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Antibiotic Solutions for Surgical Irrigation

Rapid Review

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Abbreviations

CC	capsular contracture
CDC	Centers for Disease Control and Prevention
CHG	chlorhexidine gluconate
CRP	C-reactive protein
MA	meta-analysis
NICE	National Institute for Health and Care Excellence
NMA	network meta-analysis
RCT	randomized controlled trial
SR	systematic review
SSI	surgical site infection
TAS	triple antibiotic solution
UTI	urinary tract infection

Key Messages

- During surgery, wounds can be washed out, or irrigated, using antibiotic, antiseptic, or saline solutions to prevent infections; the evidence in this report found over 20 different antibiotic solutions used across trials.
- Most studies showed that antibiotic irrigation solutions were better or no different compared to using antiseptic, saline, or no irrigation; however, a small number of studies indicated otherwise. One study reported in a systematic review showed fewer infections and complications for antiseptic compared to a triple antibiotic solution, while another study included in the same systematic review found a higher percentage of implant loss when a triple antibiotic solution was compared to antiseptic; data were poorly reported in these studies.
- Bacitracin-specific evidence was found in 2 studies; 1 study reported in 1 systematic review showed a higher percentage of infection when bacitracin irrigation was compared to cefazolin and saline irrigation; however, this was not statistically significant. Another study showed no differences in infections requiring surgical intervention or in hospitalization when bacitracin irrigation was compared to no irrigation.
- One guideline recommends that wound irrigation and intracavity lavage should not be conducted during surgery, and that applying antibiotics before wound closure should only be done as part of a research trial.
- Due to the mixed findings across studies, high-quality research is needed to clarify the role of antibiotic irrigation during surgery. Because guideline recommendations about wound irrigation, specifically, are based on research published before 2008, updated guidelines to include research from more current studies are needed to reflect current practice.

Context and Policy Issues

A surgical site infection (SSI) is an infection localized to the site where a surgery was performed.[1] SSIs occur after surgery and can involve skin, tissues, organs, or implanted material below the skin.[1] According to the Canadian Patient Safety Institute, 26,000 to 65,000 patients are affected by SSIs per year.[2] Several practices may be undertaken to prevent SSIs, and these can take place before (preoperative), during (intraoperative), and after (post-operative) surgery.[3] One method to manage wounds from surgeries is intraoperative irrigation with a fluid to remove loose material and decrease bacterial load.[4] A similar technique called intracavity lavage also reduces the risk of SSI when body cavities are exposed during surgery.[5] Saline, antiseptic, and antibiotic fluid solutions have been used to perform irrigation during surgery.[4] However, there are several concerns about using irrigation, including whether fluid can wash away important inflammatory cells needed for healing.[6] In addition, there are questions about the potential of antibiotics to prevent normal healing, damage tissue, or contribute to antimicrobial resistance with overuse.[6] Further to these concerns, Health Canada conducted a safety review that showed that the antibiotic bacitracin may increase the risk of hypersensitivity, nephrotoxicity, allergic contact dermatitis, or anaphylaxis.[7] The guidance from Health Canada is that bacitracin is not indicated as an irrigation solution for prophylaxis during surgical procedures because patients may experience nephrotoxicity and anaphylactic reactions.[7]

Given the uncertainty around using antibiotic solutions for surgical irrigation, a review to determine the clinical effectiveness of antibiotic solutions for irrigation during surgery is necessary. In 2021, CADTH compiled a reference list of relevant publications identified from a literature search.[8] The current report is an upgrade to that CADTH reference list.[8] The objectives of this rapid review are to summarize the evidence regarding the clinical effectiveness of antibiotic solutions used for irrigation in any surgery, and to determine evidence-based guidelines regarding the use of antibiotic irrigation solutions to prevent surgical infections.

Research Questions

1. What is the clinical effectiveness of antibiotic solutions used in surgical irrigation?
2. What are the evidence-based guidelines regarding the use of antibiotic solutions for surgical irrigation to prevent infection?

Methods

Literature Search Methods

This report makes use of a literature search developed for a previous CADTH report.[8] For the previous report, a limited literature search was conducted by an information specialist on key resources, including MEDLINE, Embase, the Cochrane Library, the websites of Canadian and major international health technology agencies, as well as a focused internet search. The search strategy comprised both controlled vocabulary, such as the National Library of Medicine's MeSH (Medical Subject Headings), and keywords. The main search concepts were antibiotic irrigation and surgery. Search filters were applied to limit retrieval to health technology assessments, systematic reviews (SRs), meta-analyses (MAs), or network meta-analyses (NMAs), randomized controlled trials (RCTs) or controlled clinical trials, or guidelines. Comments, newspaper articles, editorials, and letters were excluded. Where possible, retrieval was limited to the human population. The search was also limited to English-language documents published between January 1, 2011, and September 30, 2021.

Selection Criteria and Methods

One reviewer screened citations and selected studies. In the first level of screening, titles and abstracts were reviewed and potentially relevant articles were retrieved and assessed for inclusion. The final selection of full-text articles was based on the inclusion criteria presented in Table 1.

Exclusion Criteria

Articles were excluded if they did not meet the selection criteria outlined in Table 1, or if they were duplicate publications. Where the intervention included antiseptic, antifungal, steroid, or hormone, the study was excluded. Non-solution versions of the intervention (e.g., oral, powder, drops, ointment, cream, foam) or interventions where items were impregnated with

antibiotics were excluded. Only interventions that took place during the intraoperative phase were included or summarized. Comparisons between 2 antibiotics were excluded. SRs in which all relevant studies were captured in other more recent or more comprehensive SRs were excluded. Primary studies retrieved by the search were excluded if they were captured in 1 or more included SRs.

Critical Appraisal of Individual Studies

The included publications were critically appraised by 1 reviewer using the following tools as a guide: A MeaSurement Tool to Assess systematic Reviews 2[9] for SRs, the "questionnaire to assess the relevance and credibility of a network meta-analysis"[10,11] for NMAs, the Downs and Black checklist[12] for RCTs, and the Appraisal of Guidelines for Research and Evaluation II instrument[13] for guidelines. Summary scores were not calculated for the included studies; rather, the strengths and limitations of each included publication were described narratively.

Summary of Evidence

Quantity of Research Available

A total of 310 citations were identified in the literature search. Following screening of titles and abstracts, 260 citations were excluded and 50 potentially relevant reports from the electronic search were retrieved for full-text review. Seven potentially relevant publications were retrieved from the grey literature search for full-text review. Of these potentially relevant articles, 44 publications were excluded for various reasons, and 13 publications met the inclusion criteria and were included in this report. These comprised 5 SRs,[6,14-17] 7 RCTs,[18-24] and 1 evidence-based guideline reported in 2 publications.[25,26] Appendix 1 presents the PRISMA[27] flow chart of the study selection.

Additional references of potential interest are provided in Appendix 6.

Table 1: Selection Criteria

Criteria	Description
Population	Individuals (of any age) undergoing any type of surgery
Intervention	Antibiotic solutions used in surgical irrigation (e.g., bacitracin, vancomycin, cefazolin, gentamicin, metronidazole, clindamycin, ceftriaxone)
Comparator	Q1: Standard of care, non-antibiotic irrigation solutions (e.g., saline solution, antiseptic solutions [e.g., chlorhexidine, povidone-iodine, acetic acid, sodium hypochlorite]), and/or IV infusion of preoperative antibiotic prophylaxis Q2: Not applicable
Outcomes	Q1: Clinical effectiveness (e.g., surgery-related infections, post-operative infections up to 30 days post-surgery, wound healing, length of stay in hospital, and safety). Q2: Recommendations regarding the use of antibiotic solutions in surgical irrigation
Study designs	Health technology assessments, systematic reviews, randomized controlled trials, evidence-based guidelines

Summary of Study Characteristics

Study Design

The 5 included SRs[6,14-17] were published between 2018 and 2021 and they had broader inclusion criteria than the scope of this review. An SR by Baker et al.[14] looked at irrigation during implant-based breast surgery using various irrigation solutions of antibiotics and/or antiseptics. The search dates for the SR[14] were unclear, and included 4 retrospective cohort studies that reported interventions and comparators of interest to the current review. An SR by Saeg et al.[17] included any study about wound irrigation published from January 2000 to March 2020, which comprised 1 MA, 2 SRs, and 2 retrospective cohort studies with interventions and comparators relevant to the current review. An SR about antimicrobial irrigation by Leas[15] included literature published from 2017 to 2021, and had 1 study that was relevant to the current review. It should be noted that the primary study was also included in the SR by Saeg et al.;[17] however, the relevant aspects for this report were described in more detail in the Leas publication.[15] An SR with NMA by Thom et al.[6] included literature published up to February 1, 2017, covering any surgery, and had 20 RCTs relevant to the current review. An SR with MA by López-Cano et al.[16] included literature published up to January 31, 2017, covering any surgery, and had 10 RCTs relevant to the current review. There was some overlap in the primary studies that were included in the SRs; therefore, the narrative summaries and pooled estimates from the SRs may contain some data from the same RCTs. This overlap is presented in Appendix 5, Table 17. Across all 5 SRs[6,14-17] in the current report, population sizes ranged from 14 patients to 8,892 patients, all studies reported on infections, and follow-up time ranged from 8 days to 1 year.

Seven RCTs[18-24] published between 2018 and 2021 were included. One study by Krahn et al.[19] was a cluster randomized crossover trial. All studies included some form of blinding. Six studies were conducted at 1 centre[18,20-24] and 1 study was conducted across 28 centres in Canada and the Netherlands.[19] In 6 RCTs, patients were randomized,[18-21,23,24] and in 1 RCT, mastectomy pockets were randomized.[22] Across the 7 RCTs,[18-24] population sizes ranged from 40 to 19,603 and follow-up time ranged from 1 week to 606 days.

One guideline published in 2019[26] by the National Institute for Health and Care Excellence (NICE) on prevention and treatment of SSIs is included in the current review. This guideline was an update to a 2008 guideline.[25] In this report, both the 2019[26] and 2008[25] publications are referenced for completeness of reporting. The recommendations for wound irrigation and intracavity lavage were based on the 2008 guideline,[25] and the recommendations for antiseptics and antibiotics before wound closure were based on the 2019 guideline.[26] Although the NICE guidelines do not provide recommendations specifically for antibiotics, they provide recommendations for wound irrigation, intracavity lavage, and general antiseptic and antibiotic application before wound closure.

Both the 2008 and 2019 versions of the guideline were developed by searching in 6 or more databases and scanning reference lists. The 2008 guideline assessed quality using 8 hierarchical levels with informal and formal consensus steps, while the 2019 guideline used Risk of Bias in Systematic Reviews, the Cochrane risk of bias tool, Risk Of Bias In Non-randomised Studies – of Interventions, and Grading of Recommendations Assessment, Development and Evaluation, depending on study design with a committee discussion of the evidence.

Country of Origin

Three SRs[14,15,17] were from the US, 1 SR[6] was from England, and 1 SR was from Spain.[16] Among the included RCTs, 3 were from the US,[20,22,24] 1 from Egypt,[18] 1 from Iran,[21] 1 from Nigeria,[23] and 1 was a study conducted across multiple centres in Canada and the Netherlands.[19] The included guideline is for those working in the UK or using services of the National Health Service in England, Wales, and Northern Ireland.[25]

Patient Population

Three SRs included relevant studies of patients undergoing breast surgery,[14,15,17] 1 SR included relevant studies of patients undergoing surgeries with primary site closures,[6] and 1 SR included relevant studies of patients undergoing various procedures such as abdominal, trauma, biliary tract, colorectal, hernia, breast, soft tissue, or cardiovascular surgeries.[16] One SR[6] reported that studies had patients of varying age groups, mostly adults, and that some studies such as those with Caesarean sections enrolled only women. Other SRs did not specify age, gender, or sex of included populations.

Across RCTs, included populations were patients undergoing breast reconstruction,[22] open appendectomy,[18] laparoscopic colectomy,[21] neurosurgical procedures,[23] benign gynecologic surgery,[24] nonemergent open pancreatoduodenectomy,[20] or cardiac implantable electronic device procedures.[19] The mean age ranged from 27.9 to 72.0 years across the RCTs. Two RCTs included only female patients,[22,24] 2 RCTs did not specify gender,[20,21] 1 RCT had a greater proportion of patients who were female,[18] 1 RCT had a greater proportion of patients who were male.[23] One RCT[19] reported 33.9% patients who were female and did not specify gender for the remaining population. Recognizing that gender and sex are different, gendered terms used in this report reflect the reporting in the included studies, and it is unclear how these terms were defined and measured.

For the included guideline,[25,26] the target population is children, young people, and adults undergoing surgery involving a skin cut. The intended users of the guideline are people having surgeries and their carers, health care professionals, and commissioners and providers.

Interventions and Comparators

Relevant interventions across studies varied and included irrigation and lavage with single or multiple antibiotics solutions such as ampicillin, bacitracin, cefamandole, cefazolin, cefotaxime, cefotetan, cefoxin, cefoxitin, cefuroxime, cephaloridine, cephalothin, cephapirin, cephradine, chloramphenicol, gentamicin with clindamycin, gentamicin, kanamycin with cephalothin, kanamycin, moxalactam, neosporin, polymyxin B, triple antibiotic solution (TAS), taurolin, or tetracycline. All studies that reported TAS as an intervention were included in this report because TAS used in Canada commonly includes a mixture of bacitracin, cefazolin, and gentamicin, which are applicable to the current review. Relevant comparators across studies included saline irrigation and lavage, chlorhexidine gluconate irrigation, or no irrigation. One SR with MA[16] included studies that compared antibiotic irrigation to placebo, where the placebo arm comprised patients who did not have prophylactic topical antibiotic agents, other antibiotics, or antiseptic. In this report, the results for this study are reported in the results for antibiotic irrigation compared to no irrigation.

The specific procedures for surgeries varied across studies. Only antibiotic-related surgical processes are described in this report. In the Nguyen et al. study,[22] all patients were given cefazolin intravenously at least 30 minutes before the surgery. The TAS intervention consisted of 50,000 U of bacitracin, 1 g of cefazolin, and 80 mg of gentamicin in 500 mL of normal

saline.[22] The chlorhexidine gluconate control contained 0.05% chlorhexidine gluconate in sterile water.[22] After surgery, all patients were given cefazolin intravenously for 24 hours or until discharge followed by a 14-day treatment of oral sulfamethoxazole and trimethoprim DS 800 mg/160 mg 2 times per day (100 mg doxycycline 2 times per day for patients who had sulfa allergies).[22]

In the Emile et al. study,[18] all patients were given 2 g of cefotaxime and 500 mg of metronidazole at anesthesia induction as part of antibiotic prophylaxis. The interventions were either 160 mg of gentamicin in 400 mL of normal saline (0.9% sodium chloride) or normal saline alone applied using a 20 cm syringe to irrigate each layer of the wound before closure.[18] In the control group, layer-by-layer wound closure was performed with polyglactin 2/0 sutures and no irrigation.[18] All patients received 1 g of cefotaxime intravenously within 12 hours of their incisions being closed.[18]

In the Negahi et al. study,[21] the intervention group received lavage with a suction-irrigation machine containing 240 mg of gentamicin and 600 mg of clindamycin dissolved in 500 mL of sterile saline, and the control group received lavage with 500 mL of sterile saline only.

In the Okunlola et al. study,[23] both study groups were given 2 g of parenteral ceftriaxone intravenously when anesthesia commenced and 1 g of ceftriaxone intravenously every 12 hours for 24 hours after surgery. In addition, the intervention group received irrigation with 250 mg/mL of ceftriaxone in normal saline and the control group received plain normal saline irrigation using jet and droplets from a 50 mL syringe.

In the Slopnick et al. study,[24] the intervention group received irrigation of a solution containing 200,000 U polymyxin B sulphate and 40 mg neomycin sulphate, while the control group had irrigation with normal saline only. All patients received cefazolin for antibiotic prophylaxis and metronidazole for hysterectomy in patients who were premenopausal unless patients were allergic.[24]

In the Maatman et al. study,[20] the intervention group received irrigation with polymyxin B, 500,000 U in 1 L of normal saline, and the control group received irrigation with 1 L of 0.9% sodium chloride. In both cases, 2 L of each solution was used for irrigation.[20] All patients were given 2 g of IV ceftriaxone and 1 g of IV metronidazole within 60 minutes of skin incision.[20]

In the randomized crossover trial,[19] there were 4 randomly assigned 6-month periods where participating centres used different sequences of incremental or conventional procedures. In the conventional period, a single dose of cefazolin (1 g to 2 g) was given intravenously 60 minutes before skin incision. If patients were allergic to penicillin, vancomycin (1 g to 1.5 g) was given intravenously 120 minutes before skin incision. In addition to the aforementioned procedure with cefazolin or vancomycin, the incremental period applied an intraoperative wound pocket wash using bacitracin 50,000 U diluted in 50 mL of saline before skin closure, and patents were given oral cephalexin (500 mg 4 times per day) or cephadroxil (1,000 mg 2 times per day for 2 days) after the operation. For patients who were allergic to penicillin, clindamycin 150 mg to 300 mg was prescribed 3 times per day. Thus, regarding this report, the relevant comparison in the study[19] was between antibiotic irrigation with bacitracin pocket wash and no irrigation. Authors of the study[19] reported that bacitracin was not available at 1 Canadian site and at all Netherlands sites, so cefazolin or saline pocket wash was administered. Limitations of this procedural change are discussed in the Summary of Critical Appraisal section.

The NICE guideline[25,26] considered all methods before, during, and after surgery to minimize surgery risk. However, the current review focuses only on aspects relating to intraoperative methods for wound irrigation, intracavity lavage, and antibiotic application before wound closure.

Outcomes

Several outcomes were reported across the SRs and RCTs: infection-related outcomes (including SSI, infection requiring surgical intervention, white blood cell count, C-reactive protein [CRP]), capsular contracture (CC), hospital-related outcomes (hospital stay, hospitalization for infection), pain-related outcomes (pain, painkiller needed), patient satisfaction, wound-related outcomes (necrosis, hematoma, seroma, wound dehiscence, wound infection), adverse events and complications (including surgical site occurrence, urine retention or ileus, intra-abdominal abscess, bowel obstruction, intestinal fistula, urinary tract infection (UTI), implant loss, allergic reaction, pancreatic fistula, organ failure, sepsis, delayed gastric emptying, bile leak, venous thromboembolism, cholangitis, myocardial infarction), and death.

Several studies did not provide definitions or had unclear definitions for outcomes. For studies that defined outcomes, 1 SR[6] and 2 RCTs[18,22] referenced the Centers for Disease Control and Prevention (CDC) definition for SSIs. The CDC definition of an SSI is an infection that happens after surgery in the area of the body (incision, organ, or space) where the surgery occurred.[28,29] In the Nguyen et al. study,[22] SSIs were further classified as minor if patients required oral antibiotics; major if patients required IV antibiotics, hospitalization, or incision and washout; or referred to as explantation if patients needed a bilateral explant after developing a persistent non-infectious rash. In the Krahn et al. study,[19] hospitalization for pocket or cardiac implantable electronic device infections was categorized as pocket infection, endocarditis, or bloodstream infection. In the Maatman et al. study, SSIs were defined using another study[30] that monitored and reported on SSIs over a 2-year period.

Pain was measured in the Emile et al. study[18] at the 1-week follow-up using the Visual Analogue Scale, which ranged from 0 to 10, with 0 indicating absence of pain at incision site and 10 implying worse severe pain at incision site.

Patient satisfaction with the outcome of the surgery was measured in the Emile et al. study[18] at the 6-week follow-up as unsatisfied, partly satisfied, or completely satisfied indicating causes of dissatisfaction, if applicable.

Surgical site occurrence was measured in the Emile et al. study[18] and included SSI, necrosis, cellulitis, serous or purulent drainage, chronic and/or non-healing wound, seroma, hematoma, wound dehiscence, or fistula at the surgical site.

UTI was measured in the Slopnick et al. study[24] at 6 weeks post-surgery. This study adapted the CDC's definition of a symptomatic UTI: "(1) at least one sign or symptom accompanied by positive urine culture with ≥105 colony-forming units/mL, (2) symptomatic UTI with clinician decision to treat as reported by the patient, or (3) at least one sign or symptom with positive urine dipstick."[24]

Post-operative pancreatic fistula was defined using the definition from the International Study Group on Pancreatic Fistula with a fluid drain output at 3 or more days after surgery and amylase greater than 3 times the upper limit of laboratory normal. Clinically relevant post-

operative pancreatic fistula were those graded as B or C as defined by the International Study Group on Pancreatic Fistula.

The 2008 version[25] of the NICE guideline considered wound infection rates and SSI, and the 2019 version[26] of the guideline considered SSI, mortality, hospital stay, post-operative antibiotic use, adverse events, and complications.

Additional details regarding the characteristics of the included publications are provided in Appendix 2, Table 2, Table 3, and Table 4.

Summary of Critical Appraisal

Systematic Reviews

All 5 SRs[6,14-17] described the interventions and outcomes of interest clearly, 4 SRs[6,14-16] described the specific study populations of interest, and 3 SRs[6,15,16] stated comparator groups of interest. All SRs[6,14-17] included literature from at least 2 databases, which is a strength; however, only 3 SRs[6,16,17] supplemented searches with reference list scanning, and 1 SR with NMA[6] consulted clinical trial registries and reference lists of other relevant SRs. No SRs reported searching grey literature, which limits the breadth of literature found in these SRs. Only 2 SRs[15,16] established protocols before review conduct; it is unclear, for the remaining SRs,[6,14,17] whether outcomes of interest were established before review conduct.

In 3 SRs,[14,16,17] screening and data extraction were conducted by at least 2 reviewers. In 1 SR,[6] 2 reviewers screened articles and appraised risk of bias; however, it is unclear whether data extraction was also conducted in duplicate. In 1 SR,[15] it is unclear whether study selection and extraction was conducted in duplicate. In SRs where screening and data extraction were not completed in duplicate, is unclear if there was any bias in the study selected or potential errors in the data extracted and reported from these publications.

The level of detail provided about each included study varied across SRs and no SRs provided sufficient detail on all study characteristics. In 4 SRs,[6,15-17] authors described interventions, comparators, outcomes, and study designs in detail, which is a strength, but patient populations were not described in sufficient detail. One SR[14] did not provide further details on populations, interventions, comparators, and outcomes. Insufficient detail on any study characteristics may limit how the results from these SRs can be applied to other contexts. Three SRs[6,15,16] used an appropriate method to assess risk of bias. One SR[14] did not report assessing risk of bias. Another SR[17] used a method to assess bias but it did not consider study design, confounding, unconcealed allocation, outcome measurement, or reporting bias, and bias was not accounted for when reporting results. For these latter 2 SRs,[14,17] since the risk of bias assessment was not sufficiently completed, the interpretation of results may be limited because the quality of the evidence is unknown. In addition, for 3 SRs,[6,14,17] it is unclear how the reported conflicts of interest or funding may have affected the reporting of the results.

Heterogeneity across studies was considered and described in 4 SRs,[6,14,16,17] which is a strength. In the 1 SR[15] that did not discuss heterogeneity, the impact of potential heterogeneity on the results is unknown. Strengths of the 2 SRs[6,16] that conducted quantitative analyses include that both studies applied appropriate methods for combination of results while taking heterogeneity and risk of bias of individual studies into account. Further, the strengths of the SR with NMA[6] are that both direct and indirect comparisons were included, inconsistency was assessed, results from individual studies were provided,

treatment effect estimates with measures of uncertainty and a rank probability plot with uncertainty were provided, heterogeneity was explored through additional analyses by important patient or publication characteristics. The limitations of the SR with NMA[6] are that the results are likely biased due to unexplained high heterogeneity and the low quality of individual studies. This limits the conclusions that can be drawn from this SR with NMA.[6]

Randomized Controlled Trials

All 7 RCTs[18-24] sufficiently described their objectives, interventions, and main outcomes, and 4 RCTs[18,20,22,24] clearly described patient characteristics, which is a strength. Further, randomization occurred in all 7 RCTs[18-24] to balance intervention and control groups as much as possible so that effects could be attributed to the intervention; however, in the Nguyen et al. study,[22] it remains unclear whether the investigators used appropriate allocation techniques to prevent selection bias. In the randomized crossover trial,[19] since bacitracin was unavailable at 1 Canadian site and all Netherlands sites, a cefazolin or saline pocket wash was administered instead; the results may have been biased because the intervention and comparator groups did not match across study groups. All SRs[18-24] included blinding of study personnel. Three RCTs[19,21,22] had no blinding or unclear blinding of patients; however, because the intervention took place during surgery, it is unlikely that patients would discover what infection prevention protocol they received.

Five RCTs[18,21-24] occurred at single centres and patients were likely from the same population; however, these patients may not be generalizable to other populations beyond these clinical settings. One RCT[20] did not clarify if it took place at a single centre or multiple centres.

Five RCTs[18-20,22,23] described main findings and 5 SRs[18-20,22,24] described covariates in sufficient detail. Two RCTs[21,24] did not report complete details, which may limit understanding of the results. Further, 4 RCTs[20-23] did not report clearly on controlling for potential confounders so it is unclear if the results may be biased. It is unclear if statistical tests could adequately answer the research question in 6 RCTs.[18,20-24] In 2 RCTs,[22,23] authors noted that their studies had small sample sizes; these studies may not have been sufficiently powered to detect any effects. In 1 RCT,[21] a power calculation was not provided so the power is unclear, and in another RCT,[24] the study sample was smaller than what the power calculation required. In 1 RCT,[18] the study had sufficient power, but the data were analyzed using a per-protocol approach that did not reflect the randomization assignment and may have biased results. In 1 RCT,[24] some covariates were not adjusted for, and in another RCT,[20] the low infection rate could not be explained.

Four RCTs[18-20,24] had minimal to no loss to follow-up. In 1 RCT,[19] there was higher noncompliance in the intervention group, which was mainly attributed to administration of oral antibiotics before surgery. In addition, 2 RCTs[21,23] had unclear follow-up and 1 RCT[22] had early termination. Within each study, these differences between groups may have biased the results. Loss to follow-up may have affected results if reasons for dropout were related to the intervention.

Guideline

This section considers research included in both the 2008[25] and 2019[26] versions of the NICE guideline. The overall objectives, health questions, and populations were described in sufficient detail. The guideline described the target population and included important stakeholders in guideline development. Sufficient methods were used to search for evidence, describe evidence selection, appraise the quality of the evidence, considered benefits and harms in formulating recommendations, ensure the guideline was reviewed, and implement

a process for updating the guideline. For the 2019 version[26] of the guideline, the methods for formulating the recommendations were not described in sufficient detail, and the link between recommendations and supporting evidence was unclear. Key recommendations were clearly visible and auditing criteria were posted. However, the recommendations are to not conduct wound irrigation in general; there are no detailed recommendations about specific antibiotics or preparations to avoid, clear advice on alternative options, or barriers and facilitators to implementing the guidance. Although competing interests of the guideline development group members were recorded, it is unclear how any funding affected formation of the guideline as funding was not reported in the publication.

Additional details regarding the strengths and limitations of included publications are provided in Appendix 3, Table 5, Table 6, and Table 7.

Summary of Findings

Appendix 4 presents the main study findings by outcome in Table 8, Table 9, Table 10, Table 11, Table 12, Table 13, Table 14, Table 15, and Table 16.

Clinical Effectiveness of Antibiotic Irrigation Solutions on Infection

Two SRs[6,14] and 1 RCT[22] reported results comparing antibiotic solution to antiseptic solution. In 1 SR with NMA,[6] results showed that antibiotic irrigation was not statistically superior to antiseptic irrigation. The other SR[14] had relevant data from 2 retrospective cohort studies; 1 demonstrated a statistically significant reduction in risk of infection in the chlorhexidine gluconate (CHG) group compared to the TAS group, while the other study did not report analyses comparing TAS and CHG. One RCT[22] included in the current review found that SSI did not differ statistically between TAS and CHG groups, even when results were broken down by infection type (minor, major, explantation).

Four SRs[6,14,15,17] and 4 RCTs[18,20,21,23] reported results comparing antibiotic solution to saline with mixed findings. Two SRs showed that infections were reduced in a cefuroxime and gentamicin group compared to a saline group,[15] a cephalothin group compared to a saline group,[15] and an antibiotic group compared to a normal saline group,[17] based on MA and NMA results. However, 1 SR with MA[16] showed that based on 3 RCTs and 753 patients, beta-lactam antibiotic irrigation solutions were not effective in reducing SSIs compared to no antibiotic solution irrigation. In addition, 1 SR and 3 RCTs showed no statistically significant differences in infection for bacitracin compared to saline,[14] cefazolin compared to saline,[14] gentamicin-saline compared to saline,[18] ceftriaxone compared to saline,[23] and polymyxin B compared to saline.[20] One RCT[21] reported that CRP levels after 12 hours were better in a gentamicin-clindamycin lavage group compared to normal saline lavage group; no further details were provided.

Two RCTs[18,19] compared antibiotic irrigation to no irrigation. One RCT[18] demonstrated a statistically significant lower value of SSIs for a gentamicin-saline group compared to a no irrigation group; however, post hoc analyses showed no statistically significant difference. In a randomized crossover trial,[19] there was no statistically significant difference in infections requiring surgical intervention between bacitracin and no irrigation.

Clinical Effectiveness of Antibiotic Irrigation Solutions on Capsular Contracture

One SR[14] reported results from a retrospective cohort study that found no difference in CC between the TAS and CHG groups.

Three SRs[14,15,17] had mixed results on the effect of antibiotic solution irrigation on CC when compared to saline solution. Two SRs found no differences in CC between a TAS group compared to a saline group in a retrospective cohort study,[14] between a cefuroxime and gentamicin group compared to a saline group,[15] or a cephalothin group compared to a saline group. In 1 SR[17] that included 2 SRs and 2 RCTs, there were mixed findings; 1 retrospective cohort study found a statistically significant reduction in CC in a TAS groups compared to a normal saline group, 1 included MA reported reduced CC with antibiotic irrigation compared to normal saline irrigation, no differences in CC between TAS and normal saline from another retrospective cohort study, and no differences in CC between antibiotic irrigation and normal saline from another included SR.

No studies examined the effectiveness of antibiotic irrigation compared to no irrigation on CC.

Clinical Effectiveness of Antibiotic Irrigation Solutions on Hospital-Related Outcomes

No studies examined the effectiveness of antibiotic irrigation compared to antiseptic irrigation on hospital-related outcomes (e.g., hospital stay, hospitalization). Three RCTs[18,20,21] reported results for the effect of antibiotic irrigation compared to saline irrigation on hospital stay. One RCT[21] showed that hospital stay in days was lower for the gentamicin-clindamycin lavage group compared to the normal saline lavage group and this was statistically significant. The other 2 RCTs showed no statistically significant differences in hospital stay for a gentamicin-saline group compared to a saline group,[18] and a polymyxin B group compared to saline group.[20]

Two RCTs comparing gentamicin-saline to no irrigation[18,19] found no statistically significant differences between the 2 regarding hospital stay or hospitalization for infection after surgical procedures.

Clinical Effectiveness of Antibiotic Irrigation Solutions on Pain-Related Outcomes

One RCT[18] showed no difference in pain visual analogue scores between a gentamicin-saline group and a saline group. Another RCT[21] showed statistically significant differences in mean pain score between gentamicin-clindamycin lavage and normal saline lavage groups at both 3 hours and 24 hours after surgery, and the amount of acetaminophen needed after 24 hours was significantly lower in the gentamicin-clindamycin lavage group. However, no statistically significant differences were seen for the amount of acetaminophen needed after 3 hours of surgery or pethidine needed after 24 hours of surgery.

One RCT[18] showed that pain visual analogue scores were similar between a gentamicin-saline group and a no irrigation group.

No studies examined the effectiveness of antibiotic irrigation compared to antiseptic irrigation on pain-related outcomes.

Clinical Effectiveness of Antibiotic Irrigation Solutions on Patient Satisfaction

One RCT[18] found that a significantly higher percentage of patients in gentamicin-saline and saline groups were completely or partly satisfied with the outcome of their procedures compared to no irrigation; this was statistically significant.

No studies examined the effectiveness of antibiotic irrigation compared to antiseptic irrigation on patient satisfaction.

Clinical Effectiveness of Antibiotic Irrigation Solutions on Wound-Related Outcomes

Results from 3 SRTs[18,21,22] showed no differences in necrosis, hematoma, seroma, and wound infection across study groups.

Clinical Effectiveness of Antibiotic Irrigation Solutions on Adverse Events and Complications

One SR[14] reported that in 1 retrospective cohort study, patients who received irrigation with CHG showed a greater reduction in complications compared to those who had TAS irrigation; this was statistically significant. Another retrospective cohort study in the same SR[14] showed a lower percentage of implant loss in the CHG group compared to the TAS group; however, the level of statistical significance in the difference was not reported. One RCT[22] showed that no patients in TAS or CHG groups had any allergic reactions.

Three RCTs[18,20,24] that compared antibiotic to saline irrigation found no statistically significant differences in adverse events or complications between the groups. One RCT[18] showed no differences in surgical site occurrences, or urine retention or ileus between gentamicin-saline and saline groups. Another RCT[24] showed no difference in treatment required for UTI between neosporin compared to saline groups, even when limiting results by UTI timing or those needing vaginal prolapse repair. This study[24] also reported finding no association between antibiotic irrigation and new urinary frequency or urgency after surgery, and there were no adverse events related to antibiotic irrigation. Another RCT[20] found no difference in post-operative pancreatic fistula or clinically relevant post-operative pancreatic fistula between polymyxin B and saline groups. Other complications that showed no statistically significant differences between groups were organ failure, sepsis, delayed gastric emptying, bile leaks, UTIs, venous thromboembolism, cholangitis, or myocardial infarction.

In the RCT[18] that compared gentamicin-saline to no irrigation, surgical site occurrences were significantly lower for gentamicin-saline compared to no irrigation and there were no differences in urine retention or ileus between groups.

A randomized crossover trial[19] showed that adverse events were rare in both bacitracin and no irrigation groups.

Clinical Effectiveness of Antibiotic Irrigation Solutions on Mortality

One RCT[22] comparing TAS to CHG indicated that overall, there were 2 patient deaths out of a study population of 88 patients. One RCT[23] comparing ceftriaxone to saline showed that 30-day mortality was 10.6% overall and was not associated with SSI; a breakdown by study groups was not provided. Another RCT[20] showed that both 30-day and 90-day mortality were not significantly different for polymyxin groups compared to saline groups.

No studies examined the effectiveness of antibiotic irrigation compared to no irrigation on mortality.

Guidelines Regarding the Use of Antibiotic Solutions for Surgical Irrigation to Prevent Infection

The NICE guideline[25,26] does not recommend wound irrigation to reduce the risk of SSI based on evidence from well-conducted MAs, SRs of RCTs, or RCTs with a low risk of bias. The NICE guideline[25,26] does not recommend intracavity lavage to reduce the risk of SSI based on mixed evidence from well-conducted MAs, SRs of RCTs, or RCTs with a low risk of bias; and 3 trials with high risk of bias. The NICE guideline[26] recommends application of antibiotic to the would before closure only when conducting clinical trials, based on 1 low-quality RCT and moderate quality RCT.

Limitations

Limitations to the body of evidence include high heterogeneity, low generalizability, and a lack of guidelines with more recent evidence. Included SRs[6,14-17] noted the high heterogeneity across studies, which varied by surgery type, specific antibiotics used for irrigation, comparator groups, and outcomes measured. Patients undergoing surgery varied greatly and procedures included breast implant surgeries, neurologic procedures, cardiac device operations, gynecological surgeries, and appendectomies, among others. Two SRs[6,16] were conducted on any surgery. The antibiotics studied also varied across studies and comprised over 20 different agents that were used alone or in combinations of 2 or 3 antibiotics in a solution. Comparator groups included antiseptic, saline solution, or no irrigation. Outcomes across studies also varied and were grouped into 8 categories in the current report.

The evidence is also limited by low generalizability. Of the 7 RCTs[18-24] included in this report, 1[19] enrolled patients within Canada and from the Netherlands, whereas the others did not include patients from Canada. Six RCTs[18,20-24] were conducted at single centres; it is unclear whether their results are applicable to populations beyond surgical patients presenting to specific departments in these institutions. Therefore, overall, the generalizability of the findings in the Canadian context is unclear. In addition, it is unclear whether findings in the current report may be replicated for surgeries other than those mentioned in the included evidence.

The current report found 1 evidence-based guideline,[25,26] which included recommendations about wound irrigation and intracavity lavage based on a 2008 version[25] of the guideline, and recommendations about antibiotic use before wound closure based on a 2019 version[26] of the guideline. For the wound irrigation guideline based on evidence up to 2008, it is unclear whether there are newer studies published in 2008 and later that may change the conclusions. Given that Health Canada recommendations for bacitracin changed in December 2020,[7] new guidelines may be required to reflect current practice.

Conclusions and Implications for Decision- or Policy-Making

A rapid review was conducted to examine the effectiveness of antibiotic solutions for surgical irrigation, and to summarize recommendations for using antibiotic irrigation to prevent surgical infection. The review is an upgrade of a 2021 CADTH report[8] that provided a reference list of relevant studies on the topic identified from the literature. The rapid review identified 5 SRs[6,14-17] (1 with MA and 1 with NMA), 7 RCTs,[18-24] and 1 guideline reported in 2 publications,[25,26] published between 2018 and 2021. The current report includes more studies than the CADTH 2021 reference list report[8] because it evaluated full-text articles to determine relevancy of studies that may have had unclear information from only titles and abstracts. Over 20 different solutions of antibiotics were reported in included studies as interventions, and comparators included antiseptic, saline, or no irrigation.

For studies comparing antibiotic solution to antiseptic solution, no significant effects were found in higher-level evidence (SR[6] or RCT[22]) on infection, while 1 retrospective study included in 1 SR[14] found a significant effect of antibiotic compared to antiseptic solution on infection. One retrospective study included in an SR[14] showed a significant effect of antibiotic irrigation on complications. Across all the included studies, there were no significant effects of antibiotic solution over antiseptic solution on CC or wound-related outcomes, and mixed effects for hospital-related outcomes, pain, and painkiller use.

For studies comparing antibiotic solution to saline, 3[6,15,17] out of 4 SRs showed significant effects on infection, while 3[18,20,23] out of 4 RCTs showed no effects on infection. One RCT[21] showed that CRP levels were better in the gentamicin-clindamycin lavage group compared to the normal saline lavage group. One RCT[18] found that patients in the antibiotic group were more satisfied with the outcome of their surgery. Across all studies, there were no significant effects or mixed effects of antibiotic solution over saline on CC, hospital stay, pain, and wound-related outcomes. Findings on mortality were unclear due to poor reporting.

For studies comparing antibiotic solution to no irrigation, 1 RCT[18] found higher patient satisfaction when comparing antibiotic to no irrigation. There were mixed effects for antibiotic irrigation on infection, adverse events, and complications, and no effects found for hospital stay, pain, and wound-related outcomes.

The included guideline[25,26] recommended that wound irrigation and intracavity lavage should not be used to reduce SSIs, and that antibiotics should only be applied before closure as part of clinical research trials.

Most studies included in the current review indicated that antibiotic solutions for irrigation were better or no different compared to antiseptic, saline, or no irrigation on various outcomes; however, 1 retrospective study included in 1 poorly reported SR[14] found a significant reduction in infections and complications in a CHG group compared to a TAS group while another retrospective study included in the same SR[14] found a higher percentage of implant loss in the TAS group compared to the CHG group, although no data on statistical significance was reported.

Regarding bacitracin-specific evidence, 1 retrospective cohort study included in 1 poorly reported SR[14] showed a higher percentage of infection in a bacitracin irrigation group when comparing it to cefazolin and saline irrigation groups; however, this was not statistically

significant. One randomized crossover trial[19] showed no statistically significant differences between bacitracin irrigation and no irrigation on infections requiring surgical intervention or hospitalization for infections from cardiac rhythm device implants.

The findings of the current review suggest that the literature is mixed regarding any potential benefits or harms of antibiotic solutions for surgical wound irrigation. There was high heterogeneity across studies and most RCTs were either not powered sufficiently to detect any effects or had potential selection bias. No high-quality SRs were found, and several had methodological weaknesses such as search strategies that were not comprehensive, lack of reporting on duplicate screening and extraction, and insufficient reporting of the details of each included study. Future high-quality SRs and RCTs can be conducted to target some of the limitations of the current review, and new primary research where evidence gaps currently exist can be added to the literature (e.g., the effectiveness of antibiotic irrigation compared to no irrigation on CC in breast surgery, antibiotic irrigation compared to antiseptic irrigation on hospital-related outcomes). Because the 1 included guideline[25,26] includes recommendations from 2008 for wound irrigation specifically, an updated guideline with more recent literature that reflects current practice for this type of intervention may be helpful for practitioners.

Because of the mixed findings from the literature, contraindication of bacitracin in recent Health Canada guidance,[7] and NICE guidelines[25,26] that do not recommend wound irrigation, decision-makers may also consider the resources needed to perform wound irrigation or stop using this process altogether. For example, clinicians may consider whether current non-irrigation infection prevention protocols that take place before, during, and after surgery (e.g., preoperative hand decontamination, post-operative wound cleansing with saline) may be sufficient until updated guidelines with more recent research becomes available.

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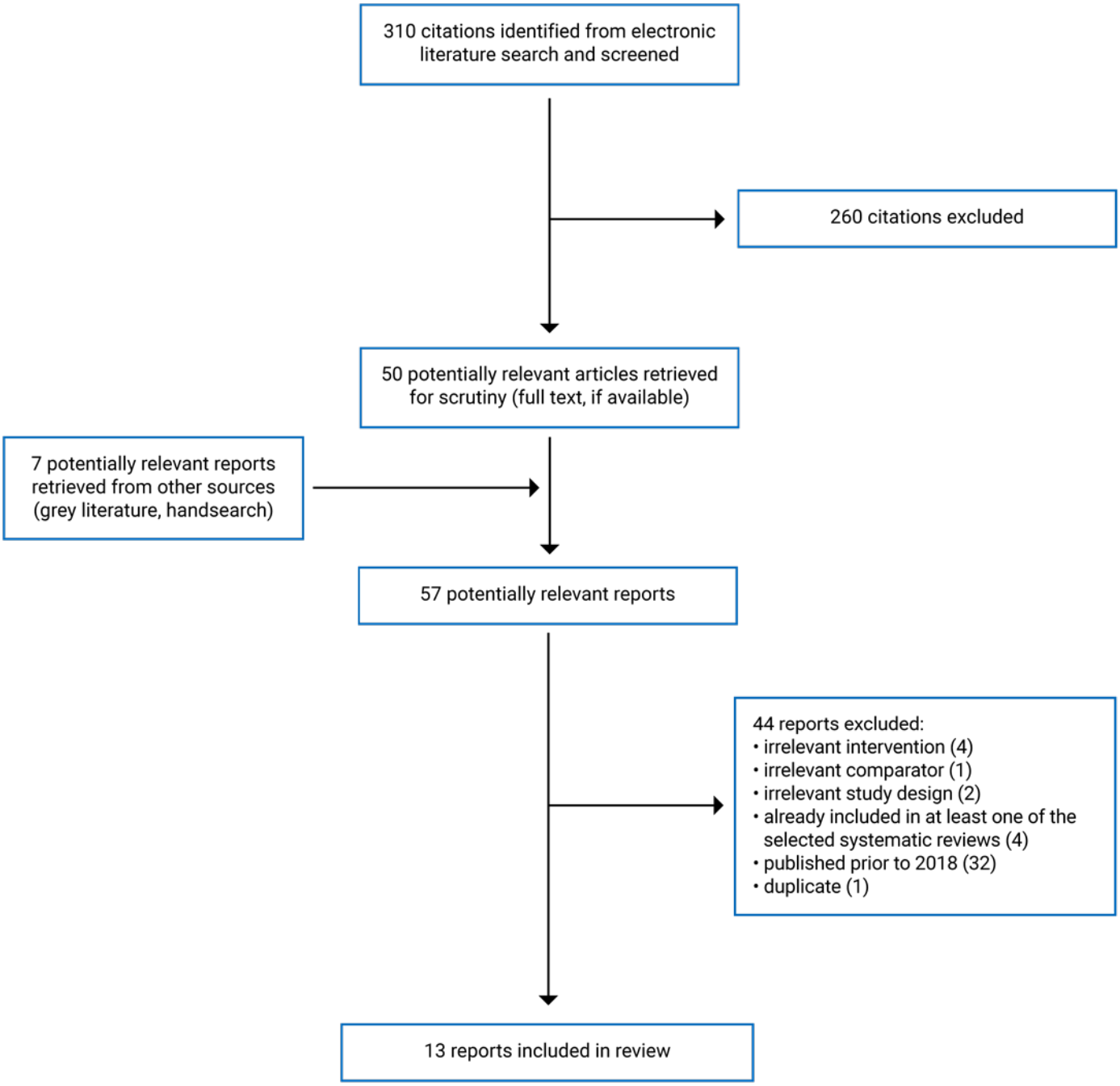
Appendix 1: Selection of Included Studies

Note that this appendix has not been copy-edited.

Figure 1: Selection of Included Studies



Appendix 2: Characteristics of Included Publications

Note that this appendix has not been copy-edited.

Table 2: Characteristics of Included Systematic Reviews and Network Meta-Analysis

Study citation, country, funding source	Study designs and numbers of primary studies included	Population characteristics	Intervention and comparator(s)	Clinical outcomes, length of follow-up
Baker 2021[14] US Funding source: consultancy to RTI Surgical	Unclear search dates 8 retrospective cohort studies, 1 prospective cohort study; 4 retrospective cohort studies relevant to the present review with sufficient detail	Patients undergoing implant-based breast surgery	Intervention: breast pocket irrigation using TAS, bacitracin, or cefazolin Comparator: saline or CHG irrigation	Outcomes: infection, complications, CC Follow-up: NR
Leas 2021[15] US Funding source: University of Pennsylvania Health System	Literature published 2017 to 2021 1 SR, 4 RCTs, 8 NRS, 1 narrative review; 1 narrative review relevant to the present review	Patients undergoing plastic surgery for breast augmentation 5,556 patients	Intervention: irrigation using cephalothin, or cefuroxime and gentamicin Comparator: saline irrigation	Outcomes: infection, CC Follow-up: up to 1 year
Saeg 2021[17] US Funding source: royalties from Thieme and Springer Publishing	Literature published January 2000 to March 2020 5 MAs, 6 SRs, 8 RCTs, 3 prospective cohort studies, 9 retrospective cohort studies; 1 MA, 2 SRs, and 2 retrospective cohort studies relevant to the present review	Patients undergoing breast implant surgery 55 to 8,892 patients across studies	Intervention: TAS or antibiotic irrigation Comparator: normal saline irrigation	Outcomes: infection, CC Follow-up: NR
Thom 2021[6] England Funding sources: UK NIHR Manchester BRC, NIHR Biomedical Research Centre University Hospitals Bristol NHS Foundation Trust, University of Bristol, NIHR via Cochrane Infrastructure, Cochrane Programme Grant	Literature published up to February 1, 2017 59 RCTs in SR, 42 RCTs in NMA; 20 RCTs relevant to the present review	Patients undergoing surgeries with primary site closure 14 to 360 patients across studies	Intervention: irrigation with ampicillin, cefazolin, tetracycline, cephapirin, cefamandole, moxalactam, cefoxitin, cefotetan, kanamycin, taurolin, cefoxin, kanamycin and cephalothin, cephalothin, gentamicin, gentamicin and clindamycin, or chloramphenicol Comparator: saline or no irrigation	Outcome: SSI Follow-up: 8 days to 8 weeks

Study citation, country, funding source	Study designs and numbers of primary studies included	Population characteristics	Intervention and comparator(s)	Clinical outcomes, length of follow-up
López-Cano 2019[16] Spain Funding source: no financial support received	Literature published up to January 31, 2017 40 RCTs in SR, 35 RCTs in NMA; 10 RCTs relevant to the present review	Inclusion criteria: patients undergoing colorectal, hernia, soft tissue, breast, cardiovascular, biliary tract, abdominal, trauma surgeries Exclusion criteria: eye surgery, antibiotic dressings, antibiotic-impregnated beds, cements 62 to 401 patients across studies	Intervention: topical antibiotic irrigation solution (cephaloridine, cephradine, cefamandole, cefotaxime, ampicillin, gentamicin) at incision site before primary closure Comparator: patients with surgical incisions where prophylactic topical antibiotic agents were not used	Outcome: SSI Follow-up: NR

BRC = Biomedical Research Centre; CC = capsular contracture; CHG = chlorhexidine gluconate; MA = meta-analysis; NHS = National Health Service; NIHR = National Institute for Health Research; NMA = network meta-analysis; NRS = nonrandomized study; NR = not reported; RCT = randomized controlled trial; SR = systematic review; SSI = surgical site infection; TAS = triple antibiotic solution

Table 3: Characteristics of Included Primary Clinical Studies

Study citation, country, funding source	Study design	Population characteristics	Intervention and comparator(s)	Clinical outcomes, length of follow-up
Nguyen 2021[22] US Funding source: no financial support received	RCT (1:1; each patient served as own control, mastectomy pockets were randomized), blinded, single centre	Inclusion criteria: females 18 to 81 years old undergoing bilateral mastectomy and eligible for immediate TE breast reconstruction Exclusion criteria: allergy to antibiotic intervention or CHG; undergoing bilateral reconstruction using other techniques, or unilateral mastectomy and reconstruction 88 female patients, mean age 47 years	Intervention: TAS breast pocket irrigation (cefazolin, bacitracin, gentamicin in saline) Comparator: CHG breast pocket irrigation	Outcomes: SSI, necrosis, hematoma, seroma, allergic reaction, allergic reaction, death Follow-up: 28 to 606 days
Emile 2020[18] Egypt Funding source: no sources of funding	RCT, double-blind, single centre	Inclusion criteria: 16- to 65-year-olds with acute appendicitis Exclusion criteria: appendicular abscess/ mass, appendicitis associated with generalized peritonitis, acute abdomen, normal appendix, steroid or immunosuppressive medication 113 female, 92 male, mean age 27.9 (SD 8.7)	Interventions: • gentamicin-saline solution wound irrigation (n = 69) • normal saline wound irrigation (n = 67) Comparator: no irrigation (n = 69)	Outcomes: SSI, complications, hospital stay, pain, patient satisfaction, seroma, hematoma, wound dehiscence Follow-up: 1, 2, 4, and 6 weeks after surgery
Negahi 2020[21] Iran Funding source: NR	RCT, double-blind, single centre	40 patients undergoing laparoscopic colectomy	Intervention (n = 20): gentamicin-clindamycin lavage Comparator (n = 20): normal saline lavage	Outcomes: pain, painkiller need, white blood cell count, hospital stay, C-reactive protein level, wound infection Follow-up: up to 30 days

Study citation, country, funding source	Study design	Population characteristics	Intervention and comparator(s)	Clinical outcomes, length of follow-up
Okunlola 2020[23] Nigeria Funding source: NR	RCT, blinded, single centre	Adults undergoing neurosurgical procedures 50 female, 82 male, mean age 48.5	Intervention (n = 66): intravenous ceftriaxone at induction of anesthesia followed by 12 hourly for 24 hours post-operatively and intraoperative wound irrigation with ceftriaxone in saline Comparator (n = 66): intravenous ceftriaxone at induction of anesthesia followed by 12 hourly for 24 hours post-operatively and intraoperative wound irrigation with plain normal saline	Outcomes: SSI, wound edge necrosis, mortality Follow-up: up to 30 days
Slopnick 2020[24] US Funding source: no extra-institutional funding	RCT (1:1), double-blind, single centre	Inclusion criteria: female adults undergoing gynecological surgery requiring intraoperative cystoscopy Exclusion criteria: history of UTIs, neurogenic bladder, neomycin or polymyxin allergy, nephrolithiasis, congenital urogenital anomaly, pregnancy, or surgery with intradetrusor onabotulinumtoxin A injection, mesh excision, or fistula repair; positive urine culture Mean age 51.6 (range 29 to 86)	Intervention (n = 111): Neosporin irrigation (200,000 U polymyxin B sulfate and 40 mg neomycin sulfate) Comparator (n = 116): normal saline irrigation	Outcomes: treatment of UTI, adverse events Follow-up: 6 weeks

Study citation, country, funding source	Study design	Population characteristics	Intervention and comparator(s)	Clinical outcomes, length of follow-up
Maatman 2019[20] US Funding source: Department of Surgery, Indiana University School of Medicine	RCT, double-blind, single centre	Inclusion criteria: adults undergoing nonemergent open pancreato-duodenectomy Exclusion criteria: imprisoned, pregnant, undergoing concomitant colectomy/hepatectomy; allergic to study medications; preoperative serum creatinine >2.0 mg/dL Intervention group: mean age 63.7 (SEM 1.3) Comparator group: mean age 64.4 (SEM 1.5)	Intervention (n = 95): intraperitoneal irrigation with polymyxin B in saline Comparator (n = 95): saline irrigation	Outcomes: SSI, hospital stay, POPF, complications, mortality Follow-up: up to 90 days
Krahn 2018[19] Canada and Netherlands Funding source: CANNeCTIN network and clinical trial grant from CIHR	Cluster randomized crossover trial, blinded, multi-centre (24 centres Canada, 4 centres Netherlands)	19,603 patients undergoing cardiac implantable electronic device procedures Mean age 72.0 (SD 13.1) 33.9% female	Incremental therapy: IV cefazolin and preoperative vancomycin (vancomycin only for penicillin-allergic patients); intraoperative wound pocket wash of bacitracin in saline; post-operative oral cephalexin 4 times/day, or cephadroxil 2 times/day for 2 days (clindamycin 3 times/day for penicillin-allergic patients; sites where bacitracin was not available used cefazolin or saline instead Conventional therapy: single dose of preoperative IV cefazolin 60 minutes before skin incision (vancomycin within 120 minutes before skin incision in penicillin-allergic patients)	Outcome: hospitalization for device infection, infection requiring surgical intervention, adverse events Follow-up: within 1 year

CANNeCTIN = The Canadian Network and Centre for Trials Internationally; CHG = chlorhexidine gluconate; CIHR = Canadian Institutes of Health Research; IV = intravenous; NR = not reported; POPF = post-operative pancreatic fistula; RCT = randomized controlled trial; SD = standard deviation; SEM = standard error of the mean; SSI = surgical site infection; TAS = triple antibiotic solution; TE = tissue expander; UTI = urinary tract infection

Table 4: Characteristics of Included Guideline

Intended users, target population	Intervention and practice considered	Major outcomes considered	Evidence collection, selection, and synthesis	Evidence quality assessment	Recommendations development and evaluation	Guideline validation
NICE 2019[25,26]						
Intended users: health care professionals; commissioners and providers; people having surgery (their families and carers) Target population: adults, young people, children undergoing surgery involving a cut through the skin	Methods for before, during, and after surgery to minimize infection risk; only guidelines for intraoperative wound irrigation, intracavity lavage, and antibiotic application before wound closure are relevant to the present review	SSIs	**2008 guideline** Searches in 6 databases for English publications; scoping searches to identify other guidelines with reference lists checked; additional evidence submitted by stakeholders **2019 guideline** New evidence found; searches in 10 databases for English publications; additional searches from reference lists and other SRs' reference lists	**2008 guideline** 8 levels of hierarchical evidence across study designs **2019 guideline** SRs: ROBIS, RCTs: Cochrane ROB or ROBINS-I tool, GRADE for quality of evidence	**2008 guideline** Informal consensus methods seeking evidence where needed, followed by formal consensus methods **2019 guideline** Committee discussion of evidence	Experts were involved in the guideline development; regular surveillance for 2008 guideline after 3, 6, and 8 years prompted an update; external stakeholders asked to review guideline draft

GRADE = Grading of Recommendations Assessment, Development and Evaluation; RCT = randomized controlled trial; ROB = risk of bias; ROBINS-I = Risk Of Bias In Non-randomised Studies - of Interventions; ROBIS = Risk of Bias in Systematic Reviews; SR = systematic review; SSI = surgical site infection

Appendix 3: Critical Appraisal of Included Publications

Note that this appendix has not been copy-edited.

Table 5: Strengths and Limitations of Systematic Reviews and Network Meta-Analyses Using AMSTAR 2[9] and the ISPOR Questionnaire[10,11]

Strengths	Limitations
Baker 2021[14]	
• The population, intervention of interest and outcomes were clearly stated. • At least 2 databases were searched and keywords were provided. • Two reviewers conducted screening and data extraction. • Authors considered and listed examples of heterogeneity in methods across studies.	• The comparators of interest and publication languages to be searched for were not explicitly stated. Additional sources of studies beyond databases were not searched. • It is unclear whether a review protocol was established before conducting the review. • An explanation for including both RCTs and NRS was not provided. • The methods for consensus for screening and extraction were not reported. • Excluded studies with justifications were not provided. • Authors did not describe all included studies in sufficient detail. • Review authors did not assess the risk of bias of primary studies or report on funding of included studies. • It is unclear how the conflict of interest reported affected the conduct or reporting of the review.
Leas 2021[15]	
• The population, intervention, comparators, outcomes, and follow-up times were clearly stated. • A protocol for the systematic review was provided. • At least 2 databases were searched, keywords for the search strategy were provided, and publication restrictions were justified. • Authors described interventions, comparators, outcomes, and study designs of included studies in detail. • Authors used a satisfactory technique for assessing risk of bias for individual studies. • Risk of bias of individual studies and overall evidence summary was provided. • The authors declared no conflicts of interest.	• Justification for study design was not provided. • It is unclear whether additional sources of studies beyond databases were searched. • It is unclear whether study selection and extraction was conducted in duplicate. • It is unclear if the authors considered overlap between primary studies and studies in included reviews, or if included reviews were assessed for risk of bias with consideration of primary studies. • Excluded studies with justifications were not provided. • Patient characteristics were not provided in sufficient detail. • Review authors did not report on funding of included studies. • Heterogeneity was not reported on.

Strengths	Limitations
Saeg 2021[17]	
• The intervention and outcomes were clearly stated. • At least 2 databases were searched, keywords were provided, and reference lists were reviewed for potentially relevant studies. • Two reviewers independently screened articles and extracted data. • Authors described interventions, comparators, outcomes, and study designs of included studies in detail. • Authors described heterogeneity across studies.	• The specific populations and comparators of interest were not clearly stated. • It is unclear whether a review protocol was established before conducting the review. • It is unclear if the authors considered overlap between primary studies and studies in included reviews and MAs or if included reviews were assessed for risk of bias with consideration of primary studies. • An explanation for including both RCTs and NRS was not provided. • Publication restrictions for the search were not justified, and additional sources beyond databases and reference lists were not searched. • Excluded studies with justifications were not provided. • Patient characteristics and follow-up time were not provided in sufficient detail. • The method for assessing risk of bias did not consider study design, confounding, unconcealed allocation, outcome measurement, or reporting bias. Risk of bias was not accounted for when presenting results. • Review authors did not report on funding of included studies. • It is unclear how the conflicts of interests mentioned affect the results of the study.

Strengths	Limitations
Thom 2021[6]	
• The population, intervention, comparators, and outcomes were clearly stated and relevant to the current review. • An explanation for including only RCTs was provided. • At least 2 databases, clinical trial registries, references of included studies, and references of relevant systematic reviews were searched. There were no publication restrictions. • Two reviewers independently screened articles and appraised risk of bias. • Reasons for excluding studies from the NMA were provided. • The network for the NMA contained direct and indirect comparisons between antibiotic, antiseptic, saline and no irrigation. • Authors described interventions, comparators, outcomes, follow-up times, and study designs of included studies in detail. • Authors used a satisfactory technique for assessing risk of bias for individual studies. • Appropriate methods were employed for statistical combination of results with heterogeneity, inconsistency, and risk of bias across studies being taken into account. • Sensitivity analyses were conducted to determine if publication dates affected results. • Inconsistency was assessed and there was no evidence of inconsistency in the NMA results. Both direct and indirect evidence was included in the NMA. • A valid rationale for use of random-effects models was provided. Assumptions about heterogeneity were explored. Subgroup analyses were performed where possible due to high heterogeneity. • Individual study results were reported in an online supplement. • Treatment effect estimates are presented with measures of uncertainty. • A rank probability plot with uncertainty is provided. • Separate results were reported by important patient characteristics.	• It is unclear whether a review protocol was established before conducting the review. • The search strategy or keywords were not provided. It is unclear if grey literature was searched. • Further details about included populations were not specified. • It is unclear whether 2 reviewers conducted data extraction. • Excluded studies with justifications were not provided. • Review authors did not report on funding of included studies. • It is unclear how funding potentially affected the review. • The conclusions were likely biased due to unexplained high heterogeneity across studies, and high or unclear risk of bias of individual studies. There is low confidence in the results of the NMA. • Other potentially relevant outcomes such as wound healing, length of stay in hospital, and safety were not included in the NMA and the reason for this is unclear. • It is unclear how treatment effect modifiers affected the results of the NMA. • It is unclear whether statistical methods preserved within-study randomization. • It is unclear whether there are separate results for direct and indirect comparisons.

Strengths	Limitations
López-Cano 2019[16]	
• The population, intervention, comparators, and outcomes were clearly stated. • A protocol with review methods was established before the review was conducted. • The authors provided justification for including only RCTs so that strong evidence could be used to inform recommendations. • At least 2 databases were searched and keywords for the search strategy were provided. References of retrieved studies were also considered. • Study screening and extraction was conducted independently by 3 reviewers. • Authors described interventions, outcomes, follow-up times, and study designs of included studies in detail. • The technique used for assessing risk of bias for individual studies was appropriate as it included consideration of randomization, concealment, blinding, and the timing of when the outcome was measured. • Appropriate methods for statistical combination of results were used, with heterogeneity in meta-analyses considered. Analyses were conducted with and without low-quality studies to detect differences. • According to the authors, an analysis revealed that there was no publication bias among included RCTs. • The authors declared no conflicts of interest.	• Additional literature from study registries and grey literature were not included. • Excluded studies with justifications were not provided. • Patient characteristics and comparators were not provided in sufficient detail. • Review authors did not report on funding of included studies.

AMSTAR 2 = A MeaSurement Tool to Assess systematic Reviews 2; ISPOR = International Society for Pharmacoeconomics and Outcomes Research; MA = meta-analysis; NMA = network meta-analysis; NRS = nonrandomized study; RCT = randomized controlled trial

Table 6: Strengths and Limitations of Clinical Studies Using the Downs and Black Checklist[12]

Strengths	Limitations
Nguyen 2021[22]	
• The objective, main outcomes, patient characteristics, interventions, control for confounders, and main findings were clearly described. • Adverse events were reported. • Exact probability values were reported. • Surgeons were blinded to study group. • Main outcome measures were clearly described. • Since the same patients were used for intervention and comparator groups, there is likely high internal validity. • Patients were recruited over the same time period.	• Random variability of the outcome data was not clearly described. • It is unclear whether the patients recruited, patients prepared to participate, or the staff, places, and facilities where patients were treated were representative. The surgical group prescribed post-operative oral antibiotics for 14 days which may not be comparable to practices in other surgical settings. • It is unclear whether patients or those measuring outcomes were blind to assignment. • The definitions for infections were subjective and may have been assessed differently by clinicians. • It is unclear whether differences in follow-up time for measured outcomes were adjusted for. Further, the study was terminated early due to the withdrawal of bacitracin from the market in January 2020. • It is unclear whether statistical tests were appropriate as 359 total patients were required for analysis and the study had a small sample size of 88 patients in total. Due to the small sample size, it is likely the study did not have sufficient power. • It is unclear whether there was any noncompliance or misclassification bias. • It remains unclear whether the investigators used appropriate allocation techniques to prevent selection bias. • Authors indicated that if there were differences in characteristics between bilateral pockets, they were not adjusted for.

Strengths	Limitations
Emile 2020[18]	
• The objectives, main outcomes, patient characteristics, interventions, confounders, random variability of the outcomes, and main findings were clearly described. • Adverse events were reported. • There was minimal loss to follow-up. • Exact probability values were reported. • Patients and outcome assessors were blind to study assignment. • Lengths of follow-up were the same for all patients. • Statistical tests were appropriate, and the normality of the data was considered. • The patients in different intervention groups were likely from the same population as they presented to the same emergency department and were recruited over the same time period. • Patients were randomized to study groups and allocation was concealed in sealed opaque envelopes. • The study had sufficient power to detect an effect since the number of randomized patients was greater than the number of patients required in the study from the power calculation.	• It is unclear whether the patients recruited, patients prepared to participate, or the staff, places, and facilities where patients were treated were representative. • Data were analyzed using a per-protocol approach which may have biased the results.
Negahi 2020[21]	
• The objectives, main outcomes, and interventions were clearly described. • Exact probability values were reported. • The surgeons and residents visiting patients after the operation were not aware of study assignment. • Pain outcomes were measured at the same time points for both study groups (3, 6, 12, 24 hours after surgery). • The patients in different intervention groups were likely from the same population as they are from the same hospital and were recruited over the same time period. • Patients were randomized to study groups.	• Patient characteristics, confounders, and main findings were not clearly described. • Random variability values were provided; however, whether the values provided were standard deviations, standard errors, or standard error of the mean is unknown • It is unclear if all relevant adverse events were measured. • It is unclear if there was any loss to follow-up or missing data, and how any differences were accounted for. • It is unclear whether the patients recruited, patients prepared to participate, or the staff, places, and facilities where patients were treated were representative. • Patients were not blind to study assignment. • It is unclear if statistical tests were appropriate. • It is unclear whether allocation to study assignment was concealed. • It is unclear whether a statistical power calculation was done since a power calculation was not reported in the publication.

Strengths	Limitations
Okunlola 2020[23]	
• The objectives, main outcomes, interventions, and main findings were clearly described. • Adverse events such as mortality were measured. • When provided, probability values are exact. • Patients and surgeons were blinded to study assignment. • The patients in different intervention groups were likely from the same population as they were in the same hospital and were recruited over the same time period. • Patients were randomized to study groups.	• Patient characteristics were not clearly described. • Random variability of outcomes was not clearly reported. • It is unclear if there was any loss to follow-up or missing data, and how any differences were accounted for. • It is unclear whether the patients recruited, patients prepared to participate, or the staff, places, and facilities where patients were treated were representative. • It is unclear if statistical tests were appropriate. • It is unclear whether allocation to study assignment was concealed. • According to the authors, the study had a small sample size. It is unclear whether there was sufficient power to detect an effect since a power calculation was not reported in the publication .
Slopnick 2020[24]	
• The objectives, main outcomes, patient characteristics, interventions, and confounders were clearly described. • Adverse events were measured. • There was minimal loss to follow-up. • Exact probability values were provided for the main outcomes. • Patients and surgeons were blinded to study assignment. • Statistical tests were appropriately described. • The patients in different intervention groups were likely from the same population as they were in the same medical centre and were recruited over the same time period. • Patients were randomized to study groups and allocation was concealed in opaque envelopes.	• Simple outcome data and random variability of this data was not reported. • It is unclear whether the patients recruited, patients prepared to participate, or the staff, places, and facilities where patients were treated were representative. • It is unclear if outcomes measured at different time points were adjusted for. • Statistical analyses accounted for some important covariates, however there were differences in surgical procedures across patients, and factors such as duration of post-operative catheterization and operative time were not adjusted for. • According to the authors, the study was underpowered to detect an effect because of low UTI rates. In addition, the study sample was lower than what the power calculation required.
Maatman 2019[20]	
• The objectives, main outcomes, patient characteristics, interventions, confounders, and main findings were clearly described. • Outcomes were measured for all patients. • Exact probability values were reported. • The patient, research nurse coordinator, and treating surgeon were blinded to study assignment. • Statistical tests were appropriately described. • Patients were randomized to study groups. • According to the authors, the study had sufficient power to detect an effect. The numbers of patients in each study arm was greater than the number needed to detect an effect.	• Random variability of the outcome data was not clearly reported. • Adverse events were not evaluated. • It is unclear whether the patients recruited, patients prepared to participate, or the staff, places, and facilities where patients were treated were representative. • It is unclear whether patients were recruited to the same location over the same time period. • It is unclear if allocation was concealed. • The intervention group had more patients with a history of tobacco use and pulmonary disease which may have affected the results.

Strengths	Limitations
Krahn 2018[19]	
• The objectives, main outcome, interventions, confounders, random variability of the results, and main findings were clearly described. • Adverse events were reported in the appendix. • There was minimal loss to follow-up. • Actual probability values were reported. • Outcome assessors were blinded. • Statistical tests were appropriate; confounders were considered, intention-to-treat analyses were conducted, and sensitivity analyses were performed. • Patients were recruited over the same time period. • Patients were randomized to study groups. • According to the study authors, the study had sufficient power to detect an effect	• Patient characteristics were not clearly described. • It is unclear whether the patients recruited, patients prepared to participate, or the staff, places, and facilities where patients were treated were representative. • It is unclear if patients were blinded. • It is unclear how differences in follow-up time of outcomes were adjusted for. • There was higher noncompliance in the intervention group compared to the comparator group. • Any potential conflicts of interest were not reported on. • Since bacitracin was unavailable at 1 Canadian site and all Netherlands sites, meaning a cefazolin or saline pocket wash was administered, this may have biased the results since the intervention was not compared to the same comparator irrigation solution at some study sites.

Table 7: Strengths and Limitations of Guideline Using AGREE II[13]

Item	Nice 2019[25,26]
Domain 1: Scope and Purpose	
1. The overall objective(s) of the guideline is (are) specifically described.	Yes
2. The health question(s) covered by the guideline is (are) specifically described.	Yes
3. The population (patients, public, etc.) to whom the guideline is meant to apply is specifically described.	Yes
Domain 2: Stakeholder Involvement	
4. The guideline development group includes individuals from all relevant professional groups.	Yes
5. The views and preferences of the target population (patients, public, etc.) have been sought.	Yes
6. The target users of the guideline are clearly defined.	Yes
Domain 3: Rigour of Development	
7. Systematic methods were used to search for evidence.	Yes
8. The criteria for selecting the evidence are clearly described.	Yes
9. The strengths and limitations of the body of evidence are clearly described.	Yes
10. The methods for formulating the recommendations are clearly described.	Unclear
11. The health benefits, side effects, and risks have been considered in formulating the recommendations.	Yes
12. There is an explicit link between the recommendations and the supporting evidence.	Unclear
13. The guideline has been externally reviewed by experts prior to its publication.	Yes
14. A procedure for updating the guideline is provided.	Yes

Item	Nice 2019[25,26]
Domain 4: Clarity of Presentation	
15. The recommendations are specific and unambiguous.	Unclear
16. The different options for management of the condition or health issue are clearly presented.	Unclear
17. Key recommendations are easily identifiable.	Yes
Domain 5: Applicability	
18. The guideline describes facilitators and barriers to its application.	Unclear
19. The guideline provides advice and/or tools on how the recommendations can be put into practice.	Unclear
20. The potential resource implications of applying the recommendations have been considered.	Unclear
21. The guideline presents monitoring and/or auditing criteria.	Yes
Domain 6: Editorial Independence	
22. The views of the funding body have not influenced the content of the guideline.	Unclear
23. Competing interests of guideline development group members have been recorded and addressed.	Yes

AGREE II = Appraisal of Guidelines for Research and Evaluation II

Appendix 4: Main Study Findings and Authors' Conclusions

Note that this appendix has not been copy-edited.

Table 8: Summary of Findings for Infection-related Outcomes

Study citation and study design	Detailed findings
Antibiotic solution irrigation compared to antiseptic solution irrigation	
Baker 2021[14] SR	**Retrospective cohort studies** **Merceron et al. (2019)** • Statistically significant reduction in risk of infection in CHG group compared to TAS group (P = 0.006). ◦ CHG: 6.4% ◦ TAS: 12.7% **Haynes (2018)** • Infection rate across study groups. (Comparison between TAS alone and CHG alone was not provided) ◦ TAS and CHG: 3% ◦ CHG alone: 5.9% ◦ TAS alone: 5.8%
Nguyen 2021[22] RCT	• SSI did not differ statistically between TAS and CHG groups (P = 0.35) ◦ TAS: 4 patients (4.5%) ◦ CHG: 7 patients (8.0%) • Minor infections did not differ statistically between TAS and CHG groups (P = 0.56) ◦ TAS: 2 patients (2.3%) ◦ CHG: 1 patient (1.1%) • Major infections did not differ statistically between TAS and CHG groups (P = 0.15) ◦ TAS: 2 patients (2.3%) ◦ CHG: 6 patients (6.8%) • Explantation did not differ statistically between TAS and CHG groups (P = 0.25) ◦ TAS: 2 patients (2.3%) ◦ CHG: 5 patients (4.5%)
Thom 2021[6] SR	Based on NMA results of 42 RCTs and 11, 726 patients, antibiotic is not statistically superior to antiseptic: SSI OR 0.77 (95% CrI, 0.4 to 1.54)
Antibiotic solution irrigation compared to saline irrigation	
Baker 2021[14] SR	**Boustany et al. (2018)** • No statistically significant reduction in infection rates comparing antibiotic to saline irrigation in a retrospective cohort study of 292 patients. (P value was not provided) ◦ Bacitracin: 19.7% ◦ Cefazolin: 18.6% ◦ Saline: 9.09%

Study citation and study design	Detailed findings
Leas 2021[15] SR	**Campbell (2018)** • Infections reduced in cefuroxime and gentamicin group compared to saline group (statistically significant, P < 0.05) based on 4 studies from an SR with 5,556 patients. • Infections reduced in cephalothin group compared to saline group (statistically significant, P = 0.03) ◦ Cephalothin: 6.7% ◦ Saline: 12.8%
Saeg 2021[17] SR	**Lynch et al. (2018)** • Statistically significant reduction in clinical infection from antibiotic irrigation compared to normal saline based on MA results from 4,725 patients: RR = 0.52 (95% CI, 0.33 to 0.81)
Thom 2021[6] SR	Based on NMA results, antibiotic agents have statistically lower odds of SSI compared to saline. • SSI mean OR 0.439 (95% CrI, 0.282 to 0.667) • Aminoglycoside compared to saline ◦ SSI OR 0.301 (95% CrI, 0.135 to 0.588) • Penicillin compared to saline ◦ SSI OR 0.349 (95% CrI, 0.099 to 0.823) • Cephalosporin compared to saline ◦ SSI OR 0.579 (95% CrI, 0.307 to 1.16) • Other antibiotics (not specified) compared to saline ◦ SSI OR 0.498 (95% CrI, 0.265 to 0.977) "Antibiotic irrigation most likely to have lowest SSI rates relative to non-antibacterial irrigation (p. 150)."[6]
Emile 2020[18] RCT	No statistically significant differences in SSI between gentamicin-saline compared to saline irrigation (P = 0.99) • Gentamicin-saline: 3 (4.3%) • Saline: 2 (2.9%) Based on post hoc analyses, the gentamicin-saline group had similar SSI rate compared to saline irrigation group (not statistically significant, P = 0.67). Overall, there was superficial incisional SSI in 15 patients and deep incisional SSI in 2 patients who were given antibiotics based on sensitivity and culture tests. (Values not broken down by study group) Five patients (29.4%) needed infected surgical wound drainage. (Values not broken down by study group)
Negahi 2020[21] RCT	Specific measure for random variability (e.g., standard deviation, standard error of the mean) not defined in study • WBC count after 12 hours (statistically significant, P = 0.0001) ◦ Gentamycin-clindamycin lavage: 10.5 mm^3 (± 1.4) ◦ Normal saline lavage: 12.8 $per.mm^3$ (± 1.9) • CRP level after 12 hours was better in gentamycin-clindamycin lavage group compared to normal saline lavage group. (No further values reported).
Okunlola 2020[23] RCT	No statistically significant difference in SSI between ceftriaxone and normal saline groups (P = 1.00) • Ceftriaxone irrigation: 2 (3.0%) • Normal saline irrigation: 1 (1.5%)

Study citation and study design	Detailed findings
Maatman 2019[20] RCT	No statistically difference between groups for SSI (P > 0.61) • Polymyxin B: 10% • Saline: 15% "The overall incidence of superficial SSI and organ-space SSI was 4.7% (n = 9) and 7.9% (n = 15), respectively. The diagnosis of superficial SSI was made by (n = 4) purulent discharge (criteria 1), (n = 4) symptoms of infection with surgical opening of the wound (criteria 3), and (n = 1) culture positivity (criteria 2). The diagnosis of organ-space SSI was made by culture positivity (criteria 2) in all cases. The rate of superficial SSI was 3% vs 6%, and the rate of organ space infection was 7% vs 8% (P > .31 each) (p. 471)."[20]
Antibiotic solution irrigation compared to no irrigation	
Emile 2020[18] RCT	SSI significantly lower for gentamicin-saline and saline groups compared to no irrigation (statistically significant, P = 0.005). SSI significantly lower for gentamicin-saline compared to no irrigation (statistically significant, P = 0.02). • Gentamicin-saline: 3 (4.3%) • No irrigation: 12 (17.4%) Posthoc analysis: Gentamicin-saline group lower SSI rate compared to no irrigation group which was not statistically significant (Authors report P = 0.02; unclear whether there is statistical significance or not).
Krahn 2018[19] RCT	Infection requiring surgical intervention was not statistically significant between groups • Bacitracin group: 62 (0.95% overall, 94% of infections) • No irrigation group: 66 (1.05% overall, 86% of infections) • OR 0.90 (95% CI, 0.64 to 1.28, P = 0.57)
Antibiotic solution irrigation compared to no antibiotic solution irrigation	
López-Cano 2019[16] SR	**Surgical site infections** **Evans et al. (1974)** • Cephaloridine:17/188 • Control: 47/213 **Pitt et al. (1980)** • Cephradine group: 3/113 • Control: 14/62 **Freischlag et al. (1984)** • Cefamandole group: 4/26 • Control group: 1/36 **Moesgaard et al. (1989)** • Cefotaxime group: 15/87 • Control group: 14/90 **Seco et al. (1990)** • Ampicillin group: 5/126 • Control group: 15/120 **Lazorthes et al. (1992)** • Cefamandole group: 0/162 • Control group: 7/162

Study citation and study design	Detailed findings
López-Cano 2019[16] SR (continued)	**Al-Shehri et al. (1994)** • Ampicillin group: 1/117 • Control group: 7/132 **Moesgaard et al. (1988)** • Gentamicin group: 19/41 • Control group: 18/38 **Praveen et al. (2009)** • Gentamicin group: 7/100 • Control group: 7/102 **Ruiz-Tovar et al. (2012)** • Gentamicin group: 2/52 • Control group: 7/51 **Evans et al. (1974), Pitt et al. (1980) and Moesgaard et al. (1989)** (2 RCTs, 753 patients) • β-lactams as irrigation solution are not effective for reducing SSIs • RR 0.42 (not statistically significant, 95% CI, 0.15 to 1.18), I^2 = 83%

CHG = chlorhexidine gluconate; CI = confidence interval; CrI = credible interval; CRP = C-reactive protein; MA = meta-analysis; OR = odds ratio; RCT = randomized controlled trial; RR = relative risk; SR = systematic review; SSI = surgical site infection; TAS = triple antibiotic solution; WBC = white blood cells

Table 9: Summary of Findings for Capsular Contracture

Study citation and study design	Detailed findings
Antibiotic solution irrigation compared to antiseptic solution irrigation	
Baker 2021[14] SR	**Merceron et al. (2019)** • No statistically significant differences in CC between groups (P = 0.086) in a retrospective cohort study. ◦ CHG group: 4.7% ◦ TAS group: 8.1%
Antibiotic solution irrigation compared to saline irrigation	
Baker 2021[14] SR	**Drinane et al. (2014)** • CC rates were not reduced after TAS irrigation in a retrospective cohort study of 55 patients. (P value was not provided) ◦ TAS group: 3.70% ◦ Saline group: 3.57%
Leas 2021[15] SR	**Campbell et al. (2018)** • No differences in cefuroxime and gentamicin compared to saline group, or cephalothin compared to saline group based on 4 studies from an SR with 5,556 patients. (Further details not provided)

Study citation and study design	Detailed findings
Saeg 2021[17] SR	**Retrospective cohort studies** **Blount et al. 2013** • There was a statistically significant reduction in CC rate compared to normal saline (P = 0.04) in a study of 856 patients. ◦ TAS: 0.4% ◦ Normal saline: 3.9% **Drinane et al. (2016)** • No differences between TAS and normal saline in a study of 55 patients. (P value was not provided) **SRs/MAs** **Samargandi et al. (2018)** • No differences between antibiotic irrigation and normal saline in this SR. (P value was not provided) **Lynch et al. (2018)** • A statistically significant reduction in CC from antibiotic irrigation compared to normal saline irrigation based on MA results from 4,725 patients. ◦ RR 0.36 (95% CI, 0.16 to 0.83) • "Triple antibiotic irrigation may be more effective than NS at reducing the risk of capsular contracture; however, large studies have reported antimicrobial irrigation to increase the risk of capsular contracture (p. 609e)."[17] • "Gravity lavage with antibiotics is more effective than NS at reducing infection rate and may improve risk of capsular contracture (p. 609e)."[17]

CC = capsular contracture; CHG = chlorhexidine gluconate; CI = confidence interval; MA = meta-analysis; RR = relative risk; SR = systematic review; TAS = triple antibiotic solution

Table 10: Summary of Findings for Hospital-Related Outcomes

Study citation and study design	Detailed findings
Antibiotic solution irrigation compared to saline irrigation	
Emile 2020[18] RCT	Mean hospital stay in days similar across groups (not statistically significant, P = 0.18) • Gentamicin-saline: 1.1 (SD 0.26) • Saline: 1.05 (SD 0.24)
Negahi 2020[21] RCT	Hospital stay in days significantly lower in antibiotic group (statistically significant, P = 0.014) • Gentamycin-clindamycin lavage: 4.2 days (± 0.41) • Normal saline lavage: 4.65 days (± 0.67)
Maatman 2019[20] RCT	Post-operative duration of hospital stay in median number of days (not statistically significant, P = 0.69) • Polymyxin B irrigation group: 7 days (range 4 to 32) • Saline group: 8 days (range 4 to 24)

Study citation and study design	Detailed findings
Antibiotic solution irrigation compared to no irrigation	
Emile 2020[18] RCT	Mean hospital stay in days similar across groups (not statistically significant, P = 0.18) • Gentamicin-saline: 1.1 (SD 0.26) • No irrigation: 1.14 (SD 0.3)
Krahn 2018[19] RCT	No statistically significant differences in hospitalization across groups • Overall (hospitalization for device infection) ◦ Bacitracin group: 78 (0.78%) ◦ No irrigation group: 99 (1.03%) ◦ OR 0.77 (95% CI, 0.56 to 1.05, P = 0.10) • High-risk patients (hospitalization for device infection) ◦ Bacitracin group: 66 (1.01%) ◦ No irrigation group: 77 (1.23%) ◦ OR 0.82 (95% CI, 0.59 to 1.15, P = 0.26)

CI = confidence interval; OR = odds ratio; RCT = randomized controlled trial; SD = standard deviation

Table 11: Summary of Findings for Pain-Related Outcomes

Study citation and study design	Detailed findings
Antibiotic solution irrigation compared to saline irrigation	
Emile 2020[18] RCT	Pain visual analogue score was similar across groups (not statistically significant, P = 0.83) • Gentamicin-saline: 4.04 (SD 1.4) • Saline: 3.68 (SD 1.2)
Negahi 2020[21] RCT	**Specific measure for random variability (e.g., standard deviation, standard error of the mean) not defined** Mean pain score after 3 hours of operation (statistically significant, P = 0.0011) • Gentamycin-clindamycin lavage: 3.4 (± 1.2) • Normal saline lavage: 4.8 (± 1.3) Mean pain score after 24 hours of operation (statistically significant, P < 0.0001) • Gentamycin-clindamycin lavage: 2.6 (± 0.81) • Normal saline lavage: 3.7 (± 0.64) Acetaminophen needed after 3 hours (not statistically significant, P = 0.06) • Gentamycin-clindamycin lavage: 8 patients • Normal saline lavage: 14 patients Acetaminophen amount needed after 24 hours (statistically significant, P = 0.004) • Gentamicin-clindamycin lavage: 1.75g (± 0.72) • Normal saline lavage: 2.4g (± 0.60) Pethidine amount needed after 24 hours (not statistically significant, P = 0.12) • Gentamicin-clindamycin lavage: 0.3mg (± 0.57) • Normal saline lavage: 1.9mg (± 4.5)

Study citation and study design	Detailed findings
Antibiotic solution irrigation compared to no irrigation	
Emile 2020[18] RCT	Pain visual analogue score was similar across groups (not statistically significant, P = 0.83) • Gentamicin-saline: 4.04 (SD 1.4) • No irrigation: 4.13 (SD 1.6)

RCT = randomized controlled trial; SD = standard deviation

Table 12: Summary of Findings for Patient Satisfaction

Study citation and study design	Detailed findings
Antibiotic solution irrigation compared to saline irrigation	
Emile 2020[18] RCT	Patient satisfaction, rated as completely or partly satisfied, was higher in the gentamicin-saline and saline groups compared tothe no irrigation group (statistically significant, P <0.001) • Gentamicin-saline: 92.8% • Saline: 97% • No irrigation: 78.2%
Antibiotic solution irrigation compared to no irrigation	
Emile 2020[18] RCT	Patient satisfaction, rated as completely or partly satisfied, was higher in the gentamicin-saline and saline groups compared to the no irrigation group (statistically significant, P <0.001) • Gentamicin-saline: 92.8% • Saline: 97% • No irrigation: 78.2%

RCT = randomized controlled trial

Table 13: Summary of Findings for Wound-Related Outcomes

Study citation and study design	Detailed findings
Antibiotic solution irrigation compared to antiseptic irrigation	
Nguyen 2021[22] RCT	Necrosis did not differ between TAS and CHG groups (not statistically significant, P = 0.45) • TAS: 20 (22.7%) • CHG: 16 (18.2%) Hemotoma did not differ between TAS and CHG groups (not statistically significant, P = 0.56) • TAS: 1 (1.1%) • CHG: 2 (2.3%) Seroma did not differ between TAS and CHG groups (not statistically significant, P = 0.65) • TAS: 2 (2.3%) • CHG: 3 (3.4%)

Study citation and study design	Detailed findings
Antibiotic solution irrigation compared to saline irrigation	
Emile 2020[18] RCT	Seroma was similar across study groups (not statistically significant, P = 0.11) • Gentamicin-saline: 12 (17.4%) • Saline: 6 (8.9%) Overall, 4 patients with wound hematoma and 33 patients with wound seroma had one stich removed and collected fluid under antibiotic coverage was evacuation. Results were not broken down by study groups. Hematoma was similar across study groups (not statistically significant, P = 0.84) • Gentamicin-saline: 2 (2.8%) • Saline: 1 (1.5%) Wound dehiscence was similar across study groups (not statistically significant, P = 0.22) • Gentamicin-saline: 0 • Saline: 0 Two patients had superficial wound dehiscence secondary to SSI and were given daily dressing until complete healing by secondary intention.
Negahi 2020[21] RCT	**Specific measure for random variability (e.g., standard deviation, standard error of the mean) not defined** • Wound infection at 1 month follow-up ◦ Gentamicin-clindamycin lavage: 1 patient ◦ Normal saline lavage: 1 patient
Okunlola 2020[23] RCT	"The six patients with superficial epidermolysis of the wound edge had satisfactory wound healing but three out of the four patients with full thickness wound edge necrosis developed SSI (p. 2)."[23]
Antibiotic solution irrigation compared to no irrigation	
Emile 2020[18] RCT	Seroma was similar across study groups (not statistically significant, P = 0.11) • Gentamicin-saline: 12 (17.4%) • No irrigation: 15 (21.7%) Overall, 4 patients with wound hematoma and 33 patients with wound seroma had one stich removed and collected fluid under antibiotic coverage was evacuation. Hematoma was similar across study groups (not statistically significant, P = 0.84) • Gentamicin-saline: 2 (2.8%) • No irrigation: 1 (1.4%) Wound dehiscence was similar across study groups (not statistically significant, P = 0.22) • Gentamicin-saline: 0 • No irrigation: 2 (2.8%) Two patients had superficial wound dehiscence secondary to SSI and were given daily dressing until complete healing by secondary intention.

CHG = chlorhexidine gluconate; RCT = randomized controlled trial; SSI = surgical site infection; TAS = triple antibiotic solution

Table 14: Summary of Findings for Adverse Events and Complications

Study citation and study design	Detailed findings
Antibiotic solution irrigation compared to antiseptic irrigation	
Baker 2021[14] SR	**Retrospective cohort studies** **Merceron et al. (2019)** • Significant reduction in complications for CHG group compared to TAS group. (P value and 95% CI not provided) ◦ CHG group: 22.4% ◦ TAS group: 31.8% **Haynes (2018)** • Implant loss results (No further data provided) ◦ TAS and CHG: 0.3% ◦ CHG: 1.6% ◦ TAS: 3.4%
Nguyen 2021[22] RCT	No patients in either TAS or CHG groups had any allergic reactions.
Antibiotic solution irrigation compared to saline irrigation	
Emile 2020[18] RCT	"Surgical site occurrence (includes SSI, necrosis, cellulitis, chronic and/or non-healing wound, wound dehiscence, serous or purulent drainage, seroma (pocket of sterile clear serous fluid at the site of the incision), hematoma (collection of blood or clots in the surgical wound), or fistula at surgical site (p.142)."[18] • No statistically significant differences between gentamicin-saline compared to saline irrigation (P = 0.15) ◦ Gentamicin-saline: 17 (24.6%) ◦ Saline: 9 (13.4%) Results for urine retention or ileus (not statistically significant, P = 0.45) • Gentamicin-saline: 2 (2.8%) [1 urine retention, 1 ileus] • Saline: 3 (4.4%) [2 urine retention, 1 ileus] Intra-abdominal abscess: no events Bowel obstruction: no events Intestinal fistula: no events Adverse effects due to gentamicin use: no events

Study citation and study design	Detailed findings
Slopnick 2020[24] RCT	No difference between groups for treatment of UTI (not statistically significant, P = 0.718) • Neosporin group: 11.4% (95% CI, 5.0% to 18.0%) • Normal saline group: 9.9% (95% CI, 4.0% to 16.0%) • Adjusted OR 1.30 (CI, 0.53 to 3.16, P = 0.569) No difference between groups remained after limiting UTI timing to 2 weeks after surgery (not statistically significant, P = 509) • Neosporin group: 7.6% • Normal saline group: 5.4% No difference between groups remained after limiting to those needed vaginal prolapse repair (not statistically significant, P = 0.768) • Neosporin group: 18.5% • Normal saline group: 15.6% No association between antibiotic irrigation and new urinary frequency or urgency after surgery (not statistically significant, P = 0.07) • Neosporin group: 12.6% • Normal saline group: 21.9% "There were no adverse events related to the use of antibiotic irrigation (p. 2389)."[24]
Maatman 2019[20] RCT	Overall POPF 28.4% (n = 54). No statistically significant difference between study groups (P = 0.63) • Polymyxin B irrigation group: 26% • Saline group: 31% Overall, clinically relevant POPF 11.1% (n = 21). No statistically significant difference between groups (not statistically significant, P = 1.0) • Polymyxin B irrigation group: 12% • Saline group: 11% "All patients in this study underwent a duct to mucosa anastomotic technique for the pancreaticojejunostomy. No difference was observed in estimated blood loss, pancreatic duct size, gland texture, operative time, blood transfusion rates, or fistula risk score between the treatment and control groups (p. 471)."[20] Organ failure (not statistically significant, P = 1.0) • Polymyxin B irrigation group: 1 patient • Saline group: 2 patients Sepsis (not statistically significant, P = 0.50) • Polymyxin B irrigation group: 0 patients • Saline group: 2 patients Delayed gastric emptying (not statistically significant, P = 0.75) • Polymyxin B irrigation group: 4 patients (4%) • Saline group: 6 patients (6.3%)

Study citation and study design	Detailed findings
Maatman 2019[20] RCT (continued)	Bile leak (not statistically significant, P = 1.0) • Polymyxin B irrigation group: 4 patients (4%) • Saline group: 4 patients (4%) UTI (not statistically significant, P = 0.62) • Polymyxin B irrigation group: 3 patients (3%) • Saline group: 1 patient Venous thromboembolism (not statistically significant, P = 0.25) • Polymyxin B irrigation group: 0 patients • Saline group: 3 patients (3.2%) Cholangitis (not statistically significant, P = 1.0) • Polymyxin B irrigation group: 0 patients • Saline group: 1 patient Myocardial infarction (not statistically significant, P = 1.0) • Polymyxin B irrigation group: 0 patients • Saline group: 1 patient
Antibiotic solution irrigation compared to no irrigation	
Emile 2020[18] RCT	"Surgical site occurrence (includes SSI, necrosis, cellulitis, chronic and/or non-healing wound, wound dehiscence, serous or purulent drainage, seroma (pocket of sterile clear serous fluid at the site of the incision), hematoma (collection of blood or clots in the surgical wound), or fistula at surgical site (p.142)."[18] • Surgical site occurrence significantly lower for gentamicin-saline and saline groups compared to no irrigation (statistically significant, P < 0.001). Surgical site occurrence significantly lower for gentamicin-saline compared to no irrigation (statistically significant, P = 0.03). ◦ Gentamicin-saline: 17 (24.6%) ◦ No irrigation: 30 (43.5%) Results for urine retention or ileus (not statistically significant, P = 0.45) • Gentamicin-saline: 2 (2.8%) [1 urine retention, 1 ileus] • No irrigation: 1 (1.4%) [1 urine retention] Intra-abdominal abscess: no events Bowel obstruction: no events Intestinal fistula: no events Adverse effects due to gentamicin use: no events
Krahn 2018[19] RCT	Overall, adverse events were rare (0.26%) and similar in both study groups.

CHG = chlorhexidine gluconate; CI = confidence interval; OR = odds ratio; POPF = post-operative pancreatic fistula; RCT = randomized controlled trial; SR = systematic review; SSI = surgical site infection; TAS = triple antibiotic solution; UTI = urinary tract infection

Table 15: Summary of Findings for Mortality

Study citation and study design	Detailed findings
Antibiotic solution irrigation compared to antiseptic irrigation	
Nguyen 2021[22] RCT	2 patients died, with a mean follow-up time to death of 446.5 days
Antibiotic solution irrigation compared to saline irrigation	
Okunlola 2020[23] RCT	Overall, 30-day mortality was 10.6% and was not associated with SSI.
Maatman 2019[20] RCT	30-day mortality (not statistically significant, P = 1.0) • Polymyxin B irrigation: 1 patient • Saline: 2 patients 90-day mortality (not statistically significant, P = 1.0) • Polymyxin B irrigation: 4 patients (4%) • Saline: 4 patients (4%)

RCT = randomized controlled trial; SSI = surgical site infection

Table 16: Summary of Recommendations in Included Guideline

Recommendations and supporting evidence	Quality of evidence and strength of recommendations
NICE 2019[25,26]	
2008 guideline Wound irrigation and intracavity lavage: • "Do not use wound irrigation to reduce the risk of surgical site infection (p. 11)."[25] • "Do not use intracavity lavage to reduce the risk of surgical site infection (p. 11)."[25]	**2008 guideline** "There is evidence of no difference in SSI incidence after intraoperative subcutaneous wound irrigation using antibiotics or saline. [EL = 1+]. There is evidence from one study of decreased SSI incidence following intraoperative subcutaneous wound irrigation using povidone-iodine compared with saline. [EL = 1+]. There is evidence from one study of no difference in SSI incidence following use of subcutaneous wound irrigation compared with the use of a drain but with no irrigation. [EL = 1+]. There is evidence from one study that wound irrigation of the muscles and subcutaneous fat tissue (using saline under pressure with a syringe) compared with no irrigation decreases the incidence of SSI. [EL = 1+] (p. 71-72)"[25] "There is evidence of no difference in SSI incidence after antibiotic compared with saline lavage. [EL = 1+]. There is evidence from one study that the incidence of SSI is decreased when tetracycline lavage is compared with saline lavage. [EL = 1+]. There is evidence of no difference in SSIs incidence between antiseptic and saline intraoperative intracavity lavage. [EL = 1+]. There is evidence from one small study of fewer wound infections when povidone-iodine is used for post-operative lavage of the perineal space compared with saline. [EL = 1+]. There is evidence from one small study that there is no difference in wound infection rates between use of AOPW compared with saline for lavage. [EL = 1−]. There is evidence from one trial that the incidence of SSI is lower following treatment with intravenous latamoxef compared with lavage with tetracycline. [EL = 1+]. There is evidence of no difference in SSI incidence following the use of drains alone compared with saline lavage. [EL = 1+] There is evidence from one study of fewer SSIs occurring following pulsed saline lavage compared with saline lavage with a jug or syringe during hemiarthroplasty for displaced intracapsular fractured neck of femur. [EL = 1−] There is evidence from one small study that there is a significant increase in wound infection rates using saline CPPL compared with no CPPL. [EL = 1−]. Evidence from one small trial suggests that there is no difference in SSI rates between use of IV cefamandole or lavage and irrigation with cefamandole or lavage and irrigation and IV cefamandole. [EL = 1+]. Evidence from one small trial suggests that there is no difference in wound infection rate following lavage and wound irrigation with either saline or cefazolin. [EL = 1+] (p. 71-72)"[25]

Recommendations and supporting evidence	Quality of evidence and strength of recommendations
2019 guideline Antibiotics before wound closure: • "Only apply an antiseptic or antibiotic to the wound before closure as part of a clinical research trial (p. 12)."[26]	**2019 guideline** **Topical cefotaxime** Outcomes at 1 month after surgery • Very low-quality evidence from 1 RCT, including 177 people, could not differentiate the following outcomes between people who received topical cefotaxime before wound closure during abdominal surgeries and those who did not receive topical antibiotic: • SSI • Septicemia • Mortality post-surgery These results were also consistent in the following subgroups: • appendectomy • biliary surgery • colonic surgery • drainage of intra-abdominal abscess (p. 21)[26] **Topical cephaloridine** Outcomes at 1 month after surgery • Moderate quality evidence from 1 RCT, including 401 people, indicated that people who received topical cephaloridine before wound closure had a lower incidence of SSI compared to those who did not receive topical antibiotic. This result was also consistent in the following subgroups: • clean surgery • contaminated surgery (p. 22)[26]

AOPW = acidic oxidative potential water; CPPL = closed saline post-operative peritoneal lavage; EL = evidence level; IV = intravenous; RCT = randomized controlled trial; SSI = surgical site infection.

Appendix 5: Overlap Between Included Systematic Reviews

Table 17: Overlap in Relevant Primary Studies Between Included Systematic Reviews

Primary study citation	Baker 2021[14]	Leas 2021[15]	Saeg 2021[17]	Thom 2021[6]	López-Cano 2019[16]
Merceron TK, et al. Mod Plast Surg. 2019;9(4):74-85.	Yes	No	No	No	No
Boustany AN, et al. Indian J Plast Surg. 2018;51(1):7-14.	Yes	No	No	No	No
Campbell CA. Ann Plast Surg. 2018;80(6S Suppl 6):S398-S402	No	Yes	Yes	No	No
Haynes DA. Conference abstract presented at SESPRS 61st Annual Meeting; June 2018.	Yes	No	No	No	No
Lynch JM et al. Aesthetic Plast Surg. 2018;42:1179–1186	No	No	Yes	No	No
Samargandi OA et al. Plast Surg (Oakv.) 2018;26:110-119.	No	No	Yes	No	No
Drinane JJ et al. Ann Plast Surg. 2016;77:32-36.	No	No	Yes	No	No
Ruiz-Tovar J et al. Surg Infect (Larchmt). 2016;17(1):65-70.	No	No	No	Yes	No
Blount AL et al. Aesthet Surg J. 2013;33:516-521.	No	No	Yes	No	No
Drinane JJ et al. Plast Reconstr Surg Glob Open. 2013;1:e55.	Yes	No	No	No	No
Ruiz-Tovar J et al. J Am Coll Surg. 2012;214:202-207.	No	No	No	Yes	Yes
Ruiz-Tovar J et al. Conference abstract presented at 24th European Congress on Surgical Infections. May 2011	No	No	No	Yes	No

Primary study citation	Baker 2021[14]	Leas 2021[15]	Saeg 2021[17]	Thom 2021[6]	López-Cano 2019[16]
Praveen S and Rohaizak M. Asian J Surg. 2009;32:59-63	No	No	No	No	Yes
Mirsharifi SR et al. Tehran Univ Med J. 2008;65(11):71-5.	No	No	No	Yes	No
Carl SH and Hampton RS. Am J Obstet Gynecol. 2000;182(1):S96-S.	No	No	No	Yes	No
Al-Shehri MY et al. Ann Saudi Med. 1994;14:233–236.	No	No	No	Yes	Yes
Magann EF et al. Obstet Gynecol. 1993;81(6):922-5.	No	No	No	Yes	No
Lazorthes F et al. Surg Gynecol Obstet. 1992;175:569–570.	No	No	No	No	Yes
Schein M et al. Arch Surg. 1990;125(9):1132-5.	No	No	No	Yes	No
Seco JL et al. Am J Surg. 1990;159:226–230.	No	No	No	No	Yes
Moesgaard F et al. Dis Col Rectum. 1989;32:36–38.	No	No	No	No	Yes
Moesgaard F et al. Acta Chir Scand. 1988;154:589–592.	No	No	No	No	Yes
Case WG et al. Surg Res Commun. 1987;2:103–105.	No	No	No	Yes	No
Greig J et al. Chemioterapia. 1987;6(2 Suppl):595–6.	No	No	No	Yes	No
Dashow EE et al. Obstet Gynecol. 1986;68:473–8.	No	No	No	Yes	No
Elliott JP and Flaherty JF. Obstet Gynecol. 1986;67(1):29–32.	No	No	No	Yes	No

Primary study citation	Baker 2021[14]	Leas 2021[15]	Saeg 2021[17]	Thom 2021[6]	López-Cano 2019[16]
Silverman SH et al. Dis Colon Rectum. 1986;29(3):165–9.	No	No	No	Yes	No
Freischlag J et al. Surgery. 1984;96:686–693.	No	No	No	No	Yes
Levin DK et al. Am J Obstet Gynecol. 1983;147(3):273–7.	No	No	No	Yes	No
Lord JW et al. Am J Surg. 1983;145(2):209–12.	No	No	No	Yes	No
Halsall AK et al. Pharmatherapeutica. 1981;2(10):673–7.	No	No	No	Yes	No
Oleson A et al. Ugeskrift for Laeger. 1980;142(22):1415–8.	No	No	No	Yes	No
Pitt HA et al. Ann Surg. 1980;192:356–363.	No	No	No	No	Yes
Evans C et al. Br J Surg. 1974;61:133–135.	No	No	No	No	Yes
Rambo WM. Am J Surg. 1972;123(2):192–5.	No	No	No	Yes	No
Moylan JA et al. Surg Forum. 1968;19(d):66–7.	No	No	No	Yes	No

Note: This table has not been copy-edited.

Appendix 6: References of Potential Interest

Previous CADTH Reports

CADTH. 2021; https://www.cadth.ca/antibiotic-solutions-surgical-irrigation.

Review Articles

31. Awad AN, Heiman AJ, Patel A. Implants and breast pocket irrigation: outcomes of antibiotic, antiseptic, and saline irrigation. *Aesthet*. 2021;09:09.

32. Mann M, Wright CH, Jella T, et al. Cranial surgical site infection interventions and prevention bundles: a systematic review of the literature. *World Neurosurg*. 2021;148:206-219.e4. PubMed

33. Pop-Vicas AE, Abad C, Baubie K, Osman F, Heise C, Safdar N. Colorectal bundles for surgical site infection prevention: a systematic review and meta-analysis. *Infect Control Hosp Epidemiol*. 2020;41(7):805-812. PubMed

34. Lynch JM, Sebai ME, Rodriguez-Unda NA, Seal S, Rosson GD, Manahan MA. Breast pocket irrigation with antibiotic solution at implant insertion: a systematic review and meta-analysis. *Aesthetic Plast Surg*. 2018;42(5):1179-1186. PubMed

35. Nelson RL, Iqbal NM, Kravets A, et al. Topical antimicrobial prophylaxis in colorectal surgery for the prevention of surgical wound infection: a systematic review and meta-analysis. *Tech Coloproctol*. 2018;22(8):573-587. PubMed

36. Yao R, Tan T, Tee JW, Street J. Prophylaxis of surgical site infection in adult spine surgery: a systematic review. *J Clin Neurosci*. 2018;52:5-25. PubMed