate the efficacy of one dose of antimicrobial vs. 3 doses covering the 24h postoperative period using a new antimicrobial prophylaxis consisting of cefotaxime plus metronidazole or cefoxitin	**Number of patients: N=1010** **Patient Characteristics** There was an even distribution of patients for each antimicrobial regimen. **Procedures:** Elective and emergency intra-abdominal surgeries. **Setting:** 2 hospitals. **Location:** Australia **Dates:** September 1989 - January 1992 **Inclusion Criteria:** Patients 16 years and older, admitted to the two hospitals for all types of intra-abdominal surgery (elective and emergency) **Exclusion Criteria:** if there was a history of allergy to cephalosporins, penicillin, or metronidazole, had received antimicrobials. Also if operative findings indicated the need for prolonged	**Intervention group: n=516** 1dose CFX: n=252: 2g cefoxitin intravenously on induction of anesthesia 1dose CTX+M: n=264: 1g cefotaxime + 500mg metronidazole on induction of anesthesia **Timing of intervention:** pre and postop **Duration of intervention:** preop and up to 12h postop **Device/agent:** cefoxitin or cefotaxime plus metronidazole **Control group: n=** 3dose CFX: n=254: 2g cefoxitin intravenously on induction of anesthesia followed by another 2g at 6 & 12h postop 3dose CTX+M: n=240: 1g cefotaxime + 500mg metronidazole on induction of anesthesia followed by 1g of cefotaxime at 6 & 12h postop. **Standard preventive measures:** Skin prep: PI Solution Plastic wound protectors:	**SSI** All procedures Total: 58/1010 (5.7%) 1dose: 31/516 (6.0%) 3dose: 27/494 (5.5%) P>0.19 1dose CFX: 17/252 (6.7%) 3dose CFX: 17/254 (6.7%) 1dose CTX+M: 14/264 (5.3%) 3dose CTX+M: 10/240 (4.2%) <u>Elective colorectal procedures</u> CTX+M: suggests no difference Total: 12/138 (8.7%); 1dose: 5/71(7.0%) 7/67(10.4%); p =0.48 (28-41 day follow up) CFX: suggests no difference: Total: 16/135 (11.9%); 1dose: 8/65(12.3%) 3dose: 8/70(11.4%); p=0.87 <u>Emergency colorectal procedures</u>: Total: 6/46 (13.0%);	**Definitions:** Wound infection: the presence of purulent discharge from the wound or a serous discharge with positive culture of pathogenic organisms. **Perioperative care:** NR **Other notes:** Study was not sufficiently powered for smaller sub analyses. **Follow-up:** 28-41 day follow-up. **Funding Source Conflicts:** Authors: NR Institution: NR Study: Industry Supplies: NR

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			antimicrobials, or the need for delayed primary wound closure were excluded. Also if a patient died in the 14 days after the operation with no evidence of infection, they were excluded from the analysis.	not allowed. Bowel Prep: all patients undergoing elective colorectal surgery were given mechanical (non-antimicrobial) bowel prep of up to 3 L of a colonic lavage solution prior to operation.	1dose: 4/21 (19.0%) vs. 3dose: 2/25 (8.0%); p=0.28 <u>Appendectomy</u>: Drug regimen 1: n=112: 1doseCFX: 4/54 (7.4%) 3dose CFX: 4/58 (6.9%) Drug regimen 2: n=117 1doseCTX+M: 2/63 (3.2%) 3dose CTX+M: 0/54 <u>Esophageal, gastric, and small bowel surgery</u> Drug regimen 1: n=82: 1doseCFX: 1/42 (2.4%) 3dose CFX: 3/40 (7.5%) Drug regimen 2: n=81 1doseCTX+M: 1/41 (2.4%) 3dose CTX+M: 1/41 (2.4%) <u>Biliary Surgery:</u> Drug regimen 1: n=158: 1doseCFX: 2/83 (2.4%) 3dose CFX: 2/75 (2.7%) Drug regimen 2: n=140 1doseCTX+M: 3/76 (3.9%) 3dose CTX+M: 0/64	

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
McArdle 1995 [47] (ES)	**RCT** 1, 7, 8	To compare an oral ciprofloxacin/ parenteral metronidazole regimen with a parenteral aminoglycoside/metronidazole combination commonly used for prophylaxis in colorectal surgery, and the value of 1day versus 3 days of antimicrobial cover.	**Number of patients N=87** **Patient Characteristics:** the groups were comparable in in terms of characteristics. **Procedures:** colorectal surgery **Setting:** 1 university hospital **Location:** United Kingdom **Dates:** NR **Inclusion Criteria:** patients undergoing colorectal surgery. **Exclusion Criteria:** NR	**Intervention group: n=45** Patients administered gentamicin 120mg and metronidazole 500mg intravenously at induction of anesthesia followed by gentamicin 80mg and metronidazole 500mg at 8h & 16h post-op (3doses total) **Timing of intervention:** pre and postop **Duration of intervention:** 1 shot or 3 days postop **Device/agent:** gentamicin 120mg or 80mg and metronidazole 500mg **Control group: n=42** Patients administered gentamicin 120mg and metronidazole 500mg intravenously at induction of anesthesia followed by 80mg gentamicin and metronidazole 500mg 3times/ day for 3 days postop. **Standard preventive measures:** NR	**SSI** Total: 20/87 (23.0%) Single day: 13/45(28.9%) 3day: 7/42(16.7%); p=0.18	**Definitions:** Wound sepsis: the presence of pus either discharging spontaneously or requiring drainage. Major wound sepsis: the discharge of pus with constitutional disturbance Minor wound infections: patients with cellulitis and a positive wound culture. **Perioperative care:** NR **Other notes:** NR **Follow-up:** 4 weeks post discharge **Funding Source Conflicts:** Authors: NR Institution: NR Study: Industry Supplies: NR

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
Nooyen 1994 [33] (ES)	**RCT** 1, 2, 4, 7, 8	To compare a single dose of cefuroxime with their currently recommended 3-day course of cefuroxime with regard to effectiveness in preventing postoperative wound infection.	**Number of patients: N=844** **Patient Characteristics:** Risk factors and patient characteristics were similar between groups. ·Age range Intervention: 34-86 Control: 33-86 Age>70 years Intervention: 79/419 (18.9%) Control: 86/425 (20.2%) ·Gender: m/f Intervention: 329/90 Control: 353/72 ·Obesity: NR ·Comorbidities Diabetes Mellitus Intervention: 34/419 (8.1%) Control: 41/425 (9.6%) COPD Intervention: 14/419 (3.3%) Control: 11/425 (2.6%) History of smoking Intervention: 354/419 (84.5%) Control: 363/425 (82.4%) Use of corticosteroids Intervention: 10/419	**Intervention group:** n=419 After placement of a peripheral line in the operating room, patients received 20mg/kg cefuroxime intravenously at induction of anesthesia. **Timing of intervention:** Pre, intra and postoperatively **Duration of intervention:** From induction of anesthesia to 3 days postop **Device/agent:** Cefuroxime **Monitoring intervention:** NR **Control group:** n=425 After placement of a peripheral line in the operating room, patients received 20mg/kg cefuroxime intravenously at induction of anesthesia then continued cefuroxime three times a day intravenously for 3 consecutive days. **Standard preventive measures:** SA Decolonization: Starting two days prior to surgery, all patients undergoing cardiopulmonary	**SSI: (7 day follow up)** **Overall (sternal + leg wounds):** 54/844 (6.3%) Note: authors report it as 5.3% using N=1016 even though they excluded 172 patient from all other final analysis (see NOTE at bottom of results) **Sternal Site** Total complications of healing Intervention: 58/419 (13.8%) Control: 56/425 (13.2%) P=0.35 Mediastinitis Intervention: 2/419 (0.5%) Control: 0/425 No cases of late onset mediastinitis were reported after discharge from hospital.(but they don't indicate how long postop) Wound infection Intervention: 5/419 (1.2%) Control: 4/425 (0.9%) Minor Complication Intervention: 51/419 (12.2%) Control: 52/425 (12.2%) **Donor site leg** Intervention: n=377 Control: n=389	**Definitions:** Wound infection: diagnosed if all of the following criteria were met: • Redness • Purulent discharge • Positive culture (if pathogenic organisms were isolated) Infection of the sternum was differentiated into superficial infection or mediastinitis Mediastinitis: fever>38°C, chest pain or sternal instability and a purulent discharge from the mediastinal area from which pathogenic microorganisms could be isolated. Respiratory Tract infection: If patients were febrile, Gram stain of sputum demonstrated many polymorphonucl ear leukocytes

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			(2.4%) Control: 10/425 (2.4%)<u>Operative:</u> Primary/ re-operation Intervention: 398/21 Control: 398/27 Emergency/ elective Intervention: 411/8 Control: 407/18 (18 vs. 8, P<0.08) though the rate of infection was not higher among emergency procedures. Donor vessels Leg veins only// Left internal mammary artery +/- leg veins// Both internal mammary arteries +/- leg veins Intervention: 94//223//102 Control: 118//212//95 **Procedures:** Coronary Artery Bypass Grafting (CABG) **Indications:** NR **Setting:** 1 hospital **Location:** The Netherlands. **Dates:** October 1989 - December 1990 **Inclusion Criteria:** All patients undergoing coronary artery bypass grafting	surgery are treated intra-nasally with a cream consisting of 0.1% chlorhexidine and 0.5% neomycin to eliminate possible *Staphylococcus aureus.* Closure: All skin wounds were closed with intra-cutaneous re-absorbable sutures Jugular Vein Catheter Removal: catheter was removed after 48 hours in all cases	<u>Total complications of healing</u> Intervention: 118/377 (31.3%) Control: 130/389 (33.4%) P=0.41 <u>Wound infection</u> Intervention: 5/377 (1.3%) Control: 2/389 (0.5%) <u>Minor complications</u> Intervention: 95/377 (25.2%) Control: 110/389 (28.3%) <u>Wound dehiscence</u> Intervention: 18/377 (4.8%) Control: 18/389 (4.6%) **Other infections:** <u>UTI</u> Intervention: 4/377 (1.0%) Control: 1/389 (0.2%) <u>Respiratory tract infection</u> Intervention: 5/377 (1.3%) Control: 3/389 (0.7%) **Topic-specific outcomes:** NR **Reoperations:** NR-See NOTE below **Length of stay:** NR **Mortality:** none- See NOTE below **Adverse events:** NR- see NOTE below	and a predominant organism, and the chest X-ray showed a new pulmonary infiltration <u>Urinary Tract Infection (UTI):</u> if the urine culture was positive ($\geq 10^5$ cfu/ml) in the presence of fever for which no other cause could be found. **Perioperative care:** Graft: The internal mammary artery graft, when used, was harvested on a pedicle of soft tissue equal in width to that of both mammary veins. Leg veins were obtained by standard measures Postoperative samples of sputum and urine and if necessary wound exudates were collected on first and

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			(CABG) including elective and emergency surgery, primary and reoperation. **Exclusion Criteria:** Exclusion from randomization: Refusal of consent, administration of systemic antimicrobial treatment within the previous 48 h, hypersensitivity to cefuroxime or the presence of prosthetic valves or a vascular prosthesis.		**NOTE: Of 1016 patients included in the study, 172 were excluded from final analysis for the following reasons** (in some more than one reason was present): Reason: Intervention (n)/control (n) Chest open>6h: 42/27 Repeat thoracotomy within 7 days: 22/30 Intra-aortic balloon pump: 8/6 Artificial ventilation >24h: 7/10 Death within 7d (non-infectious): 1/8 (all died in OR or did not come off IABP) Additional antimicrobials: 15/3 Other operative procedure: 0/5 No wound inspection: 1/1 They report that neither wound infection nor mediastinitis occurred in any of these patients	following days. **Other notes:** See results for reasons for exclusion from final analysis **Follow-up:** On the seventh day postop, the sternotomy and donor site wounds were examined for healing, redness, discharge of fluid without signs of infection, or infection by a blinded physician **Funding Source Conflicts:** Authors: Industry Institution: NR Study: Industry Supplies: NR
Bernard 1994 [36] (ES)	**RCT** 1, 2, 3, 4, 5, 7, 8, 9	To determine whether a longer antimicrobial prophylaxis regimen for 48 hours after pulmonary operation	**Number of patients: N=203** **Patient Characteristics:** All characteristics were balanced except those with a P-value below ·Age, y: mean (range)	**Intervention group:** n= 101 48 hour cefuroxime A 1.5g dose of cefuroxime was delivered intravenously at the moment of induction of anesthesia. A second dose was	**SSI: (follow up 8 days)** Total deep infections: Intervention: 47/101 46% Control: 66/102 (65%) P=0.005 Difference in infection rates (19%±11%) remained significant (p=-.01) after adjusting for	**Definitions:** Deep Infections: Wound infections + Pneumonia + severe bronchopneumonia +empyema+ fistula)

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
		decreases the rate of deep infections in pleura, bronchi and parenchyma.	Intervention: 56 (19-78) Control: 61 (17-81) P=0.02 ·Gender: m/f Intervention: 91/10 Control: 85/17 ·Obesity: NR ·Comorbidities Tobacco packs/year: mean (range) Intervention: 33 (0-120) Control: 33 (0-120) Quit Smoking more than 1 month Intervention: 18/101 (18%) Control: 15/102 (15%) P(not significant) Alcohol: (L/day), mean (range) Intervention: 0.4 (0-3) Control: 0.5 (0-5) Chronic bronchitis: Intervention: 30/101 (29.7%) Control: 36/102 (35.3%) Diabetes Intervention: 5/101 (5.0%) Control: 4/102 (3.92%) Cardiac insufficiency Intervention: 5/101 (5.0%) Control: 6/102 (5.9%) Previous	systematically delivered 2 hours later to obtain high seric concentrations until the end of the procedure. 1.5g cefuroxime was given every 6 hours after the operation for 48 hours. The first postoperative infusion was given exactly 6 hours after the second infusion. **Timing of intervention:** Pre, intra and postoperatively **Duration of intervention:** From induction of anesthesia until 48 hours after the second dose during surgery **Device/agent:** Cefuroxime **Monitoring intervention:** NR **Control group:** n=102 Flash cefuroxime. A 1.5g dose of cefuroxime was delivered intravenously at the moment of induction of anesthesia. A second dose was systematically delivered 2 hours later to obtain high seric concentrations until the end of the procedure. A placebo was administered every 6	multiple variables) Wound infection Intervention: 1/101 (1%) Control: 1/102 (1%) P=0.9 Empyema Intervention: 1/101 (1%) Control: 6/102 (6%) P=0.03 Pneumonia Intervention: 17/101 (17%) Control: 31/102 (30%) P=0.01 Severe Bronchopneumonia Intervention: 25/101 (25%) Control: 25/102 (25%) P=0.9 Fever (>38°C) Intervention: 5/101 (5%) Control: 10/102 (10%) P=0.09 **Other infections:** Fistulas Intervention: 2/101 (2%) Control: 7/102 (7%) P=0.045 **Topic-specific outcomes:** Antimicrobial resistance: Pathogens cultured from pleura, bronchi, drains and blood were similar in the two groups. Did not specify	Pneumonia: defined on the basis of the x-ray film with specific parenchymal features associated with temperatures between 37.5° – 38°C. X-ray appearance Class 1: normal Class 2: moderate infiltrate Class 3: important infiltrate/atelectasis Severe Bronchopneumonia an association of purulent expectorations and atelectasis on the plain chest x-ray film associated with a temperature higher than 38°C. Empyemas and septicemias: when associated with a temperature higher than 38°C. As soon as a septic

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			Chemotherapy Intervention: 16/101 (15.8%) Control: 8/102 (7.8%) P=0.07 Previous Radiotherapy Intervention: 5/101 (5.0%) Control: 3/102 (2.9%) Transfusion, units: mean(range) Intervention: 0.32(0-8) Control: 0.5 (0-12) **Procedures:** Lobectomy: 108/203 (53.2%) Pneumonectomy: 71/203 (35.0%) Wedge resection: 23/203 (11.3%) **Indications:** Lung cancer: 160/203 (78.8%) Lung metastasis: 17/203 (8.4%) Benign tumor: 20/203 (9.9%) Chronic pulmonary emphysema with blebs: 6/203 (3.0%) **Setting:** 1 hospital **Location:** France **Dates:** January 1, 1991- June 30, 1992 **Inclusion Criteria:** All patients undergoing thoracotomy with lung resection for lung cancer, lung	hours after the operation for 48 hours. **Standard preventive measures:** Skin prep: local cutaneous disinfection with povidone-iodine at 12 and 1 hour pre-op. Analgesic: all patients were given the same analgesia: Morphinic antalgic drugs were infused intravenously every 4 hours.	antimicrobial resistance. **Reoperations:** NR **Length of stay,** days**: mean±SD** Intervention: 13±1 Control: 15±1.6 **Mortality:** 4/203 (2%) Intervention: 3/101 (3%) Control: 1/102 (1%) 1/4: Pulmonary embolism 1/4: Cerebral hemorrhage 1/4: Mesenteric infarction 1/4: Respiratory failure with acute bronchopneumonia **Adverse events:** No side effects of the treatment were noted. <u>Duration of chest drainage:</u> Intervention: 5.5±0.8 days Control: 5.7±1 days	condition, bacteriologic samples were obtained from expectorations, pleura, drains, and blood. **Perioperative care:** Respiratory recovery: aerosols were given to each patient on a regular basis and a respiratory program of physiotherapy followed. **Other notes:** **Statistical** α & β errors fixed at 5% level. Infection estimated risk was 30% with aim to reduce risk to 10% (20% reduction). Needed to include 200 patients (total or each arm?) Five patients included in the analysis (2 intervention, 5 controls were not given full

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			metastasis or chronic pulmonary emphysema with blebs. **Exclusion Criteria:** Temperature > 38°C, purulent expectoration, curative antimicrobial therapy that had been stopped less than 8 days prior, infected tumor, purulent pleurisy, lung abscess, bronchiectasis, exploratory thoracotomy, mediastinal tumor, chronic renal insufficiency, or β-lactamase allergy.			treatment because of missing prescriptions) **Follow-up** Abnormal pulmonary features on plain x-ray, expectorations and temperature were recorded daily from postoperative day 3 up to 8 days) No specific about wound follow up. **Funding Source Conflicts:** Authors: NR Institution: NR Study: NR Supplies: NR
Karran 1993 [50] (ES)	**RCT** 1, 7, 8	To investigate the use of the antimicrobial imipenem for perioperative prophylaxis in elective colorectal surgery at both single dose and multiple dose regimens.	**Number of patients: N=227** **Patient Characteristics** Patients were well matched for demographic and surgical data collected. ·Age, y: NR ·Gender: NR ·Obesity: NR ·Comorbidities: NR **Procedures:** elective	**Intervention group:** n=113 2dose: patients received intravenously imipenem 1g at induction of anesthesia with a single further dose of imipenem 1g at 3h postop. **Timing of intervention:** pre and postop **Duration of intervention:** up to 16h postop **Device/agent:** imipenem	**SSI** All SSI (some patients suffered more than 1 infection) 2dose: 34/113 (30.1%) 4dose: 29/114 (25.4%); Intra-pelvic abscess: 2dose: 2/113 (1.8%) 4dose: 2/114 (1.8%); Intra-abdominal abscess 2dose: 2/113 (1.8%) 4dose: 1/114 (0.9%);	**Definitions:** Surgical Infection: if a purulent discharge occurred from the wound, a positive bacteriological culture was obtained, or a deep abscess developed at the site of operation.

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			colorectal **Setting:** 1 University hospital **Location:** UK **Dates:** NR **Inclusion Criteria:** Patients over 18 years of age undergoing elective colorectal surgery. **Exclusion Criteria:** Pregnancy, known allergy to any study drug, concomitant infection, serious comorbidity or inflammatory bowel disease. Also, patients who had been treated with antimicrobials in the preceding 72h or who had received steroids, antineoplastic agents or radiotherapy before surgery.	**Control group:** n=114 4dose: patients received imipenem 1g intravenously at induction of anesthesia with further doses and of imipenem: 1g at 3h postop and 500mg at 8h and 16h postop **Standard preventive measures:** skin prep: use of antiseptic lavage was left to the discretion of the operating surgeon.	p=0.56; Peritonitis 2dose: 0/113 4dose: 1/114 (0.9%) Abdominal wound: 2dose: 23/113 (19.5%) 4dose: 22/114 (19.3); p=0.84 Perineal wound: 2dose: 7/113 (6.2%) 4dose: 3/114 (2.6%); p=0.20 **Adverse events** Adverse events possibly related to antimicrobial agent included 2 patients with phlebitis in the group receiving <24 AMP and in the group receiving longer AMP 2 cases of hypotension, 1 phlebitis, 1 erythema, and 1 rash	**Perioperative care:** NR **Other notes:** None **Follow-up:** 6-8 weeks postop **Funding Source Conflicts:** Authors: NR Institution: NR Study: Industry Supplies: NR
Mayer 1993 [27] (ES)	**RCT** 1, 7	To perform a prospective randomized study comparing single dose antimicrobials prophylaxis with multiple-dose regimen	**Number of patients: n=66** **Patient Characteristics** Groups were not significantly different. ·Age, y: NR ·Gender: NR ·Obesity: NR ·Comorbidities: NR	**Intervention group:** n=37 1dose: 4g piperacillin and 800mg tinidazole intravenously 30 min before surgery **Timing of intervention:** pre and postop **Duration of intervention:** 1 dose or 3 does. (up to 16h postop)	**SSI** 1 abdominal wound infection was reported in each group 1dose: 1/37 (3.0%) 3dose: 1/29 (3.5%) **Length of stay:** No differences:	**Definitions:** NR **Perioperative care:** NR **Other notes:** none **Follow-up:** 8 days postop **Funding Source Conflicts:** Authors: NR Institution: NR

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
		in patients undergoing radical surgery for gynecologic malignancy	**Procedures:** Radical surgery for a gynecological malignancy **Setting:** 1 university hospital **Location:** Austria **Dates:** June 1987 – September 1988 **Inclusion Criteria:** Patients undergoing radical surgery for a gynecological malignancy. **Exclusion Criteria:** Patients who had infections within the last two weeks, received antimicrobials or had a history of allergic reaction to either study antimicrobial. Also if radical surgery was not possible or indicated.	**Device/agent:** piperacillin and tinidazole **Control group:** n=29 patients who received 4g piperacillin and 800 mg tinidazole 30 min before surgery and at 8 & 16h postop. **Standard preventive measures:** NR	1dose: 18 days (range 12-23) 3dose: 19 days (range, 12-23 days)	Study: NR Supplies: NR
Bates 1992 [25] (ES)	**RCT** 1, 2, 4, 7, 8	To study a large number of patients in two hospitals within the same health district to determine if there is a significant difference between	**Number of patients: N=900** **Patient Characteristics:** patients were matched between groups except for: ·Age: age>80y 1 dose: 57/446 (12.8%) 3 dose: 46/550 (8.4%) ·Gender: NR	**Intervention group: n=449** One dose of antimicrobials given on induction of anesthesia **Timing of intervention:** Pre and post op **Duration of intervention:** 1 pre op dose or 16h postop. **Device/agent:** augmentin (1:10 combination of	**SSI** All procedures: None: 48/449 ≤24h: 49/451 Colorectal Sub-Population: (N=224) in at-risk abdominal surgery 1 dose: 23/113(20.4%) 3 doses: 17/111(15.3%) P>0.2 Appendectomy Sub-	**Definitions:** Wound sepsis: Major minor or late **Perioperative care:** NR **Other notes:** None **Follow-up:** 1 month **Funding Source Conflicts:** Authors: NR

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
		single and multiple dose regimes of amoxicillin 250mg/ clavulanic acid 125mg for prophylaxis in at-risk surgery.	·Obesity: NR ·Comorbidities: NR **Indications**: Inflamed appendix 1 dose: 71/114 (62%) 3 dose: 101/133 (76%) Dose violation 1 dose: 3/446 (0.7%) 3 dose: 13/550 (2.4%) **Procedures:** Appendectomies and all open gastric, esophageal, colonic or biliary surgery. All patients coming to laparotomy for intestinal obstruction including that due to strangulated hernia were entered into the study as well as patients with intra-abdominal malignancy **Setting:** 2 General Hospitals **Location:** United Kingdom **Dates:** May 1986 – June 1988 **Inclusion Criteria:** All patients aged 16 or over admitted under 2 surgical firms at 2 adjacent district general hospitals for at-risk abdominal surgery with	amoxicillin and clavulanic acid.) **Control group: N = 551** Three doses of antimicrobials with the first given on induction of anesthesia and two additional injections at 8 & 16h later. **Standard preventive measures:** NR	Population: (n=247): 1 dose: 11/114 (9.6%) 3 dose: 21/133(15.8%) p=0.16	Institution: NR Study: NR Supplies: Industry

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			potential opening of a viscus. **Exclusion Criteria:** All patients known to be allergic to penicillin. If patients had received antimicrobials within the previous 48h or if the surgeon considered that pre-operative antimicrobial administration were essential, they were also excluded. Also, declination of consent was excluded although all received prophylactic antimicrobials. Patients found to have purulent (fecal) peritonitis were withdrawn from the study			
Turano 1992 [29] (ES)	**RCT** 1	To compare the efficacy and safety of two schedules of prophylactic cefotaxime in abdominal gynecologic and urologic surgery	**Number of patients: N=608** **Patient Characteristics** Recorded, not reported ·Age, y: NR ·Gender: NR ·Obesity: NR ·Comorbidities: NR **Procedures:** unspecified gynecologic	**Intervention group: n=385** 1dose: 1g cefotaxime intravenously 30 min before incision and might be repeated in 6h if the surgery lasted more than 3h. **Timing of intervention:** pre and postop **Duration of intervention:** preop or	**SSI** All Surgeries 1dose: 28/1802 (1.6%) 3dose: 39/1765 (2.2%) subpopulation of 608 patients undergoing unspecified gynecologic procedures, 1dose: 12/385 (3.1%) 3dose: 4/223 (1.8%) p=0.53	**Definitions:** Wound infection: discharge of serous or seropurulent material from the wound within 7 days of operation. **Perioperative care :** NR **Other notes:** None

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			procedures. **Indications:** NR **Setting:** 226 Surgical units **Location:** Italy **Dates:** January 1, 1990 – June 30, 1991 **Inclusion Criteria:** patients of any age undergoing gynecologic procedures (abdominal and vaginal hysterectomy and myomectomy.) **Exclusion Criteria:** known or suspected β-lactam sensitivity, treatment with any antimicrobial in the 7 days preceding surgery, requirement for combination antimicrobial treatment resulting from the nature of the patient's condition or type of surgical procedures (e.g. immunosuppression or colorectal surgery) or terminal illness.	**Device/agent:** cefotaxime **Control group: n=223** 3dose: 1g cefotaxime intravenously 30 min before incision and 1.g doses at 6 and 12h postop. (3doses total). **Standard preventive measures:** NR		**Follow-up:** minimum 7 day follow-up (or until discharge). **Funding Source Conflicts:** Authors: NR Institution: NR Study: Industry Supplies: NR

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Wymenga 1992 [20] (ES)	**RCT** 1, 2, 7, 8	To establish the efficacy of a single perioperative antimicrobial dose for infection prophylaxis in joint replacement with a randomized, controlled, multicenter study.	**Number of patients: N=2651** **Patient Characteristics** The two trial arms were well matched with respect to the general and orthopedic diagnoses, risk factors and medications. ·Age, y: NR ·Gender: NR ·Obesity: NR ·Comorbidities: NR **Procedures:** THA, TKA and hemiarthroplasty procedures **Indications:** NR **Setting:** 27 hospitals **Location:** The Netherlands **Dates:** July 1, 1986 – July 1, 1988 **Inclusion Criteria:** Patients undergoing total hip replacement, hemiarthroplasty of the hip or total knee arthroplasty **Exclusion Criteria:** allergy to cephalosporin, penicillin anaphylaxis, the use of antimicrobials less	**Intervention group: n=1327** 1dose: 1500mg cefuroxime given intravenously upon induction of anesthesia 30min before the operation **Timing of intervention:** pre and postop **Duration of intervention:** preop and up to 16h postop **Device/agent:** cefuroxime **Control group: n=1327** 3dose: 1500mg cefuroxime given intravenously upon induction of anesthesia 30min before the operation then 750mg given at 8 & 16h postop. **Standard preventive measures:** **AMP Skin prep**: in 3 centers, the wound was rinsed with a fluid containing an antimicrobial, whereas 2 centers used PI to rinse the wound.	**SSI (13 months)** 1dose: 11/1327 (0.83%) 3dose: 6/1324 (0.45%); p=0.17; RR: 1.83, 95%CI (0.68-4.93).	**Definitions:** Confirmed joint sepsis: a positive bacteriologic culture at reoperation or a draining sinus Strong evidence of sepsis: four or more possible signs of infection: Category I: in patients who only showed two or three possible signs of sepsis; Category II: a definite diagnosis could not be made; Category III: were not suspected of having joint sepsis. Wound infection in postop period: erythema more than 1cm from the incision. **Perioperative care:** NR **Other notes:** Study was sufficiently powered. **Follow-up:** 13 months

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			than 48h before the operation, use of perioperative antimicrobial administration other than cefuroxime, malignancy, former or current sepsis in the joint and the use of gentamicin-impregnated bone cement for prosthetic fixation.			**Funding Source Conflicts:** Authors: NR Institution: NR Study: Industry Supplies: Industry
Aberg 1991 [26] (ES)	**RCT** 1, 7, 8	To compare the triple versus single dose of cefuroxime (with the addition of metronidazole for the surgeries of the jejunum, ileum, colon and rectum-anus). Concomitantly to introduce a system for continuous surveillance of postoperative wound infections.	**Number of patients: N=415 patients; 428 operations** **Patient Characteristics** Patients were well matched between groups. ·Age, y: NR ·Gender: NR ·Obesity: NR ·Comorbidities: NR **Procedures:** laparotomy, vagotomy, gastrectomy, gastric banding, other gastric, cholecystectomy, choledochal surgery, pancreatectomy, surgery of jejunum, ileum, or colon, rectal anterior resection, rectal amputation.	**Intervention group:** n= 200 1 dose of cefuroxime (with the addition of metronidazole for surgery of the jejunum, ileum, colon, and rectum-anus. **Timing of intervention** **Duration of intervention** **Device/agent:** cefuroxime (with metronidazole for rectal surgeries) **Control group: n=215** 3 doses of cefuroxime (with the addition of metronidazole for surgery of the jejunum, ileum, colon, and rectum-anus. **Standard preventive measures:** NR	**SSI:** All Procedures: 1dose: 8/207 (3.9%) 3dose:15/221 (6.8%) subanalysis of 48 elective rectal surgery patients: 1dose: 2/19 (10.5%) 3dose: 1/29 (3.4%); p=0.35 subanalysis gastric procedures (n=64) including gastrectomy (n=8), gastric banding (n=35) and other gastric (n=21) deep surgical sepsis: 1dose: 1/24 (4%) 3dose: 4/40 (10%); p=0.41	**Definitions:** Deep surgical sepsis: peritonitis, intra-abdominal abscess, or septicemia. **Perioperative care**: NR **Other notes:** None **Follow-up:** within 1 month **Funding Source Conflicts:** Authors: None Institution: None Study: None Supplies: None

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			Indications: NR **Setting:** 1 county hospital **Location:** Sweden **Dates:** February 1988 – May 1990 **Inclusion Criteria:** Consecutive patients 16 years or older scheduled for elective abdominal surgery during the study dates. **Exclusion Criteria:** due to unscheduled perioperative antimicrobial therapy			
Becker 1991 [43] (ES)	**RCT** 1, 3, 4, 5, 6, 7, 8, 9	To study in a prospective, double-blind randomized, fashion, the efficacy of a short perioperative course versus an extended postoperative course of intravenous antimicrobials in patients undergoing colectomy, mucosal protectomy and ileal pouch-anal anastomosis.	**Number of patients: n=40** **Patient Characteristics:** Patient characteristics were similar between groups except: **Entry into bowel lumen:** **5day:** 9/18 (50%) **12h:** 6/22 (27%) but major contamination was not statistically significantly different. ·Age, y: NR ·Gender: NR ·Obesity: NR ·Comorbidities: NR **Procedures:** Colectomy, mucosal protectomy, and ileal	**Intervention group: n=18** After 12h postop, patients received 1g cefoxitin intravenously every 6h for 5 days beginning 6h after fixed postop dose **Timing of intervention:** postop **Duration of intervention:** 5 days **Device/agent:** 1g cefoxitin intravenously. **Control group: n=22** After 12h postop, patients received placebo (dextrose in water) intravenously every 6h for 5 days beginning 6h after fixed postop dose **Standard preventive measures:** 1) clear liquid diet for 4	**SSI** no wound or intra-abdominal infections in either group at 1yr follow up: 5 day: 0/22 vs. 12h: 0/18 **Length of stay:** No difference, days: (mean±SD) 5 day: 8.7±0.4 12h: 8.4±0.2.	**Definitions:** Wound was considered uninfected if it was healing without evidence of erythema or discharge. Infected: if purulent drainage was present, regardless of culture results or if nonpu8rulent material contained pathogenic bacteria. Deep infection – if infection extended below fascia

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			pouch-anal anastomosis. **Indications:** chronic ulcerative colitis, familial polyposis, or Gardner's syndrome **Setting:** 1 university hospital **Location:** USA **Dates:** NR (9months) **Inclusion Criteria:** Patients with chronic ulcerative colitis, familial polyposis or Gardner's syndrome who required colectomy and who were candidates for mucosal protectomy with ileal pouch-anal anastomosis. **Exclusion Criteria:** Allergy to penicillin or cephalosporin; antimicrobial use within 1 week before operation, mechanical bowel obstruction or any other functional or anatomic reason precluding mechanical bowel prep; or the presence of an existing ileostomy or colostomy.	days before surgery; 2) mechanical bowel prep consisting of 300ml of oral magnesium citrate and 2 tap water enemas administered on preop day 2 and 300ml of oral magnesium citrate and tap water enemas until clear administered on preop day 1; 3) oral antimicrobial preparation consisting of 1g neomycin and 1g erythromycin base by mouth at 1:00pm, 2:00pm,. And 11:00pm on preop day 1; 4) 2g cefoxitin administered intravenously during a 20 min period immediately before surgery with additional 2g iv doses of cefoxitin given at 6h and 12h after the initial dose. Also, rectum was irrigated with PI solution via transanal rectal catheter.		Moderate – when subcutaneous tissues were involved. Possibly infected – evidence of induration and inflammatory changes of the skin but without purulent discharge **Perioperative Care:** NR **Other notes:** None **Follow-up:** 8 weeks post discharge when loop ileostomy was closed. Patients were then followed for 12 months after closure. **Funding Source Conflicts:** Authors: NR Institution: NR Study: Industry Supplies: NR

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
Garotta 1991 [19] (ES)	**RCT** 1, 2	To evaluate the relative effectiveness of two cephalosporin antimicrobials, ceftizoxime vs. cefuroxime, in preventing the development of complicating infections in patients submitted to elective surgery in orthopedic departments.	**Number of patients: N=614** **Patient Characteristics:** both arms were homogeneous for several characteristics such as patients' age, sex, length and type of operation and postop procedures. ·Age, y: NR ·Gender: NR ·Obesity: NR ·Comorbidities: NR **Procedures:** Hip or knee replacement or fracture fixation **Indications:** NR **Setting:** 30 hospitals **Location:** Italy **Dates:** NR **Inclusion Criteria:** Patients >18 years, undergoing orthopedic surgeries such as hip or knee replacement and fractures fixed by foreign bodies. **Exclusion Criteria:** Evidence of acute infection; antimicrobial treatment within 48 hours prior to operation or use of local antimicrobials;	**Intervention group:** n=301 1dose: given 2g ceftizoxime intravenously 30 minutes before the operation **Timing of intervention:** pre and postop **Duration of intervention:** preop and up to 12h after operation **Device/agent:** ceftizoxime **Control group:** n=313 2dose: given 2g ceftizoxime intravenously 30 minutes before the operation and 12h postop. **Standard preventive measures:** NR	**SSI:** 1dose: 2/301 (0.66%) Multi: 3/313 (0.96%)	**Definitions :** Wound infection: purulent exudation with positive microbiologic culture. **Perioperative care:** NR **Other notes:** none **Follow-up:** 1 year **Funding Source Conflicts:** Authors: Industry Institution: NR Study: NR Supplies: NR

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			and open fractures			
Buckley 1990 [14] (ES)	**RCT** 1, 3, 4, 5	To determine whether or not cefazolin decreased early postoperative wound infection rates, and whether single-dose cefazolin was as effective as multiple dose (4 doses) cefazolin in preventing early postoperative wound infections resulting from hip surgery. They also compared single and 3 doses to no AMP.	**Number of patients: N=312** **Patient Characteristics:** All groups similar in age (P=0.75) and sex distribution (P=0.86) ·Age, y: mean±SD (range) Intervention1: 76.3±14.9 (18-100) Intervention2: 77.1±12.1 (33-94) Control: 76.1±13.4 (29-96) ·Gender m/f Intervention1: 32/89 Intervention2: 22/61 Control: 3/75 ·Obesity NR ·Comorbidities NR **Procedures:** Prosthetic Hip: Intervention1: 56/108 (51.9%) Intervention2: 32/83 (38.6%) Control: 33121 (27.3%) Multiple Pins: (21 Total) Intervention1: 8/108 (7.4%) Intervention2: 5/83 (6.0%) Control: 8121 (6.6%) Compression Screw:	**Intervention1 group:** n= 108 AMP Four doses: 2g Cefazolin administered intravenously when anesthesia was induced, then 1g cefazolin every 6 hours intravenously for three doses making a total of four doses of cefazolin **Intervention2 group:** n= 83 AMP single dose: 2g Cefazolin administered intravenously when anesthesia was induced, then saline every 6 hours intravenously for three doses. **Timing of intervention:** Pre, intra and postoperatively **Duration of intervention:** From induction of anesthesia to 24 hours postop. **Device/agent:** Cefazolin **Monitoring intervention:** Blood cefazolin levels were examined intraoperatively for the first 14 patients and found to be 10 times the minimal inhibitory	**SSI: (Follow up 6 weeks)** Wound infection Intervention1+2: 4/191 (2.0%) Control: 4/121 (3.7%) P=0.46 When not combined Intervention1: 2/108 (1.6%) Intervention2: 2/83 (2.4%) Control: 4/121 (3.7%) All superficial except for 1 control group deep infection in a 96-year-old woman which was implicated in her death at 14 days postop. All other infected patients were discharged from the study after 6 weeks with healed wounds. Wound infection by Operation Type Prosthetic Hip: Intervention1+2: 2/191 (1.0%) Control: 2/121 (1.9%) Pins + Compression Screws Intervention1+2: 2/191 (1.0%) Control: 2/121 (1.9%) P=0.72 Average age of infected patients: 84.2 years (8	**Definitions:** Definite Wound infection: if there was a purulent discharge, whether or not organisms were cultured. Possible wound infection: inflammation without discharge and wounds that drained culture-positive serous fluid. The patient was followed up until the wound healed or drained pus. **Perioperative care:** NR **Other notes:** Due to low infection rates, groups Intervention1 & Intervention2 were combined to increase the power. **Statistics:** Sample size of 120 per arm selected to detect difference in

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			(170 Total) Intervention1: 57/108 (52.8%) Intervention2: 46/83 (55.4%) Control: 67/121 (55.4%) Type of surgery was not evenly distributed between groups: (P=0.05) but this variable did not turn out to be a confounder Drain Used (179 Total Intervention1: 67/108 (62.0%) Intervention2: 49/83 (59.0%) Control: 63/121 (52.1%) P=0.85, χ^2= 5.95, df = 2 **Indications:** Fractured hip (interochanteric or subcapital) **Setting:** 1 hospital **Location:** Canada **Dates:** December 1, 1985 – December1 , 1988 **Inclusion Criteria:** All adults with an interochanteric or subcapital hip fracture. **Exclusion Criteria:** Cephalosporin allergy, pathologic	concentration **Control group:** n= 121 No AMP: Saline administered intravenously for four doses. **Standard preventive measures:** NR **Non-standard preventive measures** Surgery: Fractured hip was treated with either hip pinning (with compression screw or multiple pins) or a hip prosthesis implant. Drain: At surgeon's discretion, a drain was placed for subcutaneous tissue drainage.	years older than non-infected patients though not statistically significant (p=0.11) **Other infections:** NR **Topic-specific outcomes:** NR Antimicrobial resistance: All infections were S. aureus sensitive to cephalothin. No gram negatives were isolated. **Reoperations:** NR **Length of stay:** NR, but no patients' length of stay was lengthened by a drug-related complication **Mortality:** Total: 15 deaths (4.8%) Intervention1: 3/108 (2.8%) Intervention2: 4/83 (4.8%) Control: 8/121 (6.6%) Cause of all deaths was cardiopulmonary except for the patient described above who died of multi-organ system failure (the deep wound infection possibly contributed) All patients who died were in their ninth or tenth decade of life. **Adverse events:** No	infection rate of 9% with probability of type a error of <0.10 and type β error of <0.20. **Follow-up:** Complete follow-up at 6 weeks post-op. **Funding Source Conflicts:** Authors: NR Institution: NR Study: NR Supplies: NR

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			fracture due to tumor, previous surgery on the fractured hip, treatment with an antimicrobial other than cefazolin, or a preoperative course in hospital longer than 7 days.		anaphylactic reactions, allergies or renal toxicity related to cefazolin administration. Also, no cefazolin cross-reactions with patients who claimed a history of "penicillin rashes"	
Hall 1989 [44] (ES)	**RCT** 1, 2, 7, 8	To evaluate the efficacy of moxalactam given as a single dose or as a 48-hour regimen for a range of potentially contaminated abdominal operations.	**Number of patients: N=1027** **Patient Characteristics:** NR ·Age, y: NR ·Gender: NR ·Obesity: NR ·Comorbidities: NR **Procedures:** Appendectomy, cholecystectomy, bile duct surgery, elective colorectal, emergency colorectal, gastroduodenal, and small-bowel surgery. **Setting:** 2 centers (both general hospitals) **Location:** Australia **Dates:** NR **Inclusion Criteria:** consecutive patients >14 years of age who were undergoing potentially contaminated	**Intervention group: n=519** patients given 1 1g moxalactam intravenously at induction of anesthesia **Timing of intervention:** pre and post-operative **Duration of intervention:** 1 dose or 48h postop. **Device/agent:** 1g moxalactam intravenously **Control group: n=508** patients who received 1g of moxalactam intravenously at induction of anesthesia followed by 1g of moxalactam intravenously every 6h for a further 7 doses. Equaling a total of 8g in 48h/ **Standard preventive measures:** Patients were given 10mg of Vitamin K intramuscularly prior to operation due to reports	**SSI** • **Total colorectal:** Total: 22/245 (9.0%) Single: 12/119(10.1%) 48h: 10/126(7.9%); p=0.56 • **Elective colorectal** procedures (n=207) Single: 11/102(10.7%) 48h: 6/105(5.6%); p=0.19 • **Emergency Colorectal (no bowel prep in emergency cases):** Single: 1/17(5.8%) 48h: 4/21(20.0%); p=0.26	**Definitions:** Wound Infection: purulent wound discharge or a serous wound discharge with culture of pathogenic organisms**.** Major wound infection: if it resulted in an extension of the hospital stay or required dressings at home for more than 7 days Minor wound infection: if neither of these features occurred. Peritoneal infection: if pus or peritoneal fluid containing pathogenic organisms were

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			abdominal surgery at one of 2 hospitals. **Exclusion Criteria:** Postop antimicrobial for residual infection; antimicrobial administration within 48h prior to operation; viscus not opened at operation; failure to give informed consent failure to give initial dose of moxalactam history of cephalosporin sensitivity or penicillin anaphylaxis; established renal or liver failure; reaction to initial dose of moxalactam.	of coagulopathy associated with moxalactam. **Skin prep –** Povidone Iodine & no local antimicrobial or antiseptic prep **Drain tubes –** were passed through a separate incision. **Bowel prep –** all patients received a two-day mechanical bowel prep (no oral antimicrobials were administered)		found at the operations, if there was spontaneous discharge or needle aspiration of pus from the peritoneal cavity or if there was a collection of pus present at autopsy. **Other notes:** Study was sufficiently powered to detect a difference in wound infection rates. **Follow-up:** 5th postoperative week.
Ritter 1989 [21] (ES)	**RCT** 1, 7, 8	To identify the relationship between the duration of prophylaxis and the incidence of latent wound infection-	**Number of patients: N=196** **Patient Characteristics** Reported but not significant intergroup differences. **Procedures:** primary unilateral or bilateral TKA or THA **Indications:** NR **Setting:** 1 university Hospital **Location:** USA **Dates:** NR **Inclusion Criteria:**	**Intervention group: n=98** 2dose: Two intraoperative doses of cefuroxime (1500mg & 750mg) **Timing of intervention:** intra and postop **Duration of intervention:** intraop up to 24h postop **Device/agent:** cefuroxime **Control group: n=98** 5dose: Two intraoperative doses of cefuroxime (1500mg & 750mg) followed by 24h of postop cefuroxime	**SSI** In the second smaller study (N=196), in unilateral or bilateral THA or TKA patients no infections (including deep wound infections) were reported in either group 2dose: 0/98 5dose: 0/98	**Definitions:** NR **Perioperative care:** NR **Other notes:** None **Follow-up:** 12month follow up **Funding Source Conflicts:** Authors: NR Institution: NR Study: NR Supplies: NR

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			Patients undergoing primary unilateral or bilateral THA or TKA **Exclusion Criteria:** NR	(750mg every 8 hours) **Standard preventive measures:** NR		
Moesgaard 1989 [48] (ES)	**RCT** 1, 2, 7, 8	To investigate the relationship between preoperative cell-mediated immunity (CMI) and postoperative infection and whether patients with impaired CMI would benefit from prolonged antimicrobial prophylaxis.	**Number of patients: N=428** **Patient Characteristics:** groups were well matched and equally distributed. ·Age, y: NR ·Gender: NR ·Obesity: NR ·Comorbidities: NR **Procedures:** elective colorectal surgery **Indications:** NR **Setting:** 1 university hospital **Location:** Denmark **Dates:** 1982-1986 **Inclusion Criteria:** all patients undergoing elective colorectal surgery. **Exclusion Criteria:** Those admitted for rectal amputation, known allergy to the antimicrobials used, pregnancy, age<15 years, and any antimicrobial therapy 5 days prior to surgery.	**Intervention group: n=209** Short-term prophylaxis: gentamicin 80mg iv + metronidazole 500mg iv at the start of the operation followed by repetition of these doses 6 hours later. **Timing of intervention:** pre and postop **Duration of intervention:** 6h or 2 days **Device/agent:** gentamicin 80mg iv + metronidazole 500mg iv **Control group: n=219** Long term prophylaxis: gentamicin 80mg iv + metronidazole 500mg iv at the start of the operation followed by repetition of these doses every 8hours for 2 days. **Standard preventive measures:** Bowel prep NR	**SSI** Total: 45/428 (11%); 6hr: 22/209 (11%) 2day: 23/219 (11%) p=0.99 Intra-abdominal abscess: Total: 14/428 (3%) 6hr: 6/209 (3%) 2day: 8/219 (4%) p=0.65	**Definitions:** Wound infection: presence of pus, either discharging spontaneously or requiring drainage. Intra-abdominal abscess: verified by surgical drainage or ultrasound guided aspiration of pus. **Perioperative Care:** NR **Other notes:** none **Follow-up:** 30 days **Funding Source Conflicts:** Authors: NR Institution: NR Study: NR Supplies: NR

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
Grundm-ann 1987 [24] (ES)	**RCT** 1	To define whether a single preoperative dose of mezlocillin/ metronidazole is sufficient in colon surgery or whether under certain circumstances (long operation time, insufficient bowel prep, high blood loss) a multiple administration of antimicrobials is more justified.	**Number of patients: N=154** **Patient Characteristics:** While statistical significance is not indicated, the 1 dose group had a higher percentage of high risk patients including patients with age>58 years, operation time >2.5h, Body weight>69kg, insufficient bowel lavage and blood transfusions. ·Age, y: NR ·Gender: NR ·Obesity: NR ·Comorbidities: NR **Procedures:** elective colorectal surgery **Indications:** NR **Setting:** 1 university hospital **Location:** Germany **Dates:** NR **Inclusion Criteria:** patients undergoing colon surgery. **Exclusion Criteria:** NR	**Intervention group: n=25** Patients who received a single dose of metronidazole and mezlocillin (5g/0.5g) prior to the operation **Timing of intervention:** pre and postoperative. **Duration of intervention:** up to 6h postop **Device/agent:** metronidazole and mezlocillin (5g/0.5g) **Monitoring intervention:** pre, intra and postop. **Control group: n=28** Patients received 5g metronidazole/ 0.5g mezlocillin prior to the operation, a second dose 90 minutes post-skin incision and 6 hours after the second dose. **Standard preventive measures:** Bowel Prep: Orthograde bowel prep with no antimicrobial ingredients. And no preop oral antimicrobial for the purpose of bowel prep**.**	**SSI** SSI: 1dose: 4/77 (5.2%) 3dose: 4/77 (5.2%) Intra-abdominal abscess 1dose: 2/77 (2.6%) 2doses: 1/77 (1.3%); p=0.57 Peritonitis 1dose: 2/77 (2.6%) 3doses: 2/77 (2.6%);	**Definitions:** NR **Perioperative care:** NR **Other notes:** None **Follow-up:** NR **Funding Source Conflicts:** Authors: NR Institution: NR Study: NR Supplies: NR

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
Juul 1987 [45] (ES)	**RCT** 1, 2, 7, 8	To evaluate the prophylactic effect of a single dose versus multiple doses of systemic ampicillin and metronidazole in elective colorectal surgery.	**Number of patients: N=294** **Patient Characteristics:** No significant differences between groups. ·Age, y: NR ·Gender: NR ·Obesity: NR ·Comorbidities: NR **Procedures:** Elective colorectal surgery **Indications:** NR **Setting:** 1 university hospital **Location:** Denmark **Dates:** October 1983-April 1986 **Inclusion Criteria:** Patients 18y or older, undergoing elective colorectal surgery during the study dates. **Exclusion Criteria:** Patients receiving antimicrobials in the preoperative period or those with a history of hypersensitivity to ampicillin or metronidazole. Also, patients not receiving full does or the bowel note being opened during surgery.	**Intervention group:** Patients received 1.5g metronidazole and 3g ampicillin intravenously at induction of anesthesia **Timing of intervention:** Pre and postoperative **Duration of intervention:** 1 dose or 3 postop days **Device/agent:** metronidazole & ampicillin **Control group:** Patients received 1.5g metronidazole and 3g ampicillin intravenously at induction of anesthesia followed by Metronidazole 0.5g and ampicillin 1g each 3 times during the second and third postoperative days. **Standard preventive measures :** Bowel prep: bowel was emptied either conventionally or by whole gut irrigation.	**SSI** Deep wound infections: Total: 17/294 (5.8%); Single Dose: 9/149 (6%) Multiple: 8/145 (6%) Intra-abdominal abscess: Total: 3/294 (1.0%) Single: 1/149 (1%) Multiple 2/145 (1%) **Topic Specific outcomes:** No difference in bacterial isolates and no report of antimicrobial resistance	**Definitions :** Deep wound infection: accumulation of pus either with spontaneous discharge or requiring surgical drainage. Wound dehiscence: subcutaneous and fascial breakdown, but without pus accumulation. Intra-Abdominal Abscess-intraperitoneal or pelvic collection of pus with spontaneous discharge or which required surgical drainage. **Perioperative care:** NR **Other notes:** None **Follow-up :** 30 days **Funding Source Conflicts:** Authors: NR Institution: NR Study: NR Supplies: NR

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
Mendel 1987 [46] (ES)	**RCT** 1	To assess the prophylactic value of a one-shot regimen of antimicrobials.	**Number of patients: N=100** **Patient Characteristics:** NR ·Age, y: NR ·Gender: NR ·Obesity: NR ·Comorbidities: NR **Procedures:** elective excision of colorectal carcinoma or diverticulitis. **Indications:** NR **Setting:** 1 Hospital **Location:** Germany **Dates:** NR **Inclusion Criteria:** Patients requiring excision of colorectal carcinoma or diverticulitis **Exclusion Criteria:** Patients with a colostomy or who had received other antimicrobials within 72h of operation.	**Intervention group: n=54** Patients receiving a "single shot" of 5g mezlocillin and 500mg metronidazole **Timing of intervention:** pre and postop **Duration of intervention:** 1dose or 3 days postop **Device/agent:** mezlocillin5g and metronidazole 500mg **Control group:** n=46 patients receiving 9 doses of 5g mezlocillin and 500mg metronidazole (a 3 day regimen) **Standard preventive measures:** Bowel prep: all patients underwent standard preop bowel prep (from 4 days preop!)	**SSI** Total: 3/100 (3.0%); Single dose: 2/54 (3.7%) 3day: 1/46 (2.1%); p=0.66	**Definitions:** NR **Perioperative care:** NR **Other notes:** none **Follow-up:** NR **Funding Source Conflicts:** Authors: NR Institution: NR Study: NR Supplies: NR
Gatell 1987 [18] (ES)	**RCT** 1, 3, 4, 5, 7, 8, 10	To compare the use of five doses of cefamandole with a single preoperative dose for preventing wound infection s after so-called	**Number of patients:** N=717 **Patient Characteristics:** Characteristics were similar between groups. ·Age, y: NR ·Gender: NR ·Obesity: NR ·Comorbidities: NR	**Intervention group: n=382** 1dose: 1 preoperative intravenous dose of cefamandole (2g) given ½ hour before starting the operation. This was followed by 4 doses of placebo following the control drug schedule **Timing of intervention**	**SSI** 1dose: 20/382 (5.2%) 5dose: 3/335 (0.9%) p=0.004 Hemiarthroplasties: 1dose: 5/76 (6.5%) 5dose: 0/74 (0%); p=0.03 All other procedures	**Definitions:** Wound infection: diagnosed when the wound drained pus spontaneously or was inflamed to the point that it had to be opened by the surgeon and

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
		clean orthopedic operations in which there was implantation of a metal device.	**Procedures:** Clean orthopedic operations in which there was a metal device implanted. **Indications:** NR **Setting:** 1 university hospital **Location:** Spain **Dates:** NR **Inclusion Criteria:** All adults scheduled for an orthopedic surgical procedures that required insertion of a metal device for fixation of bone. **Exclusion Criteria:** total joint replacement, a known allergy to penicillin or cephalosporins, and those who had immunosuppressive treatment, those who had an open fracture or a previous infection of the operative field, and those receiving any antimicrobials.	**Duration of intervention** **Device/agent:** cefamandole **5dose:** patients receiving a 2g cefamandole dose intravenously 30 min preop and 2g intravenously at 2h after the start of surgery. This was followed by 1 gram intravenously or intramuscularly at 8, 14, & 24 hours thereafter. **Control group: n=335** **Standard preventive measures:** Skin prep: skin was shaved with disposable razor & cleaned with antiseptic soap just before entering OR. Alcoholic PI was applied to the operative site and allowed to remain for 2min. Patients in both groups were hospitalized for approximately 5 days before surgery.	combined: 1dose: 15/306 (5%) 5dose: 3/261(1%); p=0.006. **Antimicrobial Resistance** 31 organisms isolated from 23 wound infections: 9 Staphylococcus aureus, 4 S. epidermis and 4 E. coli all sensitive to the AMP. In addition, 4 Pseudomonas aeruginosa, and 3 Streptococcus faecalis all resistant to the AMP and 7 strains of other gram negative bacilli, 2 of them resistant to the AMP. **Mortality** There were 30 deaths (4%); 1 patient had an uncontrolled wound infection but the cause of death was a stroke.	then drained purulent material. A hematoma or wound draining serous material was considered to be infected only when it cultured positive. **Perioperative care:** NR **Other notes:** None **Follow-up:** Minimum 12months (range 12-24 months) or if patients had an infection, until metal device was removed. **Funding Source Conflicts:** Authors: None Institution: None Study: None Supplies: None

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
Oostvogel 1987 [16] (ES)	**RCT** 1, 2, 3, 5, 6, 7	To compare a short term antimicrobial regimen (1 preop & 2 postop doses) with a single-dose regimen of intravenous antimicrobials.	**Number of patients N=169** **Patient Characteristics:** the two groups did not differ significantly. ·Age, y: NR ·Gender: NR ·Obesity: NR ·Comorbidities: NR **Procedures:** vascular surgery **Indications:** NR **Setting:** 1 general hospital **Location:** the Netherlands **Dates:** November 1983 – January 1985 **Inclusion Criteria:** All patients admitted for emergency or elective surgery during the study dates if the operation was classified as "clean-contaminated" or "contaminated" according to the NRC criteria; or when a vascular operation was planned ("Clean" operation) **Exclusion Criteria:** patients with multiple trauma or mechanical intestinal	**Intervention group: n=80 (1dose)** Received 2 million U benzylpenicillin i.v. + 120mg tobramycin i.m. 1hr preop **Timing of intervention:** pre and postop **Duration of intervention:** 1 dose or 12h postop. **Device/agent:** benzylpenicillin + tobramycin **Control group: n=89 (3dose)** Received 2 million U benzylpenicillin i.v. + 120mg tobramycin i.m. 1hr preop plus 1million U benzylpenicillin i.v. + 80mg tobramycin i.m. at 6h & 12h postop. **Standard preventive measures:** NR	**SSI** Vascular surgery Single Dose: 3/80 (2.3%) 3 Dose: 2/89 (3.8%) p>0.5	**Definitions:** Wound infection: presence of pus discharging spontaneously or requiring drainage **Perioperative care:** NR **Other notes:** None **Follow-up:** 1 month **Funding Source Conflicts:** Authors: NR Institution: NR Study: NR Supplies: NR

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			obstruction or who were already receiving antimicrobials for reasons other than prevention of wound infections, or who had severely impaired renal function or known hypersensitivity to one of the study antimicrobials. Also excluded were all patients found at operation to have bacterial peritonitis. Also perineal wounds.			
Wenzel 1985 [49] (ES)	**RCT** 1, 2, 7, 8, 9	To investigate and compare the extent of the reduction in post-operative infection risk in patients undergoing elective colonic surgery using two prophylaxis regimens. 1) A "one shot" method versus 2) pre-op combined with postop	**Number of patients:** N=60 **Patient Characteristics** No significant differences in patient parameters. ·Age, y: NR ·Gender: NR ·Obesity: NR ·Comorbidities: NR **Procedures:** Surgery of the colon and rectum **Indications:** NR **Setting:** 1 hospital. **Location:** Germany **Dates:** NR **Inclusion Criteria:** Patients who had to	**Intervention group: n=30** 1dose: 1 dose of 100mg ornidazole and 80mg gentamicin administered intravenously 45min before operation with pre-medication. **Timing of intervention:** pre and postop **Duration of intervention:** up to 48h postop **Device/agent:** ornidazole and gentamicin **Control group n=30** 48h: 1 dose of 100mg ornidazole and 80mg gentamicin administered intravenously 45min	**SSI** **Total SSI** 1dose: 6/30 (20%) 48hDose: 10/30 (33.3%) p=0.25 Intra-abdominal abscess: No difference: 1dose: 2/30 (7%) 48hdose: 2/30 (7%); Peritonitis :no difference: 1dose: 1/30 (3%) 48hdose: 3/30 (10%); p=0.32 Superficial SSI: 1dose: 3/30 (10%) 48h Dose: 5/30 (16.7%)	**Definitions:** Wound infection: edematous and/or red wound with a purulent secretion. **Perioperative care:** NR **Other notes:** Complication rates were high for both groups. **Follow-up:** NR **Funding Source Conflicts:** Authors: NR Institution: NR Study: NR Supplies: NR

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
		antimicrobial infusions for up to 48h.	undergo abdominal surgery involving opening of the colon. **Exclusion Criteria:** Patients who were to have appendectomies, those known hypersensitivity to ornidazole or aminoglycosides, those who received antimicrobial treatment less than 5d before the operation and those with pre-operative fecal contamination.	before operation with pre-medication. Followed by 3 further doses of 500mg ornidazole at 12h intervals and 3 doses of 80mg gentamicin at 8h intervals. **Standard preventive measures:** patients with non-stenosing tumors were fed a full calorie diet and were fed orally or enterally up to the day preceding the operation. Patients with stenosing tumors were given parenteral feeding additionally or exclusively. Bowel Prep: NR		
Carr 1984 [23] (ES)	**RCT** 1, 3	To establish whether additional doses of intravenous metronidazole for up to 24h after elective colorectal surgery would reduce the wound infection rate further.	**Number of patients:** N=90 **Patient Characteristics:** the four groups of patients were well matched. ·Age, y: NR ·Gender: NR ·Obesity: NR ·Comorbidities: NR **Procedures:** Intestinal anastomoses. **Indications:** NR **Setting:** 1 teaching hospital **Location:** United Kingdom	**Intervention group: n=22** Patients receiving only a pre-operative bolus of 500ml intravenous metronidazole. **Timing of intervention:** pre and postop **Duration of intervention:** up to 24h **Device/agent:** metronidazole **Control group: n=68** Patients receiving postoperative intravenous 500mg injections of metronidazole every 8h up to 24h postop.	**SSI:** all durations ≤24h combined suggest no difference between groups for Total Wounds 1 dose: 8/25 (32%) 2-4doses: 18/81 (22.2%) Abdominal wounds: Total 18/90 (20%): 1dose: 7/22 (31%) 2-4doses: 11/68 (16%) p=0.12 Perineal wounds: 1/3 (33.3%) vs. 7/13 (53.8%);	**Definitions:** Infected wound: one from which there was a purulent discharge from the main suture line even if culture was negative. **Perioperative care:** NR **Other notes:** None **Follow-up:** 6 weeks post op. **Funding Source Conflicts:** Authors: NR

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			Dates: April 1980 – February 1982 **Inclusion Criteria:** Patients who underwent elective colorectal surgery during the study dates. **Exclusion Criteria:** Patients who received antimicrobials in the preceding 2 weeks and patients with inflammatory bowel disease who had abscesses, fistulas or toxic dilatation of the colon.	**Standard preventive measures:** Bowel prep consisted of magnesium sulphate 2g TDS for 3 days before the operation and a standard mechanical method of bowel prep containing no antimicrobials.	p=0.53, at 6 week follow up.	Institution: NR Study: NR Supplies: Industry
Hasselg-ren 1984 [37] (ES)	**RCT** 1, 3, 4, 5, 6, 7, 8	To evaluate the effects of a 1 day versus a 3-day course of cefuroxime on infection rates in peripheral vascular surgery.	**Number of patients: N=121** **Patient Characteristics:** relative distribution of risk factors did not differ significantly between the study groups. ·Age, y: NR ·Gender: NR ·Obesity: NR ·Comorbidities: NR **Procedures:** vascular surgery **Indications:** NR **Setting:** 1 university hospital **Location:** Sweden **Dates:** January 1981 –	**Intervention group:** 1day: patients administered 3 doses of cefuroxime 1.5g intravenously beginning 1 hour before surgery and then every 8 hours (up to 16h postop) **Timing of intervention:** pre and postop **Duration of intervention:** 1 or 3 days postop **Device/agent:** 1.5g cefuroxime iv **Control group:** 3day: patients administered 9 doses of cefuroxime 1.5g intravenously beginning 1 hour before surgery	**SSI** 1day: 2/52 (3.8%) 3day: 3/69 (4.3%) p=0.89	**Definitions:** Wound infection: accumulation of pus that drained spontaneously or after debridement. Graft infection: defined as any persistent wound infection communicating with graft material. **Perioperative care:** NR **Other notes:** NR **Follow-up:** 30 day follow up

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			June 1983 **Inclusion Criteria:** Patients scheduled for vascular reconstructive surgery of the lower limbs and patients undergoing acute femoral embolectomy or thrombectomy. **Exclusion Criteria:** Patients scheduled for an aortic bifurcation graft; patients having received antimicrobials within 1 week prior to surgery; patients with cellulitis or wet gangrene on lower extremities; and patients with a history or penicillin or cephalosporin allergy.	and then every 8 hours (up to 64h postop) **Standard preventive measures:** Skin prep: wash with chlorhexidine soap 3 times on day prior to surgery. Hair removal: shaving immediately prior to surgery.		**Funding Source Conflicts:** Authors: NR Institution: NR Study: NR Supplies: NR
Hemsell 1984 [28] (ES)	**RCT** 1, 2, 4, 5, 6, 7, 8	To compare a preoperative dose with three perioperative doses of cefoxitin given to premenopausal women scheduled for vaginal	**Number of patients: N=112** **Patient Characteristics** Clinical and surgical variables were statistically similar between groups. ·Age, y: NR ·Gender: NR ·Obesity: NR ·Comorbidities: NR	**Intervention group:** n=58 1 dose: patients received 1 preoperative dose of 2g cefoxitin i.m. when called into the operating room. Cefoxitin was diluted with 0.5% lidocaine without epinephrine in the hip **Timing of intervention:** preop or postop **Duration of intervention:**	**SSI** 1dose: 1/58 (1.7%) 3dose: 2/54 (3.7%) **Length of stay:** No difference, days: mean ±SD: 1dose: 4.4±1.1 3dose: 4.7±1.2 days	**Definitions:** Minor postop infection: cystitis – when a woman had lower urinary tract irritative symptoms and 10^5 or more colonies of a single uropathogen per

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
		hysterectomy.	**Procedures:** vaginal hysterectomy **Indications:** NR **Setting:** 1 university hospital **Location:** USA **Dates:** February – December 1982 **Inclusion Criteria:** premenopausal women undergoing vaginal hysterectomy **Exclusion Criteria:** known allergy to cephalosporins, cephamycins, or lidocaine; history of immediate hypersensitivity reaction to penicillin; history of antimicrobial therapy within the 48h before surgery; temperature of greater than or equal to 38^{o}C during the 24h before surgery, concomitant infection or any other condition that might preclude accurate evaluation of response to therapy.	up to 12h postop **Device/agent:** cefoxitin **Control group:** n=54 3dose: patients received 1 preoperative dose of 2g cefoxitin i.m. when called into the operating room. Cefoxitin was diluted with 0.5% lidocaine without epinephrine in the hip; this was followed by intravenous infusion of 2g cefoxitin dose at 6 & 12h postop. **Standard preventive measures:** Povidone-iodine douche was taken the night before the surgery		milliliter of urine. Major postop infection: pelvic cellulitis – an extra-peritoneal infection involving primarily the parametrial tissues. This involved complaints of increasing lower abdominal and/or pelvic pain, tenderness to the gentle deep palpation of the inferolateral abdominal wall, and an elevated temperature. Tenderness was always asymmetrical. **Perioperative care:** NR **Other notes:** none **Follow-up:** 3-6 weeks post-surgery. **Funding Source Conflicts:** Authors: NR Institution: NR Study: Industry Supplies: NR

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
Austin 1980 [34] (ES)	**RCT** 1	To examine the effect the need for chemoprophylaxis beyond the immediate operative period in Aortocoronary Bypass procedures.	**Number of patients: n=85** **Patient Characteristics** Findings of the two groups were similar ·Age, y: NR ·Gender: NR ·Obesity: NR ·Comorbidities: NR **Procedures:** aortocoronary bypass **Indications:** NR **Setting:** 1 university hospital **Location:** Canada **Dates:** Sept 1, 1977 – June 30, 1978 **Inclusion Criteria:** All patients who underwent aortocoronary bypass operation at the study hospital during the study dates. **Exclusion Criteria:** IF patients had a history of an accelerated allergic reaction to penicillin or allergy to cephalosporins, or if they refused to give consent.	**Intervention group: n=38** 2dose: Patients who received cephalothin 2g intravenously immediately before cardiac bypass was begun and 2g at the end of the operation. **Timing of intervention:** pre and postop. **Duration of intervention:** either for the surgery or up to 3days postop. **Device/agent:** cephalothin **Control group: n=47** 3days: Patients who received cephalothin 2g intravenously immediately before cardiac bypass was begun and 2g at the end of the operation. This was then followed by 1g cephalothin q6h for 3 days. **Standard preventive measures:** Skin prep: surgical field was sprayed with a combination of polymyxin and bacitracin.	**SSI** **Superficial sternal SSI** 2dose: 1/38 (2.6%) 3days: 1/47 (2.1%) f/u NR **Antimicrobial resistance:** Both incisional SSIs were Staphylococcus aureus **Length of stay, days** Significantly shorter length of stay with postoperative AMP in one small (N=85) RCT with data collected 35 years ago: 2dose: 12.03±4.2 3day: 14.6±7.5 P<0.05	**Definitions:** Infections: diagnosed clinically and supported by total and differential leukocyte counts, by local cultures and by blood cultures and roentgenograms where indicated. Duration of hospitalization: defined as the number of days form operation until discharge. **Perioperative care:** NR **Other notes:** None **Follow-up:** NR **Funding Source Conflicts:** Authors: NR Institution: NR Study: NR Supplies: NR

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
Conte 1972 [32] (ES)	**RCT** 1, 3, 4, 5, 6, 7	To evaluate single-dose versus multiple dose regimens of cephalothin in patients undergoing cardiac surgery.	**Number of patients: N=64** **Patient Characteristics** The groups were randomly distributed and did not differ significantly. ·Age, y: NR ·Gender: NR ·Obesity: NR ·Comorbidities: NR **Procedures:** cardiac surgery **Indications:** NR **Setting:** 1 university hospital **Location:** USA **Dates:** 1969 – December 1970 **Inclusion Criteria:** patients scheduled for cardiac surgery with cardiopulmonary bypass. **Exclusion Criteria:** unwilling to participate, if there was a language barrier, or if there was difficulty in comprehension to prevent performed consent. If they were under 21 years of age, if the case was an emergency, if they had received	**Intervention group: n=30** 1dose 1g cephalothin intravenously during surgery. **Timing of intervention:** pre, intra and postop **Duration of intervention:** intraop or from the night before surgery until 4th day postop **Device/agent:** cephalothin **Control group: n=34** 20dose: received 1g cephalothin before, during and after surgery at 6 hour intervals from 6pm the night before the surgery until noon of the 4th postop day. **Standard preventive measures :** NR	**SSI** Organ/Space Sternal SSI 1dose: 1/30 (3.3%) 20dose: 1/34 (2.9%) Superficial Sternal SSI 1 dose: 2/30 (6.7%) 20 dose: 2/34 (5.9%) **Antimicrobial resistance:** Incisional SSI: The "no postoperative AMP group" 1dose: had 1 Staphylococcus aureus and 1 Staphylococcus epidermis infection as compared to 20dose: 1 Serratia marcescens and 1 Enterococcus infection Organ/Space Sternal SSI: 1dose: The one case of endocarditis was a Staphylococcus epidermis	**Definitions:** Major infection: a wound infection with purulent drainage and positive cultures with our without bacteremia that required surgical drainage and prolonged the postoperative course. Minor infection was defined as wound infection with little or no purulent drainage, a positive culture, minimal edge separation, and a rapid response to local care. **Perioperative care:** NR **Other notes:** None **Follow-up:** 6months - 2 years **Funding Source Conflicts:** Authors: Industry Institution: NR Study: Industry Supplies: Industry

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			penicillin in doses greater than 400,000 units/day or any other antimicrobials during the 2 weeks prior to surgery, or if they had a history of allergic reaction to the protocol drug. Also, death from a noninfectious cause within 24h after surgery, significant deviations from the protocol or apparent allergy to the protocol drug.			

2.1A3. RISK OF BIAS ASSESSMENTS: Q1 PARENTERAL AMP STUDIES

eTABLE 29. Risk of Bias Assessments of Randomized Controlled Trials for Q1 Parenteral AMP

Author Year	Q	Described as randomized	Randomization appropriately performed	Described as double-blind	Outcome assessor blinded	Study participant blinded	Investigator blinded	Attrition described	Attrition smaller than 10-15% of assigned patients	Attrition appropriately analyzed	Funding source(s) disclosed and no obvious conflict of interest	Overall Risk of Bias
Question 1: Parenteral Antimicrobial Prophylaxis (AMP)												
Aberg 1991 [26]	1	✓						✓	✓			Moderate
Akinyoola 2011 [1]	1	✓	✓									High
Ali 2006 [17]	1				✓	✓						High
Austin 1980 [34]	1	✓										High
Bates 1992 [25]	1	✓	✓		✓			✓	✓			Moderate
Becker 1991 [43]	1	✓		✓	✓	✓	✓	✓	✓	✓		Low
Bernard 1994 [36]	1	✓	✓	✓	✓	✓		✓	✓	✓		Low
Buckley 1990 [14]	1	✓		✓	✓	✓						Moderate
Carr 1984 [23]	1	✓		✓								High
Carroll 2003 [40]	1	✓			✓				✓	✓	✓	Moderate
Chang 2005 [41]	1	✓	✓							✓	✓	Moderate
Conte 1972 [32]	1	✓		✓	✓	✓	✓	✓				Low
Cuthbertson 1991 [10]	1	✓	✓		✓			✓				Moderate
Fujita 2007 [15]	1	✓	✓					✓	✓	✓	✓	Low
Garotta 1991 [19]	1	✓	✓									High
Gatell 1987 [18]	1	✓		✓	✓	✓		✓	✓		✓	Low
Grundmann 1987 [24]	1	✓										High

Author Year	Q	Described as randomized	Randomization appropriately performed	Described as double-blind	Outcome assessor blinded	Study participant blinded	Investigator blinded	Attrition described	Attrition smaller than 10-15% of assigned patients	Attrition appropriately analyzed	Funding source(s) disclosed and no obvious conflict of interest	Overall Risk of Bias
Haga 2012 [52]	1	✓					✓					High
Hall 1998 [38]	1	✓	✓				✓	✓	✓	✓		Low
Hall 1989 [44]	1	✓	✓					✓	✓			Moderate
Hasselgren 1984 [37]	1	✓		✓	✓	✓	✓	✓	✓			Low
Hemsell 1984 [28]	1	✓	✓		✓	✓	✓	✓	✓			Low
Hirokawa 2013 [54]	1	✓	✓				✓	✓	✓	✓	✓	Low
Hussain 2012 [31]	1	✓					✓	✓	✓		✓	Moderate
Imamura 2012 [51]	1	✓	✓		✓						✓	Moderate
Juul 1987 [45]	1	✓	✓					✓	✓			Moderate
Karran 1993 [50]	1	✓						✓	✓			Moderate
Kow 1995 [22]	1	✓	✓					✓				Moderate
Lin 2011 [35]	1	✓										High
Liu 2008 [39]	1	✓	✓	✓	✓		✓	✓	✓		✓	Low
Lyimo [30] 2013	1	✓			✓			✓	✓	✓	✓	Moderate
Macones 2011 [4]	1	✓	✓	✓	✓	✓	✓			✓		Low
Mayer 1993 [27]	1	✓						✓				High
McArdle 1995 [47]	1	✓						✓	✓			Moderate
Mendel 1987 [46]	1	✓										High
Moesgaard	1	✓	✓					✓	✓			Mode-

Author Year	Q	Described as randomized	Randomization appropriately performed	Described as double-blind	Outcome assessor blinded	Study participant blinded	Investigator blinded	Attrition described	Attrition smaller than 10-15% of assigned patients	Attrition appropriately analyzed	Funding source(s) disclosed and no obvious conflict of interest	Overall Risk of Bias
1989 [48]												rate
Mohri 2007 [53]	1	✓			✓		✓	✓	✓	✓		Low
Mui 2005 [11]	1	✓					✓	✓	✓	✓		Moderate
Nooyen 1994 [33]	1	✓	✓		✓			✓	✓			Moderate
Oostvogel 1987 [16]	1	✓	✓	✓		✓	✓	✓				Low
Osman 2013 [3]	1	✓	✓	✓	✓						✓	Moderate
Ritter 1989 [21]	1	✓						✓	✓			Moderate
Soriano 2008 [2]	1	✓		✓	✓	✓					✓	Moderate
Su 2005 [13]	1	✓	✓									High
Sullivan 2011 [8]	1	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	Low
Suzuki 2011 [42]	1	✓	✓					✓	✓	✓		Moderate
Tamayo 2008 [12]	1	✓	✓		✓			✓	✓	✓		Low
Thigpen 2005 [7]	1	✓	✓	✓	✓	✓	✓	✓	✓	✓		Low
Togo 2007 [55]	1	✓	✓				✓	✓	✓	✓	✓	Low
Turano 1992 [29]	1	✓										High
Wax 1997 [9]	1	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	Low
Wenzel 1985 [49]	1	✓	✓					✓	✓	✓		Moderate
Witt 2011 [5]	1	✓	✓	✓	✓	✓	✓	✓	✓	✓		Low
Wymenga 1992 [20]	1	✓	✓					✓	✓			Moderate

Author Year	Q	Described as randomized	Randomization appropriately performed	Described as double-blind	Outcome assessor blinded	Study participant blinded	Investigator blinded	Attrition described	Attrition smaller than 10-15% of assigned patients	Attrition appropriately analyzed	Funding source(s) disclosed and no obvious conflict of interest	Overall Risk of Bias
Yildirim 2009 [6]	1	✓						✓	✓	✓		Moderate

2.1B. Q2 NON-PARENTERAL AMP

2.1B1. GRADE TABLE Q2: NON-PARENTERAL AMP

eTABLE 30. GRADE Table for Q2 Non-Parenteral AMP

Comparison	Outcome	Quantity and Type of Evidence	Findings	Starting GRADE	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Confounders		
Q2. What are the most effective strategies for administering non-parenteral AMP at the surgical incision to reduce the risk of SSI? Q2A. How safe and effective is antimicrobial irrigation?														
Colorectal Surgeries														
Clindamycin-Gentamicin Solution vs. normal saline	SSI*	1 RCT [56]	• In one small RCT (N=103), in elective colorectal cancer surgeries, use of clindamycin-gentamicin was associated with a reduction in SSI: 4% vs. 14%; p<0.01. OR: 4.94 (1.27-19.19) • Antimicrobial solution was allowed to rest in the abdominal cavity for 3 minutes. • Both groups received preoperative AMP with an intraoperative bolus after 4 hours, with no mechanical bowel prep	High	0	0	0	-1	0	0	0	0	Moderate	Moderate
	Antimicrobial resistance	1 RCT [56]	• Post- irrigation samples were taken only in the intervention group (post antimicrobial irrigation). These cultures were positive in 2 patients (4%). Detected microorganisms were *Klebsiella spp and Streptococcus salivarius.* Both of these organisms were resistant to clindamycin and gentamicin.	High	0	0	0	-2	0	0	0	0	Low	Low

Comparison	Outcome	Quantity and Type of Evidence	Findings	Starting GRADE	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Confounders		
Acute Appendectomies														
Ampicillin Solution vs. Normal saline	SSI*	1 RCT [57]	• In one RCT (N=246), in acute appendectomies, irrigation with ampicillin solution was associated with an overall reduction in SSI: 1/117 (0.9%) vs. 7/132 (5.3%); p<0.05 • A reduction was specifically seen in SSI for acute appendicitis cases: 0/88 vs. 6/102 (5.9%); P<0.05	High	0	0	0	-2	0	0	0	0	Low	Low
	Product Related Adverse Events	1 RCT [57]	• One patient in each group noted some redness in the wound	High	0	0	0	-2	0	0	0	0	Low	
	Antimicrobial resistance	1 RCT [57]	• Almost all *Streptococci* and *Enterococci* were sensitive to Ampicillin and 30% of *E. coli* isolates were sensitive to ampicillin in samples cultured from intraoperative peritoneal and wound swabs. *E. coli* results were not reported by group.	High	0	0	0	-2	0	0	0	0	Low	
Q2B. How safe and effective are topical antimicrobial agents applied to the surgical incision?														
Topical Ampicillin - Solution														
Colorectal Surgeries														
Ampicillin solution vs. no topical antimicrobial	SSI*	1 RCT [58]	• In 1 RCT (N=203) in elective colorectal surgeries, use of topical ampicillin was associated with no difference in SSI: 5/105 (4.8%) vs. 5/98 (5.1%), (95%CI: -5.6-6.2), p=NS • Both groups received preoperative AMP of ampicillin and metronidazole which was continued 3 times daily for 3 days postoperatively, and standard or whole-gut bowel prep • These surgeries included some patients	High	0	0	0	-2	0	0	0	0	Low	Low

Comparison	Outcome	Quantity and Type of Evidence	Findings	Starting GRADE	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Confounders		
			with known infections including one with Fournier's Gangrene (not indicated which group)											
	Product Related Adverse Events	1 RCT [58]	• No product related hypersensitivity or any other adverse events were observed	High	0	0	0	-2	0	0	0	0	Low	
Acute Appendectomies														
Ampicillin solution vs. No topical antimicrobial agent	SSI*	1 RCT [59]	• In 1 RCT (N=246) of emergency acute appendectomies, cleaning the subcutaneous tissues with ampicillin solution soaked gauze reduced surgical site infections: 5/126 (4%) vs. 15/120 (13%); p<0.02. • Differences were not significant in the simple appendicitis cases, but were significant in the gangrenous and perforated cases (advanced) 5/58 (9%) vs. 14/52 (27%); p<0.02 • Both groups received intramuscular antimicrobial prophylaxis.	High	0	0	0	-1	0	0	0	0	Moderate	Moderate
Topical Ampicillin - Powder														
Ampicillin powder vs. No topical antimicrobial agent	SSI*	1 RCT [60]	• In 1 RCT (N=170) in elective colorectal surgeries, ampicillin powder applied to the subfascial and subcutaneous layers of the wound before closure was not associated with a reduction in SSI: 5/81 (6.2%) vs. 6/89 (6.7%); p>0.05 • Both groups received parenteral antimicrobial prophylaxis preoperatively and 2 additional doses up to 12h postop. • Follow up was not reported	High	0	0	0	-1	0	0	0	0	Moderate	Moderate
Topical Chloramphenicol														

Comparison	Outcome	Quantity and Type of Evidence	Findings	Starting GRADE	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Confounders		
Chloramphenicol vs. No topical antimicrobial agent	SSI*	1 RCT [61]	• In a study of 92 hip fracture repairs, no difference between groups: 12 (13.0%), 4/47 (8.5%) vs. 8/45 (17.8%); p=0.20. • Both groups received parenteral antimicrobial prophylaxis • Chloramphenicol ointment was applied to the surgical site at the end of the procedure and on postoperative day 3	High	0	0	0	-1	0	0	0	0	Moderate	Moderate
Topical Rifampin														
Rifampin vs. No topical antimicrobial agent	SSI*	1 RCT [62]	• In a small (N=48), lower-quality study of patients after video laparoscopic cholecystectomy, use of rifampin associated with reduced risk of umbilical port site infection (defined as purulent wound leakage: (p<0.005) and fewer local signs of inflammation (p<0.001) • According to results reported in a histogram, at 12 hours postoperatively, purulent wound leakage was present among 34/48 (70.8%) of the study population: 10/24 (41.7%) vs. 24/24 (100%). At 24 hours: 0/24 vs. 24/24 and by postoperative day seven: 0/24 vs. 2/24 of the normal saline group. Unclear if any of these were truly infections. • Both groups received parenteral AMP • Sterile rifampin (250mg) applied to the umbilicus (formulation not specified) preoperatively, intraoperatively, and postoperatively (every 12 hours for 72 hours)	High	-1	0	0	-1	0	0	0	0	Low	Low
	Wound Dehiscence	1 RCT [62]	• Rifampin associated with reduced risk for dehiscence (p<0.01)	High	0	0	0	-1	0	0	0	0	Moderate	

Comparison	Outcome	Quantity and Type of Evidence	Findings	Starting GRADE	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Confounders		
Vancomycin Paste														
Vancomycin powder mixed with hemostatic paste vs. Hemostatic paste	SSI* Mediastinal /sternal	1 RCT [63]	• In one RCT at high risk of bias, in 416 heart operations performed via median sternotomy there was a reduction in sternal / mediastinal SSI with vancomycin powder mixed with a hemostatic paste made from absorbable gelatin and topical thrombin and applied to the cut sternal edges vs. hemostatic paste alone: 1/223 (0.45%) vs. 7/193 (3.6%); p=0.02	High	-1	0	0	-1	0	0	0	0	Low	Low
Autologous Platelet Rich Plasma														
Autologous Platelet rich plasma-APRP (gel or spray) vs. No APRP	SSI*	4 RCT [64-67]	• In a meta-analysis (N=452) of 4 small RCTs in cardiac surgery and total knee arthroplasty, use of autologous platelet rich plasma was not associated with a difference in SSI OR: 1.14 (0.56-2.31); p=0.72; I^2=0 • Each individual study did not find a difference	High	0	0	0	-1	0	0	0	0	Moderate	Moderate
	Total wound closure	1 RCT [65]	• At two weeks after surgery, use of a spray was associated with decreased likelihood of total wound closure: 11% vs. 35%; p=0.02	High	0	0	0	-1	0	0	0	0	Moderate	
Q2C. How safe and effective are antimicrobial-coated sutures; when and how should they be used?														
Antimicrobial-coated suture (absorbable) vs. Non-antimicrobial-coated suture (absorbable and non-absorbable)	SSI*	14 RCT [68-81]	• In a meta-analysis (N=5388) of 14 RCTs that included heterogeneous surgeries and patients, sutures, closure levels, and closure types in both intervention and comparator arms across studies, there was a reduction in SSI: OR: 0.69 (0.55 – 0.86); p<0.01; I^2=28%. All studies used triclosan-coated suture as the antimicrobial-coated suture.	High	0	0	0	0	0	0	0	0	High	Moderate

Comparison	Outcome	Quantity and Type of Evidence	Findings	Starting GRADE	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Confounders		
	Organ/ Space SSI	4 RCT [74,78-80]	• In a meta-analysis (N=1081) of 4 RCTs that included heterogeneous surgeries and patients, no difference in organ/space SSI rates was observed: OR: 0.49 (0.07 – 3.43); p=0.47; I^2=71%. All studies used triclosan-coated suture as the antimicrobial-coated suture. • 1 RCT[74] abdominal wound was closed with interrupted sutures using either triclosan coated vs. uncoated 910 braided polyglactin. Skin was closed with staples • 1 RCT[78] abdominal sheath was closed using either triclosan coated vs. uncoated 910 braided polyglactin. Skin closure was not reported • 1 RCT[79] wound was closed using either triclosan coated vs. uncoated 910 braided polyglactin. Skin closure was not reported • 1 RCT[80] galea and fascia were closed with using either triclosan coated vs. uncoated 910 braided polyglactin. Skin closure was with absorbable monofilament sutures	High	0	-1	0	-1	0	0	0	0	Low	
	Deep SSI*	2 RCT [77,78]	• In a meta-analysis (N=1285) of 2 RCTs that included colorectal and abdominal surgeries, no difference in deep SSI rates was observed: OR: 0.86 (0.49 – 1.54); p=0.62; I^2=0. • 1 RCT [77] fascia closure occurred via continuous mass closure using triclosan coated or uncoated polydioxanone sutures. Skin was closed using staples • 1 RCT[78] abdominal sheath was closed using either triclosan coated vs. uncoated 910 braided polyglactin. Skin closure was	High	0	0	0	-1	0	0	0	0	Moderate	

Comparison	Outcome	Quantity and Type of Evidence	Findings	Starting GRADE	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Confounders		
			not reported.											
	Superficial SSI	4 RCT [72,77-79]	• In a meta-analysis (N=1922) of 4 RCTs that included heterogeneous surgeries, no difference in superficial SSI rates was observed: OR: 1.06 (0.76 – 1.48); p=0.72; I^2=0. • 1 RCT [77] fascia closure occurred via continuous mass closure using triclosan coated or uncoated polydioxanone sutures. Skin was closed using staples • 1 RCT[78] abdominal sheath was closed using either triclosan coated vs. uncoated 910 braided polyglactin. Skin closure was not reported • 1 RCT[79] wound was closed using either triclosan coated vs. uncoated 910 braided polyglactin. Skin closure was not reported • 1 RCT[72] the subcutaneous and subcuticular layers were closed with triclosan coated or uncoated braided 910 polyglactin or with triclosan coated or uncoated poliglecaprone 25 at the surgeon's discretion. Wounds were dressed with butterfly stitches, sterile adhesive dressing and either transparent adhesive wound covering or non-transparent adhesive wound covering or wound covering alone	High	0	0	0	0	0	0	0	0	High	
	ASEPSIS score	2 RCT [72,73]	• In 1 RCT[73] mean ASEPSIS score was lower in the triclosan coated suture group at all times measured (day 4, 30, 60) but never reached statistical significance at all specified endpoints	High	0	0	0	-1	0	0	0	0	Moderate	

Comparison	Outcome	Quantity and Type of Evidence	Findings	Starting GRADE	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Confounders		
			• In 1 RCT[72] mean ASEPSIS score was lower in the triclosan-coated suture group at two weeks postop but this did not reach statistical significance. There was no difference at 6 weeks postop.											
	Antimicrobial resistance	8 RCT [68,69,71,74, 75,78-80]	• No studies reported specific testing for triclosan resistance. • In 3 RCT[68,69,71] wounds were cultured and no antibiotic resistant strains were reported at 30 days follow up. • In 1 RCT[78] wounds were cultured and no antibiotic resistant strains were found at 1 year follow up. • In 1 RCT[79] wounds were cultured and no MRSA was recovered from wounds in either group at 30 days follow up. • In 1 RCT[75] preoperatively screened patients at risk for MRSA or with previous MRSA incidence and decontamination had wounds cultured 2 weeks post op with no resistant bacteria reported. • In 1 RCT[80] in pediatric cerebrospinal fluid shunt implants and revisions, wounds were cultured: MRSA: 1/2 (50%) vs. 1/8 (12.5%) for antimicrobial suture vs. standard, both in revision surgeries at up to 6 months follow up. • In 1 RCT[74] in elective colorectal surgeries, wounds were cultured and suggested no difference in the incidence of MRSA: 0/9 vs. 1/19 (5.3%); missing data: 2/9 (22.2%) vs. 6/19 (31.6%) at 30 days follow up.	High	0	0	0	-2	0	0	0	0	Low	
	Wound Dehiscence	3 RCT [70,73,77]	• Meta-analysis of 3 RCTs (N=1582): OR: 0.89 (0.31 – 2.58); p=0.83; I^2=76%	High	0	-1	0	-1	0	0	0	0	Low	

Comparison	Outcome	Quantity and Type of Evidence	Findings	Starting GRADE	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Confounders		
			• 1 RCT[73] of 374 CABG leg harvesting sites suggested no difference in non-infectious leg wound dehiscence within 60 days: 11/161 (6.8%) vs. 13/152 (8.5%); p=NS • 1 RCT[77] (N=1185) in mixed open abdominal surgeries suggested no difference in non-infectious wound dehiscence: 66/587 (13.4%) vs. 81/598 (16.3%), OR: 0.80 (0.56-1.14); p=0.21; however the study suggested a decrease in reoperation for burst abdomen with triclosan-coated sutures as compared to controls: 9/587 (1.9%) vs. 22/598 (4.5%); OR: 0.80 (0.18-0.88); p=0.02. • 1 RCT[70] suggested a reduction in dehiscence with triclosan coated sutures: 1/91 (1.1%) vs. 7/93 (7.7%); p=0.03.										
	Adverse events-product related	4 RCT 77,78,80,81	• 4 RCT[77,78,80,81] no serious adverse events reported for either suture type.	High	0	0	0	-2	0	0	0	0	Low	
Colorectal Surgery														
Antimicrobial-coated suture (absorbable) vs. Non-antimicrobial-coated suture (absorbable and non-absorbable)	SSI*	5 RCT 70,71,74,75, 77,82	• In a meta-analysis (N=1912) of 5 RCTs in colorectal surgery, no difference in SSI: OR: 0.71; (0.47 – 1.08); p=0.11; I^2=48%. • 2 RCTs suggested a reduction in SSI: 1 large RCT[74] (N=410) at 30 day follow up where abdominal wounds were closed with interrupted sutures using either triclosan coated vs. uncoated 910 braided polyglactin and skin was closed with staples. 1 small RCT [70] (N=182), with follow up not reported, the abdominal wall was closed with single-layer mass technique (peritoneum, muscle & fascia)	High	0	0	0	-1	0	0	0	0	Moderate	Moderate

Comparison	Outcome	Quantity and Type of Evidence	Findings	Starting GRADE	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Confounders		
			using triclosan coated or uncoated braided size 0 polyglactin 910. Skin was closed with non-absorbable monofilament polyamide. Both suggested a reduction in SSI 9/206 (4.3%) vs. 19/204 (9.3%); p=0.05; and 4/91 (4.3%) vs. 12/91 (13/2%); p=0.04 respectively. Preoperative AMP was followed by an intraoperative bolus delivered at 3h and antibiotics were continued for 48h postop in the larger study. AMP was delivered at induction of anesthesia in the smaller study and wound infection was not defined. • 1 subanalysis[75] of 243 colorectal surgeries in a study of abdominal surgeries where abdominal fascia was closed with coated or uncoated 2-0 monofilament polydioxanone loop; no subcutaneous sutures were used; skin was closed with staples; suggested a reduction in SSI though not significant: 17/143 (12%) vs. 19/100 (19%). This study was conducted as a part of a clinical care pathway. • 1 subanalysis of a large, multicenter RCT[77,82] (N=690) and 1 RCT[71] (N=385) suggested no difference in SSI at 30 days.1 Subanalysis[77,82] of 690 colorectal surgeries suggested no difference: 62/344 (18.0%) vs. 60/346 (17.3%); p=0.81. Continuous mass closure with triclosan-coated or uncoated polydioxanone sutures were used for the fascia, skin closure was achieved with staples and antimicrobial prophylaxis was given prior											

Comparison	Outcome	Quantity and Type of Evidence	Findings	Starting GRADE	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Confounders		
			to skin incision, 1 RCT [71] (N=385) suggested no difference: 23/188 (12.2%) vs. 24/197 (12.2%); Preoperative AMP was delivered 30 minutes before incision. Triclosan coated sutures were used in skin closure for both intervention and control groups.											
Abdominal Surgeries, Laparotomies & Appendectomies (excluding colorectal)														
Antimicrobial-coated suture (absorbable) vs. Non-antimicrobial-coated suture (absorbable and non-absorbable)	SSI*	3 RCT [75,77,78]	• In a meta-analysis (N=1208) of 3 RCTs, antimicrobial sutures reduced SSI: OR: 0.63; 95% CI: 0.42 – 0.95; p=0.03; I^2=0. • 1 subanalysis[75] of 612 abdominal surgeries suggested a reduction in SSI: 14/341 (4.1%) vs. 23/271 (8.5%). This study was conducted as a part of a clinical care pathway where abdominal fascia was closed with coated or uncoated 2-0 monofilament polydioxanone loop; no subcutaneous sutures were used; and skin was closed with staples. • 1 subanalysis[77] of 495 mixed abdominal surgeries where fascia closure occurred via continuous mass closure using triclosan coated or uncoated polydioxanone sutures and skin was closed using staples at 30 day follow up: no difference in SSI: 25/243 (10.3%) vs. 36/252 (14.3%); Preop AMP was administered 30-60 minute before incision in both studies. • 1 small (N=100) RCT[78] in appendectomies, where the abdominal sheath was closed using either triclosan coated vs. uncoated 910 braided polyglactin and skin closure was not	High	0	0	0	0	0	0	0	0	High	High

Comparison	Outcome	Quantity and Type of Evidence	Findings	Starting GRADE	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Confounders		
			reported, suggested no difference at 1 year follow up: 5/50 (10%) vs. 4/50(8%); p=0.73; all were superficial SSIs except for 1 deep SSI in the control group											
All Surgeries except Colorectal and Abdominal Surgeries, Laparotomies & Appendectomies														
Antimicrobial-coated suture (absorbable) vs. Non-antimicrobial-coated suture (absorbable and non-absorbable)	SSI*	8 RCT [68,69,72,73,76,79-81]	• In a meta-analysis (N=2183) of 8 RCTs in heterogeneous surgeries and patient populations, antimicrobial sutures reduced SSI OR: 0.68 (0.49 – 0.95); p=0.02; I^2=24%.	High	0	0	0	0	0	0	0	0	High	High
Cardiac Surgery														
Antimicrobial-coated suture (absorbable) versus non-antimicrobial-coated suture (absorbable and non-absorbable)	Sternal SSI*	1 RCT [79]	• One RCT [79] (N=510) suggested no difference in sternal infections at 30 day follow up: 4/170 (2.4%) vs. 12/340 (3.5%); OR: 0.66 (0.21-2.07); p=0.48. Triclosan coated or uncoated polyglactin 910 sutures were used, but the level of closure was not specified, AMP and skin prep were not reported.	High	0	0	0	-1	0	0	0	0	Moderate	Moderate
	Donor Site Superficial SSI*	3 RCT [69,73, 79]	• In a meta-analysis (N=1099) of 3 RCTs in cardiac surgeries, there was a suggestion that antimicrobial sutures reduced SSI (OR: 0.72 (0.48 – 1.09); p=0.12; I^2=0. • 2 RCT (N=510 [79] and N=328[69]) suggested no difference in donor site SSI at 1 month follow up: 5/142 (3.5%) vs. 10/260 (3.8%); p=1.00; and 16/160 (10%) vs. 17/163 (10.4%) respectively. The larger of the two did not report AMP or standard preventive measures and wounds were closed with either triclosan coated or uncoated polyglactin 910 (level of closure not	High	0	0	0	0	-1	0	0	0	Moderate	

Comparison	Outcome	Quantity and Type of Evidence	Findings	Starting GRADE	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Confounders		
			specified). The smaller RCT utilized triclosan coated or uncoated polyglactin 910 (level of closure was not specified), alcohol CHG skin prep and preoperative AMP, an intraoperative bolus at 3h with antibiotics administered up to 24h postop. • 1 RCT [73] (N=374) suggested a decrease in donor site SSI at 60 days follow up: 23/184 (12.5%) vs. 38/190 (20.0%); p=0.05. Patients were administered AMP 30 minutes prior to incision, an intraoperative bolus at 2h and were given 2 additional antibiotic doses up to 24h postop. Normothermia was maintained. This study utilized antimicrobial sutures in both the subcutaneous and cutaneous layers in the intervention arm.											
Breast Cancer Surgery														
Antimicrobial-coated suture (absorbable) vs. Non-antimicrobial-coated suture (absorbable and non-absorbable)	SSI*	1 RCT [72]	• 1 RCT [72] in mixed breast cancer surgeries (N=146) suggested no difference at 6 weeks follow up: 10/66 (15.2%) vs. 14/61 (22.9%); p=NS. Triclosan coated sutures were used in both subcutaneous and subcuticular closure in the intervention arm. 8/146 patients were administered preoperative AMP and 0/8 developed SSI. Not reported which group these 8 belonged.	High	0	0	0	-1	0	0	0	0	Moderate	Moderate
Mixed Surgeries														
Antimicrobial-coated suture (absorbable) vs. Non-antimicrobial-coated suture	SSI*	2 RCT [76,81]	• A meta-analysis (N=597) of 2 RCTs of mixed surgical populations, suggested no difference SSI OR: 0.76 (0.13-4.46); p=0.76; I^2=45%. • 1 RCT [76] in mixed surgeries (N=450) suggested a decrease in SSI at 60 days	High	0	0	0	-1	0	0	0	0	Moderate	Moderate

Comparison	Outcome	Quantity and Type of Evidence	Findings	Starting GRADE	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Confounders		
(absorbable and non-absorbable)			follow up: 17/230 (7%) vs. 33/220 (15%); p=0.01. • Triclosan coated or uncoated polyglactin 910 sutures were used in all surgical steps, except in some cases polypropylene sutures were used for laparotomy closure and vascular sutures. Poliglecaprone 25 was used for skin closure for the entire uncoated suture group. In the triclosan coated suture group, skin closure was not uniform across surgical specialties. Standard of care was not uniform and not in line with current standards in some instances. It is not reported which group these patients belonged to. • 1 RCT [81] (N=147) in mixed pediatric general surgery patients used coated or uncoated polyglactin 910 for unspecified levels of closure and suggested an increase in SSI with triclosan coated sutures 80 days follow up, however this difference was not significant: 3/98 (3.1%) vs. 0/49; p=0.22. AMP was not reported												
Lower Limb Revascularization														
Antimicrobial-coated suture (absorbable) vs. Non-antimicrobial-coated suture (absorbable and non-absorbable)	SSI*	1 RCT [68]	• 1 RCT in lower limb revascularization surgeries (N=276) where triclosan coated or uncoated polyglactin was used for subcutaneous closure, and triclosan coated or uncoated poliglecaprone sutures were used for intracutaneous closure; suggested no difference in SSI at 30 days follow up: 31/139 (22.3%) vs. 30/137 (21.9%); OR: 1.02 (0.58-1.81); p=0.94. Although AMP was not	High	0	0	0	-1	0	0	0	0	Moderate	Moderate

Comparison	Outcome	Quantity and Type of Evidence	Findings	Starting GRADE	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Confounders		
			standardized across hospitals, differences were evenly distributed across groups. Triclosan coated sutures were used in both subcutaneous and intracutaneous closure in the intervention arm.											
Pediatric Cerebrospinal Fluid Shunt Surgeries														
Antimicrobial-coated suture (absorbable) vs. Non-antimicrobial-coated suture (absorbable and non-absorbable)	SSI*	1 RCT [80]	• 1 RCT in pediatric cerebrospinal shunt fluid surgeries (N=61) where galea and fascia were closed with triclosan coated or uncoated polyglactin 910 and skin was closed with absorbable poliglecaprone 25 sutures, suggested a reduction in SSI at 6 month follow up: 2/46 (4.3%) vs. 8/38 (21%); OR: 0.17 (0.03-0.86); p=0.03. Skin prep with CHG & PI; Pre-op AMP; iodine-impregnated adhesive drapes; antibiotic wound irrigation prior to closure. Silicone shunt components were soaked in antibiotic solution before implantation	High	0	0	0	-1	0	0	0	0	Moderate	Moderate
Q2D. How safe and effective are antimicrobial dressings applied to surgical incisions following primary closure in the operating room?														
Silver impregnated dressing vs. standard dressing or gauze	SSI*	2 RCT [83,84]	• One small RCT [83] (N=112) in elective colorectal cancer surgeries suggested no difference in SSI rates when comparing a moisture retentive dressing containing 1.2% ionic silver with standard dressing: 9/58 (15.5%) vs. 11/54 (20.4%); p=0.62 • One small RCT[84] (N=109) in elective colorectal surgeries suggested a reduction in SSI using silver nylon dressing vs. standard gauze and tape: 7/ 55 (13%) vs. 18/54 (33%); p=0.01. Any questionable SSI treated with antibiotics was included in SSI definition	High	0	-1	0	0	0	0	0	0	Moderate	Moderate

Comparison	Outcome	Quantity and Type of Evidence	Findings	Starting GRADE	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Confounders		
	Organ/ Space SSI*	1 RCT [83]	• One small RCT [83] (N=112) in elective colorectal cancer surgeries suggested no difference in organ/space SSI rates when comparing a moisture retentive dressing containing 1.2% ionic silver with standard dressing: 1/58 (1.7%) vs. 1/54 (1.9%)	High	0	0	0	-1	0	0	0	0	Moderate	
	Deep SSI*	2 RCT [83,84]	• One small RCT [83] (N=112) in elective colorectal cancer surgeries suggested no difference in deep SSI rates when comparing a moisture retentive dressing containing 1.2% ionic silver with standard dressing: 3/58 (5.2%) vs. 2/54 (3.7%). • One small RCT[84] (N=109) in elective colorectal surgeries suggested no difference in deep SSI using silver nylon dressing vs. standard gauze and tape: 2/ 55 (4%) vs. 4/54 (7%); p=0.4. Any questionable SSI treated with antibiotics was included in SSI definition.	High	0	0	0	-1	0	0	0	0	Moderate	
	Superficial SSI*	2 RCT [83,84]	• One small RCT [83] (N=112) in elective colorectal cancer surgeries suggested no difference in superficial SSI rates when comparing a moisture retentive dressing containing 1.2% ionic silver with standard dressing: 5/58 (8.6%) vs. 8/54 (14.8%); p=0.80 • One small RCT[84] (N=109) in elective colorectal surgeries suggested a reduction in superficial SSI using silver nylon dressing vs. standard gauze and tape: 5/ 55 (9%) vs. 14/54 (26%); p=0.02. Any questionable SSI treated with antibiotics was included in SSI definition.	High	0	0	0	-1	0	0	0	0	Moderate	

Comparison	Outcome	Quantity and Type of Evidence	Findings	Starting GRADE	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Confounders		
	Length of Stay	1 RCT [83]	• No difference in median length of stay between groups: 6 (3-21) vs. 6.5 (2-17) days	High	0	0	0	-1	0	0	0	0	Moderate	
	Adverse events	1 RCT [83]	• No adverse events were noted relating to the study intervention	High	0	0	0	-1	0	0	0	0	Moderate	

*Critical outcome; OR: Odds Ratio; RR: Risk Ratio; CI: Confidence Interval

2.1B2. EVIDENCE TABLES: Q2 NON-PARENTERAL AMP

Q2. What are the most effective strategies for administering non-parenteral antimicrobial prophylaxis at the surgical incision to reduce the risk of SSI?

eTABLE 31. Evidence Table for Q2A. How safe and effective is antimicrobial irrigation?

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
Ruiz-Tovar 2012 [56] (ES)	**RCT** 1, 2, 4, 5, 7, 8, 9, 10	To evaluate the effects of peritoneal lavage with normal saline or an antibiotic solution (clindamycin-gentamicin) on intra-abdominal abscesses and wound infection, and to determine the microbiologic impact of both irrigations on	**Number of patients: N= 108** **Patient Characteristics:** ·Age, y: (mean±SD) Intervention: 69.9±11.5 Control: 68.5±10.2 ·Gender: female/male Intervention: 60/40 Control: 62/38 ·Obesity: NR ·Comorbidities: Diabetes Mellitus Intervention: 32% Control: 29% **Procedures:** Sigmoidectomy, right colectomy, upper	**Intervention group:** n= 52 Irrigation of the entire abdominal cavity was performed with 500mL normal saline followed by a second lavage with a 500mL gentamicin-clindamycin solution (gentamicin 240mg – Clindamycin 600mg) During this lavage; the solution was allowed to sit in the abdominal cavity for 3 minutes. **Timing of intervention:** Intraoperatively **Duration of intervention:** Intraoperatively	**SSI: (30 days)** Wound infection: Intervention:4% (2/54) Control:14% (7/51) P=0.009 OR: 4.94 (1.27-19.19) Intraabdominal abscess: Intervention: 0/54 Control: 6% (3/51) P=0.014 OR: 2.14 (1.13-3.57) All abscesses were smaller than 4cm and were managed without requiring percutaneous drainage. **Other infections:** NR **Topic-specific**	**Definitions:** Wound infection: presence of a purulent discharge from the surgical wound and confirmed with microbiologic culture. Intra-abdominal abscess: the presence of fluid collection at CT scan in a symptomatic patient, presenting with fever, abdominal

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
		peritoneal contamination.	anterior resection of rectum, Hartmann procedure, Miles procedure, Lower anterior resection of rectum, left colectomy, total colectomy, palliative colostomy, palliative ileostomy. No significant difference between groups in surgery distribution. **Indications:** Tumor stage I Intervention: 26% Control: 22% II Intervention: 50% Control: 54% III Intervention: 20% Control: 24% **Setting:** 1 hospital **Location:** Spain **Dates:** January 2010 – December 2010 **Inclusion Criteria:** Diagnosis of colorectal neoplasms and elective colorectal surgery. **Exclusion Criteria:** Preoperative diagnosis of chronic renal failure (due to risk of nephrotoxicity	**Device/agent:** 500mL gentamicin-clindamycin solution (gentamicin 240mg – Clindamycin 600mg) **Monitoring intervention:** NA **Control group:** n=51 Irrigation of the entire abdominal cavity was performed with 500mL normal saline followed by aspiration of the liquid and abdominal wall closure. **Standard preventive measures:** Antimicrobial Prophylaxis: ciproflaxin 400mg and metronidazole 1,500 mg. Single dose preoperatively, within 30 minutes of incision and redosed after 4 hours when surgery is prolonged. Mechanical bowel prep: none. Surgical Approach: open Bowel clamping: performed by all surgeons Closure: abdominal wall was closed using continuous sutures of absorbable monofilament polydioxanone (size no 2). Skin was closed with	**outcomes:** NR **Reoperations:** NR **Length of stay:** NR **Mortality:** NR **Adverse events:** NR **Antimicrobial Resistance:** Post- irrigation samples were taken only in the intervention group (post antimicrobial irrigation). Cultures were positive in 2 patients (4%) Detected microorganisms were *Klebsiella spp and Streptococcus salivarius.* Both of these organisms were resistant to gentamicin and clindamycin.	pain, prolonged postoperative ileus, or septic status. Anastomotic leak: evidence of rectal contrast extravasation at CT scan. **Perioperative care:** NR **Other notes:** NR **Follow-up:** 30 days post discharge **Funding Source Conflicts:** Authors: None Institution: None Study: None Supplies: None

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			associated with intraperitoneal gentamicin absorption) or anastomotic leak in the postoperative course which would represent a bias in the diagnosis of intra-abdominal infection.	staples.		
Al-Shehri 1994 [57] (ES)	**RCT 1, 6, 7, 8,**	To investigate the efficacy of the addition of topical ampicillin to systemic antimicrobials in reducing post appendectomy wound infection rate in a properly controlled randomized prospective trial	**Number of patients: N= 249** **Patient Characteristics:** groups were comparable by characteristics listed below ·Age, y: mean (range) Intervention: 24 (4-66) Control: 21 (5-80) ·Gender: male Intervention: 77/117 (65.8%) Control: 90/132 (68.2%) ·Obesity: NR ·Comorbidities: NR **Procedures:** appendectomy through gridiron incision **Indications:** Normal Appendix: Intervention: 26/117 (22.2%) Control: 27/132 (20.5%)	**Intervention group:** n=117 Wounds were irrigated with 1g ampicillin in 100 ml sterile normal saline at closure **Timing of intervention:** intraoperatively **Duration of intervention:** NA **Device/agent:** 1 g ampicillin on 100ml sterile normal saline **Monitoring intervention:** NA **Control group: n=132** Wounds were irrigated with 100 ml sterile normal saline at closure. **Standard preventive measures:** Mechanical bowel prep: AMP: intravenous metronidazole (500mg for adults and 15mg/kg/body weight for children) and	**SSI: (1 month)** Total Intervention: 1/117 (0.9%) Control: 7/132 (5.3%) P<0.05 Acute appendicitis: Intervention: 0/88 Control: 6/102 (5.9%) P<0.05 **Other infections:** NR **Topic-specific outcomes:** Intraabdominal pelvic abscesses: none in either group Postoperative ileus Intervention: 1/117 (0.9%) Control: 2/132 (1.5%) Fever (attributed to atelectasis and treated with chest physiotherapy and early ambulation) Intervention: 3/117 (2.6%)	**Definitions:** Wound infection: purulent discharge in the wound regardless of the culture results or occurrence of serous discharge with a positive growth on culture. **Perioperative care:** NR **Other notes:** **Follow-up:** one month **Funding Source Conflicts:** Authors: NR Institution: NR Study: NR Supplies: NR

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			Acute Appendix: Intervention: 88/117 (75.2%) Control: 102/132 (77.3%) Advanced appendicitis (histologically proven gangrenous or perforated appendix) Intervention: 3/117 (2.6%) Control: 3/132 (2.3%) **Setting:** 1 University Hospital **Location:** Saudi Arabia **Dates:** **Inclusion Criteria:** patients undergoing appendectomy through gridiron incision for clinically suspected acute appendicitis **Exclusion Criteria:** Allergy to ampicillin and other systemic diseases requiring systemic antibiotic administration	gentamicin (75mg for adults and 1.5mg/kg/body weight for children) one hour before surgery. If appendix was found to be gangrenous or perforated antibiotics were continued for 5 days postoperatively.	Control: 2/132 (1.5%) **Length of stay:** Intervention: 77/117 (65.8%) Control: 90/132 (68.2%) **Mortality:** **Adverse events:** Redness in wound Intervention: 1/117 (0.9%) Control: 1/132 (0.8%) **Antimicrobial Resistance:** Almost all streptococci and enterococci were sensitive to ampicillin besides 30% of the *E. coli* isolates. (overall numbers not reported)	

eTABLE 32. Evidence Table for Q2B. How safe and effective are antimicrobial agents applied to the surgical incision?

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
Dorge 2013 [67] (ES)	**RCT 1**	To investigate whether the topical application of autologous PRP (platelet rich plasma) reduces the incidence of deep sternal wound infections in patients at high risk undergoing cardiac surgery with full sternotomy.	**Number of patients: N=196** **Patient Characteristics:** There were no differences with respect to age, sex, type of operation, and operative data between groups. Risk factors were distributed equally between groups ·Age, y: mean±SD Intervention: 68 (±8.6) Control: 67 (±9.5) ·Gender male Intervention: 76/97 (78.4%) Control: 66/99 (66.6%) ·Obesity: BMI >30 kg/m^2 Intervention: 29/97 (29.9%) Control: 37/99 (37.4%) ·Comorbidities Diabetes mellitus Intervention: 43/97 (44.3%) Control: 32/99 (32.3%) Renal failure: Intervention: 0/97 Control: 3/99 (3.0%) **Procedures:** elective cardiac surgery with	**Intervention group:** n= 97 PRP and thrombin were injected simultaneously between the sternal edges after the sternal wires had been placed and to the presternal tissue using the recommended dual spray applicator immediately prior to sternal closure. **Timing of intervention:** intraoperative **Duration of intervention:** intraoperative **Device/agent:** blood was drawn just prior to surgery and mixed with 6 and 1.2mL anticoagulant calcium citrate 5.5% respectively. The anticoagulated blood was then processed using a platelet separation system to yield 12mL autologous PRP and 8mL thrombin. **Monitoring intervention:** NA **Control group: n=99** Thrombin injected only during closure. **Standard preventive measures:** Preop Skin prep: shower	**SSI: (at 30 days)** Deep sternal wound infection: Intervention: 6/97 (6.2%) Control: 3/99 (3.0%) P=0.293 **Other infections:** NR **Topic-specific outcomes:** NR **Reoperations:** all DSWI required reoperation. **Length of stay:** NR **Mortality:** NR **Adverse events:** NR	**Definitions:** Deep sternal wound infection requiring revision surgery: CDC definition and clinical evidence of mediastinitis seen at revision surgery. **Perioperative care:** **Other notes:** **Follow-up:** 30 days **Funding Source Conflicts:** Authors: NR Institution: NR Study: Industry Supplies: NR

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			full sternotomy on cardiopulmonary bypass and cardioplegic cardiac arrest. **Indications:** NR **Setting:** 1 university hospital **Location:** Germany **Dates**: 9 months NR when. **Inclusion Criteria:** at least one risk factor for deep sternal wound infection (DSWI)including diabetes mellitus (oral anti-diabetic medication or insulin dependent), chronic obstructive lung disease (inhalative steroids), renal insufficiency (chronic dialysis), obesity (BMI>30kg/m^2), reduced left ventricular function (*ejection fraction <35), old age (>80 years) use of double IMA, and chronic use of systemic corticosteroids. **Exclusion Criteria:** emergency operation (operation within 24 hours of admission) and	morning prior to surgery Hair Removal: patients were shaved the morning prior to the operation. AMP: intravenous antibiotic prophylaxis with 3 x 2g cefazolin. Skin prep: operative field was wiped with povidone-iodine alcohol. Drapes: patients were draped in standard fashion & operative field was covered in an adhesive transparent drape.		

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			acute infection. Patients were excluded postoperatively if the thorax had to be left open with a secondary closure, or if they had to undergo rethoracotomy of any cause except DSWI.			
Almdahl 2011 [64] (ES)	**RCT** 1, 2, 7, 8, 9	To explore the potential of Platelet-rich plasma (PRP) spray treatment to prevent leg wound infections from open saphenous vein harvesting for Coronary Artery Bypass Graft (CABG)	**Number of patients: N=139** **Patient Characteristics:** Relevant baseline variables were well matched between groups except the lesser preoperative use of statins in the control group (see below) ·Age, y: mean±SD Intervention: 64.8±8.6 Control: 66.0±8.8 ·Gender, male: Intervention: 84.1% Control: 84.3% ·Obesity: BMI kg/m^2 mean±SD Intervention: 27.2±3.9 Control: 27.7±3.8 ·Comorbidities Current smoker Intervention: 21.7% Control: 14.3% Previous smoker	**Intervention group:** n= 69 PRP was sprayed on the wound immediately before closure. Platelet pure plasma (PPP) was applied after wound closure. **Timing of intervention:** Intraoperatively **Duration of intervention:** Intraoperatively **Device/agent:** Platelet-rich plasma spray (made using autologous thrombin). A measure of 55cc whole blood was collected giving about 7ccof PRP and about 30cc of platelet pure plasma (PPP). **Monitoring intervention:** NR **Control group:** n= 70 Standard surgical technique with no additional wound	**SSI: (Day 3 and 6 w postop)** <u>Harvest Site Infection (6 weeks):</u> <u>Overall: 17/139 (12%)</u> Intervention: 9/69 (13%) Control: 8/70 (11%) P=0.80 (95%CI: -13% to 9%) There was no correlation between early (day 3) secretion and development of wound infection (p=0.64) Positive cultures Intervention: 6 Control: 4 All contained S. aureus except in one with B. fragilis and one betahemolytic Streptococcus **Other infections:** NR **Topic-specific outcomes:** <u>Cosmetics (Self scored: 1-10)</u>	**Definitions:** SSI: ASEPSIS Score (day 3); CDC definitions (6w postop). **Perioperative care:** Same between groups. **Other notes:** The confounding effect of statins is explained to have minor importance and it doesn't affect the conclusions. They had expected an SSI rate of 20% with goal of 15% reduction to 5% with PRP treatment (not achieved). **Follow-up:** Wounds were inspected at day 3 (ASEPSIS

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			Intervention: 31.9% Control: 47.1% Diabetes Intervention: 23.2% Control: 18.6% Statin Intervention: 94.2% Control: 78.6% P=0.01 **Procedures:** CABG-related open saphenectomy **Indications:** NR **Setting:** I hospital **Location:** Norway **Dates:** January – October 2008 **Inclusion Criteria:** Patients undergoing first-time CABG using cardiopulmonary bypass and cold crystalloid cardioplegic arrest **Exclusion Criteria:** Patients with bleeding disorders and those on immunosuppressive medication (including cyclooxygenase (COX)-II inhibitors).	spraying or applications. **Standard preventive measures:** Vein harvesting: undertaken by the full open technique. Closure: harvest wound was closed with intracutaneous poliglecaprone according to local routine. Antimicrobial prophylaxis: 2g intravenous cephalothin 5 times until the first postoperative day.	Intervention: mean 8.7 (range 2-10, median 9) Control: mean 8.6 (range 5-10, median 9) P=0.34 Top Score (10) Intervention: 29 (42.0%) Control: 18 (25.7%) P=0.50 ASEPIS Score (Day 3) Intervention: 13 patients & total scores 33 Control: 14 patients and total scores 34 P=0.51 **Reoperations:** NR **Length of stay:** NR **Mortality:** All patients survived **Adverse events:** No treatment related adverse events were observed. Note: 3 intervention and 4 control patients who fulfilled SSI criteria received antimicrobial treatment without prior microbiological specimen.	Score). 6 weeks postoperatively, the patients were called and assessment of wound infection occurrence was made according to a specific form (CDC criteria). Follow-up was 100%. **Funding Source Conflicts:** Authors: NR Institution: NR Study: NR Supplies: Industry
Litmathe 2009 [66] (ES)	**RCT** 1, 3, 4, 5	To answer whether the application of autologous platelet gel	**Number of patients: N=44** **Patient Characteristics:** ·Age, y:mean±SD	**Intervention group:** n= 22 Autologous platelet gel (APG) was applied to the surgical wounds.	**SSI: (follow up 40 days)** No statistically significant differences in healing between groups. Major sternal bone and	**Definitions:** NR **Perioperative care:** Surgical techniques:

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
		(APG) will lead to a reduction in sternal wound and vessel harvest site infections and a reduction in postoperative blood loss in high-risk patients undergoing cardiac surgery.	Intervention: 65.8±8.1 Control: 66±9.1 ·Gender: m:f Intervention:14:8 Control: 17:5 ·Obesity, BMI; kg/m^2, mean±SD Intervention: 32.4±4.3 Control:34.2±12.3 ·Comorbidities Diabetes Mellitus: 44/44 patients IDDM: 10/22 (45.5%) in each group **Procedures:** Elective Coronary artery bypass grafting (CABG) or combined coronary surgery and valve replacement without redo. **Indications:** NR **Setting:** 1 hospital **Location:** Germany **Dates:** NR **Inclusion Criteria:** All patients at risk for the development of surgical wound infections who required cardiac surgery including those with diabetes mellitus, obesity (BMI>25kg/m^2, active smoker, peripheral vascular	This included the sternal bone, the presternal soft tissue, and the vein-harvesting site. **Timing of intervention:** Intraoperatively **Duration of intervention:** Application time **Device/agent:** Autologous platelet gel (APG) prepared using a max of 16ml whole blood collected through an existing line and anticoagulated with citrate dextrose solution. Per patient a maximum of 9-30ml of platelet-rich plasma was produced. **Monitoring intervention:** NR **Control group:** n= 22 The sternal wound and vein harvesting site received conventional treatment only **Standard preventive measures:** Anti-platelet drug medication: (at least aspirin) 7 days prior to surgery.	soft tissue complication leading to surgical revision (with satisfactory results after secondary surgery): Total: 4/44 (9%) Intervention: 1/22 (4.5%) Control: 3/22 (13.6%) Major healing complications at vein harvest site (successfully treated with vacuum assisted closure therapy) Total: 4/44 (9%) Intervention: 2/22 (9%) Control: 2/22 (9%) **Other infections:** NR **Topic-specific outcomes:** The need of transfusion was lower in the intervention group but not statistically significant. <u>Cumulative ventilation time</u> Intervention: 11.7±8.4h Control: 14±12.2h P=0.5 Drainage blood loss at 6, 12h and before removal of chest tube was slightly higher for intervention group but not statistically significant Total ~1000ml vs. 800ml; P=0.14	CABG was performed using the standard approach of a median sternotomy using the extracorporeal circulation (ECC) and warm blood cardioplegia according to Calafiore. Combined procedures were carried out using cold crystalloid cardioplegic solution **Other notes:** Wound healing data was presented in bar graphs. **Follow-up:** at 4, 15 and 40 days. **Funding Source Conflicts:** Authors: NR Institution: NR Study: NR Supplies: NR

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			disease and heart failure according to NYHA III-IV. **Exclusion Criteria:** Emergency operations, active endocarditis, lung infections or pneumonia, i.v. drug abuse, HIV or thrombopenia.		**Reoperations:** Surgical revision: Intervention: 1/22 (4.5%) Control: 3/22 (13.6%) Calculated and microbiologically specific antimicrobial drug therapy was applied in all 4 cases. Vacuum assisted closure therapy was utilized to heal vein harvesting site was used in 2 patients in each group (9.1%) **Length of stay:** ICU stay slightly shorter in intervention group: 48.6±44.4 h vs. 51.3 ±53.3h; p=0.67 **Mortality:** NR **Adverse events:** One patient in each group (4.5%) underwent re-intubation due to cardiopulmonary failure. **NOTE**: Lowest rectal temperature showed hypothermia in both groups but they do not specify when this was recorded or if it was corrected 34.2°C±1.4 vs. 34.4°C±1.4; p=0.5	

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
Peerbo-oms 2009 [65] (ES)	**RCT** 1, 3, 4, 5, 6, 7, 8, 9	To investigate whether the application of a platelet concentrate (in spray form) might improve the repair of wounds after primary unilateral total knee arthroplasty (TKA) with a primary focus on wound healing and a secondary focus on knee function, use of analgesics, and hemoglobin values.	**Number of patients: N=102** but complete data were recorded for 73 patients. Denominators in results vary. **Patient Characteristics:** Baseline patient characteristics were similar between groups. Both groups had normal wound healing. Missing data was analyzed to compare per protocol and ITT populations and no differences were found ·Age, y: mean(SD) Intervention: 77 (4.4) Control: 78 (5.1) ·Gender: male Intervention: 13 (26%) Control: 11 (21%) ·Obesity (exclusion criteria) Height, cm: mean(SD) Intervention: 168 (9.1) Control: 168 (8.1) Weight, kg: mean(SD) Intervention: 83 (16) Control: 79 (12) ·Comorbidities: NR (exclusion criteria) **Procedures:** Primary	**Intervention group:** n=32 The wound was dried and subcutaneous tissues were sprayed with approximately 6mL of Platelet-Rich Plasma (PRP) at a distance of 10-15 cm with the knee flexed at 90 degrees which exposes the knee cavity. After closure of the joint capsule, with the platelet poor plasma (PPP) fraction (approx. 10mL) and the skin was closed with staples. **Timing of intervention:** Intraoperatively **Duration of intervention:** Intraoperatively (duration of spray time). **Device/agent:** Autologous platelet gel (APG) prepared using a max of 16ml whole blood collected through an existing line and anti-coagulated with citrate dextrose solution. Per patient a maximum of 9-30ml of platelet-rich plasma was produced. **Monitoring intervention:** NR **Control group:** n-41 Received no spraying with PRP or PPP **Standard preventive**	**SSI: (follow up 3 months)** Superficial wound infection at 2 weeks Intervention: 1/32 (2.8%) Control: 1/41 (2.2%) Both were successfully treated with antibiotics. Total wound closure Third day postop Intervention: 7/32 (21.8%) Control: 6/41 (14.6%) 95% CI: 7% (-11% to 25%) P=0.5 Fourth day postop Intervention: 7/32 (21.8%) Control: 13/41 (31.7%) 95% CI: -9% (-30% to 10%) P=0.4 Two weeks postop Intervention: 4/36 (11.1%) Control: 16/46 (34.9%) 95% CI: -24% (-41% to 17%) P=0.02 **Other infections:** NR **Topic-specific outcomes:** Using N=102, Drop in hemoglobin, pain at rest, pain during walking, use of pain medication, WOMAC score, and Range of	**Definitions:** SSI: a wound score form was used for scoring wound healing: where 0 = dry wound with no signs of infection and 100=wound leakage with signs of infection. Wound scoring was conducted by a blinded trained orthopedics resident Wound Closure: wound score 0: no leakage or signs of infection Wound leakage: scores>0 WOMAC Score utilized to determine pain, stiffness and physical function **Perioperative care:** Knee incision was dressed postoperatively wit compression bandages and rehabilitation was started on the day after surgery using crutches according to the

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			unilateral total knee arthroplasty. (TKA) **Indications:** Osteoarthritis of the knee. **Setting:** 1 training hospital **Location:** The Netherlands **Dates:** June 2005 – March 2007 **Inclusion Criteria:** No age limit for inclusion but the criteria for participation included pain and radiographic knee osteoarthritis. **Exclusion Criteria:** Platelet count ≤150x10^9/L, hemoglobin level ≤6.5mmol/L, BMI>33kg/m2, and systemic disorders such as diabetes, rheumatoid arthritis, and hepatitis.	**measures:** Surgical procedure: all procedures took place in a training hospital using the same surgical procedure performed by an orthopedic consultant or a supervised senior orthopedic resident. Surgical Approach: The medial parapatellar approach was used, averting the patella laterally. Tourniquet: was used and after implantation, the tourniquet was deflated and primary hemostasis was achieved. Prosthesis: A cemented posterior cruciate retaining prosthesis was used in all cases. Irrigation: before closure of the wound layers, the soft tissues and knee joint were rinsed with saline solution to remove all debris Drains: Deep or subcutaneous drains were not used. Analgesic: paracetamol (3g daily) and diclofenac (50mg 3 times daily) with pantaprazol (40mg daily) for protection	motion were not statistically significantly different between control and intervention. **Reoperations:** NR **Length of stay:** NR **Mortality:** NR **Adverse events:** NR	Joint Care Program (created by the medical instrumentation company who sponsored this study). **Other notes:** Due to a partial reorganization of the ward, no or partial measurements were recorded for a number of the study patients. Missing data were attributed to the "last known result carried forward" principle. This resulted in a loss of power for the study. **Follow-up:** Wound and function scores were measured at days 3-5, and at regular control every 2 weeks. Functional scores were also measured at 6 and 12 weeks postoperatively.

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
				against ulcers. Anticoagulant: subcutaneous injection of 0.3mL low-molecular-weight-heparin daily before the operation and continued until a sufficient effect of oral anticoagulants (acenocoumarol) was achieved. **Non-standard preventive measures:** Anticoagulant: oral anticoagulants were used up to 12 weeks postoperatively.		**Funding Source Conflicts:** Authors: NR Institution: NR Study: Industry Supplies: NR
Neri 2008 [62] (ES)	**RCT** 1, 7, 8, 9	To evaluate the use of topical prophylactic antimicrobial (i.e., rifamycin) for prevention of post- video laparoscopic cholecystectomy (VLC) at the umbilical port-site.	**Number of patients: N=48** **Patient Characteristics:** ·Age, y: mean (range): 38 (21-64) ·Gender m:f: 418:30 ·Obesity: NR ·Comorbidities: NR **Procedures:** Video-laparoscopic cholecystectomy (VLC) **Indications:** uncomplicated cholelithiasis **Setting:** 1 university hospital. **Location:** USA **Dates:** September 2006 – April 2007 **Inclusion Criteria:**	**Intervention group:** n=24 12 hr. Preop: • Disinfection of the umbilical and periumbilical skin with iodopovidone • Application of a sterile medication with 3ml of rifamycin (250mg) on the umbilicus Intraop: • Suture of the umbilical access: muscular fascia and of the skin wound with polyglycolic sutures • Disinfection of the umbilical wound and peri-umbilical skin with iodopovidone first then with 0.9% saline solution. • Application of a sterile medication with 3mL of	**All data presented in bar graph rather than numerical form.** **SSI: (follow up 60 days)** Topical administration of rifamycin reduced the incidence of omphalitis (statistically significant) Mean values of local signs of inflammation was statistically significantly higher in the control versus the intervention group (P<0.001) Occurrence of umbilical wound leakage was statistically significantly lower at 12, 24, 36, and 48, and day 3, 4, 5, 6 and 7 in the intervention versus control group (p<0.005)	**Definitions:** NR Parameters evaluated: • Umbilical region pain (pain scale 0-5) • Analgesic drug administration for localized umbilical region pain • Signs of inflammation (rubor, calor, tumor) of the umbilical wound (on a scale of 1-5) including wound warmness, hyperemia, umbilical wound swelling and redness

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			Patients with uncomplicated cholelithiasis undergoing uncomplicated video-laparoscopic cholecystectomy (VLC) **Exclusion Criteria:** Acute cholecystitis with localized peritonitis; umbilical hernia; immunodepressed patients; uncompensated diabetes; perforation of the gallbladder in the peritoneal cavity during VLC; and perforation of the gallbladder during removal through the umbilicus with bile leakage.	rifamycin (250mg) on the umbilical wound. Postoperative. • At 12, 24, 36, 48 & 72 h post-VLC, rifamycin was applied in a sterile fashion to the umbilical wound of all the patients. **Timing of intervention:** Pre, intra and postoperative **Duration of intervention:** from 12hours prior to VLC to 72 hours postoperatively. **Device/agent:** Topical rifamycin **Monitoring intervention:** NR **Control group:** n=24 12 hr. Preop: • Disinfection of the umbilical and periumbilical skin with iodopovidone Intraop: • Suture of the umbilical access: muscular fascia and of the skin wound with polyglycolic sutures • Disinfection of the umbilical wound and peri-umbilical skin with iodopovidone first then with 0.9% saline solution. **Standard preventive measures:**	Dehiscence of umbilical wound sutures occurred in fewer patients in the intervention versus control groups at 12, 24, 36, and 48, and day 3, 4, 5, 6 and 7 ($p<0.001$) **Other infections:** NR **Topic-specific outcomes:** Pain- postoperative observation of pain localized in umbilical region in patients in both groups statistically less in intervention group ($P<0.001$) Number of patients requiring additional analgesics (yes/no) presented in bar graph form but shows fewer patients in intervention than control requiring additional analgesics at hour 12, 24, 36, and 48, and day 3, 4, 5,and 6 $P<0.005$ **Reoperations:** NR **Length of stay:** Mean (range) Intervention: 3 (1-8) days Control: 4 (3-8) days. **Mortality:** NR **Adverse events:**	• Purulent leakage through the umbilical wound. • Dehiscence of the umbilical skin sutures. • Incisional hernia in umbilical region at postoperative day #60 **Perioperative care:** NR **Other notes:** none **Follow-up:** Clinical data were registered at 12, 24, 36 and 48h after VLC and on the 3rd, 4th, 6th, and 7th post-VLC day. For patients dismissed before 3rd postoperative day, there was an ambulatory outpatient control on the 60th day post-VLC, the possible presence of incisional hernia in the umbilical region was registered. **Funding Source Conflicts:**

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
				Laparoscopic technique: Hasson open technique AMP: IV administration of 2g ceftriaxone, followed by a second intraoperative dose and a final dose after 24 hours.		Authors: NR Institution: NR Study: NR Supplies: NR
Kamath 2005 [61] (ES)	**RCT** 1, 4, 6, 7, 8, 9	To study the role of the topical antimicrobial chloramphenicol in reducing the incidence of superficial surgical site infection following surgery for hip fractures.	**Number of patients: N=92** **Patient Characteristics:** ·Age, y: mean 78.6 (44-101) ·Gender: m:f = 28:72 ·Obesity NR ·Comorbidities**:** Rheumatoid arthritis:4 Diabetes: 9 Cardiac, respiratory, renal or other systemic pathology: 91 Smoking history (current or past): 100% Preop hospitalization: average 1.7 days (1-8) **Procedures:** Hemiarthroplasty (uncemented prosthesis) 54/92 (58.7%) Internal fixation of the fracture with dynamic hip screw:	**Intervention group:** n= 47 Topical chloramphenicol ointment was applied to the surgical site at the end of procedure and 3rd day postoperatively and wound dressed with low adherence dressing (rayon absorbent pad with adhesive border) **Timing of intervention:** Intra and postoperatively **Duration of intervention:** intra and postoperatively **Device/agent:** Chloramphenicol **Monitoring intervention:** NR **Control group:** n=45 No antimicrobial ointment administered. Wound dressed with low adherence dressing (rayon absorbent pad with adhesive border)	**SSI: (follow up 30 days)** Superficial Infection: Intervention: 4/47 (8.5%) Control: 8/45 (17.8%) Positive wound swabs in 5 of 8 in control group: 1 Pseudomonas, 2 MRSA, and 2 MSSA. None in the intervention group had positive wound swabs. Univariate estimated relative risk (95% CI) of infection Smoking (no infected (%)) Current: 8/31 (25.8%) Former/never: 4/61 (6.6%) RR: 4.957 (1.359-18.084) Gender (no infected (%)) Male: 5/25 (20%) Female: 7/67 (10.4%) RR: 2.143 (0.611-7.512) Age (no infected (%)) >71 years: 10/70 (14.3%) >70 years: 2/22 (9.1%) RR: 1.667(0.335-8.259)	**Definitions:** Surgical site surveillance was based on the guidelines issued by the Scottish Centre for Infection and Environmental Health (SCIEH) Superficial SSI 1. infection occurs w/in 30 days after operation 2. and involves only skin and subcutaneous tissue of incision 3. Patient has at least one of the following ·purulent discharge form the superficial incision ·organisms isolated form an aseptically obtained culture

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			46/92 (23.9%) **Indications:** fracture of the neck of femur Intracapsular fracture: 54/92 (58.7%) Extra capsular fracture: 46/92 (23.9%) **Setting:** 1 hospital **Location:** Scotland **Dates:** April 2002 – March 2003 **Inclusion Criteria:** Patients who could give informed consent and who were admitted with fracture neck of femur. **Exclusion Criteria:** Pathological fractures and undisplaced intracapsular neck of femur fractures needing internal fixation.	**Standard preventive measures:** AMP: intravenous cefuroxime Anticoagulant: postoperative subcutaneous injection of enoxaparin for DVT prophylaxis **Non-standard preventive measures:** Closure: Clips: 97/100 (97%) (removed 12 days postop) Subcuticular stitches: 2/100 (2%) Interrupted nylon: 1/100 (1%) Grade of surgeon: Middle grades: 82/100 (82%) Senior house officers under senior supervision: 10/100 (10%) Consultant: 8/100 (8%)	Treatment (no infected (%)) Intervention: 4/47 (8.5%) Control: 8/45 (17.8%) RR: 0.430 (0.120-1.544) <u>Multivariate estimated relative risk (95% CI) of infection</u> Current Smoker: ARR: 7.29 (1.62-32.67); P=0.009 Male Gender ARR: 0.92 (0.19-4.31); P=0.912 Age<70 years ARR: 0.30 (0.05-1.96) P=0.209 IC Fracture: ARR: 0. 52 (0.06-1.13); P=0.072 Treatment: Intervention: ARR: 0.36 (0.08-1.56); P=0.172 **Other infections:** Chest infections: 7/92 (7.6%) 1/7: intervention and also had wound infection 1/7: control and also had wound infection UTI: 5/92 (5.4%) 1/5: control and also had wound infection **Topic-specific outcomes:** 9 patients in the study had	of fluid or tissue form the superficial incision ·at least one of the following signs or symptoms of infection: pain or tenderness, localized swelling, redness or heat and superficial incision, is deliberately opened by surgeon unless incision is culture negative. ·Diagnosis of SSI by physician. The following are NOT SSI 1. Stitch abscess (minimal inflammation and discharge confined to the points of suture penetration) 2. Infected burn wound 3. incisional SSI that extends into the fascial and muscle layers (Deep incisional SSI) **Perioperative**

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
					no associated illness and none of these had wound infections. **Reoperations:** NR **Length of stay:** average inpatient stay: 18.5 (10-90) days either in an orthopedic ward or rehabilitation ward following which patients were either sent back to their own home or care home as appropriate. **Mortality:** 7 patients died because of unrelated causes during follow up. 1/7 hemiarthroplasty had malignancy confirmed on histology & excluded. **Adverse events:** 1 Intervention and 2 control patients' wounds continued to discharge through sinuses for up to 3 months but all eventually settled down with oral antimicrobials and dressings.	**care:** Mobilization: according to standard protocol. **Other notes:** None **Follow-up:** The wound was checked on the 3rd, 6th, 12th and 30th day postop **Funding Source Conflicts:** Authors: NR Institution: NR Study: NR Supplies: NR
Seco 1990 [59] (ES)	**RCT 1, 2, 5, 6, 7, 8, 9**	To compare the results of systematic clindamycin , with our without topical ampicillin to determine if	**Number of patients: N= 246** **Patient Characteristics:** the median age and sex ratio were similar between groups ·Age y: median (range)	**Intervention group:** n=126 Patients were treated with 1g Ampicillin in 20ml Saline as topical solution. Gauze was impregnated with ampicillin solution. The	**SSI: (4-6 weeks by mail)** Total: Intervention: 5/126 (4%) Control: 15/120 (13%) P<0.02 (only one infection occurred post-discharge)	**Definitions:** Wound infection: patients in whom pus appeared or if there was serious discharge and a positive culture

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
		the combination of the antibiotics is more effective than the clindamycin alone is sufficient	Intervention: 29 (12-93) Control: 29 (12-79) ·Gender: male Intervention: 83/126 (66%) Control: 82/120 (68%) ·Obesity: NR ·Comorbidities: NR **Procedures:** emergency appendectomy for acute appendicitis **Indications:** acute appendicitis: Simple: Intervention: 68/126 (54%) Control: 68/120 (57%) Gangrenous: Intervention: 32/126 (25%) Control: 29/120 (24%) Perforated: Intervention: 26/126 (21%) Control: 23/120 (19%) **Setting:** 1 Tertiary hospital **Location:** Spain **Dates:** 1 year, when NR. **Inclusion Criteria:** Patients undergoing emergency appendectomies for acute appendicitis.	subcutaneous tissues were cleaned with this gauze and the remaining solution was allowed to rest in the wound. **Timing of intervention:** intraoperatively **Duration of intervention:** NA **Device/agent:** 1g ampicillin in 20mL saline **Monitoring intervention:** NA **Control group**: n=120 Patients did not receive topical ampicillin **Standard preventive measures:** AMP: 600mg clindamycin intramuscularly. Skin prep: with povidone-iodine.	**Simple:** Intervention: 0/68 Control: 1/68 (1%) P=NS Advanced: Intervention: 5/58 (9%) Control: 14/52 (27%) P<0.02 Appendicitis with Peritonitis with or abscess (only percentages given. Numerator and denominator not reported) Intervention: 13% Control: 35% **Other infections:** NR **Topic-specific outcomes:** Intervention: 83/126 (66%) Control: 82/120 (68%) **Reoperations:** Retroperitoneal abscess as cause (*E. coli* was isolated) Intervention: 0/126 Control: 1/120 (1%) **Length of stay:** Median (range), days Intervention: 7 (3-18) Control: 7 (3-40) **Mortality:** NR **Adverse events:** **Fever** Intervention: 3/126 (1%) Control: 1/120 (1%) Wound hematoma	**Perioperative care:** Approach: 96% through a grid-iron incision **Other notes:** **Follow-up:** 7-10 days postop in person. 4-6 weeks via mail. **Funding Source Conflicts:** Authors: NR Institution: NR Study: NR Supplies: NR

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			Exclusion Criteria: Patients <12 years old, those who underwent elective surgeries, and those who had previously been treated with antibiotics		Intervention: 1/126 (1%) Control: 1/120 (1%) Postoperative ileus Intervention: 0/126 Control: 2/120 (1%) Pulmonary embolism: Intervention: 0/126 Control: 1/120 (1%) Acute respiratory insufficient Intervention: 1/126 (1%) Control: 0/120 Unspecific diarrhea Intervention: 1/126 (1%) Control: 0/120	
Raahave 1989 [60] (ES)	**RCT 1, 5, 7, 8**	To conduct a randomized controlled trial to investigate the effect of ampicillin applied locally in combination with a 12 hour parenteral antibiotic regimen with cefotaxime.	**Number of patients: N= 170** **Patient Characteristics:** ·Age, y: median (range) Intervention: 72 (32-90) Control: 69 (28-90) ·Gender: male Intervention: 39/81 (48.1%) Control: 46/89 (51.7%) ·Obesity: NR ·Comorbidities: NR **Procedures:** Elective colorectal surgeries: Right transverse colonic resection: Intervention: 22/81 (27.8%) Control: 22/89 (24.7%)	**Intervention group:** n= 81 Patients had 2g ampicillin powder applied in the wound subfacially and subcutaneously during closure. **Timing of intervention:** intraoperatively **Duration of intervention:** NA **Device/agent: Monitoring intervention:** NA **Control group:** n= 89 Not described **Standard preventive measures:** Mechanical bowel prep: three day liquid diet plus 250ml of a complete nutrient powder in 500ml of water twice per day; 30ml of 50%	**SSI: (follow up NR)** Intervention: 5/81 (6.2%) Control: 6/89 (6.7%) P>0.05 **Other infections:** NR **Topic-specific outcomes:** Wound dehiscence: Intervention: 2/81 (2.5%) Control: 1/89 (1.1%) P>0.05 Intra-abdominal abscess Intervention: 3/81 (3.7%) Control: 2/89 (2.2%) P>0.05 Patients with anastomoses Intervention: 66 Control: 71 Anastomotic leakage Intervention: 3/66 (4.5%) Control: 6/71 (8.5%) P>0.05 **Reoperations:** NR	**Definitions:** Wound infection: a collection of pus, draining either spontaneously or at the site of incision. Wound rupture – recorded separately Evidence of anastomotic leakage: air or feces or both delivered by the drains. **Perioperative care:** NR **Other notes:** None **Follow-up:** NR **Funding Source Conflicts:** Authors: NR Institution: NR

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			Left colonic & sigmoid resection: Intervention: 21/81 (25.9%) Control: 23/89 (25.8%) Low anterior resection: Intervention: 20/81 (24.7%) Control: 21/89 (23.6%) Abdominoperineal excision: Intervention: 6/81 (7.4%) Control: 12/89 (13.5%) Laparotomy with colostomy: Intervention: 4/81 (4.9%) Control: 5/89 (5.6%) Other: Intervention: 4/81 (4.9%) Control: 2/89 (2.2%) **Indications:** Adenocarcinoma: Intervention: 70/81 (86.4%) Control: 72/89 (80.9%) Benign neoplasms: Intervention: 4/81 (4.9%) Control: 2/89 (2.2%) Diverticulitis: Intervention: 4/81 (4.9%)	magnesium sulfate twice/ day Anastomoses: done in two layers through and through polyglycolic acid and seroserous silk sutures. Low anterior resections: stapling instrument was often used instead of sutures and an extraperitoneal drain was inserted. Closure: all abdominal wounds were closed with PGA sutures in the peritoneum, fascia and subcutis; nylon sutures were used in the skin AMP: 2g cefotaxime intravenously at induction of anesthesia. Dose was repeated at 6h and 12h postop.	**Length of stay:** NR **Mortality:** NR **Adverse events:** Patients showed no allergic reactions to or other side effects from the antibiotics used.	Study: NR Supplies: NR

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			Control: 8/89 (9.0%) Other: Intervention: 3/81 (3.7%) Control: 7/89 (7.9%) **Setting:** 1 University Hospital **Location:** Denmark **Dates:** NR **Inclusion Criteria:** Consecutive patients scheduled for elective colorectal surgery. **Exclusion Criteria:** Patients who were allergic to the antibiotics used patients under antibiotic treatment during the last three preoperative days, patients who did not adhere to the planned antibiotic regimen and patients whose colon was not opened.			
Vander Salm 1989 [63] (ES)	**RCT** 1	To test the hypothesis that topical vancomycin (to which *S.* non-*aureus* is almost always sensitive) applied to the cut sternal edges will	**Number of patients: N=417** **Patient Characteristics:** Characteristics of patients were indistinguishable between groups except for repeat operations ·Age, y: mean	**Intervention group:** n= 223 Hemostatic paste mixed with 250g powdered vancomycin was applied to sternum: At end of operation before sternum closure, a hemostatic paste containing 1gm powdered absorbable	**SSI: (at 1 month)** Sternal/ mediastinal infection Intervention: 1/223 (0.45%) Control: 7/193 (3.6%) P=0.02 **Other infections:** NR **Topic-specific outcomes:** NR	**Definitions:** SSI not defined: Sternal & mediastinal necessitated a major reoperation and both were counted as sternal infections.

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
		reduce the incidence of these infections.	Intervention: 62.5 Control: 62.0 ·Gender, male Intervention: 154/223 (69%) Control: 129/193 (67%) ·Obesity: NR ·Comorbidities Diabetes mellitus Intervention: 47/223 (21%) Control: 37/193 (19%) Repeat operations Intervention: 29/223 (13%) Control: 11/193 (5.7%) P=0.008 **Procedures:** heart operations performed via median sternotomy. **Indications:** NR **Setting:** 1 university medical center **Location:** USA **Dates:** May 1986 – July 1986 **Inclusion Criteria:** all patients of 3 surgeons who had heart operations performed via a median sternotomy during the study dates (including emergency operations)	gelatin, and topical thrombin was applied to the cut edges of the sternum. **Timing of intervention:** intraoperative **Duration of intervention:** intraoperative **Device/agent:** hemostatic paste containing vancomycin powder **Monitoring intervention:** NA **Control group:** n=193 Hemostatic paste alone was applied to sternum: At end of operation before sternum closure, a hemostatic paste containing 1gm powdered absorbable gelatin, and topical thrombin was applied to the cut edges of the sternum. **Standard preventive measures:** Hair removal: with an electric razor the day before the operation for scheduled operations AMP: cefazolin or vancomycin in case of penicillin allergy. Preoperatively and for 36h postop.	*S. aureus infections* Intervention: 1/223 (0.4%) Control: 2/193 (1.0%) *S.* non-*aureus infections* Intervention: 0/223 Control: 5/193 (2.6%) **Reoperations:** **Length of stay:** NR **Mortality:** Intervention: 15/223 (6.7%) Control: 9/193 (4.6%) P=NS **Adverse events:** No complication resulted from the topical vancomycin	Superficial infections were counted as “no sternal infections” **Perioperative care:** NR **Other notes:** NR **Follow-up:** 1 month **Funding Source Conflicts:** Authors: NR Institution: NR Study: NR Supplies: NR

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			Exclusion Criteria: NR			
Juul 1985 [58] (ES)	**RCT 1, 2, 3, 4, 5, 7, 8**	To evaluate the role of topical ampicillin when systemic perioperative antibiotic prophylaxis with ampicillin and metronidazole is used.	**Number of patients: N= 203** **Patient Characteristics:** the two groups were considered similar according to gender age, efficiency of preoperative bowel prep, and type of surgery. ·Age, y: mean (range) Intervention: 69 (21-96) Control: 69 (26-91) ·Gender: male Intervention: 56/105 (53.3%) Control: 61/98 (62.2%) ·Obesity: NR ·Comorbidities: NR **Procedures:** Abdominoperineal resection Intervention: 11/105 (10.5%) Control: 12/98 (12.3%) Low anterior resection Intervention: 21/105	**Intervention group:** n=105 Received subcutaneous and subfascial application of 1g of ampicillin in 10ml of saline in each of the surgical wounds. **Timing of intervention:** intraoperatively **Duration of intervention:** NA **Device/agent:** 1g ampicillin in 10ml saline **Monitoring intervention:** NA **Control group: n=98** Received no further prophylactic antibiotic treatment. Unclear if wounds were irrigated with saline. **Standard preventive measures:** Mechanical bowel prep: Either conventional or whole-gut irrigation Blind evaluation of bowel prep efficiency	**SSI: (days)** Deep wound infection Intervention: 5/105 (4.8%) Control: 5/98 (5.1%) P=NS **Other infections:** NR **Topic-specific outcomes:** Dehiscence Intervention: 7/105 (6.7%) Control: 4/98 (4.1%) P=NS Hernia Intervention: 10/105 (10.8%) Control: 3/98 (3.3%) P=NS **Reoperations:** **-** 7 patients with dehiscence were re-operated upon because of rupture of the fascia. Not reported which group. - 6 patients had temporary transverse colostomies	**Definitions:** Deep Wound infection: accumulation of pus requiring surgical drainage. Wound dehiscence: included subcutaneous as well as fascial breakdown but not pus accumulation. **Perioperative care:** **Other notes:** **Follow-up:** observed daily until the cutaneous sutures were removed. **Funding Source Conflicts:** Authors: NR Institution: NR Study: NR Supplies: NR

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			(20%) Control: 19/98 (19.4%) Colonic resection Intervention: 44/105 (41.9%) Control: 47/98 (48.0%) Colostomy n1 Intervention: 15/105 (14.3%) Control: 7/98 (7.1%) Closure of colostomy n1 Intervention: 11/105 (10.5%) Control: 7/98 (7.1%) Other Intervention: 3/105 (2.9%) Control: 6/98 (6.1%) **Indications:** Colorectal cancer Intervention: 80/105 (76.2%) Control: 89/98 (90.8%) Diverticulitis Intervention: 11/105 (10.5%) Control: 8/98 (8.2%) Inflammatory bowel disease Intervention: 7/105 (6.7%) Control: 2/98 (2.0%) Other Intervention: 7/105 (6.7%) Control: 3/98 (3.1%) **NOTE – other includes previously	was conducted during surgery AMP: all received ampicillin 1g 3x/day and metronidazole 0.5g 3x/day intravenously from induction of anesthesia to 3 days postoperatively. Closure: abdominal and perineal wounds were closed primarily with absorbable sutures in peritoneum and fascia, Drains: retroperitoneal drainage was used after low anterior resection and abdominoperineal excision of the rectum.	because of anastomotic breakdown after low anterior resection. Not reported which group. **Length of stay:** **Mortality:** 2 patients died from cardiopulmonary complications in the first postoperative week. Not reported which group. **Adverse events:** No hypersensitivity reactions or other side effects were encountered from treatment with antibiotics.	

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			known infections including one case of Fournier's gangrene which resulted in a deep wound infection. **Setting:** 1 University Hospital **Location:** Denmark **Dates:** April 1982 – September 1983 **Inclusion Criteria:** Patients undergoing elective colonic and rectal surgery. **Exclusion Criteria:** Patients receiving antibiotics in the preoperative period or those with a history of hypersensitivity to ampicillin or metronidazole			

eTABLE 33. Evidence Table for Q2C. How safe and effective are antimicrobial-coated sutures; when and how should they be used?

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
Diener 2014 [77,82] (ES)	**RCT** 1, 2, 4, 5, 6, 7, 8, 9	To yield reliable data for the effectiveness of triclosan coated polydioxanone sutures for abdominal fascia closure in the prevention of surgical site infections, compared with non-coated polydioxanone sutures. The null hypothesis to be tested states that the rate of superficial and deep incisional surgical site infections within 30 days after midline incision is equal in both treatment groups.	**Number of patients: N=1185** **Patient Characteristics:** the study was balanced in terms of patient and operation characteristics ·Age, y: mean (SD) Intervention: 64.7 (11.8) Control: 65.0 (12.1) ·Gender: female, Intervention: 226/587 (38.5%) Control: 230/598 (38.5%) ·Obesity, BMI (mg/kg^2): mean (SD) Intervention: 26.1 (4.3) Control: 26.1 (4.6) ·Comorbidities: Diabetes mellitus: Intervention: 81/587 (13.8%) Control: 96/598 (16.1%) COPD Intervention: 38/587 (6.5%) Control: 51/598 (8.5%) Malignant disease Intervention: 407/587 (69.3%) Control: 442/598 (73.9%) Anemia	**Intervention group:** n=587 Closure of the abdominal fascia after midline laparotomy with triclosan-coated polydioxanone sutures. **Timing of intervention:** intraoperative **Duration of intervention:** closure until absorption **Device/agent:** triclosan-coated or uncoated polydioxanone sutures. **Monitoring intervention:** assessed in person and validated via assessment of photographs of abdominal wound by an independent primary outcome validation committee consisting of 3 board-certified surgeons who reviewed all photographs blinded to group. **Control group:** n=598 Closure of the abdominal fascia after midline laparotomy with uncoated polydioxanone sutures. **Standard preventive measures:** Closure: achieved by	**SSI:** Composite SSI within 30 days Intervention: 87/587 (14.8%) Control: 96/598 (16.1%) OR: 0.91 (0.66-1.25) P=0.64 Multiple imputations of the missing data yielded in a similar result (p=0.62) Superficial Intervention: 53/587 (9.2%) Control: 56/598 (9.4%) Deep Intervention: 22/587 (3.7%) Control: 25/598 (4.2%) Missing Intervention: 12/587 (2.0%) Control: 15/598 (2.5%) SSI By Surgery Colorectal: N=690 Intervention: 62/344 (18.0%) Control: 60/346 (17.3%) P=0.81 Hepatiopancreato-biliary: N=74 Intervention: 4/34 (11.8%) Control: 3/40 (7.5%) P=0.53 Upper-gastrointestinal	**Definitions:** Superficial & deep SSI: CDC: Superficial SSI: within 30 days postop and involved only skin or subcutaneous tissue around the incision plus at least one of the following: purulent drainage from the incision site; organisms isolated by culture from the incision; pain or tenderness, localized swelling, redness, or heat and the incision is opened deliberately by a surgeon unless the culture is negative; or diagnosis of superficial surgical site infection by a surgeon or attending physician.

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			Intervention: 167/587 (28.4%) Control: 166/598 (27.8%) Chronic Renal insufficiency Intervention: 23/587 (3.9%) Control: 20/598 (3.3%) Surgeon Experience: No certificate Intervention: 58/587 (9.9%) Control: 75/598 (12.5%) Wound Status Clean Intervention: 144/587 (24.5%) Control: 138/598 (23.1%) Clean-contaminated Intervention: 430/587 (73.3%) Control: 450/598 (75.3%) Contaminated Intervention: 11/587 (1.9%) Control: 9/598 (1.5%) Dirty Intervention: 2/587 (0.3%) Control: 1/598 (0.2%) Duration of surgery, min (SD)	continuous mass closure with use of two loops – one from the cranial and the caudal end of the incision in a continuous suture technique Skin closure – staples. Drains – no drains allowed. Antibiotic prophylaxis – patients had to receive antibiotic prophylaxis before the incision.	tract: N=140 Intervention: 5/67 (7.5%) Control: 15/73 (20.5%) P=0.03 Factors associated with SSI within 30 days OR (95%CI); p BMI: 1.09 (1.05-1.14); P<0.0001 Chronic renal insufficiency: 2.96 (13.6-6.46); p=0.0064 Anemia: 1.73 (1.16-2.59); p=0.0071 No Antibiotic prophylaxis 5.19 (1.56-17.1); 0.0074 Malignant disease: 0.060 (0.38-0.93); 0.0236 Combination of target organ (vs. other) – colon, rectum, liver, pancreas, & stomach. 6.37 (2.71-14.98), 0.0193 Surgeon's expertise 1.73 (1.02-2.93); p=0.0405 **Other infections:** NR **Topic-specific outcomes:** Wound dehiscence Intervention: 66 (13.4%) Control: 81 (16.3%)	Deep SSI: occurred within 30 days postop, were related to the procedure, and involved deep soft tissues, such as the fascia, and muscles, plus at least one of the following: purulent drainage form the incision but not from the organ or space of the surgical site; dehiscence of a deep incision or a deep incision is opened by a surgeon because of pain, fever or tenderness; abscess or other evidence of infection at the incision site or diagnosis of deep surgical site infection by a surgeon or attending physician. **Perioperative**

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			Intervention: 179.3 (87.1) Control: 185 (90.9) Blood loss ml, mean(SD) Intervention: 478.9 (639.6) Control: 503.0 (666.7) Antibiotic Prophylaxis Intervention: 578/587 (98.5%) Control: 586/598 (98.0%) Antibiotic Therapy Intervention: 126/587 (21.5%) Control: 112/598 (18.7%) **Procedures:** Abdominal midline laparotomy. Resection & anastomosis Intervention: 422/587 (71.9%) Control: 442/598 (73.9%) Resection & resection + exploration Intervention: 72/587 (12.3%) Control: 63/598 (10.5%) Exploration Intervention: 12/587 (2.0%)		OR: 0.80 (0.56-1.14) P=0.21 Missing Intervention: 96 (13.4%) Control: 81 (16.3%) Burst abdomen Intervention: 9/587 (1.9%) Control: 22/598 (4.5%) OR: 0.40 (0.18-0.88) P=0.0194 Missing Intervention: 104/587 (17.6%) Control: 109/598 (18.2%) **Reoperations:** NR **Length of stay:** Postop hospital stay, days, mean (SD) Intervention: 13.0 (7.4) Control: 12.5 (6.3) MD: 0.47 (-0.32-1.25) P=0.99 ICU Stay, days, mean (SD) Intervention: 2.3 (3.8) Control: 2.3 (3.6) MD: 0.01 (-0.41 – 0.43) P=0.54 **Mortality:** Intervention: 9/587 (1.5%) Control: 20/598 (3.3%) OR: 0.46 (0.21-1.01)	**care**: NR **Other notes:** Wounds were inspected at postop days 10 & 30 **Follow-up:** 30 days postop **Funding Source Conflicts:** Authors: NR Institution: NR Study: Industry Supplies: NR

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			Control: 14/598 (2.3%) Resection or anastomosis & other Intervention: 5/587 (0.9%) Control: 3/598 (0.5%) Resection & other Intervention: 0/587 Control: 3/598 (0.5%) Exploration & other Intervention: 2/587 (0.3%) Control: 2/598 (0.3%) Resection & resection or anastomosis Intervention: 0/587 Control: 1/598 (0.2%) **Indications:** Target Organ for surgery Colon Intervention: 189/587 (32.2%) Control: 214/598 (35.8%) Rectum Intervention: 145/587 (24.7%) Control: 117/598 (19.6%) Stomach Intervention: 67/587 (11.4%) Control: 73/598 (12.2%) Pancreas Intervention: 32/587 (5.5%)		P=0.48 All deaths classified as unrelated to intervention and most were due to septic shock, multiple organ failure or cardiac and pulmonary decompensation. **Adverse events:** Wound dehiscence Intervention: 66/587 (13.4%) Control: 81/598 (16.3%) OR: 0.80 (0.56-1.14) P=0.21 Missing Intervention: 96/587 (13.4%) Control: 81/598 (16.3%) Burst abdomen Intervention: 9/587 (1.9%) Control: 22/598 (4.5%) OR: 0.40 (0.18-0.88) P=0.0194 Missing Intervention: 104/587 (17.6%) Control: 109/598 (18.2%) Serious Adverse Events Unrelated to intervention: 130/146 (86.1%) vs. 137/138 (87.3%) Possibly related to intervention: 21/146 (13/9%) vs. 17/138	

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			Control: 37/598 (6.2%) Liver Intervention: 2/587 (0.3%) Control: 3/598 (0.5%) Combination of the above Intervention: 33/587 (5.6%) Control: 37/598 (6.2%) Other Intervention: 119/587 (20.3%) Control: 117/598 (19.6%) **Setting:** Multi-center (24 secondary and tertiary care centers) **Location:** Germany **Dates:** April 7, 2010 (as single center trial) and Jan 24, 2011 as multicenter trial. Both ended October 19, 2012 **Inclusion Criteria:** Adults (≥18 years) who underwent midline abdominal laparotomy for any reason. **Exclusion Criteria:** Impaired mental state or language problems or if they were participating in another intervention trial that interfered		(87.3%) Probably related to intervention: 0/146 vs. 2/138 (1.3%) Not Assessable: 0/146 vs. 1/138 (0.6%) Missing: 0/146 vs. 1/138 (0.6%) Surgical site infection: 7 (4·6%) vs. 10 (6·3%) Burst abdomen 8 (5·3%) vs. 10 (6·3%) Anastomotic insufficiency: 39 (25·8%) vs. 34 (21·5%) Intra-abdominal fluid collection or abscess: 14 (9·3%) vs. 7 (4·4%) Bleeding: 12 (7·9%) vs. 14 (8·9%) Cardiovascular: 9 (6·0%) vs. 14 (8·9%) Pulmonary: 15 (9·9%) vs. 13 (8·2%) Renal 7 (4·6%) vs. 8 (5·1%) Other gastrointestinal problems: 21 (13·9%) vs. 24 (15·2%) Other: 15 (9·9%) vs. 21 (13·3%) Not assessable: 4 (2·6%) vs. 3 (1·9%)	

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			with the intervention or outcome of this trial.			
Thimour-Bergstr-om 2013 [73] (ES)	**RCT** 1, 2, 3, 4, 5, 6, 7, 8	To test the hypothesis that wound closure with sutures coated with triclosan would reduce SSI after open vein harvesting.	**Number of patients: N=374** **Patient Characteristics:** baseline patient characteristics not significantly different between groups ·Age, y: mean ±SD Intervention: 67.6±8.3 Control: 66.9±8.1 P=0.45 ·Gender: Female Intervention: 39/184 (21.1%) Control: 31/190 (16.3%) P=0.23 ·Obesity: BMI, kg/m^2: Mean±SD Intervention: 27.6±4.1 Control: 27.6±4.1 P=0.67 ·Comorbidities: Diabetes: Insulin treatment: Intervention: 22/184 (11.9%) Control: 21/190	**Intervention group:** n= 184 Wound closed subcutaneously with triclosan coated monofilament polyglactin suture and intracutaneously with a 4.0 triclosan coated monofilament polyglecaprone suture. **Timing of intervention:** intraoperative **Duration of intervention:** closure until absorption **Device/agent:** triclosan coated or conventional monofilament polyglactin suture and 4.0 triclosan coated or conventional monofilament polyglecaprone suture. **Monitoring intervention:** trained nurse **Control group:** n=190 Wound closed subcutaneously with conventional	**SSI:** CDC Criteria Intervention: 23/184 (12.5%) Control: 38/190 (20.0%) P=0.0516 (by Fisher's exact test) P=0.497 (by χ^2 test) RR: 0.63 (0.39-1.00) Culture Proven Intervention: 14/184 (7.6%) Control: 23/190 (12.1%) P=0.15 Antibiotic Treated Intervention: 20/184 (10.9%) Control: 35/190 (18.4%) P=0.039 (by χ^2 test) P=0.042 (by Fisher's exact test) Leg SSI and Demographics BMI SSI: 28.3±4.3 No SSI: 27.4±3.8 P=0.081 Diabetes – Insulin	**Definitions:** SSI: CDC – Superficial SSI must have at least one of the following features: (i) purulent drainage; (ii) positive culture, (iii) pain, tenderness, swelling, redness and deliberately opened incision by surgeon and culture proven or not cultured, and (iv) infection diagnosis by physician. Deep SSI: had to involve fascia or muscle layers Secondary endpoints: (i) purulent drainage;

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			(11.1%) P=0.78 Oral Treatment: Intervention: 20/184 (10.8%) Control: 22/190 (11.6%) P=0.83 Dietary Treatment Intervention: 4/184 (2.2%) Control: 7/190 (3.7%) P=0.38 Smoking On-going Intervention: 29/184 (15.8%) Control: 31/190 (16.3%) P=0.88 Number of bypasses Intervention: 3.0±0.9 Control: 3.2±1.0 P=0.008 **Procedures:** CABG Intervention: 164/184 (89.1%) Control: 167/190 (87.9%) P=0.71 CABG+ AVR Intervention: 17/184 (9.2%) Control: 22/190 (11.6%) P=0.46 CABG+mitral repair	monofilament polyglactin suture and intracutaneously with a 4.0 conventional monofilament polyglecaprone suture. **Standard preventive measures:** Surgical technique: all patients were performed Cardiopulmonary bypass Normothermia: was maintained **(**35-36^{o}C) Transfusion: cold intermittent blood cardioplegia. Antibiotic prophylaxis: all patients received 4 parenteral doses of cloxacillin 2g. First administered 20min prior to skin incision, second 2h after first does and following doses 6h & 24h later. Patients with allergy to cloxacillin received clindamycin. Closure: leg incision closed with one subcutaneous continuous suture and one continuous intracutaneous suture. Covered with drape, compresses and elastic	treatment Intervention: 12/61 (19.7%) Control: 31/313 (9.9%) P=0.029 Operative Characteristics and Infections Number of bypasses SSI: 3.4±1.0 No SSI: 3.1±1.0 P=0.014 **Other infections:** NR **Topic-specific outcomes:** Noninfectious dehiscence Intervention: 11/161 (6.8%) Control: 13/152 (8.5%) P=0.57 ASEPSIS score, day 4 Mean and SD Intervention: 0.4±1.2 Control: 0.3±0.8 P=0.44 Median and range Intervention: 0 (0-12) Control: 0 (0-5) P=0.78 ASEPSIS score, day 30 Mean and SD Intervention: 3.0±7.6 Control: 4.7±9.4 P=0.070 Median and range Intervention: 0 (0-45) Control: 0 (0-43) P=0.20	(ii) antibiotic-treated SSI according to CDC's definition within 60 days postop. (iii) ASEPSIS score at Days 30 & 60 postop (iv) non-infectious leg-wound dehiscence within 60 days postop **Perioperative care:** NR **Other notes:** Study power: Based on a 20% infection rate found by a pilot study, an 80% power and a p-value of 0.05 showed 180 patients were needed in each group to show a 50% reduction in SSI Wounds inspected at postop days 4 & 30 by trained research nurse and at 60 days postop, patients interviewed by telephone. **Follow-up:** 60 days postop

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			Intervention: 3/184 (1.6%) Control: 1/190 (0.5%) P=0.30 **Indications:** NR **Setting:** 1 university hospital **Location:** Sweden **Dates:** March 2009 – February 2012 **Inclusion Criteria:** Patients planned for Coronary Artery Bypass Graft, CABG+Aortic Valve replacement (AVR) or CABG+mitral valve repair or replacement **Exclusion Criteria:** ongoing sepsis or septicemia, ongoing bacterial infections or antibiotic treatment, participation in other clinical studies, or other severe disease that might influence wound healing, emergency surgery or known allergy to triclosan.	bandages. Drape removed on Postop Day 4.	ASEPSIS score, day 60 Mean and SD Intervention: 3.7±8.7 Control: 5.4±10.0 P=0.097 Median and range Intervention: 0 (0-45) Control: 0 (0-43) P=0.46 Operation Time, min: Leg vein harvesting Intervention: 61±32 Control: 48±19 P<0.001 (This significance remained after adjusting for operating surgeon level of experience Cultures taken: No resistant bacteria reported *Staphyloccous aureus*: Intervention: 7/23 (44) Control: 15/38 (52) p=0.61 **Reoperations:** NR **Length of stay:** NR **Mortality:** considered lost to follow up Intervention: 1/184 (0.5%) Control: 1/190 (0.5%) **Adverse events:** Postoperative bleeding (ml/12h) Intervention: 470 (95-1950) Control: 482 (110-4550) P=0.94	**Funding Source Conflicts:** Authors: None Institution: NR Study: Industry Supplies: NR

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
					Postoperative Bleeding SSI: 430 (95-1485) No SSI: : 500 (140-4550) P=0.050	
Justinger 2013 [75] (ES)	**RCT** 1, 3, 4, 5, 6, 7, 8	To investigate the effect of impregnating, with triclosan, polydioxanone sutures used for abdominal wall closure on the rate of SSI	**Number of patients: N=856** **Patient Characteristics** ·Age, y: mean±SD, Intervention: 63±13 Control: 63±13 P=0.923 ·Gender: M:F Intervention:301:184 Control: 224:147 ·Obesity: BMI>30 Intervention: 76/485 (16.4%) Control: 54/371 (15.8%) P=0.713 ·Comorbidities Diabetes mellitus Intervention: 49/485 (10.1%) Control: 35/371 (9.4%) P=0.4.19 **Procedures:** Wound classification: p<.05 Clean: Intervention: 286/485 (59%) Control: 245/371 (66%) Clean contaminated Intervention: 162/485 (33.4%)	**Intervention group:** n=485 Abdominal fascia closed with triclosan-impregnated polydioxanone loop. **Timing of intervention:** intraoperative **Duration of intervention:** closure until absorption **Device/agent:** polydioxanone sutures either conventional or triclosan coated. **Monitoring intervention:** postop wounds were assessed daily by 2 blinded observers. **Control group:** n=371 Abdominal fascia closed with conventional polydioxanone loop. **Standard preventive measures:** MRSA- patients with previous methicillin-resistant *Staphylococcus aureus* contamination of patients at risk for MRSA contamination were screened preoperatively and decontaminated, if elective	**SSI** Total: Intervention: 31/485 (6.4%) Control: 42/371 (11.3%) OR: 0.501 (0.3-0.9) P<0.05 <u>SSI by Wound Classification:</u> P<0.05 Clean: Intervention: 14/286 (4.8%) Control: 22/245 (8.9%) Clean-Contaminated: Intervention: 14/162 (8.6%) Control: 16/97 (16.5%) Contaminated: Intervention: 3/37 (8.1%) Control: 4/25 (16%) Septic Intervention: 0/0 Control: 0/4 <u>SSI by Surgery</u> Upper GI Tract Intervention: 3/59 (5%) Control: 2/41 (5%) Hepatopancreatobiliary Intervention: 9/201 (4%) Control: 14/173 (8%) Small Intestine Intervention: 1/19 (5%)	**Definitions:** SSI- CDC NHSN definitions used: Wound infection was identified by the presence of erythema, induration, pain and discharge of serous or contaminated fluid. **Perioperative care:** A standardized clinical pathway was used **Other notes:** Sample size: An assumed SSI reduction from 12% to 6% resulted in a calculated sample size of 350 patients for each arm to achieve a power of 1-b=0.08 for the one-sided χ^2 test at a level a=0.025 and a low dropout rate of 5% Study used groups

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			Control: 97/371 (26.1%) Contaminated Intervention: 37/485 (7.6%) Control: 25/371 (6.7%) Septic Intervention: 0/485 Control: 4/371 (1.1%) **Indications:** NR **Setting:** One University Hospital **Location:** Switzerland **Dates:** September 2009 - September 2011 **Inclusion Criteria:** all patients scheduled to undergo open abdominal exploration and surgery and closure of the incision in a standard fashion (laparotomy) who gave consent. **Exclusion Criteria:** Refusal of surgery, minimally invasive procedures or nonsurgical therapies, burst abdomen, planned revision within 30 days, or an on-demand re-laparotomy for organ/space infections. Mortality	Bowel Prep- all patients undergoing colorectal resections had preop bowel prep with 3L of prepacol Preop shower – all patients had a regular shower without iodine within 24h preop Hair removal: abdominal wall hair removed but when and how was not described. Antibiotic prophylaxis: all patients received metronidazole and ceftriaxone; metronidazole and clindamycin in case of allergy) within 60 minutes prior to incision. Additional doses were administered in surgeries >4h Skin prep: Alcohol-based povidone-iodine Drape: skin drape used and wound edges were protected with surgical swaps. Swabs were soaked in povidone iodine solution for patients with a contaminated abdominal cavity. Normothermia: temperature was kept >35^{o}C in patients with a	Control: 3/14 (21%) Vascular Surgery Intervention: 0/26 Control: 0/24 Other Intervention: 1/27 (4%) Control: 4/19 (21%) *Colorectal* Intervention: 17/143 (12%) Control: 19/100 (19%) Total SSI Colorectal Procedures: SSI/Colo Procedures = 36/243 (14.8%) OR: 3.3 (1.9-5.7) P<0.05 <u>BMI >30 and SSI</u> 14/130 (10.8%) OR: 1.68 (*0.8-3.2) P=0.12 **Other infections:** NR **Topic-specific outcomes:** Wound culture results (reported in %) *Staphylococci* Intervention: 23.1% Control: 23.1% *Enterococci* Intervention: 23.1% Control: 30.1% *Streptococci* Intervention: 5.1% Control: 5.1% *Pseudomonas spp.* Intervention: 0	of 50 – 100 consecutive patients either to control or the triclosan treatment group **Follow-up:** within 2 weeks post-discharge **Funding Source Conflicts:** Authors: NR Institution: NR Study: Industry Supplies: NR

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			in the follow up period and abdomen not closed during the initial procedure.	warming device. Found organ/space infection: patients with an organ/space infection upon laparotomy underwent an abdominal lavage with Ringer's lactate solution of at least 5L Closure: abdominal wall closed with continuous suture & peritoneum was not closed separately. Skin closed with staples. Wound rinsing: post-closure, wound rinsed with Ringer's solution. Oxygenation: in patients with a history of Cardiovascular disease, oxygen was supplied via nasal tube to maintain oxygen saturation of >95% postop. Glycemic control: patients requiring intensive care treatment had a tight postoperative glucose control and correction of hyperglycemic states by continuous or intermittent insulin administration.	Control: 2.5% *Enterobacteriacae* Intervention: 15.4% Control: 23.1% Others Intervention: 15.4% Control: 23.1% MDRO not reported **Reoperations:** NR **Length of stay:** In hospital stay: mean±SD (range), days Intervention: 15±13 (2-134) Control: 11±18 (2-209) P=0.300 **Mortality:** Exclusionary 10 patients died. Cause of death an d study arm not reported **Adverse events:** NR	

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
Nakamura 2013 [74] (ES)	**RCT** 1, 4, 5, 7, 8, 9	To evaluate whether the incidence of wound infections can be reduced when triclosan-coated sutures are used for abdominal wound closures and to evaluate the impact on costs associated with wound infections after colorectal surgery.	**Number of patients: N=410** **Patient Characteristics:** no significant difference existed between groups ·Age, y: mean±SD Intervention: 69.4±11.3 Control: 70.2±11.1 P=0.44 ·Gender M:F Intervention: 130:76 Control: 112:92 P=0.09 ·Obesity: BMI, kg/m^2: mean±SD Intervention: 23.2±3.6 Control: 23.4±3.8 P=0.61 ·Comorbidities: Diabetes mellitus: Intervention: 41/206 (19.9%) Control: 31/204 (15.2%) P=0.21 **Procedures:** colorectal surgeries including right, left, and transverse colectomy; sigmoidectomy; low anterior and abdominoperineal resection; total colectomy; and simple colostomy	**Intervention group:** n=206 Wounds closed with triclosan-coated polyglactin 910 antimicrobial sutures **Timing of intervention:** intraoperative **Duration of intervention:** closure until absorption **Device/agent:** polyglactin 910 sutures either conventional or triclosan coated **Monitoring intervention:** daily checks until discharge followed by 30 day postop checkup **Control group:** n=204 Wounds closed with conventional polyglactin 910 antimicrobial sutures **Standard preventive measures:** Antibiotic prophylaxis: intravenous cephalosporin 30 min prior to incision; every 3h of operative time; and for 48h postop in both groups. Wound protectors: used during open surgery, and lap protectors used during delivery of specimens during laparoscopic surgery. Closure technique:	**SSI:** Total: 28/410 (6.8%) Wound Infection Intervention: 9/206 (4.3%) Control: 19/204 (9.3%) P=0.047 Organ/space Intervention: 5/206 (4.3%) Control: 4/204 (9.3%) P=0.74 Wound infection by surgery type Laparoscopic: 12/227 (5.3%) Open: 16/183 (8.7%) P=0.16 Laparoscopic surgery: Intervention: 5/119 (4.2%) Control: 7/108 (6.5%) P=0.43 Open Surgery Intervention: 4/87 (4.6%) Control: 12/96 (12.3%) P=0.061 **Other infections:** NR **Topic-specific outcomes:** Cultured organism (note some infections had were multi-organism) *Enterococcus* Intervention: 5/9 Control: 6/19	**Definitions:** Wound infection: CDC 1999 Guideline. **Perioperative care** **Other notes:** The assumed expected wound infection rates of 4% to 5% for the study group and 10% to 11% for the control group. With a 2-sided alpha=0.05, the study was expected to have 80% power to detect a relative risk reduction of 5%; a total of 400 patients were estimated to be needed. **Follow-up:** 30 days post discharge. **Funding Source Conflicts:** Authors: NR Institution: NR Study: NR Supplies: NR

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			Laparoscopic Surgery Intervention: 119/206 (57.8%) Control: 108/204 (52.9%) P=0.33 Open Surgery Intervention: 87/206 (42.2%) Control: 96/204 (47.1%) P=0.33 **Indications** **Setting:** 1 hospital **Location:** Japan **Dates:** April 2009 – March 2011 **Inclusion Criteria:** Patients undergoing elective colorectal surgery during the study dates. **Exclusion Criteria**: NR	interrupted sutures and surgical staples for skin by 7 surgeons.	*Enterobacter* Intervention: 0/9 Control: 3/19 *Bacteroides* Intervention: 3/9 Control: 5/19 *MRSA: 0/9 vs. 1/19 (5.3%)* *Missing data: 2/9 (22.2%) vs. 6/19 (31.6%)* **Reoperation:** NR **Length of stay:** (patients with infected wounds were discharged and wounds were managed from outpatient clinic) Postop Hospital Stay, days: median (SD), Intervention: 11 (6-79) Control: 11.5 (6-93) P=0.08 Postop Hospital Stay, days: mean ±SD Intervention: 15.2±11.6 Control: 15.6±10.4 P=0.71 **Mortality:** NR **Adverse events:** NR	
Turtiainen 2012 [68] (ES)	**RCT** 1, 2, 3, 5, 6, 7, 8, 9	To determine whether the use of triclosan-coated sutures for wound closure would reduce the risk of surgical wound infection after peripheral	**Number of patients: N=276** **Patient Characteristics** No significant differences seen between groups. ·Age, y: mean (SD) Intervention: 72 (11) Control: 72 (11) ·Gender: m/f Intervention: 87/25	**Intervention group:** n=139 Arterial exposure and vein harvest incisions closed with triclosan-coated polyglactin 910 and poliglecaprone 25 sutures. **Timing of intervention:** intraoperative **Duration of intervention:** closure until absorption	**SSI** Overall: 22% Intervention: 31/139 (22.3%) Control: 30/137 (21.9%) Superficial: Intervention: 24/139 (17.3%) Control: 22/137 (16.2%) Deep Intervention: 5/139	**Definitions:** Surgical wound infection: any complication of surgery was designated an infection if bacteria were isolated from the wound or if localized redness,

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
		vascular surgery.	(63%/37%) Control: 86/51 (63%/37%) ·Obesity: BMI (kg/m^2) mean (SD) Intervention: 26 (5) Control: 26 (4) ·Comorbidities Diabetes Intervention: 43/139 (31%) Control: 44/137 (32%) COPD Intervention: 16/139 (12%) Control: 23/137 (1%) Concurrent use of corticosteroids: Intervention: 19/139 (14%) Control: 15/137 (11%) **Procedures:** lower limb arterial reconstruction **Indications:** Claudication Intervention: 44/139 (32%) Control: 27/137 (31%) Rest pain Intervention: 48/139 (35%) Control: 42/137 (31%) Ischemic ulcer Intervention: 34/139 (25%) Control: 39/137 (29%) Other	**Device/agent:** Triclosan-coated or standard polyglactin 910 and poliglecaprone 25 sutures. **Monitoring intervention** **Control group:** n=137 Arterial exposure and vein harvest incisions closed with standard polyglactin 910 and poliglecaprone 25 sutures. **Standard preventive measures:** Antibiotic prophylaxis: At 3 hospitals: 3g cefuroxime administered intravenously within 1h prior to incision. At 2 hospitals: 1.5g cefuroxime administered intravenously 1h prior to incision and then every 8h for the first 24h after operations. At 1 hospital: if a prosthetic graft was used, patients also received intravenous vancomycin.	(3.6%) Control: 5/137 (3.7%) Graft Infection Intervention: 2/139 (1.5%) Control: 3/137 (2.2%) **Other infections:** NR **Topic-specific outcomes:** Graft Thrombosis: Intervention: 7/139 (5.0%) Control: 6/137 (4.4%) P=0.80 Stroke Intervention: 4/139 (2.9%) Control: 1/137 (0.7%) P=0.18 Cultures taken: no resistant bacteria reported. **Reoperations:** NR **Length of stay:** days (SD) Intervention: 5.5 (6.5) Control: 5.2 (4.3) P=0.68 **Mortality:** 10 patients died within 30 days of surgery. (9 had no SSI) 30 day mortality Intervention: 6/139 (4.3%) Control: 4/137 (2.9%) P=0.55 **Adverse events:** Major amputation	warmth, swelling, and pain around the wound appeared within 30 days after the operation (CDC definition) Superficial: if only skin and subcutaneous tissue are involved Deep: if wound infection involves both fascia and muscle layers Graft/O/S: if an artery or a graft (vein or prosthesis) becomes infected. **Perioperative care:** NR **Other notes:** Sample size: for the study to provide an 80% power for detecting a 50% reduction in infection rate at α=0.05, there should be at least 137 patients in both

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			Intervention: 13/139 (9%) Control: 29/137 (21%) **Setting:** 3 tertiary referral hospitals and two secondary referral hospitals. **Location:** Finland **Dates:** July 2010 – January 2011 **Inclusion Criteria:** adult patients who underwent nonemergency lower limb arterial surgery. **Exclusion Criteria:** Aortoiliac procedures and the patient's refusal to participate.		Intervention: 4/139 (2.9%) Control: 5/137 (3.6%)	groups. **Follow-up:** At least 1 month postop or until the wound healed **Funding Source Conflicts:** Authors: NR Institution: NR Study: NR Supplies: NR
Seim 2012 [69] (ES)	**RCT** 1, 5, 6, 7, 8	To evaluate the effects of Triclosan coated polyglactin 910 suture on standard polyglactin 910 suture with regard to surgical leg wound infections following saphenous vein harvesting in a prospective randomized	**Number of patients: N-=323** **Patient Characteristics:** demographic and perioperative characteristics between groups are comparable at baseline except for blood glucose (see below). ·Age, y mean±SD Intervention: 63.5±0.7 Control: 63.1±0.8 ·Gender: female Intervention: 17/160 (10.6%) Control: 19/163	**Intervention group:** n=163 Let wound closure with triclosan-coated polyglactin 910 suture **Timing of intervention:** Intraoperative **Duration of intervention:** Intra and postoperative **Device/agent:** Standard or triclosan-coated polyglactin 910 sutures **Monitoring intervention:** by hospital staff in hospital, by patient postdischarge. **Control group:** Leg wound closure with conventional polyglactin	**SSI** Overall infection rate: 33/323 (10.2%) Intervention: 16/160 (10%) Control: 17/163 (10.4%) BMI and infection (kg/m^2) mean±SD: Infection (n=33): 29.5±0.8 No-infection (m=290): 27.5±0.2 p=0.02 IDDM General Perioperative Data There were no significant	**Definitions:** SSI – positive bacterial culture and clinical judgment **Perioperative care:** NR **Other notes:** Study power: a-priori, in order to detect an estimated 50% reduction in infection rate in the triclosan-coated suture group and a statistical power level of 0.8, this

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
		study. Secondly, to examine patient- and operative characteristics, which are assumed to predict leg wound infections.	(11.7%) ·Obesity: BMI (kg/m^2), mean±SD Intervention: 27.7±0.3 Control: 27.5±0.3 ·Comorbidities Diabetes mellitus, Intervention: 31/160 (19.4%) Control: 40/163 (24.5%) IDDM Intervention: 9/160 (5.6%) Control: 17/163 (10.4%) Blood Glucose (mmol/l), mean±SD Intervention: 6.6±0.3 Control: 8.5±0.8 P=0.05 **Procedures:** Coronary Artery Bypass Graft (CABG) **Indications:** NR **Setting:** 1 university hospital **Location:** Switzerland **Dates:** September 2009 - September 2011 **Inclusion Criteria:** patients undergoing CABG at the study center **Exclusion Criteria:** Patients with leg wounds, bilateral	910 suture **Standard preventive measures:** Hair removal: with electric razor on the afternoon of the day before surgery. Pre-Op bathing: in the evening before the operation, all patients took a shower including washing with soap and chlorhexidine gluconate 40mg/ml. This shower repeated on the day of surgery. Standard CABG technique: using CPB, moderate hypothermia (32^{o}C), cold crystalloid or cold blood cardioplegia and aortic cross clamping. Skin disinfection: with chlorhexidine solution, 5 mg/ml with 70% ethanol. Saphenous vein harvesting: from the medial malleolus by a continuous skin incision, ending either below or over the knee. Side branches were ligated or clipped. For practical reasons, the left leg was predominantly preferred.	differences except: *Cardiopulmonary bypass time* (min) Infection (n=33): 86.4±5.5 Control/intervention (n=17/n=16): 81.3±9.1/92.2.9±6.0 No-infection (m=290): 77.2±1.2 Control/intervention (n=146/n=144): 75.7±1.7/79.2±1.9 p=0.03 *Aortic cross clamping time* (min) Infection (n=33): 48.3±4.1 Control/intervention (n=17/n=16): 44.4±5.8/53.7.9±5.8 No-infection (m=290): 41.4±1.1 Control/intervention (n=146/n=144): 40.1±1.1/43.5±3.5 p=0.05 **Other infections:** NR **Topic-specific outcomes:** Bacterial cultures taken for confirmation results not reported **Reoperations:** NR **Length of stay:** NR **Mortality:** NR **Adverse events:** NR	study required a minimum sample size of 302 patients **Follow-up:** 4 weeks post discharge (a registration form was returned at 4 weeks postop) **Funding Source Conflicts:** Authors: None Institution: None Study: None Supplies: None

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			vein harvesting, harvesting of the short saphenous vein, varicose veins and those undergoing emergency CABG	Antibiotic prophylaxis: cefalotine as a single dose of 2g intravenously before skin incision and continued with 3-h intervals to a total of 8g in both groups. Drape: wound covered with drape, compresses and elastic bandages. First day postop, the compresses and elastic bandages were removed and third postop day the drape removed.		
Isik 2012 [79] (ES)	**RCT** 1, 3, 4, 5, 10	To evaluate whether the incidence of sternal and leg wound infections is reduced when coated sutures are used for wound closure, compared with non-coated sutures	**Number of patients: N=510** **Patient Characteristics:** patients were similar in demographic and lab characteristics. ·Age >65 y: Intervention: 70 (41.2%) Control: 138 (40.6%) ·Gender: Male Intervention: 111 (64.7%) Control: 228 (67.1%) ·Obesity: BMI>30kg/m^2 Intervention: 41 (24.1%) Control: 84 (24.7%) ·Comorbidities: Diabetes mellitus Intervention: 57	**Intervention group:** n=170 Wound closure with triclosan-coated polyglactin 910 suture **Timing of intervention:** intraoperative **Duration of intervention:** closure until absorption **Device/agent:** Polyglactin 910 suture either coated or uncoated **Monitoring intervention:** Patients inspected daily by nurse in hospital. Post discharge, patients were seen every 10 days in the cardiac rehabilitation center for 30 days. **Control group:** n=340 Standard polyglactin 910	**SSI** Superficial Sternum SSI Total: 16/510 (3.1%) Intervention: 4/170 (2.4%) Control: 12/340 (3.5%) P=0.596 Mediastinitis: 0 cases Leg Site SSI Total: 17/402 (3.7%) Intervention: 5/142 (3.5%) Control: 10/260 (3.8%) P=1.000 Gender and SSI Male No SSI 324/338 (95.9%) SSI 14/338 (4.1%) Female No SSI 158/172 (91.9%) SSI 14/172 (8.1%)	**Definitions:** SSI – CDC definitions. **Perioperative care:** NR **Other notes:** Study power was calculated on the assumption that SSI would be reduced from 6% to 1%, the study group was to be ½ the size of the control group with a total of 510 patients. Which was performed with a risk coefficient (α) of 0.05, a

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			(33.5%) Control: 120 (35.3%) EuroSCORE Risk Score <5 Intervention: 119 (70.0%) Control: 210 (61.8%) EuroSCORE Risk Score >5 Intervention: 51 (30.0%) Control: 130 (38.2%) P=0.077 **Procedures:** Emergency: Intervention: 2 (1.2%) Control: 14 (4.1%) P=0.104 Procedures: p=0.78 CABG Intervention: 147 (86.5%) Control: 263(77.4%) Valve repair Intervention: 17 (10.0%) Control: 50 (14.7%) CABG and valve repair Intervention: 6 (3.5%) Control: 25 (7.4%) Other operations Intervention: 0 Control: 2 (0.6%) **Indications:** NR **Setting:** Single private hospital **Location:** Turkey **Dates:** April 2008 – September 2009	suture **Standard preventive measures:** NR	P=0.067 Both sternal and leg infections developed in 3 patients (not stated which group they belong to) SSI in patient with diabetes OR 3.23 (1.45-7.23), p=0.04 SSI in patients with EuroSCORE > 5 OR 0.98 (0.91-1.05); P=0.164 **Other infections:** NR **Topic-specific outcomes:** Wound Culture Results *S. aureus* Intervention Sternum: 0 Intervention Leg: 0 Control Sternum: 4 Control Leg: 1 *S. epidermis* Intervention Sternum: 1 Intervention Leg: 0 Control Sternum: 1 Control Leg: 1 *Corynebacterium spp.* Intervention Sternum: 0 Intervention Leg: 0 Control Sternum: 1 Control Leg: 0 *Pseudomonas aeruginosa* Intervention Sternum: 1	confidence interval (1-α) of 0.95, a risk coefficient (β) of 0.20 and a power (1-β) of 0.80 **Follow-up:** 30 days postop **Funding Source Conflicts:** Authors: None Institution: None Study: None Supplies: None

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			Inclusion Criteria: Patients undergoing cardiac surgery during the study period **Exclusion Criteria:** NR		Intervention Leg: 0 Control Sternum: 0 Control Leg: 0 *Klebsiella pneumonaie* Intervention Sternum: 1 Intervention Leg: 2 Control Sternum: 0 Control Leg: 0 *Swabs taken for suspected wounds. MRSA was not recovered from any wounds in study* **Reoperations:** NR **Length of stay:** NR **Mortality:** NR **Adverse events:** NR	
Williams 2011 [72] (ES)	**RCT** 1, 2, 4, 5, 6, 7	To assess the effect of triclosan coating of polyglactin and poliglecaprone sutures for skin closure after elective breast cancer surgery.	**Number of patients: N=150** **Patient Characteristics:** ·Age: media, years (Range) Intervention: 61 (32-87) Control: 59 (30-80) ·Gender: all female ·Obesity: NR ·Comorbidities: NR **Procedures:** Breast cancer surgery: Wide lump excision, sentinel node biopsy, Axillary node clearance, mastectomy and localized wire excision or some combination of the	**Intervention group:** n=75 Wounds closed with triclosan-coated subcutaneous polyglactin and triclosan-coated subcuticular poliglecaprone. **Timing of intervention:** intraoperative **Duration of intervention:** closure to absorption **Device/agent:** triclosan-coated subcutaneous polyglactin and triclosan-coated subcuticular poliglecaprone or standard polyglactin and poliglecaprone **Monitoring intervention:** patients reviewed	**SSI** Overall rate 2 weeks Postop: 13.7% (20/146) Intervention: 9/73 (12.3%) Control: 11/73 (15.1%) P=NS 6 weeks postop: 18.9% (24/127) Intervention: 10/66 (15.2%) Control: 14/61 (22.9%) P=NS **Other infections:** NR **Topic-specific outcomes:** <u>Patients lost to follow up Two weeks (n=4)</u> Patient request Intervention: 1 Control: 1	**Definitions:** SSI – all investigators were conversant with the CDC definition of SSI and the ASEPSIS and Southampton wound scores. **Perioperative care:** Anesthesia: general anesthesia **Other notes:** patients given diaries to record events occurring within the 6 weeks postop. Significant

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			above **Indications:** NR **Setting:** Single center **Location:** United Kingdom **Dates:** November 2008 – February 2011 **Inclusion Criteria:** Women >18 years undergoing primary elective breast surgery under the care of two breast surgeons at the study center **Exclusion Criteria:** Inflammatory breast cancer or skin ulceration; neo-adjuvant chemotherapy or radiotherapy; surgery for benign or reconstructive reasons; known immune deficiency or allergy to triclosan; and inability to give consent or suspicion that the patient was unlikely to comply with the follow-up.	regularly by nurses and at two and six weeks postop as outpatients or at a home visit. **Control group:** n=75 Wounds closed with subcutaneous polyglactin and subcuticular poliglecaprone. **Standard preventive measures:** Antibiotic prophylaxis: 8 patients considered high risk received a single intravenous dose of 1g of amoxicillin clavulanate. (high BMI, mastectomy or axillary clearance_ none of these developed SSI) Closure: wounds closed after surgery using subcutaneous polyglactin and subcuticular poliglecaprone at the discretion of the operating consultant surgeon. Wound dressing: butterfly stitches and waterproof, transparent dressing or one of two types of adhesive wound dressing. OR an adhesive wound dressing alone.	Lost to follow up Intervention: 0 Control: 1 Need for further surgery Intervention: 0 Control: 1 <u>Six weeks (n=19)</u> Patient request Intervention: 1 Control: 0 Lost to follow up Intervention: 1 Control: 2 Need for further surgery Intervention: 5 Control: 10 **Reoperations:** exclusionary criteria 6/24 SSI needed an intervention to open/pack or aspirate axillary collections. 3/6 required readmission 1/24 had a delay in starting adjuvant chemotherapy. Need for further surgery: Intervention: 5/9 (55.6%) Control: 10/14 (71.4%) **Length of stay:** NR **Mortality:** NR **Adverse events:** NR	events were corroborated by an attending physician. Power: estimated sample size of 150 patients (75 in each group) was considered to have 80% power to show a statistically significant difference of $p<0.05$ **Follow-up:** 6 weeks postop. **Funding Source Conflicts:** Authors: Industry Institution: NR Study: Industry Supplies: NR

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
				All other interventions such as pre-medication, anesthesia, and phlebothrombosis prophylaxis were standard for both groups.		
Baracs 2011 [71] (ES)	**RCT** 1, 2, 5, 7, 10	To compare polydioxanone suture with and without triclosan in seven high-volume Hungarian surgical institutions over a one-year period	**Number of patients:** N=385 **Patient Characteristics:** groups showed homogeneity in demographic features ·Age, y: mean Intervention: 62.6 Control: 63.5 ·Gender: m:f Intervention: 110:78 Control: 111:86 ·Obesity: mean BMI of patients with SSI Intervention: 23.14 Control: 27.97 ·Comorbidities: Type II Diabetes mellitus Intervention: 27/188 (14.4%) Control: 26/197 (13.4%) Neoadjuvant therapy: Intervention: 47/188 (25%) Control: 40/197 (20.3%)	**Intervention group:** n=188 Triclosan-coated running looped polydioxanone used to close the abdominal fascia. **Timing of intervention:** intraoperative **Duration of intervention:** closure and up to 30 days until absorption **Device/agent:** Running looped polydioxanone sutures either triclosan-coated or standard **Monitoring intervention:** examination of incision site during hospital stay and telephone call follow up at 30 days post discharge **Control group:** n=197 Standard running looped polydioxanone used to close the abdominal fascia. **Standard preventive measures** Closure: separate	**SSI** Intervention: 23/188 (12.2%) Control: 24/197 (12.2%) P=NS Late infection (post discharge) Intervention: 4/188 (2.1%) Control: 9/197 (4.6%) P=0.41 SSI By Operations Right-sided colon resection Intervention: 11/46 (24%) Control: 5/44 (11%) P=0.006 Rectal resection Intervention: 6/89 (7%) Control: 14/95 (15%) P=0.033 Left sided colon and sigmoid resection Intervention: 4/40 (10%) Control: 3/45 (7%) P=NS Segmental resection and	**Definitions:** SSI – SSI described as divided into superficial incisional, deep incisional, abdominal dehiscence but these were not defined. **Perioperative care:** Adjuvant therapy was not allowed to be started within the 30-day follow-up period **Other notes:** Pilot study of 50 patients showed a 5% SSI rate in the Triclosan coated polyglactin 910 suture and a 20% SSI rate in the standard 910 suture. This study showed

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			Procedures: hemicolectomies, transversectomies, cecal resection, colostomies, A-P resections of the rectum, sigmoid resections, abdominal resections of the rectum, subtotal colectomies, total colectomy and abdominal resection of the rectum. **Indications:** Benign or malignant colon or rectal disease **Setting:** 7 hospitals (3 university, 4 high-volume hospitals) **Location:** Hungary **Dates:** December 2009 – November 2010 **Inclusion Criteria:** Patients between the ages of 18-80 years old with benign or malignant colon or rectal disease undergoing and elective open surgical procedure involving an enterotomy **Exclusion Criteria:** Patients with systemic disease	peritoneal closure and subcutaneous sutures were optional depending on surgeon's preference. If employed, 2-0 suture utilized. Interrupted 2-0 poliglecaprone 25 used for the skin closure. Antibiotic Prophylaxis: a second-generation cephalosporin and metronidazole 30 minutes before incision) Drapes – disposable drapes used. Incision locations: not standardized in either rectal or hemicolectomy surgeries)	colectomy Intervention: 2/10 (20%) Control: 1/8 (13%) P=NS Total and subtotal colectomy Intervention: 0/3 Control: 1/5 (20%) <u>BMI and SSI</u> BMI<20kg/m^2 Intervention: 3/7 (42.8%) Control: 3/11 (27.3%) Normal BMI (20-30 kg/m^2): Intervention: 16/147 (10.9%) Control: 16/139 (11.5%) Obese (BMI >30kg/m^2): Intervention: 3/34 (11.8%) Control: 5/47 (10.6%) Normal BMI (20-30 kg/m^2): 11.2% (32/286) BMI<20kg/m^2: 33.3% (6/18) P<0.05 **Other infections:** NR **Topic-specific outcomes:** Cultured Organisms Gram Positive: *Pseudomonas aeruginosa, Enterococcus faecium, E. coli, Enterococcus spp*. – cultured from both groups, numbers not reported.	SSI was about 10% in each group. Polyglactin is braided and polydioxanone is monofilament. **Follow-up:** 30 days post discharge via telephone call. **Funding Source Conflicts:** Authors: None Institution: None Study: None Supplies: None

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			influencing local surgical site healing (e.g. type I diabetes mellitus, Child-Pugh class B-C liver cirrhosis, and chronic kidney disease necessitating dialysis) or those having immunosuppressive treatment or inflammatory bowel disease. Also, acute operations with unprepared bowel (9 cases) & patients who refused consent. Some patients with intraoperative findings such as locally incurable tumor or sepsis (abscess, necrotic tumor), or with postoperative findings such as further surgical intervention through the site and patients who withdrew the consent later. Undesirable complications such as sterile surgical site dehiscence and suture breakage		Gram Negative: S. epidermis: Intervention: 0 Control: 2 **Reoperations:** NR **Length of stay:** NR **Mortality:** NR **Adverse events:** NR	

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			during the post-operative period also led to exclusion from the trial.			
Galal 2011 [76] (ES)	**RCT** 1, 2, 3, 4, 5, 6	To assess the incidence of surgical site infection using triclosan-coated polyglactin 910 antimicrobial	**Number of patients: N=450** **Patient Characteristics:** there were no significant differences between groups regarding age ·Age: 21-30 y Intervention: 42/230 (18.3%) Control: 40/220 (18.2%) 31-40 y Intervention: 75/230 (32.6%) Control: 85/220 (38.6%) 41-50 y Intervention: 90/230 (39.1%) Control: 75/220 (34.1%) 51-60 y Intervention: 23/230 (10.0%) Control: 20/220 (9.1%)	**Intervention group:** n=230 Surgeries where absorbable, braided polyglactin 910 triclosan coated suture used in all steps except in some cases polypropylene was used for laparotomy closure and vascular suture. Poliglecaprone 25 used in skin closure. **Timing of intervention:** intraoperative **Duration of intervention:** suturing to absorption **Device/agent:** absorbable, braided polyglactin 910 suture coated with triclosan. Or polyglactin 910 suture. **Monitoring intervention:** NR **Control group:** n=230 Surgeries where conventional absorbable, braided	**SSI:** Total SSI: 50/450 (11%) Intervention: 17/230 (7%) Control: 33/220 (15%) P=0.011 (please note that the numbers for clean, clean contaminated and contaminated surgery do not add up to the "n" for the intervention & control group) **Other infections:** NR **Topic-specific outcomes:** NR **Reoperations:** NR **Length of stay:** mean±SD (range) days SSI 7.10±3.92 (3-16) No SSI 3.39±1.48 (1-13) P<0.001 **Mortality:** NR **Adverse events:** NR	**Definitions:** CDC definitions: an infection within 30 days of surgery (or within a year in case of prosthetic surgery): (1) diagnosis consists of infection of an anatomic plane by one of the following manifestations: collection; inflammatory signs (pain, tenderness, edema, redness); dehiscence; or positive culture; (2) classification according to anatomic plane as follows: superficial

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			P=0.567 ·Gender male Intervention: 148/230 (64.3%) Control: 127/220 (57.7%) P=0.1499 ·Obesity: NR ·Comorbidities: Diabetes: Intervention: 32/230 (13.9%) Control: 42/220 (19.1%) P=0.1386 **Procedures:** Vascular surgery: n=86 Intervention: 50/230 (21.7%) Control: 36/220 (16.4%) Plastic Surgery: n=82 Intervention: 40/230 (17.4%) Control: 50/220 (19.1%) Gastrointestinal surgery: n=65 Intervention: 38/230 (16.5%) Control: 27/220 (12.3%) Biopsy: n=64 Intervention: 32/230 (13.9%) Control: 3/220 (14.5%) Hernia: n=63 Intervention: 30/230 (13.0%)	polyglactin 910 suture was used in all surgical steps except in some cases, polypropylene was used for laparotomy closure and vascular suture, and Poliglecaprone 25 was used in skin closure. **Standard preventive measures:** Closure: in both groups, monofilament sutures were the only kind of suture material used for the following applications: polyglecaprone used for skin closure in plastic surgery, hernia, thyroidectomy, mastectomy, lipoma and hand surgery; polypropylene used for vascular, fascial closure, and skin in surgeries other than aforementioned surgeries. **In this study, they followed the local protocol of the infection control unit at their institute. This may deviate from current modern practices. This protocol used for both**		incisional surgical site infection: infection of skin and subcutaneous tissue; deep incisional surgical site infection: infection of deep soft tissue (fascia and muscles); or organ/space surgical site infection: infection of organ/space. **Perioperative care** **Other notes:** Patients were assessed daily in the hospital. Post discharge patients were requested to return to the outpatient clinic weekly for 30 days (then monthly until the end of the first year in the case of prosthetic surgery) This was a multicenter study, however,

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			Control: 33/220 (15%) Thyroidectomy: n=30 Intervention: 9/230 (3.9%) Control: 21/220 (9.5%) Mastectomy: n=15 Intervention: 10/230 (4.3%) Control: 5/220 (2.3%) Lipoma: n=13 Intervention: 7/230 (3.0%) Control: 6/220 (2.7%) General surgical procedures: n=11 Intervention: 4/230 (1.7%) Control: 7/220 (3.2%) Exploration: n=9 Intervention: 3/230 (1.3%) Control: 6 /220 (2.7%) Amputation: n=5 Intervention: 3/230 (1.3%) Control: 2/220 (0.9%) Also, the following surgeries had no SSI: Hand surgery: n=4 Shoulder Tumor: n=1 Knee tumor: n=1 Orchiectomy: n=1 **Indications** **Setting:** 1 university hospital **Location:** Egypt **Dates:** NR **Inclusion Criteria:** All	**groups.** (Modern protocol is considered by this study to be: clippers rather than razors for hair removal; local skin warming; antibiotic prophylaxis given before clean surgery involving the placement of a prosthesis or implant, clean contaminated surgery, and contaminated surgery. This antibiotic prophylaxis is not routinely used for clean non-prosthetic uncomplicated surgeries and it should be timely and appropriate for the organisms expected.)		results were only reported for 1 center **Follow-up:** 30 days or 1 year in the case of orthopedic surgery. **Funding Source Conflicts:** Authors: NR Institution: NR Study: NR Supplies: NR

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			patients of different age, sex, and risk factors who were candidates for surgical intervention during the study period **Exclusion Criteria:** Patients with an established preoperative infection at the surgical site			
Rasic 2011 [70] (ES)	**RCT** 1, 2, 4, 5, 6	The aim of this study was to compare the effect of triclosan coated polyglactin 910 or polyglactin 910 on abdominal wall healing in patients undergoing elective surgery for colorectal carcinoma	**Number of patients: N=184** **Patient Characteristics:** there was no statistical difference in demographic or preoperative data between groups. ·Age, years, mean±SD Intervention: 58±14.5 Control: 57±14.7 ·Gender: male, Intervention: 49/91 (54%) Control: 50/91 (54%) ·Obesity: BMI>25 kg/m^3, Intervention: 7/91 (8%) Control: 9/91 (9%) ·Comorbidities: NR Duration of surgery Intervention: 95.5±17.3 Control: 91.3±18.6	**Intervention group:** n=93 Abdominal wall was closed with a continuous single-layer mass technique (peritoneum, muscle, & fascia) with triclosan coated polyglactin 910 sutures **Timing of intervention:** intraoperative **Duration of intervention:** closure **Device/agent:** triclosan coated or standard polyglactin 910 sutures **Monitoring intervention:** biochemical markers of inflammation were monitored: white blood cell count (WBC); postoperative procalicitonin –PCT; and C-reactive protein –CRP) **Control group:** n=91 Abdominal wall was closed	**SSI** Presence of wound infection: Intervention: 4/91 (4.3%) Control: 12/91 (13.2%) P=0.035 **Other infections:** NR **Topic-specific outcomes:** Postop inflammatory reactions to skin sutures: Intervention: 7/91 (7.5%) Control: 16/91 (17.5%) P=0.039 Dehiscence Intervention: 1/91 (1.1%) Control: 7/91 (7.7%) P=0.027 Incisional hernia Intervention: 2/91	**Definitions:** wound infection not defined. Postoperative data: was collected from operation reports, nurses wound reports, chart review and microbiology reports. **Perioperative care:** NR **Other notes:** None **Follow-up:** NR **Funding Source Conflicts:** Authors: NR Institution: NR Study: NR Supplies: NR

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			P=0.8933 **Procedures:** surgery for removal of colorectal carcinoma **Indications:** Colorectal cancer **Setting:** 1 university hospital **Location:** Croatia **Dates**: September 2008 - September 2009 **Inclusion Criteria:** patients diagnosed with colorectal cancer scheduled for elective surgery. **Exclusion Criteria:** NR	with a continuous single-layer mass technique (peritoneum, muscle, & fascia) with polyglactin 910 **Standard preventive measures:** Antibiotic prophylaxis: Gentamycin 160mg and metronidazole 500mg, given intravenously during induction of anesthesia. Operative technique: all operations performed through a midline incision. Skin was incised (15-18cm length) with a scalpel; all other layers transected with diathermy. Closure: running sutures were 1cm apart and 1.5cm from the wound edge. Skin closed with a polyamide.	(2.2%) Control: 5/91 (5.5%) P=0.235 **Reoperations:** Intervention: 1/91 (1.1%) Control: 8/91 (8.8%) P=0.015 Intervention Reoperations: 1/1 = Dehiscence Control Reoperations 7/8 = dehiscence 1/8 = peritonitis **Length of stay:** Mean hospitalization period Intervention: 1.2±1.3 days Control: 21.4±2.8 days P<0.05 **Mortality:** no deaths in either group **Adverse events:** Inflammatory reactions to skin sutures: Intervention: 7/91 (7.5%) Control: 16/91 (17.5%) P=0.039	
Mingma-lairak 2009 [78] (ES)	**RCT** 1, 2, 3, 4, 5, 6, 7, 8, 9, 10	To evaluate the efficacy of triclosan coated absorbable suture in reducing the surgical site	**Number of patients: N=100** **Patient Characteristics:** No statistically significant differences in demographic	**Intervention group:** n=50 Antibacterial-coated absorbable suture (triclosan) used to close the abdominal sheath. **Timing of intervention:** Intraoperatively **Duration of intervention:**	**SSI: (follow up 12 months)** SSI (total) Overall rate: 9/100 9% Intervention: 5/50 (10%) Control: 4/50 (8%) P=0.727 Superficial	**Definitions:** NR **Perioperative care:** NR **Other notes:** All patients completed the study Authors set the

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
		infection rate associated with appendectomy compared with traditional, non-coated braided absorbable suture.	characteristics, preoperative information and operative information between groups. ·Age, y: mean Intervention: 29.1 Control: 29.8 ·Gender: m:f Intervention: 26:24 Control: 35:15 ·Obesity Height: cm ,mean Intervention: 161.5 Control: 164.0 P=0.039 Weight, kg, mean Intervention: 59.73 Control: 59.53 ·Comorbidities: NR White Blood Cell count, cell/mm^3, mean: Intervention: 16,564 Control: 15,062 P=0.036 Operative: Preop time, operative time, type of appendicitis and degree of contamination not statistically significant Type of appendicitis: Intervention/control Acute: 24/24 Suppurative: 56/48 Gangrene: 6/10 Ruptured: 14/18 Degree of contamination:	Intraoperatively **Device/agent:** Antibacterial absorbable suture (triclosan coated) **Monitoring intervention:** NR **Control group:** n=50 Traditional braided absorbable suture used to close the abdominal sheath. **Standard preventive measures:** AMP: Gentamicin 240mg and metronidazole 500mg given intravenously 30-60 minutes before the operation. Surgery: appendectomy done with standard technique, mainly by a second year physician.	Intervention: 5/50 (10%) Control: 3/50 (6%) Deep Intervention: 0/50 Control: 1/50 (2%) Organ/Space Intervention: 0/50 Control: 0/50 Infections were more common in cases of ruptured appendicitis (Infected 5/9 vs. Non-infected 11/91 P=0.007) The rate of SSI was higher in men than in women. (3:2) Risk factors associated with infection Infected patients tended to be older, with slightly higher temperature, higher white blood cell counts, and slightly longer operative times, but these differences were not statistically significantly different. Appendicitis case type Suppurative: Non- infected: 50/91 (54.9%) Infected: 2/9 (22.2%) P=0.050 Ruptured: Non-infected: 11/91	discontinuation criteria infection rate >10% in the intervention group or >2 times in the control group compared with the intervention. Or mechanical problems in the intervention group such as strength, knot tight and anaphylactic allergy. **Follow-up:** At day 1, 3, 7, 14, and 30, and at 6 and 12 months **Funding Source Conflicts:** Authors: None Institution: None Study: None Supplies: None

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			Intervention/Control Mild: 86/80 Moderate: 8/12 Severe: 6/8 **Procedures:** Appendectomy Via grid-iron incision: 86% **Indications:** Acute and ruptured appendicitis. Uncomplicated: 76% Acute Intervention: 24% Control: 24% Suppurative Intervention: 56% Control: 48% Gangrene Intervention: 6% Control: 10% Ruptured Intervention:14% Control: 18% **Setting:** 1 university hospital **Location:** Thailand **Dates:** August 2006 – March 2007 **Inclusion Criteria:** Patients aged 15-60 years, both sexes, appendicitis diagnosed intraoperatively through a right lower quadrant incision and included both acute and ruptured		(12.1%) Infected: 5/9 (55.6%) P=0.007 **Other infections:** NR **Topic-specific outcomes:** Cultures: No Resistance reported Intervention: 1 *S. aureus* Control: 1 (deep) *P. aeruginosa* **Reoperations:** NR **Length of stay:** days (mean) Intervention: 3.7 Control: 3.7 P=0.500 Infected vs. uninfected. Uninfected: 3.6 days Infected: 7.4 days P=0.006 **Mortality:** NR (all available for follow-up) **Adverse events:** No medical complications during the present study and no complications related to suture identified after 1 year of follow-up.	

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			appendix. **Exclusion Criteria:** Patients with diabetes, immunocompromised host, HIV, on immunosuppressive drug, malignancy, missed diagnosis intraoperative, history of allergy to the substance, or pregnancy			
Rozzelle 2008 [80] (ES)	**RCT** 1, 2, 3, 4, 5, 6, 7, 8, 9, 10	To determine whether wound closure with triclosan-coated absorbable sutures after cerebrospinal fluid (CSF) shunt surgery would reduce the incidence of early shunt infection (<6 months postoperatively)	**Number of patients: N = 61 patients with 84 shunt procedures** **Patient Characteristics:** Groups differed slightly but no significant difference was found in patient characteristics, shunt type, indication, or which surgeon between groups. ·Age median (range): 6.3 y (1 day – 48 y) ·Gender: male no (%) Intervention: 30/46 (65%) Control: 18/38 (47%) P=0.154 (Distribution unequal between groups with a weak statistical trend towards the	**Intervention group:** n=46 Antimicrobial (triclosan) coated absorbable sutures were utilized to close the subcutaneous layer around the CSF shunt **Timing of intervention:** Intraoperatively **Duration of intervention:** Intraoperatively **Device/agent:** Antimicrobial (triclosan) coated sutures **Monitoring intervention:** CSF cultures. **Control group:** n= 38 Standard (uncoated) absorbable sutures were utilized to close the subcutaneous layer around the CSF shunt (not the same kind of material as the intervention)	**SSI: (follow up 6 months)** SSI at 2nd interim period Overall: 10/84 (11.9%) Intervention: 2/46 (4.3%) Control: 8/38 (21%) P= 0.038 There was no statistically significant difference between historical rate and either the intervention or control group rates. Intervention was associated with Absolute risk reduction 0.167 (95% CI 0.027-0.235) Relative risk reduction 3.84 (95% CI 0.257 – 18.78) Predict intervention suture wound closure would prevent 1 shunt infection for every 6.0 procedures in which it is used:	**Definitions:** Shunt infection: diagnosis obtained by positive culture from CSF sampled through the shunt or from explanted shunt components. **Perioperative care:** NR **Other notes:** No patients were lost to follow up. Patients requiring a new shunt within the 6-month surveillance window were reenrolled in the program using the same suture assignment as before. Patients receiving new

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			Intervention group for males.) ·Obesity: NA weight <4kg Intervention: 7/46 (15%) Control: 6/38 (16%) ·Comorbidities Recent CSF infection Intervention: 6/46 (13%) Control: 3/38 (8%) Mean shunt procedure time was slightly longer in intervention group but not statistically significant. **Procedures:** Implantation or revision of implantation for cerebrospinal fluid (CSF) shunting devices. Implants: 40 (47.6%) Revisions: 44 (53.4%) VP Shunt type: 68 operations (81%) VPI Shunt type: 9 operations (10.7%) Subdural-peritoneal shunt: 6 operations (7.1%) VA shunts: 1 operation (1.2%) **Indications:** hydrocephalus. **Setting:** 1 hospital	**Standard preventive measures:** Surgeon Grade: all shunt procedures performed by one of two attending pediatric neurosurgeons. AMP: all participants received preoperative intravenous antimicrobials (cefazolin, or vancomycin if allergic to cephalosporins) Skin Prep: all patients received preoperative chlorhexidine skin cleansing, povidone-iodine skin prep. Drapes: all surgeries utilized iodine-impregnated adhesive drapes Wound irrigation: all patients received antibiotic wound irrigation prior to closures. Shunt cleaning: Silicone shunt components were soaked in bacitracin solution before implantation. No antibiotic-impregnated shunt components used in this study. Closure: skin closures for all procedures performed with	Number to treat=6.0; 95%CI 4.2-36.5) 8/10 diagnosed w/in 6 weeks 2/10 diagnosed at 12 and 14 weeks postop. 8/10 (+) CSF cultures 1/10 blood and distal catheter cultures grew same organism (VA Shunt) 1/10 (-) CSF culture, (+) wound purulence over distal tubing **Other infections:** NR **Topic-specific outcomes:** 60 shunts (71.4%) remained functional and apparently infection free at 6 months. Pathogenic isolates n=10 SSIs: Intervention: 1 MRSA 1 coagulase negative (coag neg) Staphylococcus Control: 1 MRSA 3 MSSA 3 coag neg Staph spp. 1 P. aeruginosa **Reoperations:** 10/84 (11.9%) shunts were removed due to infection prior to 6 month follow up.	shunts following successful treatment of a shunt infection and patients undergoing revision >6 months after randomization were re-randomized. Enrollment ceased at the second interim analysis due to a marked difference in infection rates between groups. No additional shunt infections diagnosed after enrollment ceased **Follow-up**: 6 months **Funding Source Conflicts:** Authors: Industry Institution: None Study: None Supplies: None

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			Location: USA **Dates:** April 2005 - December 2006. **Inclusion Criteria:** Patients of all ages requiring CSF shunt implantation or revision surgery. **Exclusion Criteria:** Patients receiving ventricular access devices or ventriculosubgaleal shunts, patients with active shunt infections, and immunocompromised patients.	poliglecaprone 25 sutures.	14/ 84 (16.7%) Revision procedures w/in 6 mo where infection was not suspected. (Shunt tap CSF cultures remained negative) 2/84 (2.4%) revision procedures >6mo postop. Reasons for revisions NR 7/61 (11.5%) patients receiving new shunts were re-randomized after removal of an infected shunt that had been placed during the study and appropriate antimicrobial therapy Wounds cultured, MRSA: 1/2 (50%) vs. 1/8 (12.5%) both in revision surgeries MSSA: 0/2 vs. 3/8 (37.5%) all in primary implant surgeries **Length of stay:** NR **Mortality:** 2 patients with shunt infections died (3.3%). Both were infants with severe congenital anomalies whose parents ultimately decided to withdraw care. **Adverse events:** All shunt infections treated with complete shunt removal, external	

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
					ventricular drainage, and appropriate intravenous antimicrobial therapy until daily CSF cultures remained negative for ≥5 days, followed by the replacement of a new shunt.	
Ford 2005 [81] (ES)	**RCT** 1, 4, 5, 7, 8, 9	To characterize further the clinical performance of antimicrobial (triclosan) coated absorbable suture and traditional non-antimicrobial coated absorbable suture in pediatric patients undergoing various general surgical procedures.	**Number of patients: N=147** **Patient Characteristics:** no differences in baseline characteristics between groups. ·Age, y: mean (range): 9.8 y (1-18) ·Gender: 52% male ·Obesity: NR Mean Height: 137.2 cm (range 67-191 cm) Mean Weight: 41.3 kg (range 8-130 kg) ·Comorbidities "Risk factors that could affect wound healing were present in similar proportion": individual results by risk factor not reported Intervention 29% Control: 33% "The most common risk factors were obesity and chemotherapy"	**Intervention group:** n= 98 Antimicrobial (triclosan) coated absorbable suture was used as suture of various sizes dependent on surgery **Timing of intervention:** Intraoperatively **Duration of intervention:** Intraoperatively **Device/agent:** Triclosan-coated absorbable suture. **Monitoring intervention:** NR **Control group:** n=49 Non-antimicrobial coated absorbable suture was used as suture of various sizes dependent on surgery **Standard preventive measures:** NR **Non-Standard Preventive Measures:** Perioperative antimicrobial administration: Intervention: 24%	**SSI: (follow up 80 days)** Infection Day 1-2 Intervention: 0% Control: 0% Infection Day 14 Intervention: 2% Control: 0% Infection Day 80 Intervention: 1% Control: 0% Edema, any day 1 Intervention: 10% Control: 18% Edema, any Day 14 Intervention: 3% Control: 2% Edema, any Day 14 Intervention: 0% Control: 3% Erythema Day 1 Intervention: 9% Control: 7% Erythema Day 14 Intervention: 9% Control: 2% Erythema Day 80 Intervention: 1% Control: 3% **Other infections:** 3 infections developed	**Definitions:** Infection: observed redness >3-5 mm from the wound margins, edema (characterized by increased tissue firmness), purulent discharge, pain, and increased skin temperature. Confirmatory culture was not required. FLACC behavior pain assessment scale was used in non-verbal patients (infants) unable to provide reports of pain. (face, legs, activity, cry, consolability) Intraoperative handling:

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			Actual numbers not reported Received IV antimicrobials (they do not specify if AMP or AMP and treatment) Intervention: 65% Control: 82% Taking other medications Intervention: 5% Control: 10% **Procedures:** NR (variable) **Indications:** NR (variable) **Setting:** 1 center **Location:** USA **Dates:** NR **Inclusion Criteria:** Pediatric patients aged 1-18 years undergoing clean or clean-contaminated general surgical procedures. **Exclusion Criteria:** Contaminated wound sites; use of retention sutures; inappropriate age; evidence of malnutrition or debilitation; coexisting conditions that may impair wound healing including acquired	Control: 31%	and judged not to be related to the suture. 1/3: Day 14 a 13 year old male undergoing pilonidal cystectomy developed a new sinus tract that was related to the location of the cyst 1/3: on day 14, a 14-year old female who had undergone laparoscopic cholecystectomy developed a superficial fungal rash around the umbilicus that was believed to be due to body habitus. 1/3: day 80, a 14 year old female patient who underwent a pilonidal cystectomy developed a new sinus tract distal to the original site of excision that was filled with hair (most likely represented a new lesion) **Topic-specific outcomes:** <u>Intraoperative handling:</u> <u>Overall:</u> Intervention mean 71% Control mean 59% Both sutures>94% "very good" or "excellent" Not statistically significant <u>Specific:</u> Excellent Intervention mean 75%	overall, ease of passage, first throw, tie-down, security, hand, memory, and non-fraying. **Perioperative care:** NR **Other notes:** Patient population at each wound evaluation: 1-2 days: Intervention: 88 Control:45 14 days: Intervention: 91 Control:44 80 days Intervention: 76 Control:38 **Follow-up:** Wound healing evaluated at follow-up visits at 1-2 days, 14 (±2) days and 80 (±5) days post-implantation. **Funding Source Conflicts:** Authors: Industry Institution: NR Study: Industry Supplies: NR

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			immunodeficiency syndrome (AIDS); incision sites prone to expand, stretch, distend, or require support; ophthalmic, cardiovascular, or neurologic surgical sites; a need for more than one surgical procedures; prior participation in this study; or allergy to triclosan.		Control mean 62% Both sutures>94% "very good" or "excellent" Not statistically significant Pain Day 1 Intervention: 68% Control: 89% P=0.01 Pain Day 14 Intervention: 12% Control: 9% Pain Day 80 Intervention: 3% Control: 0% **Reoperations:** Adverse events requiring surgery Intervention: 17/98 (17%) Control: 10/49 (20%) **Length of stay:** NR **Mortality:** NR **Adverse events:** The most common events consisted of admissions for chemotherapy. Any Adverse Events: Intervention: 17/98 (17%) Control: 10/49 (20%) Severe Adverse Events: Intervention: 1/98 (1%) Control: 1/49 (2%) Serious Adverse Events: Intervention: 13/98 (13%) Control: 8/49 (16%) **Requiring Surgery: 17/98 (17%) vs. 10/49 (20%)** **Device Related: 0/98 vs.**	

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
					0/49 Day 1 Antimicrobials received: Intervention: 24% Control: 31% Day 14 Antimicrobials received: Intervention: 13% Control: 23% Day 80 Antimicrobials received: Intervention: 22% Control: 29% Received other medications that could impede wound healing: Day 1 Intervention: 10% Control: 13% (not significant) Day 14 Intervention: 14% Control: 14% Day 80 Intervention: 12% Control: 21% Suture sinus: none	

eTABLE 34. Evidence Table for Q2D. How safe and effective are antimicrobial dressings applied to surgical incisions following primary closure in the operating room?

Author Year (Data Extrac-tor)	Study Design Quality Score	Study Objective	Population and Setting	Intervention	Results	Comments
Biffi 2012 [83] (ES)	**RCT** 1, 2, 3, 4, 5, 6 7, 8, 9	To compare the efficacy of a sterile moisture retentive dressing with 1.2% iconic silver with that of a common postoperative dressing for preventing SSIs in elective colorectal cancer surgery.	**Number of patients: N=112** **Patient Characteristics:** patients were similar with regards to their demographic characteristics between groups. ·Age, y: mean ±SD Intervention: 63.6±9.2 Control: 62.9±9.0 ·Gender: female Intervention: 22 (37.9%) Control: 25 (46.3%) ·Obesity: BMI Mean±SD Intervention: 25.7±4.3 Control: 25.4±4.4 ·Comorbidities **Procedures:** colorectal cancer surgery rectal: Intervention: 17/58 (29.3%) Control: 18/54 (33.3%) P=0.687 **Indications:** colorectal cancer **Setting:** Two university-affiliated hospitals **Location:** Italy **Dates:** June 2008 -	**Intervention group:** n=58 Surgical incision was dressed with a sterile moisture retentive dressing with 1.2% iconic silver covered by a self-adherent breathable dressing. **Timing of intervention:** postoperative **Duration of intervention:** removed 7th postoperative day **Device/agent:** sterile moisture retentive dressing with 1.2% iconic silver **Monitoring intervention:** NR **Control group:** n=54 Surgical incision was dressed with a self-adherent breathable dressing which was then covered by another self-adherent breathable dressing to maintain blinding **Standard preventive measures:** AMP: 30 minutes before initial incision. Skin prep; preoperative scrub and paint with 10% povidone-iodine; Mechanical bowel prep: all patients received it	**SSI (30 days)** Overall: 20/112 (17.9%) Intervention: 9/58 (15.5%) Control: 11/54 (20.4%) P=0.623 Superficial SSI Overall: 13/112 (11.6%) Intervention: 5/58 (8.6%) Control: 8/54 (14.8%) P=0.802 Deep SSI Overall: 5/112 (4.5%) Intervention: 3/58 (5.2%) Control: 2/54 (3.7%) Organ/space SSI Overall: 2/112 (1.8%) Intervention: 1/58 (1.7%) Control: 1/54 (1.9%) **Other infections:** Infection within 30 days Overall: 14/112 (12.5%) Intervention: 6/58 (10.3%) Control: 8/54 (14.8%) P=0.802 **Topic-specific outcomes:** NA **Reoperations:** NR **Length of stay:** NR **Mortality:** NR **Adverse events:** None related to this study	**Definitions:** SSI: CDC Definitions **Perioperative care:** NR **Other notes:** NR **Follow-up:** 30 days **Funding Source Conflicts:** Authors: None Institution: NR Study: Industry Supplies: NR

Author Year (Data Extrac-tor)	Study Design Quality Score	Study Objective	Population and Setting	Intervention	Results	Comments
			September 2010 **Inclusion Criteria:** Patients aged 18-75 years old undergoing elective colorectal cancer surgery by laparotomic approach. **Exclusion Criteria:** History of allergy to dressing components, evidence of active infection at or adjacent to the operative site, coagulopathy (defined as platelet count less than 50,000 cells/ µL or a prothrombin time >18 seconds), intestinal obstruction, active bowel bleeding, life expectancy less than 6 months, inability to give written informed consent or a program of minimally invasive surgery (laparoscopy or robot-assisted)			
Krieger 2011 [84] (ES)	**RCT** 1, 2, 7, 8, 9	To conduct a prospective, randomized, controlled trial directly comparing	**Number of patients: N=109** **Patient Characteristics** ·Age, y: median Intervention: 62	**Intervention group:** n=55 Silver nylon dressing, hydrated in sterile water before application. Instructions were to rehydrate the dressing	**SSI** Total Intervention: 7/55 (13%) Control: 18/54 (33%) P=0.011 Superficial	**Definitions:** SSI: CDC Definitions. Superficial incision definition was modified to

Author Year (Data Extrac-tor)	Study Design Quality Score	Study Objective	Population and Setting	Intervention	Results	Comments
		silver nylon with standard gauze dressings in patients undergoing elective colorectal operations.	Control: 58 P=0.49 ·Gender: female: Intervention: 27/55 (49%) Control: 28/54 (52%) ·Obesity: NR ·Comorbidities Diabetes mellitus: Intervention: 5/55 (9%) Control: 4/54 (7%) P=1.00 Transfusion: Intervention: 7/55 (13%) Control: 0 /54 P=0.013 **Procedures:** elective colorectal surgery. **Indications:** Neoplastic, IBD, Other **Setting:** One university-based hospital **Location:** USA **Dates:** July 2009 – April 2010 **Inclusion Criteria:** Patients undergoing elective colorectal surgery with anticipated abdominal incision of at least 3cm. **Exclusion Criteria:** Incision <3cm,	daily and then replace with a new dressing after 7 days. On discharge patients had a new dressing applied that remained for an additional 7 days. **Timing of intervention:** postoperative **Duration of intervention:** **Device/agent:** silver nylon wound dressing **Monitoring intervention** **Control group:** n=54 Incisions were dressed only with sterile gauze and paper tape. On discharge, patients instructed to replace their dressings as needed. **Standard preventive measures:** Food restriction: clear liquid diet 24 hours before surgery. Mechanical Bowel Prep not used with the exception of patients undergoing left colon or rectal surgery, who were given an enema the morning of their operation. Antimicrobial prophylaxis: 30-60 minutes prior to surgery. Standard coverage is ertapenem. Patient with penicillin	Intervention: 5/55 (9%) Control: 14/54 (26%) P=0.021 Deep Intervention: 2/55 (4%) Control: 4/54 (7%) P=0.438 **Other infections**: NR **Topic-specific outcomes:** NR **Reoperations** Debridement Intervention: 0/55 Control: 2/54 (4%) P=0.234 **Length of stay**: median (range) Intervention: 6 (3-21) days Control: 6.5 (2-17) days P=0.210 **Mortality:** NR **Adverse events:** NR	include all patients who were placed on antibiotics specifically for these signs or symptoms. **Perioperative care:** NR **Other notes:** NR **Follow-up:** 30 days **Funding Source Conflicts:** Authors: None Institution: Industry Study: Industry Supplies: NR

Author Year (Data Extrac-tor)	Study Design Quality Score	Study Objective	Population and Setting	Intervention	Results	Comments
			known allergy to silver, signs of abdominal wall infection, conditions that would prevent full closure of the skin at the primary operation, or prior abdominal mesh that was not planned to be fully removed at the time of operation. Pregnant or lactating women and patients who had received antibiotics within 1 week of surgery also excluded.	allergies given alternative prophylaxis with ciprofloxacin and flagyl or gentamicin and clindamycin. All perioperative antibiotics discontinued within 24 hours.		

2.1B3. RISK OF BIAS ASSESSMENTS OF STUDIES: Q2 NON-PARENTERAL AMP

eTABLE 35. Risk of Bias Assessments of Randomized Controlled Trials for Q2 Non-Parenteral AMP

Author Year	Q	Described as randomized	Randomization appropriately performed	Described as double-blind	Outcome assessor blinded	Study participant blinded	Investigator blinded	Attrition described	Attrition smaller than 10-15% of assigned patients	Attrition appropriately analyzed	Funding source(s) disclosed and no obvious conflict of interest	Overall Risk of Bias
Question 2: Non-Parenteral Antimicrobial Prophylaxis												
Almdahl 2011 [64]	2	✓	✓					✓	✓	✓		Moderate
Al-Sheri 1994 [57]	2	✓					✓	✓	✓			Moderate
Baracs 2011 [71]	2	✓	✓			✓		✓			✓	Moderate
Biffi 2012 [83]	2	✓	✓	✓	✓	✓	✓	✓	✓	✓		Low
Diener 2014 [77]	2	✓	✓		✓	✓	✓	✓	✓	✓		Low
Dorge 2013 [67]	2	✓										High
Ford 2005 [81]	2	✓			✓	✓		✓	✓	✓		Low
Galal 2011 [76]	2	✓	✓	✓	✓	✓	✓					Low
Isik 2012 [79]	2	✓		✓	✓	✓					✓	Moderate
Justinger 2013 [75]	2	✓		✓	✓	✓	✓	✓	✓			Low
Juul 1985 [58]	2	✓	✓	✓	✓	✓		✓	✓			Moderate
Kamath 2005 [61]	2	✓			✓		✓	✓	✓	✓		Low
Krieger 2011 [84]	2	✓	✓					✓	✓	✓		Moderate
Litmathe 2009 [66]	2	✓		✓	✓	✓						Moderate
Mingmalairak 2009 [78]	2	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	Low
Nakamura 2013 [74]	2	✓			✓	✓		✓	✓	✓		Low
Neri	2	✓						✓	✓	✓		Mode-

Author Year	Q	Described as randomized	Randomization appropriately performed	Described as double-blind	Outcome assessor blinded	Study participant blinded	Investigator blinded	Attrition described	Attrition smaller than 10-15% of assigned patients	Attrition appropriately analyzed	Funding source(s) disclosed and no obvious conflict of interest	Overall Risk of Bias
2008 [62]												rate
Peerboo-ms 2009 [65]	2	✓		✓	✓	✓	✓	✓	✓	✓		Low
Raahave 1989 [60]	2	✓				✓		✓	✓			Mode-rate
Rasic 2011 [70]	2	✓	✓		✓	✓	✓					Mode-rate
Rozzelle 2008 [80]	2	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	Low
Ruiz-Tovar 2012 [56]	2	✓	✓		✓	✓		✓	✓	✓	✓	Low
Seco 1990 [59]	2	✓	✓			✓	✓	✓	✓	✓		Mode-rate
Seim 2012 [69]	2	✓				✓	✓	✓	✓			Mode-rate
Thimour-Bergstrom 2013 [73]	2	✓	✓	✓	✓	✓	✓	✓	✓			Low
Turtiainen 2012 [68]	2	✓	✓	✓		✓	✓	✓	✓	✓		Low
Vander Salm 1989 [63]	2	✓										High
Williams 2011 [72]	2	✓	✓		✓	✓	✓	✓				Low

2.1C. Q3 GLYCEMIC CONTROL

2.1C1. GRADE TABLE: Q3 GLYCEMIC CONTROL

eTABLE 36. GRADE Table for Q3 Glycemic Control

Comparison	Outcome	Quantity and Type of Evidence	Findings	Starting GRA-DE	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Confounders		
Q3. How do perioperative blood glucose and hemoglobin A1C levels impact the risk of SSI and what are their optimal perioperative target levels in diabetic and non-diabetic patients?														
Strict glycemic control vs. standard glycemic control	SSI*	2 RCT [85,86]	• Two RCTs in 480 cardiac surgery predominantly non-diabetic (70%-80%) populations. Glycemic control protocol instituted intraoperative and postoperatively in the SICU for 24-36 hours. Both RCTs report a primary composite outcome variable that includes SSI (underpowered to detect differences in individual outcomes). • 1 large [85] (N=371) and one small [86] (N=109) RCT, comparing strict (80-100mg/dL) to standard (<200mg/dL) glycemic control found no difference in either the composite outcome variable which included SSI: RR 1.0 (0.8-1.2); p=0.71 (adjusted OR: 0.09 (0.6-1.4); p=0.68; or in deep sternal SSIs: RR 0.9 (95%CI, 0.3-2.5); p=0.79. In subanalyses of separate diabetic (n=73) and non-diabetic (n=298) populations, no difference was noted between groups for either the composite (p=0.40) or deep sternal SSI (p=0.61) variables. The study could not examine whether outcomes differed by diabetes status. • 1 small RCT [86] (N=109), comparing strict (80-130mg/dL) to standard (160-200mg/dL) glycemic control found no difference in either the composite infection outcome variable: 19.2% vs. 35.3%; p=0.12.and no difference in SSIs: 11.1% vs. 16.7%; p=0.09.	High	0	0	-1	0	0	0	0	0	Moderate	Moderate

Comparison	Outcome	Quantity and Type of Evidence	Findings	Starting GRA-DE	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Confounders		
	Hypo-glycemia*	2 RCT [85,86]	• 1 large RCT [85] defined hypoglycemia as <60mg/dL, reported it as number of episodes in each treatment group. While the study found no difference between groups for hypoglycemic episodes in the SICU, it did find that for both groups a higher proportion of the episodes occurred in the SICU: 8 (4%) vs. 14 (8%); p=1.00, RR 1.01 (0.06-15.95) as compared to intraoperatively: 1 (1%) vs. 1 (1%); p=0.19, RR 1.76 (0.76-4.09). • 1 small RCT [86] defined hypoglycemia as <50mg/dL and reported it as the ratio of hypoglycemic episodes per number of glucose measurements. It also noted no difference between groups for hypoglycemic episodes: 2.9% vs. 2.1%, (0.84-1.43); p=0.67. • Neither study reported clinical complications resulting from hypoglycemia.	High	0	0	0	0	0	0	0	0	High	
	Mortality	1 RCT [85]	• Mortality was rare, reported only in the strict glycemic control group, and not associated with blood glucose target levels: 4/185 vs. 0/186.	High	0	0	0	-1	0	0	0	0	Moderate	
	Length of stay	1 RCT [85]	• Length of hospital stay (p=0.66) and length of SICU stay (p=0.37) were not associated with blood glucose targets.	High	0	0	0	-1	0	0	0	0	Moderate	

*Critical outcome; OR: Odds Ratio; RR: Risk Ratio; CI: Confidence Interval

eTABLE 37. Evidence Table for Q3. How do perioperative blood glucose and hemoglobin A1C levels impact the risk of SSI and what are their optimal perioperative target levels in diabetic and non-diabetic patients?

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting (N)	Intervention	Results	Comments
Chan 2009 [86] (ES)	**RCT 1, 5, 7, 10**	To investigate whether different targets of intraoperative and postoperative glucose (80-130 mg/dl, 4.4-7.2 mEq/l or 160-200 mg/dl, 8.8-11.1 mEq/l) could affect postoperative clinical outcomes after cardiac surgery with cardiopulmonary bypass.	**Number of patients:** N=109 **Patient Characteristics:** the groups were comparable with respect to age, gender and height. ·Age: NR ·Gender: NR ·Obesity: BMI Intervention: 24 (±3.4) Control: 26 (±4.9) ·Comorbidities: ASA status P4: Intervention: 70.2% Control: 86.3% Length of CBP (min) Intervention: 97.9 (±45.3) Control: 116.3 (±54) P=0.060 **Procedures:** Open-heart surgery requiring cardiopulmonary bypass (CBP). **Indications:** NR **Setting:** 1 university hospital **Location:** Brazil **Dates:** NR (over a period of 12 months) **Inclusion Criteria:** adults from both genders who were older than 21 years of age and who	**Intervention group (intensive) n=54** Intervention: 80 -130mg/dL glucose **Timing of intervention:** perioperative **Duration of intervention:** from arrival in OR until36h postop **Device/agent:** Glucose **Monitoring intervention:** Measurements of whole blood glucose in undiluted arterial blood every 1-4h using a glucose analyzer. Glucose dose was adjusted by ICU nurses according to a titration algorithm (Leuven modified). algorithm given as guidance rather than exact targets **Control group: (less intensive) n=55** Control: 160-200mg/dL glucose **Standard preventive measures:** AMP: 2nd generation cephalosporin Transfusion threshold: hematocrit<30%	**SSI** Intervention: 11.1% Control: 16.7% P=0.09 **Other infections:** NR **Topic-specific outcomes:** Hypoglycemia Reported as: hypoglycemic episodes per number of glucose measurements 2.9% vs. 2.1% P=0.67 (0.84-1.43) **Reoperations:** NR **Length of stay: (days)** Intervention: 12 (±7) Control: 17 (±16) P= 0.060 (0.24-1.01) **Mortality:** (%) Intervention: 6.4% Control: 5.9% **Adverse events:** No clinical complications reported resulting from hypoglycemia at follow up (30 days).	**Definitions:** Hypoglycemia: Defined as <50mg/dL **Perioperative care:** parenteral care was not prescribed for any patients in the study. **Other notes:** authors indicate that 11 patients were lost to follow up and "may have biased the results" AND "this pilot study sample size was not large enough to allow for any definite conclusions or recommendations on the effect of strict glucose control vs. less intensive control" **Follow-up:** 30 days **Funding Source Conflicts:** Authors: None Institution: None Study: None Supplies: None

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting (N)	Intervention	Results	Comments
			were undergoing open-heart cardiac surgery requiring CBP. **Exclusion Criteria:** (1) renal failure (creatinine>1.5g/dl), (2) neurological dysfunction (diagnosis from medical records), (3) chronic pulmonary obstructive disease (COPD), (4) current use of any type of antimicrobial, (5) current use of inotropic support, (6) emergency and urgent surgeries, and (7) reoperations.			
Ghandi 2007 [85] (ES)	**RCT 1, 4, 5, 7, 8**	To determine whether maintenance of near normoglycemia during cardiac surgery by using intraoperative intravenous insulin infusion reduced perioperative death and morbidity when added to rigorous postoperativ	**Number of patients** N=371 **Patient Characteristics:** Baseline characteristics did not differ statistically significantly between groups. ·Age: NR ·Gender: NR ·Obesity: NR ·Comorbidities: 20% had known diabetes **Procedures:** Cardiopulmonary bypass surgery **Indications:** NR **Setting:** 1 tertiary care teaching hospital **Location**: USA **Dates** July 2004 – April 2005	**Intervention group:** n=185 Intraoperative glycemic control of 80mg/dL – 100mg/dL (4.4mmol/L – 5.6 mmol/L) **Timing of intervention:** intraoperative **Duration of intervention:** intraoperative only **Device/agent:** Glucose **Monitoring intervention:** Arterial blood glucose levels were measured with a glucometer. **Control group:** n=186 Intraoperative glycemic control target of <200mg/dL (11.1mmol/L) if glucose level reached >250mg/dL (13.9mmol/L), then intraoperative bolus was	OR: 0.9, 95%CI (0.3-2.5) P=0.79 **Other infections:** NR **Topic-specific outcomes:** Hypoglycemia Intraoperative (1 patient in each group) RR 1.01 (95%CI 0.06-15.95) Postoperative (ICU): Intervention: 14 (8%) Control: 8(4%) RR 1.76 (95% CI 0.76-4.09) All mild without adverse consequences **Reoperations:** NR **Length of stay:** median and mean LOS in hospital and ICU P=-.66 and p=0.37 **Mortality:**	**Definitions:** Primary outcome = composite of death, sternal wound infections, prolonged pulmonary ventilation, cardiac arrhythmias, stroke, and acute renal failure within 30 days postop. Hypoglycemia: glucose <60mg/dL; **Perioperative care :** NR **Other notes:** this single center study used a composite end point and could not examine whether outcomes differed by diabetes status. Primary outcome variable was a composite variable because "not feasible to power study to detect

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting (N)	Intervention	Results	Comments
		e glycemic control.	**Inclusion Criteria:** Adults undergoing elective cardiac surgery during study dates **Exclusion Criteria:** Patients who had off-pump cardiopulmonary bypass procedures.	given until level was less than 150mg/dL (8.3mmol/L) **Standard preventive measures:** Both groups had strict postoperative glycemic control of 80mg/dL – 100mg/dL)	Overall& In hospital 4/185 (2%) vs. 0% Post discharge (up to 30d postop) 0% vs. 0%; P=0.061 NOTE: POST DISCHARGE F/U in only 4% vs. 5% of patients **Adverse events:** None reported	differences in individual components such as death, because the rare occurrences would mandate a very large sample size." **Follow-up:** 30 days **Funding Source Conflicts:** Authors: Industry Institution: NR Study: NR Supplies: NR

2.1C3. RISK OF BIAS ASSESSMENTS: Q3 GLYCEMIC CONTROL

eTABLE 38. Risk of Bias Assessments of Randomized Controlled Trials for Q3 Glycemic Control

Author Year	Q	Described as randomize-ed	Randomizati-on appropriately performed	Described as double-blind	Outcome assessor blinded	Study participant blinded	Investigato blinded	Attrition described	Attrition smaller than 10-15% of assigned patients	Attrition appropriate-ly analyzed	Funding source(s) disclosed and no obvious conflict of interest	Overall Risk of Bias
Question 3: Glycemic Control												
Chan 2009 [86]	3	✓				✓		✓			✓	High
Gandhi 2007 [85]	3	✓			✓	✓		✓	✓			High

2.1D. Q4-5 NORMOTHERMIA

2.1D1. GRADE TABLE: Q4-5 NORMOTHERMIA

eTABLE 39. GRADE Table for Q4-5 Normothermia

Comparison	Outcome	Quantity and Type Of Evidence	Findings	Starting GRADE	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Confounders		
Q4. How safe and effective is the maintenance of perioperative normothermia in reducing the risk of SSI?														
Warming vs. no warming	SSI*	2 RCT [87,88]	• Meta-analysis of 2 RCT (N=616) found that maintenance of normothermia associated with reduced risk for SSI (OR: 0.29; 95% CI: 0.16 – 0.53; p<0.0001; I^2=0) • Mixed surgical populations, multiple warming techniques • Maintenance of perioperative normothermia with warming techniques associated with reduced risk of surgical site infection • 1 RCT [87] in 416 patients undergoing elective hernia repair, varicose vein and breast surgery, preoperative systemic warming only : 13/277 (5%) vs. 19/139 (14%); p<0.01 at 2-6 week follow up • 1 RCT [88] in 200 elective colorectal surgery patients using intraoperatively only warming: 6/104 (6%) vs. 18/96 (19%); p<0.01 at 2 week follow up.	High	0	0	0	0	0	0	0	0	High	High
	ASEPSIS score	2 RCT [87, 88]	• ASEPSIS wound scores were higher in control groups (p<0.01 [87 88]) • In a meta-analysis of the two studies, warmed patients were less likely to have ASEPSIS wound scores >20 (Relative Risk: 0.19; (95% CI, 0.09 – 0.39); p<0.01; I^2=26%	High	0	0	0	0	0	0	0	0	High	
	Mortality, 30 days	1 RCT [88]	• Mortality within 30 days was rare (4 deaths in 200 patients), with no difference observed between groups	High	0	0	0	-1	0	0	0	0	Moderate	

Comparison	Outcome	Quantity and Type Of Evidence	Findings	Starti-ng GRA-DE	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Confounders		
	Blood Loss	1 RCT [88]	• Normothermia associated with lower mean units of blood transfused per patient: 0.4±1.0 vs. 0.8±1.2; p=0.01 and fewer patients transfused: 23/104 (22%) vs. 34/96 (35%)	High	0	0	0	-1	0	0	0	0	Moderate	
	Core Temperatu-re	2 RCT [87,88]	• 1 RCT [87] found that core temperature was increased by either local or systemic warming techniques, delivered pre-operatively for 30 minutes. The impact of systemic warming (mean increase: 0.35^0 C; p<0.01) was greater than local warming (mean increase: 0.13^0 C; p=0.03). The mean core temperature after surgery was within normal limits. • 1 RCT[88] found that core temperature at end of surgery was increased with intraoperative systemic warming (p<0.01), and remained higher for more than 5 hours following surgery	High	0	0	0	0	0	0	0	0	High	
	Length of Hospital Stay	1 RCT [88]	• Normothermia associated with reduced length of stay (net reduction: 2.6 days; p<0.01); difference remained when analysis was limited to uninfected patients	High	0	0	0	-1	0	0	0	0	Moderate	
	Duration of Surgery	2 RCT [87,88]	• Normothermia not associated with increased duration of surgery	High	0	0	0	0	0	0	0	0	High	
Warming: perioperative (carbon polymer mattress [2hours preop, intraop, and 2 hours postop], forced air warming and	SSI*	1 RCT [89]	• Perioperative warming associated with decreased incidence of SSI (12.8% vs. 26.8%), but this finding was not significant OR 0.4 (0.14-1.13); p=0.08; sample size based on all complications	High	0	0	0	-1	0	0	0	0	Moderate	Moderate
	Mortality	1 RCT [89]	• 3 deaths in 103 patients, with no difference observed between groups	High	0	0	0	-1	0	0	0	0	Moderate	

Comparison	Outcome	Quantity and Type Of Evidence	Findings	Starti-ng GRA-DE	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Confounders		
fluid warmer intraop) vs. intraoperative only (carbon polymer mattress, forced air warming and fluid warmer)	Blood Loss	1 RCT [89]	• Perioperative warming associated with lower blood loss (p<0.01)	High	0	0	0	-1	0	0	0	0	Moderate	
	Core Temperatu-re	1 RCT [89]	• Perioperative systemic warming group, higher core temperature achieved immediately after 2 hours of preoperative warming (p<0.01) • Perioperative systemic warming group maintained higher core temperature during the first 90 minutes of surgery (median 36.2 vs. 36.1) but not at 2 hours postoperatively (p=0.47)	High	0	0	0	-1	0	0	0	0	Moderate	
	Length of Hospital Stay	1 RCT [89]	• Perioperative warming not associated with reduced length of hospital stay (p=0.22)	High	0	0	0	-1	0	0	0	0	Moderate	
	Duration of Surgery	1 RCT [89]	• Perioperative systemic warming was not associated with increased duration of surgery (p=0.15)	High	0	0	0	-1	0	0	0	0	Moderate	
Q5. What are the most effective strategies for achieving and maintaining perioperative normothermia? Our search did not identify RCTs or SRs that evaluated the most effective strategies for achieving and maintaining perioperative normothermia and their impact on the risk of SSI.														

*Critical outcome; OR: Odds Ratio; RR: Risk Ratio; CI: Confidence Interval

2.1D2. EVIDENCE TABLE: Q4-5 NORMOTHERMIA

eTABLE 40. Evidence Table for Q4. How safe and effective is the maintenance of perioperative normothermia in reducing the risk of SSI?

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting (N)	Intervention	Results	Comments
Wong 2007 [89] (SIBT)	**RCT** 1, 2, 4, 6, 7, 8, 9	To examine the effects of extending systemic warming duration to include pre- and postoperative periods and the potential benefits in reducing postoperative complications in patients undergoing elective major abdominal surgery..	**No. patients**: N=103 **Patient Characteristics:** (age, sex, ASA score, MBI, POSSUM scores, baseline temperature, pulse rate and mean arterial pressure were similar in both groups/not statistically significant except for core temperature before start of surgery (see results) Age: ≥ 18years of age Median (range) Intervention:62.0 (24-88) Control: 60.5 (20-84) Gender: m/f Intervention: 24/23 Control: 29/27 BMI: median (range) Intervention: 23.0(15.5-39.2) Control: 25.0 (16.5-36.3) ASA score ASA1:29/103 (28.2%) ASA2: 50/103 (38.5%)	**Intervention:** n=47 Mattress **w**armed to 40°C 2 hours before surgery, during surgery, and for 2 hours after surgery in addition to standard practice of systemic warming with forced air warming device set at 40°C and with a fluid warmer **Timing of Intervention:** pre, intra and post operatively. **Duration of intervention :** 2h preoperatively, intraoperatively and 2 hours post operatively **Device**: conductive carbon polymer mattress can provide sustained heat up to 40°C. **Monitoring:** Pre and postoperatively: before and immediately after surgery tympanic thermometer Intraoperative: nasopharyngeal temperature probe (every 30 minutes) **Control:** n=56 Mattress warmed to 40°C only during surgery in addition to standard	**SSI** Intervention: 6/47(12.8%) Control: 15/56 (26.8%) **Other Infections** Chest infection Intervention: 2/47 (4.3%) Control: 6/56 (10.7%) Urinary tract infection: Intervention: 3/47 (6.4%) Control: 2/56 (3.6%) **Topic specific outcomes** median (range) ; P value Core Temperature Immediately after preoperative systemic warming: Intervention 36.4 (35.1-37.4) Control: 36.0 (35.1-36.9) *P* <0.001 Intraoperative: 90 minutes Interventions group "maintained a significantly higher temperature during the first 90 minutes of surgery" (median 36.2) vs. controls (36.1). Core Temperature Postop (2hours): Intervention: 36.3 (34.3-38.1) Control: 36.2 (34.3-37.9) P=0.471 Blood loss (ml): Mean (range) Intervention: 200 (5-1000) Control: 400 (50-2300) *P*=0.011 All other outcome variables (IV fluids, urine output, blood	**Definitions:** **SSI- CDC:** (1) when pus could be expressed from the surgical incision or aspirated from a loculated mass inside the wound (2) if the pus culture was positive for pathogenic bacteria (3) if there was localized tenderness, localized swelling, redness or temperature at the surgical site, or (4) if the treating medical practitioners had diagnosed them as infected and treated them with antimicrobials. Hypothermia: <36°C **Normothermia**: ≥36°C **Perioperative care:** Anesthesia: Fentanyl and vecoronium bromide. Isoflurane (in 60% nitrous oxide) titrated to maintain MAP within 20% of pre-induction values. Additional fentanyl at end to improve analgesia. **Other notes:** NR **Follow up:** every day during hospitalization and at 6-8 weeks postoperatively (usually in the home) **Funding Source Conflicts:** Authors: NR Institution: NR Study: NR Supplies: NR

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting (N)	Intervention	Results	Comments
			ASA3:24/103 (23.3%) More than 75% of procedures performed by consultant (senior) surgeon **Procedure**: Elective major abdominal surgery Right hemicolectomy n=31 Anterior resection n=24 **Indications:** Colorectal cancer n=71 Inflammatory bowel disease n=15 Diverticular disease n=7 Gastric carcinoma n=3 Benign colonic tumor n=2 Others n=5 **Setting**: 1 university hospital **Location:** United Kingdom **Dates**: October 2002 to December 2003 **Inclusion criteria**: major open abdominal surgery requiring bowel resection, with or without anastomosis **Exclusion criteria**:	practice of systemic warming with forced air warming device set at 40°C and with a fluid warmer **Standard Preventive Measures** **AMP**- not described AMP duration: mean (range) Intervention:1 (0-28) Control: 2(0-12) P=0.200 **Bowel Prep-**not described	transfusion units (none), duration of antimicrobials, flatus passed, bowels opened, diet tolerated, duration of hospital stay and follow up) showed no statistically significant difference **Reoperations:** NR **Length of Stay:** mean (range); P value Intervention: 11.0 (5-119) Control: 9.0 (5-40) P value 0.217 **Mortality**- 1 (surgical emphysema from intubation complication) vs. 2 (renal & respiratory failure) (*P*=0.566) Adverse events: Total Number of Adverse events: Intervention: 15/47 (32%) Control: 30/56 (54%) *P*=0.027 Ileus 7/103 (14.9%) Pelvic collection 3/103 (2.9%) Cardiac complications 2/47 (4.3%) Renal Failure 2/47(4.3%) Anesthetic complications 1/47(2.1%) Clostridium difficile diarrhea 1/47(2.1%) Pressure ulcer 1/47(2.1%) For SSI, chest infection and urinary tract infection see "Other Infections" above .	

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting (N)	Intervention	Results	Comments
			laparoscopic procedures, use of corticosteroids or other immunosuppressive drugs (including cancer chemotherapy_ during the 4 weeks before surgery, recent history of fever, infection or both, serious malnutrition (serum albumin <3.3g.dl, a white cell count <2500 cells per ml or the loss of more than 20% of body weight within 3 months of surgery) and bowel obstruction.			
Melling 2001 [87] (SIBT)	**RCT** 1, 2, 4, 6, 7, 8, 9	To assess the use of a local warming device and a warm air blanket for the reduction of infection after clean wound surgery.	**No. patients:** N= 416 **Patient characteristics:** similar in all groups. Including age, BMI, gender, fasting>8h, hair removal (shaving) >6 h, type of surgery, surgery in last 3 months, cancer diagnosis, initial core temperature, AMP, length of surgery, seniority of surgeon.	**Intervention1-Systemic** n=139 group-standard preoperative care plus minimum 30 minutes preoperative warming to the whole body using forced-air, warming blanket. **Intervention 2- Local** n=138 standard preoperative care plus minimum 30 minutes preoperative warming to just the planned wound area using a non-contact, radiant heat	**SSI (2-6 weeks)** Overall rate of infection 32/416 (8%) **SSI**: Interventions1&2 13/277 (5%) Control: 19/139(14%) P=0.001 **ASEPSIS wound scores** significantly higher in control group vs. combined interventions (p=0.007) **ASEPSIS >20** Interventions 1&2 10/277 (4%) Control: 17/138 (12%) Other wound complications	**Definitions:** **SSI-** purulent discharge or a painful erythema that lasted 5 days and was treated with antimicrobials within 6 weeks of surgery. Wounds swabbed for culture if purulent discharge present at time of review. Note: only 14 wound swabs were obtained because Postoperative antimicrobials- "Patients seen at 2 and 6 weeks had often been prescribed antimicrobial treatment by their general practitioner without having

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting (N)	Intervention	Results	Comments
			Age, years: ≥18 years Mean (SD) Intervention 1:49.7(13.7) Intervention 2: 50 (14.1) Control: 50.4 (15.3) Gender m/f: 174/242 Obesity: BMI (mg/kg^2): Intervention 1:25.7(4.3) Intervention 2:25.8(4.1) Control:25.6(4.1) **Procedure**: Elective hernia repair n=155 varicose vein surgery n=86 breast surgery n=175 **Indications:** NR **Setting**: 1 district general hospital **Location:** United Kingdom **Dates**: April 1999 to May 2000 **Inclusion criteria**: Elective hernia repair, varicose vein surgery, or breast surgery that would result in a scar longer than 3 cm in length. **Exclusion criteria**: Pregnant, taking long-term oral steroids, had	dressing. **Timing of intervention:** preoperative **Duration of Intervention:** for a minimum of 30 minutes until just before surgery **Device:** **Systemic-**Forced-air warming blanket **Local**- non-contact, radiant heat dressing. **Monitoring intervention:** tympanic thermometers before any treatment, after any warming and after surgery **Control: -** (n=139) standard preoperative care plus no warming **Standard Preventive Measures:** Antimicrobial prophylaxis- AMP: 119/416 (29%) Hair Removal- Shaving No shaving 110/416(26.4%) Shaving <7h preop: 116/416 (27.9%) Shaving>7h preop: 183/416 (20%) Info missing n = 9	including hematoma, seroma, and wound aspiration no statistically significant difference between groups. **SSI : Intervention 2 -local vs. Intervention 1-systemic warming** No differences in outcomes between two warming methods. Individually both local (p=0.003) and systemic (p=0.026) warming had a significant effect on rate of SSI. **Effect of warming interventions compared with control:** Absolute risk reduction (95% CI): Intervention 1 systemic 10.1% (3.6-16.6) Intervention 2 Local 7.9% (1.0-14.8) Relative risk reduction: Intervention 1 systemic 73.7% Intervention 2 local 57.7% Numbers needed to treat: Intervention 1 systemic 15 patients. Intervention 2 local 10 **SSI vs. No SSI** Mean (SD) Stepwise logistic regression yielded only body mass index as significant variable at the 5% level OR 1.12 (95% CI 1.02-1.21) BMI	wound swabbed" Normothermia: NR Hypothermia: NR **Perioperative care:** Anesthesia- not described **Follow up:** 2-6 weeks postoperatively in outpatient clinic or home. Direct observation, patient diary, if not available for examination then telephone assessment patient questionnaire (6/10 questionnaires returned) **Funding Source Conflicts:** Authors: NR Institution: NR Study: Industry Supplies: Industry

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting (N)	Intervention	Results	Comments
			received radiotherapy (to the incision site) or chemotherapy in the last 4 weeks, or had an infection at the time of surgery		SSI: 28.04 (4.44) No SSI 25.31(3.98) Breast surgery had higher SSI rate than hernia repair and varicose veins Hair Removal: <u>No shaving:</u> SSI 9/32 (28%) No SSI 101/384 (27%) <u>Shaving within 7h of surgery</u> SSI 6/32 (19%) No SSI 110/384 (30%) <u>Shaving >7hrs before surgery</u> SSI 17/32 (53%) No SSI 166/384 (44%) SSI and AMP: Had AMP SSI: 6/32 (19%) No SSI 115/384 (30%) **Topic-specific outcomes** mean (SD); P value <u>Initial core temperatures</u> were significantly increased by intervention 1 and 2 vs. control Intervention 1Systemic 0.35°C(0.58) P=0.001 Intervention 2 Local: 0.13°C(0.57) P=0.028 Control initial core temp: 36.5 (0.55) <u>Postoperative core temperatures</u> were within normal limits: 36.41 (0.59) Intervention 2-Local received longer period of warming (min) as compared to Intervention 1-systemic (44.94 vs. 38.73,	

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting (N)	Intervention	Results	Comments
					p=0.005) **Length of stay:** NR **Mortality:** NR **Adverse events:** Prescribed postop antimicrobials: Intervention1&2: 18/277(7%) Control: 22/139 (16%) P=0.002	
Kurz 1996 [88] (SIBT)	**RCT** 1, 2, 4, 5, 6, 7, 8, 9	To test hypothesis that hypothermia both increases susceptibility to surgical wound infection and lengthens hospitalization	**No. patients:** N=200 **Patient Characteristics:** characteristics, diagnoses, types of surgical procedure, duration of surgery, hemodynamic values, and types of anesthesia were similar in both groups -no statistically significant difference Age: 18 to 80 years mean±SD Age: Gender: m/f 108/92 Height ,cm: Intervention:170±9 Control: 169±9 P=0.43 Weight, kg Intervention:73±14 Control: 71±14 P=0.31 **Procedure**: Elective colorectal resection **Indication:**	**Intervention:** n=104 Fluid warmer on. Forced-air cover 40°C **Patient target core temp** maintain near 36.5°C **Timing of Intervention:** intra-operative **Duration of intervention:** intraoperative **(** from induction of anesthesia to end of surgery) **Device:** Fluid warmer and forced-air cover **Monitoring:** Temperature: tympanic thermometer Preop- recorded Intraop- 10 min intervals Postop-20 min intervals for 6h Thermal comfort-visual analog scale (VAS) Pain- VAS Shivering-scale all evaluated at 20min intervals for 6 hours postop.	**SSI**: 2 weeks Overall: 24/200 (12%) Intervention: 6/104 (6%) Control: 18/96 (19%) P=0.009 SSI in smokers(n=62) vs. non-smokers (n=138) Smokers: 14/62 (23%) Non-smokers10/138 (7%) P=0.004 SENIC score (1/2/3) Intervention:3/95/6 Control:3/88/5 NNISS scores (0/1/2) Intervention:32/49/23 Control:31/39/26 P=0.6 ASEPSIS scores: Intervention: 7±10 Control: 13±16 P=0.002 ASEPSIS scores>20: Intervention: 6% of patients Control: 32% of patients P<0.001 ASEPSIS Score in smokers(n=62) vs. non-smokers (n=138) Smokers:15±18 Non-smokers: 8±10	**Definitions** Wound Infection (Suspected**):** If pus could be expressed from the surgical incision or aspirated from a loculated mass inside the wound Wound Infection (Confirmed) - if pus culture was positive for pathogenic bacteria. ASPESIS score >20 Hypothermia 34.5°C Normothermia 36.5°C **Perioperative care:** Anesthesia standardized: thiopental sodium, fentanyl, vecuronium bromide, isoflurane, and fentanyl at completion for analgesia. **Follow up:** 2 weeks: daily in hospital and at 2 weeks postop. 94% returned for 2 week visit, those who did not were evenly distributed between the study groups and most returned to visit private offices of attending surgeons. Wound status determined by calling physician. No previously unidentified SSIs detected in clinic for the first time

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting (N)	Intervention	Results	Comments
			Cancer 182/200 (91%) Inflammatory bowel disease 18/200 (9%) **Setting**: 3 hospitals 1 University n=155 1 University n=30 1 other hospital n=15 **Location:** Austria **Dates**: July 1993 through March 1995 **Inclusion criteria**: Abdominal intraperitoneal pull-through procedures **Exclusion criteria**: minor colon surgery (e.g., polypectomy or colostomy performed as the only procedure), use of corticosteroids or other immunosuppressive drugs (including cancer chemotherapy) during the 4 weeks prior to surgery, a recent history of fever, infection or both, serious malnutrition (serum albumin <3.3g/dL, white blood cell count <2500 cells/mL, or the loss of more than 20% of	**Control:** n=96 Fluid warmer off. Forced-air cover ambient temperature **Patient target core temp**: allowed to decrease to ~34.5°C. **Standard preventive measures:** Bowel Prep- standard mechanical bowel prep with an electrolyte solution. AMP-standardized- IV cefamandole and metronidazole at induction of anesthesia and maintained for 4 days postoperatively Fluids: "hydrated aggressively during and after surgery" – see details Transfusion: Leukocyte depleted blood at surgeon's discretion O_2- supplemental, nasal prongs at 6L/min first 3hours postop, gradually eliminated to maintainO_2 sat >95% Pain- opioids postop (patient controlled)	P<0.001 SSI Risk Factors, multivariate analysis OR (95%CI) Tobacco use (Y/N): 10.5 (3.2-34.1) Group assignment (Intervention vs. Control) 4.9 (1.7-14.5) Surgical site (rectum vs. colon) 2.7 (0.9-7.6) NNISS score (per unit increase) 2.5 (1.2-5.3) Age (per decade) 1.6 (1.0-2.4) **Other infections:** **Topic-specific outcomes:** mean ± SD; P value: **Intraoperative** Transfusions (allogeneic blood) Intervention: 0.4±1.0 Control 0.8 ± 1.2 P=0.01 Vasoconstriction Intervention: 6% of patients Control: 74% of patients P<0.001 Core Temperature at end of surgery Intervention:36.6±0.5°C Control: 34.7±0.6°C P=<0.001 and remained significantly different for >5 hours postoperatively **Postoperative** Vasoconstriction Intervention: 22% (short-lived) Control: 78% (continued	**Funding Source Conflicts**: Authors: None Institution: NR Study: Industry Supplies: NR

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting (N)	Intervention	Results	Comments
			body weight), or bowel obstruction.		throughout 6h recovery) P<0.001 Shivering: Intervention: “a few” Control: 59% of patients Thermal comfort score- VAS 1h postop: Intervention: 73±14mm Control: 35±17mm Remained statistically significant for 3h Other: Pain score and amount of opioid administered “virtually identical” in the two groups at every postop measurement; hemodynamic values also similar. Collagen deposition µg/cm Intervention: 328±135 Control: 254±114 P=0.04 Days to first solid food: Intervention: 5.6±2.5 Control: 6.5±2.0 P=0.006 Remained statistically significant even when analysis was limited to uninfected patients: Intervention: 5.2±1.6 Control: 6.1±1.6 P<0.001 Days to suture removal Intervention: 9.8±2.9 Control: 10.9±1.9 P=0.002 Remained statistically significant even when analysis	

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting (N)	Intervention	Results	Comments
					was limited to uninfected patients: Intervention: 9.6±2.6 Control: 10.6±1.6 P=0.003 Days to suture removal in smokers (n=62) vs. non-smokers (n=138) Smoker: 10.9±3.5 Non-smoker10.1±2.0 P=0.04 **Length of stay, days:** Intervention:12.1±4.4 Control: 14.7±6.5 P=0.001 Remained statistically significant even when analysis was limited to uninfected patients: Intervention: 11.8±4.1 Control:13.5±4.5 P=0.01 Analysis: smokers(n=62) vs. nonsmokers (n=138) Smokers: 14.9±6.7 days Non-smokers: 12.9±5.0 P=0.02 **Mortality:**30 days Intervention: 2/104(1.9%) Control: 2/96 (2.1%) **Adverse events:** **ICU Admission-** (wound dehiscence, colon perforation, peritonitis) Intervention: 4/104 (3.9%) Control: 7/96(7.3%) P=0.47	

Q5. What are the most effective strategies for achieving and maintaining perioperative normothermia? Our search did not identify RCTs or SRs that evaluated the most effective strategies for achieving and maintaining perioperative normothermia and their impact on the risk of SSI.

2.1D3. RISK OF BIAS ASSESSMENTS OF STUDIES: Q4-5 NORMOTHERMIA

eTABLE 41. Risk of Bias Assessments of Randomized Controlled Trials for Q4-5 Normothermia

Author Year	Q	Described as randomize-ed	Randomizati-on appropriately performed	Described as double-blind	Outcome assessor blinded	Study participant blinded	Investigat-or blinded	Attrition described	Attrition smaller than 10-15% of assigned patients	Attrition appropriately analyzed	Funding source(s) disclosed and no obvious conflict of interest	Overall Risk of Bias
Question 4: Normothermia												
Kurz 1996 [88]	4	✓	✓		✓	✓	✓	✓	✓	✓		Low
Melling 2001 [87]	4	✓	✓		✓		✓	✓	✓	✓		Low
Wong 2007 [89]	4	✓	✓		✓		✓	✓	✓	✓		Low

2.1E. Q6-7 OXYGENATION

2.1E1. GRADE TABLE: Q6-7 OXYGENATION

eTABLE 42. GRADE Table for Q6-7 Oxygenation

Comparison	Outcome	Quantity and Type of Evidence	Findings	Starting GRADE	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Confounders		
Q6. In patients with normal pulmonary function, how safe and effective is the perioperative use of increased fraction of inspired oxygen (FiO_2) in reducing the risk of SSI?														
General Anesthesia														
Intraoperative only (mechanical ventilation)														
80% oxygen vs. 30% oxygen (Both groups without nitrous oxide)	SSI, All*	1 RCT [90]	• In one RCT of 434 routine gynecological and abdominal surgeries, analysis suggested no difference between groups: 15/226 (6.6%) vs. 15/208 (7.2%); RR: 0.92 (0.46 – 1.84); p= 0.81. However, this study did not describe maintenance of normothermia or adequate volume replacement. There were significant differences in deviation from protocol between study groups: 3/226 (1.3%) vs. 13/208 (6.3%), p<0.01, with reasons for deviation in the control group including desaturation and bradycardia.	High	0	0	0	-1	0	0	0	0	Moderate	Moderate
	Organ/ Space	1 RCT [90]	• No difference between groups: 4/226 (1.8%) vs. 5/208 (2.4%)	High	0	0	0	-1	0	0	0	0	Moderate	
	Deep Infection	1 RCT [90]	• No difference between groups: 5/226 (2.2) vs. 4/208 (1.9)	High	0	0	0	-1	0	0	0	0	Moderate	
	Superficial Infection	1 RCT [90]	• No difference between groups: 6/226 (2.7%) vs. 6/208 (2.9%)	High	0	0	0	-1	0	0	0	0	Moderate	
	Adverse Events	1 RCT [90]	• No difference between groups in sternal pain, 5/226 (2.2%) vs. 6/208 (2.9%), p=0.66 • No significant difference between groups in nausea and vomiting (17/226 (7.5%) vs. 11/208 (5.3%), p=0.34 or hypotension 3/226	High	0	0	0	-1	0	0	0	0	Moderate	

Comparison	Outcome	Quantity and Type of Evidence	Findings	Starting GRADE	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Confounders		
			(1.3%) vs. 0/208, p=0.10)											
Intraoperative mechanical ventilation and postoperative non-rebreathing facemask or nasal cannula for 2-6 hours														
All Surgeries														
80% oxygen vs. 30% oxygen (Both groups without nitrous oxide)	SSI, All*	6 RCT [91-96]	• A meta-analysis (N=2622) of 6 RCTs that included heterogeneous surgeries and patients, and differences in optimization of normothermia and adequate tissue perfusion suggested 80% oxygen was associated with reduction in SSI: OR: 0.63 (0.43 – 0.92); p=0.02; I^2=52% • 3 high quality RCT[91-93] totaling 1001 colorectal (n=791) and open appendectomy (n=210) patients, each reported a 40% reduction in SSI with 80% oxygen. Each study optimized perioperative tissue oxygen delivery by standardizing patient core temperature regulation strategies targeted at maintenance of normothermia and fluid replacement to avoid hypo or hypervolemia • 1 high quality RCT of 217[96] patients undergoing open reduction and internal fixation of 235 high-energy tibial plateau (n=78), tibial pilon (n=86) and calcaneus (n=61) fractures reported a 40% reduction in SSI with 80% oxygen though this difference was not significant with a multivariate adjusted OR: 0.54 (0.22-1.29); p=0.17. Normothermia and adequate fluid replacement were not described. • 1 high quality RCT[94] in 1386 patients undergoing a variety of general and gynecologic surgical procedures found no	High	0	-1	0	0	0	0	0	0	Moderate	Moderate

Comparison	Outcome	Quantity and Type of Evidence	Findings	Starting GRADE	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Confounders		
			difference between groups. However, this study did not optimize tissue oxygen delivery as it failed to maintain perioperative normothermia and instituted aggressive perioperative fluid restriction.											
	Organ/ Space Infection	2 RCT [94,95]	• Organ/space infections reported in 5% of 1386 patients, and comprised 28% of all SSI • No difference between groups: 36/685 (5%) vs. 39/701 (6%)	High	0	0	0	-1	0	0	0	0	Moderate	
	Deep Infection	2 RCT [94,95,]	• Deep infections reported in 3% of 1386 patients, and comprised 15% - 18% of all SSI; no difference between groups OR: 0.80 (0.42 – 1.51); p=0.52	High	0	0	0	-1	0	0	0	0	Moderate	
	Superficial Infection	2 RCT [94,95]	• Superficial infections reported in 11% of 1386 patients, and comprised 54% - 57% of all SSI; no difference between groups OR: 1.15 (0.71 – 1.85); p=0.63	High	0	0	0	-1	0	0	0	0	Moderate	
	ASEPSIS Scores	4 RCT [91-94]	• 2 RCTs [92,93] found that 80% oxygen was associated with lower ASEPSIS scores • 2 RCTs [91,94] suggested that 80% oxygen was associated with fewer patients scoring ≥20 on ASEPSIS scale, but this finding was not significant	High	0	0	0	0	0	0	0	0	High	
	Mortality, 14-30 Days	4 RCT [91,93-95]	• 1% mortality reported in elective colorectal surgery patients at 14days[91,93] • 5% mortality reported in mixed emergency and elective laparotomy patients at 30 days[94] • No difference between groups • Mortality unrelated to use of increased fraction of inspired oxygen	High	0	0	0	0	0	0	0	0	High	

Comparison	Outcome	Quantity and Type of Evidence	Findings	Starting GRADE	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Confounders		
	Respiratory Failure (14 Days)	2 RCT [94,95]	• Respiratory failure, defined as the need for controlled ventilation or arterial oxygen saturation below 90% despite supplemental oxygen was reported in 5% of patients • No difference between groups	High	0	0	0	-1	0	0	0	0	Moderate	
	Atelectasis (14 Days)	2 RCT [94,95]	• Atelectasis diagnosis based on a radiologist's evaluation and description on chest radiograph or computed tomography • Reported in 8% of patients • No difference between groups	High	0	0	0	-1	0	0	0	0	Moderate	
	Tissue Oxygen Tension	1 RCT [93]	• Subcutaneous tissue oxygen tension was higher in patients receiving 80% oxygen. This was noted both intraoperatively (109 mmHg vs. 59mmHg; p<0.01) and postoperatively (73 mm Hg vs. 54 mm Hg; p=0.02)	High	0	0	0	-1	0	0	0	0	Moderate	
	Length of Stay	5 RCT [91-94,96]	• 3 RCTs[91-93] found no statistical difference between groups • The 2 colorectal surgery studies[91,93] suggested that 80% oxygen was associated with one day longer duration of hospital stay but the findings were not significant: 12 vs.11 days; P=0.26 [93] and p=0.09 [91] respectively • Only the 1 open appendectomy RCT[92] reported a significantly longer hospital stay in the 30% oxygen group (p=0.01). • One RCT[96] (N=235 fractures in 217 patients) in fracture fixation surgeries reported a longer length of hospital stay for the 80% oxygen group, but this difference was not significant: 3.5 days (SD 4.1 days) vs. 2.8 days (SD 2.6 days), p=0.11. • The 1 large, mixed surgical population	High	0	-1	0	0	0	0	0	0	Moderate	

Comparison	Outcome	Quantity and Type of Evidence	Findings	Starting GRADE	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Confounders		
			RCT[94] (N=1,386) suggested 80% oxygen was associated with one day shorter duration of hospital stay but the findings were not significant: 6 days (range, 1-34 days) vs. 7 days (range, 2-36 days); p=0.09											
Colorectal Surgeries														
80% oxygen vs. 30% oxygen (Both groups without nitrous oxide and with oral bowel prep, maintenance of tissue perfusion and normothermia)	SSI*	3 RCT [91,93,94]	• A meta-analysis of 2 RCTs[91,93] and a subanalysis from a third RCT[94] (N=1424) in colorectal surgeries with preoperative oral bowel prep and maintenance normothermia and adequate tissue perfusion suggested no benefit to 80% oxygen OR: 0.64 (0.40 – 1.04); p= 0.07; I^2=59%	High	0	0	0	0	0	0	0	0	High	High
Intraoperative mechanical ventilation and postoperative 30 minutes with nitrous oxide														
80% oxygen vs. 35% oxygen (both groups with nitrous oxide 30 minutes after incision)	SSI, All*	1 RCT [97]	• One interim analysis 1 RCT (n=160) reported 29 (18%) SSIs • 80% oxygen was associated with an increased risk of SSI: OR: 2.63; (1.1 – 6.2); p=0.02; RR: 2.22 (1.1-4.6)	High	0	0	0	-1	0	0	0	0	Moderate	Moderate
	Deep Structures Infection	1 RCT [97]	• Deep structures infection reported in 4/160 (3%) of patients an no difference between group: 3/80 (4%) vs. 1/80 (1%); OR 3.08 (0.31-30.24); p=0.62 • Comprised 11% - 15% of all SSI	High	0	0	0	-1	0	0	0	0	Moderate	
	Wound Infection	1 RCT [97]	• Wound infection reported in 18/160 (11%) patients, comprising 56% - 65% of all SSI • No difference between groups: 13/80 (16.25%) vs. 5/80 (6.25%): OR 2.91 (0.99 - 8.59); p=0.08	High	0	0	0	-1	0	0	0	0	Moderate	

Comparison	Outcome	Quantity and Type of Evidence	Findings	Starting GRADE	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Confounders		
	Both Deep Structures and Wound Infection	1 RCT [97]	• Both deep structures and wound infection reported in 7/140 (4%) patients, comprising 20%-33% of all SSIs. • No difference between groups: 3/80 (3.75%) vs. 4/80 (5%) OR: 0.74 (0.16 - 3.42); p=1	High	0	0	0	-1	0	0	0	0	Moderate	
	Mortality	1 RCT [97]	• 1 death reported, in the control group	High	0	0	0	-1	0	0	0	0	Moderate	
	Length of Stay	1 RCT [97]	• This study suggested that 80% oxygen was associated with a longer mean length of stay (8.3 days vs. 6.4 days), but the finding was not significant (p=0.07)	High	0	0	0	-1	0	0	0	0	Moderate	
NEURAXIAL ANESTHESIA (Intraoperative and postoperative non-rebreathing facemask)														
	SSI, All*	3 RCT [98-100]	• A meta-analysis (N=1559) of 3 RCTs in heterogeneous patients undergoing cesarean section surgeries with Neuraxial anesthesia, and differences in optimization of normothermia and adequate tissue perfusion suggested no benefit to 80% oxygen: OR: 1.31 (0.90 – 1.90); p=0.16; I^2=17% • 1 large RCT[99] (n=831) in cesarean section patients found no difference in SSI incidence between groups: 8.2% (34/416) vs. 8.2% (34/415), p=0.89. This study ensured adequate tissue perfusion, fluid replacement and normothermia. Antimicrobial prophylaxis was administered post cord-clamp • 1 large RCT[100] (n=585) and 1 small interim analysis[98] (n=143) in cesarean section patients suggested 80% oxygen delivered through a non-rebreathing facemask was associated with non-significant increase in	High	0	-1	0	0	0	0	0	0	Moderate	Moderate

Comparison	Outcome	Quantity and Type of Evidence	Findings	Starting GRADE	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Confounders		
			risk of SSI:: 35/288 (12.2%) vs. 26/297 (8.8%), p=0.18 and 25% (95% CI, 15-35%) vs. 14% (95% CI, 6-22%); p=0.13 respectively . Normothermia and adequate fluid replacement were not described in either study.											
80% oxygen vs. 30% oxygen	SSI-Endometr-itis	3 RCT [98-100]	• A meta-analysis (N=1559) of 3 RCTs in heterogeneous patients undergoing cesarean section surgeries with Neuraxial anesthesia, and differences in optimization of normothermia and adequate tissue perfusion suggested no benefit to 80% oxygen OR: 1.62 (0.86 – 3.05); p=0.14; I^2=0 • 1 large RCT[100] (n= 585) and 1 small[98] (n=143) interim analysis suggested 80% oxygen was associated with an increase in endometritis, , but this was not statistically significant in either study 7/288 (2.4%) vs. 2/297 (0.7%), p=0.08, and 9/69 (13%) vs. 5/74 (7%), p=0.26 respectively. Neither study was adequately powered to detect a statistical difference in this outcome. • 1 large RCT[99] (n=831) suggested no difference in the incidence of endometritis with 80% oxygenation (2.4% vs. 2.7%, p=0.66). This study ensured adequate volume replacement and normothermia.	High	0	-1	0	0	0	0	0	0	Moderate	
	Length of Stay	1 RCT [98]	• No difference between groups: median days (range): 3 (2-5) vs. 3 (2-6); p=0.92	High	0	0	0	-1	0	0	0	0	Moderate	
POSTOPERATIVE ONLY (Facemask and/or nasal cannula)														
28-30 % oxygen vs. room air	SSI, All*	2 RCT [101,102]	• In1 RCT[102] of 274 lower limb vascular surgeries, multivariate analysis suggested no difference between groups: 18% vs.	High	-1	0	0	0	0	0	0	0	Moderate	Moderate

Comparison	Outcome	Quantity and Type of Evidence	Findings	Starting GRADE	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Confounders		
			28%; OR: 0.56 (0.30 – 1.04); p = 0.07. Isolated groin incision SSIs were significantly lower in the supplemental (30%) oxygen group: 5.8% vs. 23.5%; OR:0.20 (0.04-0.95) ;p=0.04 • One lesser quality study[101] of 24 cervical spine surgeries reported no SSIs											
	Organ/ Space	1 RCT [102]	• No infections in the intervention group vs. 2 infections (3%) in the control group	High	0	0	0	-1	0	0	0	0	Moderate	
	Deep Infection	1 RCT [102]	• No difference : 5.1% in each group	High	0	0	0	-1	0	0	0	0	Moderate	
	Superficial Infection	1 RCT [102]	• No difference: 18/137 (13%) vs. 29/137 (21%); OR 0.56; (0.30-1.07); p=0.11.	High	0	0	0	-1	0	0	0	0	Moderate	
	ASEPSIS Scores	1 RCT [101]	• All within satisfactory healing (Score 0-10) • No difference observed between groups	High	-1	0	0	-1	0	0	0	0	Low	
	Mortality, 30 Days	1 RCT [102]	• Mortality was rare (4 deaths among 274 patients) and did not differ by group: 3/137 (2.2%) vs. 1/137 (0.7%); OR 3.0 (0.31-28.99); p=0.62.	High	0	0	0	-1	0	0	0	0	Moderate	
	Adverse Events	2 RCT [101,102]	• Adverse events were rare and did not differ between groups • Reported adverse events include: wound complications, graft thrombosis, cardiac complications, pneumonia, stroke, renal insufficiency, major amputation	High	-1	0	0	-1	0	0	0	0	Low	
	Tissue Oxygen Tension	1 RCT [101]	• Subcutaneous tissue oxygen tension was higher in patients receiving supplemental oxygen (63 mm Hg vs. 48 mm Hg; p<0.01)	High	-1	0	0	-1	0	0	0	0	Low	

Comparison	Outcome	Quantity and Type of Evidence	Findings	Starting GRADE	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Confounders		
	Length of Stay	1 RCT [102]	• No difference observed between groups: 6.5d vs. 5.4d; p-=0.13.	High	0	0	0	-1	0	0	0	0	Moderate	
Q7. What is the optimal target FIO2 to reduce the risk of SSI; how and when should it be administered? Our search did not identify RCTs or SRs that both evaluated the optimal fraction of inspired oxygen, how and when it should be administered, and included SSI as an outcome. All studies evaluating the use of supplemental increased oxygenation both intraoperative and postoperatively used 80% FiO2 as the target level. \														

*Critical outcome; OR: Odds Ratio; RR: Risk Ratio; CI: Confidence Interval

2.1E2. EVIDENCE TABLE: Q6-7 OXYGENATION

eTABLE 43. Evidence Table for Q6. In patients with normal pulmonary function, how safe and effective is the perioperative use of increased fraction of inspired oxygen (FiO_2) in reducing the risk of SSI?

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
Duggal 2013 [99] (ES)	**RCT** 1, 2, 3, 4, 5, 7, 9,	To evaluate whether supplemental perioperative oxygen could reduce the occurrence of surgical site infection or endometritis in women undergoing cesarean deliver	**Number of patients N=831** **Patient Characteristics:** the two groups were well matched for age, race, parity, BMI number of previous cesarean deliveries, elective cesarean deliveries, history of diabetes, cardiac or pulmonary disease, anemia, smoking, or chronic steroid use. ·Age: mean ±SD, y Intervention: 29.2±5.6 Control: 29.5±5.8 ·Gender: all female ·Obesity: (kg/m^2) Total ≥30 Intervention: 331/416 (79.6) Control: 306/415 (73.7) BMI 30-34.9 Intervention: 142/416 (34.1) Control: 127/415 (30.6) BMI 35-39.9 Intervention: 100/416 (24.0) Control: 97/415 (23.4) BMI 40 or greater Intervention: 89/416 (21.4) Control: 82/415 (19.8) ·Comorbidities Diabetes	**Intervention group** n=416 80% oxygen – an aerosol face mask delivered oxygen at 80% concentration during surgery and for 1h postop. Flow rate 10L/min. **Timing of intervention**: intra- and post-operatively **Duration of intervention:** intraoperative and for 1h postoperative **Device/agent:** Aerosol face mask was used for both intervention and control **Monitoring intervention** **Control group** n=415 30% oxygen – an aerosol face mask delivered oxygen at 30% concentration during surgery and for 1h postop. Flow rate 10L/min. **Standard preventive measures:** AMP: usually cefazolin (2g) intravenously after cord clamping. If allergic to penicillin, patient received clindamycin (900mg). Closure: if subcutaneous tissue was >4cm thick, it was closed with 2-0 plain catgut. Method of skin closure was determined in operating room. Fluid Replacement: care was taken to ensure the patients received adequate fluid	**SSI** Composite infection (ITT) (SSI + Endometritis) % (n calculated by extractor) Intervention: 8.2% (34/416) Control: 8.2% (34/415) P=0..89 SSI at discharge (usually PO day 3) Intervention: 2.4% (10/416) Control: 2.9% (10/415) P=0.70 SSI assessed by 6wk Intervention: 3.1% (13/416) Control: 2.9% (12/415) P=0.72 Total SSI Intervention: 5.5% (23/416) Control: 5.8% (24/415) P=0.98 Total Endometritis Intervention: 2.7% (11/416) Control: 2.4% (10/415) P=0.66 Diabetes Subanalysis Composite (SSI + Endometritis) % (n/N) Intervention: 14.4% (13/90) Control: 6.9% (6/87) P=0.11 SSI at discharge, % (n/N) Intervention: 6.7% (6/90) Control: 2.3% (2/87)	**Definitions:** Surgical site infection – CDC Definition: at least 1 of the following criteria was required: 1) purulent discharge from incision site; 2) organisms isolated from an aseptically obtained culture or tissue from the superficial incision; 3) at least one of the following signs or symptoms: pain or tenderness, localized swelling, redness or heat, and the superficial incision was opened by the surgeon unless the incision culture was negative; and 4) diagnosis of superficial incisional surgical site infection by the surgeon. Endometritis: diagnosed by the clinical finding of a temp of more than 38°C associated with uterine tenderness without any other source of fever identified. **Perioperative care:** NR **Other notes:** Study was powered to demonstrate a 50% difference in infection rate with a two-sided α of 0.05 and a power of 80%. The sample size estimation of 778 patients was determined for the composite outcome of

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			Intervention: 91/416 (21.9) Control: 87/415 (20.9) **Procedures:** Cesarean delivery **Indications:** NR **Setting:** 1 tertiary medical center **Location: USA** **Dates:** August 2006 – August 2010 **Inclusion Criteria:** Women undergoing elective or emergency cesarean delivery. **Exclusion Criteria:** Fever (temp ≥38^{o}C), chorioamnionitis (temp of 38^{o}C or higher with fetal or maternal tachycardia), patients who were group B Streptococci-positive and had been started on antibiotics, immunocompromised or HIV-positive patients, planned general anesthesia, age <18 years, and incarcerated patients.	resuscitation to ensure adequate tissue perfusion. Normothermia: optimal room temperature was maintained to ensure normothermia. A warming blanket was used at the discretion of the anesthesiologist. Normoglycemia: a finger-stick blood glucose test was done on day of surgery to ensure normoglycemia during surgery	P=0.17 SSI at 6week postop Intervention: 3.3% (3/90) Control: 1.1% (1/87) P=0.34 Total SSI Intervention: 10% (9/90) Control: 3.4% (3/87) P=0.09 Total endometritis Intervention: 4.4% (4/90) Control: 3.4% (3/87) P=0.75 **Other infections:** NR **Topic-specific outcomes:** NR Diabetic patients were analyzed separately **Reoperations:** NR **Length of stay:** NR **Mortality:** NR **Adverse events:** NR	SSI and Endometritis (baseline rate 12%) **Follow-up: 6 weeks** (postpartum visit) 135 (16.5%) lost to follow up. Intervention: 70/416 (16.8%) Control: 65/415 (15.7%) P=NS **Funding Source Conflicts:** Authors: NR Institution: NR Study: NR Supplies: NR
Stall 2013 [96] (ES)	**RCT** 1, 2, 3, 4, 5, 6, 7, 8, 9, 10	To assess the benefits of supplemental perioperative oxygen in an orthopedic patient population undergoing	**Number of patients: N=222 patients with N=235 fractures** **Patient Characteristics:** demographics and perioperative risk factors were similar in the two groups overall. Although no statistically significant	**Intervention group:** n=119 After intubation, FiO_2 was adjusted to 80%. After extubation patients were placed on high-flow nonrebreather masks at 15L per minute for 2 hours postop. **Timing of intervention:** Intra- and postop	**SSI:** Overall – 33/222 (13%) Deep – 27/33 (82%) Superficial – 6/33 (18%) Overall intervention: 14/119 (12%) Overall control: 19/116 (16%) P = 0.31 (40% decrease in	**Definitions:** High Energy Fracture: one requiring delayed (>5 days after injury) definitive fixation because of soft tissue concerns Surgical Site infection: based on CDC definitions. Deep infections: involve

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
		open reduction and internal fixation of high-energy tibial plateau, tibial pilon and calcaneus fractures.	differences were observed in the distribution, some imbalances were shown. ·Age: mean (SD) y Intervention: 42.3 (12.1) Control: 42.5 (12.2) ·Gender: female Intervention: 24/119 (20.2%) Control: 35/116 (30.2%) ·Obesity: BMI mean (SD) kg/m^3 Intervention: 28.4 (6.4) Control: 28 (5.9) ·Comorbidities: Diabetes Intervention: 7/119 (5.9%) Control: 9/116 (7.8%) **Procedures:** open reduction and internal fixation of high-energy tibial plateau, tibial pilon and calcaneus fractures. **Indications:** high tibial plateau, tibial pilon or calcaneus fractures **Setting:** University Hospital **Location:** USA **Dates:** April 2007 – November 2010 **Inclusion Criteria:** all adult patients (≥18 years) who sustained high-energy tibial plateau, tibial pilon, or calcaneus fractures undergoing open reduction and internal	**Duration of intervention:** intraoperative and 2 h postop. **Device/agent:** Nonrebreather mask for intervention group, nasal cannula for control group. **Monitoring intervention:** pulse oximetry Adherence to protocol was verified by postanesthesia care unit records. **Control group** n= 116 After intubation, FiO_2 was adjusted to 30%. After extubation patients were placed on nasal cannulae at 4L per minute to maintain oxygen saturation of at least 92% as determined by pulse oximetry for 2 hours postop **Standard preventive measures:** Multiple operations: - Patients with tibial plateau and tibial pilon fractures were first managed with surgery to place a temporary external fixator. These patients were not yet enrolled in the study so the oxygenation for the initial surgery was standard practice. A small group of patients in the tibial pilon group underwent two definitive operations, typically one approach from the posterior ankle and another anterior approach separated by a number of days. In these cases, the patients	infection rate in the treatment group) Multivariate OR of all injuries = 0.54 (95%CI: 0.22-1.29), p=0.17 No statistically significant difference was seen between groups in subanalyses of the three types of surgeries Deep - 27/222 (12.2%) Superficial – 6/222 (2.7%) **Other infections:** NR **Topic-specific outcomes:** NR **Reoperations:** NR **Length of stay:**, mean (SD) d Intervention: 3.5 (4.1) Control: 2.8 (2.6) P=0.11 **Mortality:** NR **Adverse events:** NR	debridement Superficial infections: treated with antibiotics alone. Treatment-Related Complications: unexpected pulmonary complication, prolonged intubation, and any other adverse outcome thought to be related to oxygen treatment by the anesthesiologist or primary team. Fractures: classified according to AO classifications as determined by one fellowship-trained orthopedic traumatologist blinded to treatment and outcome. **Perioperative care:** NR **Other notes:** Study is underpowered to detect a statistically significant difference in composite SSI. Trial stopped because funding ran out. Prespecified criteria for early termination of the trial were any adverse event directly attributable to the treatment (hyperoxygenation) and a reduction in surgical site infections of greater than 50% in the treatment group at annual review. **Follow-up:** median follow up =344 days (range 84-1771 days; IQR 153-573 days) Wound monitoring: per routine clinical practice, that is, on a

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			fixation, **Exclusion Criteria:** The above surgeries except those requiring flap coverage (Gustilo and Anderson grade IIIB open fracture) and those with open fractures requiring vascular repair for limb salvage (Grade IIIC open fractures). Also, evidence of infection at the fracture site before definitive fixation. During the 1st year of the trial, patients were excluded for any diagnosis of infection requiring antibiotics, even if it was distant to the site of surgical incision. That criterion was removed because it became apparent that many of the patients received orally administered antibiotics at rehabilitation centers before their definitive surgery for diagnosis of pin tract infections or other infections unrelated to the study fracture. Excluding them was detrimental to study design because patients who had recent infection might have been at increased risk of surgical site infection and therefore benefitted most.	received the same treatment for both operations. There were also a small number of patients with more than one eligible study fracture, and each fracture was randomized individually AMP – Standardized for both groups. Unless contraindicated, patients typically received 1 or 2 g of cefazolin administered intravenously preoperatively and every 8 hours for a total of 3 doses, per standard care of the institution. For open fractures, surgeons were allowed to continue antibiotics for up to 48h postop according to their clinical practice. Normothermia: NR Adequate volume replacement:: NR		daily basis until discharge and at the 2, 6, and 12 week outpatient follow-up visits. All wound assessments were blinded **Funding Source Conflicts:** Authors: None Institution: None Study: None Supplies: None

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			Also, preoperative arterial hemoglobin saturation <90% without supplemental oxygen and a history of preexisting pulmonary disease that can be worsened by high-dose oxygen such as COPD and bleomycin toxicity. Also patients who were unable to provide informed consent and those who were unable to speak English or Spanish.			
Thibon 2012 [90] (ES)	**RCT** 1, 2, 4, 5, 6, 7, 8, 9	To evaluate the effects of hyper-oxygenation to 80% FiO_2 in routine abdominal and gynecologic surgery on the frequency of SSI occurring during the 30 days following surgery, and to compare the frequencies of peri- and immediate postoperative adverse effects between a group of hyper-	**Number of patients: N=434** **Patient Characteristics:** The two groups displayed no significant differences in baseline characteristics. ·Age: y, mean (SD) Intervention: 52.1 (13.7) Control: 518 (13.3) ·Gender: female Intervention: 208/226 (92.0) Control: 184/208 (88.5) ·Obesity: BMI>30 Intervention: 29/226 (12.8) Control: 27/208 (13.0) ·Comorbidities: Diabetes: Intervention: 7/226 (3.1) Control: 12/208 (5.8) Current Smoker: Intervention: 39/226 (17.3) Control: 42/208 (20.2) **Procedures:** Gastric/hernia:	**Intervention group:** n=226 Pre-oxygenation, induction, emergence and extubation: FIO_2 100% After pre-oxygenation, patients were ventilated with an anesthesia respirator. Following induction of anesthesia and tracheal intubation, patients received 80% FiO_2 **Timing of intervention:** Intraoperative (postoperative at physician's discretion) not intended for postop. **Duration of intervention:** intraoperative **Device/agent:** facemask for both intervention and control **Monitoring intervention:** NR Protocol not maintained for the entire duration of the operation: Intervention: 3/226 (1.3) Control: 13/208 (6.3)	**SSI :** Total: 30/434 (6.9%) Intervention: 15/226 (6.6) Control: 15/208 (7.2) P=0.84 RR- 0.92 (95%CI [0.46-1.84]) Superficial Intervention: 6/226 (2.7) Control: 6/208 (2.9) Deep Intervention: 5/226 (2.2) Control: 4/208 (1.9) Organ/Space Intervention: 5/226 (2.2%) Control: 5/208 (2.4%) **Other infections:** NR **Topic-specific outcomes:** Oxygen saturation on pulse oximetry at closure (mmHg) mean (SD)	**Definitions:** SSI: CDC definitions were used. An investigator blinded to the randomization conducted a systematic review of the patient's medical records including the documentation provided by physicians and nurses and lab reports. **Perioperative care:** NR **Other notes:** Due to intention to treat analysis, patients remained in their group even if the oxygen concentration was increased during the intervention to maintain saturation **Follow-up:** 30 days (if patients did not attend their 30 day follow-up visit, their infection status was assessed by calling the patient or their physician) Loss to follow up: 4 patients were lost to follow up (2 in

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
		oxygenated patients and a group of patients receiving 30% oxygen.	Intervention: 13/226 (5.8) Control:16/208 (7.7) Hepatobiliary Intervention: 7/226 (3.1) Control: 11/208 (5.3) Colon/Rectum: Intervention: 19/226 (8.4) Control: 11/208 (5.3) Small Bowel Intervention: 4/226 (1.8) Control: 5/208 (12.4) Gynecologic Intervention: 73/226 (32.3) Control: 66/208 (31.8) Breast Intervention: 110/226 (48.7) Control: 99/208 (47.6) **Indications:** NR **Setting:** Multi-center (1 cancer institute, 1 university hospital& 2 private hospitals) **Location:** France **Dates:** June 1, 2003-June 30, 2007 **Inclusion Criteria:** Patients >18 years old, and scheduled to undergo elective abdominal, gynecologic, and breast surgery provided that anesthesia was provided **Exclusion Criteria:** Recent history of fever and/or infection, chronic respiratory failure (oxygen PaO_2 below 60 mmHg, 8.9kPa at rest), and	P=0.007 Reasons for deviation - Intervention = intraoperative complications including one case of septic shock Control = desaturation and/or bradycardia **Control group** n= 208 Pre-oxygenation, induction, emergence and extubation: FIO_2 100% After pre-oxygenation, patients were ventilated with an anesthesia respirator. Following induction of anesthesia and tracheal intubation, patients received 30% FiO_2 **Standard preventive measures:** Pre-Oxygenation: before the induction of anesthesia, each patient was pre-oxygenated (100% FiO_2) via facemasks for at least 3 minutes until the tele-expiratory fraction of oxygen was at least 90%. Normothermia: NR Adequate volume replacement: NR	Intervention: 98.9 (1.1) Control: 98.6 (1.3) P=0.01 **Reoperations:** NR **Length of stay:** NR Time until diagnosis of SSI Overall: 15.4 days±8.2 Intervention: 16.9 days±8.0 Control: 13.9 days±8.4 **Mortality:** NR **Adverse events:** Nausea and vomiting, Intervention: 17/226 (7.5%) Control: 11/208 (5.3)% P=0.34 Sternal pain, Intervention: 5/226 (2.2) Control: 6/208 (2.9) P=0.66 Cough: Intervention: 1/226 (0.4) Control: 0/208 (0) Hypotension: Intervention: 3/226 (1.3) Control: 0/208 (0) P=0.10 No auditory or visual disorder was noted	each group). They were uninfected when they left the hospital and were considered uninfected in the final analysis. **Funding Source Conflicts:** Authors: NR Institution: NR Study: Industry Supplies: NR

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			bleomycin treatment (which may induce sensitivity to oxygen toxicity).			
Scifres 2011 [100] (ES)	**RCT** 1, 6, 7, 8, 9, 10	To assess the effect of a high perioperative oxygen concentration on postcesarean delivery infectious morbidity in women undergoing cesarean delivery.	**Number of patients: N=585** **Patient Characteristics:** patient and operative characteristics were not statistically significantly different unless listed below ·Maternal Age Intervention: 27.5±6.4y Control: 27.8±5.9y ·Gender: all female ·Obesity –BMI at delivery >30kg/m^2 Intervention: 208/288 (72.22%) Control: 230/297 (77.44%) ·Comorbidities: Preterm Delivery <32wks: Intervention: 20/288 (6.9%) Control: 9/297 (3.3%) P=0.03 Chronic hypertension: Intervention: 34/288 (11.8%) Control: 21/297 (7.1%) P=0.05 Previous abdominal surgery including C-section, laparoscopy, laparotomy, Intervention: 181/288 (62.9%) Control: 210/297 (70.7%) P=0.04 Rupture of membranes before cesarean delivery.	**Intervention group:** n=288 Women received oxygen at a flow rate of 10 L/min (corresponding to approx. 80% FiO_2) by nonrebreather mask both during surgery and for 2 hours after cesarean delivery. **Timing of intervention:** Intra and postoperatively **Duration of intervention:** during and for 2 hours after cesarean delivery. **Device/agent:** intervention group used a nonrebreather mask and control group used a nasal cannula **Monitoring intervention:** Compliance with the supplemental oxygen by face mask (intervention group) was assessed by anesthesiologist intraoperatively and by the postpartum nurse at 30, 60, 90 and 120 minutes postop. Oxygen saturation was assessed both intraoperatively and postoperatively for both groups Compliance with intervention postop: Intervention at 30min: 214/288 (74.3%) Intervention at 60min: 189/288 (65.6%) Intervention at 90min: 172/288	**SSI:** Endometritis: Intervention: 7/288 (2.4%) Control: 2/297 (0.6%) RR: 3.6; 95%CI, 0.8-17.2 P=0.08 Wound infection: Intervention: 33/288 (11.5%) Control: 26/297 (8.8%) RR: 1.3; 95%CI, 0.8-2.1 P=0.28 Composite (wound infection +endometritis) Intervention: 35/288 (12.2%) Control: 26/297 (8.8%) RR: 1.4; 95%CI, 0.9-2.3 P=0.18 **Other infections:** Wound hematoma or seroma: Intervention: 16/288 (5.4%) Control: 17/297 (5.9%) RR: 1.1; 95%CI, 0.6-2.1 P=0.79 **Topic-specific outcomes** Intravenous antibiotics >24h after delivery Intervention: 38/288 (13.2%) Control: 35/297 (11.8%) RR: 1.1; 95%CI, 0.7-1.7 P=0.61 Hospital readmission Intervention: 15/288 (5.2%) Control: 10/297 (3.4%)	**Definitions:** Endometritis: oral temp of >38^{o}C after the first 24h following procedure and either (1) fundal or lower abdominal tenderness greater than expected or (2) foul-smelling purulent lochia. Patients were diagnosed with endometritis only if other causes for signs and symptoms were not identified. Patients also had to be treated with IV antibiotics to be diagnosed with endometritis. Wound infection: only if wound opening >1cm or other surgical intervention (such as laparotomy or debridement of tissue) plus at least 1 of the following: (1) purulent drainage from the wound, (2) erythema or induration of the surrounding tissues, (3) maternal oral temperature >38^{o}C, or (4) radiographic evidence of infection. **Perioperative care:** NR **Other notes:** Study utilized infectious morbidity composite measure. (A combination of endometritis and wound infection). Especially for

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			Intervention: 84/288 (29.2%) Control: 59/297 (19.9%) P<0.01 **Procedures:** Cesarean section **Indications:** scheduled or intrapartum cesarean delivery. **Setting:** One University Hospital **Location:** USA **Dates:** February 2008 – March 2010 **Inclusion Criteria:** Patients who underwent scheduled or intrapartum cesarean delivery with regional anesthesia **Exclusion Criteria:** Emergency surgery in which participant was unable to provide informed consent, human immunodeficiency virus infection, chronic corticosteroid therapy or other immunosuppressive therapy, general anesthesia, and a diagnosis of extra-uterine infection (i.e., pyelonephritis or pneumonia) before cesarean delivery. Acute chorioamnionitis was not an exclusion criterion.	(59.7%) Intervention at 120min: 97/288 (33.7%) **Control group**: n=297 Women received oxygen at a flow rate of 2 L/min (corresponding to approx. 25-30% FiO_2) via nasal cannula during cesarean delivery only. **Standard preventive measures:** Additional supplemental oxygen: with oxygen saturation <95% were supplied supplemental oxygen as needed to maintain appropriate oxygenation Intervention: 0/288 Control: 18/297 (5.9%) Skin Prep: Both groups received standard preoperative skin prep. AMP: both groups received standard AMP (cefazolin was primary antibiotic; clindamycin was used in the case of penicillin allergy. Closure: Subcutaneous sutures were left to the decision of the surgical team Adequate fluid replacement: NR Normothermia: NR	RR: 1.5; 95%CI, 0.7-3.4 P=0.27 <u>Neonatal outcomes</u> Umbilical artery pO_2 (mmHg) Intervention: 19.4±9.6 Control: 17.1±6.8 P<0.01 <u>Umbilical artery CO_2 (mmHg)</u> Intervention: 57.0±11.4 Control: 58.9±11.0 P=0.05 <u>Antibiotics after birth</u> Intervention: 75/288 (26.0%) Control: 55/297 (18.5%) P=0.03 **Reoperations:** NR **Length of stay:** NR **Mortality:** Neonatal mortality Intervention: 8/288 (2.7%) Control: 1/297 (0.34%) P=0.06 All deaths were analyzed and none were attributable to supplemental oxygen **Adverse events**: NR	subgroup analysis to determine effect of differences between populations for causes such as rupture of membranes, labor before cesarean, etc. Most non-compliance was related to discomfort associated with wearing the non-rebreather mask. Particularly in the period of 60-120min post-op. **Follow-up:** 2-4 weeks postop during the postop visit. Anyone who did not return for postop visit within 4 weeks or who had planned follow up visit at an outside clinic were contacted by the research nurse by telephone with the data collection form used as a prompt. **Funding Source Conflicts:** Authors: NR Institution: NR Study: NR Supplies: NR

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Staehr 2011 [95] (ES)	**RCT** 1, 2, 3, 4, 5, 6, 7, 8, 9, 10	To evaluate the effect of a high inspiratory oxygen fraction (80%) on SSI and pulmonary complications in obese patients undergoing laparotomy.	**Number of patients: N**: 213 **Patient Characteristics:** All demographic and perioperative characteristics were similar between groups. Population Characteristics Age: ≥18 years Gender: m/f: 86/127 Morbidly Obese: 73/213 (32%) **All characteristics below are given are for the intervention group N=102:** Median [5-95% range] or Age: 63y [37-81] Gender: m/f:43/59 Obesity: Median BMI: 34 kg/m^2 [30-44] BMI≥35kg/m^2:39 (38%) Comorbidity: Current smoker: 31 (30%) Diabetes mellitus: 16 (16%) Pulmonary Disease: 16 (16%) Hypertension: 48 (47%) Other cardiovascular disease: 15 (15%) Duration of surgery: 145 [45-309] min Epidural analgesia: thoracic/lumbar/none: 66/4/32 Type of anesthesia: Volatile: 25 (25%) Total IV: 77(75%) **Procedure:** Laparotomy	**Intervention:** n=102 Intraop: Patients were pre-oxygenated with 100% FiO_2 until tracheal intubation. Patients were given 80% FIO_2 from intubation until the end of surgery when 100% FIO_2 was given immediately before extubation. FIO_2 was increased to ensure arterial oxygen above 94%. Postop: The first 2h after surgery patients received 80% FIO_2 from the Nonrebreathing facemask and an oxygen flow of 14 l/min and an air flow of 2 l/min. 2 hrs. after surgery, supplemental O_2 was administrated according to clinical practice **Timing of Intervention:** Intra and Postoperatively **Duration of Treatment:** Intubation to 2 hours after surgery. **Device:** Nonrebreathing facemask with a reservoir **Control:** n=111 Intraop: Patients were pre-oxygenated with 100% FiO_2 until tracheal intubation. Patients were given 30% FIO_2 from intubation until the end of surgery when 100% FIO_2 was given immediately before extubation. FIO_2 was increased to ensure arterial oxygen above 94%.	**SSI** (Follow up 14 days postop) Overall: 29% Intervention: 32/102 = 31% Control: 29/111= 26% Univariate OR: 1.29 (95% CI, 0.71-2.34) *P*= 0.40 Adjusted OR: 1.22 (95%CI, 0.63-2.39) P=0.57 Superficial infection Intervention: 16/32 (50%) Control: 21/29 (73%) Deep Infection Intervention: 8/32 (25%) Control: 5/29 (29%) Organ/Space Infection Intervention: 8/32 (25%) Control: 3/29 (10%) **Incidence of SSI** Obese Patients = 27% Morbidly Obese Patients n=73(32%) **Sub-analysis of SSI between Intervention groups distributed by weight class. (interpreted from graph (%SSI [upper 95% CI])** Underweight (BMI<18.5kg/m^2) Intervention: 10% [25%] Control:19% [37%] Normal Weight (BMI 18.5-24.9 kg/m^2) Intervention: 17% [20%] Control:18% [21%] Over Weight (BMI 25.0-29.9kg/m^2)	**Definitions:** SSI**:** CDC definitions (Within 14 days) Pneumonia**:** CDC (Within 14 days) Adverse Event: ND Serious adverse event: Serious if fatal, life threatening, caused permanent disability, or required prolonged hospitalization Obese: BMI 30-34.9kg/m^2 Morbidly Obese: BMI ≥ 35kg/m^2 Overweight: BMI= 25.0-29.9kg/m^2 Normal Weight: BMI= 18.5-24.9kg/m^2 Underweight: BMI<18.5 kg/m^2 **Perioperative Care:** Anesthesia-standardized, non-nitrous oxide **Other notes:** This was a planned subgroup analysis of the PROXI trial; Meyhoff 2009 Adjusted OR adjusted for study center, diabetes mellitus, acute surgery, COPD, current smoker, upper abdominal incision, duration of surgery, and age (≥40 years or <40 years) where possible Preoperative SSI Risk Stratification: SENIC 1/2/3/4 Intervention: 24/32/42/4 Control: 25/35/47/4 NNIS, 0/1/2/3 Intervention: 20/50/26/6

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			Colorectal: Intervention: 40/102 (39%) Control: 49/111 (44%) Primary Anastomic: Intervention: 31/102 (30%) Control: 41/111 (37%) Other surgeries: Intervention: 62/102 (61%) Control: 41/111 (56%) Acute procedures: Intervention: 19/102 (19%) Control: 20/111 (18%) Operation Classification Clean: 36 (35%) Clean Contaminated: 21 (21%) Contaminated: 43 (42%) Dirty-infected 2 (2%) **Indications:** Cancer Diagnosis Intervention: 56/102 (57%) Control: 57/111 (51%) Other: Intervention: 46/102 (45%) Control: 54/111 (49%) **Setting:** Multi-Center **Location:** Denmark **Dates of Study:** October 8, 2006 - October 6, 2008 **Inclusion Criteria:** 18 years or older, BMI≥ 30kg/m^2, scheduled for acute or elective laparotomy **Exclusion Criteria:** Inability to give informed consent, chemotherapy for malignancy within 3	Postop: The first 2h after surgery patients received a mixture of O_2 (2 l/min) and air (14 l/min) through above face mask. 2 hrs. after surgery, supplemental O_2 was administrated according to clinical practice **Monitoring Intervention:** Pulse oximetry **Standard Preventative Measures:** Analgesia: epidural Normothermia: ensured adequate temperature Glycemic: ensured adequate glucose control AMP: appropriate and timely prophylactic antimicrobials Received Adequate AMP Intervention n=90(88%) Control n=91 (82%) Received Timely AMP Intervention n=64 (63%) Control n=75 (71%) Bowel Prep: absence of preoperative oral bowel prep Fluids: Given only once to replace measured or calculated deficits aiming at body weight increase of less than 1kg. Blood loss was replaced 1:1 with colloids and blood transfusion was initiated if blood loss exceeded 20ml/kg	Intervention: 19% [24%] Control:22% [28%] Obese (BMI 30.0-34.9 kg/m^2) Intervention: 30% [42%] Control:26% [36%] Morbidly Obese (BMI ≥35.0 kg/m^2) Intervention: 33% [49%] Control:30% [48%] Per-protocol analysis (N= 167) of primary and secondary outcomes showed results similar to those in the ITT analysis (N=213): SSI-per protocol analysis Intervention: 31/91 (34%) Control: 24/76 (32%) P=0.73. **Other infections:** Pneumonia (Follow up 14 days) Intervention:5.9% Control: 4.5% Obese:6% Morbidly obese: (3%) **Reoperation:** n=43(20%); Intervention: 22/102 (22%) Control: 21/111 (19%) Reoperation for SSI n=24 (11%) Debridement n=5 (2%) **Length of stay:** Intervention: 6 (1-35) days Control: 5 (2-45) days **30 Day Mortality:** Total: 2%	Control:28/47/29/7 Pulmonary complications monitored by clinical exam (attending physician), including chest radiographs or computed tomography evaluated by radiologist blinded to allocation **Follow-Up:** visit conducted between postoperative day 13 and 30. Most outcomes measured at 14 days post op except for mortality at 30days. **Funding Source Conflicts:** Authors: None Institution: None Study: None Supplies: None

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			months, surgery performed under general anesthesia within 30 days, preoperative arterial oxygen saturation less than 90% w/o supplemental oxygen assessed by pulse oximetry.		Intervention: 1/102 (1%) Control: 3/111 (2.7%) **Adverse Events:** Any adverse event Intervention: 52/102 (51%) Control: 58/111 (52%) Wound related: Intervention: 18/102 (18%) Control: 20/111 (18%) Any serious event: Intervention: 22/102 (22%) Control: 22/111 (20%) Sepsis Intervention: 4/102 (3.9%) Control: 3/111 (2.7%) Pulmonary Complications: Not significantly different Atelectasis (Follow up 14 days postop) Intervention: 9/102(8.8%) Control: 7/111 (6.3%) Obese:9% Morbidly Obese:5% Respiratory Failure(Follow up 14 days postop) Intervention: 8/102 (7.8%) Control: 5/111 (4.5%) Obese: 6% Morbidly obese:5% Anastomotic leak Intervention: 2/31 (6%) Control: 2/41 (5%) Rupture of abdominal fascia 15/213 (7%) of patients had ruptured abdominal fascia compared with 9/658 (1%) of normal weight patients in	

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					PROXY trial Intervention: 9/102 (9%) Control: 6/111 (5%) Admission to ICU (within 14 days if not part of normal routine care) Intervention: 11/102 (10%) Control: 9/111 (8%)	
Turtiainen 2011 [102] (ES)	**RCT** 1, 2, 4, 6, 7, 8, 9	To test the hypothesis that supplemental postoperative oxygen decreases the incidence of Surgical Wound Infection (SWI) after lower limb revascularization	**Number of patients:** N=274 **Patient Characteristics:** Characteristics were analyzed and not found to be statistically different between groups. **Characteristics reported below are for the intervention** Age: ≥ 18 (Mean: 73.5 [SD 11]) Gender (m/f): 78/59 Obesity: BMI, mean: 26 kg/m^2 (SD 4) Co-Morbidities: Coronary artery disease: 65 (47%) Diabetes: 50 (36%) Hypertension: 89 (65%) Rheumatoid arthritis: 7 (5%) COPD: 13 (9%) Asthma: 11 (8%) Dialysis: 5 (4%) Current smoking: 37 (27%) Blood loss (ml [SD]): 341 (337) **Procedure: N=274** Non-emergency, lower limb arterial surgery	**Intervention:** n=137 Postop: 30% FIO_2 was delivered via face mask in the recovery room and on the 1st postoperative day. On the 2nd postoperative day supplemental oxygen was delivered via nasal cannula at a constant flow rate of 5l/min. **Timing of Intervention:** Postoperatively **Duration of Treatment:** From the end of surgery until 10PM on 2nd postoperative day (at least 48hrs)**Device:** A face mask for the 1st day to deliver 30% O^2. On 2nd postop day, FIO^2 delivered via nasal cannula. **Monitoring Intervention:** Oxygen level of a toe on operated limb measured w/ pulse oximeter every 4 hours for 1st 2 days. **Control:** n=137 Postop: Breathed room air **Standard Preventative Measures:** AMP: Antimicrobial prophylaxis	**SSI** **Total SSI:** 63/ 274 (23%) Superficial: 47/63 (74%) Deep: 14/63 (22%) Organ/Space: 2/63 (3%) **Intervention vs. Control SSI:** Intervention: 25/137 patients (18.2%) Control: 38/137 patients (27.7%) *P*=0.06 Multivariate OR 0.56 (95% CI, 0.30-1.04; *P*=0.07) Superficial SSI: Intervention: 18/137 (13%) Control: 29/137 (21%) Deep SSI: Intervention: 7/137 (5.1%) Control: 7/137 (5.1%) Organ/Space SSI (vascular graft) Intervention:0/137 (0% Control: 2/137 (3%) Factors associated w/ SSI (multivariate analysis) Prosthetic material use 0.02 (95%CI 0.08-0.50) p=0.001	**Definitions:** **SSI – CDC definition** Surgical wound infection (SWI) was considered infection if there were bacteria isolated from the wound or if there were areas of localized redness, heat, swelling and pain around the wound appearing w/in 30 days after operative procedure. Surgical wounds evaluated by vascular surgeon blinded to study arm. Pneumonia: clinical diagnosis and correlative changes in chest x-ray film **Perioperative Care:** Shaving around intended surgical wound site done in operating room just before surgery. **Other notes:** Primary study design was to deliver supplemental oxygen via face mask for the first two postoperative days but patients found the face masks to be uncomfortable so the initial plan was

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			(revascularization) - 173 bypass procedures 44/173 (25%) prosthetic grafts Femoral endarterectomy n=84 Femoral bypass n=12 Femoropopliteal bypass n=92 Crural bypass n=46 Pedal bypass n=19 Embolectomy n=3 Other n=18 Operative area Inguinal:n-105 Infrainguinal: n=169 **Indications:** Claudication: 94/ 274 (34%) Rest pain: 68/ 274 (24.8%) Ischemic ulcer: 100/274 (36.5%) Other: 7//274 (4.4%) **Setting:** 5 Secondary referral hospitals & 1 tertiary referral hospital **Location:** Finland **Dates of Study:** May 2009-February 2010 (Varied between 3 and 6 months between 6 hospitals.) **Inclusion Criteria:** Adult patients who underwent non-emergency lower limb arterial surgery **Exclusion Criteria** Refusal to participate,	was standardized to 3g cefuroxime via IV w/in 1h before incision. If operation > 4h or blood loss>1,500ml then another 1.5g Cefuroxime was administered. AMP per protocol: n=244 (89%) No AMP n=4 Received 1.5g cefuroxime n=10 Treated for infected ulcer n=11 Treated for UTI n=3 Treated for sepsis n=2	Asthma 4.83 (95%CI 1.72-13.53) p=0.003 Infrainguinal incision 2.24 (95%CI 1.07-4.67) p=0.03 Coronary Artery Disease 1.94 (95%CI 1.04-3.62) p=0.04 Supplemental oxygen 0.56 (95%CI 0.30-1.04) p=0.07 **Sub-group analysis** 103 patients w/ inguinal (isolated groin) incision only SSI Total SSI 15/103 (15%) Intervention: 3/52 (6%) Control: 12/51 (24%) *P*=0.01 No differences in secondary outcomes between groups in the sub-group analysis BMI>25kg/m^2 was independent risk factor for SWI OR 1.22, 95%CI 1.03-1.45;P=0.02 Supplemental oxygen was associated with reduced risk OR, 0.20, 95%CI, 0.04-0.95;P=0.04 **Other infections:** Pneumonia: *p*=0.18 Intervention: 1/137 (0.7%) Control: 4/137 (2.9%)	changed 2 weeks after data collection had started. Whether patient received AMP per protocol or not, did not affect incidence of SWI. **Follow-Up:** For 30 days or until the SWI healed **Funding Source Conflicts:** Authors: NR Institution: NR Study: NR Supplies: NR

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			hypercapnic chronic obstructive pulmonary disease (COPD), or oxygen saturation less than 90% measured by a finger pulse oximeter when breathing room air.		**Topic-specific outcomes:** Mean toe tip oxygen saturation after surgery. Was not significantly different between 2 groups except at: <u>24hrs after surgery</u> Intervention: 94.4% Control: 91.9% *P*=0.034 <u>28hrs after surgery</u> Intervention: 95.0% Control: 92.4% *P*=0.025 **Reoperation:** 58/63 (92%) SSI patients were cured with treatment2/63 (3%) SSI patients required limb amputation due to SSI (one study one control group) **Length of Stay:** Postoperative stay Intervention: 6.5d (SD9.4) Control: 5.4d (SD4.3) *P*=0.13 **Mortality:** at 30 days Intervention: 3/137 (2.2%) Control: 1/137 (0.7%) Cause of death: 1 aspiration pneumonia 3 myocardial infarction (MI) including one intervention patient died from an MI on POD#30 and SWI had not yet healed, 3 had no SWI at the time of death	

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					Of note: 1 control group patient died of renal failure on POD#64 and had a SWI not cured at the time of death **Adverse Events** Graft Thrombosis: *p*=0.39 Intervention: 5/137 (3.6%) Control: 8/137 (5.8%) Cardiac complication: *p*=0.81 Intervention: 6/137 (4.4%) Control: 5/137 (3.6%) Stroke: *p*=0.08 Intervention: 3/137 (2.2%) Control: 0/137 (0%) Renal insufficiency: *p*=0.31 Intervention: 3/137 (2.2%) Control: 1/137 (0.7%)	
Bickel 2011 [92] (ES)	**RCT** 1, 2, 3, 4, 5, 6, 7, 8 10	To assess the influence of hyper-oxygenation on surgical site infection by using the most homogeneous study population: single diagnosis (acute appendicitis) using 1 standard surgical approach (open appendectomy through a	**Number of patients :** N=210 **Patient Characteristics:** No statistically significant difference in characteristics between the 2 groups. (Including smoking history, obesity, shaving, and timing of antimicrobial administration). All patients categorized as having ASA score of 1 or 2. Age, years: 28.0 (SD 11.5; range 15-71) Gender (m/f): 152/57 Obesity: NR Co-morbidities (out of n=210) Ischemic heart disease: 3.1%	**Intervention:** n= 107 Intraop: FIO_2 80% combined with 20% air. Postop: In recovery room, flow rate was 10L/min (high-flow) for 2 hours via non-rebreathing mask. **Timing of Intervention:** Intra- & post-operatively **Duration of Treatment:** From Induction of anesthesia to 2 hours post-operatively **Device**: Nasal cannula for control and nonrebreathing mask with a reservoir for the intervention **Monitoring Intervention:** Pulse oximetry during anesthesia & recovery period. Arterial blood obtained after anesthesia induction & during surgery and 2 hours after recovery from anesthesia.	**SSI** Total SSIs: 20/210 (9.5%) Intervention: 6/107 (5.6%) Control: 14/103 (13.6%) *P*=0.04 **SSI by patient subgroup** Normal appendix (n=9) Intervention: 0/4 Control: 0/4 P >.99 Acute appendicitis (n= 35) Intervention: 2/18 (11%) Control: 0/17 P=0.20 Phlegmonous appendicitis (n=123) Intervention: 1/63 Control: 6/60 *P*=0.049	**Definitions:** **SSI:** Evaluated clinically according to obvious signs and symptoms such as local induration & erythema, purulent discharge & need to explore the wound. Supportive results included increased white blood cell count, fever, and radiological evidence of infectious collections, positive culture findings and resolution of mild infectious findings following antimicrobial treatment. ASEPSIS score taken **Perioperative Care:** Anesthesia introduced with fentanyl citrate, propfol, or thiopental sodium, and

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		McBurney incision in the right lower quadrant of the abdomen).	Hypertension: 7.4% Diabetes: 0.6% Pulmonary disease: 1.3% **Procedure:** Open appendectomy through a McBurney incision in the right lower quadrant of the abdomen **Indications:** acute appendicitis diagnosed by clinical criteria (right lower quadrant pain, local tenderness, etc.), blood test results & results of imaging modalities (ultrasonography or abdominal computed tomography) suggestive of acute appendicitis **Setting:** Department of surgery in a Government Hospital **Location:** Israel **Dates of Study:** November 1, 2006 – May 31, 2009 **Inclusion Criteria:** Adults (>15 years) with acute appendicitis having open appendectomies **Exclusion Criteria** Chronic obstructive pulmonary disease, severe malnutrition (serum albumin conc. <3g/dL) or immunodeficiency disease	Surgical wounds evaluated daily. After discharge, evaluation was done at surgical outpatient clinic by senior surgeon w/in 2 weeks of surgery **Control:** n=103 Intraop: FIO_2 30% O_2 combined with 70%N. Postop: In recovery room, flow rate was 4L/min for 2 hours. **Standard Preventative Measures:** Antimicrobial prophylaxis-: Preoperative antimicrobials: aminoglycosides (gentamicin sulfate) and metronidazole. When intraoperative findings indicated gangrenous or perforated appendicitis, antimicrobial treatment lasted 5 days. Fluids: Adequate hydration was strictly maintained during the operation and convalescence Ventilation: mechanically controlled at a frequency and tidal volume to maintain normocapnea. Normothermia: Core temperature was strictly maintained during the operation and convalescence Wound closure: Following resection of inflamed appendix, the surgical wound in the lower right quadrant of the abdomen was meticulously irrigated and sutured with absorbable	Gangrenous appendicitis (n=43) Intervention: 3/22 (13.6%) Control: 8/21 (38.1%) *P*=0.06 **ASEPSIS Score** Satisfactory Healing Intervention: 101 (94.4%) Control: 89 (86.4%) Disturbance of healing Intervention: 2 (1.8%) Control: 5 (4.9%) Minor wound infection: Intervention: 2 (1.8%) Control: 3 (2.9%) Moderate wound infection: Intervention: 2 (1.8%) Control 5 (4.9%) Severe wound infection: Intervention: 0 (0%) Control 1 (1.0%) ASEPSIS Score: "A significant difference was recorded between the two study populations" (P=0.03)" Wound problems Intervention: 6/ 107 (5.6%) Control: 14/ 103 (13.6%) **Other infections:** NR **Topic-Specific outcomes:** Partial pressure of oxygen (PO_2) in arterial blood: mean (SD);P-value Before starting surgery: Intervention: 263.30 (87) Control: 179.95(78) P=0.001	rocuronium bromide or atracurium besylate following pre-oxygenation via mask. It was maintained with nitrous oxide and oxygen, isofluorane, 1% rocronium bromide, or atracurium besylate, and fentanyl citrate. **Other Notes:** Preoperative SSI Risk Stratification: SENIC & NNIS They note that while the rate of SSI reached statistical significance (P=0.04), using the 2-tailed Fisher exact test will lead to a P=0.06 **Follow up:** 14 days for SSI, then length of hospital stay Funding Source Conflicts: Authors: None Institution: None Study: None Supplies: None

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				sutures. Skin was closed with metal clips (including cases of gangrenous appendicitis).	<u>During surgery before wound closure</u> Intervention: 275.47 (95) Control: 149.37 (48) P=0.001 <u>In recovery room</u> Intervention 188.6 (73) Control 142.3 (65) P=-0.02 **Reoperation:** <u>Wound exploration 12/20 SSIs</u> Intervention: 4/6 (66.7%) Control: 8/14 (57.1%) P>0.99 **Length of stay**: mean (SD) Total: 2.71 days (1.25) Intervention: 2.51 days (0.88) Control: 2.92 days (1.05) *P*=0.1 **Mortality:** NR **Adverse Effects:** NR	
Meyhoff 2009 [94] (ES)	**RCT** 1, 2, 3, 4, 5, 6, 7, 8, 9, 10	To assess whether use of 80% oxygen reduces the frequency of surgical site infection without increasing the frequency of pulmonary complications in patients undergoing abdominal surgery	**Number of patients:** N = 1395 in per protocol analysis. 1386 in intention to treat analysis **Patient characteristics:** Pre-operative and perioperative characteristics compared and no statistically significant difference found between groups. (data below listed for intervention) Age: (median(5-95%)) : 64y (27-85) Gender:	**Intervention:** n=690 in per protocol analysis. 685 in intention to treat analysis <u>Intraop:</u> 100% FIO_2 at induction of anesthesia until intubation. Then 80% FIO_2 from intubation until the end of surgery. Postop: The first two hours following intubation patients received 80% FIO_2 via a nonrebreathing mask with a reservoir w/ a flow of 14L O_2 & 2L air per minute **Timing of Intervention:** Intra & Postoperatively **Duration of Treatment:** From	**SSI: Follow up 14 days** Intervention: 131/685 (19.1%) Control: 141/701 (20.1%) Univariate OR 0.94 (95%CI 0.72-1.22) p=0.64 Adjusted OR 0.91 (95%CI 0.69-1.2) p=0.51 **Infection Location:** <u>Superficial:</u> Intervention: 75/131 (57.3%) Control: 76/141 (53.9%) <u>Deep</u> Intervention: 20/131 (15.3%) Control: 26/141 (18.4%)	**Definitions:** **SSI**: CDC definitions Pneumonia- CDC Criteria (NNIS) Respiratory failure - the need for controlled ventilation or arterial oxygen saturation below 90% despite supplemental oxygen BMI: <30 or ≥30 calculated as weight in kg divided by height in m^2 Risk of SSI assessed with NNIS and SENIC. **Perioperative Care:**

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
		(laparotomy).	Men (no (%)): 228/690 (41.7%) Obesity: BMI, median (5-95%): 25kg/m^2 (18-35) BMI≥30, no (%): 102/690 (14.8%) Comorbidity: Current smoker: 207/690 (30.0%) Alcohol consumption >48g/d: 29/690 (4.2%) Previous abdominal surgery: 298/690 (43.2%) Diabetes mellitus 51/690 (7.4%) COPD: 35/690 (5.1%) Other pulmonary disease: 45/690 (6.5%) Hypertension: 209 (30.3%) Other cardiovascular disease: 125/690 (18.1%) Current signs of infection: 76/690 (11.0%) Immune deficiency: 27/690 (3.9%) Other disease209/690 (30.3%) **Procedure: (N=1386)** Colorectal: 633/1386 (45.7%) Gynecological: 268/1386 (19.3%) Small Bowel surgery: 158/1386 (11.4%) Appendectomy: 124/1386 (8.9%) Other: 203/1386 (14.6%) Operation Classification:	induction of anesthetic to 2hrs postop **Device:** High concentration oxygen mask **Monitoring Intervention:** Pulse Oximetry **Control:** n=705 in per protocol analysis. 701 in intention to treat analysis Intraop: 100% FIO_2 at induction of anesthesia until intubation. Then 30%FIO_2 from intubation until end of surgery. Postop: During the first two hours after surgery, patient received O_2 via Nonrebreathing mask w/ a flow of 14L air & 2L O_2 per minute. In both groups FIO_2 was increased if hypoxia was detected or suspected to ensure arterial oxygen saturation >94% and arterial oxygen tension >9kPa. **Standard Preventative Measures:** Analgesia - Epidural Normothermia: control of temperature Glycemic: Control of glucose level Bowel Prep: absence of pre-operative bowel preparation. AMP**:** first and second antimicrobial administered w/in 60 minutes of skin incision. Cefuroxime & metronidazole	Organ/ Space (Intra-abdominal) Intervention: 36/131 (27.5%) Control: 39/141 (27.7%) ASEPSIS Score>20: Intervention: 32(4.7) Control: 36 (5.1) Per protocol analysis (N=1081) SSI Intervention: 122/555 (22.0%) Control: 116/526 (22.1%) P=0.98 **Other infections:** Pneumonia: (14 days) Intervention: 41/685 (6.0%) Control: 44/701 (6.3%) Univariate OR 0.95 (95%CI 0.61-1.48) p=0.82 Adjusted OR 0.95 (95%CI 0.60-1.49) p=0.81 **Topic Specific outcomes:** NR **Reoperations:** For all reasons**-** does not specify how many for SSI Intervention: 104/685 (15.2%) Control: 104/701 (14.8%) **Length of stay:** Postoperative hospitalization (Mean? (range)) Intervention: 6d (1-34) Control: 7d (2-36)	Standardized inhalational or intravenous anesthesia without nitrous oxide depending on attending anesthetist. **Other notes:** Adjusted OR adjusted for study center, BMI (<30 or ≥30), diabetes mellitus, acute or elective surgery, COPD, current smoker, incision extending above umbilicus, duration of surgery, and age (≥40 years or <40 years) **Follow-Up**: SSI monitoring for 14 days, Then postop day 13-30 via telephone if necessary **Funding Source Conflicts:** Authors: None Institution: None Study: None Supplies: None

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			Clean: 318/1386 (22.9%) Clean-contaminated: 796/1386 (57.4%) Contaminated: 235/1386 (17.0%) Dirty-Infected: 37/1386 (2.7%) **Indications:** (# of patients/1386) Cancer: 714 (51.5%) Benign neoplasm: 108 (7.8%) Appendicitis: 121 (8.7%) Intestinal obstruction due to benign disease: 124 (8.9%) Inflammatory bowel disease: 79 (5.7%) Diverticulitis: 57 (4.1%) Other: 183 (13.2%) **Setting:**14 Hospitals **Location:** Denmark **Dates of Study:** Oct 2006-Oct 2008 **Inclusion Criteria:** Patients ≥18yrs who underwent acute or elective laparotomy. (When laparotomy was indicated for gynecological disease, only patients with suspected malignancy [risk of ovarian malignancy index>200 or a specimen showing atypical or neoplastic cells] were included.) **Exclusion Criteria:**	given intravenously was standard choice, but ampicillin or benzylpenicillin in combination with gentamicin and metronidazole were also allowed. 1305/1386 (94%) received AMP. Of those that received AMP: 1169/1305 (90%) Appropriate AMP 880/1305 (67%) Timely AMP Fluids: given only to replace measured or calculated deficits aiming at a post-op weight increase of less than 1kg Transfusion: blood replaced 1:1 with colloids & transfusion initiated if blood loss exceeded 20 mL/kg.	OR -0.69 (-2.3-0.93) P=0.09 **Mortality:** at 30 days Intervention: 30/685 (4.4%) Control: 20/701 (2.9%) Univariate OR 1.56 (95%CI 0.88-2.77) p=0.13 Adjusted OR 1.55 (95%CI 0.86-2.85) p=0.15 **Adverse Effects:** Wound-related, UTI, Postoperative nausea or vomiting, respiratory, circulatory, gastrointestinal tract, sepsis, or other recorded and not statistically different between groups. **Topic specific outcomes** Hypoxia: NR <u>Atelectasis: (14 days)</u> Intervention: 54/685 (7.9%) Control: 50/701 (7.1%) Univariate OR 1.11 (95%CI 0.75-1.66) p=0.60 Adjusted OR 1.13 (95%CI 0.75-1.72) p=0.56 Respiratory Failure (14 days) Intervention: 38/685 (5.5%) Control: 31/701 (4.4%) OR 1.27 (95% CI, 0.78-2.07) P=0.34 Adjusted OR 1.22 (95% CI,0.74-2.03) P=0.44	

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			Operations performed under general anesthesia w/in 30 days, chemotherapy for malignancy w/in 3 months, inability to provide informed consent, and preoperative arterial hemoglobin oxygen saturation below 90% without supplemental oxygen assessed by pulse oximetry		Admission to ICU (other than normal postop-not statistically significant	
Gardella 2008 [98] (ES)	**RCT** 1, 2, 3, 4, 5, 6, 7, 8, 9, 10	To test the hypothesis that high-concentration, inspired oxygen delivered during cesarean delivery and for 2 hours postoperatively decreases the incidence of surgical site infection	**Number of patients:** N=143 **Patient characteristics:** The study groups were similar for a large number of clinical variables, including body mass index, maternal diabetes, group B streptococcus colonization, gestational age at delivery, and duration of surgery, surgical blood loss & prophylactic usage of antimicrobials. Though not statistically significant, more patients with diabetes mellitus were randomized to the intervention group. Hypertensive disorders were more prevalent in the control group. Age**:** 16-47 y Gender: 100% female Obesity:	**Intervention:** n=69 80% Oxygen at 15L/min **Timing of Intervention:** Intra and post-operatively **Duration of Treatment:** From anesthesia induction to 2hrs post-operatively. **Device:** Covered oxygen blender was set to predetermined mixture of O2 & air to an adult nonrebreathing mask **Monitoring Intervention:** Venous Blood Gas collection from the dorsum of the foot in a subset of the high-oxygen group **Control:** n=74 30% oxygen at 15L/min **Standard Preventative Measures:** Skin Prep: Routine surgical preparation with betadyne scrub. AMP: All but one received	**SSI: Follow up 14 days** Intervention: 17/69 (25%, 15-35%) Control: 10/74 (14%, 6-22%) Relative risk of outcome associated with High O2 1.8 (95%CI, 0.9-3.8)*P*=.12 <u>Cellulitis</u>**:** Intervention: 10/69 (14%) Control: 7/74 (9%) RR (95%CI): 1.5 (0.6-3.8) *p*=.44 <u>Postpartum endometritis:</u> Intervention: 9/69 (13%) Control: 5/74 (7%) RR (95%CI): 1.9 (0.67-5.5) *p*=.26 <u>Wound separation:</u> Intervention: 5/69 (7%) Control: 2/74 (3%) RR (95%CI): 2.7 (0.5-13.4) *p*=.26 <u>Subanalysis of SSI risk factors:</u> <u>Surgical blood loss</u>	**Definitions:** **SSI**: Administration of intravenous antimicrobials for postpartum endometritis or oral and intravenous antimicrobial for wound infection during the initial hospital stay or within 14 days of surgery. Included cellulitis as well as deeper incisional infections that required wound to be opened. Endometritis: Fever ≥38.5^{o}C within the first 24 hours postpartum or>38.0^{o}C for at least 4 hours after the first 24 post-partum associated with uterine tenderness greater than expected without other identified fever sources (Ernest 2000) Relative Risk Adjustment-adjusted for gestational or chronic hypertension

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			BMI median (range): 32 kg/m^2 (22-51) Comorbidities: NR **Procedure:** Cesarean section **Indications:** Not Recorded **Setting:**1 University Hospital **Location:** USA **Dates of Study:** October 2001 – April 2007 **Inclusion Criteria:** Women who underwent a clinically indicated caesarian delivery after the onset of labor or rupture of membranes **Exclusion Criteria:** Cesarean delivery before the onset of labor or rupture of membranes, emergent cesarean delivery, general endotracheal anesthesia (those who started with regional anesthetic and converted to general were not excluded), clinical chorioamnionitis, & HIV infection	prophylactic antimicrobials. 97 received it at cord clamp; 45 received it at case start.	Intervention: 900cc (range, 600-1250) Control: 800cc (range, 300-1500) P=0.04 All other factors not statistically significant, including Intraoperative partial pressure of venous oxygen mean and range (P=0.91) and intraoperative partial pressure of venous oxygen >200mmHg or ≤200mmHg (P=0.76) **Other infections:** NR **Topic Specific outcomes:** <u>Venous Oxygen saturation, median % (range)</u> Intervention: 99 (23-99) Control: 99 (57-99) P=0.006 <u>Partial pressure of venous oxygen, median mm Hg (range)</u> Intervention: 177 (20-449) Control: 122 (20-449) P=0.001 <u>Surgical Estimated Blood Loss: median (range)</u> Intervention: 900cc (600-1,250) Control: 800cc (300-1,500) *p*=.04 **Reoperation: NR** **Length of stay:** days median (range) Intervention: 3 (2-5) Control: 3 (2-6) *p*=.92	**Perioperative Care:** Regional not general anesthetic (standard for cesarean section delivery) **Other notes**: The *P*-value exceeded the *P*-value for futility suggesting these differences were unlikely to reach statistical significance with continued recruitment. The study was ended early Eight documented protocol deviations occurred in each group, most due to intermittent mask use due to nausea/vomiting during surgery or patient request post-partum to facilitate infant bonding. **Follow-Up:** 14 days- All participants followed throughout hospitalization; of those without SSI during initial hospitalization, 7 controls and 2 interventions were lost to 2 week postpartum follow up (they were kept in analysis and considered to not have an SSI) **Funding Source Conflicts:** Authors: None Institution: None Study: None Supplies: None

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					Mortality: NR **Adverse Events:** Readmission: Intervention: 3/69 (5%) Control: 2/74 (4%) RR (95%CI): 1.4 (0.2-8.4) *p*=.99 Intravenous antimicrobial treatment: Intervention: 10/69 (14%) Control: 5/74 (7%) RR (95%CI): 2.1 (0.8-6.0) *p*=.17	
Belda 2005 [91] (ES)	**RCT** 1, 2, 3, 4, 5, 6, 7, 8, 10	To test the hypothesis that supplemental oxygen reduces infection risk in patients following elective colorectal surgery	**Number of patients: N**= 291 **Patient Characteristics:** Morphometric, demographic, & other preoperative characteristics were similar in the 2 treatment groups. Except that intervention was shorter in height & had more women. Age**:** Specifics NR = 18-80 years Gender: m/f Intervention: 71/77 Control: 91/52 Obesity: BMI: mean (SD): Intervention: 27.1 (4.5) Control: 26.5 (3.8) BMI> 30: Intervention: 26/148 (17.5%) Control: 21/143 (14.9%) Other than percentage of inspired FIO_2 and	**Intervention:** n=148 Intraop: At intubation-Oxygen/ air mixture with an FIO_2 of 80%. Intraop: At extubation increased to 100% at extubation. Postop: First 6hrs non-rebreathing facemask with reservoir with oxygen administered at the randomly designated concentration (80%) at a total flow of 16L/min Postop after 6 hours-ambient air with supplemental oxygen provided as necessary to maintain pulse oximetry of at least 92% **Timing of Intervention:** Intra and postoperatively **Duration of Treatment:** From anesthesia induction until 6 hours postoperatively. **Device:** Intraop- intubated; Post-op= non-rebreathing face masks w/ a reservoir. **Monitoring Intervention:** FIO_2, pulse oximetry were	**SSI (Follow up 14 days)** Total: 57/ 291 (39.3%) Positive cultures for pathogenic bacteria: 50/57 Intervention: 22/ 148 (14.9%) Control: 35/ 143 (24.4%) Analysis for increased risk of SSI 80% FIO_2 Unadjusted univariate RR, 0.61; 95%CI 0.38-0.98; *P*=0.04 80%FiO_2: Adjusted multivariate RR 0.46; CI 95%, 0.22-0.95; *P*=0.04 (Risk of SSI reduced 54%) Coexisting Respiratory disease: Unadjusted univariate RR 2.15 (95% CI, 1.03-4.48) Adjusted multivariate RR 3.23 (95% CI, 1.18-8.86) *P*=0.04 **ASEPSIS Score >20 on any postoperative day**:	**Definitions:** **SSI** CDC definitions Surgical wounds assessed daily by blinded surgeon. Purulent exudates were cultured & when positive for pathogenic bacteria, appropriate antimicrobial given. **Wound Healing** Evaluated using ASEPSIS score (>20 =infection) Respiratory Disease- - history of COPD, asthma requiring routine medication or other clinically important respiratory impairment. **Perioperative Care:** Anesthesia induction & treatment were standardized across all patients. Blinded attending surgeon administered analgesic agents, determined initiation of feeding, ambulation & the duration of hospitalization.

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			resulting PaO_2 there were no significant differences between the groups for >30 other potential intra or postoperative confounding factors. Comorbidities: Respiratory disease: Intervention: 25/148 (17.1%) Control: 16/143 (11.2%) PaO_2 mmHg 1h post-induction Intervention: 285.9 (96.6%) Control: 117.5(40.6%) P<0.05 PaO_2 mmHg 2h post-induction Intervention: 233.7 (89.7%) Control: 125.4 (49.0%) P<0.05 Excepting post-op hemoglobin, all other physiological variables, lab test results dada, ASEPSIS index & extrinsic infection risk factors were similar between groups. Postop hemoglobin: mean (SD) g/L Intervention: 11.0 (1.2) Control: 11.5 (2.5) *P*< 0.05 **Procedure:** Colorectal surgery Total or subtotal colectomy: 11/291 (3.8%)	continuously monitored during the surgery and in the recovery room. Arterial blood sample obtained 1h after anesthesia induction to evaluate PaO_2; another was again 2 hours after intubation. **Control:** n= 143 Intraop: At intubation Oxygen/ air mixture with an FIO_2 of 30% Intraop: At extubation increased to 100%. Postop: First 6hrs non-rebreathing facemask with reservoir with oxygen administered at the randomly designated concentration (30%) at a total flow of 16L/min Postop after 6 hours-ambient air with supplemental oxygen provided as necessary to maintain pulse oximetry of at least 92% **Standard Preventative Measures:** Mechanical Bowel Prep: using an electrolyte solution w/ no antimicrobials or antiseptics AMP: w/ metronidazole plus cefoxitin or a 3rd generation cephalosporin was administered 60-90 minutes before the surgical incision & continued postoperatively for up to 48 hours. Aminoglycosides used as an alternative to β-lactam antimicrobials in patients who	Intervention**:** 25 (16.9%) Control**:** 37 (25.9%) *P* = 0.06 **Other infections:** NR **Topic specific outcomes:** Partial (arterial) pressure of oxygen: 1h postinduction in mm Hg: Intervention: 285.9 (96.6%) Control: 117.5 (40.6%) P<0.05 Partial (arterial) pressure of oxygen: 2h postinduction: Intervention: 233.7 (89.7%) Control: 125.4 (49.0%) P<0.05 **Reoperations:** NR **Length of stay:** Intervention: 11.7 days (7.0) (SD??) Control: 10.5 days (4.4) *P*=0.09 **Mortality:** Control: 2 died of multi-organ failure of septic origin **Adverse Events** ICU Admission (not planned): Intervention: 4/148 (2.7%) Control: 5/143 (3.5%) P=0.74	**Other notes:** Preoperative SSI Risk Stratification: SENIC 1/2/3: (%) Intervention: 19.4/64.2/16.2 Control: 15.4/74.1/10.5 NNIS 0/1/2: (%) Intervention: 16.9/58.1/25.0 Control: 12.6/68.5/18.9 True ITT analysis was not possible cause of incomplete follow up date so they conducted a sensitivity analysis based on treatment group assignment that included all patients except 4 who should have been excluded because 2 had laparoscopic surgery and 2 had low preop albumin **Follow-Up:** 14 days after surgery **Funding Source Conflicts:** Authors: None Institution: None Study: Industry Supplies: Industry

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			Hemicolectomy: 89/291 (30.6%) Rectum resection with abdominal-perineal repair: 29/291 (10.0%) Sigmoid anterior resection: 87/291 (29.9%) Rectal anterior resection: 53/291 18.2%) Other: 22/291 (7.6%) **Indications:** Cancer Intervention: 126/148 (85.8%) Control: 124/143 (86.7%) Inflammatory bowel disease Intervention: 14/148 (9.4%) Control: 10/143 (7%) Other Intervention: 7/148 (4.7%) Control: 9/143 (6.3%) **Setting:** 14 hospitals **Location:** Spain **Dates of Study:** March 1, 2003 –October 31, 2004 **Inclusion Criteria**: Patients undergoing elective colorectal resection (abdominal-peritoneal reconstructions) **Exclusion Criteria:** Minor colon surgery, (polypectomy, isolated colostomy), laparoscopic surgery, surgery less than 1 hour, fever, existing signs of infection, diabetes mellitus type 1 or	reported cephalosporin allergy history. Type and duration of AMP in first 48hrs similar in the two groups. Normothermia: Maintained w/ circulating-water mattresses & forced-air heaters. Fluids: administered intraoperatively at 15mL/kg per hour; blood loss restored with crystalloids or colloids &, when necessary, w/ leukocyte-filtered allogeneic red blood cell concentrate. Fluid administered at 3mL/kg per hour during first 6 postoperative hours then reduced to 2mL/kg per hour after transferred to ward. Wound Closure: They were covered with conventional gauze bandages. An antiseptic solution was applied to the surface of the wound but neither intraperitoneal antimicrobials nor antiseptics were used. Analgesic: Patients who reported post-op pain score of more than 3cm on a 10-cm visual analog scale (0=no pain, 10= worst pain imaginable), patient was administered an intramuscular or IV morphine & non-steroidal anti-inflammatory drug.		

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			2, HIV, weight-loss >20% in the previous 3mos, serum albumin conc. < 30g/L & a leukocyte count < 2500 cells/mL			
Pryor 2004 [97] (ES)	**RCT** 1, 2, 3, 4, 5, 6, 7, 8, 9, 10	To determine whether the routine use of high FIO_2 during the perioperative period alters the incidence of SSI in a heterogeneous general surgical population in an academic setting.	**Number of patients:** N=160 **Patient Characteristics:** Preoperative patient characteristics such as sex, age, etc. were recorded and not found to be statistically significant except for BMI, Obesity & Pulse though they were not found to be indicators of SSI in multivariate analysis. Age: >18y Gender: NR BMI mean (SD) Intervention: 27.1 (6.7) Control: 25.1 (5.0) P=0.04 Obesity: BMI>30, No (%) Intervention: 19/80 (23.8%) Control: 9/80 (11.3%) P=0.04 Fifteen obese patients had BMI<35. No significant difference between groups if BMI defined as >32 or >35 Pulse, beats/min (SD) Intervention: 83 (14) Control: 79 (14) P=0.04 Comorbidities: COPD	**Intervention:** n=80 Intraop: Pre-oxygenation, induction, emergence and extubation: FIO_2 100% Intraop: 80% Oxygen (FIO_2 of 0.80) FIO_2 could be increased as required to maintain arterial oxygen saturation >94%. Postop Transport from OR: 80% Oxygen 10 L/min via closed reservoir bag-mask In recovery extubated: 80% Oxygen via a high-flow non-rebreathing, humidified, aerosol delivery system for 2 hours In recovery intubated: 80% Oxygen through ventilator for 2 h, then recovery/ICU team determined therapy **Timing of Intervention:** Intra and postoperatively **Duration of Treatment:** During surgery and for the first 2 hours postoperatively **Device:** During Transport: Intervention: Closed reservoir bag-mask system Control: Nasal cannula In recovery: high-flow nonrebreathing, humidified,	**SSI (Follow up 14 days)** No (%) Overall: 29/160 (18.1%) Intervention: 20/80 (25%) Control: 9/80 (11.3%) *P* = 0.02 OR 2.63 (95%CI, 1.1-6.2) RR 2.22(95%CI, 1.1-4.6) Multivariate analysis : FIO_2 (P=0.03) and staying intubated at the end of surgery remained predictive of infection Superficial (Wound only) Intervention: 13/20 (65%) Control: 5/9 (56%) *P* = 0.84 Deep structures Intervention: 3/20 (15%) Control: 1/9 (11%) *P* = 0.84 Wound and Deep structures Intervention: 4/20 (20%) Control: 3/9 (33%) *P* = 0.84 Time to first detection of infection Mean (SD) 5.6(2.4) days **Other infections:** NR **Topic specific outcomes:** **Arterial Oxygen Saturation (recovery)** Intervention vs. control	**Definitions:** **SSI**: SSI was assessed by investigator blinded to randomization via a retrospective chart review looking for SSI criteria being met at one of two phases: (1) during hospitalization and (2) for those discharged in <14 days without evidence of SSI, then at first postop visit with surgeon, any emergency department visits, telephone calls or other contacts within first 14 days postop. SSI Criteria prospectively defined: 1.surgical team clearly documented clinical assessment of SSI 2.SSI precipitated management action (changing antimicrobials, opening wound, aspiration, drain placement , further surgery 3.clinical assessment supported by at least 3 of the following objective criteria prospectively assigned by the study: • WBC Count>11000µL • Temperature>38.5°C • Radiological Evidence

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			Intervention: 0/80 (0) Control: 5/80 (6.3%) P=0.06 Minimum temp ,mean (SD) °C Intervention: 35.5(0.7) Control: 35.4(0.6) P=0.54 Temp at extubation ,mean (SD) °C Intervention: 36.2 (0.07) Control: 36.1 (0.6) P=0.20 **Procedure:** Colectomy (right, left, hemicolectomy & sigmoid), low anterior resection, abdominoperineal resection, gastrectomy, pancreaticoduidenectomy , exploratory laparotomy, and large gynecologic staging/ de-bulking procedures in which bowel or peritoneum was involved. **Indications:** Cancer Intervention: 36/80 Control: 30/80 Non-Cancer Intervention: 44/80 Control: 48/80 **Setting:** University Hospital **Location:** NYC, USA **Dates of Study:** September 2001-May 2003 **Inclusion Criteria:** Patients >18 y old undergoing	aerosol delivery system with selector to provide stable FIO_2 to the facemask. **Monitoring Intervention:** Pulse oximetry **Control:** n=80 Intraop: Pre-oxygenation, induction, emergence and extubation: FIO_2 100% Intraop: 35% Oxygen (FIO_2 0.35) Postop Transport from OR: 35% Oxygen at 4 L/min (nasal cannula) In recovery extubated: 35% Oxygen at 4 L/min via a high-flow nonrebreathing, humidified, aerosol delivery system. In recovery intubated: 35% Oxygen through ventilator for 2 h, then recovery/ICU team determined therapy **Standard Preventative Measures:** Bowel prep: regimen undertaken night before surgery according to surgeon's instructions. AMP choice and timing recorded. AMP: Intravenous antibiotics either immediately before arriving or upon arrival to operating room according to surgeon's usual practice. Received AMP: Intervention: 80/80 (100%) Control: 78/80 (97.5%) P=.26	p=0.005 (rank sum analysis) but values for both groups well within acceptable range (99% [1%] vs. 98% [2%]) **Estimated Blood Loss** mL mean (SD) Intervention: 230 (180) Control: 200 (190) P = 0.03 **Crystalloid** L: Intervention: 4.5(2.1) Control: 3.8(1.9) P=0.02 Blood loss and Crystalloid not significant on multivariate analysis **Nitrous oxide 30 min after incision** mean (SD), %vol/vol Intervention: 5 (10%) Control: 21 (30%) P=0.008 **Reoperations:** Intervention: 4/80 (5.0%) Control: 0/80 *P*=0.06 **Length of stay:** mean days (SD) Intervention: 8.3 (7.5) Control: 6.4 (4.7) *P*= 0.07 SSI: 13.3 (9.9) No SSI. 6.0 (4.2) P<0.001 **Mortality** POD#16 1 Control patient	of infection • Extrusion of pus from site • Positive culture from site • New erythema and induration that responded to treatment of infection **Perioperative Care:** Anesthesia- general- heterogeneity in inhalation agents used: Isoflurane Intervention: 68.8% Control: 75% Sevoflurane Intervention: 21.3% Control: 17.5% Desflurane Intervention: 10.0% Control: 7.5% **Other notes:** Preoperative SSI Risk Stratification: NNIS M/0/1/2/3 Intervention: 7/32/35/5/2 Control:9/31/34/6/0 P=0.94 NOTE: Initial power analysis does not indicate baseline SSI rate. It determined that 300 patients were needed for a detectable treatment effect of 40%. Interim analysis was planned to be performed after 160 patients recruited and study halted if P≤0.03. This study represents that interim

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			major abdominal surgical procedures under general anesthesia. Laparoscopically assisted procedures were eligible provided that laparotomy was performed at some point during the surgery. **Exclusion Criteria:** Exclusively laparoscopic procedures, patients whose respiratory status required an FIO_2 in excess of 0.35, patients with severe chronic obstructive pulmonary disease (COPD) who were likely to experience respiratory depression at FIO_2 of 0.80 (minor COPD acceptable), patients who were hemodynamically unstable prior to surgery (systolic blood pressure <90mmHg or use of vasopressors), patients who had received bleomycin at any time & patients who had an ASA status class 5 or 5E indicating patient is not expected to survive 24 hours regardless of the surgery. Fully laparoscopic procedures were excluded.	Admission to hospital: most admitted on morning of surgery.	who developed an incisional SSI, later a deep abscess, had a postoperative myocardial infarction, followed by a stroke and died **Adverse Events:** Pulmonary embolus: 1 Intervention patient had a pulmonary embolus on POD#3 but recovered without incident	analysis, enrollment stopped after statistically significant difference in SSI rates between groups noted. **Follow-Up:** 14 days **Funding Source Conflicts:** Authors: None Institution: None Study: None Supplies: None

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
Whitney 2001 [101] (ES)	**RCT** 1, 10	To determine the effects of 28% oxygen given in the first 36 hours after surgery on tissue oxygen levels, collagen deposition, and clinical healing outcomes.	**Number of patients:** N=24 **Patient Characteristics:** Subjects compared on coexisting conditions, smoking history, intraoperative & postoperative variables and there were no statistically significant differences between groups. Age: 18-80 years; Mean (SD) Intervention: 41 (9.9) Control: 42 (11.5) Gender: m/f Intervention: 69%/31% Control: 85%/15% Obesity: Body surface area m^2:mean (SD) Intervention: 2.00 (0.20) Control:2.05 (0.30) Comorbidities: Cardiac History: Yes (*p*=0.084) Intervention: 0% Control: 7.1% **Procedure:** cervical fusion and/ or excision of cervical intervertebral disk (neurosurgery or the orthopedic surgery services) **Indications:** NR **Setting:** Military regional medical center **Location:** Pacific Northwest, USA **Dates of Study:** NR (24	**Intervention:** n=13 Postop: 28% Oxygen delivered at rate of 2L/min via nasal cannula **Timing of Intervention:** Postoperative – after discharge from recovery and admission to surgical unit **Duration of Treatment:** 36 hours postop **Device:** nasal cannula for delivery of the 28% supplemental oxygen for intervention **Monitoring Intervention:** Subcutaneous tissue oxygen ($P_{sc}O_2$) measured via silastic tonometer inserted subcutaneously in subject's dorsal left upper arm after anesthetic induction. Equilibration and baseline established while patient on room air. Second equilibration at 30 minutes. $P_{sc}O_2$ readings recorded at 1, 2, 18, and 36 hours postoperatively Wound healing evaluated by hydroxyproline content in a subcutaneous polytetrafluoroethylene tube removed on the 7^{th} post-op day **Control:** n=11 Room air **Standard Preventative Measures:** NR	**Wound complications:** Clinical healing (assessed through self-report and medical chart review) showed no significant differences between groups. **Self-report:** Total Wound Problems Control: 13/ 11 Intervention: 9/ 13 Self-report included notation of any wound problem, problems with wound drainage, concerns about incision redness, problems with incision swelling, incision opening, treatment sought for wound complications, treatment prescribed for problem, and pain at surgical site that did not decrease over time. **Medical Chart Review (30 days)** Complication necessitated clinic visit: Intervention: 0/13 Control: 1/11 Incision redness Intervention: 1/12 Control: 1/8 Incision drainage Intervention: 0/13 Control: 1/8 Incision swelling Intervention: 0/12 Control: 0/8	**Definitions:** **SSI**: Retrospective medical chart review (documentation of wound complications to include presenting symptoms, wound appearance, culture results [if any] and prescribed treatment. Follow up phone calls with patient questioned about wound healing problems including wound appearance and treatment. Final wound healing classification: Primary: no wound edge separation or other indication of wound healing problems. Secondary: only if patient reported partial or complete separation of the wound edges or other indications of wound healing problems and I also confirmed by medical record documentation SSI not defined, but wound complications and infections (at a left or right neck surgical wound and in some cases a thigh skin graft)were measured by three individuals using the ASEPSIS scoring method (comparisons of the ASEPSIS method with standard clinical definitions of wound infection or complications demonstrated

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			month period) **Inclusion Criteria:** Aged 18-80 years, male & female, able to read & speak English, give informed consent, & discharged from the post-anesthesia care unit without supplemental oxygen **Exclusion Criteria:** NR		Other wound problem: Intervention: 1/12 Control: 0/8 **Wound Healing Assessment** Histology scores for cellularity and presence of connective tissue or mean amounts of hydroxyproline in the ePTFE implants- No significant difference between control & intervention groups. However, only subjects in intervention group achieved hydroxyproline levels >0.40µg/mm of ePFTE tubing. ASEPSIS Scores- all within satisfactory healing (0-10 out of 20) without significant differences between the mean scores. Wound healing classification: all primary healing **Other infections:** NR **Topic specific outcomes:** Tissue oxygen mean (SD) Intervention: 63 mm Hg ±14 Control: 48 mm Hg ±7 P=0.001 No significant effects for time or for an interaction between time and group. **Reoperations:** NR **Length of stay:** NR **Mortality:** NR **Adverse Effects:** NR	that ASEPSIS was as sensitive as and significantly more specific than the other indicators of wound problems **Perioperative Care:** NR **Other notes:** NR **Follow-Up:** for 30 days post-op via medical record review & telephone call to the subject **Funding Source Conflicts:** Authors: None Institution: None Study: None Supplies: None

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
Greif 2000 [93] (ES)	**RCT** 1, 2, 3, 4, 5, 6, 7, 8, 9, 10	To test hypothesis that supplemental administration of oxygen during perioperative period decreases the incidence of wound infections in patients undergoing elective colorectal resection.	**Number of patients: N=500** **Patient Characteristics:** Patient clinical characteristics, diagnoses, surgical procedures, duration of surgery, hemodynamic values and use of anesthetic were recorded & analyzed and not found to be statistically significant between groups except as noted. **Baseline:** Age (y) (±SD) Intervention: 57±15 Control: 57±15 Gender (m/f) 280/220 Obesity: Weight (kg) Mean ±SD Intervention: 74±17 Control: 72±17 Height (cm) Mean ±SD Intervention: 170±12 Control: 169±12 Comorbidities: Smoker Intervention: 24% Control: 29% Intraop: End-tidal isoflurane concentration-% Intervention: 0.90±24 Control: 0.84±0.24 P=0.005 Difference clinically unimportant **Procedure:** Elective colorectal resection	**Intervention: n=250** Intraop: 80% Oxygen and 20% Nitrogen after induction of anesthesia and intubation. Increased 10 100% during extubation. Postop: 80% Oxygen via nonrebreathing mask for 2 hours, then room air unless additional oxygen required to maintain oxyhemoglobin concentrations of >92%. **Timing of Intervention:** Intra and Post-operatively **Duration of Treatment:** Intraop and 2 hours postoperatively**.** **Device:** Postop-Nonrebreathing mask sealed to the patient's face and connected to a valved manifold and oxygen blender. **Monitoring Intervention:** Intraop: Concentrations of inspired oxygen and end-tidal isoflurane and carbon dioxide were measured Intraop and postop: Oxygen saturation measured with pulse oximeters Arterial blood was obtained 1h after induction of anesthesia and 2h postop to measure partial pressure of oxygen. **Control:** n=250 Intraop: 30% Oxygen and 70% Nitrogen after induction of anesthesia and intubation. Increased to 100% during extubation.	**SSI (Follow up 15 days)** **Note:** Follow up evaluations not completed in 3 patients who withdrew from the study-they had no known infections and in analysis were considered uninfected. Overall incidence was 8% (6% predicted by NNIS scores) Intervention: 13/250 (5.2%) (95%CI, 2.4-8) Control: 28/ 250 (11.2%) (95%CI, 7.3-15.1) P=0.01 Absolute difference in SSI rates: 6% (95%CI, 1.2-10.8) **ASEPSIS Scores mean ±SD** Intervention: 3±7 Control: 5±9 P=0.01 **Mixed Effects model:** Only use of 30% oxygen (controls) correlated significantly with the risk of infection OR 2.3 (95%CI, 1.2-4.6) **Analysis SSI** (N=41) vs. No SSI (N=459) ASEPSIS Scores: SSI: 25±13 No SSI: 2±4 P<0.001 WBC (X10-3/mm) mean ±SD Preop- not statistically	**Definitions:** **SSI:** Likely infected: when pus could be expressed from the incision or aspirated from a loculated mass within the wound. Infected: Wounds with culture-positive pus **Wound Healing and infection** Scoring: ASEPSIS **Perioperative Care:** Was anesthesia: standardized and induced with IV thiopental sodium (3-5mg/kg of bodyweight), fentanyl (1-3 µg/kg) and vecuronium bromide (0.1mg/kg) and maintained with isoflurane adjusted to keep mean arterial blood pressure w/in 20% of pre-induction value. Additional fentanyl administered to improve analgesia when patient emerged from anesthesia. **Other notes:** NR **Preoperative SSI Risk Stratification: NNIS & SENIC (modified)** SENIC 1/2/3 – No. patients Intervention: 71/158/21 Control: 65/165/20 P=.86 NNISS 0/1/2-No.patients Intervention: 132/100/18 Control:127/106/17 P=0.86

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			Colon: Intervention: 71% Control: 63% Rectum: Intervention: 29% Control: 37% **Indications:** Cancer: Intervention: 65% Control: 55% Inflammatory Bowel Disease (IBS) Intervention: 20% Control: 25% Other Intervention: 15% Control:20% **Setting:** 3 hospitals (2 university) **Location:** Austria (2) and Germany (1) **Dates of Study:** July 1996-October 1998 **Inclusion Criteria:** Patients 18-80 y undergoing elective open colorectal resection, including those undergoing abdominal-peritoneal pull-through procedures **Exclusion Criteria:** Patients undergoing minor colon surgery (e.g. polypectomy or isolated colostomy), recent history of fever, infection or both, serious malnutrition (serum albumin<3.3g/dl, WBC	Postop: 30% Oxygen via nonrebreathing mask for 2 hours, then room air unless additional oxygen required to maintain oxyhemoglobin concentrations of >92%. **Subgroup Analysis#1 N=54 (1 center)** **Intervention:** n=22 **Control:** n=32 Wound collagen and protein deposition: near end of surgery, 7cm expanded polytetrafluoroethylene implant inserted in subcutaneous tissue a few centimeters to one side of and parallel to the surgical incision- removed on POD#7 and assayed for hydroxyproline and protein. Subcutaneous oxygen tension: oxygen sensor within subcutaneous saline-filled tonometer in the lateral upper arm. Measurement taken after induction of anesthesia and continued at designated oxygen concentration intraop and 2 h postop. **Subgroup Analysis#2 N=24 (1 center)** Intervention: n=12 Control: n=12 **Intraop:** muscle oxygen tension: Oxygen electrode inserted into quadriceps femoris (0.35mm diameter needle inserted 1mm at a time) Oxygen tension recorded at each of 200	significant difference between groups. Postop (POD#1, 3, 6, and 9) patients with SSI had statistically significant higher counts (P value range: <0.001-0.02) Staples removed (days postop) SSI: 11.1±2.4 No SSI: 10.3±1.4 P<0.001 **Length of stay-** see below **Other infections**: NR **Topic specific outcomes:** Perioperative administration of oxygen in concentrations that exceeded those designated: Intervention: 1/500 Control: 38/500 Mean ±SD All patients N=500 Arterial oxygen saturation-% Intraoperative Intervention: 99.1±0.6 Control: 98.7±1.1 P=<0.001 Partial pressure of arterial oxygen-mm Hg Intraoperative Intervention: 348±97 Control: 121±34 P<0.001 Postoperative Intervention: 206±91 Control: 114±35 P<0.001	Initial plan was to study 1000 patients – evaluate results after 500—750 patients enrolled. A priori criterion of ending the study after enrollment of 500 patients was a difference in incidence of SSI between groups with one tailed P<0.012. **Follow-Up:** 15 days postop Wounds evaluated daily until discharge then at a clinic visit15 days) **Funding Source Conflicts:** Authors: None Institution: None Study: None Supplies: None

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			<2500 cell/ml3 or loss of >20% bodyweight), and bowel obstruction.	measurement points, histogram constructed for each patient. Muscle oxygen tension evaluated 90 minutes after induction of anesthesia at the designated FIO2. **Standard Preventative Measures:** Bowel Prep: Night before, patient underwent standard mechanical bowel prep with an electrolyte solution but no intraluminal antimicrobials. AMP: IV for a mean of 2.7±2.3 days after skin incision. Mostly metronidazole combined with cefazolin, cefamandole, amoxicillin, clavulanate or mezlocillin. Types and duration of AMP were similar in the two groups. Fluid-Patients aggressively hydrated. Intraop: Crystalloid 15ml/kg/h IV; Blood loss replacement in solution to blood ratio 4:1 or colloid at2:1. Postop: Fluids at 3.5ml/kg/h X 24h then at 2ml/kg/h X24h. Leukocyte depleted blood transfusions as deemed necessary by surgeon. Surgical wound treatment (intraop): There was no antimicrobial or antiseptic irrigation of the wound or peritoneal cavity. Wound closure: standard – all deep layers including peritoneum were closed with	Oxygen saturation-% (pulse oximetry) Postoperative Intervention: 99±2 Control: 97±2 P=<0.001 Subgroup Analysis #1 N=54 Subcutaneous oxygen tension-mm Hg Intraoperative Intervention: 109±43 Control: 59±15 P<0.001 Postoperative Intervention: 73±25 Control: 54±25 P=0.02 Collagen Deposition-ng/mm Intervention: 258±118 Control: 267±109 P=0.38 Protein Deposition-ng/mm Intervention 153±91 Control: 163±74 P=0.31 Subgroup Analysis#2 N=24 Muscle oxygen tension-mm Hg Intervention: 49±10 Control: 25±6 P<0.001 **Reoperations:** NR **Length of stay:** Intervention: 12.2±6.1 days Control: 11.9±4.0 days P=0.26 **Length of stay**	

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
				continuous sutures. Subcutaneous tissues were closed with interrupted sutures & the skin was stapled Normothermia: **I**ntraoperative core temp was maintained at 36°C with use of forced air cover over the patient and warming of intravenous fluid. Intraoperative core temps monitored in the distal esophagus; Infrared aural-canal temps or axillary temps measured throughout hospitalization. Analgesic: intravenous & intramuscular opioids and administered by a study blinded nurse blinded to treatment group assignment. Restarting feeding, staple removal, patient discharge determined by attending surgeon blinded to treatment group assignment. Discharge based on return of bowel function, control of any infections and adequate healing of incision**.**	SSI (N=41) vs. No SSI(N=459) SSI: 18.7±8.3 days No SSI: 11.4±4.1 days P<0.001 **Mortality: Follow up:** 15 days Cause of death in most cases was sepsis and multi-organ failure. Intervention: 1/250 (0.4%) Control: 6/250 (2.4%) p=0.13 **Adverse Effects** Admission to ICU: for surgical complications such as dehiscence, anastomotic leak, * peritonitis. Intervention: 5/250 (2%) Control: 12/250 (4.8%) p=0.14	

Q7. What is the optimal target FIO2 to reduce the risk of SSI; how and when should it be administered? Our search did not identify RCTs or SRs that both evaluated the optimal fraction of inspired oxygen, how and when it should be administered, and included SSI as an outcome. All studies evaluating the use of supplemental increased oxygenation both intraoperative and postoperatively used 80% FiO2 as the target level.

2.1E3. RISK OF BIAS ASSESSMENTS OF STUDIES: Q6-7 OXYGENATION

eTABLE 44. Risk of Bias Assessments of Randomized Controlled Trials for Q6-7 Oxygenation

Author Year	Q	Described as randomized	Randomization appropriately performed	Described as double-blind	Outcome assessor blinded	Study participant blinded	Investigator blinded	Attrition described	Attrition smaller than 10-15% of assigned patients	Attrition appropriately analyzed	Funding source(s) disclosed and no obvious conflict of interest	Overall Risk of Bias
Question 6: Oxygenation												
Belda 2005 [91]	6	✓	✓	✓	✓	✓	✓	✓	✓		✓	Low
Bickel 2011 [92]	6	✓	✓	✓	✓	✓	✓	✓	✓		✓	Low
Duggal 2013 [99]	6	✓	✓	✓	✓	✓		✓		✓		Low
Gardella 2008 [98]	6	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	Low
Greif 2000 [93]	6	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	Low
Meyhoff 2009 [94]	6	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	Low
Pryor 2004 [97]	6	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	Low
Scifres 2011 [100]	6	✓					✓	✓	✓	✓	✓	Low
Staehr 2011 [95]	6	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	Low
Stall 2013 [96]	6	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	Low
Thibon 2012 [90]	6	✓	✓		✓	✓	✓	✓	✓	✓		Low
Turtiainen 2011 [102]	6	✓	✓		✓		✓	✓	✓	✓		Low
Whitney 2001 [101]	6	✓									✓	High

2.1F. Q8-10 ANTISEPTIC PROPHYLAXIS

2.1F1. GRADE TABLE: Q8-10 ANTISEPTIC PROPHYLAXIS

eTABLE 45. GRADE Table for Q8-10 Antiseptic Prophylaxis

Comparison	Outcome	Quantity and Type of Evidence	Findings	Starting GRADE	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Confounders		
Q8. What are the most effective strategies for preparing the patient's skin prior to surgery to reduce the risk of SSI? Q8A. How safe and effective is preoperative antiseptic bathing or showering?														
Chlorhexidine gluconate (CHG) solution vs. placebo	SSI*	1 SR [103]	• No difference on meta-analysis of 4 RCTs [104-107] (N=7791) in clean, elective and potentially infected procedures: 356/3906 (9.1%) vs. 389/3885 (10%): RR 0.91 (0.80-1.04). • No difference on meta-analysis restricted to 2 higher quality RCTs[104,106] (N=6302): 293/3167 (9.3%) vs. 305/3135 (9.7%); RR 0.95 (0.82-1.10) • Five months into 1 large study [105] the placebo was found to have antimicrobial properties and was changed but results were not stratified nor excluded. • No difference in each individual trial • Number preoperative baths, amount of antiseptic used per bath, bathing instructions to each group, intraoperative antiseptic skin preparation agent, use of AMP, and follow up varied between studies.	High	0	0	0	0	0	0	0	0	High	High
	Product-related Adverse Reactio-ns	1 SR [103]	• No difference on meta-analysis of 2 RCTs [104, 107] (N=3589) 9/1804 (0.5%) vs. 10/1785 (0.6%); RR 0.89 (0.36-2.19). • Every study used 4% CHG • Data are driven by the large higher quality RCT [104] as no allergic reactions were reported in either group in the smaller (N=100), lesser quality RCT[107]. • 1 large study[106] (N=1813) not included in the	High	0	0	0	-1	0	0	0	0	Moderate	

Comparison	Outcome	Quantity and Type of Evidence	Findings	Starting GRADE	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Confounders		
			meta-analysis also found no difference reporting 5 patients in each group with itching or reddening of skin.											
CHG solution vs. Un-medicated bar soap	SSI*	1 SR [103]	• No difference on meta-analysis of 3 RCTs [108, 105, 109] (N=1443): 82/752 (10.9%) vs. 94/691 (13.6%); RR 1.02 (0.57-1.84) • Each study used 4% CHG • Heterogeneity for this comparison was high: P=0.08, I^2 =60%. • Only the largest (N=1315) RCT [105] reported reduction in SSI with 4% CHG: 62/689 (9.0%) vs. 80/626 (12.8%); RR: 0.70 (0.57-0.96); no special showering/bathing instructions were given to the un-medicated bar soap group whereas "great care was taken to ensure that the patients using [CHG]…complied with the instructions." • One (N=66) of the two smaller, lesser quality studies[108] suggested higher rate of SSI with CHG: 8/31 (25.8%) vs. 4/35 (11.4%): RR: 2.26 (0.75-6.77) and the other [109] (N=64) showed no difference: 12/32 (37.5%) vs. 10/30 (33.3%); RR 1.13 (0.57-2.21) • Number preoperative baths, bathing instructions, intraoperative antiseptic skin preparation agent, use of AMP, procedures, and follow up varied between studies.	High	0	0	0	0	0	0	0	0	High	High
CHG solution vs. No Wash	SSI*	1 SR [103]	• No difference on meta-analysis (N=1142) of 3 RCTs [107,109,110]: 22/623 vs. 29/519; RR 0.82 (0.26-2.62) • Each study used 4% CHG	High	0	0	0	-1	0	0	0	0	Moderate	Moderate

Comparison	Outcome	Quantity and Type of Evidence	Findings	Starting GRADE	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Confounders		
			• Heterogeneity for this comparison was significantly high: P<0.03, I^2 = 70%. • Studies included outpatient and inpatient procedures, patients undergoing vasectomy [109], plastic surgery of the trunk [107] and elective biliary tract, inguinal hernia or breast cancer procedures [110], plus differences in SSI definition • Individual study results differed with only the largest (n=978) study [110] favoring 4% CHG: 9/541 (1.7%) vs. 20/437 (4.6%): RR 0.36 (0.17-0.79), the other two suggesting no difference: 12/32 vs. 9/32; RR: 1.33 (0.65-2.72) [109] and 1/50 vs. 0/50; RR: 3.00 (0.13-71.92). • Despite instructions to not shower, it is not clear if the "No wash" groups did in fact shower.											
CHG solution: Whole body vs. partial body wash	SSI*	1 SR [103]	• Reduced risk of SSI with whole body washing in 1 RCT [110] (N=1093) in elective biliary tract, inguinal hernia or breast cancer procedures: 9/541 (1.7%) vs. 23/552 (4.1%); RR: 0.40 (0.19-0.85). • Whole body wash = entire body + scalp • Partial body wash = restricted to proposed surgical site.	High	0	0	0	-1	0	0	0	0	Moderate	Moderate
Aqueous iodophor solution vs. control ("usual personal hygiene routine")	SSI*	1 RCT [111]	• 1 RCT (N=114) in elective, clean plastic surgical procedures (thorax or abdomen) reported no infections in either group (Follow up NR). The study was designed to assess impact of preoperative showering on skin colonization, not SSI. • Study used 10% povidone iodine solution	High	-1	0	-1	-1	0	0	0	0	Very Low	Very Low

Comparison	Outcome	Quantity and Type of Evidence	Findings	Starting GRADE	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Confounders		
2% chlorhexidine gluconate-impregnated cloths vs. un-medicated bar soap	SSI*	1 RCT [112]	• 1 RCT (N=100) in elective shoulder surgeries reported no infections in either group at a minimum of 2 months postop.	High	0	0	0	-1	0	0	0	0	Moderate	Moderate
	Product-related Adverse Events	1 RCT [112]	• In 1 RCT (N=100) in elective shoulder surgeries, 12/50 (24%) patients who used 2% chlorhexidine gluconate-impregnated cloths reported mild itching or a feeling of dry skin after the application of the cloths. Adverse events were not reported for the bar soap group.	High	0	0	0	-1	0	0	0	0	Moderate	
Q8B. How safe and effective are antiseptic skin preparation agents individually and in combination?														
Iodophors														
Aqueous Iodophor: 1-step vs. 2-step	SSI*	2 RCT [113,114,]	• In a study [113] of 234 oncology surgeries, no difference was observed in incisional (10% in each group) or intra-abdominal SSI. (2% vs.3%; p=0.14) infections (30 day follow up) • In a study [114] of 108 CABG patients, no difference was observed (12% vs. 13%) in sternal infections (6 week follow up)	High	0	0	0	0	0	0	0	0	High	High
Aqueous Iodophor (1 or 2 step) vs. Iodophor in Alcohol (1 step, with or without adhesive drape)	SSI*	5 RCT [114-118]	• No difference on a meta-analysis (N=626) of 5 studies: OR: 1.80 (0.50 – 6.52); p=0.37; I^2=67%	High	0	-1	0	-1	0	0	0	0	Low	Low
CHG-alcohol vs. Aqueous Iodophor														
CHG-alcohol (1 or 2 step) vs. Aqueous Iodophor (1 or 2	SSI*	5 RCT [116,119-122]	• In a meta-analysis (N=1976) of 5 RCTs, CHG-alcohol was associated with reduced risk for SSI: OR: 0.59 (0.42 – 0.83); p=0.003; I^2=0	High	0	0	0	0	0	0	0	0	High	High

Comparison	Outcome	Quantity and Type of Evidence	Findings	Starting GRADE	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Confounders		
step)	Product-related Adverse Events	2 RCT [120,121]	• One study [120] (N=849) reported 3 (0.7%) drug-related adverse events (pruritus, erythema or both around the surgical wound) in each group (P>0.99) • One study [121] (N=500) reported two cases of skin irritation in aqueous iodophor group, and no cases in CHG-alcohol group	High	-1	0	0	0	0	0	0	0	Moderate	
CHG-alcohol vs. Iodophor-alcohol														
CHG-alcohol (1 or 2 step) vs. Iodophor-alcohol (1 or 2 step)	SSI*	6 RCT [116,123-127]	• No difference on meta-analysis of 6 RCTs (N=1323), OR: 0.64 (0.24 – 1.71); p=0.38; I^2=16%	High	0	0	0	0	0	0	0	0	High	High
CHG-alcohol (2 step) vs. Iodophor-alcohol (2 step)	SSI*	3 RCT [123-125]	• No difference among the 743 patients available for follow up at 3-4 days in a large (N=866) general surgery study[125]: 27/389 (6.9%) vs. 35/354 (9.9%); p=NS. Significance varied by procedure: biliary surgery and "other clean operations" each suggested lower incidence of SSI with CGH-alcohol (p<0.05), in contrast, there was a lower incidence of SSI (not statistically significant) with iodophor-alcohol in large bowel and other laparotomy procedures. • No difference in a study[124] of 250 elective, clean, plastic surgery breast procedures. Only 4 superficial SSIs reported at 30 day follow up, all in the iodophor-alcohol group (p=0.06) • No infections reported in either group in a small (N=50) study[123] of foot surgeries. The study was designed to evaluate the products' efficacy in reducing skin contamination, not SSI (follow up and	High	0	0	0	0	0	0	0	0	High	High

Comparison	Outcome	Quantity and Type of Evidence	Findings	Starting GRADE	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Confounders		
			definition of SSI not reported).											
CHG-alcohol (1 step) vs. Iodophor-alcohol (1 step)	SSI*	3 RCT [116,126,127]	• In a study of 80 foot/ankle surgeries[126], only 1 SSI reported (CHG-alcohol group). Follow up and definition of SSI not reported. • In a study[116] of 100 arthroscopic shoulder surgeries, no infections were reported in either group at 10-month follow up. • In a study[127] of 100 elective lumbar spinal surgeries, no infections were reported in either group at 6 month follow up • All studies were designed to evaluate the products' efficacy in reducing skin contamination, not SSI	High	0	0	0	0	0	0	0	0	High	High
Q8C. How safe and effective is the application of a microbial sealant immediately following skin preparation?														
Cyanoacrylate-based skin sealant vs. No sealant	SSI*	4 RCT [128-131]	• No difference on meta-analysis (N=609) of 4 RCTS in cardiac surgery, hernia repair, or scoliosis correction: OR: 0.46 (0.08 – 2.51); p=0.37; I^2=68%	High	0	-2	0	0	0	0	0	0	Low	Low
	Product-related Adverse Events-	4 RCT [128-131]	• In 4 RCTs there were no significant product related adverse events reported. • In one RCT[130] surgeons reported difficulty incising through the clear film in 4/166 patients but no difficulty suturing wounds. There was one report of visible "flaking" of the film at the time of procedure.	High	0	0	0	0	0	0	0	0	High	
Q8D. How safe and effective are plastic adhesive drapes?														
Non-Iodophor impregnated adhesive drape vs. No drape	SSI*	4 RCT [132-135]	• No difference on meta-analysis of 4 RCTs (N=1742) (RR: 1.05; 95% CI: 0.81 – 1.35; p=0.71; I^2=0	High	-1	0	0	0	0	0	0	0	Moderate	Moderate

Comparison	Outcome	Quantity and Type of Evidence	Findings	Starting GRADE	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Confounders		
Iodophor-impregnated adhesive drape vs. No drape	SSI*	2 RCT [114,136]	• No difference on meta-analysis of 2 RCTs (N=1113) RR: 1.03 (0.66 – 1.60); p=0.89; I^2=0	High	0	0	0	0	0	0	0	0	High	High

*Critical outcome; OR: Odds Ratio; RR: Risk Ratio; CI: Confidence Interval

Comparison	Outcome	Quantity and Type of Evidence	Findings	Starting GRADE	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Confounders		
Q9 How safe and effective is antiseptic irrigation prior to closing the surgical incision?														
Antiseptic irrigation														
Aqueous iodophor irrigation vs. Normal saline	Organ/ space Abscess*	3RCT [137-139]	• In meta-analysis (N=268) of 3 studies in general surgical contaminated and dirty abdominal cases no difference noted between groups with intraperitoneal lavage using povidone iodine OR: 0.33 (0.08 – 1.34); p=0.12; I^2=35%. Povidone iodine concentration and AMP regimens varied between studies. • In 1 study[139] in 168 patients undergoing laparotomy, peritoneal irrigation with 1 liter of 1% povidone iodine (0.1% available iodine) for 60 seconds prior to abdominal closure reduced the risk of intra-abdominal abscess formation in dirty procedures: 0/36	High	0	-1	0	0	0	0	0	0	Moderate	Moderate

Comparison	Outcome	Quantity and Type of Evidence	Findings	Starting GRADE	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Confounders		
			vs. 6/42; p<0.05 but not in contaminated procedures: 1/44 vs. 3/46: p=NS • A subanalysis [138] of peritoneal lavage with normal saline then 100ml PI solution prior to closure in dirty: 4/13 vs. 5/16; p=NS • 1 study [139] peritoneal lavage with 1L of 10% PI solution for 60 sec, repeated 3 times during the procedure, the last time before closure in contaminated and dirty combined suggested no difference: 1/37 vs. 4/34; p=0.12.											
	Deep SSI*	2 RCT [140,141]	• In meta-analysis (N=660) of 2 studies of clean spine surgeries 0.35% povidone iodine irrigation (volume not reported) and wound soaking for 3 minutes followed by irrigation with 2L normal saline was associated with reduced risk for deep SSI OR: 0.08 (0.01 – 0.58); p=0.01; I^2=0. • In both studies, irrigation was completed prior to bone grafting and instrumentation. It was not repeated prior to wound closure. Also, AMP was started preoperatively, re-dosed intraoperatively as appropriate and continued for 5 days postoperatively. • Of note, 10/12 (83.3%) SSIs were MRSA.	High	0	0	0	0	-1	0	0	0	Moderate	
	Superficial SSI*	2 RCT [142,143]	• In meta-analysis (N=329) of 2 studies in general surgical clean-contaminated, contaminated, and dirty cases (subpopulations in which both study groups were reported to have received parenteral AMP), irrigation of the subcutaneous tissues for 60 seconds with 10% povidone iodine prior to wound closure was associated with reduced risk for superficial SSI OR: 0.21 (0.10 – 0.45); p<0.01; I^2=0	High	0	0	0	0	0	0	0	0	High	

Comparison	Outcome	Quantity and Type of Evidence	Findings	Starting GRADE	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Confounders		
			• In meta-analysis (N=149) of clean-contaminated cases, PI associated with reduced risk OR: 0.15 (0.03 – 0.72); p=0.02; I^2=0 • In meta-analysis (N=90) of dirty cases, PI associated with reduced risk OR: 0.26 (0.08 – 0.91); p=0.03; I^2=0											
	Adverse Events - Product Related	3 RCT [137,141,143]	• One study [137] in 168 laparotomy patients with contaminated peritoneal cavities reported no complications from the use of povidone iodine were noted. • One study [141] in 414 mixed spine surgery patients reported no product-related adverse event with 0.35% povidone iodine followed by normal saline irrigation • One study [143] in 187 general surgical procedures reported no allergic reactions	High	0	0	0	0	0	0	0	0	High	
	Wound Healing	2 RCT [140,143]	• One study [140] in posterior spine (no trauma) reported one incidence of wound dehiscence event with 0.35% povidone iodine followed by normal saline irrigation. • One Study [143] no evidence of delayed wound healing.	High	0	0	0	-1	0	0	0	0	Moderate	
	Serum Iodine Level	3 RCT [137,139,142]	• One RCT [142]: no significant change in serum free iodine • 2 RCT[137,139]: significant increase in postop serum iodine levels at 24h. In 1 RCT[137] the increase resolved by 72h, 1 RCT[139] the increase resolved by 7 days. Both, no signs of iodine toxicity.	High	0	0	0	0	0	0	0	0	High	
Q10. How safe and effective is repeat application of an antiseptic skin preparation agent to the surgical site immediately prior to closing the surgical incision?														
Topical antiseptic agents														

Comparison	Outcome	Quantity and Type of Evidence	Findings	Starting GRADE	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Confounders		
Aqueous iodophor to skin prior to wound closure vs. no topical antiseptic	SSI*	1 RCT [144]	• In a lower quality study of 107 gastric or colorectal procedures, no difference was observed between povidone iodine and no topical antiseptic groups for combined or individual incisional or organ/space surgical site infections: • Combined: 13/54 (24.1%) vs. 12/53 (22.6%) • Gastric Organ/Space: p=0.65 • Gastric Incisional: p=0.49 • Colorectal Organ/Space: p=0.59 • Colorectal Incisional: p=0.61	High	-1	0	0	-1	0	0	0	0	Low	Low

*Critical outcome; OR: Odds Ratio; RR: Risk Ratio; CI: Confidence Interval

2.1F2. EVIDENCE TABLES: Q8-10

Q8. What are the most effective strategies for preparing the patient's skin prior to surgery to reduce the risk of SSI?

eTABLE 46. Evidence Table for Q8A. How safe and effective is preoperative antiseptic bathing or showering?

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
Webster, 2012 [103] (RA)	**SR** 1, 2, 3, 4, 5, 6, 7, 8, 10, 11	To review the evidence for preoperative bathing or showering with antiseptics for preventing nosocomial SSI	**Study types:** RCT **N**: 7 RCT, 10,157 participants **Inclusion criteria:** RCTs comparing any antiseptic preparation used for preoperative full body wash or showering, with non-antiseptic preparations. **Exclusion criteria:** Quasi-RCTs **Databases searched:** Cochrane Wounds Group Specialized Register, CENTRAL, MEDLINE, EMBASE, CINAHL, hand searching, reference lists of retrieved articles (searches ended October-November 2010) **Quality assessment:** Using the Cochrane Collaboration Tool for assessing risk of bias, low risk of bias for: Random sequence generation – 5/7 studies Allocation concealment – 3/7 studies Blinding of investigator and participant – 3/7 studies Blinding of outcome assessor – 5/7 studies Incomplete outcome data – 6/7 studies Selective reporting – 7/7 studies Other bias – 4/7 studies	**Intervention**: Any type of antiseptic solution (any strength, any regimen, at any time before the surgery) used for preoperative tub- or bed-bathing or showering. All studies used 4% chlorhexidine gluconate **Comparison**: Non-antiseptic soap, non-antiseptic soap solution, no shower or bath	**All results intervention vs. control – RR (95% CI). No significant heterogeneity unless specified** **SSI:** Chlorhexidine 4% vs. placebo – all studies (4 studies, N=7791): 0.91(0.80-1.04); Fixed effects model; I^2=0% Chlorhexidine 4% vs. placebo – high quality studies (2 studies, N=6302): 0.95(0.82-1.10); Fixed effects model; I^2=0% Chlorhexidine 4% vs. bar soap (3 studies, N=1443): 1.02(0.57-1.84); Random effects model; I^2=60% Chlorhexidine 4% vs. no wash (3 studies, N=1142): 0.82(0.26-2.62); Random effects model; I^2=70% Chlorhexidine full wash vs. partial wash (1 study, N=1092): 0.40(0.19-0.85) **Allergic reaction:** Chlorhexidine 4% vs. placebo (2 studies, N=3589): 0.89(0.36-2.19); Fixed effects model; I^2=0%	**Definitions**: SSI definition used by the studies was accepted **Perioperative care:** NR **Other Notes:** None **Follow-up** not reported **Funding Source Conflicts:** Authors: None Institution: None Study: None Supplies: None
Murray 2011 [112]	**RCT** 1, 4, 6, 9	To test the hypothesis that	**Number of patients: N=100** **Patient Characteristics**	**Intervention group**: n=50 Shower with soap and water	**SSI:** Total SSI:	**Definitions:** SSI – NR

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
(ES)		the home use of 2% chlorhexidine gluconate-impregnated cloths would be more efficacious than a standard soap-and-water shower at decreasing the preoperative cutaneous levels of pathogenic bacteria on the shoulder	·Age, years, mean±SD Intervention: 49.0±16.2 Control: 52.0±16.7 P=0.14 ·Gender: M/F Intervention: 36/14 (72% male) Control: 25/25 (50% male) P=0.04 ·Obesity: NR ·Comorbidities: Diabetes mellitus: Intervention: 4/50 (8%) Control: 4/50 (8%) P>0.99 Immunosuppressive medications: Intervention: 1/50 (2%) Control: 0/50 P=0.99 Shaved axilla Intervention: 8/50 (16%) Control: 12/50 (24%) P=0.45 Took abx prior to surgery Intervention: 1/50 (2%) (for upper respiratory infection) Control: 0/50 P=0.99 **Procedures:** shoulder surgery *[no acute trauma surgeries]* Open Intervention: 6/50 (12%) [6 primary total shoulder arthroplasties] Control: 8/50 (16%) [6 primary total shoulder arthroplasties, 1 revision total shoulder arthroplasty & 1 Weaver-	the evening before operation and wipe their entire operative extremity, including the axilla, shoulder, and ipsilateral chest and back with a 2% chlorhexidine gluconate-impregnated cloth 1h after showering. Then the morning of surgery, patients were instructed to avoid showering and apply a second 2% chlorhexidine gluconate0-impregnated cloth in the same manner as the first within 2h of departing for the hospital. **Timing of intervention:** Preoperative **Duration of intervention:** duration of chlorhexidine-impregnated cloth scrub **Device/agent:** 2% chlorhexidine gluconate-impregnated cloth and/or soap **Monitoring intervention:** NR **Control group**: n=50 Patients instructed to shower with soap and water the morning of surgery. **Standard preventive measures:** Antimicrobial prophylaxis: preop 1g of cefazolin if weight was <90kg and 2g if weight was >90kg, or 900mg clindamycin if allergic to penicillin, was	Intervention: 0/50 Control: 0/50 **Other infections:** NR **Topic-specific outcomes:** Compliance with protocol Intervention: 45/50 (90%) [4 unable to elevate arm sufficiently to apply the cloth, 1 patient showered in between applications of chlorhexidine-impregnated cloth. Control: 50/50 (100%) P=0.056 **Reoperations:** NR **Length of stay:** NR **Mortality:** NR **Adverse events:** No serious adverse events occurred in any patients Side effects (mild itching or a feeling of dry skin): Intervention: 12/50 (24%) Control: 0/50 P<0.002	**Perioperative care:** NR **Other notes:** Positive cultures were primary outcome of interest. Study was powered to detect a difference in positive cultures. It was underpowered to detect any difference in SSI **Follow-up:** 2 months post op. [follow up insufficient for implant SSI] **Funding Source Conflicts:** Authors: NR Institution: Industry Study: Industry Supplies: Industry

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			Dunn procedure] P=0.77 Arthroscopic Intervention: 44/50 (88%) Control: 42/50 (84%) P=0.77 **Indications:** NR **Setting:** 1 university hospital **Location:** USA **Dates:** January 2010 – May 2010 **Inclusion Criteria:** Patients scheduled for any type of shoulder surgery. **Exclusion Criteria:** Refusal to participate had an open wound, a current infection, or a chronic immunosuppressive condition.	administered to all patients within 1h of skin incision. Shoulder arthroplasty patients received an additional 1g vancomycin. Antimicrobial drape – antibacterial-impregnated drape used for all cases involving implantation of a prosthesis. Intraoperative skin prep: 2% chlorhexidine gluconate and 70% isopropyl alcohol. Hair removal: 6 patients reported shaving their own hair before surgery but it is not reported which group they belonged to.		
Veiga 2008 [111] (ES)	**RCT** 1, 4	To assess the influence of povidone-iodine preoperative showers on skin colonization in elective plastic surgery procedures	**Number of patients: N=114** **Patient Characteristics** ·Age: mean 38.3 y (range 18-65) ·Gender: m:f: 26:88 ·Obesity: NR ·Comorbidities: NR **Procedures**: Plastic surgery involving the thorax or abdomen: Breast reconstruction, reduction mammoplasty, augmentation mammoplasty, liposuction, gynecomasty, scar revision, supernumerary mammoplasty, and abdominoplasty. **Indications**: NR **Setting**: 1 school hospital **Location**: Brazil	**Intervention group**: n=57 Patients instructed to shower with liquid detergent-based povidone-iodine 1-% and water 2hours before surgery. Patients instructed to rinse thoroughly, lather with detergent, rinse, lather, and rinse again. **Timing of intervention:** preop **Duration of intervention:** duration of shower. **Device/agent:** Povidone–iodine 10% detergent-based soap **Monitoring intervention:** Samples for quantitative skin sampling obtained in	**SSI (follow up NR)** No SSI seen in either group. **Other infections:** NR **Topic-specific outcomes:** Patients with no microorganism growth PVP-I: 33/57 (57.9%) Control: 0/57 Patients with S. aureus growth (13/114 (11.4%) PVP-I: 1/57 (1.8%) Control: 12/57 (21.1%) P=0.0019 **Reoperations:** NR **Length of stay:** NR	**Definitions**: NR **Perioperative care**: NR **Other notes:** NR **Follow-up:** NR **Funding Source Conflicts:** Authors: None Institution: NR Study: NR Supplies: NR

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			Dates: September 15, 2004 – December 1, 2005 **Inclusion Criteria:** Patients older than 18 years scheduled for elective and clean plastic surgery procedures on the thorax or abdomen **Exclusion Criteria**: Patients with a history of hypersensitivity to povidone-iodine, presence of rashes, open sores or skin lesions, and antimicrobial use at the time of surgery.	the OR. A 5x10cm area on the anterior abdominal wall was swabbed with a sterile cotton swab pre-moistened with sterile saline. Samples were processed within 6h after obtainment and plated onto agar plates. **Control group**: n=57 No special instructions for showering implemented before surgery. Patients followed their usual personal hygiene routine on day of surgery **Standard preventive measures:** NR	**Mortality:** NR **Adverse events:** NR	

eTABLE 47. Evidence Table for Q8B. How safe and effective are antiseptic skin preparation agents individually and in combination?

Author Year (Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
Savage 2012 [127] (ES)	**RCT** 1	To identify the common bacterial flora on the skin overlying the lumbar spine and to evaluate the efficacy of two readily available skin-	**Number of patients: N=100** **Patient Characteristics:** No significant differences between groups with regards to Age or BMI. ·Age: mean, years Intervention: 51 Control: 54 ·Gender: NR ·Obesity: BMI mean (kg/m^2) Intervention: 231 Control: 175 ·Comorbidities: NR	**Intervention group:** n=50 Skin was prepared with 2% chlorhexidine gluconate and 70% isopropyl alcohol. Spine was prepared according to the manufacturer's instructions. Each preparation solution allowed to adequately dry for approximately 3-5 minutes. **Timing of intervention:**	**SSI :** Total SSI: 0/100 Superficial SSI Intervention: 0/50 Control: 0/50 Deep SSI Intervention: 0/50 Control: 0/50 **Other infections:** NR **Topic-specific outcomes:** Superficial wound	**Definitions:** SSI - NR **Perioperative care:** NR **Other notes:** study was designed with Colonization as primary outcome. SSI was secondary. Power was on the basis of the assumption that a 20% difference in positive skin culture rates would be clinically relevant, the number of patients required

Author Year (Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
		preparation solutions in the elimination of bacterial pathogens from the surgical site following skin preparation.	Diabetes mellitus: Intervention: 3/50 (6%) Control: 4/50 (8%) Smoker (>1.5 packs/day): Intervention: 3/50 (6%) Control: 3/50 (6%) Corticosteroid use: Intervention: 3/50 (6%) Control: 2/50 (4%) Immunocompromised: Intervention: 2/50 (4%) Control: 3/50 (6%) Previous Spine Surgery Intervention: 10/50 (20%) Control: 9/50 (18%) History of alcohol abuse: Intervention: 4/50 (8%) Control: 2/50 (4%) History of MRSA: Intervention: 0/50 Control: 2/50 (4%) Duration of surgery: mean (min) Intervention: 51 Control: 54 P=0.05 Estimated Blood Loss: mean (mL) Intervention: 388 Control: 175 P=0.02 **Procedures:** elective lumbar spine surgery including microdisectomy, posterior spinal fusion with or without an associated interbody fusion, decompression alone, kyphoplasty.	Pre-operative **Duration of intervention:** Application + 3-5 min drying time **Device/agent:** with 2% chlorhexidine gluconate and 70% isopropyl alcohol, or 0.7% available iodine and 74% isopropyl alcohol **Monitoring intervention:** NA **Control group:** n=50 Skin was prepared with 0.7% available iodine and 74% isopropyl alcohol. Spine was prepared according to the manufacturer's instructions. Each preparation solution allowed to adequately dry for approximately 3-5 minutes. **Standard preventive measures:** No specific cleansing or shaving protocol prior to the surgery. If necessary, hair was removed with clippers in the operating room. Antibiotic Prophylaxis: all received 1 or 2g of cefazolin (based on weight) prior to surgery except in cases of penicillin allergy where they received 900 mg of	dehiscence Intervention: 1/50 (2%) Control: 0/50 **Reoperations:** NR **Length of stay:** NR **Mortality:** NR **Adverse events:** NR	to achieve 80% power at alpha=0.05 was 50/group **Follow-up:** minimum of 6 months **Funding Source Conflicts:** Authors: NR Institution: NR Study: NR Supplies: Industry

Author Year (Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			Indications: NR **Setting:** 1 University Hospital **Location:** USA **Dates:** February – August 2010 **Inclusion Criteria:** Consecutive patients undergoing elective lumbar spine surgery **Exclusion Criteria:** If patient had an open wound at the incision site, abrasion in the vicinity of the planned incision, an active infection at or near the surgical site, or an active infection elsewhere in the body.	clindamycin. Patients who required spinal instrumentation followed the same protocol with the addition of 1g of vancomycin. Drape – same non-antimicrobial drape was used in all cases		
Sistla 2010 [119] (ES)	**RCT** 1, 4, 5, 6, 7, 9	To compare the efficacy of povidone iodine and a combination of chlorhexidine-ethanol in the reduction of skin bacterial counts and its effect on wound infection rates following hernia repair.	**No. Patients:** N=400 **Patient Characteristics:** Patient characteristics & surgical elements were similar between groups. No statistically significant difference. **All values given for entire study group. (N=400)** Age≤60 years: 306 (76.5%) Age≥60 years: 94 (23.5%) Gender (m/f): 391/9 Obesity: NR Side (bilateral/unilateral): 38/362 Comorbidity present: 23 (5.8%) ASA 3: 9 (2.3%) Preop Stay <48 h: 229 (57.3%) >48 h: 171 (42.8%) Duration of Surgery	**Intervention:** n=200 2.5% chlorhexidine with 70% ethanol applied in concentric circles beginning with the site of incision to the periphery and **allowed to dry** before the surgical site was draped **Timing of Intervention:** Preoperative **Duration of intervention:** intraoperatively **Agents:** Sterile cotton swabs pre-moistened with sterile saline, Agent brand name for intervention & control NR **Monitoring intervention:** N/A **Control:** n=200 10% povidone-iodine	**SSI- (30days)** **Overall SSI:** 33/400 (8.3%) Intervention: 14/200 (7.0%) Control: 19/200 (9.5%) *P*=0.364 Grade of SSI: Grade 1: Pus Discharge: 12/400 (3%) Intervention: 5/200 (2.5%) Control: 7/200 (3.5%) P=0.538 Grade 2:Erythema, induration or cellulitis: 18/400 (4.5%) Intervention: 8/200 (4%) Control: 10/200 (5%) P=0.605 Grade 3: Wound dehiscence: 3/400 (0.8%)	**Definitions:** Infections: CDC criteria Questionnaire: patient self-reported on 1 or more of the following conditions: no problems, redness and pain around the wound which settled without treatment, redness and pain around the wound which required antimicrobials, discharge of pus from the wound, wound break down, need for hospitalization. Note: patients reported to the hospital when they developed infection for confirmation and treatment due to limited free medical facilities. **Perioperative care** Shaving of operative site done

Author Year (Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			<55 min: 320 (80%) >55 min: 80 (20%) Grade of surgeon Resident: 378 (94.5%)**Procedures:** Open Hernia repair Herniotomy: 18 (4.5%) Herniorrhaphy: 132 (33%) Hernioplasty: 250 (62.5%) **Indications:** Suture repair: 62% Prosthetic repair: 33% Herniotomy: 5% **Setting:** Academic medical institute **Location:** India **Dates:** NR **Inclusion Criteria:** Adults undergoing elective open inguinal hernia repair **Exclusion Criteria:** Patients with recurrent or complicated inguinal hernia and patients with a history of allergy to the antiseptics	applied in concentric circles beginning with the site of incision to the periphery and **allowed to dry** before the surgical site was draped **Standard preventive measures** AMP: Patients undergoing prosthetic repair (hernioplasty) received a single dose of cefazolin intravenously an hour before surgery.	Intervention: 1/200 (0.5%) Control: 2/200 (1%) P=0.619 SSI rate in prosthetic repair: 10.6% vs. suture repair (NR) despite use of AMP; difference not statistically significant. Univariate analysis Risk of SSI Operation Side Bilateral: 8/38 (21%) infected Unilateral: 25/362(7%) infected RR 3.05 (CI 95%, 1.48-6.28) *P*= 0.007 Preoperative Stay >48 hrs. : 22/171(13%) infected <48 hrs. : 13/229(6%) infected RR 2.27 (95% CI, 1.17-4.37) *P*=0.019 Duration of surgery > 55min: 11/80 infected < 55min: 22/320 RR 2.00 (95%CI, 1.01*-3.95) *P*=0.066 Multivariate analysis found only preoperative stay to be a significant risk factor (*p*<0.001) (not age,	the night before surgery on all patients. Admission preop-patients in this series were predominantly from distant regions, admitted and then operated on next available operating day. Type of anesthesia Spinal Intervention: 172/200 (86%) Control: 169/200 (84.5%) Local Intervention: 28/200 (14%) Control: 30/200 (15%) General Intervention: 0 Control: 1/200 (0.5%) Dressing: Sterile dressings applied after surgery & wounds were left exposed after 48 hr. **Other notes:** NOTE: In Table 1 they indicate n=250 (62.5%) hernioplasties (prosthetic repair) BUT in the results text they state “Sixty-two percent of patients underwent suture repair [which should be a herniorrhaphy]; prosthetic repair was performed in 33% of patient s [which is the number of herniorrhaphies in table1) unclear which is correct. They also note that higher

Author Year (Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
					gender, side of hernia, comorbidity, ASA score, procedure, type of anesthesia, grade of surgeon or length of surgery) **Other infections:** NR **Topic Specific Outcomes:** Not relevant **Reoperations:** None of the SSIs with pus or wound dehiscence necessitated removal of the prosthetic material (mesh) **Length of Stay:** NR **Readmission:** NR **Mortality:** NR	infection rates in developing countries vs. others is partly due to "certain practices and special problems in these regions": shaving, admission prior to surgery, poor personal hygiene in some of the patients in lower socioeconomic strata and not practicing antiseptic showers preop. **Follow up:** CDC criteria used by investigators to record infections in the postoperative period. Patients were given a questionnaire to record/ report wound conditions and was returned 30 days after surgery. (72% of 400 completed the questionnaire) **Funding Source Conflicts:** Authors: NR Institution: NR Study: NR Supplies: NR
Darouic-he 2010 [120] (ES)	**RCT** 1, 2, 3, 4, 5, 6, 7, 8, 9, 10	To compare the efficacy of chlorhexidine-alcohol with that of povidone-iodine for preventing surgical-site infections	**No. Patients:** Intention to treat (ITT) N=849 Per protocol N=813 **Patient Characteristics:** Patients in the two study groups were similar with respect to demographic characteristics, coexisting illnesses, risk factors for infection, antimicrobial exposure, & duration & types or surgery.	**Intervention:** **ITT n=409** **Per protocol:** n=391 Skin at surgical site was scrubbed with an applicator that contained 2% chlorhexidine gluconate & 70% isopropyl alcohol. More than one chlorhexidine alcohol applicator was used if area exceeded 33	**SSI within 30 days** ITT N=849 Any SSI Intervention: 39/409 (9.5%) Control: 71/440 (16.1%) RR 0.59 (95% CI, 0.41-0.85) *p*=0.004 Superficial Intervention: 17/409 (4.2%) Control: 38/440 (8.6%)	**Definitions:** SSI diagnosed on basis of CDC criteria Malnutrition: Defined as > 10% decrease in weight in over 2 months **Perioperative care** NR **Other notes** None **Follow up:** 30 days; Surgical

Author Year (Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			All values given for intervention Intention to Treat intervention population n=409 Age yr.; mean (range): 53.3±14.6 (18-100) Gender: Male Sex (%) 58.9 Obesity: NR Gastrointestinal Disease: 67% Cardiopulmonary disease: 33.5% Neurologic disease: 12/5% Renal disease: 7.3% Immunologic disease: 4.7% Cancer: 58.0% Diabetes mellitus: 15.4% Liver Cirrhosis: 2.2% History of Alcohol Abuse: 17.9% History of smoking: 37.2% **Procedures** ITT population N=849 Abdominal: Intervention : 72.6% Control : 70.0% Colorectal: Intervention: 45.5% Control: 43.4% Biliary: Intervention: 10.8% Control: 12.3% Small Intestine: Intervention: 10.0% Control: 7.7% Gastroesophageal: Intervention: 6.4% Control: 6.6% Non-Abdominal Surgery Intervention: 27.4%	by 33 cm. **Timing of Intervention:** Preoperative **Duration of intervention:** Intraoperatively **Agents:** Intervention: 2% chlorhexidine gluconate & 70% isopropyl alcohol Control: 10% povidone-iodine **Monitoring intervention:** N/A **Control:** **ITT: n=440** **Per protocol** n=422 Skin at surgical site was scrubbed and painted with an aqueous solution of 10% povidone-iodine (Allowed to dry? **NR**) **Standard Preventive Measures** ITT Population, N=849 AMP: All patients received systemic prophylactic antimicrobials within 1 hour before the initial incision. No significant differences in the type or number of antimicrobials given. AMP postop Intervention :51.7% Control:48.9$ P=0.41 Shower:	RR 0.48 (95% CI, 0.28-0.84) *p*=0.008 Deep Incisional Intervention: 4/409 (1%) Control: 13/440 (3.0%) RR 0.33 (95% CI, 0.11-1.01) *p*=0.05 Organ/space Intervention: 18/409 (4.4%) Control: 20/440 (4.5%) RR 0.97 (95% CI, 0.52-1.80) P>0.99 Sepsis from SSI RR -.62; (95% CI, 0.30-1.29) Time to onset of SSI longer in intervention vs. control P=0.004 Per-protocol analysis yielded similar efficacy results. **Other Infections:** NR **Topic Specific Outcomes:** **ITT population subgroup analysis** **All Infections by Surgery type** **Abdominal:** Intervention: 37/297 (12.5%) Control: 63/308 (20.5%) 95% CI for absolute difference, -13.9to-2.1 percentage points Colorectal	site assessed 1x/day during hospitalization, on discharge & at time of follow up & whenever SSI occurred. Investigators called patients 1x/week during 30 day follow-up period. **Funding Source Conflicts:** Authors: Industry Institution: NR Study: NR Supplies: NR

Author Year (Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			Control: 30.0% Thoracic: Intervention:10.8% Control: 13.0% Gynecologic: Intervention:10.3% Control:9.1% Urologic: Intervention: 6.4% Control:8.0% **Indications:** NR **Setting:** 6 University-affiliated hospitals **Location:** USA **Dates:** April 2004-May 2008 **Inclusion Criteria:** Patients ≥18 years undergoing clean-contaminated surgery performed under controlled conditions without substantial spillage or unusual contamination. **Exclusion Criteria:** A history of allergy to chlorhexidine, alcohol or iodophors; evidence of infection at or adjacent to the operative site; and the perceived inability to follow the patient's course for 30 days after surgery	Preoperative Shower Intervention: 26.7% Control: 27%*p*=0.94 4% chlorhexidine gluconate P=0.32 10% povidone iodine P=0.26 6% triclobarban soap bar P>0.99 Hair removal- as necessary by hair clipping	Intervention: 28/186 (15.1%) Control: 42/191 (22.0%) Biliary Intervention: 2/44 (4.6%) Control: 5/54 (9.3%) Small intestine: Intervention: 4/41 (9.8%) Control: 10/34 (29.4%) Gastroesophageal Intervention: 3/26 (11.5%) Control: 6/29 (20.7%) **Non-Abdominal** Intervention: 2/112(1.8%) Control: 8/132 (6.1%) 95% CI for absolute difference, --7.9 to 2.6 percentage points Thoracic: Intervention: 2/44 (4.5%) Control: 4/57 (7.0%) Gynecologic Intervention: 0/42 Control: 1/40 (2.5%) Urologic Intervention: 0/26 Control: 3/35 (8.6%) Both the ITT and Per protocol analyses showed lower rates of SSI in the intervention group for each of the seven operations included. Trial not powered to compare SSI rates for subcategories of patients, however, SSIs	

Author Year (Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
					occurred significantly less often in intervention group for small intestinal (P=0.04), or abdominal surgery (P=0.009) or who did not shower preoperatively (P=0.02) **Factors affecting any SSIs** <u>Use of Chlorhexidine (vs. PVP-I)</u> Univariate: OR: 0.55; *p*=0.004 Multivariate: OR: 0.45 *p*=0.004 <u>Use of Abdominal Surgery (vs. Non-Abdominal Surgery)</u> Univariate: OR: 4.63; *p*<0.001 Multivariate: OR: 3.21 *p*=0.001 <u>Alcohol Abuse</u> Univariate: OR: 1.11; *p*=0.69 Multivariate: OR: 1.12 *p*<0.001 <u>Liver Cirrhosis</u> Univariate: OR: 3.28; *p*=0.02 Multivariate: OR: 2.14 *p*=0.02 <u>Immunologic Disease</u> Univariate: OR: 2.72; *p*=0.01 Multivariate: OR: 1.79 *p*=0.05 <u>Cancer</u> Univariate: OR: 2.05;	

Author Year (Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
					p=0.002 Multivariate: OR: 1.65 *p*=0.03 <u>Diabetes Mellitus</u> Univariate: OR: 1.90; *p*=0.01 Multivariate: OR: 1.75 *p*=0.03 <u>Malnutrition</u> Univariate: OR: 3.02; *p*=0.003 Multivariate: OR: 2.62; *p*=0.01 <u>Gastrointestinal Disease</u> Univariate: OR: 2.96; *p*<0.001 Multivariate: OR: 1.27 *p*=0.05 <u>Days surgical drain in place</u> Univariate: OR: 1.03; *p*=0.02 Multivariate: OR1.04 *p*<0.001 <u>Preop shower with Chlorhexidine (vs. no shower)</u> Univariate: OR: 1.56; *p*=0.38 Multivariate: OR: 0.95 *p*=0.19 <u>Preop shower with PVP-I (vs. no shower)</u> Univariate: OR: 0.135; *p*=0.01 Multivariate: OR; 0.36 *p*<0.001 <u>Use of Chlorhexidine (vs. PVP-I)</u>	

Author Year (Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
					Univariate: OR: 1.08; *p*=0.79 Multivariate: OR: 0.96 *p*=0.72 **Reoperation:** NR **Length of Stay:** NR **Readmission:** NR **Mortality:** Intervention: 4/391 (1%) None had SSIs Control: 3/422 (0.7%) All 3 died from organ/space SSI related sepsis 0.3% (95%CI -0.9-1.5); *p* =0.72 **Adverse events:** Total Serious adverse events: Intervention: 72/409 (17.6%) Control: 70/ 440 (15.9%) 1.7% (95%CI -3.3-6.7); *p* =0.52 Bloodstream Infection Intervention: 11/409 (2.7%) Control: 23/ 440 (5.2%) -2.5% (95%CI -5.1-0.1); *p* =0.08 Abscess Intervention: 6/409 (1.5%) Control: 11/ 440 (2.5%) -1.0% (95%CI -2.9-0.8); *p* =0.33 Pneumonia Intervention: 6/409 (1.5%) Control: 9/ 440 (2%)	

Author Year (Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
					-0.6% (95%CI -2.3-1.2); *p* =0.61 **Antiseptic Agent Related Adverse Events** Includes pruritus, erythema, or both around the surgical wound. Intervention: 3/409 (0.7%) Control: 3/ 440 (0.7%) 0.1% (95%CI -1.1-1.2); *p* >0.99 No cases of fire or chemical skin burns in the operating room	
Cheng 2009 [123] (ES)	**RCT** 1, 2, 10	To compare the effect of povidone-iodine and chlorhexidine gluconate (both with isopropyl alcohol) on lowering bacterial load and if any additional benefits (additional lowering of the bacterial load) were to be gained by an additional pre-scrub with a	**No. Patients**: N=50 **Patient characteristics:** No Demonstrable difference in age, sex or site of operation between groups. The only demographic information given were age and gender. Age y, mean±SD 51.1± 17.4 Gender m/f: 12/38 Obesity: NR **Procedures:** Metatarsal osteotomies for correction of hallux valgus deformity: 23/ 50 (46%) Removal of osteophytes from the first metatarsal: 15/ 50 (30%) Correction of lesser toe deformities: 12/ 50 (24%) **Indications:** See Procedures **Setting:** 1 Hospital	**Intervention** n=25 Skin prepared with chlorhexidine gluconate 0.5% in 70% alcohol) scrub and paint **Timing of Intervention:** Preoperative **Duration of intervention: i**ntraoperative **Agent:** Intervention: 0.5% Chlorhexidine gluconate in 70% alcohol Control: 10% Alcoholic tincture of povidone-iodine, 1% available iodine **Monitoring intervention:** NR **Control:** n=25 Skin prepared with alcoholic tincture, povidone-iodine 10%	**SSI & Adverse events: (Follow up NR)** None of the 50 patients developed any post-operative infections or wound complications **Other Infections:** NR **Topic specific outcomes:** Not relevant **Reoperation:** None **Length of Stay:** NR **Readmission:** None **Mortality:** None	**Definitions:** NR **Perioperative care:** NR **Other notes:** None **Follow up**: No follow up recorded **Funding Source Conflicts:** Authors: None Institution: None Study: None Supplies: None

Author Year (Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
		bristled surgical brush with either of these solutions on the non-surgical foot.	**Location:** United Kingdom **Dates**: August 2007 – January 2008 **Inclusion Criteria:** Undergoing foot surgery **Exclusion Criteria:** If there were current open wounds, skin ulcers and/ or sore, a history of onychomycosis, paronychia or nail deformity, poorly controlled diabetes mellitus or recent antimicrobial use (w/in one week of surgery)	(1% available iodine) scrub and paint **Standard Preventive Measures** AMP: All patients were given a single dose of a prophylactic broad spectrum antimicrobial prior to their procedure but after skin prep.		
Saltzman 2009 [116] (ES)	**RCT** 1, 6, 9	To examine the native bacteria around the shoulder and axilla, and to determine the efficacy of three different surgical skin-preparation solutions (2% chlorhexidine gluconate and 70% isopropyl alcohol; 0.7% iodophor and 74% isopropyl alcohol; and	**No. Patients:** N=150 **Patient Characteristics:** **Characteristics given represent the whole study.** Age: 17-79 years old Gender (m/f): 84/66 Obesity: NR<u>Intervention1:</u> Heavy Smokers (>1.5 pack per day): 1/50 Diabetes mellitus: 4/50 Rheumatoid Arthritis: 0/50 History of Alcoholism or hepatitis: 4/50 <u>Intervention2:</u> Heavy Smokers: 0/50 Diabetes mellitus: 6/50 Rheumatoid Arthritis: 2/50 History of Alcoholism or hepatitis: 2/50 <u>Control:</u> Heavy Smokers: 3/50 Diabetes mellitus: 3/50 Rheumatoid Arthritis: 0/50 History of Alcoholism or hepatitis: 1/50	**Intervention1** n=50 0.7% iodophor and 74% isopropyl alcohol **Intervention2** n=50 2% chlorhexidine gluconate and 70% isopropyl alcohol **Intervention3** n=50 Shoulder prepared with povidone-iodine scrub & paint 0.75% iodine scrub and 1.0% iodine paint **Timing of Intervention** Preoperative **Duration of intervention:** Intraoperative **Agent:** Intervention1: 0.7% iodophor and 74% isopropyl alcohol Intervention2: 2% chlorhexidine gluconate and 70% isopropyl alcohol Control: Povidone-iodine	**SSI**: **10 month minimum** No postoperative infection had developed in any of the patients in this study at a minimum follow-up **Other Infections:** NR **Topic specific outcomes:** Not relevant **Reoperation:** NR **Length of Stay:** NR **Readmission:** NR **Mortality:** NR **Adverse events:** NR	**Definitions:** Not recorded **Perioperative care** Hair removal: 37/ 150 (25%) reported voluntary shaving of axillary hair prior to enrollment. All were women. 12 in control, 9 in intervention1, 16 in intervention2 **Other notes:** None **Follow up:** 10 months **Funding Source Conflicts:** Authors: Industry Institution: None Study: Industry Supplies: Industry

Author Year (Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
		0.75% iodine scrub and 1.0% iodine paint)on the eradication of bacteria from the shoulder by evaluating the residual bacteria present following surgical skin preparation.	**Procedures** Arthroscopic Shoulder Surgery= 137/150 (91.3%) Shoulder Arthroplasties (primary) = 4 **Indications:** NR **Setting:** One hospital **Location:** USA **Dates:** September 2007 – February 2008 **Inclusion Criteria:** Patients undergoing shoulder surgery. **Exclusion Criteria:** If patient had an open wound or a current infection or were chronically immunosuppressed.	scrub (0.75% iodine scrub and 1.0% iodine paint) Prosthetic implant surgeries utilized antibacterial-barrier (adherent drape) **Monitoring intervention:** N/A **Standard Preventive Measures:** Shower: All patients were instructed to shower the day before the surgery. AMP: Preoperative antimicrobials were administered to all 150 patients. Arthroscopic or soft tissue surgeries received cefazolin or clindamycin. Arthroplasties: AMP: received the same AMP as above plus vancomycin. Skin Prep: After skin prep used an antibacterial-impregnated barriers (adhesive drapes)		
Paochar-oen 2009 [121] (ES)	**RCT** 1	To study the efficacy in the reduction of bacterial colonization and postoperative wound infection among povidone-	**No. Patients:** N=500 **Patient characteristics:** Age, operative time and wound class were all analyzed and found not to be statistically significant. **Characteristics given represent the whole study.** Age 10-60 years old Age y mean (range) Intervention: 50.5 (18-79)	**Intervention:** n=250 4% chlorhexidine in 70% isopropyl alcohol scrub (5 minutes) followed by 4% chlorhexidine in 70% isopropyl alcohol paint. **Timing of Intervention**: pre-operatively **Duration of intervention:** intraoperative **Agents:** 4% chlorhexidine	**Surgical Wound Infection:** **1 month** Total: (%) Intervention: 5/250 (2%) 2/5 arteriovenous shunt 2/5 appendectomy 1/5 right half colectomy Control: 8/250 (3.2%) 4/8 arteriovenous shunt	**Definitions:** **SSI:** if the wound drained purulent material or if the surgeon judges it to be infected and opens it. **(Dunn 2005)** **Perioperative care :** NR **Follow up:** 1 month. Surgical wounds examined twice a week for the first week and

Author Year (Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
		iodine and chlorhexidine antiseptic skin preparations in general surgery patients	Control: 56.2 (20-79) Gender (m/f): 297/213 Obesity: NR Operative time hours mean (range) Intervention: 1.45 (45min-3hr) Control: 1.43 (40 min-3 h) Wound Classification Clean (I) Intervention: 96 (38.4%) Control: 87/250 (34.8%) Clean contaminated (II) Intervention: 118/250 (47.2%) Control: 112/250 (44.8%) Contaminated (III) Intervention: 46/250 (18.4%) Control: 51/250 (20.4%) **Procedures:** All general surgery **Indications:** NR **Setting**: One university hospital **Location:** Thailand **Dates:** June 2006 – November 2008 **Inclusion Criteria**: Patients aged 18-60 years old, with clean (class 1), clean contaminated (class 2), and contaminated wounds (class 3) and ASA class 1 and 2 scores. **Exclusion Criteria:** Patient refusal, dirty wounds, uncontrolled diabetes, immunosuppressive drugs, serum albumin levels less than 3.0 mg/dl, and a history	in 70% isopropyl alcohol scrub/4% chlorhexidine in 70% isopropyl alcohol paint; povidone-iodine scrub solution and paint. **Monitoring intervention:** N/A **Control:** n=250 Povidone-iodine scrub solution (5 minutes) followed by povidone iodine paint (**Allowed to dry? NR)** **Standard Preventive Measures:** The authors allowed other pre-operative preparations under the standard guideline. What these were: NR	1/8 modified radical mastectomy 2/8 appendectomy 1/8 gastrectomy For intervention group RR 1.61 (CI 95%, 1.40-1.81) **Other infections:** NR **Topic Specific outcomes:** Not relevant **Reoperation:** NR **Length of Stay:** NR **Readmission:** NR **Mortality:** NR **Adverse events:** 2 cases of skin irritation from povidone-iodine and no allergies to chlorhexidine	every week for 1 month. **Other notes** Numbers incorrectly reported (transposed) within results table 2. **Funding Source Conflicts:** Authors: NR Institution: NR Study: NR Supplies: NR

Author Year (Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			of allergic reaction to either study agent.			
Veiga 2008 [124] (ES)	**RCT** 1	To compare povidone-iodine and chlorhexidine ethanolic solutions for skin antisepsis before elective, clean, plastic surgery procedures.	**No. Patients:** N=250 **Patient Characteristics: Characteristics given represent the whole study.** Mean operation time: Intervention: 97.9 min Control: 107.9 min Age: >18 years Gender: NR Obesity: NR **Procedures:** Breast reconstruction, mammoplasty, breast prosthesis, abdominoplasty, scar revision, zetaplasty, lipoma exeresis, gynecomasty & supernumerary mamma **Indications:** NR **Setting:** 1 hospital **Location:** Brazil **Dates:** NR **Inclusion Criteria**: Patients >18 years of age, scheduled for elective and clean plastic surgery procedures. **Exclusion Criteria:** NR	**Intervention**: n=125 Vigorous scrub with antiseptic soap followed by absorption with a sterile towel. This was followed by skin prep. Skin was painted with chlorhexidine 0.5% ethanolic solution and allowed to dry for 2 minutes **Timing of Intervention:** Preoperative **Duration of intervention:** Intraoperative **Agents: Povidone-Iodine 10%, or Chlorhexidine 0.5%** **Monitoring intervention:** Patients were followed up to 30 days to determine postoperative infections **Control group:** n=125 Vigorous scrub with antiseptic soap followed by absorption with a sterile towel. This was followed by skin prep. Skin was painted with 10% Povidone-iodine ethanolic solution and allowed to dry for 2 minutes **Standard Preventive Measures:** NR	**SSI: 30 days** Superficial incisional: Intervention = 0/125 Control =4/125 (1.6%) *P*= 0.06 *Not statistically significant* **Other infections:** NR **Topic-specific outcomes:** Not relevant **Adverse events:** NR **Reoperation:** NR **Length of Stay:** NR **Readmission:** NR **Mortality:** NR	**Definitions:** SSI: CDC definitions **Perioperative care** NR **Other notes** This paper is a "Viewpoints" in Plastic & Reconstructive Surgery **Follow up:** 30 days **Funding Source Conflicts:** Authors: None Institution: None Study: None Supplies: None
Ellenhorn 2005 [113]	**RCT** 1, 2, 10	To prove the equivalency	**No. Patients:** N=234 **Patient Characteristics:**	**Intervention:** n=119 Patients underwent only	**Wound infection-30 days** Intervention: 12/ 119	**Definitions:** Infection: defined by clinical

Author Year (Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
(ES)		for two commonly used techniques of surgical skin site preparation. [The techniques are 1) a scrub with povidone-iodine soap followed by paint with aqueous povidone-iodine OR 2) only povidone-iodine paint.]	Demographic data (mean age, obesity, diabetes, preoperative antimicrobial administration, and Mean ASA score) were analyzed and not found to be statistically significant between groups (All P≥10)**.** Age (mean) Intervention: 57.7 y Control: 60.5 y Gender: NR **The following characteristics given represent the whole study.** Obese: 43/234 (18.4%) Diabetic: 17/234 (7.3%) ASA score (mean) Intervention: 2.3 Control: 2.4 **Procedures:** Comparable between groups except as noted Colorectal: 79/234 (33.8%) Genitourinary: 38/234 (16.2%) Pancreaticobiliary: 40/234 (17.1%) Upper gastrointestinal: 38/234 (16.2%) Intervention: 24/20 (20%) Control: 14/115 (12%) Other*: 39/234 (12.3%) *Includes retroperitoneal sarcoma, lymph node dissection, second-look ovarian cancer Clean: 70/234 (29.9%) Clean-contaminated: 164/234 (70.1%)	painting of the operative site with aqueous povidone-iodine solution (available iodine 1.0%) only. **Timing of Intervention:** Preoperative **Duration of intervention-** Intraoperative **Agent:** Aqueous povidone-iodine (1.0%) and povidone-iodine detergent (0.75%) **Monitoring intervention:** NR **Control:** n=115 Patients underwent a vigorous 5-minute scrub using urethane sponges saturated with povidone-iodine detergent (available iodine 0.75%). Detergent was then absorbed with a blotting towel before painting the operative site with aqueous povidone-iodine solution (available iodine 1.0%) which was allowed to air-dry. **Standard Preventive Measures:** <u>Skin Prep:</u> All patients had all gross foreign material removed from the skin using a dry sponge and tape remover, if necessary. Shower: Patients were not	(10%) Control: 12/115 (10%) *P*=0.078 **Other infections** <u>Intra-abdominal infection</u> Intervention: 2/ 119 (2%) Control: 4/115 (3%) *P*= 0.14 **Topic-specific outcomes:** NR **Reoperation:** NR **Length of Stay:** NR **Readmission:** NR **Mortality:** NR **Adverse events:** NR	criteria as presence of wound erythema or purulence requiring therapeutic intervention within the first 30 days after the surgical procedure **Perioperative care:** Hair Removal: A razor was used to remove hair from the operative site. **Other notes:** None **Follow up:** 30 days after surgery. **Funding Source Conflicts:** Authors: None Institution: None Study: None Supplies: None

Author Year (Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			Drain: 67/234 (28.6%) **Indications:** malignancy **Setting:** cancer center **Location:** USA **Dates:** NR **Inclusion Criteria:** Patients undergoing elective abdominal operation **Exclusion Criteria:** Active infection at the time of operation, neutropenia defined as a white blood cell count of <2000 or an absolute neutrophil count of <500, history of skin reaction to iodine and anticipated use of prosthetic material as part of the surgical procedure.	instructed to shower with any antibacterial agent before the operation. **Non-Standard Preventative measures:** AMP: Use of perioperative IV antimicrobials left to the discretion of the operating surgeon. AMP given: Total: 229/234 (98%) Intervention: 98% Control: 97%		
Bibbo 2005 [122] (ES)	**RCT** 1, 10	To determine the efficacy of chlorhexidine compared with povidone-iodine as a preoperative skin preparation agent in reducing bacterial skin contamination before clean, elective foot and ankle	**No. Patients:** N=127 **Patient characteristics:** Patient characteristics were recorded and analyzed and they found no differences between the two groups **The following characteristics given represent the whole study.** Mean age (Range): 46 y (16-85y) Gender (m/f): 61/66 Obesity: NR Co-morbidities: Compromised hosts: 35% (includes smokers, diabetics, history of steroid use, or history of MRSA colonization) **Procedures:** NR **Indications:** NR	**Intervention:** n=60 A 7-minute scrub with chlorhexidine gluconate (4%) and isopropyl alcohol (70%) paint. Allowed to dry before draping. **Timing of Intervention:** Preoperative **Duration of intervention:** intraoperative **Agent:** Chlorhexidine gluconate (4%) and isopropyl alcohol (70%) paint; a Povidone-Iodine scrub (7.5%); and a povidone-iodine paint (10%) **Monitoring intervention:** Culture swabs taken from all the toes, all webs	**SSI (Follow up NR)** No Postoperative wound infections developed **Other Infections:** NR **Topic specific outcomes:** Not relevant **Reoperation:** NR **Length of Stay:** NR **Readmission:** NR **Reoperation:** NR **Mortality:** NR **Adverse events:** NR	**Definitions:** None **Perioperative care:** NR **Other notes:** None **Follow up:** NR **Funding Source Conflicts:** Authors: None Institution: None Study: None Supplies: None

Author Year (Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
		surgery.	**Setting:** One Hospital **Location:** USA **Dates:** NR **Inclusion Criteria**: Patients with intact, uninfected skin having clean, elective foot and ankle surgery **Exclusion Criteria:** Patients with open wounds, skin ulcers and/ or sores, an active acute or chronic infection, or who were on active antimicrobial therapy, which could alter skin flora.	spaces, nail folds, toe surfaces, and from the site of the proposed surgical incision. Patients having toe surgery had the dorsal foot swabbed as the matching site. Swabs were sealed and immediately transported & processed for aerobic, anaerobic, acid fast, and fungal cultures **Control:** n=67 A 7-minute scrub with povidone-iodine (7.5%) and painting of the foot and ankle with a povidone-iodine (10%) solution. Allowed to dry before draping. **Standard Preventive Measures:** Shower: No special instructions for bathing or showering implemented before surgery. Patients followed their usual personal hygiene on the day of surgery. AMP: Prophylactic intravenous antimicrobials (cefazolin or vancomycin for patients with documented penicillin and/or cephalosporin allergy) were administered in the 20 minute window before incision		

Author Year (Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
				Adhesive drapes were not used.		
Ostrander 2005 [126] (ES)	**RCT** 1, 7, 8	To assess the efficacy of three different surgical skin-preparation solutions (0.7% iodine and 75% isopropyl alcohol; 3% chloroxylenol; & 2% chlorhexidine gluconate and 70% isopropyl alcohol) in eliminating potential bacterial pathogens from the foot by evaluating the residual bacterial skin contamination following surgical skin preparation.	**No. Patients:** N= 120 **Patient characteristics:** **The following characteristics given represent the whole study.** Age y mean (range):48 (19-78) Gender (m/f): 47/78 Obesity: NR Comorbidities: Diabetes: Intervention 1: 0 Intervention 2: 0 Control: 1/ 40 (2.5%) Rheumatoid Arthritis Intervention 1: 2/40 (5%) Intervention 2: 2/40 (5%) Control: 4/40 (10%) Liver disease: Intervention 1: 2/40(5%) Intervention 2: 0 Control: 2/40 (5%) Renal issues Intervention 1: 1/40 (renal insufficiency) Intervention 2: 1/ 40 (renal transplant) Intervention 2: 1/40 (end stage renal disease) Control : 1/40 (renal failure) **Procedures:** Foot and ankle surgery **Indications:** NR **Setting:** One hospital **Location:** USA **Dates:** October 2002 – May 2003 **Inclusion Criteria**: Patients	**Intervention1:** n=40 3% chloroxylenol **Intervention2:** n=40 2% chlorhexidine gluconate and 70% isopropyl alcohol **Intervention 3** n=40 0.7% iodine and 74% isopropyl alcohol **Timing of Intervention:** Preoperative **Duration of intervention:** intraoperative **Monitoring intervention:** NR **Control:** Each group served as its own control for colonies formed (used a more proximal tibial site) **Standard Preventive Measures:** Shower**:** No home cleaning or disinfectant protocols utilized prior to surgery. AMP: All patients received intravenously administered cefazolin) within one hour of the surgical start time.	**Postoperative infection: (Follow up-NR)** Total: 3/120 (2.5%) Intervention1 Chloroxylenol: 2/40 (5%) (1 polymicrobial SSI after open reduction internal fixation (ORIF) calcaneal fracture and 1 atypical mycobacterium SSI after excision of Morton neuroma) Intervention2 Chlorhexidine gluconate and alcohol: 1/40 (2.5%) (Polymicrobial SSI after excision of large lipoma at lateral heel-portion of large tissue flap underwent necrosis with subsequent development of SSI) Control Iodine-alcohol: 0/40 *P*<1.0 **Other infections:** NR **Topic Specific Outcomes:** NA **Adverse events:** NR **Reoperation:** NR **Length of Stay:** NR **Readmission:** NR **Mortality:** NR	**Definitions:** NR **Perioperative care:** All procedures performed by one surgeon. **Other notes:** Power calculation not met. **Follow up:** NR **Funding Source Conflicts:** Authors: Industry Institution: None Study: None Supplies: None

Author Year (Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			undergoing foot and ankle surgery **Exclusion Criteria:** If patients had an open wound, abrasion, or current infection.			
Segal 2002 [114] (ES)	**RCT** 1, 2, 5, 9	To evaluate the effect of four different skin preparations on the incidence of sternal SSIs in patients undergoing coronary artery bypass graft surgery (CABG) who were identified as high risk of developing sternal SSI	**No. Patients:** N=209 **Patient characteristics:** Patient demographics compared. **The following characteristics given represent the whole study.** All patients had at least one high-risk factor (the basis of the study). 39% had 2 risk factors 4% had 3 risk factors (Percentage numbers appear larger in bar graph within paper my copy is difficult to read) Age (y): Mean 60.9 years (no SD given) Gender: Over 75% male Obesity: NR Redo sternotomies: 11.5% Procedures performed using the IMA: 88.5 Mean±SD Total OR time: 248 min ±29 Cross clamp time: 42 min±20 Last OR Glucose: 434±210 **Procedures:** elective **CABG** Surgery **Indications:** NR **Setting:** 1 tertiary/ teaching hospital **Location:** USA	**Intervention1**: n=52 Povidone-iodine five-minute scrub with paint **Intervention2:** n=50 One-step iodophor/alcohol water insoluble film **Intervention3**: n=51 one-step iodophor/alcohol water insoluble film with iodine impregnated surgical adhesive drape **Intervention 4**: n=56 Povidone-iodine paint **Timing of Intervention:** Preoperative **Duration of intervention:** Intraoperative **Agents:** Solutions, insoluble film & incise drapes not specified **Monitoring intervention:** Observation by nurses **Control:** **Standard Preventive Measures** <u>Shower</u> The nurse instructed patients to take an antimicrobial shower the evening before and the morning of surgery, or if they were inpatients, they were given a preoperative	**Sternal wound Infections: 6 weeks** Intervention1: 7/52 (13.5%) Intervention2: 1/50 (2.0%) Intervention 3: 3/51 (5.9%) Intervention 4: 7/56 (12.5%) *P*=0.117 **Infections per treatment** Aqueous Iodine (Intervention 1+4) 14/108 (13.0%) Insoluble Iodine (Interventions 2 and 3) 4/101 (4.0%) *P*=0.02 X^2=5.3 **Other infections:** NR **Topic-specific outcomes:** NR **Reoperation:** NR **Length of Stay:** Uninfected patients had a 5-6 day shorter length of hospital stay than infected patients. **Mortality:** NR **Adverse events:** NR	**Definitions** Obesity: BMI>120% of ideal weight. SSI: Clinical exam for signs of drainage, redness, tenderness, or sternal instability. Sternal surgical site exhibiting any of these signs was cultured. Positive cultures were correlated with clinical evidence according to the CDC guideline to indicate a sternal SSI **Perioperative care** NR **Other notes** Impregnated drapes in Intervention 3 shown to be ineffective as an intervention. Study deemed underpowered **Follow up:** 6 weeks postoperatively through regularly scheduled clinic visits **Funding Source Conflicts:** Authors: NR Institution: NR Study: NR Supplies: NR

Author Year (Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			Dates: Oct 1, 1994 – April 30-1997 **Inclusion Criteria:** Patients undergoing elective CABG with one or more of the following conditions: Diabetes Obesity Chronic Obstructive Pulmonary Disease (COPD) **Exclusion Criteria:** Patients with an allergy to topical iodine or with a preexisting infection indicated by a white blood cell count higher than 10,000 or by a temperature higher than 100.5^{o}F (38.06^{o}C) because their procedures were performed emergently.	antimicrobial shower in the hospital. Hair removal If necessary, a qualified patient care assistant clipped patients' hair the morning of surgery in patients' rooms. AMP: All patients received a prophylactic antimicrobial (i.e., cefuroxime) or if they had a documented allergy to penicillin, they received vancomycin in appropriate dosing window to provide adequate coverage at the time of incision.		
Hort 2002 [118] (ES)	**RCT** 1, 4, 5	To investigate the usefulness of standard surgical preparation (with chlorhexidine gluconate home scrubs and preoperative povidone-iodine or the chlorhexidine gluconate home scrubs	**No. Patients:** N=49 **Patient Characteristics:** Age, gender, weight, co-morbidities: NR Bilateral Procedures: Intervention: 2/23 Control: 6/26 **Procedures:** NR **Indications:** NR **Setting:** 1 Hospital **Location:** USA **Dates:** NR **Inclusion Criteria:** Patients undergoing foot or ankle surgery **Exclusion Criteria:** Total ankle arthroplasties	**Intervention**: n= 25 feet (23 patients[2 received bilateral procedures-]) Patient was given two chlorhexidine gluconate scrub brushes with directions to perform two separate self-scrubs several hours apart before retiring to bed the night before the operation. In the operating room, a 10 minute scrub with povidone-iodine topical solution was followed by painting of the foot with povidone-iodine topical	**SSI (Follow up NR)** NO patient in either group showed clinical signs of wound infection and all wounds healed uneventfully. **Other Infections:** NR **Topic specific outcomes:** NR **Reoperation:** NR **Length of Stay:** NR **Mortality:** NR **Adverse events:** NR	**Definitions(e.g., SSI)** Not defined **Perioperative care** NR **Other notes:** If a patient underwent a bilateral procedure, both feet assigned to the same group. **Follow up**: NR **Funding Source Conflicts:** Authors: NR Institution: NR Study: NR Supplies: NR

Author Year (Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
		plus pre-operative 70% alcohol) in prevention of surgical site contaminatio n.		solution plus the addition of a 3-minute preoperative preparation of the area with 70% alcohol. **Timing of Intervention:** Preoperatively **Duration of intervention:** intraoperative **Agents:** Povidone-Iodine solution; Scrub Brushes **Monitoring intervention:** NR **Control:** n=32 feet (26 patients;6 had bilateral procedures) Patient was given two chlorhexidine gluconate scrub brushes with directions to perform two separate self-scrubs several hours apart before retiring to bed the night before the operation. In the operating room, a 10 minute scrub with povidone-iodine topical solution was followed by painting of the foot with povidone-iodine topical solution. **Standard Preventive Measures** AMP: All patients were given one dose of broad-spectrum intravenous antimicrobial preoperatively (usually		

Author Year (Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
				cefazolin before tourniquet) Operative irrigation: Wounds were irrigated frequently during surgery with an antimicrobial solution.		
Roberts 1995 [117] (ES)	**RCT** 1, 2, 7, 8, 9	To compare the efficacy of 2 commerciall y available skin preps: a relatively new 1-step, iodophor in alcohol, film-forming, water-insoluble skin prep, versus the tradition al 5-10 minute aqueous iodophor scrub and paint. In both groups, an iodophor-containing antimicrobial incise film was also applied on the chest. No incise film was used on the	**Number of patients: n=200** **Patient Characteristics:** no significant differences in patient characteristics between groups. ·Age: NR ·Gender: NR ·Obesity: NR ·Comorbidities: NR **Procedures:** CABG **Indications:** NR **Setting:** 1 general hospital **Location:** USA **Dates:** NR just mentioned a "1 year period" **Inclusion Criteria:** consenting adults undergoing CABG **Exclusion Criteria:** if patients were allergic to iodine or its compounds	**Intervention group:** n=104 **1step:** patients underwent 1 step iodophor in water application preop. And allowed to air dry thoroughly for 2-3 min. 1 unit was used for each chest, and each leg. **Timing of intervention:** preop **Duration of intervention:** NA **Device/agent:** aqueous iodophor **Monitoring intervention:** NR **Control group: n=96** **2step:** patient underwent a traditional 2step starting with a 5-10min scrub of operative sites (chest and legs) with aqueous iodophor solution followed by an application of an iodophor solution. The sites were then blotted dry with a sterile towel. **Standard preventive measures:** Showers: patients had antimicrobial (iodophor) showers on the night prior	**SSI (30days)** Overall Infection: 1step: 10/104 (9.6%) 2step: 9/96 (9.4%) NS Chest Infection 1step: 4/104 (3.8%) 2step: 6/96 (6.3%) NS Deep Chest Infection 1step: 0/104 2step: 3/96 (3.1%) Leg Infection: 1step: 6/104 (5.8%) 2step: 5/96 (5.2%) NS **Other infections:** no evidence found for either group **Topic-specific outcomes:** NR **Reoperations:** All 3 deep wounds in control group required surgical intervention. **Length of stay:** NR **Mortality:** NR **Adverse events:** NR	**Definitions:** Infected Wounds: if purulent material drained from the incision site. Confirmation of infection by a positive culture was not necessary. Superficial infected surgical wounds: involved the skin, subcutaneous tissue or muscle located above the fascial layer. Deep infected surgical wounds: involved tissues or spaces at or beneath the fascial layer including wounds that spontaneously dehisced or were deliberately opened for drainage. Elderly: 65yo or older **Perioperative care:** In both groups, an iodophor-containing antimicrobial incise film was also applied on the chest. No incise film was used on the leg. **Other notes:** Small sample size. Too small to perform multivariate analyses. **Follow-up:** 30 days **Funding Source Conflicts:** Authors: NR

Author Year (Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
		leg.		to surgery AMP: Cefuroxime started in OR approx. 30 min prior to incision and continued every 6h for 36h postop. Hair removal: with clipper.		Institution: NR Study: NR Supplies: NR
Gilliam 1990 [115] (ES)	**RCT** 1, 8, 9	To compare the efficacy of a traditional skin preparation of an aqueous iodophor consisting of a five-minute scrub-and-paint AND a sterile non-antimicrobial plastic surgical adhesive drapes. With the efficacy of a single application of a water-insoluble iodophor-in-alcohol solution AND a sterile non-antimicrobial plastic surgical adhesive	**No. Patients:** N=60 **Patient characteristics:** Age, sex, & duration of operation were not statistically significantly different between groups. Age (average), y: Intervention: 65y Control: 61y Gender (m:f): Intervention: 11:19 Control: 8:22 Obesity: NR Length of Operation (average), Min (range): Intervention: 135 (30-310) Control: 130 (160-300) **Procedures:** Primary or revision total hip or total knee arthroplasty **Indications:** NR **Setting:** 1 hospital **Location:** USA **Dates**: NR **Inclusion Criteria:** Patients undergoing clean total joint surgery. **Exclusion Criteria:** NR	**Intervention:** n=30 Skin was prepared with a one-step application of a water-insoluble iodophor-in-alcohol solution applied as paint. Skin was allowed to dry before covering the surgical area with a sterile, non-antimicrobial plastic surgical adhesive drapes. **Timing of Intervention:** Preoperative **Duration of intervention:** Intraoperatively **Agent** Water-insoluble iodophor-in-alcohol solution **Monitoring intervention:** For liquid skin prep NR except for surgical adhesive drape, where adhesion to the skin was evaluated by the operating surgeon prior to wound closure **Control:** n=30 Skin was prepared with a traditional five-minute aqueous iodophor scrub followed by the application of an aqueous iodophor solution as	**SSI (follow up NR)** None of the patients became infected **Other Infections:** No Infections **Topic Specific Outcome:** Drape Lift: (yes or no phenomenon) Intervention: 0/30 Control: 12/30 (40%) *P*<0.01 **Reoperation:** NR **Length of Stay:** NR **Readmission:** NR **Mortality:** NR **Adverse events:** NR	**Definitions:** NR **Perioperative care** Hair Removal: All hair was removed by dry shave just prior to preparing the skin. **Other notes** Intervention was found to increase incise drape adhesion, particularly at the wound edges. **Follow up:** NR **Funding Source Conflicts:** Authors: NR Institution: NR Study: NR Supplies: NR

Author Year (Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
		drapes.		paint. Skin was allowed to dry before covering the surgical area with a sterile, non-antimicrobial plastic surgical adhesive drapes. **Standard Preventive Measures** Preop Shower: All patients showered the night before surgery with chlorhexidine gluconate soap. Environmental: Surgery was conducted under a horizontal unidirectional laminar air-flow system.		
Berry 1982 [125] (ES)	**RCT** 1, 2, 6, 7, 8, 9	To compare the effect of alcoholic povidone-iodine and alcoholic chlorhexidine (both as skin prep and surgical scrub) on the incidence of postoperative wound infection in a general surgical unit	**No. Patients:** N=866 **Patient Characteristics:** Operative & demographic information was deemed similar between study groups. Details not reported Age: <15 years Intervention: 4 (0.9%) Control: 4 (1.0%) 15-64 years Intervention: 338 (74.6%) Control: 309 (74.8%) ≥65 years Intervention: 112 (24.7%) Control: 100 (24.2%) Gender: NR Obesity: NR **Procedures, No (%): (N=886)** Operations on biliary tract: 167 (18.8%) Large bowel operations: 61 (6.9%)	**Intervention:** n=453 Two applications of 0.5% chlorhexidine alcohol. Skin preparation solution was applied with sterile sponges. **Timing of Intervention:** Preoperative **Duration of intervention:** Intraoperatively **Agent:** povidone iodine 10% in alcohol or 0.5% chlorhexidine in spirit **Monitoring intervention:** NA **Control:** n=413 Two applications of povidone-iodine 10% in alcohol. Skin preparation solution was applied with sterile sponges. **Standard Preventive**	**SSI – (Follow up: not clear- wound assessed 3-4 days postop and at discharge)** More than one type of abnormality reported on some wounds **Wound abnormality: Any abnormality agreed by both observers at discharge, all operations** Any wound abnormality Intervention: 44/453 (9.7%) Control: 61/413 (14.8%) $X^2(1)= 4.7$, $P=0.03$ Biliary tract Intervention: 6/90 (6.7%) Control: 15/77 (19.5%) $X^2(1)= 5.1$, $P<0.05$ Other clean operations Intervention: 2/105	**Definitions:** No definitions, wounds were judged at evaluator's discretion as normal, erythematous, edematous, discharging or purulent. Moist wounds were swabbed & cultured for both aerobic (**Cowan 1974)** & anaerobic (biochemical tests) organisms **Perioperative care :** NR **Other notes:** None **Follow up:** Wounds were assessed independently by one member of the nursing staff and one member of the medical staff at a "standard" period of 3-4 days post-operatively and then at discharge . If patient was discharged

Author Year (Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			Other laparotomy operations: 96 (10.8%) Hernia/genitals/varicose veins 338 (38.1%) Other 'clean' non-abdominal: 204 (23.0%) **Indications**: NR **Setting:** 1 hospital **Location:** United Kingdom **Dates**: May 1978 – February 1980 **Inclusion Criteria:** All elective surgical cases **Exclusion Criteria:** Patients known to be sensitive to either skin preparation utilized in this study.	**Measures** Surgical hand Scrub: A sterile brush was used to scrub the hands, paying particular attention to the areas under the nails and in the nail folds. The forearms were washed as far as the elbow. Skin was scrubbed for 4-5 minutes as recommended. Control: Scrub solution was alcoholic povidone-iodine (10% available iodine) Intervention: Scrub solution was alcoholic chlorhexidine with .5% available chlorhexidine. Hair removal: Skin shaving was routinely performed on hairy skin 18-24 hours preoperatively **Non-Standard Preventive Measures:** Antimicrobial Prophylaxis Only patients undergoing colonic & rectal surgery received metronidazole 3 times daily and neomycin four hourly for 3 days. Bowel Prep: Routine bowel prep was used only in large bowel surgery.	(1.9%) Control: 13/99 (13.1%) $X^2(1)= 7.9$, $P<0.05$ Differences in procedures below, not statistically significant: Large Bowel Intervention: 5/28 (17.9%) Control: 3/33 (9.1%) Other Laparotomy Intervention: 15/49 (30.6%) Control: 9/47 (19.1%) Hernia, genitalia, veins Intervention: 16/181 (8.8%) Control: 21/157 (13.4%) **Wound abnormalities: Specific abnormality agreed by both observers at discharge, all operations** Redness of wound: Intervention: 16/453 (3.5%) Control: 21/413 (5.1%) Swelling of Wound: Intervention: 12/453 (2.6%) Control: 12/413 (2.9%) Discharge from wound: Intervention: 16/453 (3.5%) Control: 21/413 (5.1%) Pus from wound: Intervention: 13/453	before the 3rd day was assessed just prior to leaving the hospital. **Funding Source Conflicts:** Authors: NR Institution: NR Study: NR Supplies: NR

Author Year (Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
					(2.9%) Control: 22/413 (5.3%) **Any abnormality agreed by both observers 3-4 days postop (**Note: *64 intervention and 59 control patients were discharged before 3 days, therefore the total population for results below is: Intervention: n=389 Control: n=354Infection was slightly more common overall in the control group but the difference was not statistically significant: Total wound abnormalities Intervention: 27/389 (6.9%) Control: 35/354 (9.9%) Biliary tract Intervention: 2/90 (2.2%) Control: 8/76 (10.5%) Large Bowel Intervention: 3/28 (10.7%) Control: 0/31 Other Laparotomy Intervention: 7/49 (14.3%) Control: 5/47 (10.6%) Hernia, genitalia, veins Intervention: 13/157 (8.3%) Control: 16/150 (10.7%) Other clean operations Intervention: 2/65 (3.1%) Control: 6/50 (12.0%)	

Author Year (Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
					Any abnormality recorded by one or both observers 3-4 day postop (i.e. disagreement between observers) Total wound abnormalities Intervention: 41/389 (10.5%) Control: 44/354 (12.4%) Biliary tract Intervention: 4/90 (4.4%) Control: 11/76 (14.5%) $X^2(1)= 3.9$, $P<0.05$ **Overall infection rate for "clean" operations (excluding colonic & biliary):** 11.9% Infection/ abnormality rates varied between surgeries and groups. NO overall statistically significant advantage for either group emerged for an all-purpose skin prep solution. **Other Infections:** NR **Topic Specific Outcomes:** NA **Reoperation:** NR **Length of Stay:** NR; Analysis of the date for each group showed no significant difference between the preparations in the mean length of patients' stay in	

Author Year (Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
					the hospital **Readmission:** NR **Mortality:** NR **Adverse events:** NR	

eTABLE 48. Evidence Table for Q8C. How safe and effective is the application of a microbial sealant immediately following skin preparation?

Author Year (Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
Dromzee 2012 [131] (ES)	**RCT** 1, 2, 10	To test the hypothesis that microbial sealant reduces surgical site infection in children and adolescent patients with scoliosis undergoing scoliosis correction.	**Number of patients: N=56** **Patient Characteristics** ·Age, year: mean (SD) Intervention: 14.93 (1.7) Control: 15.21 (1.9) P=0.570 ·Gender: B NR ·Obesity: NR ·Comorbidities: NR Number of fused levels, mean (SD) Intervention: 11.93 (2.7) Control: 12.54 (3.09) P=0.440 Intraoperative blood loss (ml) mean (SD) Intervention: 539.64 (284.09) Control: 658.93 (489.15) P=0.271 Intraoperative time (min), mean (SD) Intervention: 196.61	**Intervention group:** n=28 Sterile, film-forming cyanoacrylate liquid application before application of the incise drape **Timing of intervention:** Intraoperative **Duration of intervention:** NR **Device/agent:** film forming cyanoacrylate liquid **Monitoring intervention:** NA **Control group:** n=28 Incise drape alone. **Standard preventive measures:** AMP: NR Pre-op bathing: all patients showered with a povidone iodine skin antiseptic the day before the surgery and early in the morning of the surgery. Skin prep: in OR using 2 consecutive applications of one-step 5% povidone-iodine & alcohol solution. Drapes: both groups used sterile incise drapes Drains – one to three suction drains	**SSI :** Total: 6/56 (10.7%) Intervention: 5/28 (18.2%) Control: 1/28 (3.6%) P=0.096 There were 3 deep and 3 superficial infections but it is not report which group they belonged in All infections resolved after local wound debridement and antibiotics. Age as risk factor for early infection Mean age (SD) Infection (n=6): 17.07 (0.47) No infection (n=50): 14.83 (1.8) P<0.0001	**Definitions:** SSI – not defined **Perioperative care:** Anesthesia: general anesthesia was used **Other notes:** 50 patients = number of cases required to have an 80% chance of detecting an effect of 0.05. **Follow-up:** NR **Funding Source Conflicts:** Authors: None Institution: None Study: None Supplies: None

Author Year (Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			(62.76) Control: 234.64 (90.65) P=0.074 4-6 Week preoperative halo traction: 6/56 (10.7%) [which group NR] for stiff and severe deformity **Procedures:** Scoliosis correction **Indications:** 29 had spinal deformities from various neuromuscular causes. 27 had adolescent idiopathic scoliosis. **Setting:** 1 university hospital **Location:** France **Dates:** June 2010 and June 2011 **Inclusion Criteria:** (1) idiopathic or neuromuscular scoliosis, and (2) indicated for posterior correction and fusion **Exclusion Criteria:** (1) previous spinal surgery and (2) indicated for anterior or combined procedures.	were placed in the wound before closure. Closure: either skin staples or bioresorbable skin sutures at surgeon's discretion.	**Other infections:** NR **Topic-specific outcomes:** NR **Reoperations:** NR **Length of stay:** NR **Mortality:** NR **Adverse events:** No immediate or delayed adverse effects related to the use of sealant were noted.	

Author Year (Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
von Eckards-tein 2011 [128] (ES)	**RCT** 1, 2, 6, 7, 8, 9	To determine if the use of cyanoacrylate -based skin sealant before coronary artery bypass grafting (CABG) could reduce surgical wound contamination by skin microflora and decrease post-procedure infections.	**Number of patients: N=293** **Patient Characteristics:** There was no significant difference between groups except in occurrence of obesity (see below) ·Age, y: mean (SD) Intervention: 63.2 (8.53) Control: 62.9 (9.97) ·Gender (m:f) Intervention: 120/26 Control: 129:18 ·Obesity (BMI>30.0 to ≥37 kg/m^2) Intervention: 40 (27.6%) Control: 20 (13.6%) P=0.003 ·Comorbidities Diabetes Mellitus, Type I or Type II Intervention: 49 (33.6%) Control: 49 (33.3%) Tobacco Use, Intervention: 84 (57.5%) Control: 91 (61.9%) Alcohol use Intervention: 42 (28.8%) Control: 52 (35.4%) Duration of surgery (min): Intervention: 227.6 (42.4) Control: 211.7 (60.6)	**Intervention group:** Intention to treat (ITT): n= 146 Per protocol: n=131 Surgical sites were prepared with commonly used surgical skin preparations such as povidone-iodine or 0.7% available iodine in isopropyl alcohol 74%w/w. Skin sealant was applied on the surgical sites after surgical skin preparations and just before making the incision. Surgical incise drapes (if used) were applied after all surgical skin preparations had dried completely. Skin sealant was considered dry when a film formed on the skin. **Timing of intervention:** Intraoperatively **Duration of intervention:** Intraoperatively **Device/agent:** Cyanoacrylate-based skin sealant **Monitoring intervention:** NR **Control group:** ITT: n= 147 Per Protocol: n=138 Surgical sites were prepared with commonly used surgical skin preparations such as povidone-iodine or 0.7% available iodine in isopropyl alcohol 74%w/w. **Standard preventive measures:** NR **Non-standard preventive measures:** AMP: administered at the discretion	**SSI: (follow up 30 days postop)** Patients may have more than 1 SSI For ITT Analysis Below Intervention: n=146 Control: n=147 Total SSIs: 23/293 (7.8%) Intervention: 9/146 (6.2%) Control: 14/147 (9.5%) p=0.285 The majority were superficial SSIs: Incision site infection Intervention: 6 (2.7%) Control: 10 (6.6%) Although there frequency of patients with SSI was similar between groups, the use of skin sealant was associated with a 35% relative risk reduction in the occurrence of SSI In the subgroup of obese patients, there was a relative risk reduction for SSI of 83.3% associated with use of skin sealant. However, this is based on small patient and event numbers: Obesity	**Definitions:** SSI: CDC/ NNIS criteria Adverse events: any undesirable clinical occurrence in a patient that may be attributed to the study treatment or to SSI. **Perioperative care:** NR **Other notes:** None **Follow-up:** For the duration of hospitalization and for 30 days postop **Funding Source Conflicts:** Authors: None Institution: None Study: None Supplies: None

Author Year (Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			P=0.469 Intraaortic balloon pump: Intervention: 9 patients Control: 4 patients **Procedures:** Elective Coronary artery bypass grafting (CABG) **Indications:** NR **Setting:** 5 Centers **Location:** USA, Europe, Asia and Latin America **Dates:** April 2006 - February 2009 **Inclusion Criteria:** Patients aged 18 years or older who were undergoing elective CABG surgery with median sternotomy and the use of saphenous vein or radial artery as 1 of the graft sites. **Exclusion Criteria:** Patients undergoing additional procedures, known sensitivity or allergy to cyanoacrylate, isopropyl alcohol, iodine or iodine-containing products or tape. Also abnormal skin conditions around the surgical incision site, antimicrobial-	of the surgeon and according to hospital protocol Surgical procedure: dictated by current practice and not specified in the study protocol	Intervention: 1/40 (2.5%) Control: 3/20 (15.0%) P=0.0.015 <u>Patients with at least one SSI:</u> <u>Sternal Site Infection</u> Intervention: 4 (2.7%) Control: 7 (4.8%) P=0.363 <u>Graft Site Infection</u> Intervention: 7 (4.8%) Control: 7 (4.8%) P=0.989 NOTE: Left saphenous vein graft harvest in 74%-78% of patients Left radial artery or right saphenous vein graft harvest in 25-30% of patients Location and number of harvest sites did not appear to affect risk of SSI “but does add further variation to the study” <u>Sternal and/or Graft Site(s) Infection</u> Intervention: 9 (6.2%) Control: 14 (9.5%) P=0.285 <u>Both Sternal and Graft Site Infection</u> Intervention: 2 (1.4%) Control: 0	

Author Year (Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			impregnated incise drapes used during the operation, chemotherapy, immunosuppressive therapy or steroid therapy, use of antimicrobials for an active infection, HIV infection with CD4 count <350mm^3, therapeutic radiation or renal dialysis, morbid obesity (BMI>37kg/m^2); neutropenia, intraaortic balloon pump or mechanical assist device in place preoperatively, and hospital stay >14 days		P=0.247 **Infections for Total Population** **Denominators:** Intervention: n= 146 Control: n= 147 Arteriovenous graft site infection Intervention: 1 (0.7%) Control: 0 Incision site infection Intervention: 6 (2.7%) Control: 10 (6.6%) Mediastinitis Intervention: 3 (2.1%) Control: 2 (1.4%) Osteomyelitis Intervention: 1 (0.7%) Control: 1 (0.7%) Postoperative Wound Infection Intervention: 0 Control: 1 (0.7%) Skin graft Infection Intervention: 0 Control: 1 (0.7%) Wound Infection Intervention: 1 (0.7%) Control: 0 **Other infections:** NR **Topic-specific outcomes:** Frequency of Surgical Site infection in patients with Alcohol use, Tobacco use & Obesity	

Author Year (Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
					Alcohol Use Intervention: 2/42 (2.7%) Control: 6/52 (4.8%) P=0.291 Tobacco Use Intervention: 3/84 (3.6%) Control: 11/91 (12.1%) P=0.050 Obesity Intervention: 1/40 (2.5%) Control: 3/20 (15.0%) P=0.0.015 Skin sealant associated with a relative risk reduction of 83% for obese patients Alcohol Use or Tobacco Use or Obesity Graft Site Infection Intervention: 2/108 (1.9%) Control: 6/112 (5.4%) P=0.037 Sternal Site Infection Intervention: 4/108 (4.6%) Control: 5/112 (4.5%) P=0.546 Graft and/or Sternal Site Infection Intervention: 5/108 (4.6%) Control: 11/112 (9.8%) P=0.024 **Reoperations:**	

Author Year (Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
					Postoperative re-exploration of sternal incision site Intervention: 5/ 146 (3.4%) Control: 3/ 147 (2.0%) **Length of stay:** NR **Mortality:** 4 (1.4%) total (none considered related to study treatment) Intervention: 1/146 (0.7%) Sudden death after spasm of the graft, myocardial infarction, pulmonary embolism, and air embolism Control: 3/ 147 (2.0%) 1/3 excessive bleeding, atrial fibrillation, and global abdominal ischemia 1/3: ventricular fibrillation 1/3: hemorrhagic shock, erosion of the right atrium and mediastinitis P=0.363 **Adverse events:** Intervention: n= 146 Control: n= 147 Overall fewer than 10% of subjects experienced adverse events during the study and most were related to SSIs	

Author Year (Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
					Erythema Intervention: 1/146 (0.7 Control: 0/ 147 Surgical and medical procedures: Hospitalization Intervention: 0/ 146 Control: 1/ 147 (0.7%)	
Iyer 2011 [129] (ES)	**RCT** 1, 3, 4, 5, 10	To determine the effect of pretreatment with n-butyl cyanoacrylate-based microbial skin sealant to the saphenous vein graft harvest site in a population undergoing cardiac surgery and discuss its potential use in decreasing infections in other kinds of surgery.	**Number of patients: N=47 (94 legs)** Patients served as their own controls **Patient Characteristics:** Baseline characteristics between the treated and untreated legs were similar because the procedure was conducted on the same individual. ·Age y, mean (SD): 67.0 (7.6) ·Gender (m:f): 39:8 ·Obesity- NR ·Comorbidities Arterial hypertension: 31 (65.9%) Peripheral vascular disease: 0 (0%) Venous disease in the legs: 0 (0%) Diabetes Mellitus: 12 (25.5%) Hyperlipidemia: 40 (85.1%) Renal Failure: 4 (8.5%) Ejection fraction, mean	**Intervention group:** n= 47 The long saphenous vein grafts were taken from the below-knee segment in both legs of all patients. Skin was disinfected using alcoholic povidone-iodine solution & 3 minutes were allowed for the disinfecting solution to dry. The sealant was applied to only 1 leg per case after the disinfecting solution was allowed to dry. An applicator was used to apply a single even layer of microbial sealant over an area overlying the saphenous vein harvest site. The sealant was allowed to dry for 2 minutes. Skin sealant was NOT used at the sternal site. **Timing of intervention:** Intraoperatively **Duration of intervention:** Intraoperatively **Device/agent:** Cyanoacrylate-based skin sealant **Monitoring intervention:** NR **Control group:** n= 47 Skin was disinfected using alcoholic povidone-iodine solution & 3 minutes were allowed for the	**SSI: (follow up: 1 month)** Total saphenous vein harvest site SSI: 13/94 (13.8%) Intervention: 1/ 47 (2.1%) Control: 12/ 47 (25.5%) P=0.0011; 95% CI for difference (-0.374 to -0.0945) Intervention: The leg developed a severe infection and required incision and drainage. In the same patients, the untreated leg had no infection. Control: These 12 legs showed evidence of infection that ranged from oozing of serous fluid which responded to conservative therapy (n=7) to severely infected wound requiring incision and drainage (n=4) and	**Definitions:** Infection: if the wound showed signs of infection, it was graded by the Southampton wound grading system (Bailey 1992) Grades as follows: 0: Normal healing 1: Normal healing with bruising or erythema, subclassified as A, B, or C according to the size of bruising 2: erythema with other signs of inflammation subclassified as A, B, or C according to findings at 1 point around the suture or around the whole wound 3: hemoserous discharge (A<2cm, B>2cm, C=large volume, d>3 days) 4: purulent discharge (A<2cm, B>2cm) 5: deep or severe infection with or without tissue breakdown. **Perioperative care:** NR **Other notes:** the study was terminated after ethical committee review at the

Author Year (Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			(SD): 47.3 (13.3) **Procedures:** Coronary artery bypass graft (CABG) requiring 3 or more lengths of long saphenous vein to achieve revascularization. Additional internal thoracic conduit was also routinely used **Indications:** NR **Setting:** 1 hospital **Location:** Australia **Dates:** Began August 2008 - ???? (NR) **Inclusion Criteria:** Patients undergoing CABG requiring 3 or more lengths of long saphenous vein to achieve revascularization **Exclusion Criteria:** If the patient required ≤2 segments of vein wherein only 1 leg was used and any features that would cause dissimilarity between the legs, which included the vein in either leg not being usable, unilateral vascular disease, or skin lesion. Also if there was a discrepancy in the length of the	disinfecting solution to dry. No skin sealant. **Standard preventive measures:** Surgical technique: apart from application of the sealant, the surgical technique in both legs was identical and the vein was harvested using a single open incision. Endoscopic techniques were not employed and in most of the patients, the below portion of the vein was harvested. Hair removal: performed using an electrical clipper the day before surgery. Shower: patients washed with soap the morning of surgery Drapes: iodine impregnated drapes were used in all patients. Closure: Closure of the subcutaneous layer was with 2-0 absorbable, braided synthetic sutures, and subcuticular closure of the skin was with 3-0 synthetic absorbable sutures. A hydrocolloid dressing was used in all patients Normothermia: All patients underwent systemic cooling to 32^{o} to 34^{o}C.	debridement (n=1) There were no other infections observed at 30 days and investigators were not aware of any infections developing after this point. **Other infections:** NR **Topic-specific outcomes:** Southampton Grade Intervention: 1/1: Grade 4B Control: 3/12: Grade 5 2/12: Grade 4B 2/12: Grade 3D 4/12: Grade 3B 1/12: Grade 3A **Reoperations:** Intervention: The infected leg required incision and drainage. Control: 1 severely infected leg required debridement. **Length of stay:** NR **Mortality:** NR **Adverse events:** No patients had perioperative infarctions and there	enrollment of 47 patients **Follow-up:** 1 month (if the general practitioner involved with the care after discharge detected an infection before the 4-week follow-up, an appointment was arranged before the stipulated follow-up and the findings were recorded. **Funding Source Conflicts:** Authors: None Institution: None Study: None Supplies: None

Author Year (Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			incision between the treated and untreated legs.		were no adverse intraoperative events.	
Towfigh 2008 [130] (ES)	**RCT** 1, 2, 3, 4, 5, 7, 8, 9, 10	To compare the safety and effectiveness of microbial sealant in reducing the incidence of surgical incision bacterial contamination relative to surgical skin preparation alone in elective open inguinal hernia repair.	**Number of patients: N=166** (evaluable for effectiveness of antimicrobial sealant) Note: 148 (84%) in per protocol analysis **Patient Characteristics:** There were no statistically significant differences between the two groups. ·Age: mean (SD) y Intervention: 52.7 (15.9) Control: 54.1 (14.9) **Values below based on Total pop: N=177 Intervention n=88 Control n=89** ·Gender (male) Intervention: 84/88 (95.5%) Control: 86/89 (96.6%) ·Obesity: (BMI>30kg/m^2) Intervention: 27 (30.7%) Control: 18 (20.2%) ·Comorbidities Diabetes Mellitus Intervention: 2 (2.3%) Control: 4 (4.5%) 7 patients had comorbid clinical characteristics that have been reported to be associated with	**Intervention group:** n=83 (Per Protocol: 68) Standard surgical skin preparation including a skin prep of 10% povidone-iodine on the operative field which was allowed to dry. This was followed by a single coat application of the cyanoacrylate-based microbial sealant. The sealant was allowed to dry before the application of surgical drapes. **Timing of intervention:** Pre intra, and postoperatively **Duration of intervention:** Pre intra, and postoperatively **Device/agent:** Cyanoacrylate-based microbial sealant **Monitoring intervention:** NR **Control group:** n=83 (Per Protocol: 80) Standard surgical skin preparation including a skin prep of 10% povidone-iodine on the operative field which was allowed to dry. **Standard preventive measures:** Instruction: all principal investigators were given hands-on instruction in how to use the applicator prior to enrollment of subjects. **Non-standard preventive measures:** Surgeons were allowed to perform the open inguinal hernia repair	**SSI (2 and 4 weeks):** Total SSI: 3/148 (2%) Intervention: 0 Control: 3/80 (3.8%) All 3 SSIs were positive for *S. aureus* and 1/3 of these was a deep infection with MRSA Given the low number of events and early termination of the study, it is underpowered to detect a difference in SSI. **Other infections:** NR **Topic-specific outcomes:** Most patients did not maintain a sterile wound throughout surgery regardless of resultant SSI or not. One surgeon reported visible flaking of the microbial sealant film during the procedure. One patient in the microbial sealant group had skin irritation (resolved on its own) Surgeons reported 4 incidents of difficulty	**Definitions:** Signs of infection: swelling, erythema, drainage, warmth. And dehiscence. **Perioperative care:** NR **Other notes:** A patient was considered lost to follow up after 4 unreturned attempts at contact. **Follow-up:** at 2 and 4 weeks postoperatively to access the incision **Funding Source Conflicts:** Authors: None Institution: None Study: Industry Supplies: Industry

Author Year (Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			wound complications such as hyperhidrosis, eczema, psoriasis, or an autoimmune disease. One patient had a previous history of SSI. Procedure duration: (min) Mean (SD) Intervention: 73.7 (28.4) Control: 75.6 (31.5) **Procedures:** Open inguinal hernia repair. **Indications:** NR **Setting:** 6 Teaching hospitals **Location:** USA **Dates:** July 2005 - September 2006 (Clinical trial discontinued in September of 2006 when FDA granted regulatory approval for this product as a class II medical device. **Inclusion Criteria:** Scheduled for open, class 1 clean inguinal hernia repair; aged 18 or older; able to complete mean (SD) 30 (5) day follow-up.; and able and willing to provide informed consent	based on their personal preference with respect to hair clipping, perioperative antimicrobials, surgical techniques and use of mesh Preoperative data: Based on Total population N=176 because data missing from 1 intervention Antimicrobial shower: Intervention: 23/87 (26.4%) Control: 24/89 (27.0%) Hair removal: 173/176 (98.3%) Clipping/shaving Intervention: 45/35 Control:47/36 AMP: administered to 131/176 (74%) Intervention: 61/87 (70.1%) Control: 70 (78.7%) Mesh implanted Intervention: 71/88 (81.6%) Control: 72/89 (80.9%) Closure using sutures Intervention: 87/88 (98.9%) Control: 88/89 (98.9%) Wound covered with a dressing Intervention 77 (87.5%) Control: 80 (89.9%) P=0.62	incising through the clear film. **Reoperations:** The deep MRSA infection from the control group required readmission, debridement, mesh removal and intravenous antimicrobials. **Length of stay:** NR **Mortality:** NR **Adverse events:** Serious adverse events All serious adverse events occurred in the control group and resolved at final follow up Admission for SSI due to MRSA:1 Groin hematoma: 1 Chest pain: 1 Dyspnea: 1 Scrotal edema: 1 Knee pain: 1 Non-serious adverse events Scrotal edema, hematoma Intervention: 3 Control: 2 Wound dehiscence Intervention: 1 Control: 0 Incisional pain/ swelling Intervention: 1 Control: 1	

Author Year (Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			Exclusion Criteria: Known sensitivity to cyanoacrylate formaldehyde or acetone products or iodine or iodine containing products; surgical procedures involving mucous membranes or eyes; laparoscopic surgical procedures; evidence of coexistent infection at a remote body site; skin rashes or exfoliative condition the day of surgery; history of keloid formation; currently receiving high-dose steroid or immunosuppressive therapy; chemotherapy treatment within 30 days of current surgery; diagnoses of diabetes HbA>7.0% obtained within 90 days; use of oral, IV or topical (in expected area of incision) antimicrobials within 20 days prior to the day of surgery; pregnant or nursing; or participation in any other study of an investigational drug or		Skin irritation Intervention: 1 Control: 0 *Possibly attributable to investigational device* Constipation Intervention: 1 Control: 0 Incisional bleeding Intervention: 1 Control: 0 Urinary frequency Intervention: 0 Control: 1 Urinary retention Intervention: 1 Control: 1 Epigastric hernia drainage Intervention: 1 Control: 0 Decreased limb sensation Intervention: 0 Control: 1	

Author Year (Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			device within 2 week prior to the current procedure.			

eTABLE 49. Evidence Table for Q8D. How safe and effective are plastic adhesive drapes?

Author Year (Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
Segal 2002 [114] (ES)	**RCT** 1, 2, 5, 9	To evaluate the effect of four different skin preparations on the incidence of sternal SSIs in patients undergoing coronary artery bypass graft surgery (CABG) who were identified as high risk of developing sternal SSI	**No. Patients:** N=209 **Patient characteristics:** Patient demographics were compared. **The following characteristics given represent the whole study.** All patients had at least one high-risk factor (the basis of the study). 39% had 2 risk factors 4% had 3 risk factors (Percentage numbers appear larger in bar graph within paper my copy is difficult to read) Age (y): Mean 60.9 years (no SD given) Gender: Over 75% male Obesity: NR Redo sternotomies: 11.5% Procedures performed using the IMA: 88.5 Mean±SD Total OR time: 248 min ±29	**Intervention1**: n=52 Povidone-iodine five-minute scrub with paint **Intervention2:** n=50 One-step iodophor/alcohol water insoluble film **Intervention3**: n=51 one-step iodophor/alcohol water insoluble film with iodine impregnated surgical adhesive drape **Intervention 4**: n=56 Povidone-iodine paint **Timing of Intervention:** Preoperative **Duration of intervention:** Intraoperative **Agents:** Solutions, insoluble film & incise drapes not specified **Monitoring intervention:** Observation by nurses **Control:** **Standard Preventive Measures** <u>Shower</u> The nurse instructed patients to take an antimicrobial shower the evening before and the morning	**Sternal wound Infections: 6 weeks** Intervention1: 7/52 (13.5%) Intervention2: 1/50 (2.0%) Intervention 3: 3/51 (5.9%) Intervention 4: 7/56 (12.5%) *P*=0.117 **Infections per treatment** Aqueous Iodine (Intervention 1+4) 14/108 (13.0%) Insoluble Iodine (Interventions 2 and 3) 4/101 (4.0%) *P*=0.02 X^2=5.3 **Other infections:** NR **Topic-specific outcomes:** NR **Reoperation:** NR **Length of Stay:** Uninfected patients had a 5-6 day shorter	**Definitions** Obesity: BMI>120% of ideal weight. SSI: Clinical exam for signs of drainage, redness, tenderness, or sternal instability. Sternal surgical site exhibiting any of these signs was cultured. Positive cultures were correlated with clinical evidence according to the CDC guideline to indicate a sternal SSI **Perioperative care** NR **Other notes** Impregnated drapes in Intervention 3 were shown to be ineffective as an intervention. Study deemed underpowered **Follow up:** 6 weeks postoperatively through regularly scheduled clinic visits **Funding Source Conflicts:** Authors: NR

Author Year (Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			Cross clamp time: 42 min±20 Last OR Glucose: 434±210 **Procedures:** elective **CABG** Surgery **Indications:** NR **Setting:** 1 tertiary/ teaching hospital **Location:** USA **Dates:** Oct 1, 1994 – April 30-1997 **Inclusion Criteria:** Patients undergoing elective CABG with one or more of the following conditions: Diabetes Obesity Chronic Obstructive Pulmonary Disease (COPD) **Exclusion Criteria:** Patients with an allergy to topical iodine or with a preexisting infection indicated by a white blood cell count higher than 10,000 or by a temperature higher than 100.5^{o}F (38.06^{o}C) because their procedures were performed emergently.	of surgery, or if they were inpatients, they were given a preoperative antimicrobial shower in the hospital. Hair removal If necessary, a qualified patient care assistant clipped patients' hair the morning of surgery in patients' rooms. AMP: All patients received a prophylactic antimicrobial (i.e., cefuroxime) or if they had a documented allergy to penicillin, they received vancomycin in appropriate dosing window to provide adequate coverage at the time of incision.	length of hospital stay than infected patients. **Mortality:** NR **Adverse events:** NR	Institution: NR Study: NR Supplies: NR

Author Year (Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
Ward 2001 [132] (ES)	**RCT** 1, 2, 3, 4, 5, 6, 7, 8, 9	To evaluate the ability of the new generation of adhesive surgical drapes to prevent Post Cesarean Wound Infection.	**Number of patients: N=605** **Patient Characteristics:** Characteristics were similar between groups. **Procedures:** Caesarean Section **Setting:** 1 Regional referral hospital **Location:** South Africa **Dates:** Aug 18, 1992 – January 29, 1993 **Inclusion Criteria:** Consecutive patients undergoing Caesarean Section **Exclusion Criteria:** Women having coincidental appendix ruptured or requesting early discharge.	**Intervention group:** n=305 After drying the cleansed area, a plastic adhesive drape was carefully applied to the skin and toweling and this remained in situ until the last skin suture or staple had been inserted. The drape was then removed and a dressing applied. **Timing of intervention:** Intraoperatively **Duration of intervention:** Intraoperatively **Device/agent:** plastic adhesive drape **Control group:** n=298 Same standard preventive measures but no drape was applied. **Standard preventive measures:** Skin Prep: preoperatively, abdomen and perineum were washed with 4% chlorhexidine soap. On the Operating table, the abdomen was liberally swabbed with a solution of 0.5% chlorhexidine in 80% alcohol for at least 30s over an area extending from the xiphosternum to the flanks, down as far as the mid-thigh and across to the perineum in the midline. The surgeon then scalpel shaved an area 2cm either side of the proposed incision site. Standard sterile double towel draping followed. The site was padded dry with a sterile swab	**SSI:** Drape: 34/305 (11.1%) No Drape: 30/298 (10.1%) P=0.6933	**Definitions:** Infection: if two of the 3 following features were present: 1) Erythematous cellulitis (erythematous induration either side of the incision line 2) Seropurulent discharge from the wound. 3) Positive swab culture (organisms and leucocytes). **Perioperative care:** NR **Other notes:** None **Follow-up:** 5 days. **Funding Source Conflicts:** Authors: NR Institution: NR Study: NR Supplies: NR

Author Year (Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
				AMP: At clamping of umbilical cord, patient received 1g of cephazolin intravenously unless antimicrobials were already being administered as therapy or prophylaxis. A 1g metronidazole suppository was inserted preoperatively and repeated after 12h.		
Chiu 1993 [133] (ES)	**RCT** 1	To investigate the effectiveness of plastic adhesive skin drapes in the prevention of wound infection after acute hip fracture operations.	**Number of patients: N= 120** **Patient Characteristics:** The two groups were matched for patient characteristics. ·Age: NR ·Gender: NR ·Obesity: NR ·Comorbidities: NR **Procedures:** Acute Hip Fracture including Internal fixation with sliding hip-screw done for trochanteric fractures; Austin-Moore femoral head replacement inserted for displaced subcapital fracture in older patients; and for undisplaced fractures or for displaced fractures in young patients, the fracture was fixed with three cancellous lag screws. **Setting:** 1 University Hospital **Location:** China	**Intervention group:** n= 65 Operation site was covered with a plastic adhesive drape. **Timing of intervention:** Intraoperatively+ **Duration of intervention:** Intraoperatively **Device/agent:** plastic adhesive drape **Control group:** n= 55 Operation site was left uncovered. Same standard preventive measures but no drape was applied. **Standard preventive measures:** Ultraclean air: there was no laminar flow, ultraclean air, or exhaust suits in the operating room. AMP: cephalosporin antibiotic was given at induction of anesthesia. Skin prep: Operation site was prepared with povidone solution then wiped, dried and draped with sterile towels.	**SSI:** Total: 11/120 (9.2%) Drape: 6/65 (9.2%) Superficial: 5/65 (7.7%) Deep: 1/65 (1.5%) No Drape: 5/55 (9.1%) Superficial: 4/55 (7.3%) Deep: 1/55 (1.8%)	**Definitions:** NR **Perioperative care:** NR **Other notes:** None **Follow-up:** NR **Funding Source Conflicts:** Authors: NR Institution: NR Study: NR Supplies: NR

Author Year (Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			Dates: January – December 1991 **Inclusion Criteria:** patients with hip fracture operations done by one of two surgeons done in the same operating theater. **Exclusion Criteria:** NR			
Dewan 1987 [136] (ES)	**RCT** 1, 2, 4 7, 8	To determine if skin organism contamination of the wound made through iodophor impregnated incise drapes should be reduced and less than when a standard skin preparation is used. Thus if contamination is significantly linked to infection, a reduction in the wound infection	**Number of patients: N=1016** **Patient Characteristics:** satisfactory randomization for the non-parametrically distributed groups was confirmed for each of the major wound infection risk factors and excluded a bias from these. ·Age: NR ·Gender: NR ·Obesity: NR ·Comorbidities: NR **Procedures:** general abdominal operations including inguinal hernia repair **Indications:** NR **Setting:** One university hospital **Location:** New Zealand **Dates:** August 1983 – May 1985 **Inclusion Criteria:** Patients undergoing abdominal operation, including inguinal hernia **Exclusion Criteria:**	**Intervention group: n=529** Patients with iodophor-impregnated drape applied **Timing of intervention:** perioperatively. **Duration of intervention:** surgery **Device/agent:** Iodophor-impregnated drape **Monitoring intervention:** NA **Control group: n=487** Patients where no iodophor-impregnated drape was used. **Standard preventive measures:** Routine skin prep of an iodophor antiseptic followed by alcohol. The operative field was dried with a sterile swab.	**SSI:** Wound infection Intervention: 36/529 (6.8%) Control: 34/487 (7.0%) Not significantly different **Other infections:** NR **Topic-specific outcomes:** NR **Reoperations:** NR **Length of stay:** NR **Mortality:** NR **Adverse events:** NR	**Definitions:** Infection: present if wound discharged pus or if the discharge of fluid from the wound was as associated with appositive bacterial culture. Infection was also diagnosed if the wound showed erythema more than 1cm lateral to the wound margin, and for either one third of the length of the wound or an 8cm length of it. **Perioperative care:** NR **Other notes:** None **Follow-up:** 3weeks follow up **Funding Source Conflicts:** Authors: NR Institution: NR Study: NR Supplies: NR

Author Year (Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
		rate from skin organisms should follow.	patients under 10 years of age and patients of one surgeon when he felt the color of the drape precluded optimal incision placement. Also, patients requiring abdominoplasty and two patients with a strong history of previous iodine allergy.			
Psaila 1977 [135] (ES)	**RCT** 1, 8, 9	To assess the role of adhesive plastic skin drapes and plastic ring wound protectors in the prevention of wound infection following abdominal surgery	**Number of patients: N=144 (n=98 utilized here)** **Patient Characteristics:** ·Age: NR ·Gender: NR ·Obesity: NR ·Comorbidities: NR **Procedures:** abdominal surgery. **Indications:** NR **Setting:** One University hospital **Location:** United Kingdom **Dates:** NR **Inclusion Criteria:** Patients undergoing abdominal surgery **Exclusion Criteria:** Patients receiving preoperative antimicrobials (with exception of non-absorbable sulphonamides used for bowel prep)	**Intervention group: N=51** An adhesive plastic drape was applied over cloth towels at the abdominal surgery site. **Timing of intervention** **Duration of intervention** **Device/agent** **Monitoring intervention** **Control group: n=47** Cloth towels were applied to the abdominal wound **Standard preventive measures:** Skin prep: 1 in 30, 0.05% chlorhexidine and cetrimide 0.5% and Chlorhexidine gluconate 0.5% in alcohol.	**SSI** Wound infection: All: 26/144 (18.0%) Drape: 8/51 (16%) No Drape: 10/47 (21%) **Other infections:** NR **Topic-specific outcomes:** NR **Reoperations:** NR **Length of stay:** NR **Mortality:** NR **Adverse events:** NR	**Definitions:** Presence of infection: 1) Erythema around the sutures or along the wound edge with an accompanying pyrexia 2) Discharge of exudate or pus from the wound 3) Wound breakdown. 4) If infection was considered to be present, a swab was taken and sent. **Perioperative care:** NR **Other notes:** None **Follow-up:** daily after the 3rd postoperative day. **Funding Source Conflicts:** Authors: NR Institution: NR Study: NR Supplies: NR

Author Year (Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
Jackson 1971 [134] **(ES)**	**RCT** 1, 2	To conduct a study to determine the effectiveness of plastic adhesive drapes in preventing wound infection.	**Number of patients; n=921** **Patient Characteristics:** Recorded, not reported by study group. ·Age: NR ·Gender: NR ·Obesity: NR ·Comorbidities: NR **Procedures:** NR **Indications:** NR **Setting**: 1 hospital **Location**: England **Dates**: Started December 1967 – two years later. **Inclusion Criteria**: All suitable cases operated on by one of the 3 authors or 2 other surgeons. **Exclusion Criteria**: Operations where drapes could not be used satisfactorily (mastectomy, perineal operations, amputation, limb arterial surgery, etc.); known iodine sensitivity, cases where difficulties with adhesiveness of drapes were present or where drapes were unsatisfactory.	**Intervention group: n=473** Patients who had a plastic adhesive drape utilized at the site of surgery **Timing of intervention:** Intraoperative **Duration of intervention:** until just after incision. **Device/agent:** Plastic adhesive drape. **Monitoring intervention:** NA **Control group: n=448** Patients who had no adhesive drape utilized. **Standard preventive measures:** Skin prep: swab soaked in 2.5% alcoholic solution of iodine BP was used to paint the operation area. This was wiped dry and ether was painted around the area of the incision.	**SSI:** **Wound infection** Drape: 67/473 (14.2%) No Drape: 52/448 (11.6%) P>0.20 **Other infections:** NR **Topic-specific outcomes:** NR **Reoperations:** NR **Length of stay:** NR **Mortality:** NR **Adverse events:** NR	**Definitions :** Wound infection: defined in terms of the discharge of pus from the wound. Usually a small amount (e.g., the so-called stitch abscess), but sometimes a wound abscess developed which required evacuation by removal of a suture and spreading of the wound edges. Wherever possible, the infecting organism was isolated and the cause was assessed. If a swab grew a microorganism, but no pus was produced, the wound was not regarded as infected. The slight moistness at the site of a drainage tube was not accepted by itself as an indication of infection. **Perioperative care**: NR **Other notes**: None **Follow-up**: at least 4 weeks. **Funding Source Conflicts:** Authors: NR Institution: NR Study: NR Supplies: NR

eTABLE 50. Evidence Table for Q9. How safe and effective is antiseptic irrigation prior to closing the surgical incision?

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
Chang 2006 [140] (ES)	**RCT** 1, 2, 4, 6, 7, 8, 9, 10	To evaluate the effect of wound irrigation with povidone-iodine on wound healing, infection rate, fusion status and clinical outcome of spinal surgeries	**Number of patients: n=244** **Patient Characteristics:** patient characteristics were not statistically significantly different between groups ·Age, y: NR ·Gender: NR ·Obesity: NR ·Comorbidities: NR **Procedures:** primary instrumented lumbosacral posterolateral fusion levels for degenerative spinal disorder. **Indications:** lumbar or lumbosacral segmental instability defined by chronic back, buttock and/or leg pain and degenerative spondylolisthesis, degenerative scoliosis, or isthmic spondylolisthesis. **Setting:** 1 university hospital **Location:** Taiwan **Dates:** Jan 2002 – Aug 2003 **Inclusion Criteria:** patients undergoing primary instrumented lumbosacral	**Intervention group: n=120** Wounds were irrigated with 0.35%povidone-iodine solution to soak for 3min, followed by irrigation with 2000cc of normal saline to remove povidone-iodine solution. **Timing of intervention:** intraoperative **Duration of intervention:** 3min **Device/agent:** 0.53% povidone-iodine solution **Monitoring intervention:** NA **Control group: n=124** Wound was only irrigated with 2000cc normal saline **Standard preventive measures:** Pain control – 3 days postop. AMP: preop IV bolus injections of cefazolin and gentamicin, additional postop cefazolin and gentamicin injections were given for 48h postop followed by oral cefazolin for 3 days postop. Custom made orthosis immobilized patient whenever out of bed for 3 months postop.	**SSI:** Superficial: no infections in either group Deep: Intervention: 0/120 Control: 6/124 (4.8%) P=0.29 **Other infections:** NR **Topic-specific outcomes:** NR **Reoperations:** NR **Length of stay:** NR **Mortality:** NR **Adverse events:** one incidence of wound dehiscence event with 0.35% povidone iodine followed by normal saline irrigation.	**Definitions:** Superficial infection: above lumbosacral fascia Deep infections: below lumbosacral fascia & all deep infections were confirmed by lab parameters including the erythrocyte sedimentation rate (ESR) and level of C-reactive protein (CRP) and a positive culture of biopsy. **Perioperative care:** NA **Other notes:** none **Follow-up:** every three months until the end of the study. Duration was approx. 19months. **Funding Source Conflicts:** Authors: None Institution: None Study: None Supplies: None

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			posterolateral fusion levels for degenerative spinal disorder. **Exclusion Criteria:** prior spinal surgery, spinal trauma, malignancy			
Cheng 2005 [141] (ES)	**RCT** 1, 2, 5, 7, 8, 9 10	To evaluate the efficacy of dilute betadine solution in the prevention of infection, particularly deep infection following spinal surgery	**Number of patients:** N=417 **Patient Characteristics:** there were no statistically significant differences between groups except with age: ·Age (mean) y Intervention: 64 Control: 61 P=0.0682 ·Gender: NR ·Obesity: NR ·Comorbidities: NR **Procedures:** spinal surgery (decompression, pedicle screw fixation, discectomy, tumor excision) **Setting:** 1 university hospital **Location:** Taiwan **Dates:** January 2002 – May 2003 **Inclusion Criteria:** patients undergoing spinal surgery. **Exclusion Criteria:**	**Intervention group: n=208** Wound was soaked with povidone iodine solution for 3min (5mL of povidone-iodine diluted with normal saline to achieve 0.35% povidone iodine solution.) The wound was then irrigated with copious amounts of normal saline (2000ml) **Timing of intervention:** intraoperative **Duration of intervention:** 3min soak **Device/agent:** -.35% povidone-iodine solution **Monitoring intervention** **Control group: n=206** Patients **Standard preventive measures:** Basic aseptic technique was followed. Skin prep: with povidone iodine. AMP: 1 does parenteral cefazolin and gentamicin 1h preop then Cefazolin every 6h & gentamicin every 12 hours for 48h postop. Oral antimicrobial doses (cefazolin) were continued for 3 days.	**SSI:** Overall Intervention: 0/208 Control: 7/206 (3.4%) P=0.0072 Superficial: Intervention: 0/208 Control: 1/206 (0.5%) P=0.4976 Deep: Intervention: 0/208 Control: 6/206 (2.9%) P=0.0146 **Other infections:** NR **Topic-specific outcomes:** NR **Adverse events:** no product-related adverse event with 0.35% povidone iodine followed by normal saline irrigation	**Definitions:** Infection: suspected when unusual pain, tenderness, erythema, induration, fever, or wound drainage was noted. Findings were investigated with measurement of ESR, CRP, and bacteriological cultures from the operative site or blood. All patients with highly suspected wound infection underwent surgical debridement. **Perioperative care:** NR **Other Notes:** none **Follow-up:** at 3 month intervals until study was over. (mean length 15.5 months) **Funding Source Conflicts:** Authors: None Institution: None Study: None Supplies: None

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			Mortality in follow-up period, also, patients with overt or suspected pyogenic vertebral osteomyelitis, discitis, or any form of preoperative spinal infection; and patients with fever or other suspected sources of infection.			
Sindelar 1985 [139] (ES)	**RCT** 1, 2, 7, 8, 9	To evaluate the efficacy and toxicity of intraperitoneal irrigation with Low Molecular Weight Povidone Iodine Solution (PVP-I LMW) in surgical procedures performed in the face of bacterial contamination (i.e. intra-abdominal surgical procedures where there was likely to be bacterial	**Number of patients: N=75** **Patient Characteristics:** The experimental and control groups did not statistically differ with respect to patient characteristics. ·Age, y: NR ·Gender: NR ·Obesity: NR ·Comorbidities: NR **Procedures:** Contaminated or dirty Intra-abdominal surgical procedures **Setting:** National Institute of Health **Location:** USA **Dates:** NR **Inclusion Criteria:** Patients 18yo or older, scheduled for elective or emergency intra-abdominal surgery involving	**Intervention group: n=37** Irrigation of the intraperitoneal area was performed 3 times during the operation with 1000ml of a 10% solution of PVP-I LMW. The Solution was suctioned from the peritoneal cavity 30-60s after installation. In patients undergoing primary wound closure, irrigation of the subcutaneous tissue was performed prior to skin closure with 1000ml of PVP-I LMW 10%. **Timing of intervention:** intraoperative **Duration of intervention:** duration of lavage. **Device/agent:** low molecular weight povidone iodine solution (10%) **Control group: n=38** Irrigation of the intraperitoneal area was performed 3 times during the operation with 1000ml of saline. The Solution was suctioned from the peritoneal	**SSI:** Total Infections PVP-I LMW: 2/37 (5.4%) [dirty] Saline: 9/38 (26.7%) [7/9 contaminated; 2/9 dirty] Organ/Space Infection PVP-I LMW: 1/37 (2.7%) [dirty] Saline: 6/38 (15.8%) [4/6 contaminated; 2/6 dirty Deep wound infection PVP-I LMW: 0/37 Saline: 1/38 (2.6%) [Dirty] Superficial wound infection: PVP-I LMW: 1/37 (2.7%) [dirty] Saline: 2/38 (5.3%) [both contaminated]	**Definitions: NR** **Perioperative care:** NR **Other notes:** None **Follow-up:** 7days **Funding Source Conflicts:** Authors: NR Institution: NR Study: NR Supplies: NR

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
		contamination of the peritoneal cavity)	entry into the peritoneal cavity where the surgery was classified as contaminated or dirty (esophageal, gastric, small intestinal, colonic, hepatic, pancreatico-biliary. **Exclusion Criteria:** Patients undergoing clean operative procedures. If there was a history of iodine sensitivity, thyroid disease, renal insufficiency or surgery involving ischemic or necrotic tissues which might interfere with wound healing either in the presence or absence of infectious complications.	cavity 30-60s after installation. In patients undergoing primary wound closure, irrigation of the subcutaneous tissue was performed prior to skin closure with 1000ml of saline. **Standard preventive measures:** AMP: patients received peri-operative antimicrobials in accordance to the practice of the surgeon responsible.	CLEAN (No AMP) 0/113 vs.7/121 (6%); p<0.01 Potentially Contaminated (AMP) 1/49 vs. 7/49; p<0.05 Contaminated (AMP) 3/44 vs. 12 /46; p<0.05 Dirty (AMP) 3/36 vs. 13/42; p<0.001 **Adverse events:** Significant increase in postop serum Iodine levels at 24h resolved by 72h. No clinical signs of iodine toxicity	
Vallance 1985 [138] (ES)	**RCT** 1, 7, 8, 9	To compare a Povidone-Iodine solution against saline alone for peritoneal lavage in patients undergoing operations for generalized	**Number of patients: N=29** **Patient Characteristics:** Patient characteristics were not statistically different between the groups. ·Age, y: NR ·Gender: NR ·Obesity: NR ·Comorbidities: NR **Procedures:** dirty laparotomy	**Intervention group:** **PVP-I: n=13** Patients who received a saline lavage until solutions returned clear with 100ml PVP-I solution inserted before wound closure **Timing of intervention:** intraoperatively **Duration of intervention:** NR **Device/agent:** PVP-I or saline **Control group:** **Saline: n=16** Patients who received a saline lavage until solutions returned	**SSI:** PI: 4/13 (31%) Saline: 5/16(31%) p=NS	**Definitions:** NR **Perioperative care:** NR **Other notes:** None **Follow-up:** 30 days **Funding Source Conflicts:** Authors: None Institution: None Study: None Supplies: None

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
		purulent or fecal peritonitis	procedures **Setting:** 1 hospital **Location:** UK **Dates:** NR **Inclusion Criteria:** Patients who were confirmed at laparotomy to have generalized purulent or fecal peritonitis. **Exclusion Criteria:** Patients dying within 4 days of the operation.	clear with inserted before wound closure **Standard preventive measures** Fluid maintenance: all patients were resuscitated with iv fluids before surgery AMP: all patients were begun on broad spectrum antimicrobial postop prophylaxis which were continued for at least 5 days postop.		
Rogers 1983 [143] (ES)	**RCT** 1, 2, 7, 8, 9	To elucidate further the potential value of Povidone Iodine wound irrigation as an adjunct in the prevention postoperatively of wound infections.	**Number of patients: N=187** **Patient Characteristics:** ·Age, y: NR ·Gender: NR ·Obesity: NR ·Comorbidities: NR **Procedures:** Clean (Inguinal hernia repair, cholecystectomy, laparotomy, hiatal hernia repair, proximal gastric vagotomy, ventral hernia, and other), clean contaminated (upper gastrointestinal, colorectal, biliary tract, appendectomy and other clean contaminated surgeries), and Dirty	**Intervention group: n=86** After fascial closure, patients underwent an approximate one minute irrigation of the subcutaneous tissue with approximately 60ml of 10% Povidone Iodine (1% available iodine) solution. **Timing of intervention:** intraoperative **Duration of intervention:** approx. 1 minute **Device/agent:** PVP-I or saline **Control group: n=101** After fascial closure, patients underwent an approximate one minute irrigation of the subcutaneous tissue with saline solution. **Standard preventive measure:** AMP: administered to all patients perioperatively in both the clean-contaminated and dirty categories.	**SSI:** Clean (No AMP) P-I: 2/56 (3.6%) Saline: 6/68 (8.8%) p=?? Clean-contaminated (AMP) P-I: 1/24 (4.2%) Saline: 5/27 (18.5%) p=? Dirty (AMP) P-I: 1/6 (16.6%) Saline: 1/6 (16.6%) p=NS	**Definitions:** Wound infection: any wound in which a purulent discharge occurred during a month of observation after the operation. **Perioperative care:** NR **Other notes:** None **Follow-up:** 1 month **Funding Source Conflicts:** Authors: NR Institution: NR Study: NR Supplies: NR

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			(perforated viscus, traumatic perforation procedures) procedures. **Setting:** 1 veterans hospital **Location:** USA **Dates:** July 1, - December 31, 1979 **Inclusion Criteria:** All patients undergoing operative procedures **Exclusion Criteria:** operations on the anorectal area; also patients who died or who required reoperation within three weeks of primary operation unless the wounds were obviously infected. Vascular procedures and operations on the head and neck	Bowel Prep: mechanical (cleansing enema, cathartics & low residue liquids) and antimicrobial bowel prep (orally administered neomycin and erythromycin base) were used for elective colorectal surgeries.		
Sindelar 1979 [142] (ES)	**RCT** 1, 7, 8, 9	To evaluate the efficacy of povidone-iodine irrigations of subcutaneous tissue during wound closure in reducing the incidence of superficial	**Number of patients: N=266** **Patient Characteristics:** patient groups were similar in age, sex distribution and types of surgery. ·Age, y: NR ·Gender: NR ·Obesity: NR ·Comorbidities: NR **Procedures:** both	**Intervention group: n=129** Patients had subcutaneous tissues irrigated for 60 seconds with 10% povidone-iodine solution **Timing of intervention:** intraoperative **Duration of intervention:** 60 seconds **Device/agent:** 1% available iodine, povidone-iodine solution **Control group: n=137** Patients had subcutaneous tissues irrigated for 60 seconds with	**SSI:** Superficial SSI: PI: 7/129 Saline: 32/137 Potentially Contaminated PI: 1/49 Saline: 7/49 p<0.05 Contaminated PI: 3/44	**Definitions:** Infection: if any amount of pus was discharged within 12 weeks of operation. Serous drainage from questionable wounds was cultured and was considered infected if any bacterial growth was recovered. **Perioperative care:** NR **Other Notes:** None **Follow-up:** up to 12 weeks postop.

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
		wound infections for a variety of surgical incisions.	elective and emergency surgical procedures including abdominal & gastrointestinal procedures, oncologic procedures, vascular reconstructions, head and neck operations, thoracic and genitourinary procedures and trauma operations. **Setting:** 1 university hospital **Location:** USA **Dates:** NR **Inclusion Criteria:** patients undergoing operative procedures. **Exclusion Criteria:** Amputations for ischemic disease, drainage of subcutaneous abscesses, skin grafting and anorectal procedures. Also, patients with a history of iodine sensitivity, thyroid diseases and significant renal impairment	saline solution **Standard preventive measures** **AMP:** Parenteral AMP preop and for 48h postop	Saline: 12 /46 p<0.05 Dirty PI: 3/36 Saline: 13/42 p<0.001 **Adverse events:** no significant change in free iodine serum levels	**Funding Source Conflicts:** Authors: NR Institution: NR Study: NR Supplies: NR

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
Sindelar 1979 [137] (ES)	**RCT** 1, 5, 7, 8, 9	To study both the possible toxicity and the possible benefit of povidone-iodine peritoneal irrigations in reducing the incidence of intra-abdominal abscess formation in patients with contaminated abdomens.	**Number of patients: N=168** **Patient Characteristics:** patient groups were similar in age, sex distribution and types of surgery. ·Age, y: NR ·Gender: NR ·Obesity: NR ·Comorbidities: NR **Procedures:** **Laparotomy:** surgical explorations in the presence of bacterially contaminated peritoneal cavities. **Indications:** contaminated abdomen **Setting:** 1 university hospital **Location:** USA **Dates:** NR **Inclusion Criteria:** patients undergoing laparotomy. **Exclusion Criteria:** patients with a history of iodine sensitivity, thyroid disease, or significant renal disease.	**Intervention group: n=80** Prior to closure, the peritoneal cavity was irrigated for 60 seconds with 1L of 1% povidone-iodine solution, giving 0.1% available iodine in diluted form. Following irrigation, the peritoneum was suctioned and the majority (estimated>90%) of the irrigant was removed. **Timing of intervention:** intraoperative **Duration of intervention:** 60 seconds **Device/agent:** 1% povidone-iodine solution **Monitoring intervention:** NA **Control group: n=88** Peritoneal cavity was irrigated for 60 seconds with 1L of normal saline solution followed by suctioning. **Standard preventive measures** Amp: all patients received preoperative systemic antimicrobial prophylaxis which were continued for 48h postop or longer if clinically indicated by manifestations of sepsis. (Typically clindamycin and gentamicin except in allergy or possible renal impairment for which doxycycline was substituted).	**SSI:** Intraabdominal Abscess Overall: 10/168 (5.95%) Intervention: 1/80 (1.3%) Control: 9/88 (10.2%) P<0.05 Dirty Procedures: Intervention: 0/36 Control: 6/42 (14.3%) P<0.05 Contaminated Procedures: Intervention: 1/44 (2.3%) Control: 3/46 (6.5%) P=NS **Other infections:** NR **Topic-specific outcomes:** NR **Reoperations:** NR **Length of stay:** NR **Mortality:** NR **Adverse events:** Iodine toxicity: Intervention: 5/80 (6.25%) Control: 0/88 Serum iodine levels were elevated 24 hours after intraperitoneal irrigation with PI solution and returned to near normal by 73h postop and no complications from	**Definitions:** Intraabdominal abscess: fever, persistent pain, palpable mass, abnormal roentgenograms, or positive ultrasonographic findings. Patients with suspected abscesses underwent surgical exploration. Adverse event: iodine toxicity **Perioperative care:** NR **Other notes:** None **Follow-up:** 3 months or until death. **Funding Source Conflicts:** Authors: NR Institution: NR Study: NR Supplies: NR

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
					the use of PI	

eTABLE 51. Evidence Table for Q10. How safe and effective is repeat application of an antiseptic skin preparation agent to the surgical site immediately prior to closing the surgical incision?

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
Harihara 2006 [144] (ES)	**RCT** 1	To investigate whether incisional topical application of Povidone-iodine (PVP-I) just before skin closure can prevent wound infection or SSI.	**Number of patients: N=107 (47 Gastric & 60 colorectal)** **Patient Characteristics:** No significant difference was observed between groups. ·Age: Gastric Intervention: 62.1±11.9y Control: 65.0±11.9 Colorectal Intervention: 62.8±12.3 Control: 66.3±11.5 ·Gender: m:f Gastric	**Intervention group:** n=54 (23 gastric and 31 colorectal) Before skin closure, skin was irrigated with 500ml saline solution. Povidone-Iodine was applied to the skin around the incision twice using swabs in the same manner as the preoperative skin preparation after irrigation and just before skin closure. **Timing of intervention:** Intraoperatively **Duration of intervention:** Intraoperatively **Device/agent:** Povidone-iodine (PVP-I) **Monitoring intervention:** NR **Control group:** n= 52 (23 gastric and 29 colorectal)	**SSI: (Follow up NR)** Gastric Surgery Wound Infection: Intervention: 1/23 (4.3%) Control: 0/24 P=0.4894 SSI Intervention: 3/23 (13.0%) Control: 3/24 (12.5%) P=0.6460 Colorectal Surgery Wound Infection: Intervention: 4/31 (12.9%) Control: 4/29 (13.7%) P=0.4894 SSI Intervention: 5/31	**Definitions:** SSI: JNIS system which is a Japanese modification of the CDC NNIS System. Wound infection: infection excluding organ/space infection from SSI. **Perioperative care:** NR **Other notes:** NR **Follow-up:** NR **Funding Source Conflicts:** Authors: NR Institution: NR Study: NR Supplies: NR

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			Intervention: 18:5 Control: 20:4 Colorectal Intervention: 18:13 Control: 15:14 ·ASA Physical Status (1:2:3:4:5) Gastric Intervention: 13:10:0:0:0 Control: 12:12:0:0:0 Colorectal Intervention: 19:10:2:0:0 Control: 10:17:2:0:0 ·Obesity: BMI (only for colorectal) Colorectal Intervention: 23.1±3.4 Control: 21.8±3.2 ·Comorbidities: (only for colorectal) Colorectal Diabetes mellitus (DM) Intervention: 3/31 (9.7%) Control: 5/29 (17.2%) Smoking >30 years Intervention: 7/31 (22.6%) Control: 9/29 (31.0%) **Procedures:** Gastric and colorectal surgery. **Indications:** : NR **Setting:** 1 medical center **Location:** Japan	Povidone-Iodine was not applied to the skin around the incision just before skin closure. **Standard preventive measures:** NR	(16.1%) Control: 5/29 (17.2%) P=0.6460 <u>RISK FACTORS FOR INFECTION</u> <u>Gastric Surgery</u> No significant risk factors were identified affecting either wound infection or SSI rates in the univariate analysis using the logistic regression model in gastric surgery. <u>Colorectal Surgery</u> Univariate Analysis of Risk Factors Wound Infection ASA: OR = 3.4232; P=0.0436 DM: OR = 5.6400; P=0.0573 SSI ASA: OR = 3.7093; P=0.0206 DM: OR = 7.6667; P=0.0162 Multivariate Analysis of Risk Factors Wound Infection: OR (95% CI) ASA: 2.9039 (0.752-11.211) DM: 3.8966 (0.637-23.834)	

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			Dates: July 2004 – December 2004. **Inclusion Criteria:** Patients undergoing gastric or colorectal surgery between July 2004 and December 2004 **Exclusion Criteria:** NR		P = 0.0452 SSI: OR (95% CI) ASA: 2.6602 (0.6660-10.725) DM: 3.8336 (0.574-25.617) Smoking: 2.1090 (0.382-11.644) Wound Class: 1.7113 (0.153-19.185) P = 0.0452 **Other infections:** NR **Topic-specific outcomes:** Gastric surgery: No relation was identified between wound infection or SSI rates and skin or subcutaneous tissue positive cultures in gastric surgery. Colorectal surgery: Wound infection and SSI occurred in 2 of 5 skin culture positive cases. Wound infection and SSI occurred in 4 of 7 subcutaneous culture positive cases (2 same as in skin culture) and showed statistical significance: COLORECTAL SURGERY:	

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
					Culture Positive: 7 cases Culture Negative: 53 cases Wound Infection Culture Positive: 4/7 (57.1%) Culture Negative: 4/53 (7.5%) P=0.0042 SSI Culture Positive: 4/7 (57.1%) Culture Negative: 6/53 (11.3%) P=0.0115 **Reoperations:** NR **Length of stay:** NR **Mortality:** NR **Adverse events:** NR	

2.1F3. RISK OF BIAS ASSESSMENTS OF STUDIES: Q8-10 ANTISEPTIC PROPHYLAXIS

eTABLE 52. Risk of Bias Assessments of Systematic Reviews for Q8-10 Antiseptic Prophylaxis

Author Year	Q	Search terms described	Databases described and two or more databases searched	Inclusion/exclusion criteria described	Number of included/excluded studies along with reasons of exclusion described	Studies screened by two independent reviewers for inclusion	Data extracted by two independent reviewers	Individual study quality assessed	Heterogeneity between study results assessed qualitatively and/or quantitatively	Publication bias assessed	Characteristics of included studies reported in evidence table	Funding source(s) disclosed and no obvious conflict of interest	Overall Risk of Bias
Key Question 8-10: Antiseptic Prophylaxis													
Webster 2012 [103]	8	✓	✓	✓	✓	✓	✓	✓	✓		✓	✓	Low

eTABLE 53. Risk of Bias Assessments of Randomized Controlled Trials for Q8-10 Antiseptic Prophylaxis

Author Year	Q	Described as randomized	Randomization appropriately performed	Described as double-blind	Outcome assessor blinded	Study participant blinded	Investigator blinded	Attrition described	Attrition smaller than 10-15% of assigned patients	Attrition appropriately analyzed	Funding source(s) disclosed and no obvious conflict of interest	Overall Risk of Bias
Key Question 8-10: Antiseptic Prophylaxis												
Berry 1982 [125]	8	✓	✓				✓	✓	✓	✓		Low
Bibbo 2005 [122]	8	✓									✓	High
Chang 2006 [140]	9	✓	✓		✓	✓		✓	✓	✓	✓	Low
Cheng 2009 [123]	8	✓	✓								✓	Moderate
Cheng 2005 [141]	9	✓	✓			✓		✓	✓	✓	✓	Low
Chiu 1993 [133]	8	✓										High
Darouiche 2010 [120]	8	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	Low
Dewan 1987 [136]	8	✓	✓		✓			✓	✓			Moderate
Dromzee 2012 [131]	8	✓	✓								✓	Moderate
Ellenhorn 2005 [113]	8	✓	✓								✓	Moderate
Gilliam	8	✓							✓	✓		Modera-

Author Year	Q	Described as randomized	Randomization appropriately performed	Described as double-blind	Outcome assessor blinded	Study participant blinded	Investigator blinded	Attrition described	Attrition smaller than 10-15% of assigned patients	Attrition appropriately analyzed	Funding source(s) disclosed and no obvious conflict of interest	Overall Risk of Bias
1990 [115]												te
Harihara 2006 [144]	10	✓										High
Hort 2002 [118]	8	✓			✓	✓						Modera-te
Iyer 2011 [129]	8	✓		✓	✓	✓					✓	Modera-te
Jackson 1971 [134]	8	✓	✓									High
Murray 2011 [112]	8	✓			✓		✓			✓		Modera-te
Ostrander 2005 [126]	8	✓						✓	✓			Modera-te
Paochar-oen 2009 [121]	8	✓										High
Psaila 1977 [135]	8	✓							✓	✓		Modera-te
Roberts 1995 [117]	8	✓	✓					✓	✓	✓		Modera-te
Rogers 1983 [143]	9	✓	✓					✓	✓	✓		Modera-te
Saltzman 2009 [116]	8	✓					✓			✓		Modera-te
Savage 2012 [127]	8	✓										High
Segal 2002 [114]	8	✓	✓			✓				✓		Modera-te
Sindelar 1985 [139]	9	✓	✓					✓	✓	✓		Low
Sindelar 1979 [142]	9	✓						✓	✓	✓		Modera-te
Sindelar 1979 [137]	9	✓				✓		✓	✓	✓		Modera-te
Sistla 2010 [119]	8	✓			✓	✓	✓	✓		✓		Low
Towfigh	8	✓	✓	✓	✓	✓		✓	✓	✓	✓	Low

Author Year	Q	Described as randomiz-ed	Randomizati-on appropriately performed	Described as double-blind	Outcome assessor blinded	Study participant blinded	Investigat-or blinded	Attrition described	Attrition smaller than 10-15% of assigned patients	Attrition appropriately analyzed	Funding source(s) disclosed and no obvious conflict of interest	Overall Risk of Bias
2008 [130]												
Veiga 2008 [124]	8	✓										High
Veiga 2008 [111]	8	✓			✓							High
Vallance 1985 [138]	9	✓						✓	✓	✓		Modera-te
Von Eckardstein 2011 [128]	8	✓	✓				✓	✓	✓	✓		Low
Ward 2001 [132]	8	✓	✓	✓	✓	✓	✓	✓	✓	✓		Low

2.2. Prosthetic Joint Arthroplasty Section GRADE, Evidence, and Risk of Bias Assessment Tables

2.2A. Q11 BLOOD TRANSFUSION

2.2A1. Q11 GRADE TABLE: Q11 BLOOD TRANSFUSION

eTABLE 54. GRADE Table for Q11 Blood Transfusion

Comparison	Outcome	Quantity and Type of Evidence	Findings	Starting GRADE	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Confounders		
Q11. How do perioperative blood transfusions impact the risk of SSI in prosthetic joint arthroplasty patients?														
Transfusion vs. No Transfusion	SSI*	2 RCT [145, 146] 4 OBS [147-150]	• Meta-analysis of 6 studies (N=8493) shows increased risk with transfusion: OR:1.56 (1.18 – 2.06); p<0.01; I^2=0 • Meta-analysis of 4 OBS(N=7484) shows increased risk with transfusion: OR: 1.59 (1.15 – 2.18); p<0.01 • Both meta-analyses include a high proportion of infections in patients transfused with allogeneic blood only. • Meta-analysis of 2 RCT (N=1009) shows no increased risk of infection in patients transfused with autologous or both autologous plus allogeneic blood transfusion: OR 1.07 (0.39 – 2.89); p=0.90.	High	0	0	0	0	0	0	0	0	High	High
Q11A. Are specific blood products associated with a risk of SSI?														
Allogeneic Blood Transfusion														
Allogeneic (any) vs. No Transfusion	SSI*	4 OBS [147-150]	• In meta-analysis of 4 OBS (N=5737), combing all allogeneic transfusions without regard to buffy coat depletion or leukoreduction, transfusion associated with increased risk of infection: OR: 1.96 (1.46 – 2.63); p<0.01; I^2=0	Low	0	0	0	0	0	0	0	0	Low	Low

Comparison	Outcome	Quantity and Type of Evidence	Findings	Starting GRADE	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Confounders		
	Reoperation due to wound infection*	1 OBS [151]	• In a large retrospective OBS (N=28,087) of primary THA, using a propensity score matched population (N=4508), reoperations due to infection were rarely reported (only 5 or 0.2% in each group) and there was no difference between groups OR: 0.57 (0.11 – 2.93)	Low	0	0	0	-1	0	0	0	0	Very Low	
Allogeneic Not WBC depleted vs. No Transfusion	SSI*	1 OBS [148]	• In a large prospective study (N=3945) of primary (81%) and revision (19%) hip and knee surgeries, subanalysis of 1644 patients found allogeneic "not- WBC depleted" transfusion was associated with increased risk of wound infection OR: 2.12 (1.13 – 4.00); p=0.02 • Actual WBC content was not reported.	Low	0	0	0	-1	0	+1	0	0	Low	Low
Allogeneic WBC depleted vs. No Transfusion	SSI*	1 OBS [148]	• In a large prospective study (N=3945) of primary (81%) and revision (19%) hip and knee surgeries, subanalysis of 1817 patients suggested no difference in risk of infection with allogeneic "WBC depleted" blood: 18/637 (3%) vs. 22/1180 (2%); p=0.19 • Actual WBC content was not reported.	Low	0	0	0	-1	0	0	0	0	Very Low	Very Low
Allogeneic "Buffy Coat Depleted vs. No Transfusion	PJI*	1 OBS [149]	• In a prospective study of 444 elective primary total hip replacements, PJIs were very rare (1% of total population) and no difference was observed between groups (both groups 1%)	Low	0	0	0	-1	0	0	0	0	Very Low	Very Low
	SSI* Incisional	1 OBS [149]	• Positive wound cultures were identified in 2.3% of population, and no difference was observed between groups (3.3% vs. 2.0 %); p=0.47	Low	0	0	0	-1	0	0	0	0	Very Low	

Comparison	Outcome	Quantity and Type of Evidence	Findings	Starting GRADE	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Confounders		
	Wound-healing disturbance	1 OBS [149]	• Allogeneic buffy coat depleted blood transfusion associated with increased risk of wound healing disturbance (31% vs. 18%; p<0.05) • On univariate OR 2.1 (1.2-3.5); p=0.03 and multivariate analyses, transfusion was the only significant risk factor	Low	0	0	0	-1	0	+1	0	0	Low	
Allogeneic WBC Filtered vs. No Transfusion	SSI*	2 OBS [147,150]	• In a meta-analysis of 2 OBS (N=1637), allogeneic WBC filtered was associated with increased risk OR: 1.92; (1.12 – 3.29); p=0.02; I^2=0 • One study[147] (N=201) in primary unilateral hip or knee arthroplasty (N=201) no difference with allogeneic WBC filtered transfusion: 3/100 (3%) vs. 1/101 (1%); p=0.33 • In a second larger study[150], subanalysis (N=1436) in primary and revision TKA reported increased risk with allogeneic WBC filtered: 32/637 (5.0%) vs. 22/799 (2.8%); p=0.03	Low	0	0	0	0	0	0	0	0	Low	Low
Allogeneic "lower WBC content" vs. Allogeneic "higher WBC content	SSI*	2 OBS [148, 150]	• One study[148] (N=1101) comparing allogeneic "WBC depleted" and "WBC-not depleted" found no difference between groups: 18/637 (3%) vs. 18/464 (4%); OR: 0.72; 95% CI: 0.37 – 1.40; p=0.33 • One study [150] (N=1243) comparing allogeneic "WBC filtered" to "WBC-not filtered" found no difference between groups: No difference: 32/637 (5.0%) vs. 43/606 (7.1%); P=0.30	Low	0	0	0	0	0	0	0	0	Low	Low
Autologous Blood Transfusion														

Comparison	Outcome	Quantity and Type of Evidence	Findings	Starting GRADE	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Confounders		
Autologous (Any) vs. No Transfusion	SSI*	2 RCT [145,146] 2 OBS [147,148]	• No difference in a meta-analysis of 2 RCTs (N=970) OR: 1.15 (0.43 – 3.13); p=0.78 • In a small RCT [146] of hip arthroplasties subanalysis (N=58), no infections were observed in either group: 0/49 vs. 0/9, but study was designed to evaluate transfusion induced immunomodulation, not SSI. (7day follow up) • 1 larger RCT [145] in hip arthroplasties, subanalysis (N=912); no difference at 90 day follow up: 9/481 (1.7%) vs. 7/431 (1.6%);p>0.05 • In a large prospective (N=3945) OBS study [148] of primary and revision hip and knee surgeries, subanalysis (N=2491) found autologous transfusion was associated with a reduction in wound infections: 11/1311 (1%) vs. 22/1180 (2%); OR: 0.45 (0.22 – 0.92); p=0.03 • In an OBS study[147] (N=186) of primary hip or knee arthroplasty patients: 0/85 vs.1/101- too few events to perform additional analysis.	High	0	0	0	-1	0	0	0	0	Moderate	Moderate
Autologous ± WBC Filtration vs. No transfusion	SSI*	1 RCT [145]	• No difference in a large RCT (N=1089) in THA (regardless of WBC filtration status): • Subanalysis of 657 patients reported no difference with autologous “no WBC filtration” transfusions: 5/226 (2.2%) vs. 7/431 (1.6%); p=0.59 • Subanalysis of 686 patients reported no difference with autologous WBC filtered blood transfusions: 3/255 (1.2%) vs. 7/431 (1.6%); p=0.64	High	0	0	0	-1	0	0	0	0	Moderate	Moderate
Autologous	SSI*	1 RCT [146]	• In a small RCT of THA, subanalysis of 34	High	0	0	0	-2	0	0	0	0	Low	Low

Comparison	Outcome	Quantity and Type of Evidence	Findings	Starting GRADE	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Confounders		
Whole Blood vs. No Transfusion			patients, no infections in either group at 7 day follow up. Whole blood included autologous donated and perioperative salvage blood. • The study was designed to evaluate transfusion induced immunomodulation, not SSI.											
Autologous "Not WBC depleted" vs. No Transfusion	SSI*	1 OBS [148]	• In a large prospective (N=3945) study of primary and revision hip and knee surgeries, subanalysis (N=2491) found autologous transfusion (including autologous blood donated whole blood or packed red blood cells, cell saver, acute normovolemic hemodilution, and postoperative salvage) was associated with a reduction in wound infections: OR: 0.45 (0.22 – 0.92); p=0.03, follow up period was limited to the patient's stay in the surgical unit. Transfusion trigger for autologous blood transfusion is not reported • Autologous donated blood only: 4/610 (0.66%) vs. 22/1180 (1.86%); p=0.05 • Autologous postoperative salvage blood only: 8/191 (4.19%) vs. 22/1180 (1.86%); p<0.05	Low	0	0	0	-1	0	0	0	0	Very Low	Very Low
Autologous Buffy Coat Depleted vs. No Transfusion	SSI*	1 RCT [146] 1 OBS [147]	• In a small RCT[146] of hip arthroplasties (N=33), no infections were observed in either group at 7 day follow up. The study was designed to evaluate transfusion induced immunomodulation, not SSI. • In 1 OBS[147] (N=186) of primary hip or knee arthroplasty patients: 0/85 vs.1/101- too few events to perform additional analysis.	High	0	0	0	-2	0	0	0	0	Low	Low

Comparison	Outcome	Quantity and Type of Evidence	Findings	Starting GRADE	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Confounders		
Autologous "lower WBC content" vs. Autologous "higher WBC content"	SSI*	2 RCT [145,146]	• In a small RCT [146] of hip arthroplasties (N=49), no infections were observed in either group at 7 day follow up. The study was designed to evaluate transfusion induced immunomodulation, not SSI. • In a large RCT [145] of total hip arthroplasties (per protocol analysis, (n=481), no difference was observed between groups: OR: 0.53 (0.12 – 2.23); p=0.30. Only 1 PJI reported in each group (Intention to treat analysis n=951)	High	0	0	0	-1	0	0	0	0	Moderate	Moderate
Post-operative salvage only vs. Autologous Donated blood-only	SSI*	1 OBS [148]	• In one large OBS study of elective primary and revision hip and knee arthroplasties, subanalysis in 801 patients showed significantly higher infection rates with postoperative salvage recovery only autologous blood versus autologous donated blood only in both hip: 3/69 (4%) vs. 4/462 (1%); p<0.05 and knee arthroplasties: 5/122 (4%) vs. 0/148 (0%); p<0.05. Hip and knee arthroplasties combined: 8/191 (4.19%) vs. 4/610 (0.66%) OR: 0.15; (0.04 – 0.51); p<0.01	Low	0	0	0	-1	0	+1	0	0	Low	Low
Allogeneic vs. Autologous blood transfusion														
Allogeneic (Any) vs. Autologous (Any)	SSI*	3 OBS [147,148,152]	• When combining transfusions without regard to buffy coat depletion or leukoreduction, transfusion with allogeneic blood was associated with increased risk of SSI as compared to autologous transfusion OR: 4.53 (2.37 – 8.65); p<0.01; I^2=0	Low	0	0	0	0	0	+1	0	0	Moderate	Moderate
Allogeneic ± WBC depleted vs. Autologous	SSI*	2 OBS [148,152]	• Allogeneic NOT WBC Depleted: In a large prospective study [148] of hip and knee surgeries, subanalysis in 1775 patients showed increased risk: 18/464 (4%) vs.	Low	0	0	0	0	0	+1	0	0	Moderate	Moderate

Comparison	Outcome	Quantity and Type of Evidence	Findings	Starting GRADE	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Confounders		
Not WBC depleted			11/1311 (1%); OR: 4.77 (2.24 – 10.18); p<0.01 • WBC Not Depleted: In one prospective study [148] Allogeneic versus autologous blood donation only: 18/464 (4%) vs. 4/610 (0.66%); p=0.001 • WBC Not Depleted: One prospective study [148] Allogeneic versus postoperative salvage only: 18/464 (4%) vs. 8/191 (4.19%); p=0.85 • WBC depleted: One prospective study [148] Subanalysis in 1948 patients showed allogeneic "WBC depleted" transfusion was associated with increased risk of wound infection: 18/637 (3%) vs. 11/1311 (1%); p=0.01 • WBC Depleted: In one small observational study[152] in hip arthroplasties, allogeneic "WBC depleted" blood transfusion was not associated with increased risk of infection as compared to perioperative cell saver shed washed blood: 2/48 (4.17%) vs. 0/49; p=0.28										
Allogeneic WBC Filtered vs. Autologous Buffy coat depleted	SSI*	1 OBS [147]	• No difference: 3/100 (3%) vs. 0/85; p=0.23.	Low	0	0	0	-1	0	0	0	0	Very Low	Very Low
Both Autologous and Allogeneic Blood Transfusion														
Both Autologous and Allogeneic (Any) vs. No	SSI*	1 RCT [145] 2 OBS [147,148]	• No difference in post-hoc subanalysis[145] (N=470) : 0 of 39 transfused vs. 1.6% of 431 not transfused (p=0.82) • One study[148] No difference: 8/329 (2%) vs. 22/1180 (2%) OR: 1.31; 95% CI: 0.58 –	High	0	0	0	-1	0	0	0	0	Moderate	Moderate

Comparison	Outcome	Quantity and Type of Evidence	Findings	Starting GRADE	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Confounders		
Transfusion			2.97; p=0.52 • No difference in subanalysis [147] (n=123): 0/22 vs. 1/101 (1%)											
Both Autologous and Allogeneic vs. Autologous-only	SSI*	2 OBS [148,153]	• In a large OBS study [153] (N=2884) of primary total hip (n=2016) and knee (n=480) arthroplasties and hip revisions (n=388), transfusion with both allogeneic (buffy coat depleted) and autologous (buffy coat depleted and salvaged blood) was associated with increased risk of wound infection compared with autologous (buffy coat depleted-only) blood alone. Statistical testing was not possible (data presented in graph format). • In 1 study[148] SSI= 8/329 (2%) vs. 11/1311 (1%); p=0.02	Low	0	0	0	0	0	0	0	0	Low	Low
Q11B. If the risk of SSI is increased, can this effect be isolated from the risk associated with more complex cases?														
Revision vs. Primary Arthroplasty (Hip [THA] and knee [TKA] combined)	Transfusion*	2 OBS [148,150]	• Increased risk of transfusion among revisions (THA and TKA combined) in a meta-analysis of 2 OBS studies (N=6385): OR 3.81 (1.61 – 9.03); p<0.01; I^2=95% • In one study [148] Increased risk among revisions: 303/362 (84%) vs. 2112/3118 (68%); p<0.001 • In one observational study[150] Increased risk among revisions: 274/350 (78%) vs. 969/2555 (38%); p<0.01	Low	0	-1	0	0	0	+1	0	0	Low	Low
Revision THA vs. Revision	Transfusion*	1 OBS [148]	• Higher risk of transfusion among revision THA: 252/293 (86%) vs. 51/69 (74%); p=0.02	Low	0	0	0	-1	0	0	0	0	Very Low	Very Low

Comparison	Outcome	Quantity and Type of Evidence	Findings	Starting GRADE	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Confounders		
TKA	Calculated blood loss	1 OBS [148]	• No difference in median calculated blood loss: 2875ml vs. 2528ml; p=0.23	Low	0	0	0	-1	0	0	0	0	Very Low	
Revision THA vs. Primary THA	Transfusion*	2 OBS [148,153]	• Any blood transfusion [148]: Higher risk among revision hip arthroplasties: 252/293 (86%) vs. 1405/2066 (68%); p<0.01 • Allogeneic only[148]: More allogeneic only transfusions among transfused revision hips as compared to primary hip arthroplasties: 115/252 (46%) vs. 503/1405 (36%); p<0.01 • Autologous only[148]: More autologous only transfusions among transfused primary hip as compared to revision hip arthroplasties: 83/252 (33%) vs. 737/1405 (52%); p<0.01 • BOTH Autologous and additional allogeneic blood transfusion; Higher risk among revision THAs- Meta-analysis (N=4061): OR 2.44 (1.77 – 3.36); p<0.01; I^2=50% • One OBS[148] Higher risk among revision THAs: 54/252 (21%) vs. 165/1405 (12%); p<0.001 • One OBS [153] Higher risk among revision THAs: 76/388 (20%) vs. 159/2016 (8%); p<0.01	Low	0	0	0	0	0	0	0	0	Low	Low
	Calculated blood loss	2 OBS [148,153]	• Meta-analysis 2 OBS studies: significantly higher calculated blood loss in revision hips: mean difference 700 ml (95% CI: 323 ml – 1076 ml); p=0.0003; I^2=87% • Mean calculated blood loss higher for revision hip: 3060 ml vs. 2143 ml; p<0.01[148]; Mean blood loss significantly higher for revision hip: 1720±460ml vs. 1190±480ml; p<0.01[153]	Low	0	0	0	0	0	0	0	0	Low	

Comparison	Outcome	Quantity and Type of Evidence	Findings	Starting GRADE	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Confounders		
	Procedure duration	1 OBS [153]	• Significantly longer procedure duration for revision hip arthroplasty (mean ±SD): 183±64 minutes vs. 115±38 minutes; p<0.01	Low	0	0	0	-1	0	0	0	0	Very Low	
Revision TKA vs. Primary TKA	Transfusion*	1 OBS [148]	• Any transfusion no difference for revision knee as compared to primary knee: 51/69 (74%) vs. 707/1052 (67%); p=0.25 no difference for revision knee as compared to primary bilateral knees: 51/69 (74%) vs. 11/13 (85%); p=0.42 • Allogeneic only: No difference- 23/51 (45%) vs. 245/707 (35%); p=0.13 • Autologous only: No difference -17/51 (33%) vs. 245/707 (49%); p=0.85 • BOTH autologous and additional allogeneic blood transfusion higher risk of transfusion for revision knees: 11/51 (21%) vs. 77/707 (11%); p=0.02	Low	0	0	0	-1	0	0	0	0	Very Low	Very low
	Calculated blood loss	1 OBS [148]	• Mean calculated blood loss higher for revision knee: 2634 ml vs. 2072 ml; p<0.01	Low	0	0	0	-1	0	0	0	0	Very Low	
Primary THA vs. Primary TKA	Transfusion*	2 OBS [148, 153]	• Any transfusion [148]: No difference- 1405/2066 (68%) vs. 707/1052 (67%); p=0.65 • Allogeneic only [148]: No difference- 503/1405 (36%) vs. 245/707 (35%); p=0.60 • Autologous only[148]: No difference- 737/1405 (52%) vs. 385/707 (54%); p=0.38 • Both Autologous and additional allogeneic [148]: No difference- 165/1405 (12%) vs. 77/707 (11%); p=0.56 • BOTH autologous and additional allogeneic [153] : No difference-159/2016 (8%) vs. 43/480 (9%); p=0.44	Low	0	0	0	0	0	0	0	0	Low	Low

Comparison	Outcome	Quantity and Type of Evidence	Findings	Starting GRADE	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Confounders		
	Calculated blood loss	2 OBS [148,153]	• Meta-analysis 2 OBS: No difference- Mean difference: -19 ml (-176 ml – 137 ml); p=0.81; I^2=84% • Mean calculated blood loss no difference: 2143 ml vs. 2072 ml; p=0.24 [148] • Mean blood loss higher in primary knee arthroplasty 1190±480ml vs. 1280±403; p<0.01[153] • Median preoperative estimate blood loss was significantly lower than median calculated blood loss for both primary total hip (median 750 vs. 1944ml; p<0.01) and total knee (median, 800 vs. 1934ml; p<0.01) procedures[148].	Low	0	-1	0	0	0	0	0	0	Very Low	
Primary THA: Unilateral vs. Bilateral	Transfusion*	1OBS [148]	• Any transfusion -No difference: 1387/2039 (68%) vs. 18/27 (67%); p=0.88 • Allogeneic only: No difference: 496/1387 (36%) vs. 7/18 (39%); p=0.78 • Autologous only: No difference 728/1387 (53%) vs. 9/18 (50%); p=0.83 • BOTH Autologous and additional allogeneic blood transfusion: No difference: 163/1387 (12%) vs. 2/18 (11%); p=0.93	Low	0	0	0	-1	0	0	0	0	Very Low	Very Low
Primary TKA: Unilateral vs. Bilateral	Transfusion*	1OBS [148]	• Any transfusion: No difference: 696/1039 (67%) vs. 11/13 (85%); p=0.20 • Allogeneic only: No difference - 242/696 (35%) vs. 3/11 (27%); p=0.61 • Autologous only: No difference 377/696 (54%)vs. 8/11 (74%); p=0.23 • BOTH Autologous and additional allogeneic: Only unilateral TKA received both:- 77/696 (11%) vs. 0/11 (0%); p=0.47	Low	0	0	0	-1	0	0	0	0	Very Low	Very Low

Q11C. How does the volume of transfused blood product impact the risk of SSI? Our search did not identify data that evaluated differences in the volume of transfused blood product and their impact on the risk of SSI in prosthetic joint arthroplasty patients.

Comparison	Outcome	Quantity and Type of Evidence	Findings	Starting GRADE	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Confounders		
Q11D. How safe and effective is withholding blood transfusion to reduce the risk of SSI? Our search did not identify data that both evaluated the safety and effectiveness of withholding blood transfusions and its impact on the risk of SSI in prosthetic joint arthroplasty patients.														

*Critical outcome; OR: Odds Ratio; RR: Risk Ratio; CI: Confidence Interval

2.2A2. EVIDENCE TABLE: Q11, Q11A, AND Q11B BLOOD TRANSFUSION

Q11. How do perioperative blood transfusions impact the risk of SSI in prosthetic joint arthroplasty patients?

Q11A. Are specific blood products associated with a risk of SSI?

Q11B. If the risk of SSI is increased, can this effect be isolated from the risk associated with more complex cases?

eTABLE 55. Evidence Table for Q11. How do perioperative blood transfusions impact the risk of SSI in prosthetic joint arthroplasty patients?

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting (N)	Intervention	Results	Comments
Frietsch 2008 [145] (SIBT)	**RCT** 1, 2, 3, 4, 5, 7, 8, 9, 10 .	To determine if leukoreduction of autologous whole blood (AWB) reduces the transfusion-related immunomodulation (TRIM) effect, resulting in reduced perioperative infection rate and/or length of hospital stay.	**No. patients:** **ITT:** N=951 **Per-Protocol**=481 **Patient Characteristics:** Baseline characteristics of the patients were similar in the two groups (number, sex, age, height, weight, calculated blood volume, overall estimated perioperative blood loss, donated autologous units per patient, ASA score, Anesthesia type, surgery type [cementless, cemented, hybrid], duration of surgery, anesthesia and hypothermia. Age years median (range) Intervention:63 (28-82)	**Intervention Group**: Leukodepleted AWB (LD-AWB) **ITT** n=488 **Per Protocol** n=255 (52.3%) **Timing of Intervention:** Intra and postoperative **Duration of Intervention:** NR **Device/ Agent**: **Intervention (LD-AWB):** double bag system with inline whole-blood WBC filter for pre-storage leukoreduction. Blood was leukoreduced after storage on cooling plates at 4 to 6°C for 1-4 hours. Residual WBC content was consistently below 1 X 10^6 per unit and mean red blood cell loss (RBC) was less than 10%. **Control (non-ND AWB):** single-bag system. All units stored at 4°C until transfusion or expiry Both systems contained 70ml citrate phosphate	**SSI (3 months)** **ITT Analysis N=951** **Wound Infections** Intervention: 6/488 (1.2%); Control: 9/463 (1.9%) OR 0.63 (95% CI, 0.22-1.78); p=0.27 **Other infections** Overall, urinary, respiratory, fungal and Other (gastrointestinal, pleuritis, vascular thrombophlebitis, skin infection other than wound, gynecologic) none with statistically significant difference Note: Infections occurred while in hospital in 87.5% of cases. **Per-protocol Analysis N=481** **Wound Infections** Intervention: 3/255 (1.2%) Control: 5/226 (2.2%) 0.53(0.12-2.23);p=0.30 **Other infections** Overall, urinary,	**Definitions:** **Wound Infection:** Defined either as 1. isolation of bacteria from fluid wound secretions containing pus, 2. abscesses (verified by surgical drainage or aspiration of pus), or 3, arthritis by clinical symptoms requiring surgical drainage. **Respiratory tract infection (RTI)**: 1) positive x-ray (chest infiltration) together with fever, 20 dyspnea or cough or purulent sputum together with fever, or 3) isolation of bacteria in tracheal secretion (only intubated patients) together with fever. **ASEPSIS Index:** Daily wound inspections evaluated for the following wound conditions: clear exudate, erythema, putrid exudate, dehiscence of profound tissue layers with size of relative wound area of the total wound concerned. If more than one wound condition was existent, only the condition with the highest rating was scored. Wound inspection scores were added up (dynamic part). Each of the additional criteria (antimicrobial treatment, abscess drainage [local vs. general anesthesia], bacterial growth [positive culture of at least 100,000 colonies of a single

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting (N)	Intervention	Results	Comments
			Control:63 (26-83) Gender m/f: 470/481 mean±SD(median/ range) Height (cm) Intervention: 170±8.9 (170/150-196) Control: 170.3±9.0(170/140-197) Weight(kg) Intervention: 80.1 ±14.1(80/48-126) Control: 80.4±14.2(80/50-136) ASA1=192/951 (20.2%) ASA2=628/951(66.0%) ASA3=125/951(13.1%) •Comorbidities: NR **Procedure:** Primary hip arthroplasty (cemented n=30, cementless n=642, hybrid n=274) **Indications:** NR **Setting**: 2 university and 1 urban hospital: Center A n=696	dextrose adenine (CPDA-1) as storage medium. **Monitoring Intervention:** Hemoglobin (Hb) levels. **Transfusion Trigger:** Hemoglobin (Hb) concentration <8.0±0.5g/L during and after surgery (irrespective of whether autologous or allogeneic blood was to be transfused) **Control Group-** Non-leukodepleted AWB (non-LD AWB) **ITT** n=463 **Per Protocol** n=226 (48.8%) **Standard preventive measures** AMP (second generation cephalosporin) **,** normothermia, normovolemia, adequate oxygenation	respiratory, fungal and Other (gastrointestinal, pleuritis, vascular thrombophlebitis, skin infection other than wound, gynecologic) none with statistically significant difference **<u>In both ITT and Per-Protocol:</u>** **Overall infection rate, ASEPSIS score, Length of Stay, antimicrobial treatment, multidrug use, fever>38°C after postop day 3:** No significant difference **<u>SUBGROUP ANALYSIS 1:</u>** Not transfused (NOT-T; n=431) vs. Autologous only transfused (AUT-T; n=481) vs. Additionally allogeneically transfused (ALL-T; n=39) **Overall infection rate:** NOT-T: 14.2% AUT-T: 20.6% ALL-T: 13.2% p=0.03 **Wound infections:** NOT-T: 1.6%	organism], and prolonged hospital stay (static part) could be added once. **Perioperative Care** **Preop:** Patients were scheduled to donate 2 or 3 units of AWB (500ml each) in weekly intervals with surgery planned to take place in weeks 3 to 5 after the first donation. Hb concentration below 110g/L during donation period led to postponement of following donation by 1 week. Patients encouraged to take oral iron (300mgFe^{2+} orally per day) RBC loss was calculated as the compensated RBC loss (perioperatively transfused RBC volume) plus non-compensated RBC loss estimated from pre and postoperative (Day 3) hematocrit (Hct) levels correcting large-vessel to total body Hct: **RBC loss**= **(**Hct_{pre}-Hct_{POD3}) X Blood Volume* X 0.86+RBC-$V_{units.}$ RBC-V_{units}=RBC volume of transfused AWB *Calculated according to Nadler) **Blood loss**=RBC loss/(Hct_{pre}-Hct_{POD3})/2 **Transfusion rates by Center:** **No transfusion; autologous only; autologous and allogeneic**

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting (N)	Intervention	Results	Comments
			(73.2%); Center B n=213 (22.4%) Center C n=42 (4.4%) **Location:** Germany **Dates**: NR **Inclusion criteria**: Patients scheduled for primary hip arthroplasty and preoperative donation of at least 2 units of AWB **Exclusion criteria**: Subjects with contraindications for preoperative autologous blood donation according to the German guidelines, immune deficiency, steroid therapy and intended use of cell salvage.		AUT-T: 1.7% ALL-T: 0% p=>0.05 Urinary tract Infection: NOT-T 11.1% AUT-T 16.8% ALL-T 13.2% p=0.02 **Other infections:** Respiratory, fungal, and other infections (gastrointestinal, pleuritis, vascular thrombophlebitis, skin infection other than wound, gynecologic) all p=>0.05 **Length of Stay days:** mean±SD (median) NOT-T 13.0±2.3 (13) AUT-T 13.8±3.6 (14) ALL-T 14.3±4.2 (14) p=≤0.01 **Note:** significant difference in infection rate and length of stay was paralleled by significantly longer anesthesia and surgery duration (NR), suggesting dependency from the complexity level of surgery rather than transfusion. **SUBGROUP ANALYSIS 2:** Micro-aggregate filtration of	A n=696: 43%;52.7%;4.3% B n=213:56.8%;39.4%;3.8% C n=42: 26.2%, 71.4%, 2.4% Anesthesia Spinal: Intervention: AWB 297/488 (60.9%) Control: Non LD AWB: 312/463 (67.4%) General: Intervention: AWB 187/488 (38.3%) Control: Non LD AWB: 143/463 (30.9%) Epidural: Intervention: AWB 2/488 (0.4%) Control: Non LD AWB: 1/463 (0.2%) Other Intervention: AWB 2/488 (0.4%) Control: Non LD AWB: 3/463 (0.6%) **Follow up:** Phone, letter or an outpatient visit 3 months post op. Wound inspection: daily during the first 14 postoperative days and discharge, not on weekends **Funding Source Conflicts:** Authors: None Institution: None Study: None Supplies: Industry

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting (N)	Intervention	Results	Comments
					blood product at bedside at Centers A and C. Subgroup analysis to exclude any influence of these microfilters on overall infections rate showed no statistical significant difference (p=0.63, two-sided). **Topic specific outcomes: N/A** **Reoperation:** <u>In both ITT and Per-Protocol</u>: antimicrobial treatment, multidrug use: No significant difference <u>In ITT protocol:</u> Wound infection requiring revision or hospitalization: Intervention: 1/488 (0.2%) Control: 3/463 (0.6%) Delayed wound healing requiring revision or hospitalization: Intervention: 7/488 (1.4%) Control: 7/463 (1.5%) Surgical wound revision: Intervention: 3/488 (0.6%) Control: 8/463 (1.7%) Prosthesis infection: Intervention: 1/488 (0.2%)	

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting (N)	Intervention	Results	Comments
					Control: 1/463 (0.2%) Re-surgery - prosthesis exchange: Intervention: 1/488 (0.2%) Control: 1/463 (0.2%) **Length of stay**: Median (range) ITT Intervention (LD AWB): 14 days (7-36) Control (Non-LD AWB):14 days (8-55) *P*=0.17 Per-Protocol Intervention (LD AWB): 14 days (7-34) Control (Non-LD AWB):14 days (9-55) *P*=0.71 **Mortality:** none **Adverse events:** In ITT protocol: not significantly different between groups Total: Intervention: 1/488 Control: 1/463 Relation to LD: Possible /unlikely unrelated Intervention: 3/7/3 Control: 2/2/8 Myocardial infarction, bradycardic arrhythmia, transient cerebral, ischemic attack,	

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting (N)	Intervention	Results	Comments
					respiratory insufficiency (sleep apnea), deep venous thrombosis, dyesthesia foot	
Frietsch 2001 [146] (ES)	**RCT** 1, 2, 5, 7, 8, 9, 10	To address Transfusion-induced immunomodulation (TRIM) caused by autologous blood – stored either as Whole Blood (WB) or as buffy coat-poor packed red cells and fresh-frozen plasma (RCP) – in patients undergoing hip arthroplasty. Monocyte and neutrophil phagocytic activities, rate of systemic and wound infection, se of antimicrobials and length of hospital stay (LOS) were evaluated.	**Number of patients N=58** **Patient Characteristics** **WB=Whole Blood** **RCP=buffy coat-poor packed Red Cells and fresh-frozen Plasma** **NT-NO Transfusion** **·Age: mean±SD** WB: 58±10 years RCP: 59±10 years NT: 61±8 years **·Gender:** m/f WB: 9/16 RCP: 10/14 NT: 7/2 **·Obesity:** Weight WB: 71±16 kg RCP: 74±15 kg NT: 84±10 kg Height WB: 166±9 cm RCP: 168±7 cm NT: 171±5 cm **·Comorbidities:** NR 3Units Predeposited WB: 22/25(88%) RCP: 22/24	**Intervention group:** n=2 Transfused Autologous Blood: Blood was donated at weekly intervals (450ml each). Surgery was scheduled for the 5th week after the first donation. RCP: Buffy coat-poor packed red cells (RC) and fresh-frozen plasma (FFP): n=24 donated blood was separated into RC and FFP(80-90% of leukocytes and >98% platelets were eliminated) **Timing of intervention:** intra or postoperatively **Duration of intervention:** Intra and/or postoperatively. **Agent:** Autologous blood. Either Whole blood (WB) or buffy-coat poor packed red cells (RC) **-** Oldest blood was used first. **Monitoring intervention:** hemoglobin count and leucocyte counts were	**SSI (follow up 7 days)** None of the patients presented clinical signs of infection. Authors indicate "This study is not expected to have the statistical power to discriminate between the two types of storage regarding outcome criteria of immunomodulation, such as wound or systemic infection rates or LOS, as the infection rate in this type of surgery is generally low" **Other infections:** None occurred in either group. **Topic-specific outcomes**: **No allogeneic transfusions were required in any group.** Total Blood loss: median (Range) WB: 1740 (820-3170) ml RCP: 1760 (880-3290) ml NT: 1530 (1120-2320)	**Definitions:** NR **Perioperative care:** Anesthesia: spinal/general WB: 17/8 RCP: 20/4 NT: 8/1 **Analytical methodology:** Shapiro-Wilk test used to probe for normality of distribution (P>0.4). For repeated measurements, baseline corrected area under curve (AUC) was calculated. T-test and Wilcoxon rank sum test for independent variables were used to determine statistical significance. **Other notes:** Small sample size **Follow-up:** 7 days observation period **Funding Source Conflicts:** Authors: None Institution: None Study: None Supplies: None

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting (N)	Intervention	Results	Comments
			(91.2%) NT: 9/9 (100%) 2 Units Predeposited WB: 3/25 (12%) RCP: 2/24 (8.8%) NT: 0 Storage period (days) WB: 27.9±2.9 RCP: 28.4±2.0 NT: 28.2±1.6 Length of Surgery WB: 102±17 minutes RCP: 89±21 minutes NT: 92±25 minutes **Procedures:** Hip arthroplasty **Indications:** NR **Setting:** 1 university hospital **Location:** Germany **Dates:** NR **Inclusion Criteria:** patients who had donated autologous blood and were scheduled for hip arthroplasty **Exclusion Criteria:** contraindication	determined by routine automated laboratory methods. Differential blood cell count was measured by depolarized orthogonal light scattering **Control group:** n=32 WB Whole Blood n=25 donated blood units stored as whole blood Non-transfused patients (NT) NT 7 had donated blood stored as WB vs. 2 as RCP. **Standard preventive measures** Thromboembolic Prophylaxis: 40mg subcutaneous enoxaparin administered 1/day starting 12h prior to surgery. AMP: cefuroxime administered intravenously prior to surgery. Cemented, cementless, and hybrid prostheses were implanted. Volume replacement: modified ringer's solution and gelatin solution were used. Postop_ autologous plasma was re-transfused for volume replacement primarily in	ml Transfusion of predeposited units 3 units WB: 3/25 RCP[(RC/FFP)/n]: (9/7)/24 NT: 0 2 units WB: 8/25 RCP[(RC/FFP)/n]: (6/6)/24 NT: 0 1 unit WB: 14/25 RCP[(RC/FFP)/n]: (9/4)/24 NT: 0 P≤0.05 for all transfusion of unit values (3, 2, 1) for WB vs. RC Volume replacement (ml) Modified Ringer's Solution WB: 4376±802 RCP: 4604±642 NT: 4422±1190 Colloid Solution WB: 1540±628 RCP: 1333±602 NT: 1417±530 Patients with Cell Salvage WB: 12/25 (48%) RCP: 8/24 (33.3%) NT: 1/9 (11.1%) Volume transfused:	

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			for autologous blood donations and diseases associated with impaired immune defense.	the RCP group. Analgesic: diclofenac & prirtarmid. Cell salvage: performed in all groups if a patient had <3 units and/or presented for surgery with Hb concentration <12g/dl. Blood collected was processed and retransfused with drain blood measured and sponged blood estimated Transfusion Triggers: Hb, 9g/dl or clinical signs of myocardial ischemia.	median(range) WB: 510 (240-1200) ml RCP: 610 (4-1600) ml NT: 360 ml Laboratory Analysis: Regarding hemoglobin concentration, neutrophils, monocytes, phagocytic activity, and oxidation activity: There were no significant differences in values between the three groups. **Reoperations**: NR **Length of stay: (mean±SD)** WB: 15.3±0.8 days RCP: 15.3±0.6 days NT: 15.0±1.0 days **Mortality:** NR **Adverse events:** NR	
Pedersen 2009 [151] (ES)	**Retrosp-ective concur-ent control** 1, 2, 3, 4, 5, 6, 7, 8	To determine whether allogeneic red blood cell transfusion was associated with increased odds of complications following primary total hip replacement (THR). Complications included	**Number of patients: N=28,087** **Matched group N=4508** **Patient Characteristics:** For total group, Transfused patients were older & had more comorbid conditions. They also were more	**Intervention group**: **Receiving Transfusion Intervention1**: n=9063 (32.3%) Patients received ≥1 unit red blood cell (RBC) transfusion within 8 days of surgery **Intervention2:** n=2254 Patients receiving ≥1 unit RBC allogeneic transfusion within 8 days of surgery (matched by propensity scoring to the	**SSI (Follow Up 90 Days) (Adjusted)** Reoperation due to infection Intervention2: 5/2254 (0.2%) Control2: 5/2254 (0.2%) OR (95%CI): 0.57 (0.11-2.93) **Other infections:** Pneumonia: adjusted	**Definitions** Outcomes (within 90 days of index procedure): 1. Death, 2. Hospitalization with cardiovascular events including myocardial infarction, congestive heart failure, peripheral vascular disease, or cerebrovascular events, 3. hospitalization with venous thromboembolism, including deep venous thrombosis and/or pulmonary embolism, 4. hospitalization with pneumonia

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		hospitalization with cardiovascular and/or cerebrovascular events, venous thromboembolism, pneumonia, reoperation due to infection of primary THR, and mortality within 90 days of primary THR	likely to be female, receive a cemented prosthesis, and to have a THR procedure of more than 2 hours. For the propensity-matched population, there were no substantial differences for any of the characteristics related to the risk of transfusion Standardized mean difference (SMD)>0.1 is indicative of significant imbalance between groups ·**Age:** Age groupings were similar between groups except for 80+ years Intervention2: 404/2254 (17.9%) Control2: 411/2254 (18.2%) SMD= 0.18397 ·**Gender:** female n (%)	control2 group **Timing of intervention:** intraoperative &/or Postoperative **Duration of intervention:** within 8 days of surgery **Agent:** Allogeneic red blood cells. Intervention1: Median: 2units/patient Range: 1-20 units **Monitoring intervention:** NA **Control group: No Transfusion** **Control1:** n=19024 Patients who received no transfusion **Control2: n=**2254 Patients who received no transfusion and were matched by propensity scoring to Intervention2 **Standard preventive measures:** NR **Non-standard preventive measures:** <u>Anti-rheumatic drug Prophylaxis for heterotropic bone formations:</u>	Intervention2: 36/2254 (1.6%) Control2: 17/2254 (0.8%) OR (95%CI): 2.1 (1.2-3.8) **Topic-specific outcomes:** Median (range) number of units transfused: Intervention1: 2 (1-20) Control: 0 <u>Duration of operation: Similar between matched groups except for Longer surgeries:</u> >121 minutes: Intervention2: 151 (6.7%) Control2: 157 (7.0%) SMD: 0.20997 <u>Preoperative Hemoglobin concentration w/in 3 months prior to surgery:</u> <138.5 g/L Intervention2: 1410 (62.6%) Control2: 1362 (60.4%) SMD: 0.25041 **Length of stay:** NR **Mortality: (within 90 days of primary THR) -**	and 5. reoperation due to infection. **Perioperative care:** <u>Regional Anesthesia:</u> Intervention2: 1753/2254 (77.8%) Control2: 1757/2254 (78.0%) SMD=0.18378 **Analytical methodology:** To overcome bias due to confounding, they matched patients not receiving transfusions with patients receiving transfusion with a 1:1 ratio using propensity score matching. The propensity score for each patient was calculated using logistic regression. Patients were matched for baseline characteristics. Information on blood lost during surgery was not available for this dataset. They adjusted for hemoglobin concentration 1-7 days postoperative as a surrogate measure of blood loss. Information on smoking status, obesity/BMI, prior history of transfusion, and preoperative history of increased perioperative bleeding and pre-operative history of chronic anemia was also not available and not included in propensity matching score. **Other notes:** Data utilized in this study is from **1)** The Danish Hip Arthroplasty Registry (DHR). This registry of all

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			Intervention2: 1490/2254 (66.1%) Control2: 1439/2254 (63.8%) SMD=0.11293 ·**Obesity:** NR ·**Comorbidities:** Diabetes Intervention2: 134/2254 (5.9%) Control2: 115/2254 (5.1%) SMD=0.05238 Preoperative Hemoglobin <138.5g/L within 3 mo. before surgery Intervention2: 1410/2254 (62.6%) Control2: 1362/2254 (60.4%) SMD=0.25041 **Procedures:** Primary Total Hip Replacement (THR) **Indications:** Primary arthrosis Intervention2: 1647/2254 (73.1%) Control2:	Intervention2: 195/2254 (8.7%) Control2: 208/2254 (9.2%) SMD=0.06109	**adjusted** Intervention2: 39/2254 (1.7%) Control2: 18/2254 (0.8%) OR (95%CI) 2.17 (1.24-3.80) **Adverse events**: <u>Deep venous thrombosis/ pulmonary embolism –adjusted</u> Intervention2: 28/2254 (1.2%) Control2: 23/2254 (71.0%) OR (95%CI): 1.17 (0.67-2.06) <u>Cardiovascular or cerebrovascular disease – adjusted</u> Intervention2: 54/2254 (2.4%) Control2: 39/2254 (1.7%) OR (95%CI): 1.42 (0.93-2.15) **<u>Composite outcome – adjusted</u>** OR (95% CI): 1.67 (1.23-2.26) <u>Subanalysis of composite outcome risk by Number of transfusions/ patient:</u> Adjusted OR (95%CI)	primary THR consists of data recorded prospectively by the operating surgeons using standardized forms. (pre-, peri- and postoperative data). Reoperation data was also obtained here. **2)** The Danish Transfusion Database. Data included all allogeneic red blood cell transfusions administered to included patients within 8 days of primary THR surgery. Patients were classified as having received either no or one or more units. **3)** The Civil Registration System was utilized for data on mortality. **4)** The Danish National Registry of Patients was used for hospitalization data. Diagnoses were classified according to the Danish version of the International Classification of Diseases (ICD. The ninth edition (ICD-8) was used from 1977 to 1993 and the tenth edition (ICD-10) has been used hereafter. The physician who diagnosed the patient assessed all discharge codes. Odds estimates may partly reflect unmeasured bias due to blood loss Limitation: No information on intraoperative blood loss which may have impacted postop transfusions. Information on pre/post-operative hemoglobin concentration used as a surrogate measure of blood loss. **Follow-up:** until the occurrence of

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			1633/2254 (72.5%) SMD=0.23293 Trauma Intervention2: 323/2254 (14.3%) Control2: 319/2254 (14.2%) SMD=0.28662 Other Intervention2: 284/2254 (12.6%) Control2: 302/2254 (13.4%) SMD=0.00682 **Setting:** Multi-center 20 hospitals in North Jutland, Aarhaus, Funen, and Copenhagen). These 20 orthopaedic departments serve ~45% of the Danish population (nearly 2.3 million people). **Location:** Denmark **Dates:** January 1, 1999 – December 31, 2007 **Inclusion Criteria:** Patients with primary THR procedures registered in the		≥6 transfusions:3.4 (1.3-9.2) 3-4 transfusions: 1.5 (0.8-2.9) 2-3 transfusions: 1.2 (0.8-1.9) 1 transfusion: 2.7 (1.2-5.7) <u>Subgroup analysis for history of cardiovascular events</u> With History (matched) Intervention2: 407/2254 (18.1%) Control2: 407/2254 (18.1%) - Red blood cell transfusion was associated with odd of the composite adverse outcome within 90 days of surgery: 1.2 (0.8-1.9) Without History (matched) Intervention2: 1834/2254 (81.4%) Control2: 1834/2254 (81.4%) In THR patients without cardiovascular events prior to surgery, OR of composite outcome: 1.7 (1.1-2.7) <u>Subgroup analysis postoperative hemoglobin (matched)</u>	death, hospitalization for cardiovascular or cerebrovascular events, venous thromboembolism, pneumonia, reoperation due to infection or 90 days after surgery. **Funding Source Conflicts:** Authors: None Institution: None Study: None Supplies: None

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			Danish Hip Arthroplasty Registry (DHR) and performed at the hospitals reporting to the Danish Transfusion Database during the study dates. This includes patients who sustained right and left THR during the study period as long as surgery was not performed on the same day (those were treated as independent operations) **Exclusion Criteria:** Patients without possibility for follow up and bilateral primary THR procedures performed during the same surgery.		Hemoglobin concentration <105g/L Intervention2: 729/2254 (32.3%) Control2: 729/2254 (32.3%) - Adjusted OR: for composite adverse outcome w/in 90 days of surgery: 1.1 (0.5-2.7) for transfused vs. non transfused Hemoglobin concentration>105g/L Intervention2: 1505/2254 (66.8%) Control2: 1505/2254 (66.8%) - Adjusted OR: for composite adverse outcome w/in 90 days of surgery: 1.6 (1.0-2.5) for transfused vs. non transfused	
Monte del Trujillo 2008 [152] (ES)	**Prospect-ive concurre nt control** 1, 3, 4, 5, 6, 7, 8	To prospectively evaluate the utility of a new device that automatically provides washed salvaged blood to reduce exposure	**Number of patients N=108** **Patient Characteristics:** There were no differences in characteristics between groups	**Intervention group**: n=60 Utilization of the blood processing device designed to wash autologous blood and re-infuse the blood.	**SSI (Follow up - NR)** **Unadjusted:** Total Infection: Intervention: 1 (2%) Control: 5 (10%) P=0.086 Wound Infection Intervention: 0 (0%)	**Definitions:** Postoperative Infectious Complications (urinary tract, respiratory tract, and wound infections): CDC definitions. Adverse reactions to WSB reinfusion: Shivers, fever, bradycardia, hypotension

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting (N)	Intervention	Results	Comments
		to Allogeneic Blood Transfusions (ABT) in elective Total Hip Replacement (THR) patients. End-points include the impact of Washed Salvaged Blood (WSB) return on both the rate of postoperative infection and the length of hospital stay.	except age and Hypertension. Data expressed as mean ±SD or n (%) ·**Age (y):** Intervention: 62±14 Control: 67±9 P= 0.027 ·**Gender: f/m** Intervention: 27/33 Control: 31/17 ·**Obesity: weight (kg)** Intervention: 79±9 Control: 80±11 ·**Comorbidities** Diabetes Intervention: 7 (12%) Control: 12 (25%) Anemia (Hb<130g/l) Intervention: 4 (7%) Control: 2 (4%) Hypertension Intervention: 16 (27%) Control: 32 (67%) P=0.001 Patient distribution according to	**Timing of intervention:** intraoperative and/or postoperative **Duration of intervention:** duration of transfusion **Agent:** Perioperatively salvaged WSB. The blood was collected with non-fractionated heparin and was re-infused within the first 6h from the beginning of blood salvage. **Device:** A blood processing device designed specifically to adapt to the intermittent blood loss of orthopedic surgical patients. **Monitoring intervention:** NR **Control group** n=48 Patients received normal allogeneic blood transfusions (ABT) if necessary, one unit of leukodepleted packed red blood cell was considered to have a RBC mass of 165ml. **Standard preventive measures**: Surgical Team: All patients were operated	Control: 2 (4%) Infection Rate ABT: 12.2% (4/32) No ABT: 2.6% (2/76) p=0.046 **Other infections:** Urinary Infection Intervention: 1 (2%) Control: 2 (4%) Respiratory Infection: Intervention: 0 (0%) Control: 1 (2%) **Topic-specific outcomes:** Intervention: Enough WSB blood volume obtained to be returned: 49/60 (82%) Mean: 336±205 Hct: 63±5% RBC: 205±151ml RBC/patient: 1.3±0.9 **Calculated and total perioperative blood loss was not significantly different between groups according to age, gender, anesthesia type or hypertension. Calculated Blood Loss (ml) Cemented THR: Intervention: 1943±906 Control: 2091±747	Estimated blood volume: calculated using gender and body weight [Gross1983] Total Perioperative Blood Loss (CBL (ml)) = [Uncompensated RBC loss (ml) = Compensated RBC loss (ml)]/0.35 Uncompensated RBC loss (ml)= (preoperative Hct – postoperative day 4 Hct) x Estimated Blood Volume (EBV) Compensated RBC Loss (ml) = [Packed allogeneic red cell units x 165 (ml/unit) = [washed autologous blood volume x washed autologous blood Hct] Acute Anemia: hypotension, tachycardia, tachypnea, dizziness, fatigue. **Perioperative care:** Anesthesia: standard general or regional Cemented THR: Regional/General Anesthesia Intervention: 6/6 Control: 8/9 P=0.876 Uncemented THR: Regional/General Anesthesia Intervention: 27/21 Control: 13/18 P=0.119 Cemented components: 73% of patients (79 patients) Oral Iron Supplement Intervention: 32 (53.3%)

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			preoperative Hb levels, perioperative Hb levels, and calculated total blood loss were no different in both groups. Preoperative Hb (g/dl) Cemented THR: Intervention: 14.4±1.2 Control: 13.6±1.2 P=0.067 Uncemented THR: Intervention: 14.5±1.6 Control: 14.6±1.4 P=0.823 (note: p<0.05 within control group) **Procedures**: Unilateral Total Hip Replacement (THR) **Indications:** NR **Setting:** 1 Center **Location**: Spain **Dates**: January 2005 – June 2006 **Inclusion Criteria:** Patients undergoing THR **Exclusion**	on by the same surgical team (senior surgeons) and each attending surgeon performed two operations in each surgical session (1 intervention and 1 control) Approach: All patients were positioned supine and anterolateral approach was used to the hip. Antimicrobials: surgery performed under antimicrobial prophylaxis Anticoagulant: surgery performed under antithrombotic prophylaxis (low molecular weight heparin) Analgesia: Postop. Components: Same acetabular and femoral components were used in all hips. Drains: 2 suction drains were used in all procedures. Removed on POD 2. Transfusion was indicated when patient's Hb level decreased to less than 8g/dL or when the patient had symptoms of acute anemia (hypotension, tachycardia, tachypnea,	P=0.634 Uncemented THR: Intervention: 2336±1015 Control: 2347±971 P=0.966 **ABT rate,** Total Intervention: 15% (n=9) Control: 48% (n=23) RR:0.31; P=0.001 Preoperative Hb≥13g/dl RR: 0.32; P=0.003 Preoperative Hb3g/dl RR: 1.47; P=0.091 Age<60yo RR: 0.47; P=0.021 Age≥60yo RR: 0.17; P=0.027 ABT rate n (%) Cemented THR: Intervention: 1 (8%) Control: 10 (59%) P=0.008 Uncemented THR: Intervention: 8 (17%) Control: 13 (42%) P=0.013 Total ABT units Cemented THR: Intervention: 2 Control: 20 P=0.017 Uncemented THR: Intervention: 13 Control: 28	Control: 24 (50%) P=0.338 **Analytical methodology: Chi-square or Fisher's Exact test for qualitative variables. Parametric one-way ANOVA or non-parametric Mann-Whitney for quantitative variables.** **Other notes:** none **Follow-up:** NR **Funding Source Conflicts:** Authors: None Institution: None Study: None Supplies: None

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			Criteria: Patients with hematological diseases or coagulation disorders, hepatic or renal diseases, those receiving anticoagulant therapy or with known infection or malignancy. Also, patients with any other blood-saving strategy (e.g. preoperative autologous blood donation or erythropoietin treatment).	dizziness, fatigue, etc.)	P=0.005 Transfusion Index (ml RBC/ transfused patient) Allogeneic Overall Intervention: 53±117 Control: 371±154 P=0.001 Cemented THR: Intervention: 49±129 Control: 378±142 P=0.001 Uncemented THR: Intervention: 54±118 Control: 366±168 P=0.001 Autologous Cemented THR: Intervention: 163±77 Control: 0 Uncemented THR: Intervention: 218±153 Control: 0 Overall Total Intervention: 263±189 Control: 371±154 P=0.022 Cemented THR: Intervention: 212±167 Control: 378±142 P=0.049 Uncemented THR: Intervention: 272±192 Control: 366±168 P=0.001 **Reoperations:** NR **Length of stay (days):** Intervention: 10.1±3.1	

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					Control: 11.6±7.4 P=0.201 ABT:13.5±7.9days No ABT: 9.6±3.1 days Difference 3.9 days; 95%CI (1.8-6.0); P=0.001 **Mortality:** NR **Adverse events:** DVT Intervention: 0 (0) Control: 1 (2%) Ability to walk (days) Intervention: 4.6±1.4 Control: 5.1±3.4 NoABT:4.4±1.6 days ABT: 5.7±3.5 days Difference 1.3d; 95%CI (0.3-2.3) P=0.013	
Innerhofer 2005 [147] (ES)	**Prospective concurrent control** 1, 2, 3, 4, 5, 6,	To determine that the use of White Blood Cell (WBC) filtered blood components should cause allogeneic recipients to exhibit postoperative infection rates similar to those of patients receiving autologous blood during elective primary hip or knee arthroplasty using the incidence of postoperative	**Number of patients: N=308** Preoperative Autologous Blood Donation (PAD): n=143 No PAD: n=165 No transfusion: n=101 Autologous: n=85 Allogeneic, WBC filtered= n=100 Both, n=22 **Patient Characteristics:** **·Age: median (IQR)** No RBC: 66y (54-73) Autologous: 64y	**Intervention group:** Allogeneic (WBC-filtered)n=100 **Timing of intervention:** Intraoperative and/or postop **Duration of intervention:** duration of transfusion **Agent:** all blood components produced by hospital Autologous or Allogeneic whole blood was collected in top and bottom bags; citrate	**SSI (Follow up-discharge)** Wound infection (total=4 (1.2%) Allogeneic: 3/100 (3%) No RBC: 1/101 (1.0%) Autologous: 0 Both: 0 **Other infections:** Total infections (UTI, pneumonia, wound, purulent dermatitis): 22/308 (6.82%) resulting in antimicrobial therapy for treatment Allogeneic: 12/100 (12%) No RBC: 7/101 (6.9%)	**Definitions:** Urinary Tract Infection (UTI): diagnosed by orthopedic surgeon, established from positive results of microbiologic cultures and clinical signs of UTI Pneumonia: when signs of fever, leukocytosis, and chest infiltrate were observed Wound infection: clinically in the case of purulent secretion and painful erythema. Purulent Dermatitis (bacterial dermal infection distinct from operation site): confirmed by positive microbiologic results. **Perioperative care:** NR **Analytical methodology:** Chi-

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting (N)	Intervention	Results	Comments
		infection as an endpoint	(55-70) Allogeneic: 74y (67-78) Both: 72y (65-77) P<0.0001 ·**Gender: f/m** No RBC: 43/58 Autologous: 44/41 Allogeneic: 73/27 Both: 15/7 P=0.0001 ·**Obesity: BMI** No RBC: 28 (25-31) Autologous: 27 (24-30) Allogeneic: 26 (23-29) Both: 26 (24-32) P=0.009 ·**Comorbidities:** Existing Disease (including Coronary artery disease, congestive heart failure, COPD, Diabetes mellitus, renal and liver disease, chronic polyarthritis, intake of corticosteroids, malignant disease) No RBC: 37.6% (n=38) Autologous: 29.4% (n=25) Allogeneic: 58%	phosphate dextrose adenine-1 was used as anticoagulant. WBC reduction was provided by pre-storage inline WBC filtration of whole blood. Separated RBCs were stored in 100ml of saline-ademine-glucose-mannitol additive solution and kept at 4°C and plasma was frozen (to -30°C core temp) within 2 hour of separation. Autologous blood was donated by means of apheresis, at 400ml of RBCs 3-4 weeks before surgery. It was divided into 2 units re-suspended in 100ml saline-adenine-glucose-mannitol each. RBCs were not WBC filtered and the WBC content was 2,000-30,000 WBCs/μL **Monitoring intervention:** NR **Control group:** n=208 <u>Control1: n=101</u> No RBCs/ no Transfusion Control2: n=85 Autologous <u>Control 2: n=22</u>	Autologous: 1/85 (1.2%) Both: 1/22 (4.6%) P=0.03 Allogeneic compared with Autologous transfusions: P=0.0053 No transfusion compared with compared to autologous: P=0.06 Allogeneic + Both: 10.7% (13/122) Autologous + None: 4.3% (8/186) P=0.03 **Incidence of infection increased significantly with the number of transfused allogeneic WBC-filtered RBCs (p=0.01, data not shown) <u>Statistically significant Multivariate analysis of variables predicting postop infection</u> Allogeneic WBC-filtered RBCs OR (95%CI): 23.66 (1.33-422.06) P=0.02 Foley catheter (days) OR (95%CI): 1.23 (1.1-1.4) P=0.002 <u>UTI</u> Allogeneic: 7/100	square and U test to compare baseline data of patients. Univariate analysis was performed for factors associated with postoperative infection and transfusion supply. Chi-square and Kruskall-Wallis test were applied to analyze predictive factors of infection after allogeneic transfusion. Logistic regression model for evaluating risk factors for postoperative infection. **Other notes:** As expected, Fresh Frozen Plasma (FFP) was seldom necessary to correct coagulopathy (15/308 patients) and intraoperatively salvaged blood was processed for 44/308 (14%) of patients only and therefore was not analyzed further. **Follow-up:** Discharge **Funding Source Conflicts:** Authors: NR Institution: NR Study: NR Supplies: NR

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			(n=58) Both: 36.4% (n=8) P=0.0007 **·Hb at admission (g/dl):** No RBC: 14.3 (13.7-15.1) Autologous: 12.8 (12.3-13.9) Allogeneic: 13.1 (12.1-13.8) Both: 12.2 (11.4-12.5) P<0.0001 **·Hb at discharge (g/dl):** Not significantly different between groups. **Procedures:** Primary Hip Replacement: 189 Primary Knee Replacement: 119 **Indications:** NR **Setting:** 1 center **Location:** Austria **Dates:** 10 months **Inclusion Criteria:** Patients undergoing primary hip or knee replacement surgery **Exclusion Criteria:** Any infection (including UTI), medical	Both Autologous and Allogeneic RBCs **Standard preventive measures:** Transfusion trigger: bHb levels below 8g/dl and/or physiologic signs of anemia Warming: all patients were actively warmed with fluid warmer and a convective warming system. Transfusions: fluid warmers and 40-µm blood filters were used AMP: single dose of second-generation cephalosporin before incision. Anticoagulant: Enoxaparin administered 12h before operation. Catheters: all patients received Foley catheters on the morning of the day of surgery. **Non-standard preventive measures:** Blood Aspiration: blood was aspirated into a cell-saver system and processed when appropriate (>1000ml of blood in the reservoir. Postoperatively unwashed shed blood was also re-transfused	(7.0%) No RBC: 5/101 (5.0%) Autologous: 1/85 (1.2%) Both: 0/22 Pneumonia Allogeneic: 3/100 (3.0%) No RBC: 0/101 Autologous: 0/85 Both: 1/22 (4.5%) Purulent Dermal infection Allogeneic: 0/100 No RBC: 1/101 (1.0%) Autologous: 0/85 Both: 0/22 **Topic-specific outcomes:** ·Total RBCs (units transfused): Allogeneic: 2 (2-4) No RBC: 0 Autologous: 2 (1-2) Both: 4 (3-4) P<0.0001 ·Shed Blood (ml): Allogeneic: 500 (300-700) No RBC: 550 (500-900) Autologous: 500 (450-1000) Both: 500 (300-1000)	

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting (N)	Intervention	Results	Comments
			reason for not donating autologous blood, surgery for metastatic process, or stabilization of acute fractures.	within 6h FFP**:** was only used to treat coagulopathy 15/308 (4.9%)	P=NS **Reoperations:** NR **Length of stay:** With Infection: 16.8±4.2d No Infection: 14.0±2.1d P=0.0004 **Mortality:** NR **Adverse events:** ·Foley Catheter (days) Allogeneic: 3 (3-4) No RBC: 3 (2-4) Autologous: 3 (2-3) Both: 4 (3-5) P=0.006	
Weber 2005 [149] (ES)	**Prospect-ive concur-ent control** 1, 2, 3, 4	To determine the effects of allogeneic blood transfusion on length of hospital stay in patients undergoing elective total hip arthroplasty by examining the frequency of allogeneic blood transfusion, wound-healing disturbances, superficial and deep wound infections, and length of hospital admission.	**Number of patients: N=444** **Patient Characteristics: mean (SEM) or n (%)** **·Age: years** Intervention: 64.2 (14.5) Control: 63.1 (11.2) **·Gender: %male** Intervention: 13% (34) Control: 39% (49 P<0.01 **·Obesity** Height (cm) Intervention: 167 (8.6) Control: 171 (8.9) P<0.05 Weight (kg)	**Intervention group:** n=92 Received allogeneic blood transfusion. **Timing of intervention:** Intraoperative and postoperative **Duration of intervention:** Intraoperative with different triggers either before or after 4 hours postop. **Agent:** Packed red blood cells were supplied by local blood bank and consisted of buffy coat-depleted cells, mean vol. 320ml, Hb 17.8g/dl, Hct=0.58, and Leukocytes $0.4x10^9$/L	**SSI (follow up 6 weeks) Unadjusted results.** Deep Infection (mean(SEM)) Intervention: 1% (10%) Control: 1% (8%) P=NS Positive Wound Culture (mean(SEM)) Intervention: 3.3% (18%) Control: 2.0% (14%) P=NS Wound Disturbance (mean(SEM)) Intervention: 31% (47%) Control: 18% (39%) P<0.05 To determine impact of perioperative blood loss, they divided the group into 3 subgroups:	**Definitions:** Wound and urinary tract infections: defined by the presence of a positive culture. Wounds were examined daily by orthopedic surgeons who were trained to the assessment protocol but not blinded to transfusion. Deep infection: requires joint involvement Wound-healing disturbance: erythematous inflammation of >1cm, wound fluid discharge, purulent suture, wound dehiscence, blister, or any degree of wound necrosis. **Perioperative care:** NR **Analytical methodology:** Occurrence of wound disturbance factors in relation to blood transfusion and other potentially related factors were calculated using logistic regression

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting (N)	Intervention	Results	Comments
			Intervention: 72 (15.4) Control: 79 (13.8) P<0.001 ·**Comorbidities:** <u>Diabetes mellitus</u> Intervention: 2/92 (2.2%) Control: 18/352 (5.1%)<u>Pulmonary disease</u> Intervention: 9/92 (9.8%) Control: 29/352 (8.2%)<u>Steroids</u> Intervention: 1/92 (1.1%) Control: 12/352 (3.4%) <u>Rheumatoid Arthritis</u> Intervention: 6/92 (6.5%) Control: 16/352 (4.5%) **Procedures:** Elective primary total hip arthroplasty **Indications:** NR **Setting:** 1 hospital **Location:** The Netherlands **Dates:** October	**Monitoring intervention:** <u>Info collected</u> 1. At POD 0 - all routine clinical postop assessments, name of surgeon, Hb level. 2. POD1 - blood loss, transfusion data (including units and type of blood products given and Hb before transfusion) any blood-saving techniques used, and medications used 3. POD4 – serum prealbumin and pre-transfusion Hb (only if transfused) 4. Discharge – blood loss, transfusion data (number of units and type of blood product) and length of hospitalization. **Control group:** n=352 No transfusion received **Standard preventive measures:** All patients received standard care acceding to standard protocol by using active body warming and so on. Therefore, fraction of inspired oxygen, body	Blood loss 1-700mL Blood loss 101-1000mL Blood loss >1000mL. For each subgroup they observed “essentially the same proportion in the incidence of wound disturbances as was found for the groups as a whole.” (Study not powered for this analysis so correlation between transfusion and wound disturbances did not reach significance in these subgroups)_ <u>Unadjusted predictors of Wound healing disturbances: OR (95%CI)</u> Blood Transfusion OR: 2.1 (1.2-3.5); P=0.03 All other variables not significant **Blood transfusion was also the only significant variable using multivariate analysis **Other infections:** <u>Urinary Tract Infection (mean(SEM))</u> Intervention: 3.3% (18%) Control: 3.7% (19%)	Risk variables were calculated using stepwise conditional backward and forward selection to perform multivariate analysis. Effect of variables on Length of stay was calculated with linear regression analysis. Then log-normalized. **Other notes:** None **Follow-up:** at least 6weeks postoperatively. **Funding Source Conflicts:** Authors: NR Institution: NR Study: NR Supplies: NR

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting (N)	Intervention	Results	Comments
			29, 1998 – October 27, 1999 **Inclusion Criteria**: Patients undergoing planned elective primary total hip arthroplasty, ≥18yo, living in The Netherlands, or otherwise available for follow up for at least 6 wk. postop **Exclusion Criteria:** Any infection of any body-system at screening, as determined by symptoms or erythrocyte sedimentation rate (ESR)>20mm (unless known to be preexistent); any blood transfusion received within 6wk before surgery; and any other operation within 6wk preop. Also, patients who donated autologous blood preoperatively.	temperature, and so on was comparable between groups. Because of the length of study period, group of surgeons was limited and their distribution was comparable between groups. **Non-standard preventive measures** <u>Transfusion Trigger:</u> Hb<8.1 g/dl (5.0mmol/l) during surgery and until 4h postop and Hb<8.9 g/dl (5.5mmol/l) more than 4h postop. For patients with cardiovascular disease, all triggers were increased by 0.8g/dl (0.5mmol/l) <u>Gentamycin cement used (%) (SEM)</u> Intervention: 21% (41) Control: 14% (34) P=NS	P<0.01 **Topic specific outcomes:** **Preop ESR (mm 1st h)** Intervention: 18.3 (13.8) Control: 14.5 (11.1) P<0.05 **Preop prealbumin (mmol/L)** Intervention: 266 (51.4) Control: 285 (56.2) P<0.05 **Preop Hb (mmol/L)** Intervention: 8.0 (0.8) Control: 8.6 (0.7) P<0.001 **Operation time (min)** Intervention:80 (31.6) Control: 71 (19.5) P<0.05 **Perioperative blood loss (mL)** Intervention: 789 (551) Control: 540 (274) P<0.001 **Total Blood Loss (mL)** Intervention: 1185 (716) Control: 922 (431) P<0.001 **Reoperations**: NR **Length of stay: mean (SEM) d** Intervention: 12.3 (5.3) Control: 9.8 (3.5) P<0.001 Evaluation to determine if length of stay was affected by perioperative	

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					blood loss showed that duration of hospitalization was essentially unaffected by blood loss and a similar difference in hospitalization duration between transfused and nontransfused was maintained among the subgroups. (Study not powered to detect significant differences in sub-analysis but did reach significance in patients who lost more than 700mL of blood perioperatively) <u>Regression model to predict length of stay (days) (β (95%CI) (How much each variable adds to length of stay)</u> Age (days per 10yr) 0.9 (0.6-1.2); P<0.001 Operation time (days per 10 min) 0.2 (0.1-0.4); P=0.011 Wound disturbance (days if present) 1.3 (0.4-2.1); P=0.006 Transfusion (days if given) 2.2 (1.3-3.1); P<0.001 **Mortality:** NR	

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting (N)	Intervention	Results	Comments
					Adverse events: NR	
Llewelyn 2004 [150] (ES)	**Prospect-ive Pre-Post** 1, 2, 3, 4, 8	To conduct a two-cohort prospective study in patients undergoing elective coronary artery bypass graft or total hip and/or knee replacement surgery before and after universal leukoreduction (ULR) to examine the effects of ULR on a large group of surgical patients who received transfusion(s).	**Number of patients: N=3942 evaluable** **Patient Characteristics:** using evaluable populations: **Transfusions: n=** Before ULR: n= 997 Ortho before n=606 After ULR: n=1098 Ortho after: n=637 **No Transfusion** Before ULR: n=956 Ortho before: n=871 After ULR: n=891 Ortho after: n=799 **·Age: years** Transfusions: Before ULR:68.6±11.1 After ULR:69.2±10.2 No Transfusion Before ULR: 68.0±10.4 After ULR:68.1±10.3 **·Gender: male (%)**	**Intervention group: Received Transfusions n= 2095** **Total Orthopaedic received transfusion: 1243** **Intervention1**: n=997 **(Orthopaedic I1 n=606)** Patients receiving transfusions before mandatory ULR. These transfusions were intended to be unmodified RBC, but cohort included patients who received BC-RBC and/or WBC reduced RBCs ONLY IF they also received at least 2 u unmodified RBC. Intervention2: n=1098 **(Orthopaedic I2 n-637)**Patients receiving transfusions after mandatory ULR (Full cohort2 is WBC reduced allogeneic RBCs) **Timing of intervention:** intraoperative and postoperative **Duration of intervention**: intraoperative and postoperative **Agent:**	**SSI (Follow Up 90 days)** **Surgical wounds** Orthopedic Intervention1: 43/606 (7.1%) Intervention2: 32/637 (5.0%) Control1: 31/871 (3.6%) Control2: 22/799 (2.8%) **Proven Infections** Orthopedic Intervention1: 50/606 (8.3%) Intervention2: 26/637 (4.1%) AOR:0.45 (0.28-0.74); p=0.002 Control1: 21/871 (2.4%) Control2: 29/799 (3.6%) **Other infections** Lower Respiratory Infections Orthopedic Intervention1: 21/606 (3.5%) Intervention2: 26/637 (4.1%) Control1: 20/871 (2.3%)	**Definitions:** 2 primary outcomes of interest " Length of stay and Infections" Length of Stay (LOS): the days between the operation and discharge form the acute care ward. (Days on intensive care unit and/or high dependency unit plus orthopedic or cardiac ward) Infections: new suspected and proven postop infections for which antimicrobial s were prescribed (excluding topical antimicrobials and antimicrobials given as perioperative antimicrobial prophylaxis) plus local signs and symptoms as follows: UTI: two or more of following: 1) fever with no other recognized cause 2) urgency 3) frequency 4) dysuria Lower Respiratory Tract Infection: LRTI: new or increased production of sputum and/or fever (>38^{o}C) with appropriate chest signs including consolidation and/or chest x-rays showing new or progressive infiltrate Wound infections: with purulent discharge in or exuding from the wound. Secondary outcomes: Hospital proven postop infections: required clinical symptoms above leading to antimicrobial prescription PLUS positive microbio culture (except physician's diagnosis of pneumonia sufficed as confirmation

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			Transfusion: Before ULR: 471 (47.2%) After ULR: 600 (54.6%) P = 0.001 No Transfusion Before ULR: 422 (44.1%) After ULR: 423 (47.5%) **·Obesity (weight (kg))** Transfusion: Before ULR: 75.1±15.7 After ULR: 75.7±14.8 No Transfusion Before ULR: 79.6±15.6 After ULR: 80.6±16.0 **·Comorbidity (%)** Transfusion: Before ULR: 318 (31.8%) After ULR: 341 (31.1%) No Transfusion Before ULR: 309 (32.3%) After ULR: 249 (28.0%) **Infection (%)** Transfusion: Before ULR: 65 (6.5%) After ULR: 45	Cohort1: Unmodified RBCs or unmodified RBC and RBCs with Buffy coat removal (BC-RBCs), or WBC-reduced RBCs only if they received at least 2u unmodified RBCCohort2: all blood was WBC-reduced within 48 hours of collection by filtration either of whole blood or of BC-RBCs. **Monitoring intervention:** Transfusion recorded. **Control group:** **No Transfusions n= 1847** **Total Orthopaedic No Transfusion: n=1670** **Control1**: n=956 **Orthopaedic C1 n=871** Patients not receiving transfusions before mandatory ULR **Control2**: n=891 **Orthopaedic C2:n=799** Patients not receiving transfusions with leukocyte reduction (after mandatory ULR) **Standard preventive measures** **Non-standard preventive measures:**	Control2: 22/799 (2.8%) Urinary Tract Infections Orthopedic Intervention1: 22/606 (3.6%) Intervention2: 16/637 (2.5%) Control1: 19/871 (2.0%) Control2: 26/799 (3.3%) Bacteremia/ Septicemia Orthopedic Intervention1: 3/606 (0.5%) Intervention2: 1/637 (0.2%) Control1: 4/871 (0.5%) Control2: 0 Other Site Infections Orthopedic Intervention1: 17/606 (2.8%) Intervention2: 13/637 (2.0%) Control1: 13/871 (1.5%) Control2: 13/799 (1.6%) **Topic-specific outcomes** Drain Losses (mL) Unchanged in orthopaedic patients	of LRTI) Major non-infectious postop complications: one or more of the following: cardiac arrest, infarction, renal impairment requiring dialysis, confirmed deep vein thrombosis and/or pulmonary embolism, respiratory failure, and return to operating room for bleeding from surgical wound site. **Perioperative care:** NR **Analytical methodology:** 80% power and 5% significance, a sample size of 400-500 patients receiving transfusion was adequate to allow the study to detect an effect size of 0.125. T-test or chi square. Binary outcomes required logistic regression Time-dependent variables were analyzed by Cox proportional hazards method **Other notes:** Data were collected by research nurses or audit staff by review of hospital notes and computer information systems after the patient's discharge. **Follow-up:** 90 days after discharge **Funding Source Conflicts:** Authors: None Institution: None Study: None Supplies: None

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting (N)	Intervention	Results	Comments
			(4.1%) P=0.013 No Transfusion Before ULR: 29 (3.0%) After ULR: 32 (3.6%) **Hb level (g/dl)** Transfusion: Before ULR: 13.2±1.4 After ULR: 13.3±1.4 No Transfusion Before ULR: 13.7±151.2 After ULR: 13.8±1.2 **Procedures:** Non-emergent Coronary Artery Bypass Grafting (CABG) and elective total hip replacement and/ or total knee replacement (Primary and revisions) Primary Procedure: Orthopedic Procedures Redoes (includes bilateral and THR plus TKR) Transfusion: Before ULR: 145 (23.9%)	Transfusion Triggers; Each hospital followed its own transfusion protocols	who received transfusions vs. those who did not Lowest Hb Level (g/dL) Data not stratified by procedure type Discharge Hb level (g/dL) Data not stratified by procedure type Subgroup analysis: of storage age and dose of blood on primary outcomes before and after ULR (including postop infections, and postop LOS) found no statistically significant comparisons. TRANSFUSION DATA Number RBC units/patient Orthopedic Before ULR: 2.7±1.5 After ULR: 2.9±2.0 P=0.115 Number of patients (%) receiving – THIS IS CABG+ORTHO 1 unit of RBCs Before ULR: 114/997 (11.4%) After ULR: 78/1098 (7.1%) 2-3 units of RBCs Before ULR: 476/997	

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting (N)	Intervention	Results	Comments
			After ULR: 129 (20.2%) P=0.118 No Transfusion Before ULR: 58 (6.7%) After ULR: 26 (3.3%) P=0.001 TKR (%) Transfusion: Before ULR: 194 (32.0%) After ULR: 242 (38.0%) P=0.027 No Transfusion Before ULR: 443 (50.9%) After ULR: 408 (51.1%) P=0.934 **Indications:** variable **Setting:** Multicenter (CABG at 4 hospitals and Arthroplasty at 7 hospitals) **Location:** England **Dates:** Cohort1 (pre-ULR): Began January –May 1999 and continued until enough patients were recruited		(47.7%) After ULR: 540/1098 (49.2%) >3 units RBCs Before ULR: 407/997 (40.8%) After ULR: 480/1098 (43.7%) P=0.003 FFP/cryoprecipitate Before ULR: 84/997 (8.4%) After ULR: 108/1098 (12.1%) P=0.008 PLTs Before ULR: 75/997 (7.5%) After ULR: 110/1098 (12.3%) P=0.0004 **Reoperations:** NR **Length of stay:** postop LOS: mean (SD) days Received Transfusions Orthopedic Before ULR: 2.8±1.56 After ULR: 3.3±2.98 AR 1.16 (1.04-1.30); p=0.010 No Transfusions Orthopedic Before ULR: 8.3±3.4 After ULR: 7.9±3.8 AR 1.11 (1.00-1.22); p=0.042	

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting (N)	Intervention	Results	Comments
			(approx. 5 months) Cohort2 (Post ULR): Began January –May 2000 and continued until enough patients were recruited (approx. 5 months) **Inclusion Criteria:** CABG patients undergoing nonemergency, whether primary or redo procedures, with or without aortic or mitral valve replacement or endarterectomy. Orthopedic patients undergoing elective THR or TKR whether primary or redo operations. Bilateral procedures were included if performed during the same operation **Exclusion Criteria:** Patients receiving		**Mortality (in hospital and up to 90 days after discharge home):** Orthopedic Intervention1: 7/606 (1.2%) Intervention2: 7/637 (1.1%) Control1: 5/871 (0.6%) Control2: 3/799 (0.4%) **Adverse events:** Major Complications Orthopedic Intervention1: 40/606 (6.6%) Intervention2: 39/637 (6.1%) AOR: 0.85 (0.28-2.61); P=0.775 Control1: 34/871 (3.9%) Control2: 15/799 (1.9%) AOR: 0.44 (0.24-0.82); p=0.010	

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting (N)	Intervention	Results	Comments
			previously donated autologous transfusions Cohort1: patients receiving BR-RBC & WBC-reduced transfusions unless they had also received at least 2 units of unmodified RBCs.			
Rosenc-her 2003 [148] (ES)	**Prospect-ive Concurr-ent Cohort** 1, 3, 4, 5	To examine blood management practices before, during and after elective total knee and total hip arthroplasties in Europe (including revisions and bilateral procedures) and to determine factors predictive of the risk associated with allogeneic transfusion. Factors examined included blood wastage; pre- and postoperative Hb evolution; transfusion associated	**Number of patients: N=3996** **Patient Characteristics** ·**Age** mean±SD 69±11.2 years Allogeneic-only: 71±10.7 Autologous-only: 66±11.6 P<0.001 ·**Gender**: m/f 1393/2431 (sex data missing for 172 patients) ·**Obesity:** NR ·**Comorbidities:** Hypertension: 1631 (41%) Coronary Artery Disease: 469 (12%) Significant differences between transfusion	**Intervention group: Received Transfusions: 2762** **Allogeneic Only (±WBC filtration)** =1024/2762 (37%) **Autologous Only** =1393/2762 (50%) Autologous Blood Donation (ABD) = 1290/1393 (93%) Acute Normovolemic Hemodilution=82/1393 (6%) Cell saver=329 Postop salvage=264 **Allogeneic and Autologous**: n=345/2762 (13%) **Timing of intervention:** Intraoperative/postoperative **Duration of intervention:** Intraoperative/postopera	**SSI (Follow up discharge from Surgery Department)** Unadjusted: Overall wound infection rate: 81/3996 (2%) Allogeneic-only: 36/999 (4%) Autologous-only: 11/1311 (1%) $X^2(1) = 19.26$; p<0.001 (allogeneic only vs. autologous only) Allogeneic & Autologous: 8/329 (2%) No Transfusion: 22/1180 (2%) ABD Transfusions only: 4/615 (1%) Allogeneic Transfusion WBC-Depleted: 18/637 (3%) Not WBC-Depleted: 18/464 (4%) No statistically significant difference between WBC depleted	**Definitions:** Infection: Determination of infection was made using physical clinical judgment. Overall Infection Rates: includes wound infections, urinary tract infection, respiratory tract infection, septicemia, and "other" infections Estimated blood Loss: Physician's estimates of EBL were recorded before the surgery. Baseline Hb level: Hb level collected during the assessment office visit when the surgery was planned - 21±7 days before surgery. **Perioperative care:** NR **Analytical methodology**: Logistic regression was used for modeling the probability of transfusion based on selected predictor variables. Otherwise, descriptive statistics or Parametric and nonparametric statistical tests after consideration of distributional characteristics and statistical test assumptions were

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting (N)	Intervention	Results	Comments
		complications; and predictors of allogeneic transfusion.	method groups: $\chi^2(3)=13.82$; P<0.001 Diabetes: 382 (10%) COPD: 317 (8%) Rheumatic: 149 (4%) Significant differences between transfusion method groups: $\chi^2(3)=13.29$; P<0.001 Hematologic: 106 (3%) **Procedures:** Elective total hip and total knee arthroplasties. Primary unilateral hip**:** 2027 (51%) Primary bilateral hip: 27 (1%) Primary unilateral knee: 1036 (26%) Primary bilateral knee: 13 (0%) Hip revision: 292 (7%) Knee revision: 69 (2%) **Indications:** Variable **Setting:** 225	tive **Device/agent:** Transfused blood **Monitoring intervention:** CRF=case report forms were utilized to report, scan then analyze the perioperative data including transfusion type and amount. **Control group:** n=1234 No transfusions **Standard preventive measures:** NR	and non WBC depleted allogeneic transfusions Knee Patients only ABD only: 0/148 Postop salvage only: 5/122 (4%) $X^2(1) = 5.97$; p<0.05 (Knee ABD vs. Postop Salvage) Hip Patients Only ABD only: 4/462 (1%) Postop salvage only: 3/69 (4%) $X^2(1) = 5.60$; p<0.05 (Hip ABD vs. Postop Salvage) <u>Overall Infection Rates:</u> Allogeneic-only: 110/999 (11%) Autologous-only: 93/1311 (7%) Allogeneic & Autologous: 30/329 (9%) No Transfusion: 94/1180 (8%) ABD transfusion only: 25/615 (4%) Allogeneic Transfusion WBC-Depleted: 82/637 (13%) Not WBC-Depleted: 42/464 (9%) Knee Patients only ABD only: 6/148(4%) Postop salvage only: 13/122 (11%) Hip Patients Only	utilized. **Other notes:** The tables and data were not uniformly presented. Numbers & % were frequently mislabeled leading to problems interpreting the data. Missing data from every table resulted in "apparent discrepancies" in the counts adding to the problem of interpretation. **Follow-up:** Until discharge from Surgery Department **Funding Source Conflicts:** Authors: NR Institution: NR Study: NR Supplies: NR

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting (N)	Intervention	Results	Comments
			Centers **Location:** Europe --France, Germany, Greece, Italy, the Netherlands, and Spain **Dates:** NR **Inclusion Criteria**: All patients undergoing total hip or total knee replacement. Enrollment of consecutive patients was requested with a limit of 20 patients per center. **Exclusion Criteria:** NR		ABD only: 19/462 (4%) Postop salvage only: 12/69 (17%) **Other infections:** SEE ABOVE **Topic-specific outcomes:** <u>Donated Blood: n=</u> Baseline Hb Level was linearly regressed with the probability of allogeneic transfusion: WOMEN: Base Hb level of 8.0 = 75% prob of transfusion Base Hb level of 16.0=12% prob of transfusion MEN: Base Hb level of 8.0 = 70% prob of transfusion Base Hb level of 16.0=8% prob of transfusion **Reoperations:** NR **Length of stay:** days Allogeneic: 13.0±8.1 Autologous: 12.3±10.5 Autologous-only collected via ABD method: 11.9±7.7 and No transfusion: 10.7±12.3 vs. Allogeneic (allogeneic only or allogeneic and	

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting (N)	Intervention	Results	Comments
					autologous): 13.5±10.2 P<0.001 **Mortality:** NR **Adverse events:** Fluid volume overload: Ranged from 3-4% across transfusion methods: NS Suspected Clinical DVT: Ranged from 2-3% across transfusion methods including no transfusion. NS Transfusion Reactions: Recorded not reported	
Borghi 2000 [153] (ES)	**Prospect-ive concur-ent control** 1, 2, 3, 4, 5, 8	To evaluate the incidence and risk factors for allogeneic blood transfusion (after autologous blood transfusion) in patients scheduled for primary hip, primary knee or revision hip arthroplasties and receiving an aggressive autotransfusion regimen	**Number of patients N=2884** **Patient Characteristics** **·Age: (mean±SD) years** THA: 61±12 TKA: 68±8 HR: 64±11 **·Gender m/f** THA: 726/1290 TKA: 125/355 HR: 124/264 **·Obesity** Weight (kg) THA: 68±11 TKA: 70±10 HR: 68±10 Height (cm) THA: 162±9 TKA: 160±8 HR: 161±8	**Intervention group: n= 278** Patients receiving allogeneic concentrated red blood cell (ARBC) transfusions after all autologous blood (both pre-donations and blood recovered intra and postoperatively. **Timing of intervention** **Duration of intervention** **Agent:** Autologous Blood Collected: According to the Maximum surgery blood order on Schedule, 2 units of pre-donated blood were collected for THA and TKA and 3 units for	**SSI (follow up: discharge from orthopedic ward)** **All infection data was presented in bar graph form. The below numbers are percentages inferred.** **Statistical Significance of difference between ARBC PLUS Autologous and No ARBC across each group is as follows** **GROUP THA: p=0.0005** **GROUP TKA: p=0.008** **GROUP HR: p=0.005** Infection: THA: ARBC plus autologous: 1%	**Definitions** **Perioperative care:** MSBOS: the actual number of blood units transfused in 90% of patients receiving one individual surgical procedure. Anesthesia: either balanced general, regional or integrated epidural/general anesthesia. The type was freely decided by the attending anesthesiologist with no randomization. **Analytical methodology:** Continuous variables: Analysis of variance Post hoc comparisons: Tukey's test and student's t-test with Bonferroni's correction. Categorical variables: χ^2-square or Fisher's exact test. Multivariate analysis of variance for repeated measures with Wilks' λ-test for

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting (N)	Intervention	Results	Comments
			·**Comorbidities:** NR Duration of Surgery (min) THA: 115±38 TKA: 117±44 HR: 183±64 *P* (THA vs. HR)=0.0005 *P* (TKA vs. HR)=0.0005 **Procedures:** Total hip arthroplasty: 2016/2884 (69.9%) Total knee arthroplasty: 480/2884 (16.6%) Hip revision of arthroplasty: 388/2884 (13.5%) **Indications:** variable **Setting:** 1 orthopedic institute **Location:** Italy **Dates:** NR (5 year period) **Inclusion Criteria:** Patients undergoing Total Hip Arthroplasty (THA) Total Knee Arthroplasty (TKA) or Hip Revision of Arthroplasty (HR)	Revision of Hip Arthroplasty. Autologous blood was separated into RBC and FFP. FFP re-infused at end of surgery or within 24h; pre-donated RBCs transfused during 3d postop. **Monitoring intervention:** NR **Control group: n=2606** Patients receiving autologous blood transfusion (pre-donation separated into RBC and FFP) plus intraoperative re-infused cell-salvage and postoperative closed system drain(see details below) **Standard preventive measures** Iron Supplement: during each pre-donation of autologous blood and the first 4 POD, all patients received intravenous iron (200mg/day) **Perioperative Blood Return:** **Intraoperativel**y, uncoagulated blood was collected from wound into a reservoir using an aspirator and collection bag connected to the	No ARBC: 0.5% TKA: ARBC plus autologous: 2% No ARBC: 0.5% HR: ARBC plus autologous: 1% No ARBC: 0.5% <u>Wound Hematoma</u> THA: ARBC plus autologous: 11% No ARBC: 2% TKA: ARBC plus autologous: 11% No ARBC: 5% HR: ARBC plus autologous: 8% No ARBC: 2% **Other infections:** NR **Topic-specific outcomes:** <u>Perioperative Blood Losses (ml)</u> THA: 1190±480 TKA: 1280±403 HR: 1720±460 *P* (THA vs. HR)=0.0005 *P* (TKA vs. HR)=0.0005 <u>Intraoperative Blood recovery (ml)</u> THA: 267±168 TKA: 162±92	changes over time After univariate analysis, partial risk factors associated with the response were further evaluated by multiple logistic regression analyses. **Other notes:** None **Follow-up:** Discharge from orthopedic ward **Funding Source Conflicts:** Authors: None Institution: None Study: None Supplies: None

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting (N)	Intervention	Results	Comments
			Exclusion Criteria: NR	inferior edge of the surgical wound in order to concentrate, wash and infuse red cells. These were immediately returned to the patient. **Postoperatively**, uncoagulated blood lost from the surgical wound was monitored and collected using a closed recovery system connected to the surgical drains. If blood losses exceeded 200ml during 1st 8h postop, the units of fresh frozen plasma were re-infused at the end or within the first 24h of surgery. **Autologous Transfusion Trigger:** if Hb <11g/dl **Allogeneic concentrated Red Blood cells Transfusion Trigger:** presence of asymptomatic anemia (vertigo, dizziness, postural hypotension, headache, insomnia, confusion, tachycardia, angina, dyspnea) or when Hb<6g/dl (10g/dl in patients with cerebrovascular or coronary artery disease)	HR: 524±387 *P* (THA vs. TKA)=0.0005 *P* (THA vs. HR)=0.0005 *P* (TKA vs. HR)=0.0005 <u>Postoperative Blood recovery (ml)</u> THA: 387±237 TKA: 541±294 HR: 465±287 *P* (THA vs. TKA)=0.0005 *P* (THA vs. HR)=0.0005 *P* (TKA vs. HR)=0.0005 <u>Patients receiving ABRC plus autologous Transfusion</u> THA: 159 (8%) TKA: 43 (9%) HR: 76 (20%) *P* (THA vs. HR)=0.0005 *P* (TKA vs. HR)=0.0005 <u>(number of patients receiving ABRC transfusions was not significantly different across anesthesia types for each surgery type)</u> <u>Hb concentration:</u> Baseline Hb concentration was significantly lower for HR than for THR and TKR at 1st and 3rd POD(p<0.0005 vs. THA & P<0.001 vs. TKA) <u>Main Risk factors</u>	

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting (N)	Intervention	Results	Comments
					<u>associated with An increased incidence of Perioperative transfusion of Allogeneic blood:</u> Preoperative Hb<10g/dl: OR: 8.8 (6.5-16.8); p=0.004 Hip Revision Arthroplasty OR: 5.8 (3.9-8.5); p=0.0001 No MSBOS pre-donation: OR: 3.4 (2.7-4.1); p-0.0001 **Reoperations:** NR **Length of stay:** <u>Patient Discharge (days after Surgery)</u> THA: 12±5 TKA: 16±6 HR: 15±7 *P* (THA vs. TKA)=0.0005 *P* (THA vs. THR)=0.0005 Patients not receiving ARBC's log-rank curve showed significantly shorter durations of stay than the log-rank curve for patients receiving ARBC plus autologous transfusion (p=0.0005) **Mortality:** NR **Adverse events:** No severe adverse	

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting (N)	Intervention	Results	Comments
					effects were reported during either preoperative collection of autologous blood or iv iron administration **Statistical Significance of difference between ARBC plus autologous blood and No ARBC across each group is as follows** **GROUP THA: p=0.0005** **GROUP TKA: p=0.008** **GROUP HR: p=0.005** <u>Dysrhythmia</u> THA: ARBC plus autologous: 3% No ARBC: 0.5% TKA: ARBC plus autologous:9% No ARBC: 1% HR: ARBC plus autologous: 7% No ARBC: 1.5% <u>Respiratory Failure</u> THA: ARBC plus autologous: 2% No ARBC: 0.5% TKA: ARBC plus autologous: 0 No ARBC: 1%	

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting (N)	Intervention	Results	Comments
					HR: ARBC plus autologous: 4% No ARBC: 1% <u>Myocardial Ischemia</u> THA: ARBC plus autologous: 6% No ARBC: 0.5% TKA: ARBC plus autologous: 0 No ARBC: 0.5% HR: ARBC plus autologous: 4% No ARBC: 0.5% <u>Pulmonary Embolism</u> THA: ARBC plus autologous: 1% No ARBC: 0.5% TKA: ARBC plus autologous: 2% No ARBC: 0 HR: ARBC plus autologous: 5% No ARBC: 0.5% <u>Deep Vein Thrombosis</u> THA: ARBC plus autologous: 0.4% No ARBC: 0.5% TKA:	

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting (N)	Intervention	Results	Comments
					ARBC: 2% No ARBC: 1.5% HR: ARBC plus autologous: 0% No ARBC: 0.5%	

Q11C. How does the volume of transfused blood product impact the risk of SSI? Our search did not identify data that evaluated differences in the volume of transfused blood product and their impact on the risk of SSI in prosthetic joint arthroplasty patients.

Q11D. How safe and effective is withholding blood transfusion to reduce the risk of SSI? Our search did not identify data that both evaluated the safety and effectiveness of withholding blood transfusions and its impact on the risk of SSI in prosthetic joint arthroplasty patients.

2.2A3. RISK OF BIAS ASSESSMENTS OF STUDIES: Q 11 BLOOD TRANSFUSION

eTABLE 56. Risk of Bias Assessments of Randomized Controlled Trials for Q11 Blood Transfusion

Author Year	Q	Described as randomized	Randomization appropriately performed	Described as double-blind	Outcome assessor blinded	Study participant blinded	Investigator blinded	Attrition described	Attrition smaller than 10-15% of assigned patients	Attrition appropriately analyzed	Funding source(s) disclosed and no obvious conflict of interest	Overall Risk of Bias
Question 11: Blood Transfusion												
Frietsch 2008 [145]	11	✓	✓	✓	✓	✓		✓	✓	✓	✓	Low
Frietsch 2001 [146]	11	✓	✓			✓		✓	✓	✓	✓	Low

eTABLE 57. Risk of Bias Assessments of Other Controlled Studies for Q11 Blood Transfusion

Author Year	Q	All study groups derived from similar source/reference populations	Attrition not significantly different across study groups	Measure of exposure is valid	Measure of outcome is valid	Investigator blinded to endpoint assessment	Potential confounders identified	Statistical adjustment for potential confounders done	Funding source(s) disclosed and no obvious conflict of interest	Overall Risk of Bias
Question 11: Blood Transfusion										
Borghi 2000 [153]	11	✓	✓	✓	✓	✓			✓	Low
Del Trujillo 2008 [152]	11	✓		✓	✓	✓	✓	✓	✓	Low
Innerhofer 2005 [147]	11	✓	✓	✓	✓	✓	✓			Low
Llewelyn 2004 [150]	11	✓	✓	✓	✓				✓	Low
Pedersen 2009 [151]	11	✓	✓	✓	✓	✓	✓	✓	✓	Low
Rosencher 2003 [148]	11	✓		✓	✓	✓				Moderate
Weber 2005 [149]	11	✓	✓	✓	✓					Moderate

2.2B. Q12-16 SYSTEMIC IMMUNOSUPPRESSIVE THERAPY

2.2B.1 GRADE TABLE: Q12-16 SYSTEMIC IMMUNOSUPPRESSIVE THERAPY

eTABLE 58. GRADE Table for Q12-16 Systemic Immunosuppressive Therapy

Comparison	Outcome	Quantity and Type of Evidence	Findings	Starting GRADE	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Confounders		
Systemic Immunosuppressive Therapy: Biologic Agents (Non-Tumor Necrosis Factors [TNF] and Anti-TNFs) and Disease Modifying Antirheumatic Drugs-(DMARD)														
Q12. How does systemic corticosteroid or other immunosuppressive therapy impact the risk of SSI in prosthetic joint arthroplasty patients? Q12A. Does the type of agent impact the risk of SSI?														
Biologic-agents (non-TNF and anti-TNF) vs. DMARDs	SSI*	2 OBS [154,155]	• In meta-analysis of 2 OBS studies (N=528) , biologic agents were associated with a higher risk for SSI: OR: 5.90 (2.68 – 12.99); p<0.01; I^2=0 • In each of these studies[154,155] multivariate logistic regression analysis identified biologic agents as a significant risk factor SSI.	Low	0	0	0	0	0	0	+1	0	Moderate	Very Low
	PJI*	2 OBS [154,155]	• In a meta-analysis of 2 OBS (N=528), biologic agents were not associated with a higher risk for PJI: OR: 3.59 (0.52 – 24.88); p=0.20; I^2=0 • In one study[154], 3 (0.7%) total organ/space SSIs among 420 RA patients undergoing THA or TKA: 1/48 (2.08%) vs. 2/372 (0.54%); p=0.27 • In the other study[155], 1/54 (1.85%) vs. 0/54 (0%); p=0.50	Low	0	0	0	-1	0	0	0	0	Very Low	
	Superfic-ial SSI*	2 OBS [154,155]	• In a meta-analysis of 2OBS (N=528), biologic agents associated with increased risk for superficial SSI OR: 5.80 (2.55 – 13.18); p<0.01; I^2=0 • 1 OBS study[154]= 24 (5.7%) total superficial SSIs among 420 RA patients undergoing THA or TKA: 9/48 (18.75%) vs. 15/372 (4.03%); p<0.01 • 1 OBS Study[155]= 7/54 (12.96%) vs. 1/54	Low	0	0	0	0	0	+1	0	0	Moderate	

Comparison	Outcome	Quantity and Type of Evidence	Findings	Starting GRADE	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Confounders		
			(1.85%); p=0.06											
	Adverse events of surgical wounds	1 OBS [156]	• 1 small study (N= 113): 2/39 (5.1%) vs. 5/74 (6.8%); OR 0.7459 (0.14-4.03); p=1.00 (results include 4 ankle fusions) • No difference on subanalysis (30 THAs and 65 TKAs- THA: none in either group; TKA: 4/51 (7.8%) vs. 1/14 (7.1%); OR 0.90 (0.09-8.80). 92.3% of all patients on biologic agents (infliximab and etanercept) were also on methotrexate (DMARD).	Low	0	0	0	-1	0	0	0	0	Very Low	
	Adverse events-drug related	1 OBS [155]	• 1 small (N=90) retrospective 1:1 pair-matched case-control study of deep venous thrombosis (DVT) in joint arthroplasty (96%) and other joint procedures (4%): increased incidence of DVT with biologic agents 23/45 (51%) vs. 12/45 (26%); p=0.02. • On multivariate logistic regression analysis biologic agents (anti-TNF) were the only risk factor for DVT: OR 2.83 (1.10-7.25); p=0.03	Low	0	0	0	-1	0	0	0	0	Very Low	
DMARD: methotrex-ate vs. No DMARD therapy	PJI*	1 OBS [157]	• No difference in 1 study (N=202) total joint replacements in RA patients: 3/92 (3.26%) vs. 2/110 (1.81%); p=0.66 at 6m follow-up • Revision total joint replacements: 1/9 (11.1%) vs. 0/16; p=0.26 • Bilateral TKA: 0/3 vs. 1/11 (9.09%); p=1.00	Low	0	0	0	-1	0	0	0	0	Very Low	Very Low
	Deep wound abscess*	1 OBS [157]	• No difference: 0/92 vs. 1/110 (0.91%); p=0.57	Low	0	0	0	-1	0	0	0	0	Very Low	
	Infected Hemat-oma*	1 OBS [157]	• No difference: 2/92 (2.2%) vs. 1/110 (0.9%); p=0.47 • Bilateral TKA 1/3 (33%) vs. 0/11; p=0.14	Low	0	0	0	-1	0	0	0	0	Very Low	

Comparison	Outcome	Quantity and Type of Evidence	Findings	Starting GRADE	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Confounders		
	Necrotic eschar	1 OBS [157]	• No difference: 2/92 (2.17%) vs. 0/110; p=0.24	Low	0	0	0	-1	0	0	0	0	Very Low	
	Serous drainage	1 OBS [157]	• No difference: 1/92 (1.09%) vs. 1/110 (0.91%)	Low	0	0	0	-1	0	0	0	0	Very Low	
Q12B. Does the preoperative duration of the therapy impact the risk of SSI?														
Disease duration	SSI*	2 OBS [154,155]	• In a study[154] comparing RA patients on biologics (anti-TNF) and DMARDs undergoing arthroplasty surgery, multivariate logistic regression analysis comparing infected to non-infected patients showed years of disease duration was a risk factors for SSI: OR 1.09 (1.04-1.14); p<0.01. • Disease duration for the cohort[154] was a median of 14.5 years (interquartile range 8.9-21) but these results were not stratified by biologic agents vs. DMARDs. • In a study[155] comparing RA patients on biologic (anti-TNF) and DMARDs undergoing arthroplasty surgery multivariate logistic regression analysis also suggested disease duration as a risk factor for SSI: OR 1.17 (1.03-1.33); p=0.02.	Low	0	0	0	0	0	0	0	0	Low	Low
Q12C. Does the agent dose impact the risk of SSI?														
Biologic-agents (anti-Tumor necrosis factors) vs. DMARDs	SSI*	2 OBS [155,154]	• In a retrospective 1:1 matched pair case control study[155] 64 rheumatoid arthritis patients on biologic agents (anti-TNF) were matched to 64 patients on DMARDs. Patients in the biologic agent (anti-TNF) group were on significantly higher daily doses of prednisone (5mg/day; range 2-7)	Low	0	-1	0	0	0	0	0	0	Very Low	Very Low

Comparison	Outcome	Quantity and Type of Evidence	Findings	Starting GRADE	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Confounders		
			than the DMARD patients (3mg/day, range 0-5); p<0.01. Multivariate logistic regression analysis showed that prednisone dose OR 1.43 (1.01-2.04); p=0.05 was a risk factor for SSI. • In a retrospective study[154] of 420 THAs and TKAs in RA patients, multivariate logistic regression analysis comparing infected to non-infected patients did not show prednisone dose to be a risk factor for SSI. Both patients with SSI (n=27) and those without SSI (n=393) were on prednisone doses of 3mg/day, (range 0-5); p=0.27. Results were not stratified by biologic agents vs. DMARDs.											
Q13. What are the most effective strategies in managing systemic corticosteroids or other immunosuppressive therapy perioperatively to reduce the risk of SSI in prosthetic joint arthroplasty patients? Q13A. How safe and effective is the discontinuation of these agents preoperatively and when should they be resumed?														
DMARD: Methotrex-ate stopped vs. continued perioperat-ively	PJI*	4 OBS [157-160]	• In a meta-analysis (N=180) of 3 small observational studies, the data suggests that stopping methotrexate is associated with lower risk for PJI, but the result is not significant (OR: 0.20 (0.04 – 1.03); p=0.05; I^2=0 • 1 small OBS study[159], overall SSI: 3/41 (7.3%) • 1 OBS study[159], no difference: 0/26 y vs.3/15; p=0.08. 1y follow up. Methotrexate 2 weeks perioperatively • In each of these studies[157] - No difference: 1/47 (2.1%) vs. 2/45 (4.44%); p=0.54; 6m follow up. Methotrexate stopped indefinitely • No difference in one small (N=47) study[158]: 0/32 vs.1 /15 (6.67%); p=0.25. No PJIs	Low	0	0	0	0	0	0	0	0	Low	Low

Comparison	Outcome	Quantity and Type of Evidence	Findings	Starting GRADE	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Confounders		
			reported among 32 patients who stopped methotrexate therapy 4 or more weeks preoperatively as compared to 1 among the 15 patients who were one methotrexate within 4 weeks of surgery: • In 1 OBS study[160] (N=462) in RA patients undergoing 657 THAs and TKAs, patients were receiving at least 1 DMARD within 3 months of surgery in 336 of those 657 procedures. DMARD therapy was withheld in 192/336 (57%) of these procedures. Stopping DMARD therapy at the time of surgery lowered the risk of subsequent PJI: OR 0.65 (0.09-4.95) but this was not statistically significant.											
	RA Flare	1 OBS [159]	• "No patient in either group experienced a postoperative flare of their rheumatoid arthritis"	Low	0	0	0	-1	0	0	0	0	Very Low	
	Infected Hemato-ma	1 OBS [157]	• No difference: 2/47 (4.25%) vs. 0/45; p=0.30	Low	0	0	0	-1	0	0	0	0	Very Low	
	Necrotic eschar	1 OBS [157]	• No difference: 2/47 (4.25%) vs. 0/45; p=0.30	Low	0	0	0	-1	0	0	0	0	Very Low	
	Non-commun-icating serous drainage	1 OBS [157]	• No difference: 0/47 vs. 1/45 (2.22%);p=0.48	Low	0	0	0	-1	0	0	0	0	Very Low	
Biologic agent: Anti-tumor	PJI*	1 OBS [160]	• Subanalysis of 50/462 RA patients on biologic agent (anti-TNF) therapy (etanercept, adalimumab, infliximab, or	Low	0	0	0	-1	0	0	0	0	Very Low	Very Low

Comparison	Outcome	Quantity and Type of Evidence	Findings	Starting GRADE	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Confounders		
necrosis factor (anti-TNF): Stopped vs. continued perioperat-ively			anakinra) who underwent hip or knee arthroplasties, suggested an increase in incidence of PJIs among those in whom anti-TNF therapy was continued perioperatively, but the findings were not statistically significant: 0/12 (0%) vs. 3/38 (7.9%).											
Q13B. Should the agent dose be adjusted, and if so, for how long? Our search did not identify data that evaluated perioperative immunosuppressive therapy dose adjustment and its impact on the risk of SSI in prosthetic joint arthroplasty patients.														
Q14. What is the optimal duration of postoperative AMP to reduce the risk of SSI in prosthetic joint arthroplasty patients who are on systemic corticosteroid or other immunosuppressive therapy? Our search did not identify data that specifically evaluated differences in duration of postoperative AMP in prosthetic joint arthroplasty patients who were on systemic corticosteroids or other immunosuppressive agents and its impact on the risk of SSI. However, multiple procedures examined in the Core section, Q1.E: Postoperative AMP duration that included patients on immunosuppressive therapy showed no benefit of continuing AMP after closing the surgical incision in the operating room. Therefore, the broader recommendation for duration of postoperative AMP should be applied to prosthetic joint arthroplasty procedures irrespective of use if systemic corticosteroid or other immunosuppressive therapy.													
Intra-articular Corticosteroid Injections														
Q15. How do preoperative intra-articular corticosteroid injections impact the risk of SSI in prosthetic joint arthroplasty patients?														
History of corticoster-oid Injection vs. no injection	SSI*	5 OBS [161-165]	• Meta-analysis (N=1146) 5 OBS studies; OR: 1.91 (1.01 – 3.61); p=0.05; I^2=13% • 35/476 (7.4%) vs. 26/670 (3.9%)	Low	0	0	0	0	0	0	0	0	Low	Low
TKA: Injection vs. No Injection	SSI*	2 OBS [161,162]	• In a meta-analysis of 2 studies (N=414), no difference between groups OR: 1.89 (0.53 – 6.76); p=0.33; I^2=50%	Low	0	0	0	-1	0	0	0	0	Very Low	Very Low
	PJI*	2 OBS [161,162]	• In a meta-analysis of 2 studies (N=414), no difference between groups OR: 12.30 (0.62 – 242.88); p=0.10 • 1 study[161] (N=144) reported significant risk of PJI for TKA patients injected prior to surgery: 3/54 (5.6%) vs. 0/90 (0%); p<0.03 at 1yr	Low	0	-1	0	-1	0	0	0	0	Very Low	

Comparison	Outcome	Quantity and Type of Evidence	Findings	Starting GRADE	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Confounders		
			follow up. All 3 had received a steroid injection within 11mo of surgery; mean (range): 9.6mo (8-11) • One study[162] (N=270) matched 90 injected patients to 180 patients not injected prior to TKA and reported no infections in either group at 1 year follow up: 0/90 vs. 0/180. Half were injected within 1yr prior to surgery.											
	Superficial SSI*	2 OBS [161,162]	• In a meta-analysis of 2 studies (N=414): no difference between groups OR: 1.71 (0.68 – 4.31); p=0.26; I^2=16% • One study[161] (N=144) reported 22 (15.3%) total superficial SSIs and no difference at 30 day follow up: 12/54 (22.2%) vs. 10/90 (11.1%); p=0.1 • One study[162] (N=270) reported 7(2.6%) total superficial SSIs and no difference at 30 day follow up: 2/90(2.2%) vs. 5/180 (2.7%); RR 0.80 (0.16-4.03); p=1.0	Low	0	0	0	0	0	0	0	0	Low	
THA: Injection vs. No Injection	SSI*	3 OBS [163-165]	• In a meta-analysis of 3 studies (N=732), no difference between groups: 18/332 vs. 11/400; p=0.07; OR: 1.70 (0.58 – 4.96); p=0.34; I^2=13% • 1 OBS Study[163], SSI= 0/68 vs. 2/136 • 1 OBS Study[164], SSI= 14/224 vs. 9/224 • 1 OBS Study[165], SSI= 4/40 vs. 0/40	Low	0	0	0	-1	0	0	0	0	Very Low	Very Low
	PJI*	3 OBS [163-165]	• In a meta-analysis of 3 studies (N=732), no difference between groups7/332 (2.1%) vs. 2/400 (0.5%); OR: 2.95 (0.61 – 14.18); p=0.18; I^2=0% • One study[163] (n=202) found 66 injected patients (68 THAs) to 136 not-injected patients (136 THAs): no difference: 0/68 (0%) vs. 1/136 (0.73%); p=0.80.	Low	0	0	0	-1	0	0	0	0	Very Low	

Comparison	Outcome	Quantity and Type of Evidence	Findings	Starting GRADE	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Confounders		
			Methylprednisolone 40mg/dL injections were administered an average of 14 months before surgery (median, 11months) • One retrospective matched cohort study[164] (N=4448) in THA reported no difference: 3/224 (1.33%) vs. 1/224 (0.44%) at 2y follow up. Hazard ratio: 3 (0.3-29.8). Cumulative risk of deep infection at 5yr was 3% (95% CI, 0-7%) for the injection group and 0.6% (95%CI, 0-1.7%) for the no-injection group. Steroid dose average 20.47mg (range, 6-40) • 1 small (N=80) study[165] in joint infections requiring revision THA reported no difference: 4/80 (5%); 4/40 (10%) vs. 0/40 (0%); p=0.13 at 1y follow up (used methylprednisolone 80mg/dL)											
	Superficial SSI*	3 OBS [163-165]	• In a meta-analysis of 3 studies (N=732), no difference between groups OR: 1.32 (0.54 – 3.22); p=0.55; I^2=0 • One study[163] found no difference: 0/68 (0%) vs. 1/136 (0.73%); p=0.80. (30 day follow up) • One study[164] found no difference: 11/224 (4.9%) vs. 8/224 (3.6%) 2 year follow up; Hazard ratio 1.5 (95% CI, 0.6-3.6); Cumulative risk of superficial SSI at 5 years: 4.5% (95% CI, 2.4-8.4) vs. 3.7% (95% CI, 1.1-6.1) • One study[165] found no infections: 0/40 vs. 0/40 (1 year follow up).	Low	0	0	0	0	0	0	0	0	Low	

Q16 What are the most effective strategies for managing the preoperative use of intra-articular corticosteroid injections to reduce the risk of SSI in prosthetic joint arthroplasty patients?
Q16A. Does the length of time between intra-articular corticosteroid injection and prosthetic joint arthroplasty impact the risk of SSI?

Comparison	Outcome	Quantity and Type of Evidence	Findings	Starting GRADE	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Confounders		
THA:														
Length of time between most recent injection and surgery	SSI*	2 OBS [164,165]	• In a small (N=80) matched, cohort (injected: not injected) study: neither the total number of injections (p=0.89) before THA nor the time interval between the injection and the operation (p=0.88) differed. For this particular measure, the study was underpowered (0.052 and 0.053, respectively) • No association between the average time from intra-articular corticosteroid injection to primary THA and the development of superficial SSI or PJI • Mean time between injection and THA: 112 days (SD=81days). • Mean time between injection and THA for 3 patients who developed PJI was less than half the length of time for those who developed superficial SSI (n=11): 44 days (SD=23) vs. 112days (SD=94d).	Low	0	0	0	0	0	0	0	0	Low	Low
Q16. What are the most effective strategies for managing the preoperative use of intra-articular corticosteroid injections to reduce the risk of SSI in prosthetic joint arthroplasty patients? Our search did not identify data that evaluated preoperative strategies for managing the use of intra-articular corticosteroid injections in prosthetic joint arthroplasty patients and their impact on risk of SSI.														
Q16A. Does the length of time between intra-articular corticosteroid injection and prosthetic joint arthroplasty impact the risk of SSI? Our search did not identify data that evaluated different lengths of time between preoperative intra-articular corticosteroid injection administration and its impact on the risk of TKA.														
Q16B. Does the corticosteroid injection dose impact the risk of SSI? Our search did not identify data that evaluated different doses of preoperative intra-articular corticosteroid injections and their impact on the risk of SSI.														

*Critical outcome; OR: Odds Ratio; RR: Risk Ratio; CI: Confidence Interval

2.2B.2: EVIDENCE TABLES: Q12-16 SYSTEMIC IMMUNOSUPPRESSIVE THERAPY

Q12. How does systemic corticosteroid or other immunosuppressive therapy impact the risk of SSI in prosthetic joint arthroplasty patients?

Q12A. Does the type of agent impact the risk of SSI?

Q12B. Does the preoperative duration of the therapy impact the risk of SSI?

Q12C. Does the agent dose impact the risk of SSI?

Q13. What are the most effective strategies in managing systemic corticosteroids or other immunosuppressive therapy perioperatively to reduce the risk of SSI in prosthetic joint arthroplasty patients?

Q13A. How safe and effective is the discontinuation of these agents preoperatively and when should they be resumed?

eTABLE 59. Evidence Table for Q12-13 Systemic Immunosuppressive Therapy

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
Bridges 1991 [158] (ES)	**Retrospe-ctive concurre-nt control** 1, 2, 3, 4, 6, 7, 8	To compare the surgical outcomes of patients with Rheumatoid Arthritis (RA) in whom methotrexate (MTX) was stopped more than 4 weeks preoperatively with those in whom MTX was stopped less than 4 weeks preoperatively. All orthopedic surgeries were included.	**Number of patients: N=38 patients (6 patients in both groups) and 47 procedures** **Patient Characteristics:** no statistically significant differences between the patients in control and intervention groups with regard to any of the characteristics examined. ·Age: ·Gender: ·Obesity: ·Comorbidities: **Procedures: n/N procedures** TJA of hip or knee (n) MTX-on: 12/19 (63.2%) MTX-off: 32/34 (94.1%) MCP arthroplasty MTX-on: 2/19 (10.5%) MTX-off: 0/34 Metatarsal head resection MTX-on: 1/19 (5.3%) MTX-off: 1/34 (2.9%) Shoulder arthroplasty MTX-on: 1/19 (5.3%) MTX-off: 0/34	**Intervention group: n=19 (6 patients in both groups)** [19 procedures] MTX-On - Patients who received MTX within 4 weeks of surgery **Timing of intervention:** NA **Duration of intervention:** NA **Device/agent:** NA **Monitoring intervention:** NA **Control group: n=25 (6 patients in both groups)** [34 procedures] MTX-Off – patients in whom MTX was discontinued 4 or more weeks before the surgery, and those in whom surgery was performed before or after the MTX treatment period and who were taking no disease modifying anti rheumatic drugs (DMARDs) for at least 3 months prior to surgery. **Standard preventive measures:** NR	**SSI (6 weeks)** **PJI** MTX-on: 1/15 procedures (6.7%) MTX-off: 0/32 P=0.25 **Other infections:** NR **Topic-specific outcomes:** Flares NR **Reoperations:** NR **Length of stay:** NR **Mortality:** MTX-on: 6/19 (31.6%) MTX-off: 4/25 (16.7%) One (1) patient death overlapped both groups. **Adverse events:** NR	**Definitions:** **Complications**: prosthetic joint infection or would dehiscence or infection documented in the medical record within 6 weeks after surgery **Perioperative care:** NR **Analytical methodology:** student's t test, chi-square test, or Fisher's exact, 2-tailed as appropriate. **Other notes:** none **Follow-up:** 6 weeks postop **Funding Source Conflicts:** Authors: NR Institution: NR Study: NR Supplies: NR

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			Other MTX-on: 3/19 (15.8%) MTX-off: 1/34 (2.9%) **Indications:** Rheumatoid Arthritis (RA) **Setting:** 1 University hospital **Location:** USA **Dates:** 1981-1989 **Inclusion Criteria:** Patients with RA who began MTX therapy and who underwent elective primary orthopedic surgery before January 1990. **Exclusion Criteria**: Patients undergoing revision Total Joint Arthroplasty.			
Carpen-ter 1996 [159] (ES)	**Prospecti-ve Concurre-nt control** 1, 2, 3, 4, 6, 7	To prospectively follow all rheumatoid arthritis (RA) patients receiving Methotrexate (MTX) who underwent total joint arthroplasty to determine if continuing or stopping MTX during the perioperative period influenced the rate of postoperative	**Number of patients: N=32 patients (41 procedures)** **Patient Characteristics:** no significant differences in patient characteristics between groups **Procedures:** THA: MTXon – 8/26 (30.8%) MTXoff – 4/16 (25%) TKA: MTXon – 7/26 (26.9%) MTXoff – 3/16 (18.8%) TWA: MTXon – 3/26 (11.5%) MTXoff – 3/16 (18.8%) TMCPA: MTXon – 7/26 (26.9%) MTXoff – 4/16 (25%) TEA MTXon – 0/26	**Intervention group: n=19 (**26 procedures) Patients assigned to discontinue MTX the week prior and during the week of surgery (total of 2 weeks) **Timing of intervention:** NA **Duration of intervention:** NA **Device/agent:** Methotrexate **Monitoring intervention:** NA **Control group: n=13 (**15 procedures) Patients assigned to continue MTX through the perioperative period. **Standard preventive measures:** NR	**SSI (**1 year**)** PJI MTX-on: .3/15 procedures (20%) MTX-off: 0/26 procedures p=0.08 **Other infections:** NR **Topic-specific outcomes:** Flares: no flares reported in either group **Reoperations:** NR **Length of stay:** NR **Mortality:** NR **Adverse events:** NR	**Definitions:** none **Perioperative care:** NR **Analytical methodology:** two-sample t test. Bonferroni correction was used for multiple comparisons. Fisher's exact test. **Other notes:** none **Follow-up:** at least 1 year postop **Funding Source Conflicts:** Authors: NR Institution: NR Study: NR Supplies: NR

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
		infections.	MTXoff – 1/16 (6.25%) **Indications:** Rheumatoid Arthritis **Setting:** 1 army medical center **Location:** USA **Dates:** January 1982 – December 1991 **Inclusion Criteria:** All RA patients receiving MTX at the time they were to undergo total joint arthroplasty or joint fusion during study dates. **Exclusion Criteria:** patients on azathioprine concurrently			
Perhala 1991 [157] (ES)	**Retrospe-ctitve concurre-nt control** 1, 2, 3, 4, 6, 7	To assess whether the risk of local infectious complications or poor wound healing is increased during the postoperative course in Rheumatoid arthritis (RA) patients treated with Methotrexate (MTX)	**Number of patients: N=121 patients (202 procedures)** **Patient Characteristics:** unless listed below, no statistically significant differences in characteristics existed between groups. ·Age: mean (Y) MTX: 54.6 NoMTX: 59.0 P=0.03 ·Gender: ·Obesity: ·Comorbidities: Daily prednisone dose: mean(mg) MTX: 4.87 NoMTX: 3.69 P=0.08 **Procedures:** THA And TKA **Indications:** Rheumatoid	**Intervention Group: n=60 patients (92 procedures)** Patients who had taken MTX: **Intervention group1:** MTXoff: Patients who had taken MTX but stopped more than 4 weeks prior to the surgery **Intervention group2:** MTXon: patients who had taken MTX but who took MTX within 4 weeks of surgery **Timing of intervention:** NA **Duration of intervention:** NA **Device/agent:** Methotrexate **Monitoring intervention:** NA **Control group: n=61** Patients who had never taken MTX	**SSI (6 months)** <u>PJI</u> <u>MTX vs. NO MTX</u> All Total Joint Replacements MTX: 3/92 (3.26%) NoMTX: 2/110 (1.81%) p=0.66 Revision total joint replacements: MTX: 1/9 (11.1%) NoMTX 0/16 p=0.26 Bilateral TKA MTXon 0/3 NoMTX: 1/11 (9.09%) p=1.00 <u>Continuous MTX vs. Pausing MTX</u> <u>PJI</u> MTXon: 2/45 (4.44%) MTXoff: 1/47 (2.12%) p=0.54	**Definitions:** NR **Perioperative care:** NR **Analytical methodology:** Student's *t* test, Chi square analysis. **Other notes:** None **Follow-up:** 6 months **Funding Source** **Conflicts:** Authors: None Institution: None Study: None Supplies: None

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			Arthritis **Setting:** 1 hospital **Location:** USA **Dates:** January 1, 1978 – December 31, 1987 **Inclusion Criteria:** Patients who underwent Total hip or total knee replacement at the center during the study dates. And who were classified by the American Rheumatism Association criteria as having classic or definite RA (30). **Exclusion Criteria:** Patients who had undergone apheresis or total lymphoid irradiation or had been treated with azathioprine, cyclophosphamide, or chlorambucil concurrently	**Standard preventive measures:** All patients received antimicrobial s perioperatively (Cefazolin or vancomycin)	**Other infections:** **MTX vs. No MTX** Deep Wound Abscess MTX: 0/92 NoMTX: 1/110 (0.91%) p=0.57 Infected Hematoma MTX: 2/92 (2.17%) NoMTX: 1/110 (0.91%) p=0.47 Bilateral TKA MTX: 1/3 (33%) NoMTX 0/11 p=0.14 Necrotic eschar MTX: 2/92 (2.17%) noMTX: 0/110 p=0.24 Serous Drainage MTX: 1/92 (1.09%) NoMTX: 1/110 (0.91%) Continuous MTX vs. Paused MTX Infected Hematoma MTXoff: 2/47 (4.25%) MTXon: 0/45; p=0.30 Necrotic eschar MTXoff: 2/47 (4.25%) MTXon: 0/45 p=0.30 Serous Drainage MTXoff: 0/47 MTXon: 1/45 (2.22%) p=0.48 **Topic-specific outcomes:** NR **Reoperations:** NR **Length of stay:** NR	

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
					Mortality: NR **Adverse events:** NR	
Momoh-ara 2011 [154] (ES)	**Retrospe-ctive concurre-nt control** 1, 2, 3, 4, 5, 6, 7,	To analyze the risk ratios of SSI after total hip arthroplasty (THA) or total knee arthroplasty (TKA) in Rheumatoid Arthritis (RA) patients treated with biologic DMARDs (mainly TNF blockers) compared with RA patients treated with non-biologic DMARDs. Also to determine whether perioperative interruption of TNF blockers decreases SSI. FROM DISCUSSION	**Number of patients: N=420** **THA = 81 (19.3%)** **TKA = 339 (80.7%)** **Patient Characteristics:** given for total population given as n (%) or median (IQR) ·Age: 61 (54.8-68) y ·Gender % female: 382 (91.0%) ·Obesity: 21.4 (19.4-23.8) BMI ·Comorbidities: Diabetes: 34 (8.1%) Smoking (ever): 67 (16.0%) Surgical history: 193 (46.0%) Disease Duration: 14.5 (8.9-21.0)y Preop CRP: 0.98 (0.25-2.19) Preop Hb: 10.9 (10.2-11.8) Preop WBC: 7.25 (6.1-9.0) Revision: 16 (3.8%) **Procedures:** Total Hip Arthroplasty (THA) or Total Knee Arthroplasty (TKA) **Indications:** Rheumatoid	**Intervention group:** n= 48 Biologic DMARDS THA = 11 TKA= 37 IFX: 19 (4.5%) ETN: 23 (5.5%) ADA: 2 (0.5%) TCZ: 4 (1.0%) **Timing of intervention:** For TNF-blockers was performed in accordance with British Society for Rheumatology and Japan College of Rheumatology Guidelines.: That TNF-blocker treatment should be withheld 2-4 weeks prior to major surgical procedures: specifically ETN & ADA: 2-4 weeks IFX & TCZ: 4 weeks (TCZ was restarted 4 weeks after surgery) **Duration of intervention:** variable **Agent:** biologic Disease Modifying Antirheumatic Drugs (bDMARDS) **Monitoring intervention:**	**SSI (Follow Up NR)** TOTAL INFECTIONS 27 total Postop Complications (6.4%) Superficial incisional SSI: 24 (5.7%) **–** [treated with antimicrobials] Organ/Space SSI: 3 (0.7%) – [required surgical treatment to remove the artificial joint prosthesis] Non-biologic DMARDs: 2/3 (66.7%) IFX: 1/3 (33.3%) Statistically significant risk factors Disease Duration (years) SSI: 23.3 (17.6-26.4) No-SSI: 14.1 (8.1-19.6) OR: 1.09 (1.04-1.14); p=0.003 Biologic DMARDs SSI: 10/27 (37.0%) No-SSI: 38/393 (9.7%) OR: 5.69 (2.07-15.61); p=0.0007 Prednisone dose not a statistically significant risk factor	**Definitions:** SSI: diagnosed by surgeon according to CDC SSI Guideline 1999. **Perioperative care:** General, lumbar and/or epidural anesthesia were all utilized **Analytical methodology**: Multivariate logistic regression to test the association of SSI with putative risk factors and with the use of non-biologic DMARDs and biologic DMARDs. **Other notes:** NR **Follow-up:** NR **Funding Source Conflicts:** Authors: Industry Institution: NR Study: NR Supplies: NR

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
		The aims of this study were to assess the influence of non-biologic DMARDs and biologic DMARDs, as well as the withholding of TNF-blocker therapy on the incidence of SSI.	Arthritis (RA) **Setting**: 1 Medical University Institute of Rheumatology **Location:** Japan **Dates:** January 2005 and December 2009 **Inclusion Criteria:** Patients who full the 1987 revised American College of Rheumatology (ACR) criteria for RA who underwent THA or TKA between January 2005 and December 2009 and were treated with biologic or non-biologic DMARDs **Exclusion Criteria:** NR	NR **Control group:** n=372 THA=70 TKA=302 Non-biologic DMARDs. As a rule were continued perioperatively but were administered cautiously in individual patients if there were comorbidities or were elderly. Patients in this group received one or more immunosuppressive and/or immunomodulatory Non-biologic medication IMMUNOSUPPRESIVE AGENTS MTX: 279 (66.4%) Leflunomide: 4 (1%) Tacrolimus: 31 (7.4%) Mizoribine: 15 (3.6%) Cyclophosphamide: 3 (0.7%) IMMUNOMODULATORY AGENTS Salazosulfapyridine: 93 (22.1%) Bucillamine: 52 (12.4%) Minocycline: 7 (1.7%) Actarit: 9 (2.1%) Auranofin: 4 (1.0%) Gold Sodium Thiomalate: 1 (0.2%) D-penicillamine: 16 (3.8%) Glucocorticoids: 296 (70.4%) at average dose of 3.0mg/day **Standard preventive**	SSI: 3 (0-5 No-SSI: 3 (0-5 OR: 1.09 (0.93-1.28); p=0.27 <u>Statistically significant Medications as SSI risk factors (where n>10 administered patients)</u> IFX SSI: 4/27 (14.8%) No-SSI: 15/393 (3.8%) OR: 9.8 (2.41-39.82); p=0.001 ETN SSI: 6/27 (22.2%) No-SSI: 17/393 (4.3%) OR: 9.16 (2.77-30.25); p=0.0003 **Other infections:** NR **Topic-specific outcomes:** NR **Reoperations:** 3 Organ/Space SSI (0.7%) required removal of artificial joint prosthesis **Length of stay:** NR **Mortality:** NR **Adverse events:** No cases of sever delayed wound healing requiring additional sutures were observed.	

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
				measures: All surgeries were performed with protective clothing against infection, in a bioclean room. AMP: cefazolin or ampicillin/cloxacillin were given intravenously twice before surgery and 2h after the start of surgery. AMP was not administered regularly after the day of surgery.		
Hirano 2010 [156] (ES)	**Retrospe-ctive Concurre-nt Cohort** 2, 3, 4, 5, 8	To investigate the influences of anti-Tumor Necrosis Factor (TNF) agents on the postoperative recovery in patients with Rheumatoid Arthritis (RA) and the effects of biologics on wound healing.	**Number of patients: N=113** **Patient Characteristics:** mean ± SD (Range) or n (%) ·Age: year (range) TNF: 58.9±9.0 (31-73) Non-TNF: 62.6±9.1 (30-77) P=0.0308 ·Gender: Female (%) TNF: 32 (82.1%) Non-TNF: 65 (87.8%) ·Obesity: NR ·Comorbidities: RA Duration: years (Range): TNF: 13.5±7.8 (4-32) Non-TNF: 16.5±11.7 (1-51) Steinbrocker Stage III vs. IV TNF: 18.8% vs. 81.2% Non-TNF: 52.7% vs. 47.3% P=0.0249 %MTX use	**Intervention group:** n=39 INF: 24/39 (61.5%) ETA: 15/39 (38.5%) Tumor Necrosis Factor (TNF) group: patients treated with anti-TNF agents from both centers Administration of agents were stopped prior to surgery and restarted after complete wound healing: **Timing of intervention:** Pre and postoperatively **Duration of intervention:** variable INF: agent stopped 3-4 weeks prior to surgery. (mean 29.8 days preop) ETA: agent stopped 1-2 weeks prior to the surgery. (mean 9.6 days preop) **Agents:** Anti-TNF Infliximab (INF) or etanercept (ETA)	**SSI (follow-up NR)** Infection TNF: 1 (2.6%) TKA Agents administered – INF, MTX and oral prednisone Non-TNF: 5 (6.8%) OR: 0.7459 (0.138-4.0336) P=0.7459 **Other infections:** NR **Topic-specific outcomes:** **<u>Subanalysis: influence of anti-TNF on wound healing</u>** THA N=30 total TKA N= 65 total TNF n=13 TNF n=14 Non-TNF n=17 Non-TNF=51 <u>AE Occurrence rate for surgical wounds:</u> THA = 0 .0% in both TNF and non-TNF groups.	**Definitions:** Adverse events (AEs) of surgical wounds included wound dehiscence and continuation of discharge that were healed by conservative treatment Wound dehiscence: wound which is not completely healed in 14 POD or which requires secondary suture. Infection: positive culture results Time for complete wound healing: the period from the date of operation to the removal of surgical staples. Postop Febrile periods: body temp≥37.5^{o}C % recovery of hemoglobin (%Hb), % recovery of total protein

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			TNF: 92.3% Non-TNF: 50.0% P=0.001 **Procedures:** Ankle arthrodesis and total arthroplasty of the hip, knee, elbow, shoulder and ankle. Only the first operation for each patient was included. TKA TNF: 14 (35.9%) Non-TNF: 51 (68.9%) THA TNF: 13 (38.2%) Non-TNF: 17 (23.0%) TEA TNF: 8 (20.5%) Non-TNF: 4 (5.4%) AD TNF: 3 (7.7%) Non-TNF: 1 (1.4%) TSA TNF: 1 (2.6%) Non-TNF: 0 TAA TNF: 0 Non-TNF: 1 (1.4%) **Indications:** Rheumatoid Arthritis (RA) **Setting**: 1 University Hospital and 1 medical center **Location:** Japan **Dates:** April 2004 – July 2007 **Inclusion Criteria:** Patients with RA undergoing Ankle	**Monitoring intervention:** NR **Control group:** n=74 Non-TNF Group (traditional DMARDs) consisting of patients only from the University Hospital. **Standard preventive measures:** NR	TKA TNF: 1 (7.1%) Non-TNF: 4 (7.8%) OR= 0.9038 (0.0928-8.7992) p=NS <u>Febrile Period</u> THA TNF: 3.5±2.0 days Non-TNF: 3.1±1.9days OR= 0.9038 (0.0928-8.7992) p=NS TKA TNF: 2.6±2.5 days Non-TNF: 2.9±1.7 days <u>%Hb, %TP, %Alb:</u> The only statistically significant difference between TNF and non-TNF groups occurred in the THA subgroup for %Hb TNF: 101.0±14.4% Non-TNF: 83.8±10.0% P=0.0016 **Reoperations:** TNF infection was treated with surgical debridement without implant removal; antimicrobials were administered for 4 weeks. **Length of stay:** NR **Mortality: NR** **Adverse events:** <u>Adverse Events (AEs) of surgical wounds</u> TNF: 2 (5.1%) Non-TNF: 5 (6.8%) OR: 0.7459 (0.138-4.0336)	(%TP), and % recovery of serum albumin (%Alb): **Perioperative care:** NR **Analytical methodology:** Continuous variables evaluated with Mann Whitney *U* Test. Or Fisher's exact test to evaluate the difference in Proportions. **Other notes:** Data was collected from medical records. **Follow-up:** NR **Funding Source Conflicts:** Authors: None Institution: None Study: None Supplies: None

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			arthrodesis and total arthroplasty of the hip, knee, elbow, shoulder and ankle **Exclusion Criteria:** revision surgery and other minor operations such as foot operations and wrist operations		P=0.7459 <u>Time to Complete Wound Healing</u> TNF: 10.9±1.2 days Non-TNF: 10.8±1.3 days <u>Postop Febrile Periods:</u> TNF: 2.6±2.2 days Non-TNF: 2.9±1.7 days <u>%Hb</u> TNF: 96.3±14.3% Non-TNF: 90.1±11.5% P=0.0156 <u>%TP</u> TNF: 100.8±9.5% Non-TNF: 100.8±9.2% <u>%Alb</u> TNF: 98.9±13.5% Non-TNF: 98.0±11.3%	
Kawak-ami 2010 [155] (ES)	**Retrospe-ctive Concurre-nt control** 1, 2, 3, 4, 5, 6, 7	To validate that perioperative interruption of Tumor Necrosis Factor (TNF) blocker therapy decreases complications utilizing the British Society for Rheumatology guidelines and the Japanese College of Rheumatology recommendations for withholding infliximab (IFX) and etanercept	**Number of patients: N=128 surgeries (112 patients)** **Patient Characteristics:** Patients were matched for type of surgery and gender between groups. ·Age: years TNF: 57.0 (51.8-64.0) DMARDs: 57.0 (47.0-64.0) ·Gender: male/female TNF: 13/51 DMARDs: 13/51 ·Obesity (BMI) TNF: 21.2 (20.3-22.7) DMARDs: 21.2 (20.1-23.9) ·Comorbidities Disease Duration (y) TNF: 10.6 (8.0-19.8) DMARDs: 13.4 (8.9-19.1) Methotrexate (MTX) TNF: 56 (87.5%)	**Intervention group: n=64 surgeries (49 patients)** Anti-TNF group IFX = 35 ETN = 29 NOTE: 56 (87.5%) of TNF group was also on MTX and 53 (82.8%) were on prednisone 5mg/day (range 2-7) (see patient characteristics) **Timing of intervention:** ETN was withheld 2-4 weeks before surgery infliximab (IFX) was withheld 4 weeks before surgery. Both were restarted after there was no evidence of infection and once wound healing was satisfactory. **Duration of intervention:** Pre and postoperative	**SSI (follow up If using CDC criteria then all superficial 30d and anything with an implant wound be 1yr for deep and organ/space)** Superficial SSI TNF: 7/64 (10.9%) requiring the use of antimicrobials DMARDs: 1/64 (1.6%) P=0.016 Deep SSI: TNF 1/64 (1.6%) – IFX and required prosthesis removal DMARD: 0 <u>Multivariate analysis of putative risk factors for SSI: OR (90%CI)</u>	**Definitions:** SSI: CDC SSI Guideline criteria (1999) Flare-ups: Arthralgia was evaluated using subjective patient assessments. Serological markers like CRP and ESR have not been deemed suitable for measuring the disease activity during the perioperative period. Recurrences of Arthralgia were considered Flare-ups. Venous thromboembolism of lower extremities: diagnosed by 3 experienced medical technologists using

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
		(ETN) for 2-4 week prior to major surgical procedures then restarting treatment once there is no evidence of infection and once wound healing is satisfactory. Wound complications, Deep Venous Thrombosis and flare-ups following joint surgery were assessed.	DMARDs: 48 (75%) P=0.06 DMARDs TNF: 8 (12.5%) DMARDs: 31 (48.4%) P=7.99E-06 Prednisone (PSL) TNF: 53 (82.8%) DMARDs: 40 (62.5%) P=0.008 PLS, dose, mg/day TNF: 5 (2-7) DMARDs: 3 (0-5) P=0.006 Baseline characteristics for DVT Subanalysis (Listed below are only those factors that demonstrated statistically significant differences between groups Methotrexate (MTX) TNF: 39 (86.7%) DMARDs: 32 (71.1%) P=0.06 DMARDs TNF: 7 (15.6%) DMARDs: 24 (53.3%) P=1.54E-04 Prednisone (PSL) TNF: 38 (84.4%) DMARDs: 29 (64.4%) P=0.026 PLS, dose, mg/day TNF: 5 (2-7) DMARDs: 3 (0-5) P=0.041 **Procedures:** **1:1 pair-matched case control study so numbers**	**Agent:** Anti-Tumor Necrosis Factor (TNF) agents: Infliximab (INF) or etanercept (ETN) **Monitoring intervention:** NR **Control group: n=64 surgeries (63 patients)** Patients treated with non-biologic DMARDs. Some patients took more than 1 DMARD Methotrexate (MTX): n=48 Salazosulphapyridine: n=18 Bycillamine: n=6 ɒ=penicillamine: n=4 NOTE: 40 (62.5%) of DMARD patients were on prednisone 3mg/day (range 0-5) (see patient characteristics) **Standard preventive measures:** None	Disease duration (y): 1.169 (1.030-1.326); P=0.015 TNFα-blocker: 21.8 (1.231-386.1) p=0.036 PSL dosage: 1.433 (1.007-2.040) p=0.046 **Other infections:** Urinary Tract Infection: TNF: 1/64 (1.6%) DMARD: 0 Respiratory Inflammation TNF: 0 DMARD: 1/64 (1.6%) **Topic-specific outcomes:** Flare-ups due to interruption of anti-TNF: Arthralgia (+): IFX: 2/35 (5.7%) ETN: 9/29 (31.0%) P=0.009 The ETN patients experienced difficulty for a while during post-op rehab, but recovered after resumption of ETN Treatment. Majority of IFX patients underwent surgery in the middle of an 8-week infusion treatment. **Reoperations:** 1 deep SSI (TNF group (IFX)) required removal of artificial joint prosthesis. **Length of stay NR** **Mortality NR** **Adverse events:** Postoperative complication	ultrasonography **Perioperative care:** All surgery was performed under general or epidural anesthesia **Analytical methodology** Multivariate logistic regression was performed to test the association of SSI & DVT with putative risk factors Baseline characteristics were compared using Mann-Whitney U-test or Fisher's exact test. **Other notes** **Follow-up:** If using CDC criteria then all superficial 30d and anything with an implant wound be 1yr for deep and organ/space **Funding Source Conflicts:** Authors: Industry Institution: None Study: None Supplies: None

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			below are number of procedure PER STUDY GROUP **Arthroplasty procedures: n=54 (84%)** Shoulder Arthroplasty (SA): 1 Unilateral, elective elbow arthroplasty: 2 Implant replacement arthroplasty of the MCP joints: 2 Wrist arthroplasty:6 Unilateral, Elective THA: 8 Unilateral, elective TKA: 33 Total ankle arthroplasty (TAA): 1 Bipolar hip hemiarthroplasty: 1 **Non Arthroplasty procedures: n=10 (16%)** Arthroscopic synovectomy of the knee: 3 Foot surgery: 5 Ankle arthrodesis:1 Open reduction and internal fixation (ORIF): 1 **Indications:** Rheumatoid Arthritis **Setting:** 1 medical university **Location:** Japan **Dates:** May 2004 – March 2009**.** **Inclusion Criteria:** Patients in matched pairs either treated with anti-TNF agents or conventional DMARDS and who underwent joint surgery for		of delayed wound healing was absent in both groups. <u>DVT Subgroup analysis</u> DVT Positive TNF: 23/45 (51%) DMARDs: 12/45 (26%) P=0.015 Multivariate logistic regression showed that TNF blockers were the only statistically significant risk factor for DVT. OR= 2.83 (1.10-7.25) p=0.03	

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			RA. All patients fulfilled the 1987 revised ACR Criteria for RA **Exclusion Criteria:** Surgery in which TNF agent adalimumab (ADA) was used			
Bongar-tz 2008 [160] (ES)	**Retrospe-ctive concurre-nt cohort** 1, 2, 3, 4, 5, 6, 7	To determine the cumulative and 1-year incidence of prosthetic joint infection (PJI) in total hip arthroplasty (THA) and total knee arthroplasty (TKA) in a modern cohort of patients with RA and to further explore potential risk factors for these infections. Additionally, the frequency of this complication of patients with RA as compared with patients with OA who undergo the	**Number of patients: N=924** **Patient Characteristics** ·Age: mean±SD y RA: 63.6±13.3 OA: 67.2±10.8 P<0.001 ·Gender: n% female RA: 363 (78.6%) OA: 338 (73.2%) P=0.06 ·Obesity: NR ·Comorbidities: At least 1 comorbidity RA: 337 (73.0%) OA: 383 (83.0%) P<0.0001 Mean disease Duration: 21.1 years Previous PJI in index joint RA: 43 (9.3%) OA: 24 (5.2%) Steinbrocker functional classification at time of surgery (p<0.0001) Class1 (patient normally active): RA: 4 (0.9%) OA: 6 (1.3%) Class2 (patient able to	**Intervention group: n=462 patients with 657 surgeries.** Patients with RA undergoing either THA or TKA. **Timing of intervention:** Pre or post operatively **Duration of intervention:** If DMARD therapy was withheld around the time of surgery, the stop and start dates were abstracted based on pharmacokinetic half-life and/or data on the biologic activity of each DMARD. According to the information below, the DMARD use was judged as either withheld or maintained. Duration of days medication was withheld: Methotrexate:8 Leflunomide: 85 days or 14 days with cholestyramine wash-out Oral gold: 8 Intramuscular gold: 29 Sulfasalazine: 8 Hydroxychloroquine: 85 Azathioprine: 8	**SSI (mean follow up 4.3 years)** <u>PJI in matched cohorts at 5 years</u> RA: 15/462 (4.2%) OA: 4/ 462 (1.4%) Log rank p=0.005 HR: 4.08 (1.35-12.33) After adjusting for previous infection in the index joint: HR: 3.74 (1.23-11.33) [age, sex, functional class, and comorbidity were not significant predictors of infection) <u>PJI in matched cohorts at 1 year</u> RA: 10/462 (2.3%) OA: 1/ 462 (1.4%) p=deemed statistically significant, but P=NR OR: 10.30 (1.31-80.26) <u>PJI in RA population</u> RA: 23/657 (3.7%) (14[2.2%] infected w/in first year) Revision: 15/255 (5.9%) Primary: 8/402 (2.0%) THA: 12/328 (3.7%)	**Definitions** RA Diagnosis: verified by using validated RA classification criteria. According to the American College of Rheumatology classification criteria. OA Diagnosis: verified during chart review using physician's diagnosis of hip and/or knee OA and absence of RA PJI: diagnosed when at least 1 of the following were present: 1. Isolation of the same organism from ≥2 cultures of joint aspirates or intraoperative tissue specimens. 2. Acute inflammation consistent with infection on histopathologic examination (as determined by the pathologist). 3. Cutaneous sinus tract communicating with the

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
		same type of surgery was assessed.	maintain occupation but less active): RA: 183 (39.6%) OA: 338 (73.2%) Class3 (unable to maintain occupation): RA: 184 (39.6%) OA: 108 (23.4.2%) Class4 (largely or wholly incapacitated): RA: 86 (18.6%) OA: 8 (1.7%) Unknown: RA: 6 (1.3%) OA: 2 (0.4%) **Procedures:** Total knee arthroplasty (TKR) or total hip arthroplasty (THA) Primary THA: 164 (25.0%) Revision THA: 164 (25.0%) Primary TKA: 238 (36.2%) Revision TKA: 91 (13.8%) **Indications:** Rheumatoid Arthritis (RA) or Osteoarthritis (OA) **Setting:** 1 hospital **Location:** USA **Dates** January 1, 1996 – June 30, 2004 **Inclusion Criteria:** All patients with a diagnosis of RA or OA who underwent THA or TKA during the study dates.	Cyclosporine: 8 Cyclophosphamide: 8 D-penicillamine: 15 Etanercept: 8 Adalimumab: 15 Infliximab: 57 Anakinra:8 **Agent:** See above **Monitoring intervention:** NR **Control group: n=462 patients** Matched cohort of patients with OA instead of RA. Patients were listed in the registry as having a diagnosis of OA and no diagnosis of RA. Matching was performed according to age (±5 years), site (hip or knee), type (revision or primary arthroplasty), and time point of first surgery. **Standard preventive measures:** AMP: Preop AMP: 656 (99.9%) **Nonstandard preventive measures:** Antimicrobial impregnated cement: 209 (31.8%) surgeries were performed with antimicrobial impregnated cement	TKA: 11/329 (3.3%) Previous PJI: 7/67 (10.4%) Statistically significant risk factors for SSI (univariate) HR (95%CI) [p=NR] Revision arthroplasty: 2.99 (1.02-8.75) Previous infection of index joint: 5.49 (1.87-16.14) Operation Time: 1.36 per 60-min increase (1.02-1.81 ** NOTE** - Patients in this study who had a previous PJI had a risk of another infection of only 3.5% as compared with 29.2% after revision of the previously infected joint. DMARD Stopping DMARD therapy at the time of surgery lowered the Risk of subsequent PJI: HR 0.65 (0.09-4.95) but not statistically significant. Patients who did not stop anti-TNF therapy before surgery:3/38 (7.9%) infections Patients who stopped Anti-TNF therapy before surgery: 0/12 infections. P=NS Perioperative cortisone was not associated with increased risk of prosthesis	joint prosthesis 4. Purulence in the joint space (as determined by the surgeon). **Perioperative care** **Analytical methodology:** Proportion of surgeries complicated by a PJI was estimated by Kaplan-Meier Techniques. Cox proportional hazards models were used to examine the association between the risk of prosthetic joint inspection for explanatory variables. Also used to compare the risk of infection between the RA and OA cohorts. **Other notes:** None **Follow-up:** Length of FU. mean±SD (years) RA: 3.1±2.4 OA: 3.8±2.6 All patients were followed up by surgeon examination at least twice in the first postsurgical year and then at least every 5 years thereafter. If in-

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			Exclusion Criteria: NR		infections **Other infections:** NR **Topic-specific outcomes:** NR **Reoperation :** 16/23 (69.6%)infections were treated with prosthesis removal. 6/16 had subsequent reimplantation 7/23 (30.4%) were treated with debridement and long-term antimicrobial suppression therapy. **Length of stay:** NR **Mortality:** NR **Adverse events:** NR	person follow up was not possible, patients were contacted by letter and/or phone and asked to complete a standardized form For outstanding or unclear issues as well as for a follow-up <1 year, primary physicians were contacted. **Funding Source Conflicts:** Authors: Industry Institution: None Study: None Supplies: None

Q13B. Should the agent dose be adjusted, and if so, for how long? Our search did not identify data that evaluated perioperative immunosuppressive therapy dose adjustment and its impact on the risk of SSI in prosthetic joint arthroplasty patients.

Q14. What is the optimal duration of postoperative AMP to reduce the risk of SSI in prosthetic joint arthroplasty patients who are on systemic corticosteroid or other immunosuppressive therapy? Our search did not identify data that specifically evaluated differences in duration of postoperative AMP in prosthetic joint arthroplasty patients who were on systemic corticosteroids or other immunosuppressive agents and its impact on the risk of SSI. However, multiple procedures examined in the Core section, Q1.E: Postoperative AMP duration that included patients on immunosuppressive therapy showed no benefit of continuing AMP after closing the surgical incision in the operating room. Therefore, the broader recommendation for duration of postoperative AMP should be applied to prosthetic joint arthroplasty procedures irrespective of use if systemic corticosteroid or other immunosuppressive therapy.

eTABLE 60.Evidence Table for Q15. How does preoperative intra-articular corticosteroid injection impact the risk of SSI in prosthetic joint arthroplasty patients?

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
Desai 2009 [162] (ES)	**Retrospe-ctive Concurr-ent Control** 1, 2, 3, 4, 5	To compare the incidence of infection in patients who had an intra-articular steroid infiltration prior to a knee replacement, with those who hadn't. SSI and	**Number of patients: N=360 knees (250 patients)** **Patient Characteristics** ·Age: mean (Range) years Injection: 68 (49-87) No Injection: 72 (51-88) ·Gender: m/f Injection: 26/54 No Injection: 74/96 Knee of TKR: right/left Injection: 42/48 No Injection: 82/98 ·Obesity: NR ·Comorbidities: NR **Procedures:** Total Knee Arthroplasty (TKR) **Indications:** Osteoarthritis Injection: 58/80 (72.5%) No Injection: 133/170 (78.2%) Rheumatoid arthritis Injection: 22/80 (27.5%) No Injection: 37/170 (21.7%) **Setting:** 1 hospital **Location:** England **Dates:** 1997 - 2005 **Inclusion Criteria:** Patients who had total knee replacement within the study dates with a minimum 1-year follow-up including	**Intervention group: n=90 knees (80 patients)** Patients who had an injection prior to undergoing knee replacement surgery. 45/80 (56.3%) patients had a TKR within 12 months after the injection **Timing of intervention:** preoperative **Duration of intervention:** Variable **Agent:** (40mg/dL methylprednisolone and 5mg/mL levobupivacaine) intra-articular steroids. Infiltration was conducted in the operating theater as a day-case procedure (patients were discharged later the same day). Injection was conducted under strict aseptic precautions. 30 knees (the earlier surgeries) were performed as out-patient procedures with strict aseptic precautions. **Monitoring intervention:** NR **Control group: n=180 knees (170 patients)** Knees undergoing TKR that had no injection prior to TKR surgery. Knees were matched two control knees to one Intervention knee.	**SSI (Follow up at least 1 year)** **Unadjusted Results** Superficial Infection (All treated with antimicrobials & no further complications) Injection: 2/90 (2.2%) [both patients received injections 18 months prior to surgery as an outpatient procedure] No Injection: 5/180 (2.7%) RR 0.80 (0.16-4.03) P=1.0 6/7 Infections occurred in patients with Osteoarthritis. Deep Infection: **No Cases in either group** **Other infections:** NR **Topic-specific outcomes:** None **Reoperations:** None **Length of stay:** NR **Mortality:** NR **Adverse events:** NR	**Definitions:** Superficial Infections: cases which had discharge from superficial layers within one moth of surgery; patients who received antimicrobial cover for more than 1 week delayed wound healing and cases which had positive cultures form superficial layers which settled and did not require further surgery for the knee Deep Infection: cases with positive swab cultures or tissue biopsy from the deep tissues, patients who under-went exploration and wash out of the wound with positive culture report and cases which underwent revision surgery for infection. **Perioperative care:** NR **Analytical methodology:** Normal approximation method was utilized to assess non-inferiority of injection on risk of infection. **Other notes:** Patients were retrospectively

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			patients with diabetes mellitus and a history of smoking. **Exclusion Criteria:** A history of malignancy, immune-suppressive drugs, sero-negative inflammatory arthropathy or a previous infection in the ipsolateral knee.	Matching was done on the basis of age, sex and year of operation. Age selection was done by 10 yearly intervals and year of operation was done by 3-yearly intervals **Standard preventive measures:** Prosthesis: All TKR were cemented, fixed bearing knee systems. Approach: midvastus approach under tourniquet Suction: usage was kept to a minimum and only used during pulsed lavage irrigation prior to cementation. Irrigation: prior to wound closure and with 0.05 chlorhexidine. Hemostatis: meticulously achieved before closure over drains Tourniquet was released after wound closure AMP: 3 doses of Cefuroxime postoperatively in addition to the loading dose to ensure cover for 24 hours Postop		identified by analysis of the notes in a prospective database of TKRs performed by the primary author. Cohort matching was done prior to any evaluation of patient notes with respect to infection rates. Authors estimate that given low infection rate, sample size of ~2000 patients per group needed to rule out (with 95% CI) a 50% increase in infection rate among those injected. **Follow-up:** At least 1 year follow up. Mean follow-up was 48 months. Range 1-6years) **Funding Source Conflicts:** Authors: NR Institution: NR Study: NR Supplies: NR

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
Sreeku-mar 2007 [163] (ES)	**Retrosp-ective Concurr-ent Control** 1, 2, 3, 4, 5	To determine if intra-articular steroid injection prior to joint (hip) replacement increases the risk of injection in replaced joints relative to patients who had no intra-articular injection prior to the same surgery.	**Number of patients: N=202** **Patient Characteristics** ·Age: avg. (range) median, y Injection: 62.2 (32-89) 62.62 No-injection: NR (39-89) 64.09 ·Gender: m/f Injection: 15/51 No-injection: 32/104 ·Obesity: Any patient considered overweight (BMI>35) was advised to lose weight prior to surgery. The operation was deferred until the patient achieved target weight. ·Comorbidities Infections: patients were critically assessed for any focus of sepsis, including form the bladder, skin and lungs. Time between injection and operation for Injection Cohort: Mean 14 months (median 11 months) **Procedures:** Hip replacement Right/left Injection: 41/27 Bilateral Procedure: Injection: 2/66 **Indications:** NR **Setting:** 1 Tertiary Referral Hospital **Location:** England	**Intervention group:** n=66 patients (68 hips) Injection Cohort: received intra-articular injection of steroids prior to hip replacement surgery **Timing of intervention:** Pre-operatively **Duration of intervention:** variable **Agent:** 40mg/dL methylprednisolone and 5mg/mL levobupivacaine were injected. Patients were discharged the same day. **Monitoring intervention:** NR **Control group:** n=136 patients (136 hips) who received no intra-articular injection prior to surgery Each hip in the intervention was matched to two hips in the control (non-injection) group Matching was done on the basis of age (10-year intervals), gender, and year of operation (3-year intervals). When exact matches were unavailable, the next closest match was chosen. **Standard preventive measures:** Surgeon: all surgeries were performed by the senior author Approach: by the trans-	**SSI (F-U at least 1 year)** Infection at most recent follow up Total Infections: Injection: 0 No Injection: 2/136 (1.4%) Difference in incidence: 1.4% (-0.5%-3.3%) Superficial: Injection: 0 No Injection: 1/136 (0.7%) noticed at 4 weeks postop and responded to antimicrobials. Deep Infection Injection: 0 No Injection: 1/136 (0.7%) presented 2 months postop with pyrexia and severe pain. Patient was 75yo. Hip was aspirated and antimicrobials were started. **Other infections:** NR **Topic-specific outcomes:** NR **Reoperations:** Reattachment of trochanter Injection: 1/66 (1.5%) occurred at 2 years Postop due to persisting pain No Injection: 0 **Length of stay:** NR **Mortality:** Injection: 0 No Injection: 1/136 (0.7%) Patient with joint infection presented at 2 months postop developed acute	**Definitions:** None **Perioperative care:** NR **Analytical methodology:** Statistical analysis was performed using Stata. 95%CI was obtained by the normal approximation method **Other notes:** All procedures performed by single surgeon **Follow-up:** at least 1 year Average Follow Up: Injection: 25.33 months No Injection: 22.28 months **Funding Source Conflicts:** Authors: NR Institution: NR Study: NR Supplies: NR

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			Dates: 1997 - 2004 **Inclusion Criteria:** Patients who underwent hip replacement surgery after steroid filtration. A matched cohort of patients was created of patients who underwent hip replacement without steroid infiltration prior to surgery. **Exclusion Criteria**: Patients who had previous operations on the same hip and patients who had malignancy or were on immune-suppressive drugs. Patients with a previous infection in the same hip were excluded.	trochanteric. Trochanteric osteotomy was done and the hip was exposed. Suction: kept to a minimum used only during pulsed lavage to reduce the suction catheter sucking air towards the patient. Irrigation: regular washing of the wound was done with chlorhexidine 0.05%. Hemostatis: meticulous hemostasis was achieved before closure of the drains AMP: 3 doses of cefuroxime, postoperatively, in addition to the loading dose to ensure coverage for 24h postop.	renal shutdown and died of multi-organ system failure at 3 months. **Adverse events:** Aching hip postop Injection: 3/66 (4.5%) [had absence of infection confirmed by ESR, CRP Levels & isotope scans]	
McIntosh 2006 [164] (ES)	**Retrosp-ective Concurr-ent Control** 1, 2, 3, 4, 5, 8	To determine if the administration of an intra-articular steroid injection into an osteoarthritic hip within 1 year of subsequent primary THA would increase the rate of superficial and deep periprosthetic infection when compared with a matched	**Number of patients: N=448** **Patient Characteristics** ·Age: mean (SD) years Injection: 70 (9.8) No Injection: 69 (9.6) ·Gender m/f Injection: 93/131 No Injection: 92/132 ·Obesity: Calculated from mean height/weight reported: Injection: 30.1 No injection: 29.8 Height: mean (SD) cm Injection: 167 (24) No Injection: 168 (9.7) Weight: mean (SD) kg Injection: 84 (19.9)	**Intervention group: n=224** Patients who received intra-articular steroid injection within 1 year prior to total hip arthroplasty **Timing of intervention:** Preoperative **Duration of intervention:** Variable **Agent**: (Agent-Not standardized) Steroids delivered via intra-articular injection. All injections were performed by members of the radiology department within 1 year prior to the THA using standard aseptic protocols. Hip penetration was confirmed	**SSI (follow-up minimum 2 years)** <u>Superficial Infections</u> Injection: 11 (4.9%) No Injection: 8 (3.6%) Hazard Ratio: 1.5 (0.6-3.6) Cumulative Risk of superficial infection at 5 years: Injection 4.5% (2.4-8.4) No Injection: 3.7% (1.1-6.1) 15/19 superficial infections were treated with local wound care and 7/15 were also treated with a course of oral antimicrobial prophylaxis <u>Deep infections (developed</u>	**Definitions:** Superficial Infection: any wound infection that did not penetrate the deep fascia and included any patients with persistent postoperative wound drainage, superficial wound dehiscence, or suture abscess formation. **Perioperative care:** NR **Analytical methodology:** Kaplan-Meier method was used to estimate the cumulative risk of infections.

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
		control group who did not receive a preoperative intra-articular steroid injection.	No Injection: 84 (19.9) ·Comorbidities: NR Time from injection to THA: mean (SD) days Injection: 112 (81) No Injection: NA Operative Time: mean (SD) minutes: Injection: 182 (47) No Injection: 182 (48.1) **Procedures:** Total Hip Arthroplasty **Indications:** Osteoarthritis **Setting:** I Research Hospital **Location:** USA **Dates:** January 1998 – May 2002 **Inclusion Criteria:** Patients with OA of the hip during the study dates. **Exclusion Criteria:** Diagnosis of inflammatory arthritis, connective tissue disorders, any history of acetabular or femoral fracture, any previous surgery on the index hip, or tumor of the acetabulum or femur.	fluoroscopically by the installation of radiopaque dye before steroid administration. Type and amount of steroid dispensed was left to the discretion of the performing radiologist. **Monitoring intervention:** NR **Control group: n=224** Patients who did not receive intra-articular steroid injections prior to Total Hip Arthroplasty. Patients were matched to the Injection Group (intervention) **Standard preventive measures:** NR	<u>at a mean of 1.69 years)</u> Injection: 3 (1.3%) No Injection: 1 (0.4%) Hazard Ratio: 3 (0.3-29.8) Cumulative Risk of deep infection at 5 years: Injection: 3% (0-7%) No Injection: 0.6% (0-1.7%) None of the superficial infections had deep infections develop. 2/4 deep infections were preceded by multiple recurrent dislocations (both in injection group) 2/4 deep infections also had a chronic medical condition 1/2 had a tracheostomy for sever obstructive sleep apnea and was on chronic anticoagulation for atrial fibrillation & DVT and/or pulmonary embolism. 1/2 had type II diabetes mellitus No association was found between the average time from intraarticular injection to primary THA and the development of Superficial or Deep Infections Overall average time between steroid injection and THA for injection group: 112 (SD 81) days	Cox proportional hazard model was used to assess the difference in survivals between groups. Taking into account the timing of injection and the length of follow-up. **Other notes:** **Follow-up:** at 3 months, 1 year, 2 years, and 5 years. Or until THA revision for instability, loosening, implant resection for deep infection, or death. Minimum 2 years Average follow up (years) Injection: 2.7 (1.4) No Injection: 2.6 (1.6) **Funding Source Conflicts:** Authors: None Institution: None Study: None Supplies: None

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
					Superficial: 112 (SD 94) days Deep: 44 (SD 23) days Probability value could not be calculated because of limited number of patients with deep infections **Other infections:** NR **Topic-specific outcomes:** NR **Reoperations:** <u>Superficial infections</u> 2/15 had surgical removal of retained drains 2/15 had wounds incised followed by irrigation and debridement with documentation of fascial integrity <u>Deep Infections</u> 3/3 treated with two-stage exchange 1/3 treated by debridement with prosthesis retention and chronic suppression with oral antimicrobial therapy **Length of stay:** NR **Mortality:** Unrelated to THA: Injection: 12 (5.4%) No Injection: 13 (5.8%) **Adverse events:** Revision for aseptic loosening: Injection: 5 (2.2%) No Injection: 4 (1.8%) <u>Dislocations</u>	

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
					Injection: 6 (2.7%) No Injection: 5 (2.2%) Mean time to dislocation: (yr.) Injection: 1.41 (0.02-3.13) No Injection: 1.54 (0.02-5) 4/11: demonstrated hip stability with conservative treatment 7/11: reoperations Injection: 4 (1.8%) No Injection: 3 (1.3%)	
Papavas-iliou 2006 [161] (ES)	**Retrosp-ective Concurr-ent Control** 1, 2, 3, 4, 5, 8	To determine the rate of infection in patients who had undergone TKR and to correlate this rate with the pre-operative use of intra-articular steroids.	**Number of patients: N=144** **Patient Characteristics:** ·Age: NR ·Gender: NR ·Obesity: NR ·Comorbidities: NR **Procedures:** Total knee replacement **Indications:** See exclusion criteria **Setting:** 1 hospital **Location:** England **Dates:** February 2002 – October 2004 **Inclusion Criteria:** All patients who underwent TKR during the study dates **Exclusion Criteria:** If records were incomplete, patients who had previous surgery on the affected knee (other than arthroscopy), a diagnosis of inflammatory arthritis,	**Intervention group: n=54** Patients who had received one or more intra-articular injection of steroid in their operated knee **Timing of intervention:** variable preoperatively **Duration of intervention:** variable **Agent:** Methylprednisolone-Steroid delivered via intra-articular injection in an orthopedic clinic, rheumatology clinic, or general practice setting before surgery. **Monitoring intervention**: NA **Control group: n=90** Patients with no record of having received an intra-articular injection of steroid before surgery.	**SSI** **Superficial:** 30 days <u>Superficial wound infection:</u> Injection: 12/54 (22.2%) No injection: 10/90 (11.1%) P=0.1 <u>Deep wound infection: 1 year</u> Injection: 3/54 (5.6%) No injection: 0 P<0.025 All 3 deep infections were treated with long-term antimicrobial therapy and revision surgery. All 3 deep infections had injections within 12 months. No relationship was found between the number or timing of injections and the risk of postoperative infection	**Definitions:** Superficial incisional infection: an SSI which occurred within 30 days of surgery and involved only the skin or subcutaneous tissue around the incision. One of the following criteria had to be met: 1) purulent drainage from the incision 2) cultured organisms from a swab or tissue biopsy from the superficial wound layers. Deep Incisional infection: an SSI which occurred within 30 days of surgery and involved only the skin or subcutaneous tissue around the incision. One of the following criteria had to be met: 1) purulent drainage from the depths of the

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			immunosuppression, and a previous history of infection around the knee, smoking and diabetes.	**Standard preventive measures:** Recorded but not reported.	**Other infections:** NR **Topic-specific outcomes:** NR **Reoperations:** Revision surgery for deep infection Injection: 3/54 (5.6%) No injection: 0 P<0.025 **Length of stay:** NR **Mortality:** NR **Adverse events:** Postoperative investigations for deep infection due to symptoms of persistent pain or swelling. Injection: 5/54 (9.3%) No injection: 0	incision 2) microbiological culture from aseptically-aspirated fluid, a swab or a tissue biopsy from the deep-tissue layers or pus cells present on microscopy 3) a deep incision which spontaneously dehisced or was deliberately opened by a surgeon when the patient had a temperature >38^{o}C, localized pain, or tenderness 4) an abscess or other evidence of infection involving the deep incision which was found by direct examination, during re-operation, or by histopathological or radiological examination 5) Diagnosis of a deep incisional SSI by an attending physician **Perioperative care:** NR **Analytical methodology:** Chi-squared test **Other notes:** A pilot study of 420 patients who had received a TKR was performed by reviewing the records looking for incidences of deep

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
						infection: 6/420 (1.4%) deep infections occurred. 5/6 infections had received an intra-articular injection of steroid prior to surgery. **Follow-up:** NR **Funding Source Conflicts:** Authors: None Institution: None Study: None Supplies: None
Kaspar 2005 [165] (ES)	**Retrosp-ective Concurr-ent Control** 1, 2, 3, 4, 5, 8	To determine the influence of intra-articular steroid injection on the rate of surgical site infection in patients with osteoarthritis undergoing subsequent THA	**Number of patients: N=80 (entire database 979)** **Patient Characteristics** ·Age mean ±SEM (Range) y Injection: 71.03±1.53 (45-87) No Injection: 70.55±1.50 (46-87) ·Gender: m/f Injection: 25/15 ·Obesity: BMI Injection: 28.58±0.72 (17-39) No Injection: 29.94±0.77 (21-43) ·Comorbidities: Mean ASA score for both groups was 2.2 indicating most patients had few comorbidities Problems with the spine were present in approximately half of the population evenly distributed across groups.	**Intervention group: n=40** Received intra-articular steroids prior to THA. Details of injections were found from an examination of patients receiving injections in the fluoroscopy suite. **Timing of intervention:** Preoperatively **Duration of intervention:** variable **Agent:** Methylprednisolone 80mg with 1-5ml of bupivacaine. Steroids delivered via intra-articular injection. Injections were performed in a fluoroscopy suite under aseptic technique **Monitoring intervention:** NR **Control group: n=40**	**SSI (mean follow up 29.8 months)** <u>Deep Infection</u> Injection: 4/40 (10%) No Injection: 0 P=0.01 <u>Overall rate of established infections and possible infections</u> Injection: 12/40 (30%) No Injection: 3/40 (7.5%) **Other infections:** NR **Topic-specific outcomes:** <u>Time between most recent injection and THA: mean ±SEM (95%CI)</u> Infection and/or infection test: 11.38±3.03 (5.6-17.2) No Infection/ no infection Test: 10.86±1.74 (7.2-14.5) P=0.878 Power: 0.053 <u>Total number of injections before THA mean ±SEM</u>	**Definitions** **Perioperative care** **Analytical methodology:** Descriptive statistics, unpaired *t*-test, Fisher's exact test for categorical data, Kaplan-Meier survival analysis, and comparison of survival plots by Mantel-Cox type log-rank testing. Power analysis performed by univariate modeling. **Other notes:** Study was underpowered **Follow-up:** Mean length of follow up: 29.8±0.4 months Injection: 33.2±2.1 months No Injection: 30.2±1.6 months **Funding Source**

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			Procedures: Total hip arthroplasty Cemented: 19 in each group Non-Cemented: 21 in each group **Indications:** Osteoarthritis Injection: 1/40 (2.5%) No Injection: 1/40 (2.5%) Inflammatory Arthritis Injection: 39/40 (97.5%) No Injection: 39/40 (97.5%) **Setting:** 1 hospital **Location:** USA **Dates:**1995 - 1998 **Inclusion Criteria:** Patients undergoing THA during the study dates. **Exclusion Criteria:** prostatic malignancy, previous ipsilateral fracture of the hip or earlier surgery on the affected side. Also patients who were immunocompromised, previously or presently infected, affected with cancer in the hip or suspected tumors around the hip or who had been given an initial diagnosis of osteoarthritis.	Did not receive intra-articular steroid injections prior to THA. Matched cohort. Patients were matched in descending order of priority by gender, cemented or cementless THA, age, BMI, ASA pre-op score, year of operation, and surgeon. **Standard preventive measures:** Recorded but not reported	Infection and/or infection test: 1.43±0.25 No Infection/ no infection Test: 1.46±0.11 P=0.891 Power: 0.052 **Reoperations:** Overall rate of revision Injection: 5/40 (12.5%) No Injection: 1/40 (2.5%) Note: Authors report revision rate of 1.02% (10/979) for all unmatched controls/primary THAs performed at their hospital over the study time period (excludes those with primary THA performed elsewhere or before the database was established). **Length of stay:** Injection: 6.58±0.49 (2-18) No Injection: 7.26±0.96 (4-36) **Mortality:** NR **Adverse events:** NR	**Conflicts:** Authors: None Institution: None Study: None Supplies: None

Q16. What are the most effective strategies for managing the preoperative use of intra-articular corticosteroid injections to reduce the risk of SSI in prosthetic joint arthroplasty patients?

Our search did not identify data that evaluated preoperative strategies for managing the use of intra-articular corticosteroid injections in prosthetic joint arthroplasty patients and their impact on risk of SSI.

A. Does the length of time between intra-articular corticosteroid injection and prosthetic joint arthroplasty impact the risk of SSI? Our search did not identify data that evaluated different lengths of time between preoperative intra-articular corticosteroid injection administration and its impact on the risk of TKA.

B. Does the corticosteroid injection dose impact the risk of SSI? Our search did not identify data that evaluated different doses of preoperative intra-articular corticosteroid injections and their impact on the risk of SSI.

2.2B.3 RISK OF BIAS ASSESSMENTS: Q12-16 SYSTEMIC IMMUNOSUPPRESSIVE THERAPY

eTABLE 61. Risk of Bias Assessments of Other Controlled Studies for Q12-16 Systemic Immunosuppressive Therapy

Author Year	Q	All study groups derived from similar source/reference populations	Attrition not significantly different across study groups	Measure of exposure is valid	Measure of outcome is valid	Investigator blinded to endpoint assessment	Potential confounde-rs identified	Statistical adjustment for potential confounders done	Funding source(s) disclosed and no obvious conflict of interest	Overall Risk of Bias
Questions 12 – 16: Immunosuppressive Therapy										
Bongartz 2008 [160]	13	✓	✓	✓	✓	✓	✓	✓		Low
Bridges 1991 [158]	13	✓	✓	✓	✓		✓	✓	✓	Low
Carpenter 1996 [159]	13	✓	✓	✓	✓		✓	✓		Low
Desai 2009 [162]	15	✓	✓	✓	✓	✓				Low
Hirano 2010 [156]	12		✓	✓	✓	✓			✓	Low
Kaspar 2005 [165]	15	✓	✓	✓	✓	✓			✓	Low
Kawakami 2010 [155]	12	✓	✓	✓	✓	✓	✓	✓		Low
McIntosh 2006 [164]	15	✓	✓	✓	✓	✓			✓	Low
Momohara 2011 [154]	12	✓	✓	✓	✓	✓	✓	✓		Low
Papavasil-iou 2006 [161]	15	✓	✓	✓	✓	✓			✓	Low
Perhala 1991 [157]	12	✓	✓	✓	✓		✓	✓		Low
Sreekum-ar 2007 [163]	15	✓	✓	✓	✓	✓				Low

2.2C. Q17 ANTICOAGULATION

2.2C.1 GRADE TABLE: Q17 ANTICOAGULATION

eTABLE 62. GRADE Table for Q17 Anticoagulation

Comparison	Outcome	Quantity and Type of Evidence	Findings	Starting GRADE	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Confounders		
Q17. What are the most effective strategies for managing perioperative venous thromboembolism (VTE) prophylaxis to reduce the risk of SSI? **Q17A. Does the risk of SSI differ by individual VTE prophylaxis agent?**														
Enoxaparin vs. Fondaparinux	SSI*	1 SR [166]	• No difference in a meta-analysis of 4 RCTs [167-170] (N=7237) in primary or revision THA, TKA, or hip fracture surgery: group: 29/3621 (0.8%) vs. 37/3616 (1.0%). (11 day follow up)	High	-1	0	-1	0	0	0	0	0	Low	Low
	Drug related adverse events	1 SR [166]	• No episode of decreased platelet count was reported in either group	High	-1	0	-1	0	0	0	0	0	Low	
Enoxaparin vs. Rivaroxaban	SSI*	4 RCT [171-174]	• No difference in a meta-analysis of 4 RCTs (N=12,383): 28/6200 (0.5%) vs. 27/6183 (0.4%); OR: 1.03 (0.60 – 1.76); p=0.92; I^2=0; 30-35 day follow up • Two studies[171,172] found no difference in THA (n=6890): 14/3453 (0.41%) vs. 16/3437 (0.47%). SSIs were rare (30 or 0.40%) • Two studies[173,174] found no difference in TKA (n=5493): 14/2747 (0.51%) vs. 11/2746 (0.40%). Infections were rare (25 or 0.46%)	High	0	0	0	0	0	0	0	0	High	High
	Hemorrhagic wound complications	4 RCT [171-174]	• No difference in 4 RCTs (THA and TKA combined data) composite of excessive wound hematoma and reported surgical site bleeding: 105/6200 (1.7%) vs. 100/6183 (1.6%); p=NS • Two studies[171,172] found no difference in THA: 59/3453 (1.7%) vs. 54/3437 (1.6%); p =NS	High	0	0	0	0	0	0	0	0	High	

Comparison	Outcome	Quantity and Type of Evidence	Findings	Starting GRADE	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Confounders		
			• Two studies[173,174] found no difference in TKA: 46/2747 (1.7%) vs. 46/2746 (1.7%); p=NS											
	Drug related adverse events	4 RCT [171-174]	• No difference in 4 RCTS modified intention to treat analysis: 970/6200 (15.6%) vs. 971/6183 (15.7%) • Two studies[171,172] found no difference in THA: 15% both 514/3453 vs. 515/3437 • Two studies[173,174] found no difference in TKA: (17% both) 456/2747 vs. 456/2746	High	0	0	0	0	0	0	0	0	High	
Enoxaparin vs. ASA and mechanical prophylaxis	SSI*	1 OBS [175]	• 1 large OBS study (N=2437) Logistic regression analysis showed that enoxaparin (started 12-24 hours postoperatively) was not associated with increased risk of SSI in primary THA; OR 2.11 (0.24-18.5); p=0.499; or primary TKA: OR 1.07 (0.23-4.95); p=0.932.	Low	0	0	0	-1	0	0	0	0	Very Low	Very Low
	Time until wound was dry	1 OBS [175]	• Logistic regression analysis showed that enoxaparin (started 12-24 hours postoperatively) was associated with longer time until wound was dry for primary THA (p<0.01) but not for primary TKA (p=0.62) • Patients on enoxaparin had longer time until wound was dry as compared to those on ASA or those on warfarin; this difference was significant on the 5th (p<0.01) but not by the 8th postoperative day.	Low	0	0	0	-1	0	0	0	0	Very Low	
Enoxaparin vs. Bemiparin vs. Fraxiparin vs. Fondaparin-ux	PJI*	1 OBS [176]	• In a nested case-control study of TKA patients (n=36 infections, 106 controls) specific anticoagulation agents were not associated with increased risk of SSI: p=0.97 • Only 50 of 5496 (0.91%) patients developed an SSI; (95% CI, 0.68%-1.20%). • Hematoma identified as an independent risk	Low	0	0	0	-1	0	0	0	0	Very Low	Very Low

Comparison	Outcome	Quantity and Type of Evidence	Findings	Starting GRADE	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Confounders		
			factor for PJI. Adjusted OR 4.2 (1.1-16.6)											
Enoxaparin, dalterparin, tinzaparin or fondaparinux vs. ASA ± mechanical prophylaxis	SSI*	1 OBS [177]	• No difference in retrospective study (N=41,917) using administrative data from a national sample of primary TKAs: 4366/37,198 (12%) vs. 559/4719 (12%); adjusted OR 1.08 (0.95-1.24). • Authors indicated that subtherapeutic dosing and/or inappropriate timing of the LMWHs or synthetic Factor Xa inhibitor may have impacted the results.	Low	0	0	0	-1	0	0	0	0	Very Low	Very Low
Warfarin vs. No pharmacolo-gic or mechanical prophylaxis	SSI*	1 OBS [178]	• In a large (n=1742) study in primary unilateral TKA, infections were rare 14/1742 (0.8%) and did not differ between groups: 9/957 (0.9%) vs. 5/785 (0.6%) • Goal INR: 1.6-2.2 for 6 weeks. Follow up was 3 months. • Study excluded patients already on preoperative anticoagulation therapy for other conditions.	Low	0	0	0	-1	0	0	0	0	Very Low	Very Low
	Deep Incisional SSI	1 OBS [178]	• Deep SSIs were rare 8/1742 (0.5%) and did not differ between groups: 6/957 (0.6%) vs. 2/785 (0.3%)	Low	0	0	0	-1	0	0	0	0	Very Low	
	Superficial Incisional SSI	1 OBS [178]	• Superficial SSIs were rare 7/1742 (0.4%) and did not differ between groups: 3 (0.3%) vs. 3 (0.4%)	Low	0	0	0	-1	0	0	0	0	Very Low	
Warfarin vs. ASA ± mechanical prophylaxis	SSI*	2 OBS [175,177]	• In a large OBS study[175] (n=2437) of primary THA (n=1211) and TKA (n=1226), logistic regression analysis among THAs showed that warfarin with a target INR of 2.0, started on the day of surgery, was not associated	Low	0	0	0	0	0	0	0	0	Low	Low

Comparison	Outcome	Quantity and Type of Evidence	Findings	Starting GRADE	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Confounders		
			with an increased risk of wound infection OR 7.47 (0.62-89.3); p=0.112. On logistic regression analysis, warfarin does not appear as one of the variables influencing wound infection after TKA. Follow up was not reported • In a large OBS study[177] (N=93, 840) of administrative data on primary TKA, subanalysis (n=56,642), showed no difference; 6349/51923 (12%) vs. 559/4719 (12%); adjusted OR: 1.10 (0.96-1.26). Target INR not reported. SSIs were detected at the time of admission or on readmission within 30 days of index procedure.											
	Time until wound was dry	1 OBS [175]	• Warfarin was not associated with longer time with wound drainage after neither THA (p=0.834) nor TKA (p=0.197) • Patients on enoxaparin had longer time until wound was dry as compared to those on SAS or those on warfarin; this difference was significant on the 5th (p<0.01) but not by the 8th postoperative day.	Low	0	0	0	-1	0	0	0	0	Very Low	
Higher vs. Lower Mean INR	PJI*	1 OBS [179]	• In a 2:1 case control study (N=154) of 78 cases who underwent revision THA or TKJA for septic failure compared to 156 non-infected controls who underwent the same procedure, all on postoperative warfarin (target INR=1.5) found that while the mean INR at all time-points was higher in the infected group, it was not statistically significant (p=0.06). • INR level was significantly higher in patients with wound-related problems who later developed infection (p=0.03)	Low	0	0	0	-1	0	0	0	0	Very Low	Very Low

Comparison	Outcome	Quantity and Type of Evidence	Findings	Starting GRADE	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Confounders		
			• Twice as many infected patients with mean INR >1.5 as compared to controls: 22% vs. 11%; p=0.05 • Infected patients were more likely to have INR>1.5 at time of hospital discharge; 17% vs. 8%; p=0.04 • INR>1.5 at time of hospital discharge was more prevalent in group with wound complications vs. those with uncomplicated postoperative wound healing; 22% vs. 8%; p=0.005 • Multivariate logistic regression analysis showed the following were significant risk factors for PJI: • Wound complications including development of hematoma: OR 27.02 (11.04-91.59); <0.01 • Persistent wound drainage: OR 32.20 (8.7-119.17); p<0.01 • ASA comorbidities: OR 2.07 (1.08-0.97); p=0.03 • Postoperative transfusion: PR 1.63; (1.14-2.33); p<0.01 • 13/78 (17%) of patients in the PJI cohort were on anticoagulation therapy preoperatively for another condition. These patients were heparinized postoperatively until fully coagulated with warfarin (target INR = 2-3). 9/13 (69%) developed wound complications including hematoma (n=3), persistent wound drainage (n=5) and delayed wound healing (n=1)										
	Wound hematoma	1 OBS [179]	• Infected patients had a higher incidence of wound hematomas: 11 (14%) vs. 2 (1%); p=0.0001.	Low	0	0	0	-1	0	0	0	0	Very Low	

Comparison	Outcome	Quantity and Type of Evidence	Findings	Starting GRADE	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Confounders		
	Wound drainage-persistent	1 OBS [179]	• Infected patients had a higher incidence of wound drainage: 24 (31%) vs. 4 (3%); p<0.01	Low	0	0	0	-1	0	0	0	0	Very Low	
Q17B. What is the optimal timing and duration of perioperative VTE prophylaxis that also reduces the risk of SSI?														
Prophylaxis started preoperatively vs. Postoperatively	PJI*	1 OBS [176]	• In a nested case-control study of TKA patients (n=36 infections, 106 controls), infected patients received the first dose of anticoagulant within 12 hours (before or after) of surgery more frequently than those not infected: OR 1.5 (0.73-3.0). • After adjusting by main risk factors, no statistical association was found between close perioperative timing of the first dose of anticoagulant and risk of PJI. • Hematoma formation identified as an independent risk factor for PJI. Adjusted OR 4.2 (1.1-16.6)	Low	0	0	0	-1	0	0	0	0	Very Low	Very Low
Q17C. How safe and effective is modifying the dose of the perioperative VTE prophylaxis agent to reduce the risk of SSI? Our search did not identify data that evaluated the safety and effectiveness of modifying perioperative VTE prophylaxis and its impact on the risk of SSI.														

*Critical outcome; OR: Odds Ratio; RR: Risk Ratio; CI: Confidence Interval

2.2C.2 EVIDENCE TABLE: Q17 ANTICOAGULATION

Q17. What are the most effective strategies for managing perioperative venous thromboembolism (VTE) prophylaxis to reduce the risk of SSI?

Q17A. Does the risk of SSI differ by individual VTE prophylaxis agent?

Q17B. What is the optimal timing and duration of perioperative VTE prophylaxis that also reduces the risk of SSI?

eTABLE 63. Evidence Table for Q17. What are the most effective strategies for managing perioperative venous thromboembolism (VTE) prophylaxis to reduce the risk of SSI?

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
Turpie 2009 [174] (ES) RECORD 4	**RCT** 1, 2, 3, 4, 5, 7, 8, 9	To assess the efficacy and safety of oral rivaroxaban (Rivarox) 10mg once daily compared with 30mg enoxaparin (Enox) given subcutaneously every 12h for the prevention of venous thromboembolism after elective total knee arthroplasty.	**Number of patients: N=3034** **Patient Characteristics** ·Age: mean (SD) y Rivarox: 64.4 (9.7) Enox: 64.7 (9.7) ·Gender: Female n (%) Rivarox: 1007/1526(66.0%) Enox: 1508/1508 (64.1%) ·Obesity: mean (SD) kg/m^2 Rivarox: 30.9 (6.2) Enox: 30.7 (6.0) ·Comorbidities History of VTE: Rivarox: 38/1526(2.5%) Enox: 28/1508 (1.9%) **Procedures:** Total Knee Arthroplasty: n (%) Primary: Rivarox: 1488/1526 (97.5%) Enox: 1479/1508 (98.1%) Revision: Rivarox: 37/1526 (2.4%) Enox: 28/1508 (1.9%) None or missing data Rivarox: 1/1526 (0.1%) Enox: 1/1508 (0.1%) **Indications:** NR **Setting:** Multi-Center **Location:** Bulgaria, Canada, Denmark, India, Israel, Lithuania, Pakistan, Poland, Sri Lanka, Sweden, USA, **Dates:** June 2006 – October 2007 **Inclusion Criteria:** Patients	**Intervention group: n=1584** Rivarox: Patients assigned to receive 10 mg 1x/day rivaroxaban PO.in the evening beginning 6-8h after wound closure or after adequate hemostasis was achieved. Plus placebo injection **Timing of intervention:** Preop **Duration of intervention:** Postop until the evening before venography on POD 11-15 **Device/agent:** Rivaroxaban **Monitoring intervention:** NA **Control group: n=1564** Enox: patients assigned to receive 30mg subcutaneously every 12h beginning 12-24h post wound closure. Plus placebo tablet **Standard preventive measures:** NR	**SSI (follow up 41-50 days)** Postoperative wound infection: Rivarox: 4/1526 (0.3%) Enox: 3/1508 (0.2%) **Other infections:** NR **Topic-specific outcomes** Hemorrhagic wound complications: Rivarox: 21/1526(1.4%) Enox: 22/1508 (1.5%) **Reoperations:** NR **Length of stay:** days mean (SD) Rivarox: 8.0 (6.1) Enox: 7.9 (6.3) **Mortality:** Rivarox: 6/1526 (0.4%) Enox: 6/1508 (0.4%) **Adverse events:** Drug related Adverse Events: Rivarox: 310/1526 (20.3%) Enox: 295/1508 (19.6%)	**Definitions** SSI-NR **Perioperative care:** NR **Other notes:** None **Follow-up:** for 30-35 days after last dose of anticoagulant. (41-50 days postop) **Funding Source Conflicts:** Authors: NR Institution: NR Study: Industry Supplies: NR

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			18 and older scheduled for total knee arthroplasty **Exclusion Criteria:** Patients with active bleeding or a high risk of bleeding, or any disorder contraindicating the use of enoxaparin or that might necessitate enoxaparin dose adjustment. Also disorders preventing bilateral venography, clinically significant liver disease, severe renal impairment (creatinine clearance <30ml/min), concomitant use of drugs that strongly inhibit cytochrome P450 such as protease inhibitors or ketoconazole, pregnancy or breastfeeding, planned intermittent pneumatic compression or the requirement for ongoing anticoagulant therapy.			
Eriksson 2008 [171] (ES) RECORD 1	**RCT** 1, 2, 3, 4, 5, 7, 8, 9	To assess the efficacy and safety of a postoperative 10-mg dose of rivaroxaban (Rivarox) given once daily as compared with a 40mg subcutaneous dose of enoxaparin (a low-molecular	**Number of patients: N=4433** **Patient Characteristics** ·Age: mean (range) y Rivarox: 63.1 (18-91) Enox: 63.3 (18-93) ·Gender: female n (%) Rivarox: 1220/2209 (55.2%) Enox: 1242/2224 (55.8%) ·Obesity: BMI mean (range) Rivarox: 27.8 (16.2-53.4) Enox: 27.9 (15.2-50.2) ·Comorbidities	**Intervention group: n=2266** Patients who received 10mg oral rivaroxaban 1x/day. Rivaroxaban was started 6-8h after wound closure and administered every 22-26h in the evening. Plus placebo injection **Timing of intervention:** Postop for Rivaroxaban & pre and postop for Enoxaparin	**SSI (follow up 66-77 days)** Postoperative wound infection Rivarox: 8/2209 (0.4%) Enox: 8/2224 (0.4%) **Other infections:** NR **Topic-specific outcomes:** **Hemorrhagic wound complications:** Rivarox: 34/2209 (1.5%) Enox: 38/2224 (1.7%)	**Definitions:** SSI - none **Perioperative care:** NR **Other notes:** None **Follow-up:** 30-35 days after the last dose of the study drug. (60-77 days) **Funding Source Conflicts:** Authors: Industry Institution: NR Study: Industry Supplies: NR

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
		weight heparin), with the first [Enox]dose given the evening before surgery and subsequent doses given once daily, for extended thromboprophylaxis after Total Hip Arthroplasty	History of VTE Rivarox: 47/2209 (2.1%) Enox: 55/2224 (2.5%) **Procedures:** Total Hip Arthroplasty Primary Rivarox: 2127/2209 (96.3%) Enox: 2118/2224 (95.2%) Revision Rivarox: 66/2209 (3.0%) Enox: 86/2224 (3.9%) Missing Data Rivarox: 16/2209 (0.7%) Enox: 20/2224 (0.9%) **Indications:** NR **Setting:** Multi center **Location:** International: Argentina, Australia, Austria, Belgium, Brazil, Canada, Chile, Colombia, Czech Republic, Denmark, France, Finland, Germany Greece, Hungary, Israel, Italy, Lithuania, the Netherlands, Norway, Poland, Slovakia, South Africa, Spain, Sweden, Turkey, United States. **Dates:** February 2006 – March 2007 **Inclusion Criteria:** men and women at least 18 years of age who were scheduled to undergo elective total hip arthroplasty. **Exclusion Criteria:** Those scheduled to undergo	**Duration of intervention:** 36 days postop (range 30-42) until patient had a mandatory bilateral venography. Although further thromboprophylaxis was continued at the investigator's discretion. **Device/agent:** 10mg oral rivaroxaban or 40mg subcutaneous injections of enoxaparin. **Monitoring intervention:** NA **Control group: n=2224** Patients who received 40mg subcutaneous injections of enoxaparin administered 1x/day. It was initiated 12h before surgery and restarted 6-8h after wound closure then administered every 22-26h in the evening. Plus placebo tablet **Standard preventive measures:** NR	**Reoperations:** NR **Length of stay** **Mortality:** Death possibly related to study drug Rivarox: 3/2209 (0.01%) Enox: 1/2224 (0.04%) **Adverse events:** Drug related adverse events Rivarox: 270/2209 (12.2%) Enox: 265/2224 (11.9%)	

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			staged bilateral THA, were pregnant or breast-feeding, had active bleeding or a high risk of bleeding, or had a contraindication for prophylaxis with enoxaparin or a condition that might require an adjusted dose of enoxaparin. Also conditions preventing bilateral venography, substantial liver disease, severe renal impairment (creatinine clearance <30ml/min), concomitant use of protease inhibitors for the treatment of human immunodeficiency virus infection, planned intermittent pneumatic compression, or a requirement for anticoagulant therapy that could not be stopped.			
Lassen 2008 [173] (ES) RECORD 3	**RCT** 1, 2, 3, 4, 5, 7, 8, 9	To conduct a multicenter, randomized, double-blind trial that compares the efficacy and safety of oral rivaroxaban (Rivarox) 10mg once daily administered postoperatively, with those of enoxaparin	**Number of patients: N=1459** **Patient Characteristics** ·Age: mean (Range) y Rivarox: 67.6 (28-91) Enox: 67.6 (30-90) ·Gender: female n (%) Rivarox: 857/1220 (70.2%) Enox: 821/1239 (66.3%) ·Obesity: BMI Mean (RANGE) Rivarox: 29.5 (16.3-51.1) Enox: 29.8 (16.0-54.3) ·Comorbidities	**Intervention group: n=1220** Rivarox: Patients who received once daily oral rivaroxaban in a 10-mg tablet. Treatment was initiated 6-8h after wound closure. Then administered every 24h until POD10-14. Further thromboprophylaxis was given at investigator's discretion according to local practice. **Timing of intervention:**	**SSI (follow up 40-49 days):** Postoperative infection of wound Rivarox: 7/1220 (0.6%) Enox: 11/1239 (0.9%) **Other infections:** NR **Topic-specific outcomes:** Hemorrhagic Wound Complications Rivarox: 25/1220 (2.0%) Enox: 24/1239 (1.9%) **Reoperations:** NR	**Definitions:** SSI – postoperative infection of wound was classified according to the Medical dictionary for Regulatory Activities (MEdDRA a registered trademark of the International Federation of Pharmaceutical Manufacturers and Associations) Hemorrhagic wound complication: excessive wound hematoma or

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		(Enox), 40mg given subcutaneously once daily administered preoperatively, for the prevention of venous thromboembolism after elective total knee arthroplasty	History of VTE Rivarox: 48/1220 (3.9%) Enox: 42/1239 (3.4%) **Procedures:** Elective total knee arthroplasty Primary: Rivarox: 1176/1220 (96.4%) Enox: 1186/1239 (95.7%) Revision Rivarox: 24/1220 (2.0%) Enox: 30/1239 (2.4%) None/Missing data Rivarox: 20/1220 (1.6%) Enox: 23/1239 (1.9%) **Indications:** NR **Setting:** Multi-center **Location:** Austria, Belgium, Canada, China, Colombia, Czech Republic, Denmark, France, Germany, Israel, Italy, Mexico, the Netherlands, Poland, Peru, South Africa, Spain, Sweden. **Dates:** February 2006 – November 2006 **Inclusion Criteria:** Patients who were 18 years of age or older and scheduled for Total knee arthroplasty. **Exclusion Criteria:** Patients with active bleeding or a high risk of bleeding that contraindicated the use of low-molecular-weight-heparin and patients with any contraindication	Postop **Duration of intervention:** from 6-8h after wound closure until POD10-14 **Device/agent:** Rivaroxaban 10mg tablets **Monitoring intervention:** NA **Control group: n=1239** Enox: Patients who received a once-daily subcutaneous injection of 40mg enoxaparin sodium. This was initiated 12h before surgery and was given again 6-8h after wound closure, then administered every 24h. Study medications were continued until at least POD 10 and up to POD 14. Further thromboprophylaxis was given at investigator's discretion according to local practice. **Standard preventive measures:** NR	**Length of stay:** Rivarox: 48/1220 (3.9%) Enox: 42/1239 (3.4%) **Mortality:** Death Rivarox: 0/1201 (3.9%) Enox: 6/1217 (3.4%) **Adverse events:** Drug related adverse events: Rivarox: 146/1220 (12.0%) Enox: 161/1239 (13.0%)	bleeding at the surgical site. **Perioperative care:** NR **Other notes:** None **Follow-up.** 30-35 days after the last dose of medication. **(POD 40-49?)** **Funding Source Conflicts:** Authors: Industry Institution: NR Study: Industry Supplies: NR

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			necessitating adjustment of its dose. Also, conditions preventing bilateral venography, clinically significant liver disease, concomitant use of protease inhibitors of the human immunodeficiency virus or fibrinolytic agents, planned intermittent pneumatic compression, requirement of ongoing anticoagulation therapy, and pregnancy or breastfeeding.			
Kakkar 2008 [172] (ES) RECORD 2	**RCT** 1, 2, 3, 4, 5, 6, 7, 8, 9	To assess the efficacy of extended thromboprophylaxis with an oral factor Xa inhibitor, rivaroxaban (RivaRox), for 31-39 days, compared with a short-term LMWH enoxaparin (Enox) regimen for 10-14 days followed by placebo in patients undergoing total hip arthroplasty (THA) This is known	**Number of patients:** **N=2457 (Safety population)** **N=1923 – population for major VTE** **N=1733 – ITT population for Primary Efficacy** **Patient Characteristics:** this information is for the safety population: RivaRox: n=1228 Enox: n=1229 ·Age: mean (SD, IQR) years RivaRox: 61.4 (13.2, 53-71) Enox: 61.6 (13.7, 54-72) ·Gender: female (%) RivaRox: 667 (54.3%) Enox: 651 (53.0%) ·Obesity: BMI mean (SD, IQR) RivaRox: 26.8 (4.8, 23.5-29.4)	**Intervention group:** **n=1228;** **VTE= 961; Primary Efficacy=864** RivaRox: Patients receiving extended duration rivaroxaban as thromboprophylaxis for 5 weeks. Starting 6-8 hours after wound closure and continued for 31-39 days. In addition, they received placebo injections for 10-14 days starting 12h before surgery. **Timing of intervention:** pre and postoperative **Duration of intervention:** begun 6-8 hours after wound closure and continued for 31-39 days. **Agent:** Oral rivaroxaban (10mg) once daily **Monitoring intervention:**	**SSI (follow-up 30-35 days)** Postoperative wound infections RivaRox: 8/1228 (0.7%) Enox: 6/1229 (0.5%) **Other infections:** Infections and infestations: RivaRox: 88/1228 (7.2%) Enox: 87/1229 (7.1%) **Topic-specific outcomes:** Non-Fatal Pulmonary Embolism n (95%CI) RivaRox: 1/864 (0.1%, <0.1-0.6) Enox: 4/869 (0.5%, 0.1-1.2) Absolute Risk Reduction: (95%CI) 0.3% (-0.2-1.1), p=0.37 Deep vein thrombosis in Safety Population	**Definitions:** Deep vein thrombosis was assessed and confirmed by ascending bilateral venography. In cases of suspected pulmonary embolism, pulmonary angiography, perfusion/ventilation lung scintigraphy with chest radiography or spiral computed tomography was done. Major bleeding: bleeding that was fatal, into a critical organ (e.g. retroperitoneal, intracranial, intraocular, intra-spinal), required re-operation, or clinically overt extra-surgical-site bleeding associated with a fall in hemoglobin of 20g/L or more,

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		as the **RECORD 2 study** "Regulation of Coagulation in Orthopaedic surgery to prevent Deep-vein thrombosis and pulmonary embolism)	Enox: 27.1 (5.2, 23.6-30.0) ·Comorbidities: Previous history of VTE RivaRox: 10 (0.8%) Enox: 20 (1.6%) Duration of surgery: median (IQR) (min) RivaRox: 95.0 (72-125) Enox: 93.0(73-126) **Procedures:** Elective Hip Arthroplasty (THA) Previous Orthopedic Surgery RivaRox: 225 (18.3%) Enox: 232 (18.9%) Primary RivaRox: 1160 (94.5%) Enox: 1157 (94.1%) Revision RivaRox: 52 (4.2%) Enox: 50 (4.1%) Missing/no surgery RivaRox: 16 (1.3%) Enox: 22 (1.8%) **Indications:** NR **Setting:** Multicenter (123 centers) **Location:** Multinational (21 countries worldwide) **Dates:** February 2006 – April 2007 **Inclusion Criteria:** Patients enrolled during the study dates aged 18 years or older, scheduled to undergo elective THA. **Exclusion Criteria:** Those	Liver biochemistry and cardiovascular adverse events were monitored throughout the treatment and follow-up periods. Mandatory bilateral venography the day after the last dose of the study mediation (day 32-40) **Control group: n=1229; VTE: 962; Primary Efficacy=869** Enox: Patients receiving the heparin-based thromboprophylaxis Enoxaparin for 2 weeks. It was initiated 12h before surgery and restarted 6-8 hours after wound closure. And continued for 10-14 POD. Patients also received placebo tablets for 31-39 days starting 6-8h after surgery. **Standard preventive measures:** NR **Nonstandard preventive measures:** Use of cement RivaRox: 621 (50.6%) Enox: 608 (49.8%)	RivaRox: 37/1228 (3.0%) Enox: 86/1229 (7.0%) Deep-vein Thrombosis in ITT population: n (95%CI) RivaRox: 14/864 (1.6%, 0.9-2.7) Enox: 71/869 (8.2%, 6.4-10.2) Absolute Risk Reduction: (95%CI) 6.5% (4.3-8.5), p<0.0001 Proximal DVT: n (95%CI) RivaRox: 5/864 (0.6%, 0.2-1.3) Enox: 44/869 (5.1%, 3.7-6.7) Absolute Risk Reduction: (95%CI) 4.5% (2.9-6.0), p<0.0001 Distal DVT: n (95%CI) RivaRox: 9/864 (1.0%, 0.5-2.0) Enox: 27/869 (3.1%, 2.1-4.5) Absolute Risk Reduction: (95%CI) 2.0% (0.7-3.3), p=0.0025 Major venous thromboembolism: n (95%CI) RivaRox: 6/961 (0.6%, 0.2-1.4) Enox: 49/962 (5.1%, 3.8-6.7) Absolute Risk Reduction: (95%CI) 4.5% (3.0-6.0), p<0.0001	calculated from the POD1 baseline value or requiring infusion of two or more units of whole blood or packed cells. On-treatment non-major bleeding – any on-treatment bleeding event not adjudicated as major bleeding Hemorrhagic wound complications: composite of excessive wound hematoma and surgical-site bleeding Any post-operative bleeding: bleeding starting after the first tablet intake and ending up to 2 days after the last intake of study medication. Safety Analysis: patients who received at least 1 dose of medication Modified ITT population: patients who were valid for safety analysis, had undergone planned surgery, and had adequate assessment of thromboembolism. Patients valid for assessment of major venous thromboembolism – those valid for safety analysis and in whom the venograms were evaluable for the

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			scheduled to undergo staged bilateral hip arthroplasty, who had active bleeding or a high risk of bleeding, or had any condition contraindicating the use of enoxaparin, or that might require enoxaparin dose adjustment, including severe renal impairment. Also including significant liver disease, pregnancy or breastfeeding, concomitant use of HIV protease inhibitors, use of fibrinolytic therapy or planned intermittent pneumatic compression during the study period, conditions preventing bilateral venography, or the requirement for an anticoagulant that could not be discontinued.		<u>Symptomatic venous thromboembolism:</u> n (95%CI) RivaRox: 3/1212 (0.2%, <0.1-0.7) Enox: 15/1207 (1.2%, 0.7-2.0) Absolute Risk Reduction: (95%CI) 1.0% (0.3 -1.8), p=0.0040 <u>Symptomatic venous thromboembolism in follow-up period:</u> n (95%CI) RivaRox: 1/1212 (0.1%, <0.1-0.5) Enox: 2/1207 (0.2%, <0.1-0.6) Absolute Risk Reduction: (95%CI) 0.1% (-0.2-0.4), p=0.62 <u>Major on-treatment bleeding</u> RivaRox: 1/1228 (<0.1%) [hemorrhagic diarrhea and hematemesis and resulted in discontinuation of rivaroxaban; patient received acetylsalicylic acid w/o gastric protection before surgery] Enox: 1/1229 (<0.1%) [Blood in cerebrospinal fluid. Deemed not related to study drug but enoxaparin was discontinued] <u>Non-Major on-treatment bleeding:</u>	proximal veins, irrespective of whether they were valid for distal veins **Perioperative care:** NR **Analytical methodology:** Mantel-Haenszel weighting stratified by country with corresponding asymptotic two-sided 95%CI and two-sided p value. Unweighted RR reduction calculated with an asymptotic method. Sensitivity analysis: 1) included all randomized patients with evaluable bilateral venography (irrespective of whether it was in the time window) or a confirmed symptomatic/asymptomatic event/death irrespective of the time window. 2) All randomized participants included in Sensitivity analysis 1. Plus those who had evaluable bilateral venography/ ultrasonography as done by the investigator, irrespective of the time window, or a symptomatic/ asymptomatic event/ death, irrespective of the time window, provided

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					RivaRox: 80/1228 (6.5%) Enox: 67/1229 (5.5%) <u>Clinically relevant non-major bleeding</u> RivaRox: 40/1228 (3.3%) Enox: 33/1229 (2.7%) <u>Any bleeding after initiation of placebo or Rivaroxaban:</u> RivaRox: 56/1197 (4.7%) Enox: 49/1193 (4.1%) <u>Patients receiving blood transfusion:</u> RivaRox: 485/1228 (39.5%) Enox: 514/1229 (41.8%) **Reoperations:** No major bleeding events leading to reoperation in either group **Length of stay:** NR **Mortality up to day 30-42:** <u>Death**:** n (95%CI) RivaRox: 2/864 (0.2%, <0.1-0.8) (both of cardiovascular cause) Enox: 6/869 (0.7%, 0.3-1.5) (one of pulmonary embolism, 4 unrelated to venous thromboembolism, one unexplained) Absolute Risk Reduction: (95%CI) 0.5% (-0.2-1.1), p=0.29 <u>Death in follow-up period:</u> n (95%CI) RivaRox: 0/1228 (0.0%, 0.0-0.3) Enox: 2/1229 (0.2%, <0.1-	the symptomatic event was not adjudicated. To be a non-event by the committee. **Other notes:** Sample size based on event rate of 11% in Enoxaparin group. And a RR of 40% in rivaroxaban. Thus 914 patients per group would be enough to demonstrate a Reduction in RR with a power of 90% **Follow-up:** 30-35 days after the last dose of medication **Funding Source Conflicts:** Authors: Industry Institution: NR Study: Industry Supplies: NR

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					0.6)[one to pulmonary embolism, one unexplained] Absolute Risk Reduction: (95%CI) 0.2% (-0.1-0.6), p=0.50 **Adverse events** <u>Any on treatment adverse event:</u> RivaRox: 768/1228 (62.5%) Enox: 807/1229 (65.7%) <u>Drug related adverse events:</u> RivaRox: 245/1228 (20.0%) Enox: 249/1229 (20.3%) Drug related serious on-treatment adverse events RivaRox: 13/1228 (1.1%) Enox: 17 (1.4%) <u>Serious on-treatment adverse events:</u> RivaRox: 90/1228 (7.3%) Enox: 131/1229 (10.7%) <u>Adverse events leading to discontinuations:</u> RivaRox: 46/1228 (3.8%) Enox: 64/1229 (5.2%) <u>Edema peripheral</u> RivaRox: 55/1228 (4.5%) Enox: 48/1229 (3.9%)	

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Turpie 2002 [166] (ES)	**Meta-Analysis** 3, 4	To perform a meta-analysis of 4 randomized, double-blind trials using the same comparative drug (Enoxaparin [Enox] and Fondaparinux [Fond]), end points (venous thromboembolism, and proximal deep vein thrombosis), and adjudication committee and to report the results of the meta-analysis.	**Study types and number: N=4** Phase III clinical trials: 4/5 **Number of total patients in the review: N=7344** **Efficacy Population: N=5385** **Inclusion criteria:** 4 multicenter, randomized, double blind studies. **Exclusion criteria:** NR **Databases searched:** NA – Studies were all conducted as a part of the Phase 3 studies in a clinical trial program. **Aggregate summary score:** NR Eriksson 2001– Hip Fracture Lassen 2002– Hip Replacement Turpie 2002 – Hip Replacement Bauer 2001 – Major Knee Surgery Eriksson 2003 – Hip Fracture	**Intervention group: n=3668** **Efficacy population: = 2682** Fond: Patients administered Fondaparinux as an anticoagulant 4/4 studies: fondaparinux was administered at2.5mg qd with the time of first injection 6h±2h postop and the time to second injection ≥12h after first dose. **Timing of intervention:** Postoperatively Eriksson: 2001 if surgery was delayed 24-48h after admission, fondaparinux was initiated 12±2h preoperatively (68/626 (19.9%)). Omission of preop injections was recommended in both cohorts if a spinal or epidural anesthesia, or catheterization was planned. Lassen: Fondaparinux was initiated a mean of 6.25h after surgery in 86% of patients Turpie: Fondaparinux was initiated a mean of 6.5h after surgery in 92% of patients. Bauer: Fondaparinux was initiated a mean of 6.25h in 94% of patients	**SSI:** Wound infection (by day 11) Fond: 37/3616 (1.0%) Enox: 29/3621 (0.8%) Complications at surgical site leading to prolonged hospitalization or re-hospitalization: Fond: 52/3616 (1.4%) Enox: 52/3621 (1.4%) **Other infections:** NR **Topic-specific outcomes:** Patients treated for VTE by day 11: Fond: 199/3616 (5.5%) Enox: 351/3621 (9.7%) P<0.001 Venous thromboembolism: Fond: 182/2682 (6.8%) Enox: 371/2703 (13.7%) Any deep vein thrombosis Fond: 174/2677 (6.5%) Enox: 363/2698 (13.5%) Any Proximal Deep Vein Thrombosis Fond: 35/2756 (1.3%) Enox: 81/2775 (2.9%) Distal Deep Vein Thrombosis Fond: 141/2704 (5.2%) Enox: 293/2709 (10.8%) All odds ratios favor Fondaparinux regarding Surgery type, Obesity, age, gender, type of anesthesia,	**Definitions** VTE: deep vein thrombosis, pulmonary embolism or both up to day 11. Bleeding index: the sum of the number of units of packed red blood cells or whole blood transfused and the difference of the hemoglobin values (g/dL) before and after the bleeding occurrence (i.e. bleeding index=units of transfusion + hemoglobin before bleeding – hemoglobin after bleeding) Fatal bleeding: bleeding that was retroperitoneal, intracranial, intraspinal or involved any other critical organ, **Perioperative care:** NR **Other notes:** None **Follow up:** wound infection: 11 days (wound infection and VTE) entire study: 49 days (PE) **Funding Source Conflicts:** Authors: Industry Institution: NR

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				Duration of intervention: for 5-9 days postoperatively or until a mandatory bilateral venography was performed to assess for a new VTE after a minimum 5-day hospital stay **Agent:** Fondaparinux **Monitoring intervention:** NR **Control group: n=3676** **Efficacy population = 2703** Enox: Patients administered enoxaparin as an anticoagulant. 2/4 Studies: enoxaparin in 40mg qd with time of 1st injection 12h±2h preoperatively 2/4 studies: enoxaparin in 30mg qd with time of 1st injection 12-24h postoperatively 1/4 studies: Time to second injection 12-2h postop 3/4 studies: time to second injection NR **Standard preventive measures:** Other thromboembolic prophylaxes: Intermittent pneumatic compression, dextran and thrombolytic or anticoagulant agents were prohibited; centers	use of cement or duration of surgery with no significant difference seen in odds ratios for variations in these factors. Common Odds Ratio between studies favors Fondaparinux with regards to VTE: -55.2 (-63.1 to -45.8); p<0.001 **Post-hoc analysis of timing of Fondaparinux injection:** A statistically significant relationship was shown between the timing (between 3-9 hours postop) of the first fondaparinux injection and major bleeding (p=0.008) A statistically significant relationship also existed between the incidence of overt bleeding associated with a bleeding index ≥2 and the timing of the first fondaparinux injection (p=0.008) Efficacy was not affected by this timing: p=0.67 **Re-operations:** See Infections **Length of stay:** See infections **Mortality** Fatal bleeding	Study: NR Supplies: NR

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				were instructed to avoid the use of aspirin or nonsteroidal anti-inflammatory drugs when possible; other antiplatelet agents were prohibited Graduated compression stockings: use was allowed and physiotherapy was recommended Length of administration: investigators could extend prophylaxis during follow-up with any currently available therapy, but only after a venography was performed. VTE: after occurrence, treatment was left to the surgeon's discretion.	Fond: 0/3616 Enox: 1/3621 (0.0%) Death from any cause Fond: 15/3616 (0.4%) Enox: 21/3621 (0.6%) Death from any cause up to 49 days Fond: 48/3616 (1.3%) Enox: 52/3621 (1.4%) **Adverse events:** Adjudicated bleeding events up to day 11: Fond: 96/3616 (2.7%) Enox: 63/3621 (1.7%) P=0.008 Bleeding into critical organ Fond: 0/3616 Enox: 1/3621 (0.0%) Bleeding leading to another operation Fond: 12/3616 (0.3%) Enox: 8/3621 (0.2%) Bleeding with a bleeding index≥2 Fond: 84/3616 (2.3%) Enox: 53/3621 (1.5%) Any Transfusions Fond: 1950/3616 (53.9%) Enox: 1864/3621 (51.5%) P=0.04	

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Asenio 2010 [176] (ES)	**Prospective concurrent control with a nested case control** 1, 2, 3, 4, 5, 6, 7, 8	To investigate the independent effect of Low Molecular Weight Heparin (LMWH) timing for Deep Venous Thrombosis (DVT) prophylaxis related to the start of surgery on the risk of prosthesis infection among patients undergoing Total Knee Arthroplasty (TKA). Other objectives were to establish the risk of prosthesis infection and their microbiological characteristics and to evaluate the relative effect of other potential risk factors.	**Number of patients: N=5496** **Nested Case Control: N=142** **Patient Characteristics:** for case control patients ·Age: mean±SD y Intervention: 71.3±6.1 Control: 71.4±8.5 ·Gender male n (%) Intervention: 13 (36.1%) Control: 30 (28.3%) ·Obesity Intervention: 23 (63.9%) Control: 66 (62.3%) ·Comorbidities Diabetes mellitus Intervention: 10 (27.8%) Control: 13 (12.3%) OR:2.83 (1.08-7.38) p=0.03 Hypertension: Intervention: 27 (75%) Control: 64 (60.4%) OR: 2.07 (0.86-5.0); p=0.10 **Procedures:** Total knee arthroplasty (TKA) Non-Primary Arthroplasty Intervention: 2 (5.7%) Control: 4 (4.0%) Surgery duration Intervention: 112.8±34.2 Control: 121.4±43.1 **Indications:** NR **Setting:** Multicenter (13 Spanish hospitals)	**Intervention group: n=36** Patients who underwent TKA and developed a prosthetic joint infection. **Timing of intervention** <u>First Dose of LMWH Preoperatively</u> ≥48h Intervention: 0 Control: 2 (1.9%) 24-48h Intervention: 0 Control: 1 (1%) 13-24h Intervention: 12 (33.3%) Control: 31 (29.8%) 7-12h Intervention: 3 (8.3%) Control: 6 (5.8%) ≤6h Intervention: 0 Control: 1 (1%) <u>POSTOPERTIVELY ≤6h</u> Intervention: 3 (8.3%) Control: 6 (5.8%) <u>7-12h</u> Intervention: 10 (27.8%) Control: 29 (27.9%) <u>13-24h</u> Intervention: 4 (11.1%) Control: 17 (16.4%) <u>24-48h</u> Intervention: 4 (11.1%) Control: 11 (10.6%) <u>Timing of any dose of LMWH</u> Within 24h preop Intervention: 15(41.7%) Control: 41 (38.7%)	**SSI (Follow up 6 months postop)** For total population of 5496: Prosthetic infection incidence rate: 0.91 cases/100 patients operated (95%CI 0.68-1.2) Infection rate ranged from 0.25%-2.34% by center (p=0.14) 68% of infections were identified post-discharge. Time from procedures to infection median: 37 days (IQR: 16-63) Early Postoperative Infection: 46% Adjusted OR for independent risk factors for infection: Diabetes: 3.2 (95%CI:1.2-8.8) Hematoma formation: 4.2 95%CI (1.1-16.5) **Other infections:** NR **Topic-specific outcomes:** <u>Bleeding</u> Intervention: 12 (33.3%) Control: 32 (30.2%) <u>Wound Hematoma</u> Intervention: 19 (52.8%) Control: 50 (47.6%) OR:3.58 (0.96-13.40) p=0.06	**Definitions:** Prosthesis infection: CDC definitions – an infection involving the periprosthetic tissues and Infection: Occurring within the first 6 months postop and meeting at least 1 of the following criteria: 1. an organism was isolated from a culture of fluid or tissue aseptically obtained from an incision deliberately opened by the surgeon 2. an abscess or other evidence of infection was detected on direct examination, either during reoperation or by histopathological or radiographic examination, 3. prosthesis infection was diagnosed by a surgeon or attending physician. Early prosthesis infection: an organ/space wound infection that developed within 1 month postoperatively. Late Prosthesis infection: a prosthesis infection that developed between 1-6 months postop.

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			Location: Spain **Dates:** January 1, 2005 – December 31, 2006 **Inclusion Criteria:** All patients undergoing primary TKA or total knee replacement in 13 Spanish traumatology surgical units during the study dates. **Exclusion Criteria:** Patients with infected prostheses.	Within 24h postop Intervention: 31 (86.1%) Control: 89 (84.0%) **Duration of intervention:** variable **Agent:** Low Molecular Weight Heparin (LMWH). Doses received were stratified related to the time of surgery, and the time interval relative to surgical time. Enoxaparin Intervention: 19 (52.8%) Control: 50 (47.6%) Bemiparin Intervention: 8 (22.2%) Control: 26 (24.8%) Fraxiparin Intervention: 7 (19.4%) Control: 23 (21.9%) Fondaparinux- NOT a LMWH; synthetic pentasaccharide factor Xa inhibitor Intervention: 2 (5.6%) Control: 6 (5.7%) P=0.97 **Monitoring intervention:** NA **Control group: n=106** For every intervention patient who developed an infection, 3 control patients were chosen who did not develop an infection within the first 6 postoperative months. Patients were	**Reoperations:** NR **Length of stay:** NR **Mortality:** NR **Adverse events:** NR	**Perioperative care:** NR **Analytical methodology** Univariate logistic regression, paired *t*-test, multiple conditional logistic regression modal was developed from a saturated model containing all non-correlated risk factors that were significant at the .1 level. Only cases that could be matched to controls were included in the risk factor analysis. **Other notes:** None **Follow-up:** Active surveillance by surgeons and/or hospital epidemiologists during the 6 months post-op When clinical records did not provide enough information to rule out infection during the first 6 months, patients were interviewed by telephone. Investigators extracted all information from medical records **Funding Source Conflicts:** Authors: None Institution: None Study: None Supplies: None

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
				matched by medical center and date of index case procedures ±2 weeks. **Standard preventive measures:** AMP: AMP were given across patients, however, timing was not standard and breaks down as follows: >2h preop Intervention: 2 (5.6%) Control: 12 (11.3%) ≤2h preop Intervention: 29 (80.6%) Control: 84 (79.2%) Postop Intervention: 5 (3.9%) Control: 10 (9.4%) **Non-Standard preventive measures:** <u>Hair Removal P=0.07 between groups</u> Shaving not done Intervention: 6 (22.2%) Control: 25 (28.7%) Blade Razor Intervention: 8 (29.6%) Control: 12 (13.8%) OR:3.3 (0.26-42.1) Electrical Clipper Intervention: 13 (48.1%) Control: 50 (57.5%) OR: 0.18 (0.02-2.24) <u>Normothermic Blanket</u> Intervention: 8 (22.2%) Control: 38 (35.8%) OR: 0.30 (0.09-1.01) p=0.05		

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
Bozic 2010 [177] (ES)	**Retrospect-ive concurrent cohort** 1, 2, 3, 4, 5, 6, 7, 8	To utilize administrative data from a large national sample of patients undergoing primary total knee arthroplasty (TKA) to compare the risk of venous thromboembolism (VTE), surgical site bleeding, surgical site infection (SSI), and mortality between patients who received aspirin, warfarin, or injectable (LMWH and fondaparinux) VET Prophylaxis (VETP)	**Number of patients: N=93,840** **Patient Characteristics** ·Age: mean (SD) y Aspirin: 66.4 (10.7) Injectable: 66.5 (10.5) Warfarin: 67.3 (10.4) P<0.001 ·Gender: male n (%) Aspirin: 1679 (36%) Injectable: 12,505 (34%) Warfarin: 18,085 (35%) ·Obesity: Aspirin: 833 (18%) Injectable: 5105 (14%) Warfarin: 6454 (12%) ·Comorbidities Diabetes: Aspirin: 754 (16%) Injectable: 6561 (18%) Warfarin: 8839 (17%) Deficiency anemia Aspirin: 456 (10%) Injectable: 5056 (14%) Warfarin: 5824 (11%) Aspirin patients had lower baseline VTE risk score than warfarin or LMWH/fondaparinux patients (p<0.001) Aspirin Patients had fewer medical comorbidities than Injectable (p<0.001) but similar to Warfarin Patients (p=0.69) Aspirin patients less likely to have a charge for sequential compression devices in perioperative period:	**Intervention group:** Aspirin (n=4719): Patients who received aspirin ± mechanical prophylaxis and no other pharmacologic VTEP agent **Timing of intervention:** NR **Duration of intervention:** NR **Agent:** Aspirin, Warfarin, or Injectable VTEPs (LMWH Enoxaparin] or fondaparinux [Factor Xa inhibitor] **Monitoring intervention:** NA **Control group:** Warfarin (n=51,923): patients who received Warfarin as the VTEP Injectable (n=37,198): Patients who received VTEP with injectable agents (e.g. LMWHs or fondaparinux) **Standard preventive measures:** NR	**SSI (30 days)** Wound infection Aspirin: 559/4719 (12%) Injectable: 4366/37.198 (12%) Warfarin: 6349/51,923 (12%) SSI population: n=1037 Adjusted ORs (95%CI) Aspirin as referent Injectable: 1.08 (0.95-1.24) Warfarin: 1.10 (0.96-1.26) **Other infections:** NR **Topic-specific outcomes:** Any thromboembolism Aspirin: 110 (2.3%) Injectable: 1152 (3.1%) Warfarin: 2009 (4%) P<0.01 for all comparisons Adjusted ORs (95%CI) n=3271 Aspirin as referent Injectable: 1.03 (0.76-1.39) Warfarin: 1.36 (1.02 -1.82) P<0.01 for all comparisons Proximal DVT or PE Aspirin: 77 (1.6%) Injectable: 901 (2.4%) Warfarin: 1632 (3%) P<0.01 for all comparisons Adjusted ORs (95%CI) n=2610	**Definitions:** TKA – ICD-9-CM procedure code 81.45 Postoperative complications, including venous thromboembolism (any thromboembolic event including proximal or distal DVT as well as PE), proximal DVT and PE only; surgical site bleeding; and surgical site infection were defined using ICD-9-CM diagnosis codes recoded during the index admission as well as principal diagnosis associated with any readmissions occurring w/in 30 days of discharge. **Perioperative care:** NR **Analytical methodology** Alternating logistic regression models were used to assess the independent association between the 3 VTEP strategies and the risk of complications or death. A Propensity score was used in all models due to the threat of bias from group allocation. The resultant c-statistic was 0.725 which was

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			Aspirin 38% LMWH/fondaparinux 48% Warfarin 55% (p<0.001) **Procedures:** Total knee arthroplasty (TKA) **Indications:** NR **Setting:** Multicenter (307 Hospitals participating in a proprietary database developed for measuring quality and healthcare use in hospitalized patients) The centers are predominantly small to midsize nonteaching facilities serving a largely urban patient population. **Location:** USA **Dates:** October 2003 - September 2005 **Inclusion Criteria:** Patients admitted during the study dates, were ≥18 years old, and had primary TKA as their principal procedure during their hospitalization **Exclusion Criteria:** Patients with no charges for any VTEP treatments, and those who had charges for VTEP treatments in formulations representing therapeutic rather than prophylactic anticoagulation.		Aspirin as referent Injectable: 0.99(0.76-1.28) Warfarin: 1.34 (1.05 -1.70) P<0.01 for all comparisons <u>Bleeding related to wound site</u> Aspirin: 30 (0.6%) Injectable: 459 (1%) Warfarin: 548 (1%) P<0.01 for all comparisons Adjusted ORs (95%CI) n=1037 Aspirin as referent Injectable: 1.11 (0.77-1.60) Warfarin: 0.97 (0.65 -1.47) Ultrasound or venogram any time after operative day (n, %) Aspirin: 1 (0.02%) Injectable: 73 (0.20%) Warfarin: 28 (0.05%) Use of pneumatic compression devices Aspirin: 1795 (38%) Injectable: 17,756 (48%) Warfarin: 28,757 (55%) **Reoperations:** NR **Length of stay:** median (IQR) Aspirin: 1 (3-4) Injectable: 4 (3-4) Warfarin: 3 (3-4)	included in all core multivariable models as a covariate intended to adjust for allocation bias. In a secondary analysis, 3 propensity scores, including assignment to injectable VTEP vs. other VETP, etc. These scores did not substantially nor directionally alter the results, thus the first propensity score was used. **Other notes:** None **Follow-up:** 30 days **Funding Source Conflicts:** Authors: None Institution: None Study: None Supplies: None

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
					P<0.001 Patients on Aspirin also more likely to be discharged home (vs. an extended care facility) Aspirin 30% LMWH/fondaparinux 23% Warfarin: 21% P<0.001 **Mortality:** Aspirin: 9 (0.2%) Injectable: 45 (0.1%) Warfarin: 54 (0.1%) Adjusted ORs (95%CI) n=109 Aspirin as referent Injectable: 0.63 (0.30-1.34) Warfarin: 0.54 (0.25-1.15) **Adverse events:** NR	
Parvizi 2007 [179] (ES)	**Retrospect-ive Case Control** 1, 2, 3, 5, 6, 7, 8	To determine whether patients receiving excessive anticoagulation (an international normalized ratio [INR] of greater than clinically intended level) were at risk for developing wound-related problems, which in turn, predisposes them to	**Number of patients: N=234** **Patient Characteristics** ·Age: mean±SD (years) Cases: 66±10 Controls: 66±10 ·Gender: female (%) Cases: 36 (46%) Control: NR ·Obesity: BMI >30 kg/m2 Cases: 44 (56%) Control: 80 (51%) BMI 9kg/m^2 (mean±SD) Cases: 32±9 Controls: 32±7 ·Comorbidities: ASA Score (mean±SD) Cases: 2.6±0.57 Controls: 2.4±0.56 P=0.01	**Intervention group: n=78** Cases: Patients who developed periprosthetic infection **Timing of intervention:** pre-and postoperatively **Duration of intervention:** given on the day of surgery and continued for a period of 6 weeks. If patient a) was on anticoagulation before surgery for other conditions b) had known allergy to warfarin, or c) developed thromboembolism in the postoperative period; the	**SSI (adjusted results when possible; unadjusted otherwise)** Mean duration between index joint arthroplasty and development of infection was 256 days (range 4-1890 days) **<u>Multivariate analysis: Risk factors for periprosthetic infection (OR (95%CI)</u>** ASA score 2.07 (1.08-0.97); p=0.03 Postoperative Transfusions: 1.63 (1.14-2.33); P=0.007 Postoperative wound complications including development of hematoma:	**Definitions:** Periprosthetic infection: patient has at least 3 of 5 of the following criteria: 1) abnormal serology (erythrocyte sedimentation rate of >30mm/h; C-reactive protein level of >1mg/dL) 2) Strong clinical and radiographic suspicion for periprosthetic infection 3) positive joint aspiration culture for infection 4) evidence of purulence during the subsequent surgical intervention 5) Positive intraoperative

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
		periprosthetic infection. Ultimately, this study is to examine the correlation between anticoagulation and periprosthetic infection.	Diabetes mellitus Cases: 14 (18%) Control: 22 (14%) Steroid Therapy Cases: 8 (10%) Control: 5 (3%) P=0.03 NNIS≥1 Cases: 50 (64%) Control: 73 (47%) P=0.01 SURGICAL DATA Total Transfusion: mean±SD Cases: 0.78±1.15 Controls: 0.39±0.79 P=0.002 Allogeneic Transfusion Cases: 10 (13%) Control: 3 (2%) P=0.0006 Autologous Transfusion Cases: 47 (60%) Control: 111 (71%) P=0.09 **Procedures:** Primary TKA: Cases: 33/78 (%) Controls: NR Revision TKA: Cases: 10/78 (%) Controls: NR Primary THA: Cases: 12/78 (%) Controls: NR Revision THA Cases: 23/78 (%) Controls: NR	patient was given either subcutaneous and/or intravenous heparin as the sole or the bridging agent until adequate and full anticoagulation (goal INR-2-3) with oral agent could be established **Agent:** All patients in both groups were given low-dose warfarin (goal INR=1.5) unless indicated otherwise **Monitoring intervention:** INR **Control group: n=156** Controls: Patients undergoing TKA or THA who underwent same index procedure but did not develop a subsequent infection. **Standard preventive measures** AMP: Cephalosporin or an alternative for patients with penicillin allergies was administered within 60 minutes of arthroplasty procedure and continued for 24h postop. Antimicrobial was administered at a mean of 39 min pre-incision.	27.02 (11.04-91.59); p=0.0002 Wound Drainage: 32.20 (8.7-119.17); p<0.0001 **Other infections:** NR **Topic-specific outcomes:** Wound Hematoma Cases: 11 (14%) Control: 2 (1%) P=0.0001 Wound Drainage Cases: 24 (31%) Control: 4 (3%) P=0.0001 Other Complications (including PE, DVT & UTI) Cases: 18 (23%) Control: 18 (12%) P=0.02 Received injectable anticoagulant in addition to oral Cases: 13/78 (16.7%) (including 1 LMWH) Received intravenous heparin: Cases: 13/74 (16.7%) 9/13 heparinized resulted in would complications Hematoma: 3/9 Persistent wound drainage: 5/9 Delayed wound healing: 1/9 INR Mean INR>1.5 Cases: 16 (21%)	culture. Wound discharge beyond POD 7 was deemed clinically significant and abnormal. **Perioperative care:** NR **Analytical methodology:** Wilcoxon procedure: to perform unadjusted analysis to compare means across continuous variables. Fisher exact test: compare proportions across categorical variables. T-statistics for continuous variables X^2 for categorical variables Multivariate stepwise logistic regression was used to perform adjusted analysis **Other notes:** None **Follow-up:** NR **Funding Source Conflicts:** Authors: None Institution: None Study: None Supplies: None

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			Indications: Degenerative joint arthritis was the most common diagnosis in both groups. Posttraumatic arthritis: 4/234 (1.7%) Inflammatory arthropathy: 2/234 (0.9%) **Setting:** 1University Hospital **Location:** USA **Dates:** 2000 - 2005 **Inclusion Criteria:** All patients undergoing primary or revision total knee (TKA) or total hip arthroplasty (THA) for an aseptic diagnosis. **Exclusion Criteria:** NR		Control: 17 (11%) P=0.05; χ^2=3.97 INR at day of Discharge>1.5 Cases: 13 (17%) Control: 12 (8%) P=0.04; χ^2=4.39 INR>1.5 on day of discharge Wound complications:22% No Wound Complications: 8% P=0.005 INR level was statistically higher in patients with wound-related problems who later developed infection compared with patients who did not develop infection (p=0.03) **Reoperations:** Cases: 14 (18%) Control: 3 (2%) OR: 11.2; p<0.0001 <u>Indications for reoperations included:</u> CASES: Evacuation of hematoma: 9/14 (64.3%) Debridement and wash out of draining wound: 3/14 (21.4%) Debridement and closure for wound dehiscence: 2/14 (14.3%) CONTROLS Evacuation of hematoma: 2/3 (66.7%) Delayed wound healing: 1/3: (1%)	

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
					Length of stay: Cases: 6 (Range 1-11) days Controls: 4 (range 2-6) days P=0.006 **Mortality:** NR **Adverse events** Wound dehiscence developed in 2 patients both of whom later developed infection	
Patel 2007 [175] (ES)	**Retrospect-ive concurrent control** 1, 2, 3, 5, 6, 7, 8	The purpose of this study is to identify pharmacologic factors (prophylaxis against deep venous thrombosis), surgical factors (estimated blood loss and surgical time), and patient specific factors (BMI and drain output) that are associated with the time until postoperative wound is dry following primary total joint arthroplasty, and to determine whether	**Number of patients: N=2437** **Patient Characteristics** ·Age: mean (years) Infected THA: 59.1 Uninfected THA: 60.1 Infected TKA: 63.1 Uninfected TKA: 66.5 ·Gender: m/f Infected THA: 0.6%/1.2% Infected TKA: 0.3%/1.0% ·Obesity: NR ·Comorbidities: NR **Procedures:** Total Hip Arthroplasty (THA):1211 Total knee arthroplasty (TKA): 1226 **Indications:** NR **Setting:** 1 tertiary care teaching hospital. **Location:** USA **Dates:** January 1997 – July	**Intervention group: n=25** Patients undergoing THR(n=15) or TKR (n=10) assigned to receive Warfarin, LMWH or aspirin at the surgeon's preference who developed a postoperative wound infection **Timing of intervention:** postoperative **Duration of intervention:** variable **Agent:** Warfarin: target international normalized ratio (INR)= 2.0 Low-Molecular-Weight-Heparin(LMWH): started between 12-24 hours postop Aspirin (ASA): 325mg in conjunction with pneumatic compression devices started the	**SSI (unadjusted Follow Up NR)** **Overall:** 25/2412 (1.0%) THA: 15/1211 (1.2%) [5/15 had cellulitis which resolved with antimicrobials. 10/15 had persistent drainage despite 3 days IV antimicrobials and underwent operative irrigation and debridement] TKA: 10/1226 (0.8%) [7/10 had cellulitis which resolved with antimicrobials; 2/10 required component removal due to persistent infection; 1/10 underwent operative irrigation and debridement due to infected hematoma but joint components were retained] <u>Logistic regression analysis of variables influencing wound infection after THA: OR(95%CI)</u> Time until wound dry: 1.42 (1.18-1.71); p<0.001	**Definitions:** Normal Weight: BMI ≤24.9 kg/m^2 Overweight: BMI 25-29.9 kg/m^2 Obese: BMI 30.0-39.9 kg/m^2 Morbidly Obese: BMI ≥40 kg/m^2 Length of stay: time/date of admission to time/date of discharge (as determined by the surgeon) either to home or to a rehabilitation setting. The surgical wound was inspected daily with notation made of when the wound appeared dry according to the definition of Weiss and Krackow. Wound was considered actively draining if a ≥2x2-cm area of gauze covering the wound was wet or if fluid was noted to be

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
		prolonged wound drainage results in a longer hospital stay or increases the risk of early postoperative wound infection.	2004 **Inclusion Criteria:** Primary unilateral total hip and total knee arthroplasties in who closed suction drains had been utilized and who had a normal coagulation profile. **Exclusion Criteria:** NR	morning after surgery. **Monitoring intervention:** NA **Control group: n=2412** Patients undergoing THR (n=1196) or TKR (n=1216) assigned to receive Warfarin, LMWH or aspirin at the surgeon's preference who developed a postoperative infection **Standard preventive measures:** Drains: were removed at 36 hours postop or whenever drain output during any 8-h shift fell below 25mL. AMP: routine preoperative and postoperative prophylactic antimicrobials (cefazolin if patient was not allergic to penicillin, otherwise, clindamycin) including at least 30min prior to initial incision.	Coumadin vs. aspirin and pneumatic compression devices: 7.47 (0.62-89.3); p=0.112 LMWH vs. aspirin and pneumatic compression devices: 2.11 (0.24-18.5); p=0.499 <u>Logistic regression analysis of variables influencing wound infection after TKA: OR(95%CI)</u> BMI: 1.08 (1.01-1.16); p=0.018 LMWH vs. aspirin and pneumatic compression devices: 1.07 (0.23-4.95); p=0.932 **Other infections:** NR **Topic-specific outcomes:** <u>Regression Analysis of variables influencing Time until wound was dry after THA:</u> LMWH: Coefficient = 0.318 P=0.027 (compared with aspirin group) Morbidly Obese: Coefficient = 0.667; P=0.001 Drain Output: Coefficient – 0.002; P=<0.001 <u>Statistically Significant variables influencing Time until wound was dry after TKA:</u> Drain Output: coefficient = 0.0003; P=0.023 <u>Drain output:</u> THA group: every additional	originating from the site. (spotting on gauze was not considered to be actively draining) **Perioperative care:** NR **Analytical methodology:** Multiple linear regression analysis was used to model the effects of prophylaxis against deep venous thrombosis (DVT), BMI, age, & type of anesthesia on time to a dry wound. Multiple logistic regression analysis was used to calculate the OR between postop infection and the time to a dry wound while controlling for DVT prophylaxis, BMI, surgical time, EBL 7 Drain output. **Other notes:** None **Follow-up:** NR **Funding Source Conflicts:** Authors: None Institution: None Study: None Supplies: None

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
					100-mL increase in postop drain output resulted in an additional 0.20 day of wound drainage time. TKA group: every additional 100-mL increase in postop drain output resulted in an additional 0.03 day of wound drainage time. **Reoperations:** THA: 10/1211 (0.8%) 10/15 underwent operative irrigation and debridement TKA: 3/1226 (0.2%) 2/3 required component removal due to persistent infection; 1/3 underwent operative irrigation and debridement due to infected hematoma but joint components were retained **Length of stay:** There was a strong positive correlation between the length of hospital stay and the number of days until surgical wound was dry: r=0.29; p<0.001 THA: r=0.34; p<0.001 TKA: r=0.26; p<0.001 **Mortality:** NR **Adverse events:** NR	

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
Sachs 2003 [178] (ES)	**Retrospect-ive concurrent control** 1, 2, 3, 4, 5, 6	To determine the safety and efficacy of 6 weeks of low-dose warfarin when compared with no thromboprophylaxis in total knee arthroplasty using infection and complication rates as the primary outcome measures	**Number of patients: N=1742** **Patient Characteristics** ·Age: Median Age for both groups was 70 years. ·Gender: both groups included approximately 44% men and 56% women ·Obesity: NR ·Comorbidities: NR **Procedures:** Unilateral, Primary Total Knee Arthroplasty (TKA) **Indications:** NR **Setting:** Multicenter **Location:** USA **Dates:** 1995 - 2000 **Inclusion Criteria:** Patients who were treated with postoperative warfarin as recorded in the records of the "warfarin clinic" during the study dates. Patients underwent total knee arthroplasty and were operated on by one of 4 surgeons who were using warfarin on an unselected basis for several years. Controls were identified who were treated without any chemical or mechanical thromboprophylaxis and were operated on by 1 of 3 surgeons whose routine	**Intervention group:** n=957 Received low-dose warfarin as thromboprophylaxis **Timing of intervention:** Postoperative **Duration of intervention:** 6 weeks **Agent:** low-dose warfarin maintained at an international normalized ration (INR) from 1.6-2.2 for 6 weeks **Monitoring intervention:** NR **Control group: n=**785 Patients received no thromboprophylaxis. While in the hospital, this group did not receive any aspirin or NSAIDs and were not placed on any type of venous compression device. **Standard preventive measures:** Postoperative protocol: Continuous passive motion (CPM), physical therapy, and weight bearing, as well as most orders for pain control and nausea were essentially	**SSI (follow-up 3 months)** <u>Overall:</u> Warfarin: 9/957 (0.94%) No Prophylaxis: 5/785 (0.64%) <u>Superficial infection</u> Warfarin: 3 (0.4%) [two required readmission and IV antimicrobial therapy; one treated with an oral antimicrobial and developed wound necrosis and required readmission and plastic surgery] No Prophylaxis: 3 (0.3%) [two required readmission and IV antimicrobials] <u>Deep Wound Infection</u> Warfarin: 6 (0.6%) [6 required surgery, 5 with successful resolution; 1 required 5 subsequent surgeries without resolution; 1 developed necrosis requiring readmission and surgery for wound coverage and closure] No Prophylaxis: 2 (0.3%) [both required readmission and surgery] Wound Necrosis(described above) Warfarin: 2 (0.2%) No Prophylaxis: 0 (0%) <u>Total Complication Rate (including infections)</u> Warfarin: 17 (2.2%) No Prophylaxis: 45 (4.7%)	**Definitions:** NR **Perioperative care:** Patients were encouraged to undergo spinal anesthesia **Analytical methodology:** Chi-square analysis, Mann-Whitney test **Other notes:** None **Follow-up:** 3 months postop **Funding Source Conflicts:** Authors: None Institution: None Study: None Supplies: None

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			was to avoid thromboprophylaxis during TKA **Exclusion Criteria:** Patients undergoing bilateral or revision TKA, patients on warfarin prophylaxis for previous chronic arterial fibrillation or thromboembolic events	the same for all patients. Both groups received initial wound care from a small group of orthopedic "special care nurses" who performed dressing changes, suture removal and wound observations for the first month after surgery.	P<0.01 <u>One or more complication</u> Warfarin: 5% No Prophylaxis: 2% **Other infections:** Pneumonia Warfarin: 5 (0.5%) No Prophylaxis: 1 (0.1%) **Topic-specific outcomes:** DVT Warfarin: 2 (0.2%) [two calf vein DVTs] No Prophylaxis: 0 (0%) PE Warfarin: 1 (0.1%) [required readmission] No Prophylaxis: 2 (0.3%) [these two events were non-fatal occurring within initial hospitalization and resolved with treatment **Reoperations:** Subsequent surgeries Warfarin: 11 (1.1%) No Prophylaxis: 2 (0.3%) X^2=4.66; P<0.01 **Length of stay- NR** **Mortality:** Deaths (within 90 days) Warfarin: 1 (0.1%); patient admitted 1w postop with GI bleed, unsuccessful attempts to control resulted in myocardial infarction and death No Prophylaxis: 2 (0.3%); 1 in 91yo patient who sustained a fata myocardial infarction 5w postop; 1 in a 73yo patient without prior	

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
					history of cardiac disease readmitted in congestive heart failure 11 days postoperatively, contracted pneumonia and expired None due to thromboembolic disease **Adverse events:** New Arrhythmia Warfarin: 6 (0.6%) No Prophylaxis: 1 (0.1%) All recovered Angina Warfarin: 5 (0.5%) No Prophylaxis: 0 (0%) MI Warfarin: 3 (0.3%) No Prophylaxis: 2 (0.3%) TIA Warfarin: 1 (0.1%) No Prophylaxis: 1 (0.1%) CVA Warfarin: 2 (0.2%) No Prophylaxis: 1 (0.1%) GI Bleeding Warfarin: 3 (0.3%) No Prophylaxis: 0 (0%) Other Warfarin: 7 (0.7%) No Prophylaxis: 4 (0.5%)	

Q17C. How safe and effective is modifying the dose of the perioperative VTE prophylaxis agent to reduce the risk of SSI? Our search did not identify data that evaluated the safety and effectiveness of modifying perioperative VTE prophylaxis and its impact on the risk of SSI.

2.2C.3. RISK OF BIAS ASSESSMENTS OF STUDIES: Q17 ANTICOAGULATION

eTABLE 64. Risk of Bias Assessment of Systematic Reviews for Q17 Anticoagulation

Author Year	Q	Search terms described	Databases described and two or more databases searched	Inclusion/exclusion criteria described	Number of included/excluded studies along with reasons of exclusion described	Studies screened by two independent reviewers for inclusion	Data extracted by two independent reviewers	Individual study quality assessed	Heterogeneity between study results assessed qualitatively and/or quantitatively	Publication bias assessed	Characteristics of included studies reported in evidence table	Funding source(s) disclosed and no obvious conflict of interest	Overall Risk of Bias
Question 17: Anticoagulation													
Turpie 2002 [166]	17			✓	✓								High

eTABLE 65. Risk of Bias Assessments of Randomized Controlled Trials for Q17 Anticoagulation

Author Year	Q	Described as randomized	Randomization appropriately performed	Described as double-blind	Outcome assessor blinded	Study participant blinded	Investigator blinded	Attrition described	Attrition smaller than 10-15% of assigned patients	Attrition appropriately analyzed	Funding source(s) disclosed and no obvious conflict of interest	Overall Risk of Bias
Question 17: Anticoagulation												
Eriksson 2008 [171]	17	✓	✓	✓	✓	✓		✓	✓	✓		Low
Kakkar 2008 [172]	17	✓	✓	✓	✓	✓	✓	✓	✓	✓		Low
Lassen 2008 [173]	17	✓	✓	✓	✓	✓		✓	✓	✓		Low
Turpie 2009 [174]	17	✓	✓	✓	✓	✓		✓	✓	✓		Low

eTABLE 66. Risk of Bias Assessments of Other Controlled Studies for Q17 Anticoagulation

Author Year	Q	All study groups derived from similar source/reference populations	Attrition not significantly different across study groups	Measure of exposure is valid	Measure of outcome is valid	Investigator blinded to endpoint assessment	Potential confounders identified	Statistical adjustment for potential confounders done	Funding source(s) disclosed and no obvious conflict of interest	Overall Risk of Bias
Question 17: Anticoagulation										
Asensio 2010 [176]	17	✓	✓	✓	✓	✓	✓	✓	✓	Low
Bozic	17	✓	✓	✓	✓	✓	✓	✓	✓	Low

Author Year	Q	All study groups derived from similar source/reference populations	Attrition not significantly different across study groups	Measure of exposure is valid	Measure of outcome is valid	Investigator blinded to endpoint assessme-nt	Potential confoun-ders identified	Statistical adjustment for potential confounders done	Funding source(s) disclosed and no obvious conflict of interest	Overall Risk of Bias
2010 [177]										
Parvizi 2007 [179]	17	✓	✓	✓	✓	✓	✓	✓	✓	Low
Patel 2007 [175]	17	✓	✓	✓		✓	✓	✓	✓	Low
Sachs 2003 [178]	17	✓	✓	✓	✓	✓	✓			Low

2.2D. Q18 ORTHOPAEDIC SPACE SUIT

2.2D.1. GRADE TABLE: Q18 ORTHOPAEDIC SPACE SUIT

eTABLE 67. GRADE Table for Q18 Orthopaedic Space Suit

Comparison	Outcome	Quantity and Type of Evidence	Findings	Starting GRADE	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Confounders		
Q18. How safe and effective are orthopaedic space suits in reducing the risk of SSI in prosthetic joint arthroplasty patients and then which healthcare personnel should wear them?														
Space Suit vs. No suit	Deep SSI requiring reoperation*	1 OBS [180]	• One retrospective study (N=8288) in TKA using Medicare claims data, found no difference in risk of deep SSI requiring reoperation within 90 days of surgery: 0.28% (0.11-0.46) vs. 0.38% (0.20-0.55); RR 0.75 (0.34-1.62) • Deep Infections identified through ICD9-CM diagnosis codes for multiple joint/bone infection, debridement, and implant removal codes (not revision total joint arthroplasty codes). In this study deep infection might be referring to PJI. • Use of laminar flow varied between groups.	Low	0	0	0	-1	0	0	0	0	Very Low	Very Low
	Deep SSI requiring revision*	1 OBS [181]	• One study large joint registry study (N=88,311) with multiple subgroup analyses, found use of space suits was associated with an increased number of deep SSIs requiring revision surgery within 6 months of THA or TKA (P<0.01) but this evidence is limited in size (only 96 events or 0.109%): • The results did not differ in the presence or absence of laminar flow • Deep SSI in this study might be referring to PJI. • 60% of primary procedures used antimicrobial impregnated cement.	Low	0	0	0	-1	0	0	0	0	Very Low	

Comparison	Outcome	Quantity and Type of Evidence	Findings	Starting GRADE	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Confounders		
	Deep SSI*	1 OBS [182]	• One small study (N=62) evaluating contamination using space suit or conventional gowns with single hood plus surgical mask, during THA or hip hemiarthroplasty reported only 1 deep SSI in the exhaust suit group (11 days postop) but this evidence is limited in size: 1/31 (3.2%) vs. 0/31. (24 month follow up). • Statistical significance was not reported. • HEPA filtration was present in both study groups. • Deep SSI was not defined-in this study might be referring to incisional SSI • Study was designed to evaluate contamination	Low	0	0	0	-1	0	0	0	0	Very Low	
	Superfi-cial SSI	1 OBS [182]	• One study (14,484) found no difference in risk of superficial SSI for patients undergoing THA or hip hemiarthroplasty: 1 (3.2%) superficial SSI in each group at 16 and 15 days postoperatively, respectively. Follow up 24 months. • Statistical significance was not reported. • HEPA filtration was present in both study groups.	Low	0	0	0	-1	0	0	0	0	Very Low	

*Critical outcome; OR: Odds Ratio; RR: Risk Ratio; CI: Confidence Interval

2.2D.2. EVIDENCE TABLE: Q18 ORTHOPAEDIC SPACE SUIT

eTABLE 68. Evidence Table for Q18. How safe and effective are orthopaedic space suits in reducing the risk of SSI in prosthetic joint arthroplasty patients and then which healthcare personnel should wear them?

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
Hooper 2011 [181] (ES)	**Retrospe-ctive concurre-nt control** 1, 2, 3, 4, 5, 6, 8	To review the New Zealand Joint Registry to determine if the use of laminar flow and protective suits with hoods and self-contained exhaust systems (space suits) would reduce the rate of early deep infection requiring a revision procedure following total hip (THR) and knee (TKR) replacements at 10 years	**Number of patients: N=88,311** Primary THR: 51,485 Primary TKR: 36,826 **Patient Characteristics:** recorded, not reported but narrative details that there were no significant differences in clinical details between the groups and there was similar duration of operations ·Age: NR ·Gender: NR ·Obesity: NR ·Comorbidities: NR **Procedures:** Total Hip replacement (THR) and total knee replacement (TKR) and revisions due to early infections. **Indications:** Osteoarthritis: 94% for both THR and TKR Inflammatory Arthritis: THR: 3% TKR: 4%	**Intervention group:** Intervention1: Space Suit n=20,385 THR: 21% (n=10,811) TKR: 26% (n=9,574) Intervention2: Laminar Flow Theater: n=30,983 THR: 33% (n=16,990) TKR: 38% (n=13,993) Note: Authors only provide percentages; "n" was calculated. Intervention3: Both Space Suit and Laminar Flow-Numbers not reported (See Other Notes) **Timing of intervention:** intraoperative **Duration of intervention:** intraoperative **Device:** either laminar air flow or protective suits with hoods and self-contained exhaust systems (space suits) or both. Laminar Flow: All hospitals confirmed that they had a regular maintenance program for filters. There were no hospitals which used laminar flow combined with a complete surgical enclosure. Space Suits: All the suits	**SSI (Follow up: ≥ 6 months)** **Unadjusted results:** **THR** Early revision for deep infection: 46/51485 (0.089%) Intervention1- Space Suit: 0.186% Control1-No Space Suit: 0.064% P<0.0001 Intervention2- Laminar Flow theater: 0.148% Control2-conventional theater: 0.061% P<0.003 Intervention3-BothSpace suit + laminar flow: 0.198% Control3 -Neither No Space suit in a conventional OR: 0.053% P<0.001 From Figure 1c (Bar Graph- details not reported in text) Conventional OR: Suit: ~0.15% No Suit: 0.053% Laminar Flow OR: Suit: 0.198% No Suit:~ 0.10% P values for above NR SURGEON SPECIFIC SURGICAL PRACTICE INFECTION RATES	**Definitions:** SSI- deep (joint space) Revision due to early infection: any such procedure performed within 6months of the initial operation **Perioperative care:** NR **Analytical methodology:** Percentages with revision for deep infection were compared between groups using the Chi-squared test or Fisher's exact test when expected frequencies were low. A p-value of <0.05 was considered significant **Other notes:** There was a steady increase in the use of intervention procedures and In 2008 almost half of all procedures were performed in laminar-flow theaters with space suits

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			Setting: Multi-center (64 hospitals) **Location:** New Zealand **Dates:** 1999-2008 **Inclusion Criteria:** All primary THR & TKR and revisions due to early infections with full information on theater environment and a minimum follow up of 6 months. Specifically surgeons who had experience in both conventional and laminar-flow operating theaters and who had performed at least 50 procedures in both. Also surgeons who had used space-suits in both settings and who had completed at least 50 procedures in each **Exclusion Criteria:** NR	were contemporary in design and no surgeon worked in a fully-enclosed space. No surgeon worked with all staff in the theater. **Monitoring intervention:** NR **Control group:** n=NR Control1: (n=67,926) THR or TKR performed without Space Suit THR: 79% (n=40,674) TKR: 74% (n=27,252) Control2: (n=57,328)THR or TKR performed In Conventional theater THR: 67% (n=34,495) THR:62% (n=22,833) Control3: in conventional theater with no space suit **Standard preventive measures:** **Non-standard preventive measures:** AMP: in New Zealand, prophylactic antimicrobials are given for most THR and TKR procedures. (Registry shows 96%) Antimicrobial agent in cement: Registry data shows 60% utilization rate	33 surgeons did or did not wear space suits Intervention1 (with space suit): 0.082% Control1 (without space suit) :0.057% P=0.755 43 surgeons performed more than 50 operations in both operating environments Intervention2(Laminar Flow): 0.110% Control2 (Conventional OR): 0.028% P<0.03 30 surgeons used both space suit AND laminar flow or neither Intervention3 (space suit AND laminar flow): 0.1035% Control3 (NO space suit AND conventional OR): 0/3598 procedures P=0.09 **TKR** Early revision for deep infection: 50/36826 (0.136%) Intervention1- Space Suit: 0.243% Control1-No Space Suit: 0.098% P<0.001 Intervention2- Laminar Flow theater: 0.193% Control2-conventional theater: 0.100% P<0.019	The registry captures 98% of both primary and revision arthroplasties performed in New Zealand and records revision procedures secondary to deep infection. **Surgeon Questionnaire**: They compared rates for surgeons who used space suits in both operating room settings (laminar flow and conventional) and completed at least 50procedures in each (similar surgical practices). Questionnaire requested information on frequency of suit use, members of the team who wore them, whether practice changed depending on OR team and whether they wore full suits or just hood/exhaust system.

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
					Intervention3-Both Space suit AND Laminar Flow: 0.25% Control3-Neither (No Space suit AND Conventional OR): 0.087% P<0.001 From Figure 2c (Bar Graph- details not reported in text) Conventional OR: Suit: ~0.25% No Suit:0.087 % Laminar Flow OR: Suit: 0.25% No Suit:~0.12 % P values for above NR SURGEON RELATED INFECTION RATES 23 surgeons ± space suits: Intervention1 (Space suit): 0.251% Control1 (No Space suit):0.028% P=0.016 32 surgeons performed more than 50 operations in both operating environments Intervention2 (Laminar Flow): 0.147% Control2 (Conventional OR): 0.189% P=0.597 NOTE: One hospital of 64 was identified as having a significantly increased rate of revision for early deep infection when the use of a	Discussion comments regarding potential reasons for increased rate of infection with use of space suit include: Observers in OR have noted surgeons often adjust suit or hood during procedure and subsequently unknowingly contaminate their gloves. Exhaust system – there is no information as to the flow of the expelled air from exhaust systems and whether air is concentrated with debris and significant numbers of colony forming units close to the surgical site. **Follow-up:** Minimum 6 months **Funding Source Conflicts:** Authors: None Institution: None Study: None Supplies: None

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
					conventional theater and no space suit was compared with laminar flow with a space suit. The hospital contributed only a small number to the database and when these were removed from the analysis, there was no change in the significance of the results. **Other infections:** NR **Topic-specific outcomes:** Surgeon Questionnaire 35/60 (58.3%) response rate Space suit used in all replacement procedures: 35/35 Surgical technique the same regardless of laminar flow vs. conventional OR: 35/35 Full space suit: 28/31 OR team members wearing full suit: surgeon, assistant and scrub nurse. OR team members NOT wearing space suit: anesthetist or technician **Reoperations:** All infections were reoperations **Length of stay:** NR **Mortality**: NR **Adverse events**: **Surgeon Questionnaire:** Spatial awareness limited by hood (space suit)	

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
					"Easier to contaminate themselves while wearing space suit since there was an apparent false sense of security within it"	
Miner 2007 [180] (ES)	**Retrospe-ctive concurre-nt control** 1, 2, 3, 5, 8	To assess the current effects of laminar airflow systems and body exhaust suits on the risk of postoperative infections via a secondary analysis of data collected for a larger study of hospital characteristic and patient outcomes after total knee replacement (TKR)	**Number of patients: N=8288 procedures** **Patient Characteristics:** NR ·Ag: NR ·Gender: NR ·Obesity: NR ·Comorbidities: NR **Procedures:** Unilateral primary total knee replacement (TKR) **Indications:** NR **Setting:** 256 centers in Illinois, Ohio, North Carolina and Tennessee that submitted a claim for TKR during 2000 **Location:** USA **Dates:** January 1 – August 30, 2000	**Intervention group**: Intervention1: n=3538 Patients in Hospitals which used exhaust suits in more than 75% of procedures Intervention2: n=3513 Patients in Hospitals which used laminar air flow in more than 75% of procedures **Timing of intervention:** Intraoperative **Duration of intervention:** Intraoperative **Device:** Laminar air flow or Exhaust suits. Laminar air flow: horizontal and vertical laminar airflow systems were combined into a single group that represented regular use of laminar air flow. Exhaust Suit: Not indicated: who wore	**SSI (follow up 90 days) Unadjusted results** Overall 90-day cumulative incidence of deep infection requiring reoperation: 28/8288 TKR (0.34%)BODY EXHAUST SUIT Intervention1: 10/3538 (0.28% (95%CI: 0.11-0.46)) Control1: 18/4750 (0.38 (95%CI: 0.20-0.55)) Risk Ratio (95%CI) for Body Exhaust Suit: 0.75 (0.34-1.62) LAMINAR AIR FLOW Intervention2: 15/3513 (0.43% (95%CI: 0.21-0.64)) Control2: 13/4750 (0.27 (95%CI: 0.12-0.42)) 28 TKR were performed in 25 hospitals. **Other infections:** NR **Topic-specific**	**Definitions**: SSI-deep prosthetic joint infection Infection: International Classification of Diseases, Ninth revision (ICD-9) diagnosis and procedures codes for evidence of postoperative deep infection that required additional operation. Reoperations within 90 days **Perioperative care**: NR **Analytical methodology:** None Did not adjust for clustering of events within hospitals bb/c 22/25 hospitals with infections reported only a single infection and

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			Inclusion Criteria: Data from Medicare claims parts A and B to identify unilateral primary TKRs. For patients with a second TKR during a separate hospitalization, only the first procedure was considered. Hospitals had to meet the following criteria: 1. The orthopedic administrator returned the survey on use of laminar airflow systems (horizontal or vertical) and body exhaust suits during TKR in year 2000, 2. The survey contained information regarding use of laminar airflow systems and body exhaust suits as infection control measures, and 3. There was evidence of at least 1 Medicare claim for a TKR performed during January 1	exhaust suits, specifics of design. OR Flow or traffic **Monitoring intervention**: NR **Control group:** Control1: n=4750 Patients in Hospitals which used exhaust suits at frequencies of "not at all", "used in less than 26% of procedures," "used in 26%-75% of procedures"Control2: n=4775 Patients in Hospitals which used Laminar Air Flow at frequencies of "not at all", "used in less than 26% of procedures," "used in 26%-75% of procedures" **Standard preventive measures:** Use of laminar air flow and exhaust suit was distributed roughly independently among hospitals. Most hospitals reported that these methods were either part of their standard infection control practices (used>75% of time) or not at all.	**outcomes:** 30% of hospitals in analysis reported regular use of laminar airflow systems 41% of hospitals in this analysis reported regular use of body exhaust suits. **Reoperations:** All incidences of infection were reoperations within 90 days. **Length of stay:** NR **Mortality:** NR **Adverse events:** NR	because no hospital reported more than 2 infections. **Other notes:** UV Light use-collected data on use of UV lights but this was used only at 13/256 hospitals and did not allow analysis of effect on infectious outcomes. Low number of events (n=28) yielded low power to exclude potential benefits. Also precluded analysis of subgroups and interactions between infection control techniques. Also potential for misclassification of individual procedures (focus on hospital standard practice)-infections associated with hospitals classified as using intervention technique most of the time, could have occurred in patients for whom the technique was

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			and August 1, 2000 **Exclusion Criteria:** Bilateral TKR during the same hospitalization.			not use. **Follow-up:** 90 days **Funding Source Conflicts:** Authors: None Institution: None Study: None Supplies: None
Pasquar-ella 2003 [182] (ES)	**Prospecti-ve Concurre-nt control** 1, 2, 3, 4, 5,	To evaluate the effect on aerobic bacterial sedimentatio n of a mixed operating theater ventilation with separate operating and anesthetic areas and to compare the contaminatio n using body exhaust gowns or conventional clothing during hip joint Arthroplasty (THR and hemiarthropl asty)	**Number of patients: N=62 operations** **Patient Characteristics** ·Age: mean 70.80 years range= 30-95 years SD=12.39 ·Gender: m/f: 33/29 ·Obesity: NR ·Comorbidities: NR **Procedures:** Total hip replacements (THR) or hemiarthroplasties **Indications:** Hemiarthroplasties: either coxoarthrosis or fracture (trauma) THR: NR **Setting:** Orthopedic department in 1 hospital **Location:** Switzerland **Dates:** December 1997-January 1998 **Inclusion Criteria:** Patients scheduled for THR or hemiarthroplasties	**Intervention group:** n=31 Body exhaust suits were worn by one surgeon, the first assistant and the scrub nurse who remained seated throughout the whole operation. The circulating nurse wore a conventional gown. Operation was conducted in a diluted airflow system with separation zones. **Timing of intervention:** Intraoperative **Duration of intervention**: Intraoperatively **Device:** Diluted airflow system with separation zones: Unidirectional airflow system where the air is forced through a 0.3µm H14 99.995% HEPA (high efficiency particulate air) filter and supplied through eight air ceiling diffusers located over the operating table	**SSI (follow up 24 months)** **Unadjusted:** Total: 3/61 (4.8%) Deep: 1/61 (1.6%) Superficial: 2/61 (3.2%) Intervention (Exhaust suit): Deep: 1/31 (3.2%) postop day 11 Superficial: 1/31 (3.2%) postop day 16 Control (conventional gown): Deep: 0/31 Superficial: 1/31 (3.2%) postop day 15 **Other infections:** NR **Topic-specific outcomes:** NA **Reoperations:** NR **Length of stay:** NR **Mortality:** NR **Adverse events:** NR	**Definitions:** Deep and superficial wound infections not defined but recorded. **Perioperative care:** Anesthesia: either general or spinal. **Analytical methodology:** Settle plate results were compared between patient and anesthetist areas and between conventional gowns and body exhaust suits using Mann-Whitney U tests after normality checking to establish significant differences between variables. **Other notes:** None **Follow-up:** 24 months **Funding Source Conflicts:**

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			for either coxoarthrosis or fracture between the study dates **Exclusion Criteria:** NR	and the instrument table. The air is extracted by means of two floor-level return air grilles in the walls of the anesthetic area. Air turnover rate ≈24 air changes /h with a positive pressure of 2 Pa. A plexiglass barrier separates the OR into the patient area and the anesthetic area. The Patient's head and the anesthesiologist remain outside the patient area during the operation. Body exhaust suit: Manufacturer named but suit not described. Conventional Gowns: 65% polyester 35% cotton with the head cover consisting of a single hood plus surgical mask and the neck remaining partially exposed. **Monitoring intervention:** NA **Control group**: n=31 Conventional gowns worn by all surgical staff during operation in diluted airflow system with separation zones **Standard preventive measures:** AMP: IV injection of cefamandole 30min before anesthesia		Authors: NR Institution: NR Study: NR Supplies: Industry

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
				followed by a second dose of cefamandole in operations lasting longer than 2h. <u>Operating Room Traffic:</u> Operating Team (1 surgeon, 2 assistants, 2 nurses) same for all procedures. Surgeon first assistant and scrub nurse remained seated entire operation (second assistant stood at opposite end of room and circulating nurse moved around). Extraneous personnel were excluded from the OR. Swing doors were closed to all personnel after the final preparation of the patient on the operating table.		

2.2D.3. RISK OF BIAS ASSESSMENTS: Q18 ORTHOPAEDIC SPACE SUIT

eTABLE 69. Risk of Bias Assessments of Other Controlled Studies for Q18 Orthopaedic Space Suit

Author Year	Q	All study groups derived from similar source/reference populations	Attrition not significantly different across study groups	Measure of exposure is valid	Measure of outcome is valid	Investigator blinded to endpoint assessme-nt	Potential confound-ders identified	Statistical adjustment for potential confounders done	Funding source(s) disclosed and no obvious conflict of interest	Overall Risk of Bias
Question 18: Surgical Attire										
Hooper 2011 [181]	18	✓	✓	✓	✓	✓	✓		✓	Low
Miner 2007 [180]	18	✓	✓	✓		✓			✓	Low
Pasquarel-la 2003 [182]	18	✓	✓	✓	✓	✓				Low

2.2E. Q20 BIOFILM

2.2E.1. GRADE TABLE: Q20 BIOFILM

eTABLE 70. GRADE Table for Q20 Biofilm

Comparison	Outcome	Quantity and Type of Evidence	Findings	Starting GRADE	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Confounders		
Q20. What are the most effective strategies to reduce the risk of biofilm formation and SSI in prosthetic joint arthroplasty patients? **Q20A. How effective are cement modifications (i.e., antimicrobial and nanoparticle loading)?**														
Cefuroxime loaded cement vs. plain cement; both groups with perioperat-ive AMP	Deep SSI*	2 RCT [183,184]	• Meta-analysis 2 RCTs (N=418), reduced risk for deep SSI in primary hybrid TKA (cemented tibial and patellar components) with cefuroxime 2g in 40g polymethylmethacrylate loaded cement: OR: 0.08 (0.01 – 0.59); p=0.01; I^2=0 • 1 study[183] in 350 TKAs, non-diabetics: 0/178 vs. 5/162 (3.1%); p=0.02 • 1 study[184] in 78 TKAs, all diabetics: 0/41 vs. 5/37 (13.5%); p=0.02 • Based on definition deep SSI included PJI • All TKAs performed by same surgeon, in operating rooms without ultraviolet light, laminar flow, or orthopaedic space suit • AMP included parenteral cefazolin and gentamycin preoperatively then every 6 and 12 hours, respectively postop for 36 hours followed by cefazolin orally for 7 more days.	High	0	0	0	0	-1	0	0	0	Moderate	Moderate
	Superfi-cial SSI	2 RCT [183,184]	• Meta-analysis 2 RCT (N=418), no difference OR: 0.91 (0.18 – 4.55); p=0.90; I^2=0 • In one study[183] of 350 TKAs for osteoarthritis with no diabetes mellitus: 2/178 vs. 2/162; p=1.00 • In one study[184] of 78 TKAs all with diabetes mellitus: 1/41 vs. 1/37; p=0.84	High	0	0	0	-1	-1	0	0	0	Low	

Comparison	Outcome	Quantity and Type of Evidence	Findings	Starting GRADE	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality	Consistency	Directness	Precision	Publication Bias	Large Magnitude	Dose-response	Confounders		
Q20B. How effective are prosthesis surface modifications (i.e., antimicrobial coating, galvanic couples, "printing" technologies, and nanotechnology)? Our search did not identify in vivo studies that evaluated the safety and effectiveness of prosthesis modifications and their impact on biofilm formation and the risk of SSI.														
Q20C. How effective are vaccines? Our search did not identify in vivo studies that evaluated the safety and effectiveness of vaccines and their impact on biofilm formation and the risk of SSI.														
Q20D. How effective are other biofilm control agents (e.g., biofilm dispersants, quorum-sensing inhibitors, novel antimicrobial agents)? Our search did not identify in vivo studies that evaluated the safety and effectiveness of biofilm control agents and their impact on biofilm formation and the risk of SSI														

*Critical outcome; OR: Odds Ratio; RR: Risk Ratio; CI: Confidence Interval

2.2E.2. EVIDENCE TABLE: Q20 BIOFILM

Q20. What are the most effective strategies to reduce the risk of biofilm formation and SSI in prosthetic joint arthroplasty patients?

eTABLE 71. Evidence Table for Q20A. How effective are cement modifications (i.e., antimicrobial and nanoparticle loading)?

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
Chiu 2002 [183] (ES)	**RCT** 1, 5, 10	To evaluate the efficacy of cefuroxime-impregnated cement in the prevention of deep infection after primary total knee arthroplasties performed without clean-air measures such as laminar flow and body-exhaust suits.	**Number of patients:** N=285 patients (340 knees) **Patient Characteristics:** Age, tourniquet time, operative time, amount of blood transfusion, The Hospital for Special Surgery Knee Score (pre & post operatively), sex, side of operation, and preoperative diagnosis were all analyzed and were found to be similar between groups. Age: Mean ±SD Intervention :70±7.4yr Control:68±6.9yr Gender: (m/f) Intervention :69%/31% Control:70%/30% Obesity: NR Comorbidities: NR Operation Side: (left/right) Intervention :51%/49% Control:55%/45% **Procedures**: Primary total knee arthroplasties with cementless fixation of the femoral	**Intervention group:** n=178 knees Cefuroxime-impregnated cement (2g of cefuroxime in 40 g cement) was utilized for fixation of the tibial an patellar components only **Timing of intervention**: Intra and postoperatively **Duration of intervention**: The duration of implantation (indefinitely). **Device:** Cefuroxime-impregnated cement; pure cement without cefuroxime; prosthetic knee **Monitoring intervention:** Radio graphic evaluation at every visit & functional evaluation (Hospital for Special Surgery score) performed at every visit starting with the 3rd postop visit. **Control group:** n= 162 knees Cement did not contain cefuroxime. Only tibial and patellar components were fixed with cement. **Bilateral TKAs:** n=55 patients ; one knee treated with intervention, the other	**SSI: (range 26-80 months)** Early Superficial Infections: Intervention: 2/178 (1.1%) Control: 2/162 (1.2%) *P*=1 Early or Intermediate Deep Infections: Intervention: 0/178 Control: 5/162 (3.1%) Early: 3/5 (60%) Intermediate: 2/5 (40%) *P*=0.0238 *No deep infections in bilateral procedures* **Other infections**: NR **Topic-specific outcomes:** NR **Re-operations attributable to SSI:** All four early superficial wound infections were treated with wound debridement & intravenous antimicrobials for 1 week then oral antimicrobials for another week. **Length of stay:** Mean Stay, days (range): 8 days (5-15 days) **Mortality:** NR **Adverse events:** Loose femoral component at 2 years: Intervention: 1/178 (0.6%) – underwent revision of the femoral component Not significant statistically with	**Definitions: (McQueen 1990)** Superficial Infection – infection superficial to the deep fascia with positive or negative cultures and no delays in wound healing. Deep Infection – Infection extending deep to the deep fascia, with persistent wound discharge or joint pain, positive or negative cultures from deep tissues and delays in wound healing. Deep Infections also confirmed by laboratory parameters (the erythrocyte sedimentation rate & level C-reactive protein) & positive culture of joint fluid. Early Infections: Developing <2 months after operation Intermediate Infections: Developing 2-24 months after operation Late Infections: Developing >24 months after operation. **(Rand 1993)**

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			component and cement fixation (mixing method of cement NR) of the patellar and tibial components. **Indications**: <u>Osteoarthritis:</u> Control: 146/162 (90.1%) Intervention: 154/178 (86.5%) <u>Rheumatoid Arthritis</u> Control: 6/162 (3.7%) Intervention: 10/178 (5.6%) <u>Posttraumatic arthritis:</u> Control: 6/162 (3.7%) Intervention: 10/178 (5.6%) <u>Gouty arthritis</u> Control: 2/162 (1.2%) Intervention: 1/178 (0.6%) <u>Osteonecrosis:</u> Control: 1/162 (0.6%) Intervention: 3/178 (1.7%) **Setting:** 1 Hospital **Location:** Taiwan, China **Dates:** 1994-1998 **Inclusion Criteria:** Patients undergoing primary total knee arthroplasty **Exclusion Criteria:** Patients with diabetes mellitus, peripheral arterial occlusive	with controls **Standard preventive measures:** Environmental: No ultraviolet light for disinfection; no laminar flow nor body-exhaust suits were used. AMP Preop: intravenous bolus injections of cefazolin & gentamicin. AMP Postop: Intravenous injections of cefazolin every 6hrs for 36 hours; Intravenous injections of gentamicin every 12hrs for 36 hours; and oral cefazolin every 6hrs for 7 days. Drain: Used routinely and removed on the 2nd day. Continuous passive motion: used every day until discharge Weight bearing: on the involved knee was allowed form the second postoperative day and crutches were used as needed	available numbers Patellar fracture after traumatic episode: Control: 1/162 (0.6%) – treated with ORIF with tension band wiring	**Follow-up:** at 3 weeks, 8 weeks, and 6 months then every 6 months thereafter. Average was 49 months (Range 26-80 months) **Perioperative care:** NR **Other notes:** All surgeries performed by 1 surgeon The authors report the operating room was not modern like more developed countries with better facilities. This study was an effort to show that antimicrobial impregnated cement could be utilized as part of a bundle to reduce SSI without clean air facilities. **Funding Source Conflicts:** Authors: None Institution: None Study: None Supplies: None

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			disease, psoriasis, prior knee surgery, any kind of lower-extremity infection, osteomyelitis, or a malignant tumor who were being treated with immunosuppressive agents.			
Chiu 2001 [184] (ES)	**RCT** 1, 5, 10	To evaluate the effect of antimicrobial (cefuroxime) impregnated cement on the prevention of deep infection after primary total knee arthroplasty (TKA) in patients with diabetes mellitus (DM).	**Number of patients**: N=78 **Patient Characteristics:** Age; sex; side of operation; type of diabetes; type of diabetic treatment; duration of diabetes mellitus; tourniquet time; operation time, volume of blood transfusion; preoperative fasting blood sugar; preoperative "2 hours post meal" blood sugar; postoperative fasting blood sugar, postoperative "2 hours post meal" blood sugar; preoperative knee score; and postoperative knee score were all analyzed and found to be similar between groups except postoperative knee score (HHS-functional) Age: mean (range) Intervention: 72y (56-	**Intervention group:** n=41 knees (35 patients-6 Bilateral TKA) Cefuroxime-impregnated cement (2g of cefuroxime in 40 g cement) was utilized for fixation of the tibial and patellar components only. **Timing of intervention:** Intra and post-operatively **Duration of intervention:** The duration of implantation (indefinitely). **Device:** Cefuroxime-impregnated cement; pure cement without cefuroxime; prosthetic knee **Monitoring intervention:** Patients were examined at 3 weeks, 8 weeks & 6 months post-operatively. Then every 6 months there-after. Radio graphic evaluation at every visit & functional evaluation (Hospital for Special Surgery score) performed at every visit starting with	**SSI: (range 26-88 months)** Early superficial wound infection: Intervention: 1/ 41 (2.4%) Control: 1/37 (2.7%) *P*= 0.835 Deep infection Intervention: 0/41 Control: 5/37 (13.5%) *P*=0.021 Relative probability of not developing a deep infection in intervention group 0.865 (95%CI 0.769-0.973) All deep infections were in unilateral TKAs All deep infections were considered late (1-6mo postop) and were deemed healing satisfactorily until after the first follow-up visit. *No deep infections occurred in bilateral surgeries.* **Other infections:** NR **Topic-specific outcomes:** Deep infections Type 1 Diabetes: 1/5 6mo postop 70yoMale Type 2 Diabetes: 4/5 (1,2,3 and 6 mo. postop in 67-73yo Males)	**Definitions:** **SSI** Classified according to (**McQueen et al 1990)** and confirmed by measurement of the ESR & level of C-reactive protein and culture of joint fluid. **Perioperative care:** Authors report patients had poor control of blood glucose and the operating room was "not modern". Also used 7 day course of a systemic antimicrobial because operating environment was poor and patients were in poor state of hygiene. They report trying to shorten regimen by using antimicrobial impregnated cement **Other notes:** All surgeries performed by 1 surgeon **Follow-up:** Patients were examined at 3 weeks, 8 weeks & 6

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			90) Control: 69y (54-81) Gender: m/f (%) Intervention: 80/20 Control: 67/33 Obesity: NR Comorbidities: NIDDM/IDDM: Intervention: 32/3 Control: 28/4 Duration of Diabetes: y (SD) Intervention: 12y (8.7) Control: 10y (7.8) Left/right: (%) Intervention: 80/20 Control: 52/48 **Procedures:** Total knee arthroplasty with cementless fixation of the femoral component and cement fixation (mixing method of cement NR) of the patellar and tibial components. **Indications**: Osteoarthritis **Setting:** 1 hospital **Location:** Taiwan, China **Dates:** 1993-1998 **Inclusion Criteria**: Patients with diabetes mellitus undergoing total knee arthroplasty **Exclusion Criteria:** Patients with rheumatoid arthritis,	the 3rd postop visit. **Control group:** n= 37 knees (32 patients-5 Bilateral TKA) Cement did not contain cefuroxime. Only the tibial and patellar components were fixed with cement. Bilateral TKAs: cefuroxime-impregnated cement used on one side (Intervention n=6) and not the other (Control n=5). All undertaken in sequence under difference anesthetics **Standard preventive measures:** Environmental: No ultraviolet light for disinfection; no laminar flow nor body-exhaust suits were used. AMP Preop: intravenous bolus injections of cefazolin & gentamicin. AMP Postop: Intravenous injections of cefazolin every 6hrs for 36 hours; Intravenous injections of gentamicin every 12hrs for 36 hours; and oral cefazolin every 6hrs for 7 days. Drain: (not vacuum) Were used for 36 hours Continuous passive motion: Prescribed immediately and used	Infecting organism in deep infections: *Staphylococcus aureus:* 3/5 *Staphylococcus epidermis*: 2/5 Postoperative knee score (HHS-functional) Intervention: 91 (SD 2.8) Control: 86 (SD 9.2) *P*= 0.0093 Caused by five cases of deep infection in control group **Re-operations:** Both early superficial wound infections were successfully treated with debridement and intravenous antimicrobials administered for 1 week and orally for another week. Deep Infections 3/5 – radical debridement was followed by four weeks of intravenous antimicrobials and then two months of oral antimicrobials 2/5 –deep SSIs underwent two stage re-implantation procedures. **Length of stay:** Mean lengths was 8 days (Range 5-14 days) **Mortality:** NR **Adverse events:** NR	months post-operatively. Then every 6 months there-after Mean follow up was 50 months (Range 26-88 months) **Funding Source Conflicts:** Authors: None Institution: None Study: None Supplies: None

Author Year (Data Extractor)	Study Design Risk of Bias Score	Study Objective	Population and Setting	Intervention	Results	Comments
			psoriasis, previous knee surgery, any type of infection of the lower limb, osteomyelitis, malignant tumor or those who were undergoing immunosuppressive therapy.	every day until discharge Weight bearing: on the operated knee was allowed immediately & crutches used as needed.		

Q20B. How effective are prosthesis surface modifications (i.e., antimicrobial coating, galvanic couples, "printing" technologies, and nanotechnology)? Our search did not identify in vivo studies that evaluated the safety and effectiveness of prosthesis modifications and their impact on biofilm formation and the risk of SSI.

Q20C. How effective are vaccines? Our search did not identify in vivo studies that evaluated the safety and effectiveness of vaccines and their impact on biofilm formation and the risk of SSI.

Q20D. How effective are other biofilm control agents (e.g., biofilm dispersants, quorum-sensing inhibitors, novel antimicrobial agents)? Our search did not identify in vivo studies that evaluated the safety and effectiveness of biofilm control agents and their impact on biofilm formation and the risk of SSI.

2.2E.3. RISK OF BIAS ASSESSMENTS: Q20 BIOFILM

eTABLE 72. Risk of Bias Assessments of Randomized Controlled Trials for Q20 Biofilm

Author Year	Q	Described as randomized	Randomization appropriately performed	Described as double-blind	Outcome assessor blinded	Study participant blinded	Investigator blinded	Attrition described	Attrition smaller than 10-15% of assigned patients	Attrition appropriately analyzed	Funding source(s) disclosed and no obvious conflict of interest	Overall Risk of Bias
Question 20 Biofilm												
Chiu 2002 [183]	20	✓				✓					✓	Moderate
Chiu 2001 [184]	20	✓				✓					✓	Moderate

3. EVALUATION OF THE RISK OF BIAS OF AN INDIVIDUAL STUDY

3.1. Instructions

Check off each item in the appropriate checklist if it is present in the study
Divide the total number of checked items by the total number of questions on the checklist
Rate the risk of bias as follows:

- If < 25% of checklist items were present in study, the Risk of Bias was rated as High
- If > 25% and ≤ 50% of checklist items were present in study, the Risk of Bias was rated as Moderate
- If >50% of checklist items were present in study, the Risk of Bias was rated as Low

3.2. Checklist for Systematic Reviews

1) Search terms described
2) Databases searched described and two or more databases searched
3) Inclusion/exclusion criteria described
4) Number of included/excluded studies along with reasons of exclusion described
5) Studies screened by two independent reviewers for inclusion
6) Data extracted by two independent reviewers
7) Individual study quality assessed
8) Heterogeneity between study results assessed qualitatively and/or quantitatively
9) Publication bias assessed
10) Characteristics of included studies reported in evidence table
11) Funding source(s) disclosed and no obvious conflict of interest

3.3. Checklist for Randomized Controlled Trials

1) Described as randomized
2) Randomization appropriately performed (e.g. random number table, computerized scheme)
3) Described as double-blind
4) Outcome assessor blinded
5) Study participant blinded (e.g. interventions identical in appearance)
6) Investigator blinded (e.g. opaque sealed envelopes)
7) Attrition described
8) Attrition smaller than 10-15% of assigned patients
9) Attrition appropriately analyzed (e.g. intention to treat analysis)
10) Funding source(s) disclosed and no obvious conflict of interest

3.4. Checklist for Observational Studies

1) All study groups derived from similar source/reference populations
2) Attrition not significantly different across study groups
3) The measure of exposure is valid
4) The measure of outcome is valid
5) Investigators blinded to endpoint assessment
6) Potential confounders identified

7) Statistical adjustment for potential confounders done
8) Funding source(s) disclosed and no obvious conflict of interest

3.5. Translating Risk of Bias into GRADE Tables

When the risk of bias was rated as "High" for ≥50% of studies making up the evidence base for a given outcome, one point was deducted for Study Quality in the GRADE table.

4. EVIDENCE TABLE EXTRACTION TEMPLATES

eTABLE 73. Systematic Review (SR) Extraction Template

Author Year (Data Extrac-tor)	Study Design Quality Score	Study Objective	Population and Setting	Intervention(s)	Results (by intervention)	Comments
	SR Quality Score	Narrative	**Study types and number:** **Number of total patients in the review:** **Inclusion criteria:** **Exclusion criteria:** **Databases searched:** **Aggregate summary score:**	**Intervention group:** **Timing of intervention:** **Duration of intervention:** **Device:** **Monitoring intervention:** **Control group:** **Standard preventive measures:**	**SSI:** **Other infections:** **Topic-specific outcomes:** **Re-operations:** **Length of stay:** **Mortality:** **Adverse events:**	**Definitions:** **Perioperative care:** **Other notes:** **Follow up:** **Funding source conflicts:**

eTABLE 74. Randomized Controlled Trial (RCT) Extraction Template

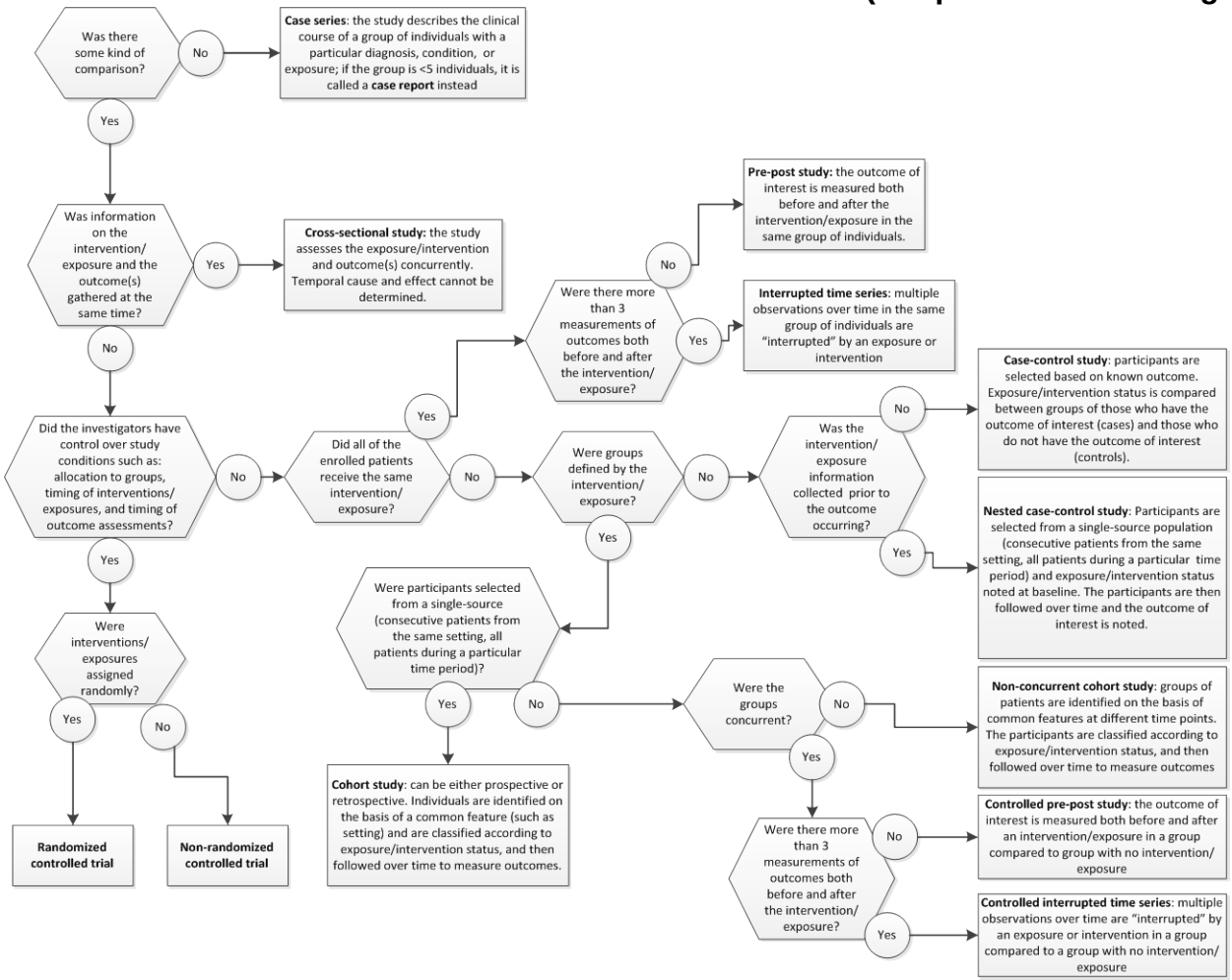
Author Year (Data Extrac-tor)	Study Design Quality Score	Study Objective	Population and Setting	Intervention	Results	Comments
	RCT Quality Score	Narrative	**Number of patients:** **Patient Characteristics:** ·Age: ·Gender: ·Obesity: ·Comorbidities: **Procedures:** **Indications:** **Setting:** **Location:** **Dates:** **Inclusion Criteria:** **Exclusion Criteria:**	**Intervention group:** **Timing of intervention:** **Duration of intervention:** **Device/agent:** **Monitoring intervention:** **Control group:** **Standard preventive measures:**	**SSI:** **Other infections:** **Topic-specific outcomes:** **Reoperations:** **Length of stay:** **Mortality:** **Adverse events:**	**Definitions:** **Perioperative care:** **Other notes:** **Follow-up:** **Funding source conflicts:**

eTABLE 75. Other Observational Studies (OBS) Extraction Template

Author Year (Data Extract-or)	Study Design Quality Score	Study Objective	Population and Setting	Intervention	Results	Comments
	Study Design Quality Score	Narrative	**Number of patients:** **Patient Characteristics:** ·Age: ·Gender: ·Obesity: ·Comorbidities: **Procedures:** **Indications:** **Setting:** **Location:** **Dates:** **Inclusion Criteria:** **Exclusion Criteria:**	**Intervention group:** **Timing of intervention:** **Duration of intervention:** **Device/agent:** **Monitoring intervention:** **Control group:** **Standard preventive measures:**	**SSI:** **Other infections:** **Topic-specific outcomes:** **Reoperations:** **Length of stay:** **Mortality:** **Adverse events:**	**Definitions:** **Perioperative care:** **Analytical methodology:** **Other notes:** **Follow-up:** **Funding source conflicts:**

5. STUDY TYPE DETERMINATION

eFIGURE A. STUDY TYPE DETERMINATION ALGORITHM (Adapted from: Hartling et. al. 2010[185])



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