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Systematic Review

Antiseptic wound irrigation to prevent surgical site infection after laparotomy: meta-analysis

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Abstract

Background: Surgical site infection after laparotomy is a major postoperative complication. The efficacy of prophylactic laparotomy wound irrigation to reduce surgical site infection rates remains controversial. This study evaluates the impact of antiseptic wound irrigation on surgical site infection prevention.

Methods: A systematic review and meta-analysis, following PRISMA 2020, included randomized clinical trials and observational studies (published after 1999) comparing antiseptic or saline irrigation *versus* saline or no irrigation before laparotomy closure in adult patients with surgical site infection as the primary outcome. Databases searched included MEDLINE, EMBASE, Cochrane Library, and Google Scholar (September 2024). Risk of bias was assessed using RoB 2 and ROBINS-I; Grading of Recommendations Assessment, Development, and Evaluation evaluated evidence certainty.

Results: Eighteen studies (6368 patients) reported an overall surgical site infection rate of 14.7%. Thirteen studies compared antiseptic with saline irrigation, showing no significant effect (relative risk 0.80, 95% confidence interval 0.58 to 1.09; $P = 0.159$) with very low evidence certainty. Excluding laparoscopic cases and high-risk bias studies revealed a favourable effect for antiseptic irrigation (relative risk 0.75, 0.64 to 0.87; $P < 0.001$) with moderate certainty. Three studies compared antiseptic with no irrigation, and four compared saline with no irrigation. Meta-analysis indicated reduced surgical site infection rates with any irrigation (antiseptic or saline) *versus* no irrigation (relative risk 0.52, 0.37 to 0.74; $P < 0.001$) with moderate certainty.

Conclusion: Wound irrigation (antiseptic or saline) likely reduces surgical site infection rates after laparotomy. Evidence comparing antiseptic *versus* saline is uncertain but suggests a potential benefit after excluding the high risk of bias studies. Further high-quality, standardized trials are needed.

Introduction

Postoperative surgical site infections (SSIs) after laparotomy remain one of the big challenges in abdominal surgery, affecting 10–25% of patients, depending on the intraoperative level of contamination (LOC I = clean, LOC II = clean-contaminated, LOC III = contaminated, LOC IV = septic), and other individual risk factors[1,2]. Whereas superficial incisional SSIs (SSI °I) can often be treated conservatively, bacterial infections of the deeper layers of the abdominal wall (SSI °II) can spread along the fascia—often requiring multiple re-operations and prolonging hospital stay. In the worst case, infections of organs or the peritoneal cavity (SSI °III) can be life threatening for patients.

Prophylactic intraoperative wound irrigation to reduce SSI rates is a widespread practice, but evidence of its effectiveness remains uncertain and thus recommendations on its use are divergent. Several international organizations have published guidelines on SSI prevention, including the World Health Organization (WHO)[3] in 2016, the Centre for Disease Control and Prevention (CDC)[4], updated in 2017, and the National Institute for Health and Care Excellence (NICE)[5], updated in 2020. Whereas the CDC guideline recommends wound irrigation with aqueous iodophor solution (grade 2, weak recommendation), the WHO only suggests considering it, and the NICE guideline recommends abstaining from it due to the lack of evidence[6,7]. However, these guidelines do not specifically address abdominal surgery, nor do they take antiseptic solutions other than povidone-iodine (PVP-I) into account. They do agree that high-level evidence regarding saline or antiseptic irrigation is missing, and that antibiotic irrigation solutions should no longer be used[7].

In addition, several systematic reviews and meta-analyses have already been published on the subject. However, all of them included trials of low methodological quality, trials dating from the 1980s or even earlier, and trials mixing different types of surgeries, laparoscopic and open procedures, or obsolete antibiotic irrigation solutions[8–17]. This includes a systematic review and meta-analysis[17] from the author's group from 2014, which concluded that any wound irrigation (antibiotic, antiseptic, and saline) is better than no wound irrigation, but, on its own,

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antibiotic irrigation was the only type of wound irrigation that significantly reduced SSIs. However, wound irrigation with topical antibiotics is no longer recommended due to the possible impact on microbial resistance.

Results from recent high-quality clinical trials[18–21] have suggested that wound irrigation with antiseptics before skin closure does not reduce the rate of SSI after laparotomy for gastrointestinal surgery (LOC II). However, most of these trials also included laparoscopic procedures, which are known to have a lower SSI risk than open procedures. In addition, there is evidence from smaller trials[22–28] that patients undergoing procedures with a higher SSI risk (emergency, LOC III and IV) benefit from wound irrigation with antiseptics or saline. In conclusion, although wound irrigation is a popular procedure amongst most surgeons, the lack of procedure standardization leads to clinical trials with high heterogeneity and controversial results, so that recommendations on its use are still inconsistent[8,11,12,29,30].

The aim of this study was to evaluate the efficacy of antiseptic wound irrigation compared with saline or no irrigation to prevent SSI after laparotomy in adult patients undergoing general surgery. In contrast to two other recently published meta-analyses[31,32], other fields of surgery, laparoscopic procedures, and antibiotic irrigation solutions were specifically excluded.

Methods

This systematic review and meta-analysis are reported in line with the PRISMA[33] and the assessing the methodological quality of systematic reviews (AMSTAR)[34] guidelines. The study protocol, registration number CRD42022321458, was registered in PROSPERO ((https://www.crd.york.ac.uk/prospero/) and published in a peer-reviewed journal[35]. As an amendment to the protocol, the study team decided to use the relative risk (RR) instead of the odds ratio when reporting the results before the statistical analysis had started. This decision was guided by the suggestion of the Cochrane Handbook for Systematic Reviews[36] to use RR when reporting results.

Eligibility criteria

The following inclusion criteria were predefined, according to the recommended population, intervention, comparison, outcome, and study design (PICOS) approach[37]. As an amendment to the protocol, the population (P) description was rephrased to clarify the type of included surgeries.

- **P** (population): adult subjects (age ≥ 18 years) undergoing elective or emergency laparotomy for general surgery (including colorectal, hepato-pancreatico-biliary (HPB) and upper gastrointestinal (GI) procedures).
- **I** (intervention): prophylactic wound irrigation after closure of the peritoneum using antiseptic solutions or saline compared with saline irrigation or no irrigation.
- **C** (comparison): saline irrigation or no irrigation.
- **O** (outcome): surgical site infection within 30 days after surgery.
- **S** (study design): randomized clinical trials (RCTs), non-randomized prospective observational studies (NRSs), systematic reviews, and meta-analyses (for reference screening only).

The predefined exclusion criteria were non-abdominal surgery (orthopaedics, neurosurgery, and others); gynaecological, urological, or vascular abdominal surgery; trials testing different interventions such as antibiotic wound irrigation, intra-abdominal irrigation, application of gels or powders to the incision wound, application of topical antiseptics on the skin over closed incision (antiseptic dressings), or skin re-disinfection before wound closure; different outcomes such as bacterial counts or cost effectiveness; and insufficient reporting.

Information sources

The following databases were searched on 1 September 2024: Embase (Scopus), MEDLINE (PubMed®), Google Scholar, and the Cochrane library (CENTRAL). In addition, the reference lists of all included trials and systematic reviews, as well as the above-mentioned guidelines on SSI prevention, were screened.

Search strategy

The databases were searched using the following restrictions/filters if applicable: human subjects or medicine; language: English or German; publication date starting from 1 January 2000. Two authors (TM, RD) performed the search independently. The detailed search strategy can be found in *Table S1*.

Selection process

Search results were prescreened to identify irrelevant articles by title and abstract, and the remaining records were imported into an EndNote™ V20 library[38]. Duplicates were removed manually. The remaining articles were classified as relevant, possibly relevant, or irrelevant by two reviewers (TM, RD) independently, applying the eligibility criteria. Relevant or possibly relevant articles were retrieved for full-text reading. The selection process was performed by two authors (TM, RD) independently and any disagreements were resolved by discussion with a senior author (DR or HF).

Data collection process and data items

Data from the individual studies were extracted in a predefined data collection form. The form included details on type of study, publication date, inclusion and exclusion criteria, number of patients, type of surgical procedure and LOC, type of intervention, and control. Furthermore, the definition of primary outcome, the results (rates of SSI in each treatment group), the duration of follow-up, and the use of postoperative antibiotics were recorded. In addition, details of methods (randomization, blinding, and others) were extracted for the risk of bias assessment of individual trials. No automation tools were used in the data collection process. The selection process was performed by two authors (TM, RD) independently and disagreements were resolved by discussion with a senior author (DR or HF) and re-extraction if necessary.

Study risk of bias assessment

Data on methodological quality of RCTs were assessed using the Cochrane Collaboration's RoB 2 tool for assessing risk of bias in RCTs[39] and the ROBINS-I tool for assessing risk of bias in NRSs[40]. The assessment was performed by two authors (TM, RD) independently. Any disagreements were resolved through discussion with a senior author (DR or HF). In case of missing data, the primary authors of the studies were contacted. Publication bias was assessed using a funnel plot.

Certainty assessment

The Grading of Recommendations Assessment, Development, and Evaluation (GRADE) methodology[41] (GRADEpro software) was used to evaluate the certainty of the evidence.

Effect measures and synthesis methods

The primary outcome was SSI (any definition). No secondary outcomes from the original publications were analysed. The included studies were grouped according to comparison (antiseptic *versus* saline wound irrigation, antiseptic *versus* no wound irrigation, and saline *versus* no wound irrigation). In case of three-armed studies, the intervention arms were combined for the analysis. If studies included both open and laparoscopic cases, the latter were excluded in a sensitivity analysis. A separate meta-analysis was performed for each comparison. Furthermore, subgroup analyses were performed for type of antiseptic agent and LOC (I–II *versus* III–IV), if data were available. For each comparison, a sensitivity analysis was conducted excluding NRSs and RCTs with high risk of bias. Absolute numbers of patients and events are presented for each trial incorporated in the meta-analyses. The RRs with 95% confidence intervals (c.i.) were estimated for each trial from the numbers of events and patients treated. Due to the naturally expected heterogeneity, random effect models with Mantel–Haenszel weights were used to estimate the overall treatment effect and a corresponding 95% c.i. Forest plots are shown to illustrate treatment effects estimated for each trial and the estimated overall treatment effect for all investigated groups. For each analysis, the Q-test for heterogeneity was performed to access the variation of effect sizes across the studies, τ^2 is presented as an estimate for the variance of true treatment effects between the trials, and the estimated proportion of variability that can be referred to trial heterogeneity is indicated by the I^2 statistic. A two-sided level of significance of less than 5.0% was considered for all tests. All analyses were performed using R Statistical Software (v4.2.3; R Core Team 2023, Vienna, Austria). Effect measures and synthesis methods were calculated using the meta package (v6.5.0)[42].

Results

Study selection

The study selection process is presented in the PRISMA flow diagram (*Fig. 1*). In total, 1270 records were identified through the search. Finally, 81 articles were sought for full-text retrieval and were eligible for detailed assessment. Reasons for exclusion are shown in the PRISMA flowchart. Finally, 15 RCTs[18–24,26,28,43–48] and 3 NRSs[25,27,49] were included in the meta-analysis. According to the recommendations of GRADE[50], NRSs can be included in a meta-analysis if certainty of evidence by GRADE assessment from RCTs is very low/low. One study[51] had only 10 days follow-up and one[52] used the duration of hospital stay (median 12 days) and were therefore excluded from the meta-analysis.

Individual study characteristics and results

Main characteristics of the individual studies are shown in *Table 1*, and additional details are presented in *Table S2*. Except for one multi-centre trial[20], all studies were conducted at a single centre. Thirteen studies[18–24,27,44–48] compared antiseptic with saline wound irrigation. One of these studies[20] was three-armed, comparing antiseptic, saline, and no wound irrigation. Most studies[18,19,21,23,24,46–48] (8) evaluated PVP-I solutions in various concentrations and volumes (*Table 1*). Other antiseptic irrigation solutions were polyhexanide (PHX) 0.04%[20,22], electrolyzed strongly acidic aqueous solution (ESAAS)[44], topical ionized solution (IS)[45], and chlorhexidine gluconate (CHG) 0.05%[27]. Five studies compared PVP-I irrigation with no wound irrigation[43,49] and saline with no wound irrigation[25,26,28]. Seven of the studies[23–25,28,43,45,46] included patients undergoing open appendectomy, and the remaining trials included various types of general surgery. Of the studies, 8 included emergency surgery, 9 included elective surgery, and 2 did not specify the urgency of included procedures (*Table 1*). The studies by Takeda *et al.*[19], Maemoto *et al.*[21], and Strobel *et al.*[22] included open and 80, 70, and 35% of laparoscopic-assisted procedures, respectively.

Most trials included procedures with intraoperative LOC II–III[22,24,44,45,49] or II–IV[19,20,23,25,28]. Five trials[18,21,26,43,47] included exclusively LOC II. Only three trials focused on LOC III[27], III–IV[48], or IV[46] (*Table 1*).

As shown in *Table S2*, the most common primary outcome was SSI according to the CDC classification[18–22,25,27,44–47], followed by the South Hampton Grading (SSI > grade 2)[23,24,26,43,49]. Follow-up times were adequate (30 days) in the included studies. The type of peri-operative prophylactic intravenous antibiotics varied substantially among the included studies (*Table S2*). Furthermore, nine studies[18,23–26,28,43,44,46] routinely continued intravenous antibiotic therapy after surgery in all patients. The individual sample size and SSI rates of the included studies are presented in the corresponding forest plots. Of the 13 studies comparing antiseptic *versus* saline wound irrigation, 4 studies[22–24,27] found a significant reduction in SSI rates, 8 studies[18–21,44,45,47,48] found no significant difference between the two groups and 1 study[46] even found a lower SSI rate in the saline group compared with antiseptic wound irrigation. None of the studies[20,43,49] comparing antiseptic to no wound irrigation found a reduction in SSI rates in the intervention group. However, two of these studies[43,49] reported a reduction in the severity of infections by antiseptic wound irrigation. Three of the studies[25,26,28] comparing saline irrigation to no wound irrigation found a significant reduction in SSI rates.

Results of syntheses and certainty of evidence

Data of 6368 patients were included in the meta-analysis, the overall SSI rate being 14.7% (939). *Figure 2* shows the forest plot for the comparison of antiseptic *versus* saline wound irrigation (12 RCTs and 1 NRS). There was no significant effect in favour of antiseptic wound irrigation (RR 0.80, 95% c.i. 0.58 to 1.09; $P = 0.159$), and substantial heterogeneity was observed. This analysis contains one RCT[46] with high risk of bias and one NRS[27] with a serious risk of bias. In the sensitivity analysis excluding these two studies, the results were confirmed (see *Fig. S1* and *Table S3*). Certainty of evidence was very low for both analyses (see *Table 2*).

In addition, the same analysis was performed excluding the laparoscopic cases from the three studies that included both open and laparoscopic surgery (*Fig. S2*). In the sensitivity analysis of this comparison (11 RCTs), a significant effect in favour of antiseptic wound irrigation was observed (RR 0.75, 95% c.i. 0.64 to 0.87; $P < 0.001$) (*Fig. 3*) and certainty of evidence was moderate (*Table 2*).

The forest plot for the comparison of antiseptic *versus* no wound irrigation (2 RCTs and 1 NRS) is presented in *Fig. S3*. No significant effect in favour of antiseptic wound irrigation was observed (RR 0.74, 95% c.i. 0.49 to 1.11; $P = 0.147$). No heterogeneity was observed ($I^2 = 0\%$, $\tau^2 = 0$, P(Q-test) = 0.70). Certainty of evidence was low (*Table 2*). Due to the low number of studies, no subgroup analysis regarding antiseptic agents was possible. This analysis contained one non-randomized observational study[49]. Sensitivity analysis excluding this study was not possible as only two studies were left for the meta-analysis.

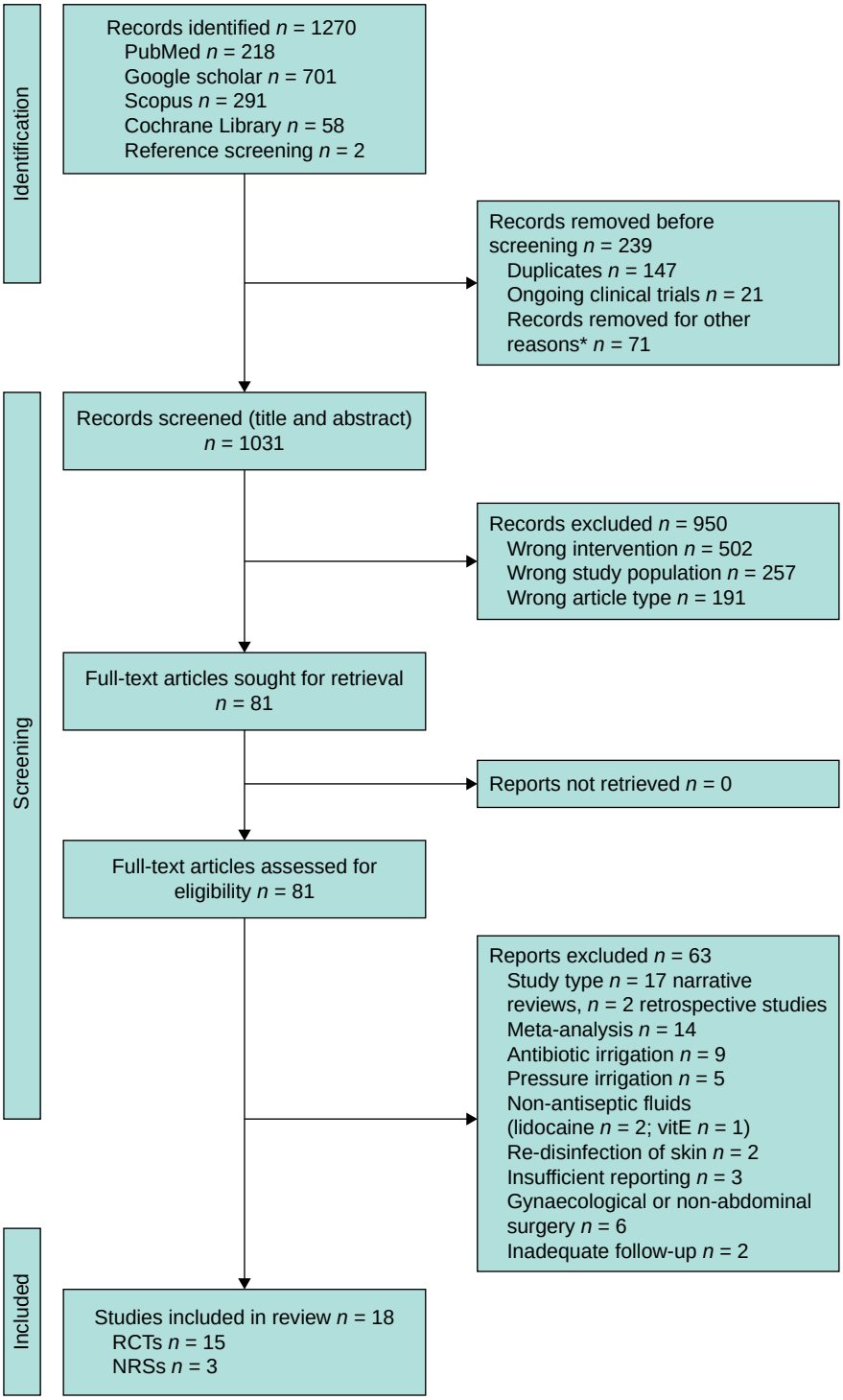


Fig. 1 PRISMA (2020) flow diagram. Identification of studies via databases and registers

RCT, randomized clinical trial; NRS, non-randomized study; vitE, vitamin E. *Language, animal studies, or publication date before 2000.

The forest plot for studies comparing saline *versus* no wound irrigation is presented in *Fig. S4*. A significant effect in favour of saline was observed (RR 0.48, 95% c.i. 0.30 to 0.77; $P = 0.002$) in the possible presence of heterogeneity ($I^2 = 63\%$, $\tau^2 = 0.14$, P(Q-test) = 0.05). This analysis contains one NRS[25] with serious risk of bias. In the sensitivity analysis excluding this trial, the effect was confirmed (*Table S3 and Fig. S5*). Certainty of evidence was low for both analyses (*Table 2*).

Lastly, *Fig. 4* shows the forest plot for studies comparing any wound irrigation (saline or antiseptic) *versus* no wound irrigation. One of the six studies included in this synthesis was three-armed, including one comparator arm with no irrigation. A significant effect in favour of any wound irrigation was observed (RR 0.52, 95% c.i. 0.37 to 0.74; $P < 0.001$) in the presence of heterogeneity ($I^2 = 45\%$, $\tau^2 = 0.08$, P(Q-test) = 0.11). The sensitivity analysis excluding NRSs and RCTs with high risk of

Table 1 Characteristics of individual studies (alphabetical order)

Author	Date	Study design	Urgency	Surgical Access	Included procedures	LOC	Agent for wound irrigation (concentration)	Control
Ali *et al.*[48]	2023	RCT	Emergency	Open	Exploratory laparotomy or appendectomy	III–IV	PVP-I (10%)	Saline
Cervantes-Sanchez *et al.*[28]	2000	RCT	Emergency	Open	Appendectomy	II–IV	Saline	No irrigation
Goztok *et al.*[27]	2018	NRS	Elective	Open	Closure of temporary loop ileostomy	II–III	CHG (0.05%)	Saline
Iqbal *et al.*[43]	2015	RCT	Emergency	Open	Appendectomy for non-perforated appendicitis	II	PVP-I (1%)	No irrigation
Kashtel *et al.*[46]	2020	RCT	Emergency	Open	Appendectomy for perforated appendicitis	III–IV	PVP-I (NS)	Saline
Khan *et al.*[26]	2019	RCT	NS	Open	Mixed abdominal surgery	II	Saline	No irrigation
Maemoto *et al.*[21]	2023	RCT	Elective	Mixed†	Gastro-intestinal surgery	II	PVP-I (10%)	Saline
Majeed and Atya[25]	2020	NRS	Emergency	Open	Appendectomy	II–IV	Saline	No irrigation
Mueller *et al.*[20]	2024	RCT*	Elective	Open	Gastro-intestinal and HPB surgery	II–IV	Arm 1: PHX (0.04%) Arm 2: Saline	Arm 3: No irrigation
Owais *et al.*[24]	2019	RCT	Emergency	Open	Appendectomy	II–III	PVP-I (1%)	Saline
Ratnakar *et al.*[23]	2023	RCT	Emergency	Open	Appendectomy	II–IV	PVP-I (1%)	Saline
Sallam *et al.*[51]	2018	NRS	NS	Open	Gastro-intestinal surgery	II–III	PVP-I (10%)	No irrigation
Strobel *et al.*[22]	2020	RCT	Elective	Mixed†	Gastro-intestinal and HPB surgery	II–III	PHX (0.04%)	Saline
Takeda *et al.*[19]	2024	RCT	Elective	Mixed†	Gastro-intestinal surgery	II–IV	PVP-I (10%)	Saline
Takesue *et al.*[44]	2011	RCT	Elective	Open	Colorectal surgery	II–III	ESAAS	Saline
Tijerina *et al.*[45]	2010	RCT	Emergency	Open	Appendectomy for non-perforated appendicitis	II–III	Ionized solution	Saline
Vinay *et al.*[47]	2019	RCT	Elective	Open	Gastro-intestinal surgery	II	PVP-I (5%)	Saline
Zhao *et al.*[18]	2022	RCT	Elective	Open	Gastrectomy	II	PVP-I (1%)	Saline

LOC, level of contamination; RCT, randomized clinical trial; PVP-I, povidone-iodine; NRS, non-randomized study; CHG, chlorhexidine gluconate; NS, not specified; PHX, polyhexanide; HPB, hepato-pancreatico-biliary; ESAAS, electrolyzed strongly acidic solution. *Multicentre. †Mixed inclusion of laparoscopic and open procedures.

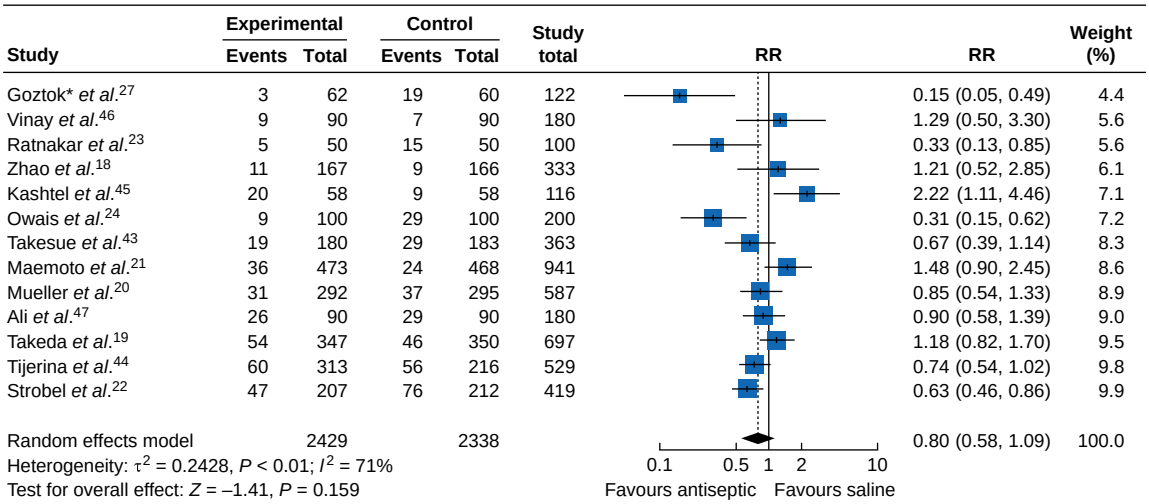


Fig. 2 Forest plot of 12 RCTs and 1 NRS* comparing antiseptic with saline wound irrigation (order by weight)

RR, relative risk; NRS, non-randomized study.

bias confirmed this result (*Table S3 and Fig. S6*). Certainty of evidence was moderate for both analyses (*Table 2*).

Results of subgroup analyses

The subgroup analysis by type of antiseptic agent restricted the data to studies using PHX or PVP-I, as the other agents (ESAAS; IS, and CHG) were only used in single studies (*Fig. S7*). Neither agent showed a significant benefit in preventing SSI compared with saline. The variation in the results of the PHX studies was smaller than in the PVP-I studies.

To investigate the effect of wound irrigation in procedures with different LOC, a subgroup analysis for patients undergoing LOC I–II or LOC III–IV procedures was conducted, as the latter are known to have a higher SSI risk. However, only ten of the trials reported the SSI rates in relation to LOC or

Table 2 GRADE evaluation of studies comparing intraoperative wound irrigation with antiseptics compared with saline or no irrigation for SSI prevention in general abdominal surgery

	No. of participants (studies)	Certainty of the evidence (GRADE)	Relative risk (95% c.i.)	Anticipated absolute effects	
				Risk with saline or no irrigation	Risk difference with antiseptic or saline irrigation
Antiseptic *versus* saline	4767 (12 RCTs + 1 NRS)	⊕◯◯◯ Very low*,†,‡	0.80 (0.58, 1.09)	165 per 1000	33 fewer per 1000 (69 fewer to 15 more)
Antiseptic *versus* saline (SA)§	4529 (11 RCTs)	⊕◯◯◯ Very low*,†,‡	0.80 (0.62, 1.03)	161 per 1000	32 fewer per 1000 (61 fewer to 5 more)
Antiseptic *versus* saline (open only)	3378 (12 RCTs + 1 NRS)	⊕◯◯◯ Very low*,†,‡	0.75 (0.56, 1.01)	192 per 1000	48 fewer per 1000 (84 fewer to 2 more)
Antiseptic *versus* saline (open only) (SA)§	3140 (11 RCTs)	⊕⊕⊕◯ Moderate*	0.75 (0.64, 0.87)	190 per 1000	48 fewer per 1000 (69 to 25 fewer)
Antiseptic *versus* no irrigation	660 (2 RCTs + 1 NRS)	⊕⊕◯◯ Low*,‡	0.74 (0.49, 1.11)	170 per 1000	44 fewer per 1000 (87 fewer to 19 more)
Saline *versus* no irrigation	1590 (3 RCTs + 1 NRS)	⊕⊕◯◯ Low*,†	0.48 (0.30, 0.77)	182 per 1000	95 fewer per 1000 (128 to 42 fewer)
Saline *versus* no irrigation (SA)§	1390 (3 RCTs)	⊕⊕◯◯ Low*,†	0.54 (0.29, 0.99)	144 per 1000	66 fewer per 1000 (102 to 1 fewer)
Any irrigation *versus* no irrigation	2148 (4 RCTs¶ + 2 NRSs)	⊕⊕⊕◯ Moderate*	0.52 (0.37, 0.74)	186 per 1000	89 fewer per 1000 (117 to 48 fewer)
Any irrigation *versus* no irrigation (SA)§	1848 (4 RCTs¶)	⊕⊕⊕◯ Moderate*	0.53 (0.35, 0.82)	149 per 1000	70 fewer per 1000 (97 to 27 fewer)

Sensitivity analyses were performed for each comparison, excluding the NRSs and RCTs with high risk of bias according to the RoB 2 tool. c.i.: confidence interval; RCT, randomized clinical trial; NRS, non-randomized observational study; RR, relative risk; SA, sensitivity analysis. Reasons for downgrading: *risk of bias evaluation result (RoB 2); †inconsistency ($I^2 > 50\%$); ‡imprecision (c.i. including 1); §indirectness. ¶comparison contains one three-armed RCT.

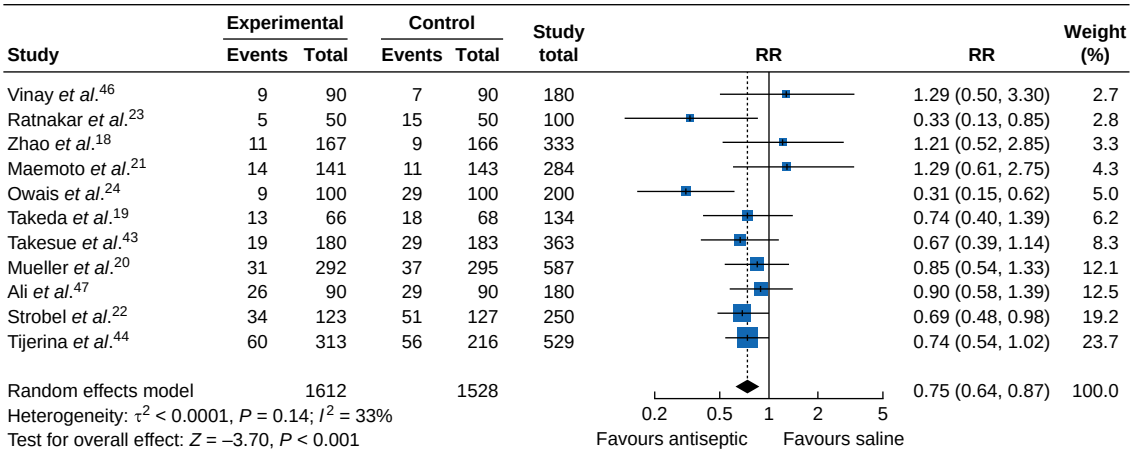


Fig. 3 Forest plot of 11 RCTs (sensitivity analysis) comparing antiseptic with saline wound irrigation in open procedures (order by weight), excluding laparoscopic cases

RR, relative risk; RCT, randomized clinical trial.

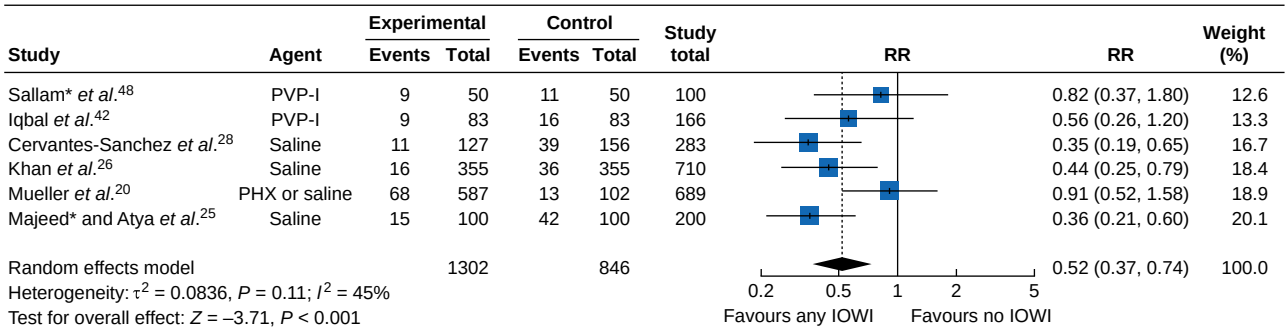


Fig. 4 Forest plot of 4 RCTs and 2 NRSs* comparing any *versus* no wound irrigation (order by weight)

RR, relative risk; PVP-I, povidone-iodine; PHX, polyhexanide; IOWI, intraoperative wound irrigation; RCT, randomized clinical trial; NRS, non-randomized study.

Table 3 Results of subgroup analysis according to level of intraoperative contamination (LOC) I–II *versus* III–IV

	LOC I–II (clean/ clean-contaminated)	LOC III-IV (contaminated/dirty)	P*	Forest plot
Included trials	Strobel *et al.*[22] Mueller *et al.*[20] Zhao *et al.*[18] Maemoto *et al.*[21] Takeda *et al.*[19]	Strobel *et al.*[22] Mueller *et al.*[20] Kashtel *et al.*[46] Ali *et al.*[48] Goztok *et al.*[27] Takeda *et al.*[19]		
Antiseptic *versus* saline wound irrigation RR (95% c.i.)	0.99 (0.62, 1.59)	0.87 (0.52, 1.48)	0.724	*Fig. S8*
Included trials	Mueller *et al.*[20](AN + SN) Iqbal *et al.*[43](AN) Khan *et al.*[26] (SN)	Mueller *et al.*[20](AN + SN), Cervantes-Sanchez *et al.*[28](SN) Majeed and Atya[25](SN)		
Any *versus* no wound irrigation RR (95% c.i.)	0.62 (0.42, 0.92)	0.37 (0.24, 0.56)	0.071	*Fig. S9*

LOC, level of contamination; RR, relative risk; c.i., confidence interval; AN, antiseptic *versus* no irrigation; SN, saline *versus* no irrigation. *Random effect models with Mantel–Haenszel weights.

the authors delivered additional information after being contacted; therefore, only limited data were available for these comparisons. Only five trials comparing antiseptic *versus* saline wound irrigation reported SSI rates for LOC I–II and III–IV separately. As shown in *Table 3* and the forest plot in *Fig. S8*, the effects in favour of antiseptic wound irrigation compared with saline were non-significant in both LOC groups, and there was no significant difference between the two subgroups ($P = 0.724$). 'Antiseptic *versus* no wound irrigation' and 'saline *versus* no wound irrigation' were combined to 'any wound irrigation *versus* no wound irrigation' to obtain enough data for a meta-analysis. As shown in *Table 3* and the forest plot in *Fig. S9*, the comparison with the strongest effect in favour of any wound irrigation was observed in the subgroup LOC III–IV (RR 0.37, 95% c.i. 0.24 to 0.56). A smaller effect was observed in the subgroup LOC I–II (RR 0.62, 0.42 to 0.92). The effect of any *versus* no wound irrigation did not differ significantly between the two subgroups ($P = 0.071$).

Risk of bias in studies

Risk of bias assessment of the individual studies revealed that most studies had some concerns regarding bias, and one trial[46] was at high risk of bias. Only one study[20] was at low risk of bias. All the observational studies were at serious risk of bias. The detailed results in the five domains from the RoB 2 tool for RCTs are presented in *Table S4* and ROBINS-I tool for NRSs in *Table S5*.

Publication and reporting bias

The funnel plot in *Fig. S10* includes the comparisons 'antiseptic *versus* saline wound irrigation (**a**), 'antiseptic *versus* no wound irrigation' (**b**), and 'saline *versus* no wound irrigation' (**c**). It depicts the RRs for SSI *versus* its standard error on a study/comparison basis. As no asymmetry was found (P(Egger) = 0.674) for antiseptic *versus* saline wound irrigation and visual inspection for the other comparisons, publication bias was assumed to be unlikely. Reporting bias must be considered, as only five of the included studies[18–22] have been registered in international trial registries.

Discussion

The current results suggest that wound irrigation with antiseptics such as PHX or aqueous PVP-I reduces SSI rates after laparotomy procedures. In addition, a significant favourable effect for any intraoperative irrigation compared with no irrigation was observed. However, the results must be interpreted with caution as heterogeneity between the trials is high. The recent high-quality trials by Takeda *et al.*[19], Maemoto *et al.*[21], Zhao *et al.*[18], and Mueller *et al.*[20] show that, in elective procedures with LOC II, wound irrigation with antiseptics did not reduce SSI rates. The smaller trial by Strobel *et al.*[22] is the only one that demonstrated a significant benefit of wound irrigation with PHX in high-risk patients and patients undergoing colorectal procedures. It must be considered that the trials by Takeda *et al.*, Maemoto *et al.*, and Strobel *et al.* included 80, 70 and 35% of laparoscopic-assisted procedures, respectively. Laparoscopic procedures are known to have a lower SSI risk than laparotomy. Although 'laparoscopic procedures' was one of the exclusion criteria for the present study, these important trials were still included and additional sensitivity analysis was performed. In the sensitivity analysis of open procedures only, the effect of antiseptic wound irrigation compared with saline is significant. This means, that the overall result is sensitive to the type of surgical access. This finding confirms the assumption that antiseptic wound irrigation is of no observable benefit in laparoscopic procedures, as the SSI risk is generally much lower than in open procedures.

Moreover, several individual studies showed a favourable effect for antiseptic wound irrigation with PHX[22], diluted PVP-I solutions[46,48], and CHG[27] in procedures with intraoperative LOC III or IV. Unfortunately, only limited data for the planned subgroup analysis were available, as most of the studies do not report SSI incidence in different LOC groups. The results of the exploratory subgroup analysis show a significant effect in favour of any wound irrigation (antiseptic or saline) *versus* no wound irrigation in all LOC subgroups. This finding is in line with the results of the authors' previous work, which includes studies from 1979 to 2014[17]. However, when comparing antiseptic with saline wound irrigation, the effects are non-significant in either of the LOC subgroups.

Compared with the recently published network meta-analysis by Groenen *et al.*[31], which included all types of surgery (neurosurgical, gynaecological, plastic, abdominal, and orthopaedic surgery), there are some interesting differences. In this meta-analysis, there was a significant reduction in SSI when comparing antiseptic with no irrigation (RR 0.60; 95% c.i. 0.44 to 0.81) or with saline irrigation (RR 0.72; 0.57 to 0.93)—whereas saline *versus* no irrigation showed no significant association (RR 0.83; 0.63 to 1.09).

This is partially explained in the editorial comment to this publication, stating that by mixing different surgical specialties the amount of heterogeneity makes it impossible to determine the true impact of wound irrigation[53]. The review included data of 17,188 patients with an overall SSI rate of 7.7%—half that observed in the overall data for abdominal surgery patients only in the present study (14.7%). This reflects the inclusion of clean procedures with a low SSI risk, common in plastic and neurosurgical surgery. Moreover, the network analysis included antibiotic irrigation solutions for wound irrigation, even though they have been abandoned by several guidelines and institutions due to the potential increase in antibiotic resistance[31]. As a consequence, the authors believe that trials using antibiotic irrigation solutions should no longer be considered for guidelines, reviews and/or meta-analyses.

Limitations of the underlying data include that most of the trials have some concerns regarding risk of bias, most of them arising from insufficient reporting. Furthermore, the studies are heterogenous regarding postoperative continuation of intravenous antibiotics, use of plastic wound drapes, and antibiotic-coated sutures, which all potentially impact the postoperative SSI rates. Eight of the studies included patients undergoing open appendectomy only. Patients undergoing this procedure are typically younger, and nine studies included paediatric patients who differ in SSI risk from adult or elderly patients. Furthermore, laparotomy is hardly representative for all gastrointestinal procedures and is rarely performed any more in high-income countries where most appendectomies are laparoscopic. The type of country (low-, middle-, high-income countries) in which the individual studies were conducted, and where different surgical standards might be employed, resulting in different SSI risks was not analysed. In addition, two different definitions of SSI were used among the included studies. First, most of the studies used the CDC criteria, which differentiate between SSI grades I–III, of which grades I–II represent incisional SSIs. Wound irrigation is most certainly a measure with effect on SSIs I–II and not on SSI III (organ/intra-abdominal infection). However, not all trials report the rates of different depths of SSI separately, which might confound the results. Second, most of the remaining studies used the South Hampton grading system for incisional wound assessment and defined SSI as a score > 2. However, due to insufficient reporting and the different outcome definitions, it was impossible to take these into account in the analysis. In addition, two studies had inadequate follow-up times: in the study by Alabdulla *et al.*, follow-up was only 10 days, and in the study by Neeff *et al.*, follow-up was restricted to the hospital stay (median 12 days), although it has been shown that up to 60% of SSIs occur after hospital discharge[54]. Therefore, both of these studies were excluded from the analysis. One study was three-armed (antiseptic *versus* saline *versus* no irrigation). For analyses of any irrigation *versus* no irrigation, the antiseptic and saline arms were combined according to recommendations of the Cochrane Handbook. Furthermore, the studies were also heterogenous in terms of the used irrigation agents, irrigation technique, concentrations, and volumes. PVP-I was used in different concentrations ranging from 0.1–10%, as no recommendations for the best dosing and volume exist. Lastly, there were three single studies on other antiseptic solutions: ESAAS and IS were experimental solutions and CHG was a non-randomized observational study. Including those studies into the analysis might have confounded the results, which is why a subgroup analysis comparing the commonly used antiseptics (PHX and PVP-I) only was conducted. However, only two trials using PHX were available and none of the antiseptic agents showed superiority.

Limitations of the search strategy are that it was not developed with a librarian, and did not include MeSH terms. However, pilot searches were performed, and the search strategy and results were compared with other recently published systematic reviews[31,32] on intraoperative wound irrigation to ensure that no eligible evidence was missed by the strategy.

Another limitation of the review process is that publications in languages other than English or German were not included. Furthermore, records published before 2000 were excluded—however, this threshold was chosen without a certain method of determining at what date trials could be considered outdated evidence. Several reviews of trials conducted from 1970 to 2000 already exist but do not reflect the choice of antiseptic agents and standards of surgical practice comparable to today.

This study has several implications for practice, policy, and future research. Regarding antiseptic wound irrigation with PVP-I, the updated CDC guideline from 2017 contains a grade 2 (weak) recommendation of wound irrigation with aqueous PVP-I solutions[4]. The WHO guideline contains a suggestion to consider wound irrigation with aqueous PVP-I solutions before closure of wounds with LOC I and II[3]. However, the underlying studies for these recommendations are heterogenous in surgical specialty, LOC, and study quality, and must therefore be interpreted with caution. Moreover, the guidelines do not specify the recommended concentration or volume of aqueous PVP-I solutions for wound irrigation. The recent large trials by Takeda *et al.*[19], Maemoto *et al.*[21], and Zhao *et al.*[18] show no benefit of PVP-I over saline in clean-contaminated abdominal procedures. Whereas Maemoto *et al.* used 40 ml 10% PVP-I solution for wound irrigation, Takeda *et al.* used 10% PVP-I solution in different volumes according to wound size and Zhao *et al.* used 500 ml 1% PVP-I solution. In addition, Maeomoto *et al.* and Takeda *et al.* included a large number of laparoscopic procedures (70 and 80%, respectively). Furthermore, in the trial by Takeda *et al.*, all patients received syringe pressure irrigation with saline before antiseptic irrigation, plastic wound retractors, and antibiotic sutures for wound closure. This underlines the importance of standardization of irrigation agents, concentrations, volumes, and other additional prevention measures to make trials comparable, and implies that the current recommendations of the CDC and WHO should be questioned, considering the allergic and endocrine potential of PVP-I.

Concerning antiseptic wound irrigation with PHX, this is a relatively new substance. In Germany, it is approved for wound irrigation and is frequently used in orthopaedic and abdominal surgery. In the USA, however, it is not FDA-approved. This explains why all three trials investigating PHX as the agent for wound irrigation are from Germany. The first pilot trial by Neeff *et al.*[52] in 2016 found no benefit of PHX over saline irrigation in 197 elective colorectal procedures, including laparoscopic procedures with mini-laparotomy. However, this study was not included in this meta-analysis as the follow-up time was limited to the duration of hospital stay. In contrast, Strobel *et al.*[22] in 2020 found a significant reduction in SSI, also including laparoscopic procedures with mini-laparotomy. This might be explained by the fact that the population of Strobel contained one-third of high-risk patients under immunosuppressive therapy for inflammatory bowel disease. The recently completed multicentre intraoperative wound irrigation for the prevention of surgical site infection after laparotomy (IOWISI) trial[20] demonstrated no benefit of PHX irrigation in clean-contaminated

laparotomy procedures. However, only 48 patients with LOC III and 2 patients with LOC IV were included across all centres in this trial. Due to these low patient numbers, no statement on the efficacy of PHX in procedures with LOC III and IV can be made, and further research is needed to address this question.

Regarding wound irrigation with other antiseptics, ESAAS and IS are not substances that are routinely used or available. ESAAS has even been shown to impair wound healing[44]. CHG, on the other hand, seems to be a promising new agent for antiseptic wound irrigation, but so far only limited evidence is available regarding its use in abdominal surgery[55]. There is one non-randomized observational study[27] of patients undergoing loop-ileostomy reversal, which was included in the present review. Other than that, there is only one pilot study[56] of patients undergoing emergency laparotomy, which was not included in the present review as it was a retrospective observational study and the outcome was primary wound closure rather than incidence of SSI. However, this study found that primary wound closure was achieved in 65 of 66 patients (98.5%) with the use of 0.05% CHG irrigation solution before closure. During follow-up, 18 of 66 patients (27.3%) required removal of staples and conversion to wet-to-dry-packaging, in most cases due to fat necrosis[56]. Another recent trial[57] showed that wound irrigation with CHG decreased the SSI rate and time to healing in pilonidal disease surgery. Overall, PHX and CHG seem to be the most promising new antiseptic agents for wound irrigation, as allergies or side effects are rare whereas antiseptic potency is high.

With regard to saline wound irrigation, the current results suggest a significant benefit of saline compared with no wound irrigation. However, three of the five trials in the analysis included patients undergoing open appendectomy. The trials were conducted in Iraq, Pakistan, and Mexico. The results of the German IOWISI trial are the only ones that showed no significant effect of saline over no wound irrigation in clean-contaminated procedures. Even though the individual setting and country of the trials was not analysed, it is conceivable that the beneficial effect of saline wound irrigation might be limited to low-resource settings or high-risk patients. A recent systematic review and meta-analysis[58] of five RCTs investigating saline wound irrigation for the prevention of SSI after caesarean section included data from 4025 patients and found no significant reduction in SSI. Another working group performed a similar analysis in 2020[14], including four RCTs with 1194 patients who underwent abdominal surgery, and found that the RR for SSI was lower after saline wound irrigation compared with no wound irrigation, but the effect was not significant (RR 0.73, 95% c.i. 0.37 to 1.43). However, two of the four RCTs were gynaecological surgery, which is why they were not included in the present review. These inconsistent findings underline the importance of separating results from different surgical subspecialties.

Another aspect of saline lavage is pressurized or pulsed lavage, which was not investigated in the present review as it is considered another type of intervention. A systematic review and meta-analysis by Bath *et al.*[59] included 11 trials in orthopaedic and general surgery, and reported a significant reduction in SSI through the use of pulsed lavage. In abdominal surgery, only two trials exist[60–62], which both show a reduction in SSI rates using pulsed lavage compared with no wound irrigation. This includes the trial by Cervantes-Sanchez *et al.*[28], which was included in the current analysis. This outlines that it is debatable whether irrigation with a simple bulb-syringe should be considered as pulsed or pressurized lavage.

Prophylactic intraoperative wound irrigation with antiseptics or saline likely reduces SSI rates after open abdominal procedures compared with no irrigation, especially if the SSI risk is high (procedures with LOC III–IV). For antiseptic compared with saline irrigation, the evidence is very uncertain about the effect. However, when laparoscopic cases and high-risk-of-bias studies were removed from the comparison, antiseptic wound irrigation likely reduced the SSI rates compared with saline irrigation.

The questions regarding which antiseptic irrigation agent is superior, as well as which types of procedures benefit most from this practice, remain unclear. To obtain answers, more high-quality trials are needed, and standardization is required regarding surgical access and level of intraoperative wound contamination (LOC I–IV), as well as the choice and concentration of irrigation agent and irrigation techniques. In addition, future trials should report SSI rates by depth of infection (grade I–III) according to the CDC classification,

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Author contributions

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Disclosure

The authors declare no conflict of interest.

Supplementary material

Supplementary material is available at *BJS Open* online.

Data availability

All relevant data extracted from included studies can be accessed in the supplemental material. Any other materials can be provided be the corresponding author on request.

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