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Incisional Wound Irrigation for the Prevention of Surgical Site Infection
A Systematic Review and Network Meta-Analysis

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IMPORTANCE Surgical site infections (SSIs) are common postoperative complications and associated with significant morbidity, mortality, and costs. Prophylactic intraoperative incisional wound irrigation is used to reduce the risk of SSIs, and there is great variation in the type of irrigation solutions and their use.

OBJECTIVE To compare the outcomes of different types of incisional prophylactic intraoperative incisional wound irrigation for the prevention of SSIs in all types of surgery.

DATA SOURCES PubMed, Embase, CENTRAL, and CINAHL databases were searched up to June 12, 2023.

STUDY SELECTION Included in this study were randomized clinical trials (RCTs) comparing incisional prophylactic intraoperative incisional wound irrigation with no irrigation or comparing irrigation using different types of solutions, with SSI as a reported outcome. Studies investigating intracavity lavage were excluded.

DATA EXTRACTION AND SYNTHESIS This systematic review and network meta-analysis is reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis statement. Two reviewers independently extracted the data and assessed the risk of bias within individual RCTs using the Cochrane Risk of Bias 2 tool and the certainty of evidence using the Grading of Recommendations, Assessment, Development, and Evaluation framework. A frequentist network meta-analysis was conducted, and relative risks (RRs) with corresponding 95% CIs were reported.

MAIN OUTCOME AND MEASURE The primary study outcome was SSI.

RESULTS A total of 1587 articles were identified, of which 41 RCTs were included in the systematic review, with 17 188 patients reporting 1328 SSIs, resulting in an overall incidence of 7.7%. Compared with no irrigation, antiseptic solutions (RR, 0.60; 95% CI, 0.44-0.81; high level of certainty) and antibiotic solutions (RR, 0.46; 95% CI, 0.29-0.73; low level of certainty) were associated with a beneficial reduction in SSIs. Saline irrigation showed no statistically significant difference compared with no irrigation (RR, 0.83; 95% CI, 0.63-1.09; moderate level of certainty).

CONCLUSIONS AND RELEVANCE This systematic review and network meta-analysis found high-certainty evidence that prophylactic intraoperative incisional wound irrigation with antiseptic solutions was associated with a reduction in SSIs. It is suggested that the use of antibiotic wound irrigation be avoided due to the inferior certainty of evidence for its outcome and global antimicrobial resistance concerns.

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Supplemental content

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Surgical site infections (SSIs) account for the majority of postoperative complications and are associated with increased morbidity, mortality, costs, and prolonged hospital stay.[1,2] The risk of SSIs can be reduced by the use of prophylactic intraoperative incisional wound irrigation (pIOWI) in which debris, metabolic waste, and exudate (possibly contaminated with microbes) are washed away just before wound closure.[3] A wide variation in irrigation solutions and application methods are used.

International guidelines on the prevention of SSIs and previously published (network) meta-analyses provide contradictory recommendations regarding the use of pIOWI, potentially impairing wider implementation. The UK National Institute for Health and Care Excellence[4] guideline recommends against the use of pIOWI. In contrast, the guidelines from the US Centers for Disease Control and Prevention (CDC)[5] and the World Health Organization (WHO)[6,7] suggest performing irrigation with povidone iodine. Furthermore, the WHO[6,7] advises against using an antibiotic solution, whereas a Cochrane Review[8] states antibacterial irrigation may be superior to nonantibacterial irrigation.

Since publication of the international guidelines, a substantial number of randomized clinical trials (RCTs) on this topic have been published. The RCTs compare various irrigation solutions or assess the efficacy of a specific solution compared with no irrigation. A traditional pairwise meta-analysis is unable to compare the multiple different irrigation solutions in 1 single meta-analysis, as it can only compare 2 interventions. A network meta-analysis allows for simultaneous comparisons of multiple interventions, even in the absence of head-to-head comparisons between interventions.

A recent network meta-analysis by Thom et al[9] found antibiotic and antiseptic solutions had the lowest odds of SSIs compared with no irrigation or nonantibacterial irrigation. However, this network meta-analysis is problematic as RCTs investigating either incisional wound irrigation or intracavity lavage (ie, intraperitoneal, intra-abdominal, or intramediastinal) have been pooled together, whereas these are distinct interventions with inherently different objectives. Incisional wound irrigation is a preventive measure, whereas intracavity lavage is considered to be part of a therapeutic intervention for infections. Therefore, further insights in pIOWI and its implications for the prevention of SSIs are warranted.[10]

We present a systematic review, network meta-analysis, and Grading of Recommendations Assessment, Development, and Evaluation (GRADE) assessment of published RCTs comparing different types of pIOWI solutions for the prevention of SSIs. In addition, we aimed to provide a recommendation, based on up-to-date evidence, on the use of pIOWI for current clinical practice for all types of surgery.

Key Points

Question What are the outcomes of different types of prophylactic intraoperative incisional wound irrigation solutions for the prevention of surgical site infections (SSIs) in all types of surgery?

Findings Results of this systematic review and network meta-analysis including 41 randomized clinical trials found high-certainty evidence that wound irrigation with aqueous antiseptic solutions was associated with a significant reduction in SSIs compared with no irrigation and low-certainty evidence that wound irrigation with antibiotic solutions was associated with a significant reduction in SSIs compared with no irrigation.

Meaning Incisional wound irrigation with aqueous antiseptic solutions was associated with a reduction in the risk of SSIs; results suggest that the use of antibiotic wound irrigation be avoided due to the inferior certainty of evidence for its outcome and global antimicrobial resistance concerns.

Methods

Search Strategy and Selection Criteria

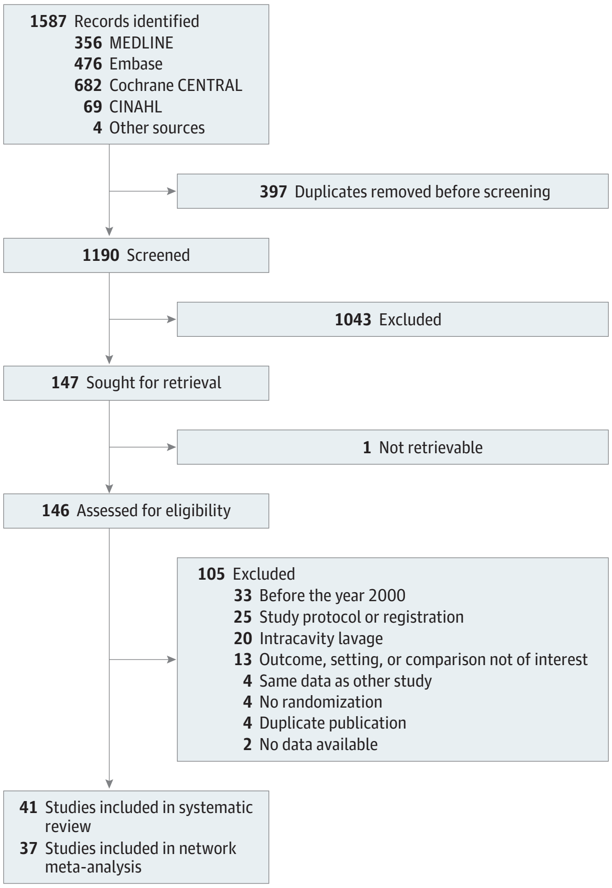
This systematic review and network meta-analysis is reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) reporting guidelines.[11] The study protocol is registered in the PROSPERO database (CRD42023403336).

We conducted a systematic review and network meta-analysis to evaluate the association of different types of pIOWI with the incidence of SSI. We included unpublished and published RCTs that investigated the effect of pIOWI on SSI rates in any type of surgery, using antiseptic, antibiotic, or saline solutions for irrigation, compared with each other or with no irrigation. The solutions were grouped based on their biochemical properties. All studies investigating irrigation of newly made incisions were included, irrespective of contamination level as described by the CDC.[12] Studies investigating intracavity lavage were excluded. In addition, studies examining any method of topical application of a nonsolution (eg, aerosols, powder, gels, sponges) were not included because no diluting effect of irrigation is present. We excluded RCTs from before the year 2000 because these likely do not adhere to the most recent standards for perioperative clinical care, as described by Mangram et al.[12] In addition, animal studies and studies investigating surgeries performed outside the operating suite were excluded. Information on patient race and ethnicity was not gathered because only a small number of studies reported these patient characteristics. There was no restriction on article language.

The literature search of the previous systematic review and meta-analysis performed by our research group was updated.[13] We carried out the search using MEDLINE (PubMed), Excerpta Medica Database (Embase), and Cochrane Central Register of Controlled Trials (CENTRAL) up to June 12, 2023. Additional articles were identified by backward and forward citation tracking of earlier published systematic reviews and included studies. The complete search strategy is presented in the eMethods in Supplement 1.

Two researchers (H.G. and N.B.) independently performed title and abstract screening and full-text review of potentially relevant studies. Disagreements were resolved by discussion or by consulting the senior author (M.A.B.).

Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Flowchart of Study Selection



Statistical Analysis

Two reviewers (H.G. and N.B.) independently extracted study data using a prespecified data abstraction form. Corresponding authors were contacted in case the data were unclear or missing from the original publication.

The primary outcome was SSI, defined at the discretion of the author of the original study. No secondary outcome was analyzed.

The frequentist method and a random-effects model were used to perform a network meta-analysis. Studies with no events in any of the arms were excluded from quantitative analysis.[14] The outcomes of the network meta-analysis are presented in pooled relative risks (RRs) with corresponding 95% CIs, displayed in forest plots and league tables containing all network RRs. Although a 2-sided P value <.05 was considered statistically significant, the results of all statistical tests are interpreted in context.[15]

The GRADE methodology was used to evaluate the certainty of the evidence using a minimally contextualized approach for direct, indirect, and the complete network meta-analysis evidence sequentially. The GRADE includes assessment on 5 domains: risk of bias, inconsistency, indirectness, imprecision, and publication bias.[16,17] Two reviewers (H.G. and N.B.) independently assessed risk of bias within individual RCTs using the Cochrane Risk of Bias 2 (RoB2) tool.[18] Inconsistency was assessed using I^2 and τ^2 statistics. Publication bias was evaluated with a comparison-adjusted funnel plot.[19] For the assessment of incoherence, both the point estimates, CIs, and outcomes from the Separate Indirect From Direct Evidence node-splitting analysis were interpreted in context.[20] A more elaborate explanation of the GRADE methodology is present in eTable 6 in Supplement 1.

We conducted a planned subgroup analysis according to the CDC wound classification.[12] Studies focusing on clean surgery exclusively were compared with all other studies (studies investigating nonclean surgery or clean and nonclean surgery mixed). Another, nonplanned, subgroup analysis was done on the income level of the country where the study was conducted, based on World Bank data, with a division between lower-income countries (low or lower middle) and higher-income countries (upper middle or high).[21]

A sensitivity analysis was conducted excluding studies with high risk of bias based on the RoB2 tool.[14] In another sensitivity analysis, we excluded studies that did not explicitly describe the use of systemic antibiotic prophylaxis.[7] All quantitative analyses were done using R, version 4.2.1 (R Core Team), using the packages meta, netmeta, metaphor, and tidyverse.

Results

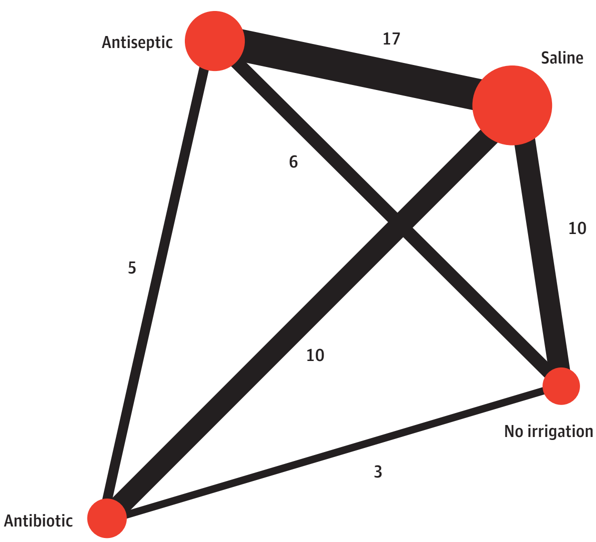
We identified 1583 records in the initial search, and 4 additional articles were identified through backward and forward citation tracking for a total of 1587 articles identified. In total, 146 full-text reports were assessed for eligibility. The systematic review flowchart study selection is shown in **Figure 1**. Reasons for exclusion after full-text review are listed in eTable 1 in Supplement 1. We included 41 RCTs[22-62] in our systematic review and 37 RCTs in the network meta-analysis, due to lack of events in all arms in 4 studies.[46,53-55] The study characteristics of the RCTs included in the systematic review are listed in eTable 2 in Supplement 1. Irrigation solutions were grouped into antiseptic, antibiotic, or saline solutions.

The antibiotics applied in a solution in the different studies were cefazolin,[32,48,51] gentamicin,[31,38,51,53,55] rifampicin,[40-42,44] imipenem,[56,61] clindamycin,[53] ceftriaxone,[52] metronidazole,[25] and bacitracin.[51] All but 2 studies[44,48] described the antibiotic solutions to be aqueous. All antiseptic solutions studied were aqueous, with 18 RCTs[22,27-30,33,37-43,45,47,57,60,62] investigating iodine solutions ranging from 0.1% to 10% in concentration. Other antiseptics used were polyhexanide,[49,50,58] chlorhexidine,[51] hydrogen peroxide,[46] and electrolyzed strongly acidic aqueous solution.[59] In the saline irrigation group, all studies described irrigation with saline 0.9%, except for 1 RCT[50] in which Ringer lactate was used. Volume of irrigation and application method varied among all studies and irrigation groups (eTable 3 in Supplement 1).

Data Analysis

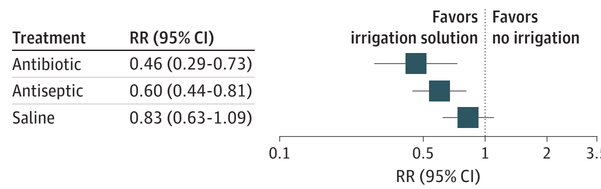
The resulting network meta-analysis consisted of 51 comparisons, which are visualized in a network graph presented in

Figure 2. Network Graph of the 41 Randomized Clinical Trials Included in the Network Meta-Analysis



The network graph shows the number of studies investigating the direct comparison of the different methods of prophylactic intraoperative incisional wound irrigation for the prevention of surgical site infections. The size of the nodes and the thickness of the lines correspond with the number of studies.

Figure 3. Forest Plot of the Outcomes of Different Wound Irrigation Solutions



The forest plot shows the outcomes of different wound irrigation solutions in the prevention of surgical site infections compared with no irrigation. Data are relative risk (RR) with corresponding 95% CI.

Figure 4. League Table of All Pairwise Comparisons in the Network Meta-Analysis

Antibiotic	1.07 (0.51-2.24)	0.57 (0.37-0.90)	0.19 (0.06-0.59)
0.77 (0.50-1.19)	**Antiseptic**	0.67 (0.51-0.88)	0.77 (0.52-1.13)
0.56 (0.37-0.83)	0.72 (0.57-0.93)	**Saline**	0.75 (0.54-1.04)
0.46 (0.29-0.73)	0.60 (0.44-0.81)	0.83 (0.63-1.09)	**No irrigation**

The league table is a square matrix showing all pairwise comparisons in the network meta-analysis. In the lower triangle of the league table, the network relative risks (RRs) with corresponding 95% CIs are shown. The upper triangle shows the RRs of only the direct comparisons (comparable with a regular pairwise meta-analysis). For instance, the first column (in the lower triangle) shows the network RR with corresponding 95% CI of antibiotic compared with the other irrigation solutions. The last column (upper triangle) shows the direct RR with corresponding 95% CI of no irrigation compared with the other irrigation solutions.

Figure 2. In total, 17 188 patients were included in the systematic review, reporting 1328 SSIs, which corresponds to an overall incidence of 7.7%.

Figure 3 shows the forest plot for the efficacy of the different types of irrigation solutions compared with no irrigation; the league table for these data is presented in **Figure 4**. Antibiotic (RR, 0.46; 95% CI, 0.29-0.73) and antiseptic (RR, 0.60; 95% CI, 0.44-0.81) solutions were both associated with a significant reduction in SSIs when compared with no irrigation. Similarly, wound irrigation with antibiotic or antiseptic solutions was favorable compared with irrigation with saline (antibiotic irrigation: RR, 0.56; 95% CI, 0.37-0.83; antiseptic irrigation: RR, 0.72; 95% CI, 0.57-0.93). Saline irrigation showed no significant association (RR, 0.83; 95% CI, 0.63-1.09) with SSIs compared with no irrigation. The association between SSI reduction and antibiotic and antiseptic solutions was not significantly different (RR, 0.77; 95% CI, 0.50-1.19).

Moderate heterogeneity between studies was found (I^2 = 42.9%; τ^2 = 0.11). The I^2 and τ^2 statistics for each comparison are presented in eTable 2 in Supplement 1. The results for node splitting are shown in eTable 4 in Supplement 1.

Subgroup and Sensitivity Analyses

We carried out a subgroup analysis on the 15 studies[27-30,33,37,38,43,46,51-55,57] that investigated clean surgery (eFigure 1A in Supplement 1).[12] Eleven[27-30,33,37,38,43,51,52,57] of these 15 RCTs reported at least 1 SSI and were, therefore, included in the network meta-analysis. The only significant benefit was found for antiseptic solutions compared with saline solutions, as seen in the league table (RR, 0.21; 95% CI, 0.08-0.51). For the remaining RCTs that did not exclusively evaluate clean surgery, a significant association between the use of antibiotic and antiseptic solutions and the reduction of SSIs was found, similar to the results of the main analysis (eFigure 1B in Supplement 1).

Twenty-six RCTs[22, 24, 26-30, 33, 35, 36, 40-45, 47, 49-51, 53-55, 58, 59, 62] were performed in either high- or upper-middle-income countries. Antibiotic (RR, 0.39; 95% CI, 0.18-0.83) as well as antiseptic (RR, 0.61; 95% CI, 0.41-0.92) solutions were associated with a reduction in SSIs for these countries compared with no irrigation (eFigure 1C in Supplement 1). The subgroup analysis of low- and lower-middle-income countries, comprising 14 RCTs[23,25,31,32,34,37-39,48,52,56,57,60,61] (eFigure 1D in Supplement 1), also showed that both antibiotic (RR, 0.50; 95% CI, 0.26-0.95) and antiseptic (RR, 0.51; 95% CI, 0.29-0.90) solutions were associated with a reduction in SSIs compared with no irrigation. Furthermore, saline irrigation was associated with a nonsignificant reduction in SSIs (RR, 0.80; 95% CI, 0.50-1.30) when compared with no irrigation in low-income countries.

The sensitivity analysis after exclusion of studies with high risk of bias comprised 33 RCTs[22,24,26-31,33-40,42-45,47-52,56-62] and showed a significant outcome for antibiotic (RR, 0.43; 95% CI, Table. Grading of Recommendations Assessment, Development, and Evaluation (GRADE) Assessment[a]

Comparison	Direct evidence (classic) RR (95% CI)	Direct evidence (classic) Certainty of evidence	Indirect evidence (transitivity) RR (95% CI)	Indirect evidence (transitivity) Certainty of evidence	Network meta-analysis (incoherence) RR (95% CI)	Network meta-analysis (incoherence) Certainty of evidence	Target
Antibiotic vs antiseptic	1.07 (0.51-2.24)	⊕OOO Very low	0.64 (0.37-1.10)	⊕⊕OO Low	0.77 (0.50-1.19)	⊕OOO Very low	Trivial to no effect
Antibiotic vs saline	0.57 (0.37-0.90)	⊕⊕⊕O Moderate	0.59 (0.20-1.75)	⊕OOO Very low	0.56 (0.37-0.83)	⊕⊕⊕O Moderate	Minimally important benefit
Antibiotic vs no irrigation	0.19 (0.06-0.59)	⊕⊕OO Low	0.55 (0.34-0.90)	⊕OOO Very low	0.46 (0.29-0.73)	⊕⊕OO Low	Minimally important benefit
Antiseptic vs saline	0.67 (0.51-0.88)	⊕⊕⊕O Moderate	1.00 (0.61-1.65)	⊕OOO Very low	0.72 (0.57-0.93)	⊕⊕⊕O Moderate	Minimally important benefit
Antiseptic vs no irrigation	0.77 (0.52-1.13)	⊕⊕⊕O Moderate	0.40 (0.24-0.66)	⊕⊕OO Low	0.60 (0.44-0.81)	⊕⊕⊕⊕ High	Minimally important benefit
Saline vs no irrigation	0.75 (0.54-1.04)	⊕⊕⊕O Moderate	1.10 (0.59-2.08)	⊕OOO Very low	0.83 (0.63-1.09)	⊕⊕⊕O Moderate	Trivial to no effect

Abbreviation: RR, relative risk.

[a] Network evidence: for all comparisons, both direct and indirect evidence are available. Therefore, we used the highest of the 2 certainty ratings as the certainty rating for the network meta-analysis estimate. The certainty of the network estimate can be upgraded if precision is greater than direct or indirect estimates.

0.24-0.76) and antiseptic (RR, 0.60; 95% CI, 0.43-0.82) solutions and no significant outcome for saline solution (RR, 0.80; 95% CI, 0.59-1.09) compared with no irrigation (eFigure 1E in Supplement 1).

We included 31 studies[22-32,35,36,38-45,47,49,51,52,57-62] in the sensitivity analysis that explicitly mention the administration of surgical systemic antibiotic prophylaxis, which is best practice. Here, results were also comparable with the main analysis (eFigure 1F in Supplement 1).

Risk of Bias

A detailed risk-of-bias assessment is shown in eTable 5 in Supplement 1. There was 1 RCT[49] with low risk of bias, 36 RCTs[22,24,26-40,42-48,50-62] had some concerns regarding bias, and 4 RCTs[23,25,32,41] had high risk of bias. The comparison-adjusted funnel plot (eFigure 2 in Supplement 1) showed no asymmetry, revealing publication bias to be unlikely.

Certainty of Evidence

Full evaluation of the certainty of evidence and considerations for grading are detailed in the **Table** and eTable 6 in Supplement 1. GRADE assessment, incorporating minimally important difference, resulted in a high certainty of evidence for 1 comparison (antiseptic vs no irrigation) and moderate certainty for 3 comparisons (antiseptic vs saline irrigation, antibiotic vs saline irrigation, and saline vs no irrigation). Low certainty of evidence was found for the comparison of antibiotic vs no irrigation, and very low certainty was found for antibiotic vs antiseptic irrigation.

Discussion

This systematic review and network meta-analysis studied the outcomes of different pIOWI solutions for the prevention of SSIs in any type of surgery from more recent data. We found high-certainty evidence that wound irrigation with aqueous antiseptic solutions was associated with a significant reduction in SSIs compared with no irrigation and moderate-certainty evidence when compared with irrigation with saline. There was low certainty of evidence that wound irrigation with antibiotic solutions was associated with a significant reduction in SSIs compared with no irrigation and moderate certainty of evidence when compared with irrigation with saline. These findings were robust to sensitivity analyses restricted to studies adequately describing the use of systemic antibiotic prophylaxis and without studies at high risk of bias.

International guidelines on the prevention of SSI[4-8] provide conflicting recommendations regarding the use of pIOWI. A considerable number of new RCTs have been conducted since the publication of these guidelines. These new RCTs often compare different irrigation solutions with one another or no irrigation, requiring network meta-analysis to efficiently use the existing evidence.

A recent network meta-analysis[9] on pIOWI analyzed studies with incisional wound irrigation and studies with intracavity lavage together. The authors found that antibiotic and antiseptic solutions were associated with a reduction in SSIs compared with no or inert (eg, saline) irrigation. However, pooling data on intracavity lavage and incisional wound irrigation likely leads to biased effect estimates of incisional wound irrigation. Intracavity lavage typically concerns part of a therapeutic intervention for infections, and complications unaffected by irrigation (eg, anastomotic leakage) contribute importantly to the incidence of organ-space infections. In contrast, an earlier meta-analysis by our group[13] discouraged the use of antibiotic solutions, and results suggested the use of aqueous antiseptic solutions for irrigation. Some data included in previous analyses are outdated and not representative of current standards of care. Fortunately, important new data have since emerged, rendering these old data redundant for the current perspective. In the present network meta-analysis, we solely included RCTs published after 1999 to ensure that the data were more homogenous with regard to infection prevention measures and more representative of the current perspective.

The most crucial aspect demanding attention when considering antibiotics is the rising concern of antimicrobial resistance.[63] The escalating ineffectiveness of antibiotics underscores a pressing need to limit their usage. Encouragingly, no indications of diminished bacterial sensitivity have been shown for antiseptics.[64,65]

A subgroup analysis for different CDC contamination categories was performed.[12] Not only is level of contamination a predicting factor for SSI occurrence, irrigation could also work differently in clean or nonclean wounds. A benefit of antiseptic solutions over saline solutions was the only significant outcome found in the exclusively clean surgery subgroup. The other comparisons show very wide CIs, most likely due to thinning of data and loss of statistical power, making it hard to draw conclusions. Moreover, meta-regression was not compatible with the frequentist method, and not using it may have influenced our subgroup analyses.

To determine the translational value of the outcomes of wound irrigation to countries of different prosperity levels, we performed a subgroup analysis wherein we divided RCTs by income level, according to the World Bank's income level data.[21] Results in both of the subgroups (higher and lower income) resembled that of our main analysis. Saline irrigation was associated with a nonsignificant reduction in SSIs when compared with no irrigation in lower-income countries. It may be worth considering the use of saline for irrigation when antiseptic or antibiotic irrigation is not readily available or is scarce.

Limitations

Interpretation of our data is challenged by the clinical and methodological heterogeneity of the body of evidence. Several studies did not report a definition for SSI or used definitions other than the diagnostic criteria outlined by the CDC.[12] We assumed that reported SSI was incisional in origin by considering the nature of the intervention. Additionally, various different application methods and exposure times were used in a range of populations (eTable 3 in Supplement 1). Despite this challenge, we strongly believe that this body of evidence is best interpreted as whole. The question at hand is relevant to all surgical specialties and given appropriate antimicrobial coverage of the irrigation agent used, there is no plausible biological mechanism for outcome modification for any specific surgical specialty. Thus, to avoid splintering of the data and to optimize the chance of finding the best available evidence, we deem the combining of specialty data justified. GRADE methodology provides important guidance on how to best interpret the data in cases of inconsistency, intransitivity, and incoherence that may result from this decision. In addition to the practical and statistical advantages, the decision to apply broad inclusion criteria leads to a very strong external validity and makes our analysis useful to surgical specialists in the broadest sense.

Interestingly, our findings suggest that the mechanical effect of irrigation itself may be of lesser importance compared with the antimicrobial properties of the fluids, as saline irrigation was not associated with a significant reduction in SSI compared with no irrigation.

Among the RCTs that investigated antiseptics for pIOWI, the majority focused on iodine solutions. However, a recent network meta-analysis on skin antiseptics found the use of chlorhexidine in alcohol to be associated with a reduction in SSI compared with iodine in alcohol.[66] In line with these findings, using aqueous chlorhexidine for prophylactic wound irrigation may be more effective than aqueous iodine in reducing SSI. We identified only 1 RCT that studied the irrigation effect of an aqueous chlorhexidine solution.[51] This might be because of concerns of potential negative effects of chlorhexidine on tissue healing from in vitro studies, although these concerns were never substantiated with clinical data.[67-69] Future studies may investigate the potential benefit of aqueous chlorhexidine solutions. Furthermore, other solutions investigated in the literature (eg, castile soap by Bhandari et al)[70] were not included because they did not fit into either an antiseptic or an antibiotic profile. The use of antibiotic wound irrigation remains controversial and should be avoided for the following reasons: (1) the certainty of evidence for its outcome is inferior compared with that of antiseptic irrigation, (2) present data show that there was trivial to no difference in outcome of SSI between antiseptic and antibiotic irrigation, and (3) there are serious concerns regarding antimicrobial resistance to antibiotics.[63] On the contrary, no signs of decreased bacterial sensitivity have been shown for either iodine or chlorhexidine over time.[64,65]

Conclusions

Results of this systematic review and network meta-analysis suggest that there was high certainty of evidence that incisional wound irrigation with aqueous antiseptic solutions was associated with a reduction in the risk of SSI. The use of antibiotic wound irrigation remains controversial and should be avoided due to the inferior certainty of evidence for its outcome, the trivial to no difference in outcome compared with antiseptics, and the rapid global antimicrobial resistance to antibiotics.

ARTICLE INFORMATION

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Invited Commentary

Solution to Pollution in Surgical Wounds—Not Just Dilution

Heather L. Evans, MD, MS; Robert G. Sawyer, MD

The systematic review and network meta-analysis by Groenen and colleagues[1] published in a recent issue of *JAMA Surgery* on incisional wound irrigation for the prevention of surgical site infection (SSI) is a commendable effort in shedding light on a controversial topic in surgery. The key premise is that network meta-analyses can compare the impact of multiple different irrigation solutions on the development of SSI, even when they were not compared in the original studies. Although the study contributes valuable insights, it is essential to scrutinize the inherent challenges in defining and standardizing SSIs, as well as the design limitations that influence the interpretation of the results.

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One of the primary challenges in understanding the impact of incisional wound irrigation lies in the vagueness of SSI definitions, which are subjective and dependent largely on the observer. In this analysis, the definition of SSI was "...at the discretion of the original study's author."[1] It is never explicitly stated, but it appears that the outcome of interest in all of these studies is superficial SSI. However, the lack of standardized criteria across the included studies may introduce significant and unquantifiable variability. Furthermore, a diverse array of surgical procedures is included, each with distinct contamination risks, dose levels, and techniques. This heterogeneity presents a formidable obstacle when attempting to generalize findings. The amalgamation of such disparate data may dilute the ability to discern the true impact of irrigation on preventing SSIs in specific surgical contexts. Interestingly, in a recent randomized clinical trial of a newer antiseptic agent, polyhexanide (published after this meta-analysis was completed), SSI rates were not decreased in the wound irrigation intervention arm, but contaminated and emergent procedures were excluded from the study.[2]

Dentists have long used chlorhexidine solutions, such as Peridex (3M), in procedures like root canals, periodontal work, and oral surgery.[3] The efficacy of chlorhexidine in preventing infections is well established in dentistry, yet we lack sufficient data on its application in surgical settings. To address these gaps in our understanding, a coordinated study of chlorhexidine-based irrigation in acute care surgery is imperative. High priority topics include intra-abdominal infection, gross contamination during emergent laparotomy, and necrotizing soft tissue infection. This targeted research approach will provide much-needed clarity on the efficacy of incisional wound irrigation in scenarios where the risk of infection is particularly high.

The study by Groenen and colleagues[1] contributes significantly to the discourse on SSIs and confirms the general approach of using antiseptic irrigation to prevent SSI. Acknowledging and addressing the aforementioned limitations will pave the way for more nuanced and context-specific insights into the role of incisional wound irrigation in preventing SSIs. The solution to pollution in surgical settings is not simply dilution, but rather a tailored and meticulous understanding of the infection risk in specific surgical procedures and circumstances.

ARTICLE INFORMATION

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Supplementary Online Content

Groenen H, Bontekoning N, Jalalzadeh H, et al. Incisional wound irrigation for the prevention of surgical site infection: a systematic review and network meta-analysis. *JAMA Surg*. Published online April 24, 2024. doi:10.1001/jamasurg.2024.0775

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

eMethods. Search strategy

Medline (via PubMed)
1. ‘‘surgical wound infection’’[Mesh] OR surgical site infection*[tiab] OR SSI[tiab] OR SSIs[tiab] OR surgical wound infection*[tiab] OR surgical infection*[tiab] OR postoperative wound infection*[tiab] OR postoperative wound infection*[tiab]
2. irrigat*[tiab] OR lavag*[tiab] OR spray*[tiab] OR soak*[tiab] OR rins*[tiab] OR ‘‘therapeutic irrigation’’[Mesh]
3. trial[ti] OR randomly[tiab] OR clinical trial as topic[mesh:noexp] OR placebo[tiab] OR randomized[tiab] OR controlled clinical trial[pt] OR randomized controlled trial[pt]
4. 1 AND 2 AND 3

EMBASE and CINAHL
1. exp surgical infection/ or (SSI or SSIs).ti,ab,kw. or ((surg* or postoperat* or post-operat*) adj3 infect*).ti,ab,kw.
2. wound irrigation/ or lavage/ or (irrigat* or lavag* or spray* or soak* or rins*).ti,ab,kw.
3. controlled clinical trial/ or randomized controlled trial/ or exp "clinical trial (topic)"/ or (randomly or randomized or placebo).ti,ab,kw. or trial.ti.
4. 1 AND 2 AND 3

Cochrane CENTRAL
1. MeSH descriptor: [Surgical Wound Infection] explode all trees
2. SSI or SSIs:ti,ab,kw (word variations have been searched)
3. (surg* or postoperat* or post-operat*) near/3 infect*:ti,ab,kw (word variations have been searched)
4. 1 OR 2 OR 3
5. irrigat* or lavag* or spray* or soak* or rins*:ti,ab,kw (word variations have been searched)
6. 4 AND 5

CINAHL
1. (MH ‘‘surgical wound infection’’) OR (TI (surgical site infection* OR SSI OR SSIs OR surgical wound infection* OR surgical infection* OR post-operative wound infection* OR postoperative wound infection*) OR AB (surgical site infection* OR SSI OR SSIs OR surgical wound infection* OR surgical infection* OR post-operative wound infection* OR postoperative wound infection*))
2. (MH ‘‘therapeutic irrigation’’) OR TI (irrigat* or lavag* or spray* or soak* or rins*) OR AB (irrigat* or lavag* or spray* or soak* or rins*)
3. (MH ‘‘randomized controlled trials’’) OR (MH ‘‘clinical trials+’’) OR TI trial OR (TI controll* AND trial*) OR AB (TI controll* AND trial*) OR (TI (randomly OR placebo OR randomi?ed) OR AB (randomly OR placebo OR randomi?ed))
4. S1 AND S2 AND S3

The search was conducted upto 12-6-2023

eTable 1. Reasons for exclusion after full text review

	Study	Reason for exclusion
1	Abdelrahman 2020[1]	No data available
2	Actrn 2020[2]	Intra-cavity lavage
3	Actrn 2012[3]	Outcome, comparison or setting not of interest
4	Akhavan-Sigari 2019[4]	Conference abstract of included study (Akhavan-Sigari 2020)[5]
5	Aneja 2022[6]	Study protocol
6	Arslan 2020[7]	No randomisation
7	Baker 1994[8]	Before the year 2000
8	Bhandari 2015[9]	Outcome, comparison or setting not of interest
9	Bourgeois 1985[10]	Before the year 2000
10	Calkins 2019[11]	Same data as Calkins 2020[12]
11	Calkins 2020[12]	Outcome, comparison or setting not of interest
12	Conover 1984[13]	Before the year 2000
13	Ctri 2023[14]	Study protocol
14	Ctri 2022[15]	Study registration: no data available
15	Ctri 2021[16]	Study registration: no data available
16	Ctri 2021[17]	Study registration: intra-cavity lavage
17	Ctri 2012[18]	Study registration: no data available
18	De Jong 1982[19]	Before the year 2000
19	Dineen 2015[20]	No randomisation
20	Donnenfeld 1986[21]	Before the year 2000
21	Drks 2022[22]	Intra-cavity lavage
22	Drks 2014[23]	No randomisation
23	Drks 2013[24]	Study registration: no data available
24	Elliott 1986[25]	Before the year 2000
25	Englund 2019[26]	No randomisation
26	Euctr 2017[27]	Study protocol of included study (Mueller 2023)[28]
27	Freischlag 1984[29]	Before the year 2000
28	Greig 1987[30]	Before the year 2000
29	Hargrove 2006[31]	Outcome, comparison or setting not of interest
30	Harrigill 2003[32]	Intra-cavity lavage
31	Irct20140503017537N, 2019[33]	Study protocol
32	Irct20200126046261N, 2020[34]	Study protocol
33	Isrctn 2005[35]	Intra-cavity lavage
34	Karuserci 2021[36]	Same data as included study (Karuserci 2022)[37]
35	Kellum 1985[38]	Before the year 2000
36	Ko 1992[39]	Before the year 2000
37	Lavery 1986[40]	Before the year 2000
38	Levin 1983[41]	Before the year 2000
39	Lindsey 1982[42]	Before the year 2000
40	Liu 2017[43]	Intra-cavity lavage
41	Lord 1983[44]	Before the year 2000
42	Lord 1977[45]	Before the year 2000
43	Maatman 2019[46]	Intra-cavity lavage
44	Maemoto 2021[47]	Study protocol of included study (Maemoto 2023)[48]
45	Magann 1993[49]	Before the year 2000
46	Mahomed 2016[50]	Conference abstract of included study (Mahomed 2016)[51]
47	Marti 1979[52]	Before the year 2000
48	Mashbari 2018[53]	Intra-cavity lavage
49	Mathelier 1992[54]	Before the year 2000
50	Mohd 2010[55]	Outcome, comparison or setting not of interest
51	Moradi 2019[56]	Intra-cavity lavage
52	Mueller 2017[57]	Study protocol of included study (Mueller 2023)[28]
53	Nct 2022[58]	Study protocol
54	Nct 2022[59]	Study protocol
55	Nct 2022[60]	Study protocol
56	Nct 2020[61]	Study protocol
57	Nct 2020[62]	Study protocol of included study (Emile 2020)[63]
58	Nct 2019[64]	Study protocol of included study (Strobel 2020)[65]
59	Nct 2018[66]	Study protocol
60	Nct 2018[67]	Study protocol of included study (Emile 2020)[63]
61	Nct 2017[68]	Intra-cavity lavage
62	Nct 2016[69]	Intra-cavity lavage
63	Nct 2015[70]	Same data as included study (Nguyen 2021)[71]
64	Nct 2015[72]	Study protocol of included study (Cohen 2020)[73]
65	Nct 2014[74]	Outcome, comparison or setting not of interest
66	Nct 2012[75]	No data available
67	Nct 2012[76]	Study protocol of included study (Etaati 2012)[77]

68	Nct 2011[78]	Intra-cavity lavage
69	Nct 2008[79]	Study protocol of included study (Bhandari 2015)[9]
70	Nikfarjam 2014[80]	Outcome, comparison or setting not of interest
71	Oestreicher 1989[81]	Before the year 2000
72	Patellugari 2020[82]	Outcome, comparison or setting not of interest
73	Pitt 1980[83]	Before the year 2000
74	Pitt 1982[84]	Before the year 2000
75	Pollock 1978[85]	Before the year 2000
76	Quiroga-Garza 2017[86]	Outcome, comparison or setting not of interest
77	Rambo 1972[87]	Before the year 2000
78	Rogers 1983[88]	Before the year 2000
79	Ruiz-Tovar 2016[89]	Intra-cavity lavage
80	Ruiz-Tovar 2011[90]	Intra-cavity lavage
81	Ruiz-Tovar 2012[91]	Intra-cavity lavage
82	Ruiz-Tovar 2016[92]	Same data as Ruiz-Tovar 2016[89]
83	Salamat 2022[93]	Outcome, comparison or setting not of interest
84	Schottel 2016[94]	Outcome, comparison or setting not of interest
85	Silverman 1986[95]	Before the year 2000
86	Sindelar 1985[96]	Before the year 2000
87	Sindelar 1979[97]	Before the year 2000
88	Sindelar 1977[98]	Before the year 2000
89	Sood 1985[99]	Before the year 2000
90	Tanaka 2015[100]	Intra-cavity lavage
91	Tanphiphat 1978[101]	Before the year 2000
92	Tctr 2021[102]	Study protocol
93	Temizkan 2016[103]	Intra-cavity lavage
94	Terzi 2015[104]	Conference abstract of Arslan 2020[7]
95	Tighe 1982[105]	Before the year 2000
96	Umin 2019[106]	Study protocol of included study (Maeomoto 2023)[48]
97	Umin 2012[107]	Intra-cavity lavage
98	Umin 2011[108]	Intra-cavity lavage
99	Vinay 2020[109]	Conference abstract of included study (Vinay 2019)[110]
100	Viney 2012[111]	Intra-cavity lavage
101	Weiss 2013[112]	Outcome, comparison or setting not of interest
102	Wu 1992[113]	Before the year 2000
103	Wu 1991[114]	Before the year 2000
104	Yang 2021[115]	Intra-cavity lavage
105	Yazdi 2014[116]	Outcome, comparison or setting not of interest

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eTable 2. Study characteristics

Study	SSI / N total	Treatment 1	Treatment 2	Type of surgery	Wound class §	SAP	ROB	Follow-up	SSI definition
Antibiotic vs Antiseptic (RR 0.77; 95% CI 0.50 – 1.19) (I^2 = 50.6%, τ^2 = 1.1247)									
Inojie 2023	8 / 80	Gentamicin in saline	3.5% PI	Open spine surgery	1	Yes	Some concerns	30 days	CDC
Karuserci 2022*	2 / 200	Rifampicin in saline	10% PI	Caeserean section	2	Yes	Some concerns	30 days	CDC
Nguyen 2021	11 / 88	Cefazolin, gentamicin, and bacitracin in saline	0.05% chlorhexidine gluconate	Bilateral mastectomy with tissue expander reconstruction	1	Yes	Some concerns	28 days	CDC
Karuserci 2020*	28 / 200	Rifampicin in saline	10% PI	Gynecologic oncology surgery	2	Yes	High	30 days	CDC
Karusersi 2019*	7 / 200	Rifampicin in saline	10% PI	Benign gynecologic surgery	2	Yes	Some concerns	30 days	¶a
Antibiotic vs Saline (RR 0.56; 95% CI 0.37 – 0.83) (I^2 = 8.3%, τ^2 = 0.3897)									
Zeb 2023	12 / 106	Imipenem in saline	Saline	Open appendectomy	2 – 4	Yes	Some concerns	3 weeks	NR
Karuserci 2022*	6 / 200	Rifampicin in saline	Saline	Caeserean section	2	Yes	Some concerns	30 days	CDC
Shah 2021	14 / 80	Imipenem in saline	Saline	Appendectomy	3 – 4	NR	Some concerns	NR	NR
Okunlola 2021	3 / 132	Ceftriaxone in saline	Saline	Neurosurgery	1	Yes	Some concerns	30 days	¶b
Karuserci 2020*	28 / 200	Rifampicin in saline	Saline	Gynecologic oncology surgery	2	Yes	High	30 days	CDC
Emile 2020*	17 / 150	Gentamicin in saline	Saline	Open appendectomy	1 – 3	Yes	Some concerns	6 weeks	CDC
Karusersi 2019*	13 / 200	Rifampicin in saline	Saline	Benign gynecologic surgery	2	Yes	Some concerns	30 days	¶a
Oller 2015	0 / 51	I. Gentamicin in saline II. Clindamycin in saline	Saline	Axillary lymph node dissection in breast cancer	1	Yes	Some concerns	2 weeks	NR
Ruiz-Tovar 2013¤	0 / 40	Gentamicin in saline	Saline	Elective axillary lymph node dissection due to axillary metastasis	1	Yes	Some concerns	NR	NR
Etaati 2012*	5 / 100	Cefazolin in saline	Saline	Caeserean section	2	Yes	High	1 week	¶c
Mirsharifi 2008	12 / 102	Cefazolin	Saline	Open cholecystectomy	2 – 3	NR	Some concerns	6 weeks	¶d
Bhargava 2006	28 / 60	Metronidazole in saline	Saline	Exploratory laparotomy	4	Yes	High	30 days	¶e
Antibiotic vs No irrigation (RR 0.46; 95% CI 0.29 – 0.73) (I^2 =0.0%, τ^2 = 0.3438)									

Emile 2020*	17 / 150	Gentamicin in saline	No irrigation	Open appendectomy	1 – 3	Yes	Some concerns	6 weeks	CDC
Etaati 2012*	5 / 150	Cefazolin in saline	No irrigation	Caeserean section	2	Yes	High	1 week	¶c
Köşüş 2010	12 / 1272	Rifamycin	No irrigation	Caeserean section	2	Yes	Some concerns	30 days	CDC
Antiseptic vs No irrigation (RR 0.60; 95% CI 0.44 – 0.81) (*I^2* = 0.0%, τ^2 = 0.0919)									
Mueller 2023*	44 / 394	0.04% polyhexanide	No irrigation	Emergency and elective abdominal laparotomy	2 – 4	Yes	Low	30 days	CDC
Al-Abdulla 2021*	16 / 80	1% PI	No irrigation	Open appendectomy	3 – 4	Yes	Some concerns	10 days	¶f
Haider 2018	43 / 600	1% PI	No irrigation	Clean elective surgery	1	Yes	Some concerns	4 weeks	¶f
Mahomed 2016	291 / 3270	10% PI	No irrigation	Caeserean section	2	Yes	Some concerns	4 weeks	CDC
Iqbal 2015	25 / 166	1% PI	No irrigation	Open appendectomy	3	Yes	Some concerns	30 days	¶f
Kokavec 2008	2 / 162	3.5% PI	No irrigation	Orthopedic surgery of proximal femur, hip and pelvis in pediatric patients	1	Yes	Some concerns	2 months	¶g
Antiseptic vs Saline (RR 0.72; 95% CI 0.57 – 0.93) (*I^2* = 48.7%, τ^2 = 0.5088)									
Mueller 2023*	68 / 587	0.04% polyhexanide	Saline	Emergency and elective abdominal laparotomy	2 – 4	Yes	Low	30 days	CDC
Maemoto 2023	60 / 950	10% PI	Saline	Elective gastroenterological surgery	2	Yes	Some concerns	30 days	CDC
Zhao 2023	20 / 340	1% PI	Saline	Radical gastrectomy	2	Yes	Some concerns	30 days	CDC
Karuserci 2022*	6 / 200	10% PI	Saline	Caeserean section	2	Yes	Some concerns	30 days	CDC
Maghsoudipour 2022	0 / 50	3% hydrogen peroxide	Saline	Rhinoplasty	1	NR	Some concerns	8 weeks	¶h
Al-Abdulla 2021*	14 / 80	1% PI	Saline	Open appendectomy	3 – 4	Yes	Some concerns	10 days	¶f
Cohen 2020¤	3 / 173	0.35% PI	Saline	Pediatric posterior spinal fusion	1	Yes	Some concerns	90 days	CDC
Akhavan - Sigari 2020	26 / 936	3.5% PI	Saline	Spinal fusion surgery	1	Yes	Some concerns	12 months	CDC
Karuserci 2020*	28 / 200	10% PI	Saline	Gynecologic oncology surgery	2	Yes	High	30 days	CDC
Strobel 2020	111 / 456	0.04% polyhexanide	Saline	Elective abdominal laparotomy	2 – 3	Yes	Some concerns	30 days	CDC
Karusersi 2019*	18 / 200	10% PI	Saline	Benign gynecologic surgery	2	Yes	Some concerns	30 days	¶a
Vinay 2019	16 / 180	5% PI	Saline	Elective laparotomy	2	Yes	Some concerns	4 weeks	CDC
De Luna 2017	3 / 50	3% PI	Saline	Spine surgery	1	Yes	Some concerns	30 days	CDC

Fei 2017	12 / 80	0.1% PI	Saline	Posterior lumbar interbody fusion surgery	1	NR	Some concerns	NR	NR
Neeff 2016	41 / 197	0.04% polyhexanide	Ringer's solution	Colorectal surgery	2 – 4	NR	Some concerns	NR	NR
Takesue 2011	48 / 400	Electrolyzed Strongly Acidic Aqueous Solution	Saline	Elective colorectal surgery	2 – 3	Yes	Some concerns	30 days	¶a
Chang 2006	6 / 244	0.35% PI	Saline	Lumbosacral posterolateral fusion surgery	1	Yes	Some concerns	14 months	NR
Cheng 2005	7 / 414	0.35% PI	Saline	Spine surgery	1	Yes	Some concerns	6 months	¶i
Saline vs No Irrigation (RR 0.83; 95% CI 0.63- 1.09) (I^2 = 20%, τ^2 = 0.2342)									
Mueller 2023*	50 / 397	Saline	No irrigation	Emergency and elective abdominal laparotomy	2 – 4	Yes	Low	30 days	CDC
Gomaa 2022	221 / 2890	Saline	No irrigation	Caeserean section	2	NR	Some concerns	30 days	¶j
Al-Abdulla 2021*	18 / 80	Saline	No irrigation	Open appendectomy	3 – 4	Yes	Some concerns	10 days	¶f
Gül 2021	18 / 230	Saline	No irrigation	Caeserean section	2	Yes	Some concerns	7 days	¶k
Emile 2020*	17 / 150	Saline	No irrigation	Open appendectomy	1 – 3	Yes	Some concerns	6 weeks	CDC
Aslan 2018	25 / 204	Saline	No irrigation	Caeserean section	2	Yes	Some concerns	30 days	NR
Etaati 2012*	5 / 150	Saline	No irrigation	Caeserean section	2	Yes	High	1 week	¶c
Güngördük 2010	36 / 520	Saline	No irrigation	Caeserean section	2	Yes	Some concerns	6 weeks	¶l
Al-Ramahi 2006	21 / 206	Saline	No irrigation	Abdominal gynecologic surgery	2	Yes	High	1 month	¶m
Platt 2003	0 / 30	Saline	No irrigation	Bilateral breast reduction	1	NR	Some concerns	8 weeks	NR
Cervantes-Sánchez 2000	12 / 255	Saline	No irrigation	Appendectomy	1 – 3	Yes	Some concerns	4 weeks	¶n

* Studies compare three wound irrigation solutions
¤ SSI secondary outcome, thus not adequately powered to detect SSI
§ 1: Clean, 2: Clean-contaminated, 3: Contaminated, 4: Dirty

SSI definitions, other than CDC:
¶a: National Nosocomial Infections Surveillance System (NNIS).[1]
¶b: a modified scoring system: grade 0, normal healing; grade I, normal healing with mild erythema or epidermolysis; grade II, superficial wound infection with galeal/fascia intact; grade III, deep wound infection below the galeal/fascia but with intact dural; grade IIIa, no osteomyelitis; grade IIIb, with osteomyelitis; grade IIIc, with pachy meningitis; grade IV, meningitis without tissue breakdown excluding chemical meningitis; grade V, meningitis with breakdown of dural and fascia; grade VI, intracranial or intraspinal intradural abscess; grade Via, subdural empyema; grade Vib, intraparenchymal abscess; grade Vic, intraventricular abscess; grade Vid, combination.
¶c: at the time of discharge, the patients of all groups were trained to go to the hospital if they had fever or if they saw any erythema, swelling or discharge at the surgical site. Then, the patients were daily followed by telephone to see if they had signs of symptoms of SSIs.
¶d: infection was defined according to clinical symptoms: purulent discharge, pain, heat, swelling or erythema at site of the wound. Final diagnosis was made by the surgeon.
¶e: postoperatively, the wound was inspected after 48 h for any discharge, soakage, erythema, tenderness and pain.

¶f: Southampton grading: grade 0, healing is normal; grade I, normal healing + mild bruising; grade II, erythema / tenderness / heat; grade III, serous discharge; grade IV, purulent discharge.
¶g: infection was assumed when there was unexpected or increased pain, redness, swelling, increased temperature or discharge from the wound.
¶h: presence of infection was examined and reported as positive or negative.
¶i: infection was suspected when unusual pain, tenderness, erythema, induration, fever, or wound drainage was noted. Such findings were investigated with measurement of erythrocyte sedimentation rate, C-reactive protein, and bacteriological cultures from the operative site or blood.
¶j: tenderness, redness, hotness, swelling, purulent discharge.
¶k: purulent discharge or erythema, fever, induration, and tenderness in the surgical site, which required separation of the incision, indicated an infection.
¶l: wound infection was diagnosed when a wound drained purulent material or serosanguineous fluid in association with induration, warmth and tenderness. Suspected wound infections were opened for confirmation and wound cultures were taken. Haematoma, seroma, or wound breakdown in the absence of the previously discussed signs was not considered a wound infection.
¶m: defined as wound discontinuation associated with purulent discharge from the wound and local tenderness, hotness, and/or redness within 1 month of surgery.
¶n: a wound was considered to be infected accordingly to Krukowski et al.[2] when there was a collection of pus or a positive bacteriologic culture from a wound discharge (as described by Ljunqvist[3]).

CDC, Centers for Disease Control and Prevention; N, number of patients; NR, not reported; PI, povidone iodine; ROB, risk of bias; RR, relative risk; SAP, systemic antibiotic prophylaxis; SSI, surgical site infection; 95% CI, 95% confidence interval

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eTable 3. Statements on method of wound irrigation

Study	Statements on method of wound irrigation
Mueller 2023	After randomization, patients received IOWI with 1000 ml of a 0·04% PHX solution, IOWI with 1000 ml NaCl 0·9%, or no irrigation. The wound was rinsed carefully with the respective solution and the excess was removed by suction. Debris and blood clots were removed from the wound using irrigation and suction. The wound was left moistened with the irrigation solution to ensure sufficient contact time (> 10 min).
Maemoto 2023	IOWI is performed for one minute with 40 mL of aqueous 10% PVP-I (POVIDONE-IODINE solution 10% “MEIJI”; Meiji Seika Pharma Co., Ltd., Tokyo, Japan) in the study group, and the same procedure is performed with 100 mL of saline (Isotonic Sodium Chloride Solution “Hikari”; Hikari Pharmaceutical Co., Ltd., Tokyo, Japan) in the control group.
Zhao 2023	After closing the peritoneal sutures with size 0 VICRYL Plus (Johnson & Johnson - Ethicon Endo-Surgery, Inc., Cincinnati, OH, USA), the wound was irrigated with either 500 mL of 1% PVI solution or 500 ml of 0.9% NS. Size 4-0 VICRYL Plus intradermic sutures were used in all patients.
Inoje 2023	Patients randomized into Group A had their spine wound irrigated with saline containing gentamicin solution (a liter of normal saline mixed with 80 mg of gentamicin injection) in a quantity sufficient to fill the wound to the level of the skin without overflow. The saline containing gentamicin solution was maintained in the incision for 3 minutes, after which the wound was flushed with the remaining saline containing gentamicin solution. Group B patients’ wounds were irrigated with a liter of 3.5% diluted PI solution. The surgical wound was filled with PI in a volume sufficient to fill the wound to the level of the skin without overflow. The PI solution was maintained in the incision for 3 minutes, after which the wound was flushed with the remaining dilute PI solution.
Zeb 2023	Before the wound was stitched up, the tissues in group I were irrigated with one litre of saline containing one gramme of imipenem (1 mg/ml), while group II received one litre of regular saline.
Karuserci 2022	All subcutaneous tissues were irrigated with 250 ml of saline. Then 3–5ml 10% povidone-iodine in group 2 and 250 mg/3 ml rifampicin in group 3 was applied directly on the subcutaneous tissue without diluting. The excess liquid was cleaned off and the subcutaneous tissue scrubbed with gauze.
Gomaa 2022	Subcutaneous irrigation by 200cc saline before closure of the skin.
Maghsoudipour 2022	Irrigation with hydrogen peroxide or placebo was performed right before closure of the surgical site with sutures, using irrigation syringes prepared by a pharmacist at the time they were needed. In the intervention group, hydrogen peroxide 3% solution was used, while 0.9% sodium chloride solution was used in the placebo group.
Al-Abdulla 2021	In this study group A, before skin closure, subcutaneous tissue was irrigated by 1% povidone iodine using 10cc syringe, kept there for 2 to 3 minute and then aspirated. Group B the subcutaneous tissue was washed by normal saline using 10cc syringe. Group C no irrigation was done.
Shah 2021	NR
Nguyen 2021	TAS contained 1 g of cefazolin, 50,000 U of bacitracin, and 80 mg of gentamicin in 500 mL of normal saline. Both the Tissue Expander and mastectomy pocket were bathed in the respective solutions, and a 1-minute dwell time was employed based on data presented on the IrriSept website reporting similar efficacy with 1- or 5-minute exposure times for most organisms.
Okunlola 2021	The patients in the subject group received 2 g of intravenous ceftriaxone (Roche-Rocephin) at induction of anaesthesia followed by 1 g 12 hourly for 24 h post-operatively and intra-operative wound irrigation with 250 mg/ml of ceftriaxone in normal saline. The patients in the control group received 2 g of intravenous (Roche-Rocephin) at induction of anaesthesia followed by 1 g 12 hourly for 24 h post-operatively and intraoperative wound irrigation with plain normal saline. The irrigation was done by jet and or droplets from 50 ml syringe.
Gül 2021	The subcutaneous tissue was irrigated with 200 ml of saline solution (0.9% NaCl) in patients in the experimental group (Group 1, n=115), and not irrigated in those in the control group (n=115) before the skin was closed.
Cohen 2020	After the initial culture collection, nonviable tissues were debrided and the wound was soaked for 3 minutes with enough 0.35% PVP-I or sterile saline to be in contact with the entire wound. No antibiotics were added to sterile saline. The wound was then irrigated with 2 L of saline regardless of randomization to limit confounding, since PVP-I must be irrigated with saline.
Akhavan - Sigari 2020	Before bone grafting, the surgical wounds in the normal ssaline group were filled and soaked with 0.9% normal saline, suction was performed; the irrigation being repeated three times. In the PVI group, surgical wounds were irrigated with PVI 3% to fill and soak the wound for two minutes followed by normal saline irrigation.
Karuserci 2020	All subcutaneous tissues were irrigated with 250 mL of saline. Then 10 mL of 10 % povidone-iodine in Group 2 and 500 mg/6 mL of rifampicin in Group 3 was applied directly on the subcutaneous tissue without being diluted. The excess liquid was cleaned off and the subcutaneous tissue scrubbed with a gauze.
Strobel 2020	At the end of the operation, the peritoneal cavity was rinsed routinely with 0.9% sodium chloride solution at body temperature (Braun, Melsungen, Germany). Before closure of fascia, instruments and gloves were changed. After the closure of fascia, subcutaneous irrigation with 250mL 0.9% saline (Braun, Melsungen, Germany) or 250mL antiseptic 0.04% polyhexanide solution (Serasept2, Serag-Wiessner) was done according to the randomization list. The application time for polyhexanide was 10 minutes and for saline as biologically inactive agent 1 minute.
Emile 2020	In group I, upon closure of the peritoneum gentamicin-saline solution (160 mg of gentamicin in 400 ml of normal saline 0.9%) was used by a 20-cm syringe for irrigation of every layer of the wound before its closure. The first layer was between the peritoneal membrane and the internal oblique muscles, the second layer was between the approximated internal oblique muscles and the external oblique aponeurosis, and finally the third layer (the subcutaneous space) after closure of the external oblique aponeurosis (Fig. 1). In group II, layer by layer irrigation of the wound with normal saline solution was performed in a similar manner. In group III, layer-by-layer closure of the surgical wound with polyglactin 2/0 sutures took place without irrigation.

Karuserci 2019	All subcutaneous tissues were irrigated with 250 ml of saline. Then 500 mg/6 ml of rifampicin in group 2 and 10 ml of povidone iodine in group 3 was applied directly on the subcutaneous tissue without dilution. The excess liquid was cleaned off and the subcutaneous tissue scrubbed with gauze.
Vinay 2019	In Group A, the incision site was treated with 400 ml, 0.9% normal saline and 100 ml 5% povidone-iodine solution. In Group B, the incision site was treated with 500 ml 0.9% normal saline solution.
Haider 2018	In group A, before skin closure subcutaneous tissues were irrigated with 5 ml 1 % PVI solution in normal saline. The solution was kept in wound for five minutes then aspirated. In group B, no irrigation was done.
Aslan 2018	Before the subcutaneous tissue closure in the saline group the subcutaneous saline irrigation was performed with a 200cc of saline (0.9%NaCl). No subcutaneous irrigation was applied in the control group before the skin closure.
De Luna 2017	In group A, before applying the bone graft, low-pressure irrigation (Bio Pulse, Leader Medica) with PVP-I diluted to a 3% concentration (30 g/l) in 2 litres of saline for between 5 and 10 minutes was performed and then washed out by 1 litre of sodium chloride solution through a pulse irrigation device. In group B, low-pressure irrigation with 2 litres of saline solution for between 5 and 10 minutes was performed before applying bone graft.
Fei 2017	The incision was flushed with 0.1% iodine solution (volume: 200 ml) and soaked for 2 min, then the incisions were flushed with normal saline under adequate hemostasis conditions. The incisions were flushed with saline solution in the usual way.
Mahomed 2016	The intervention was wound irrigation with about 50 mls of 10% aqueous PVI solution (Betadine group). The solution in a bowl was poured in and around the incision site.
Neeff 2016	NR
Oller 2015	All patients underwent a first lavage of the axillary surgical bed with physiologic saline. Group 1 underwent a second lavage with saline. Group 2 had a second lavage with a 240-mg gentamicin solution (Group 2), and Group 3 had a second lavage with a 600-mg clindamycin solution.
Iqbal 2015	In the study group A, before skin closure, the subcutaneous tissue was irrigated with 4-5 cc of 1% diluted povidone-iodine solution. The solution was sprayed into the subcutaneous wound with the help of a 5cc syringe, kept there for 2-3 minutes and was then aspirated. However, in the control group B, no irrigation was done.
Ruiz-Tovar 2013	In both groups, prior to the lavage, a microbiological sample from the surgical bed was obtained with a swab (sample 1), followed by a lavage with 500 ml normal saline. After aspiration of the saline, a new microbiological sample was obtained (sample 2). In Group 1 a second lavage with 500 ml normal saline was performed, while in Group 2 the second lavage was performed with an antibiotic solution, including gentamicin (240 mg) dissolved in 500 ml normal saline.
Etaati 2012	In one group, after the surgery and before closing up the patients, 2 grams of cefazolin in 5 cc of distilled water were used to irrigate the patients. In the second group, 150 cc of normal saline was used to irrigate the patients and in the last group, no irrigation was used.
Takesue 2011	In the ESAAS group the surgical wound was irrigated with at least 500 mL of ESAAS after the completion of fascial suture. In the saline solution group, the same amount of saline solution was used for wound irrigation.
Güngördük 2010	In the study group, before skin closure, the subcuticular tissue was irrigated with 100 ml of sterile saline with a 30–60 ml syringe. The skin was then closed using a 3-0 Vicryl suture. In the control group, the subcuticular tissue was not irrigated with sterile saline and the skin was closed using a 3-0 Vicryl suture.
Köşüş 2010	In the second group subcutaneous tissue was irrigated with rifamycin SV/ 250 mg, before closure of subcutaneous tissue.
Kokavec 2008	Approximately 1 ml of betadine was diluted by adding approx. 30 ml of sterile saline solution to a concentration of about 0.35% povidone iodine for perioperative use (2-3 minutes)
Mirsharifi 2008	One gram of injectable cefazolin was used to wash the wound after the surgery and just before closing the incision site, and the control group was without topical antibiotic.
Bhargava 2006	In group A the wound was irrigated with normal saline and in group B 50–100mL of metronidazole (from a single manufacturer). The concentration used was 500 mg/100 mL, which was infiltrated in the subcutaneous tissues making sure that the area of infiltration exceeds that of the incision.
Chang 2006	In group 1 composed of patients with odd serial numbers (study group), wounds were irrigated with 0.35% povidone-iodine solution to soak for 3 min, followed by an irrigation with 2000 c.c. of normal saline to remove povidone-iodine solution. No more wound irrigation was given after. In contrast, group 2 with patients even numbered (control group) was wound irrigated only with 2000 c.c. of normal saline.
Al-Ramahi 2006	The 104 patients in the odd number group (group 1), underwent wound irrigation with 50 mL of normal saline solution (NaCl 0.9%) following surgery and before skin closure. The 102 patients in the even-number group (group 2) received no wound irrigation.
Cheng 2005	The commercially available betadine solution used had a concentration of 10% povidoneiodine (100 mg of povidoneiodine per 1 mL of solution). Approximately 5 mL of povidoneiodine was diluted with normal saline to achieve a 0.35% povidoneiodine (3.5% betadine) solution for use during operation. The wound was irrigated with copious amounts of normal saline (2000 mL) after betadine solution irrigation. In group 2, irrigation with copious normal saline (2000 mL) was performed alone.
Platt 2003	Each breast was preinfiltrated with 300 mL saline containing adrenaline diluted to 1:500,000, lignocaine, and hyaluronidase (Hyalase; CP Pharmaceuticals Ltd, Wrexham, UK). Infiltration was performed uniformly throughout the breast using a spinal needle and syringe, sparing the pedicle.
Cervantes-Sánchez 2000	Group I (control) was treated with surgery and prophylactic systemic antibiotics and group II (experimental) was treated with surgery, antibiotics, and wound syringe pressure irrigation as follows: after closure of the fascial planes, we irrigated the subcutaneous fat tissue with 300 ml of normal saline solution, delivered with a 20-ml syringe with a 19-gauge intravenous (IV) catheter, applying to the embolus the force of one hand, at a distance of 2 cm from the wound tissues, aspirating the fluid collected in the wound with a bulb syringe.

ESAAS, Electrolyzed Strongly Acidic Aqueous Solution; IOWI, intraoperative wound irrigation; NaCl, sodiumchloride; NR, not reported PHX, polyhexanide; PI, povidone-iodine; PVI, povidone-iodine; PVP-I, povidone-iodine; TAS, Triple Antibiotic Solution; NR, not reported

eTable 4. Node splitting

With the Separate Indirect from Direct Design Evidence node splitting, the network effect estimates are split into the contribution of the direct and indirect effect estimates. Node splitting can only be performed for comparisons that have both direct and indirect evidence. The difference between the direct and indirect relative risks is expressed in the ratio of ratios, which shows significant disagreement when $p < 0.05$.

Comparison	**N**	**NMA RR**	**Direct RR**	**Indirect RR**	**ROR**	***p*-value**
Antibiotic vs antiseptic	5	0.7671	1.0678	0.6386	1.6721	0.27
Antibiotic vs saline	10	0.5557	0.5745	0.5881	0.9769	0.97
Antibiotic vs no irrigation	3	0.4592	0.1870	0.5536	0.3378	0.09
Antiseptic vs saline	17	0.7245	0.6705	1.0000	0.6705	0.17
Antiseptic vs no irrigation	6	0.5987	0.7670	0.3971	1.9313	**0.04**
Saline vs no irrigation	10	0.8264	0.7463	1.1018	0.6773	0.28

N: number of studies investigating comparison
NMA RR: network relative risk
Direct RR: relative risk of direct comparison
Indirect RR: relative risk of indirect comparison
ROR: ratio of ratios (ratio of direct RR and indirect RR)

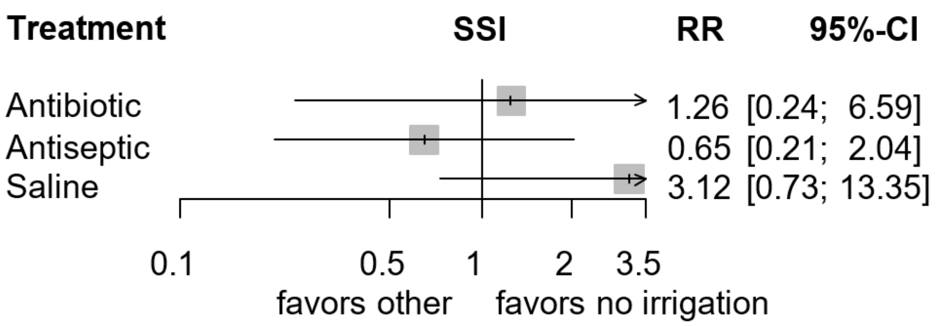
eFigure 1. Subgroup and sensitivity analyses

The forest plots show the network relative risks (RR) with corresponding 95% confidence intervals (CI) compared with no irrigation.

In the lower triangle of the league tables the network RRwith corresponding 95% CI are shown. The upper triangle shows the RR of only the direct comparisons (comparable with a regular pairwise meta-analysis).
For instance, in Appendix 6.a, the first column (in the lower triangle) shows the network RR with corresponding 95% CI of antibiotic compared with the other irrigation solutions. The last column (upper triangle) shows the direct RR with corresponding 95% CI of no irrigation compared with the other irrigation solutions.

A. Only clean surgery (CDC wound classification I)

Forest plot



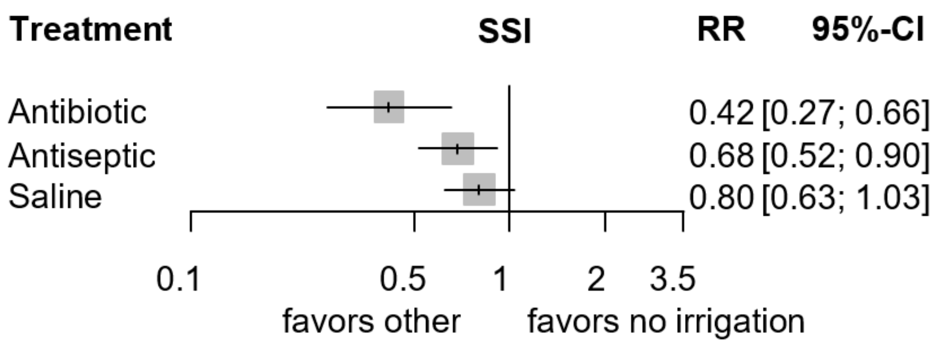
(I^2 = 22.7%, τ^2 = 0.3037)

League table

Antibiotic	1.29 [0.34; 4.84]	2.00 [0.15; 27.20]	-
1.95 [0.59; 6.42]	**Antiseptic**	**0.17 [0.07; 0.43]**	0.65 [0.21; 2.04]
0.40 [0.10; 1.60]	**0.21 [0.08; 0.51]**	**Saline**	-
1.26 [0.24; 6.59]	0.65 [0.21; 2.04]	3.12 [0.73; 13.35]	**No irrigation**

B. Excluding studies with only clean surgery

Forest plot



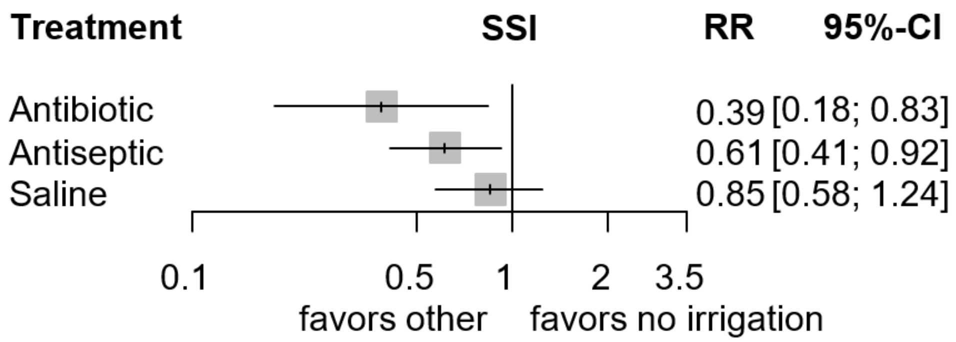
(I^2 = 34.3%, τ^2 = 0.0623)

League table

Antibiotic	1.04 [0.41; 2.60]	**0.55 [0.36; 0.84]**	**0.19 [0.06; 0.58]**
0.61 [0.39; 0.95]	**Antiseptic**	0.79 [0.62; 1.02]	0.81 [0.56; 1.17]
0.52 [0.35; 0.77]	0.85 [0.67; 1.07]	**Saline**	0.77 [0.57; 1.03]
0.42 [0.27; 0.66]	**0.68 [0.52; 0.90]**	0.80 [0.63; 1.03]	**No irrigation**

C. Only upper-middle and high income countries

Forest plot



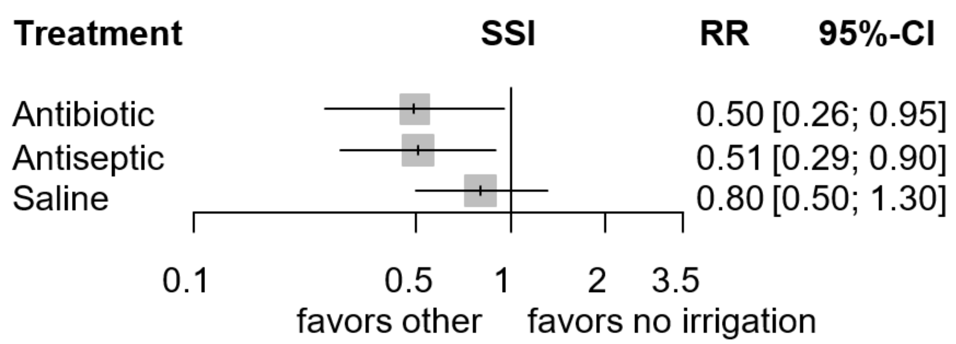
(I^2 = 46.7%, τ^2 = 0.1327)

League table

Antibiotic	0.82 [0.37; 1.84]	0.45 [0.19; 1.10]	**0.04 [0.00; 0.74]**
0.63 [0.31; 1.27]	**Antiseptic**	**0.68 [0.50; 0.92]**	0.81 [0.48; 1.35]
0.46 [0.23; 0.92]	**0.73 [0.54; 0.97]**	**Saline**	0.76 [0.48; 1.18]
0.39 [0.18; 0.83]	**0.61 [0.41; 0.92]**	0.85 [0.58; 1.24]	**No irrigation**

D. Only low and lower-middle income countries

Forest plot



(I^2 = 37.9%, τ^2 = 0.1378)

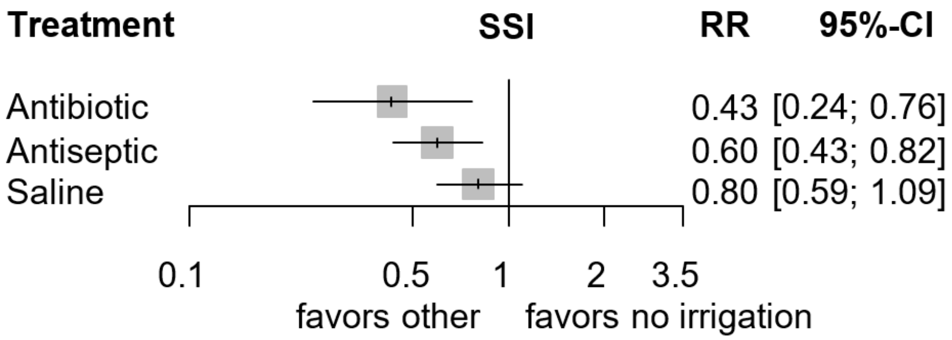
League table

Antibiotic	7.00 [0.80; 61.57]	0.63 [0.37; 1.08]	**0.25 [0.07; 0.91]**
0.97 [0.46; 2.03]	**Antiseptic**	0.56 [0.24; 1.31]	0.68 [0.34; 1.37]

0.62 [0.37; 1.03]	0.64 [0.35; 1.15]	**Saline**	0.71 [0.40; 1.25]
0.50 [0.26; 0.95]	**0.51 [0.29; 0.90]**	0.80 [0.50; 1.30]	**No irrigation**

E. Excluding studies with high risk of bias

Forest plot



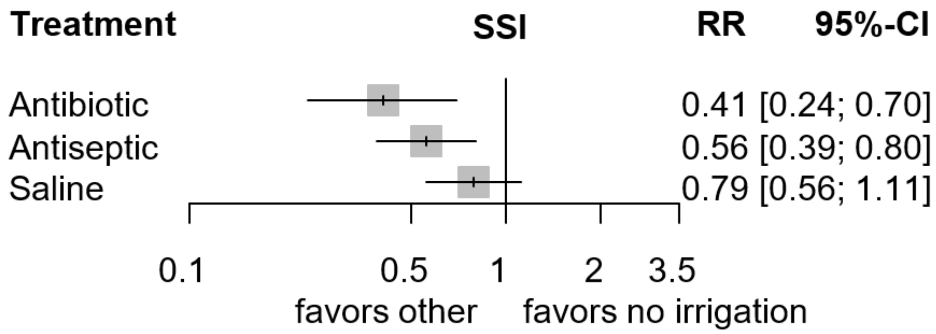
(I^2 = 47.6%, τ^2 = 0.1254)

League table

Antibiotic	0.79 [0.30; 2.09]	0.59 [0.32; 1.09]	**0.18 [0.05; 0.63]**
0.72 [0.42; 1.24]	**Antiseptic**	**0.68 [0.51; 0.91]**	0.76 [0.51; 1.14]
0.54 [0.32; 0.90]	**0.74 [0.57; 0.97]**	**Saline**	0.72 [0.50; 1.03]
0.43 [0.24; 0.76]	**0.60 [0.43; 0.82]**	0.80 [0.59; 1.09]	**No irrigation**

F. Only studies with adequate description of systemic antibiotic prophylaxis

Forest plot



(I^2 = 45.8%, τ^2 = 0.1506)

League table

Antibiotic	1.06 [0.49; 2.30]	**0.52 [0.30; 0.91]**	**0.18 [0.06; 0.61]**
0.73 [0.44; 1.21]	**Antiseptic**	**0.67 [0.49; 0.92]**	0.75 [0.46; 1.21]
0.52 [0.32; 0.83]	**0.71 [0.53; 0.95]**	**Saline**	0.71 [0.47; 1.06]
0.41 [0.24; 0.70]	**0.56 [0.39; 0.80]**	0.79 [0.56; 1.11]	**No irrigation**

eTable 5. Elaborate risk of bias assessment

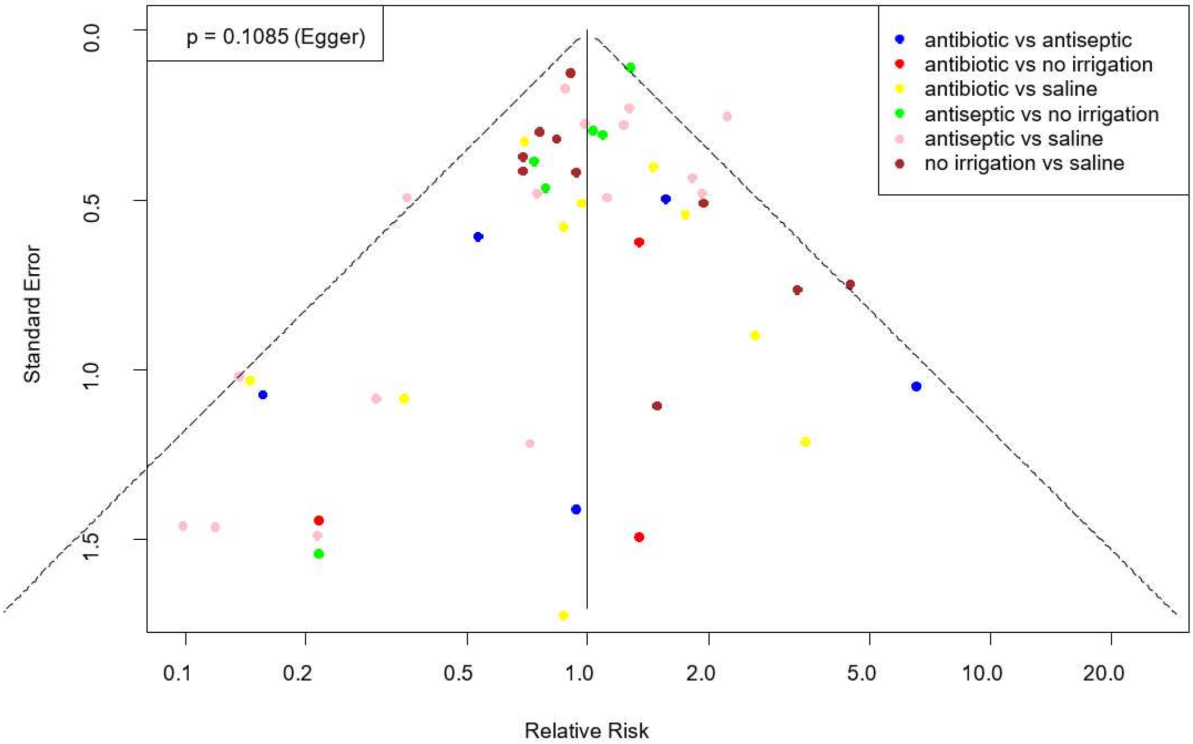
Study	Randomisation process	Deviations from the intended interventions	Missing outcome data	Measurement of the outcome	Selection of the reported result	Overall
Akhavan-Sigari 2020	!	+	+	+	!	!
Al-Abdulla 2021	!	+	+	!	!	!
Al-Ramahi 2006	-	+	+	!	!	-
Aslan Çetin 2018	+	+	!	+	+	!
Bhargava 2006	-	+	+	-	!	-
Cervantes-Sánchez 2000	+	+	+	+	!	!
Chang 2006	+	+	+	!	!	!
Cheng 2005	+	+	+	!	!	!
Cohen 2020	+	+	!	!	+	!
De Luna 2017	!	+	+	!	!	!
Emile 2020	+	!	!	+	+	!
Etaati 2012	+	+	+	-	!	-
Fei 2017	!	+	+	!	!	!
Gomaa 2022	+	+	+	!	!	!
Gül 2021	+	+	+	!	!	!
Güngördük 2010	+	+	+	+	!	!
Haider 2018	+	+	+	!	!	!
Inojie 2023	+	+	+	+	!	!
Iqbal 2015	!	+	+	!	!	!
Karuserci 2019	!	+	+	!	!	!

+	Low risk
!	Some concerns
-	High risk

Karuserci 2020	-	!	+	!	!	-
Karuserci 2022	+	+	+	!	!	!
Kokavec 2008	!	!	+	!	!	!
Köşüş 2010	!	!	!	!	!	!
Maeomoto 2023	+	!	+	+	+	!
Maghsoudipour 2022	+	+	+	!	+	!
Mahomed 2016	+	+	!	+	+	!
Mirsharifi 2008	!	+	+	+	!	!
Mueller 2023	+	+	+	+	+	+
Neeff 2016	!	+	+	!	!	!
Nguyen 2021	+	+	+	+	!	!
Okunlola 2021	+	+	+	+	!	!
Oller 2015	+	+	+	!	!	!
Platt 2003	!	+	+	!	!	!
Ruiz-Tovar 2013	+	+	+	!	!	!
Shah 2021	!	+	+	!	!	!
Strobel 2020	+	+	!	+	+	!
Takesue 2011	+	+	+	+	!	!
Vinay 2019	+	+	+	!	!	!
Zeb 2023	!	!	+	!	!	!
Zhao 2023	+	+	+	!	+	!

eFigure 2. Comparison-adjusted funnel plot

The comparison-adjusted funnel plot shows the effect estimate of a study (relative risks) versus its precision (standard error) for the outcome SSI. Asymmetry of the comparison-adjusted funnel plot can indicate that there are differences between small and large studies in regards to the effect of the treatment (small-study effect). Comparison-adjusted funnel plot asymmetry can be caused by publication bias. Since no asymmetry (no small-study effect) is found, publication bias is deemed not likely.



eTable 6. GRADE assessment

The Grading of Recommendations Assessment, Development and Evaluation (GRADE) methodology was used to evaluate the the certainty of the evidence using a minimally contextualized approach for direct, indirect and the complete network meta-analysis evidence sequentially.[1-3]

Minimally important benefit, -harm, or trivial to no effect was chosen as the target estimate based on the point estimate in relation to the minimally important difference.[4] Considering the inherently different trade-offs between saline, antiseptic and antibiotic irrigation with respect to concerns on resistance and other adverse effects we defined different minimally important differences (MID) for these interventions.[5-7] In line, the precedent set by the long standing practice to reserve surgical antibiotic prophylaxis for clean-contaminated procedures (unless special considerations such as the use of implant material apply), we defined the MID as 3.5% for the routine use of antibiotic irrigation based on the upper limit of the incidence of SSI in clean procedures at the time (5%) and the RR of SSI after the use of surgical antibiotic prophylaxis in common clean-contaminated procedures (0.35).[8,9] The MID for other interventions was defined as 2% based on the default for appreciable benefit and harm of 25% and the SSI incidence of 8% without irrigation in the presented data.

Since all included studies are randomized controlled trials, the rating for the GRADE starts high for all direct comparisons. Starting GRADE for the indirect evidence was based on the lowest of the two most dominant first order direct comparisons contributing to the indirect evidence. Starting GRADE for the network meta-analysis evidence was based on the highest certainty of evidence of the contributing direct and indirect evidence or whichever of the two was available.

Each comparison can be downgraded due to one of the following reasons:

- Risk of bias
  Of the 41 studies included in the network meta-analysis, four had an overall "High risk of bias". Due to the network meta-analysis, this may have an effect on all the network estimates of all comparisons. We performed a (network) sensitivity meta-analysis excluding studies with high risk of bias. The results were comparable with the overall analysis, and downgrading for risk of bias was not needed.
- Inconsistency
  Low, moderate, and high inconsistency were characterized using the I^2 and τ^2 statistics. An I^2 <25% is considered as low, between 25% and 50% is considered moderate, and >50% as high. For the direct evidence, -1 downgrade for inconsistency was necessary for the comparisons antibiotic versus antiseptic (I^2 = 50.6%, τ^2 = 1.12) and antiseptic versus saline (I^2 = 48.7%, τ^2 =0.5088). Coherence was only applied to the network meta-analysis evidence. For the assessment of coherence both the point estimates, confidence intervals and outcomes from the Separate Indirect from Direct Design Evidence node splitting (Appendix 5) analysis were interpreted in context.[11,12]
- Indirectness
  Transitivity was only applied to indirect evidence. Due to the broad inclusion criteria and consequential clinical heterogeneity some intransitivity was anticipated. We evaluated transitivity by comparing the SSI incidence in the common control group between the two contributing direct comparisons and considered relative differences larger than 25% sufficient concern for downgrading.[13]
- Imprecision
  Imprecision was only applied to the final evaluation of the evidence. Imprecision was evaluated taking the minimally important differences into account and assessing the optimal information size in case of large effects by calculating the ratio between the lowest and highest boundary of the confidence interval with a threshold for downgrading of 2.5.[3,14]
- Publication bias
  The comparison-adjusted funnel plot showed in Appendix 8 shows no sign of small-study effects.

Network evidence
For all comparisons, both direct and indirect evidence are available. Therefore, we used the highest of the two certainty ratings as the certainty rating for the NMA estimate. The certainty of the network estimate can be upgraded if precision is greater than direct or indirect estimates.

Comparison	Direct evidence (Classic)		Indirect evidence (Transitivity)		Network meta-analysis (Incoherence)		
	Relative Risk (95%CI)	Certainty of evidence	Relative Risk (95%CI)	Certainty of evidence	Relative Risk (95%CI)	Certainty of evidence	Target
Antibiotic vs antiseptic	1.07 (0.51 – 2.24)	⊕OOO very low	0.64 (0.37 – 1.10)	⊕⊕OO low	0.77 (0.50 – 1.19)	⊕OOO very low	Trivial to no effect
Antibiotic vs saline	**0.57 (0.37 – 0.90)**	⊕⊕⊕O moderate	0.59 (0.20 - 1.75)	⊕OOO very low	**0.56 (0.37 – 0.83)**	⊕⊕⊕O moderate	Minimally important benefit
Antibiotic vs no irrigation	**0.19 (0.06 – 0.59)**	⊕⊕OO low	**0.55 (0.34 - 0.90)**	⊕OOO very low	**0.46 (0.29 - 0.73)**	⊕⊕OO low	Minimally important benefit
Antiseptic vs saline	**0.67 (0.51 – 0.88)**	⊕⊕⊕O moderate	1.00 (0.61 – 1.65)	⊕OOO very low	**0.72 (0.57 – 0.93)**	⊕⊕⊕ O moderate	Minimally important benefit
Antiseptic vs no irrigation	0.77 (0.52 – 1.13)	⊕⊕⊕O moderate	**0.40 (0.24 – 0.66)**	⊕⊕OO low	**0.60 (0.44 – 0.81)**	⊕⊕⊕⊕ high	Minimally important benefit
Saline vs no irrigation	0.75 (0.54 – 1.04)	⊕⊕⊕O moderate	1.10 (0.59 – 2.08)	⊕OOO very low	0.83 (0.63 – 1.09)	⊕⊕⊕O moderate	Trivial to no effect

Comparison	Reasons for downgrading		
	Direct evidence	**Indirect evidence**	**Network meta-analysis**
Antibiotic vs antiseptic	-1 inconsistency -3 imprecision	-1 imprecision	-2 imprecision
Antibiotic vs saline	-1 imprecision	-3 imprecision -1 intransivity	-1 imprecision
Antibiotic vs no irrigation	-2 imprecision	-1 intransivity -1 imprecision	-1 incoherence -1 imprecision
Antiseptic vs saline	-1 inconsistency	-3 imprecision	no downgrade (starting GRADE moderate)
Antiseptic vs no irrigation	-1 imprecision	-1 intransivity	no downgrade
Saline vs no irrigation	-1 imprecision	-1 intransitivity -3 imprecision	-1 imprecision

GRADE conclusions surgical site infections (SSI)

Antibiotic vs antiseptic

Very low GRADE	Antibiotics solutions may have little to no effect on SSI when compared with antiseptic solutions in surgical patients but the evidence is very uncertain.

Antibiotic vs saline

Moderate GRADE	Antibiotic solutions likely reduce SSI when compared with saline in surgical patients.

Antibiotic vs no irrigation

Low GRADE	Antibiotic solutions may result in a reduction of SSI when compared with no irrigation in surgical patients.

Antiseptic vs saline

Moderate GRADE	Antiseptic solutions likely result in a reduction of SSI when compared with saline in surgical patients.

Antiseptic vs no irrigation

High GRADE	Antiseptic solutions result in a reduction of SSI when compared with no irrigation in surgical patients.

Saline vs no irrigation

Moderate GRADE	Saline solutions likely result in little to no difference in SSI when compared with saline in surgical patients.

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Data Sharing Statement

Groenen. Incisional Wound Irrigation for the Prevention of Surgical Site Infection. *JAMA Surg*. Published April 24, 2024. doi:10.1001/jamasurg.2024.0775

Data
Data available: No

Additional Information
Explanation for why data not available: Data can be provided upon request and in agreement of terms. No individual participant data was used.