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SYSTEMATIC REVIEW AND META-ANALYSIS

Intra-operative wound irrigation to reduce surgical site infections after abdominal surgery: a systematic review and meta-analysis

Tara C. Mueller · Martin Loos · Bernhard Haller · André L. Mihaljevic · Ulrich Nitsche · Dirk Wilhelm · Helmut Friess · Jörg Kleeff · Franz G. Bader

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Abstract
Purpose Surgical site infection (SSI) remains to be one of the most frequent infectious complications following abdominal surgery. Prophylactic intra-operative wound irrigation (IOWI) before skin closure has been proposed to reduce bacterial wound contamination and the risk of SSI. However, current recommendations on its use are conflicting especially concerning antibiotic and antiseptic solutions because of their potential tissue toxicity and enhancement of bacterial drug resistances.
Methods To analyze the existing evidence for the effect of IOWI with topical antibiotics, povidone-iodine (PVP-I) solutions or saline on the incidence of SSI following open abdominal surgery, a systematic review and meta-analysis of randomized controlled trials (RCTs) was carried out according to the recommendations of the Cochrane Collaboration.
Results Forty-one RCTs reporting primary data of over 9000 patients were analyzed. Meta-analysis on the effect of IOWI with any solution compared to no irrigation revealed a significant benefit in the reduction of SSI rates (OR=0.54, 95 % confidence Interval (CI) [0.42; 0.69], $p<0.0001$). Subgroup analyses showed that this effect was strongest in colorectal surgery and that IOWI with antibiotic solutions had a stronger effect than irrigation with PVP-I or saline. However, all of the included trials were at considerable risk of bias according to the quality assessment.
Conclusion These results suggest that IOWI before skin closure represents a pragmatic and economical approach to reduce postoperative SSI after abdominal surgery and that antibiotic solutions seem to be more effective than PVP-I solutions or simple saline, and it might be worth to re-evaluate their use for specific indications.

Keywords Surgical site infection · Abdominal surgery · Wound irrigation · Antiseptic solutions · Topical antibiotics

Introduction

Postoperative surgical site infection (SSI) represents as one of the most frequent complications following abdominal surgery. In the USA, an estimated 300,000 to 500,000 cases of SSI occur annually [1, 2]. Similar figures are reported from Germany [3, 4], the UK [5], and France [6]. The incidence of SSI varies substantially, depending on the type and site of surgery [2]. According to recent high-level randomized controlled trials (RCTs) with standardized SSI definitions, rates range from around 15 % (BaFo trial [7]; PROUD trial [8]) up to 25 % (ROSSINI trial) [9] following laparotomy for visceral surgery. SSIs contribute substantially to postoperative morbidity and mortality and have been shown to significantly increase the mean length of hospital stay and treatment costs [1, 6, 10]. Therefore, measures to prevent SSI are urgently needed.

Hypothetically, intra-operative wound irrigation (IOWI) with saline, povidone-iodine (PVP-I) solutions, or topical antibiotics represents a simple and economically reasonable measure to reduce SSI rates. Currently, clinical practice is largely variable and depends on individual preferences and hospital doctrines. Surveys have shown that epifascial IOWI with PVP-I solution is widely used by abdominal surgeons

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T. C. Mueller (✉) · M. Loos · A. L. Mihaljevic · U. Nitsche · D. Wilhelm · H. Friess · J. Kleeff · F. G. Bader
Department of Surgery, Klinikum rechts der Isar, Technische Universität München, Ismaninger Str. 22, 81675 Munich, Germany
e-mail: tara.mueller@tum.de

B. Haller
Institute for Medical Statistics and Epidemiology, Technische Universität München, Munich, Germany

[11–13]. Wound irrigation with simple saline or with saline containing antibiotics is another common clinical practice [12–14]. It seems a logical measure to reduce bacterial wound contamination and clean the wound from blood clots and necrotic tissue. However, the current clinical guideline published by the UK's National Institute for Health and Care Excellence (NICE) advises against the routine use of IOWI with topical antibiotics or antiseptics due to potential adverse effects, tissue toxicity of antiseptics, and increased development of bacterial resistances [5, 15]. Yet, the level of evidence for these recommendations is poor. Clinical trials investigating the efficacy of IOWI have been conducted mainly in the 1970–1990s, and their results are inconclusive; heterogeneous patient inclusion and outcome criteria were used. A few systematic reviews and meta-analyses on the use of PVP-I or antibiotic solutions have been conducted [12, 16–19]; however, none of them resulted in a definite conclusion, although they all observed a positive trend in the reduction of SSI rates. To determine the current state of knowledge, we conducted a systematic review, including all available clinical trials evaluating IOWI with either saline, PVP-I, or antibiotic solutions for the prevention of SSI following laparotomy.

Methods

Information sources and search strategy

Pubmed/MEDLINE, EMBASE, and the Cochrane Central Register of Controlled Trials (CENTRAL) were searched in May 2013. The following search terms were used in various combinations: prevention of surgical site infection, abdominal surgery, surgical wound infection/prevention and control [MeSH Terms], wound irrigation, wound lavage, incisional surgical site infection, intra operative irrigation, intra operative lavage, antibiotic irrigation, antibiotic irrigation solutions, iodine irrigation, povidone iodine irrigation, saline irrigation, and topical anti infective agents [MeSH Terms]. The abstract and title search was limited to clinical trials published in English or German between January 1, 1970 and May 1, 2013. In addition, all articles within the reference list of retrieved studies and reviews were hand-searched. The search was performed by two independent reviewers and followed the published protocol corresponding to the PRISMA statement [20] and the Cochrane Handbook of systematic reviews of interventions [21].

Eligibility criteria and study selection

Prospective RCTs investigating the primary outcome of postoperative SSI after IOWI of the surgical incision after closure of the fascia or peritoneum and before skin closure were eligible for inclusion. Trials with primary endpoints of infectious complications unrelated to the incision were excluded (e.g., implant infections). Eligible irrigation solutions were saline, PVP-I, or topical antibiotics in different forms and concentrations (dry powder sprays or wound powder were also acceptable), irrespective of the closure and irrigation technique. Acceptable comparators were "no irrigation" or irrigation with saline. All types of open abdominal surgeries were eligible, including visceral, gynecological, urological, or vascular procedures irrespective of the urgency of operation (elective or emergency). All trials reporting clinical SSI were included irrespective of the SSI definition used. However, purely bacteriological studies were not included [22, 23]. Trials using intra-abdominal/-cavity irrigation as well as trials on skin redisinfection of the wound edges were excluded, since this was considered to be a different intervention. In addition, retrospective studies and studies that did not report primary data were excluded. Finally, trials in which only one of the compared treatment arms received systemic prophylactic antibiotics were excluded, as this would have caused substantial bias.

Data collection and evaluation of risk of bias

When retrieved abstracts seemed to meet the inclusion criteria, both reviewers read full-text articles and extracted data independently. Disagreements were resolved by reaching a consensus with the remaining authors. Data were extracted on type of study, publication date, field of surgery, methodology and number of participants, inclusion and exclusion criteria, type of intervention, and used irrigation agent. Furthermore, the definition of outcomes and the reported SSI rates in each group were extracted. Data on potential sources of heterogeneity, like the SSI definition used and the type of surgery, were also extracted. Methodological quality of individual clinical trials was assessed by examination of the allocation sequence, allocation concealment and double blinding using the Cochrane tool for assessing the risk of bias [21]. The risk of bias was graded as low, unclear, or high. In addition, the risk of publication bias was investigated by means of a funnel plot.

Synthesis of results

Analysis of the trials was performed for two groups of trials: (1) IOWI compared to no IOWI (group A) and (2) IOWI with PVP-I/antibiotics compared to IOWI with saline (group B). Furthermore, subgroup analyses were performed for colorectal vs. non-colorectal procedures and for each irrigation solution. Absolute numbers of patients and events are presented for each trial incorporated in the meta-analyses and the corresponding subgroups. Odds ratios with 95 % confidence intervals (CIs) were estimated for each trial from the numbers of events and patients treated. Due to the naturally expected heterogeneity in performance of surgical procedures between

different types of surgery, grade of contamination, and hence trials, random effect models with Mantel-Haenszel weights were used to estimate the average treatment effect and a corresponding 95 % CI. Forest plots are shown to illustrate treatment effects estimated for each trial and the estimated average treatment effect for all investigated subgroups. For each analysis, tau^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. Additionally, the results of a χ^2 test for heterogeneity are presented. A two-sided level of significance of less than 5.0 % was considered for all tests. The software Review Manager 5.2 (The Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen, 2012) was used for analyses and generation of illustrations.

Results

Trial selection

The process of selection of trials included in this review is summarized in Fig. 1. Forty-one RCTs, reporting primary data of 9142 patients, were found eligible for inclusion in this analysis. The trials were separated into group A (IOWI vs. no IOWI), which consisted of 35 trials (8472 patients), and group B (IOWI with antibiotics of antiseptics vs. saline), which comprised 6 trials (1062 patients). One additional trial (Sindelar et al. 1979) was included for a qualitative analysis in group B, since the number of patients undergoing abdominal surgery in this trial was substantial, but SSI rates were not separately reported from other included types of surgery such as head and neck and trauma surgery [24].

Study characteristics: methods, patients, intervention and controls, outcomes

Table 1 shows the basic characteristics of trials, including types of surgeries performed, number of included patients, and the type of treatment and control interventions. Four trials were three-armed (intervention groups 1 and 2 vs. control group) [26, 30, 32, 34]. Another six trials were three-armed, but one arm had to be excluded from the analysis because patients received parenteral antibiotics [36, 37, 41, 48, 49] or a non-valid irrigation solution according to our inclusion criteria [39]. The remaining 31 studies were two-armed. Inclusion and exclusion criteria as well as SSI definitions used in all included trials are presented in the supplement information (supplement 1). Table 2 shows the reported outcomes, length of follow-up, and SSI rates in intervention and control groups. Overall, the observed total SSI rates ranged from 3.0 [40] to 58.2 % [52]. The length of follow-up varied largely between

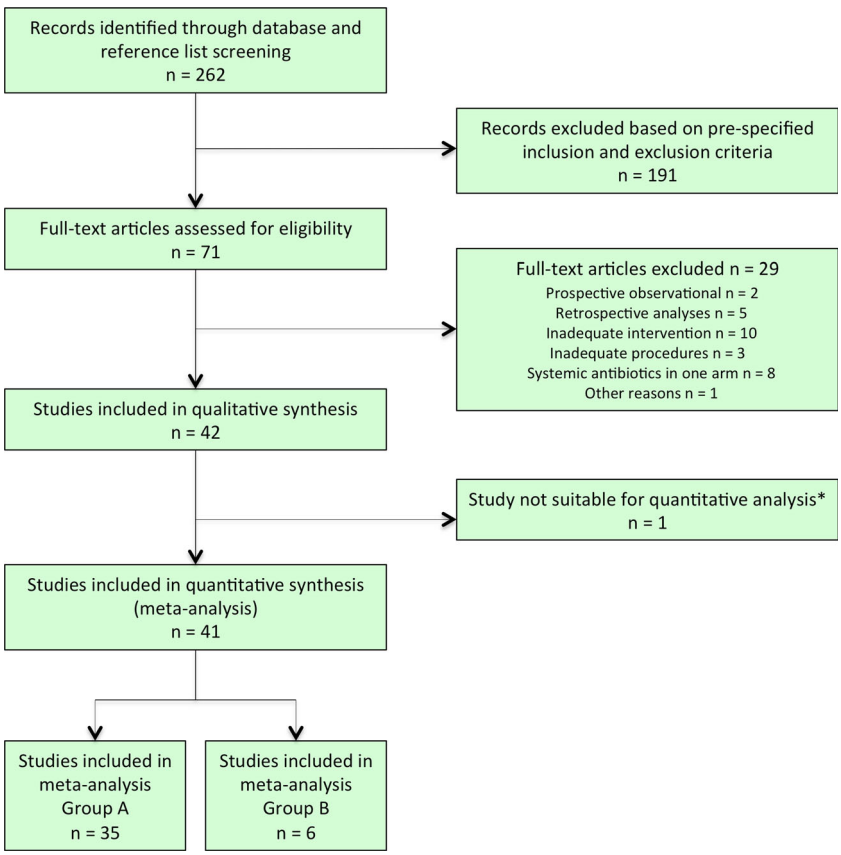


Fig. 1 Summary of the study selection process (PRISMA flow chart)

Table 1 Basic characteristics of all analyzed studies, including types of surgeries performed, number of included patients, and the type of study and control interventions

Author	Date	Type of procedures	No. of patients	Intervention group	Intervention group 2	Control group
Group A (no irrigation in the control group)						
Mountain [25]	1970	Appendectomy	150	Ampicillin powder	x	None
Longland [26]	1971	Appendectomy	300	Polymyxin B, bacitracin, and neomycin powder	Tetracyclin in saline solution	None
Madsen [27]	1971	Gastric surgery (truncal vagotomy and pyloroplasty)	64	Ampicillin powder	x	None
Andersen, Bendtsen [28]	1972	Appendectomy	490	Ampicillin powder	x	None
Andersen, Korner [29]	1972	Colonic resections or abdomino-perineal excisions of the rectum	240	Ampicillin powder	x	None
Mackie [30]	1973	Appendectomy	92	Ampicillin powder	Noxythiolin powder	None
Bates [31]	1974	Appendectomy	200	Ampicillin powder	x	None
Gilmore and Martin [32]	1974	Appendectomy	450	PVP-I dry powder spray	Polyantibiotic powder spray	None
Gilmore and Sanderson [33]	1975	Biliary, gastro-duodenal, peritonitis, intestinal, appendectomy miscellaneous	133	PVP-I dry powder spray	x	Spray with propellant only
Jensen [34]	1975	Contaminated and septic abdominal surgery (opening of hollow viscus)	267	Ampicillin powder	Ampicillin and cloxacillin powder	None
McCluskey [35]	1976	Biliary, gastroduodenal, appendectomy, colonic resection, miscellaneous	110	PVP-I solution	x	None
Galland [36]	1977	Cholecystectomy, gastrectomy, gastro-dudenal, intestinal, laparotomy, colorectal, appendectomy	78	PVP-I dry powder spray	x	None
Stokes [37]	1977	Urgent abdominal operations	117	PVP-I dry powder spray	x	None
Barr [38]	1978	Partial colectomy, subtotal gastrectomy	88	PVP-I solution	x	None
Tanphiphat [39]	1978	Appendectomy	246	Ampicillin powder	x	None
Andersen, Burcharth [40]	1980	Cholecystectomy (n=113), inguinal hernia (n=285)	398	Ampicillin powder	x	None
Foster [41]	1981	Appendectomy	236	PVP-I dry powder spray	x	None
Gray [42]	1981	Biliary, gastroduodenal, intestinal, and miscellaneous	153	PVP-I dry powder spray	x	None
Kothuis [43]	1981	Elective laparotomy (biliary, gastro-duodenal, vascular, colorectal, ileocolic)	220	PVP-I solution	x	None
Ostergaard [44]	1981	Colorectal surgery for carcinoma	240	Ampicillin powder	x	None
Walsh [45]	1981	Appendectomy, gastro-duodenal, biliary tract, colonic, miscellaneous	627	PVP-I dry powder spray	x	None
de Jong [46]	1982	Colon resection, appendectomy, gastric- and biliary surgery, hernia, various	582	PVP-I solution	x	None
Galland [47]	1983	Emergency appendectomy	200	PVP-I dry powder spray	x	None
Sherlock [48]	1984	Emergency appendectomy	75	PVP-I dry powder spray	x	None
Sood [49]	1984		55	Neosporin solution	x	None

Table 1 (continued)

Author	Date	Type of procedures	No. of patients	Intervention group	Intervention group 2	Control group
		Cholecystectomy or vagotomy with gastrojejunostomy				
Juul [50]	1985	Colorectal surgery	203	Ampicillin powder 1 g in saline	x	None
Lau [51]	1986	Appendectomy	315	PVP-I solution	x	None
Moesgaard and Nielsen [52]	1988	Abdomino-perineal excision of rectum	79	Metronidazol and genatmycin solution	x	None
Moesgaard, Nielsen and Hjortrup [53]	1989	Septic abdominal surgery (peritonitis at the time of operation)	177	Cefotaxime solution	x	None
Raahave [54]	1989	Colorectal surgery	170	Ampicillin powder	x	None
Seco [55]	1989	Emergency appendectomy	246	Ampicillin 1 g in saline	x	None
Cervantes-Sanchez [56]	2000	Appendectomy	283	Saline	x	None
Al-Ramahi [57]	2006	Abdominal gynecological procedures	206	Saline	x	None
Pradhan [58]	2009	Cesarean section (emergency)	70	Fusidic acid solution	x	None
Güngördük [59]	2012	Cesarean section	520	Saline	x	None
Group B (saline irrigation in the control group)						
Logan [60]	1973	Cholecystectomy	100	Ampicillin powder in saline	x	Saline irrigation
Ciccone [61]	1974	Major abdominal urological surgery	200	Kanamycin solution	x	Saline irrigation
Galle [62]	1980	Radical hysterectomy, abd. hysterectomy or cervicectomy	67	PVP-I solution	x	Saline irrigation
Lord [63]	1983	Biliary surgery, gastroduodenal surgery, colorectal surgery	200	Kanamycin and cephalothin in saline	x	Saline irrigation
Rogers [64]	1983	Hernias, cholecystectomy, laparotomy, biliary, colorectal, gastro-duodenal, intestinal, perforations	187	PVP-I solution	x	Saline irrigation
Mathelier [65]	1992	Cesarean section	308	Cefazolin in saline	x	Saline irrigation

Table 2 Outcomes, follow-up time, and SSI rates in different study groups

Author	Postoperative outcomes	Follow-up	Intervention group 1, SSI/*n* (%)	Intervention group 2, SSI/*n* (%)	Control group, SSI/*n* (%)	Total, SSI/*n* (%)
Group A (no irrigation in the control group)						
Mountain [25]	Wound infection	5 days	7/76 (9.2)	x	18/74 (24.3)	25/150 (16.7)
Longland [26]	Wound infection	Not specified	9/50 (18.0)	1/50 (2.0)	38/200 (19.0)	48/300 (16.0)
Madsen [27]	Wound infection	Not specified	0/32 (0.0)	x	8/32 (25.0)	8/64 (12.5)
Andersen, Bendtsen [28]	Wound infection	3 weeks	10/245 (4.1)	x	42/245 (17.1)	52/490 (10.6)
Andersen, Korner [29]	Wound infection, wound dehiscence	30 days	3/120 (2.5)	x	22/120 (18.3)	25/240 (10.4)
Mackie [30]	Wound infection	3–5 weeks	0/38 (0.0)	4/31 (12.9)	2/23 (8.7)	6/92 (6.5)
Bates [31]	Wound infection	Hospital stay	3/100 (3.0)	x	16/100 (16.0)	19/200 (9.5)
Gilmore and Martin [32]	Wound infection, wound contamination	4 weeks	12/149 (8.0)	14/150 (9.3)	24/151 (15.9)	50/450 (11.1)
Gilmore and Sanderson [33]	Wound infection, wound contamination	6 weeks	6/63 (9.5)	x	18/70 (25.7)	24/133 (18.0)
Jensen [34]	Wound infection	10 days	4/96 (4.2)	6/88 (6.8)	6/83 (7.2)	16/267 (5.9)
McCluskey [35]	Wound infection	4 weeks	21/56 (37.5)	x	14/54 (25.9)	35/110 (31.8)
Galland [36]	Wound infection	Not specified	14/39 (35.9)	x	18/39 (46.1)	32/78 (41.0)
Stokes [37]	Wound infection	Not specified	11/55 (20.0)	x	21/62 (33.9)	32/117 (27.3)
Barr [38]	Wound infection	Not specified	1/28 (3.6)	x	23/60 (38.3)	24/88 (27.3)
Tanphiphat [39]	Wound infection	2 weeks	4/122 (3.3)	x	12/124 (9.7)	16/246 (6.5)
Andersen, Burcharth [40]	Wound infection, suture sinus, recurrences, incisional hernias	1 year	5/196 (2.5)	x	7/102 (6.9)	12/398 (3.0)
Foster [41]	Wound infection, financial aspects	4 weeks	29/119 (24.4)	x	27/117 (23.1)	56/236 (23.7)
Gray [42]	Wound infection	2 weeks	7/71 (9.9)	x	20/82 (24.4)	27/153 (17.6)
Kothuis [43]	Wound infection, complicated wound healing	2 weeks	16/102 (15.7)	x	15/118 (12.7)	31/220 (14.1)
Ostergaard [44]	Wound infection	30 days	3/120 (2.5)	x	22/120 (18.3)	25/240 (10.4)
Walsh [45]	Wound infection	4 weeks	28/308 (9.1)	x	40/319 (12.5)	68/627 (10.8)
de Jong [46]	Wound infection	4 weeks	39/303 (12.9)	x	45/279 (16.1)	84/582 (14.4)
Galland [47]	Wound infection	4 weeks	13/95 (13.7)	x	14/105 (13.3)	27/200 (13.5)
Sherlock [48]	Wound infection	4 weeks	6/39 (15.4)	x	13/36 (36.1)	19/75 (25.3)
Sood [49]	Wound infection	5 days	0/29 (0.0)	x	4/26 (15.4)	4/55 (7.3)
Juul [50]	Wound infection, wound dehiscence, hernia	3–6 months	5/105 (4.8)	x	5/98 (5.1)	10/203 (4.9)
Lau [51]	Wound infection	6 weeks	9/159 (5.7)	x	3/156 (1.9)	12/315 (3.8)
Moesgaard and Nielsen [52]	Perineal or abdominal wound infection	3 months	24/41 (58.5)	x	22/38 (57.9)	46/79 (58.2)

Table 2 (continued)

Author	Postoperative outcomes	Follow-up	Intervention group 1, SSI/*n* (%)	Intervention group 2, SSI/*n* (%)	Control group, SSI/*n* (%)	Total, SSI/*n* (%)
Moesgaard. Nielsen and Hjortrup [53]	Wound infection	1 month	15/87 (17.2)	x	14/90 (15.6)	29/177 (16.4)
Raahave [54]	Wound infection, wound rupture, anastomotic leakage, intra-abdominal abscess	Not specified	5/81 (6.2)	x	6/89 (6.7)	11/170 (6.5)
Seco [55]	Wound infection	10 days	5/126 (3.9)	x	15/120 (12.5)	20/246 (8.1)
Cervantes-Sanchez [56]	Wound infection	4 weeks	11/127 (8.6)	x	39/156 (25.0)	50/283 (17.7)
Al-Ramahi [57]	Wound infection	4 weeks	11/104 (10.6)	x	10/102 (9.8)	21/206 (10.2)
Pradhan [58]	Wound infection	Not specified	1/35 (2.8)	x	6/35 (17.1)	7/70 (10.0)
Güngördük [59]	Wound infection	6 weeks	17/260 (6.5)	x	19/260 (7.3)	36/520 (6.9)
Group B (saline irrigation in the control group)						
Logan [60]	Wound infection	10 days	3/52 (5.7)	x	1/48 (2.1)	4/100 (4.0)
Ciccone [61]	Wound infection, serum and urine levels, ototoxicity and nephro-toxicity of kanamycin	Not specified	3/100 (3.0)	x	12/100 (12.0)	15/200 (7.5)
Galle [62]	Wound infection, febrile morbidity (fever index)	Not specified	9/31 (29.0)	x	9/36 (25.0)	18/67 (26.9)
Lord [63]	Wound infection	Not specified	3/100 (3.0)	x	9/100 (9.0)	12/200 (6.0)
Rogers [64]	Wound infection	4 weeks	4/86 (4.6)	x	11/101 (10.9)	15/187 (8.0)
Mathelier [65]	Wound infection or uterine infection	4 weeks	2/154 (1.3)	x	13/154 (8.4)	15/308 (4.9)

trials; however, the majority performed follow-up for 4 weeks. Ten trials did not specify the length of follow-up [26, 27, 36–38, 54, 58, 61–63].

Risk of bias evaluation

The results of the risk of bias evaluation are presented as a table in supplement 2. According to the Cochrane handbook's definition [21], 18 of the included trials were judged to be at "high risk of bias" and 23 trials were at an "unclear risk of bias" mostly due to a lack of information available from the older trials. The funnel plots (supplement 2) showed an asymmetry in the plot of group A which indicates a possible publication bias, as all included trials with a high standard error for the log odds ratio show a large benefit for the experimental group.

Meta-analysis of IOWI vs. no irrigation

The meta-analysis of trials in group A (35 RCTs including 8472 patients) for estimation of the average effect of IOWI on postoperative SSI rates showed that IOWI with any of the included irrigation solutions significantly reduced the rate of postoperative SSIs compared to no irrigation (OR=0.54, 95 % CI [0.42; 0.69], $p<0.0001$) (Fig. 2). The subgroup analysis comparing colorectal and non-colorectal procedures included 30 trials. In the remaining five trials, this subgroup analysis was not applicable, as the exact numbers of colorectal procedures were not specified. Results showed that the estimated beneficial effect of IOWI was significant only in colorectal surgeries (OR=0.51, 95 % CI [0.37; 0.72], $p=0.0001$) compared to non-colorectal surgeries (OR=0.69, 95 % CI [0.43; 1.09], $p=0.11$) (Fig. 3a, b). The subgroup analysis for each individual irrigation solution revealed that the estimated effect of IOWI with antibiotic solutions (OR=0.39, 95 % CI [0.27; 0.55], $p<0.0001$) was larger than the effect from IOWI with PVP-I (OR=0.70, 95 % CI [0.51; 0.97], $p=0.03$) compared to no irrigation. IOWI with saline compared to no irrigation did not have a significant effect (OR=0.64, 95 % CI [0.28; 1.46], $p=0.29$) (Fig. 4a–c).

Meta-analysis of IOWI with topical antibiotics or PVP-I vs. saline irrigation

Meta-analysis of trials in group B (six RCTs including 1062 patients) showed that IOWI with either antibiotics or PVP-I

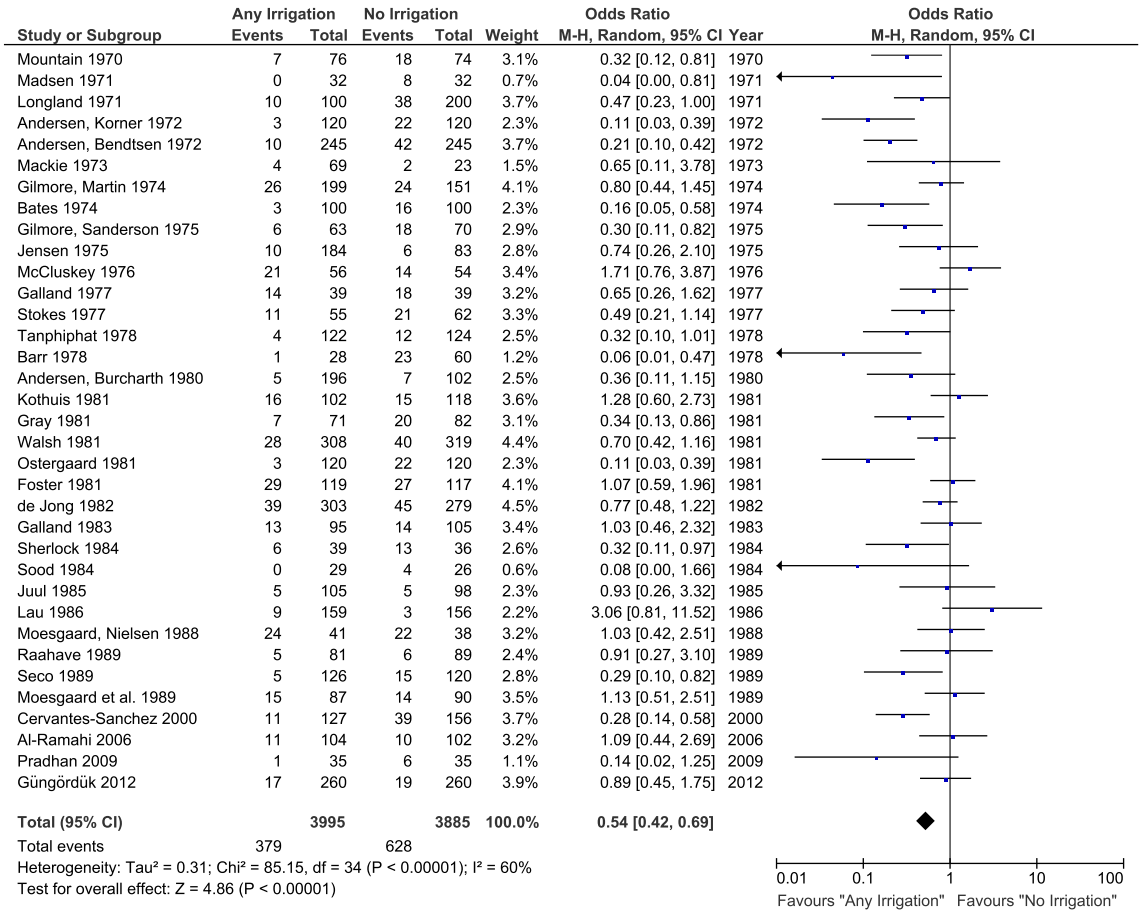


Fig. 2 Forest plot of IOWI with any irrigation solution vs. no irrigation (group A). Individual and pooled effect estimates for all 35 included studies are shown

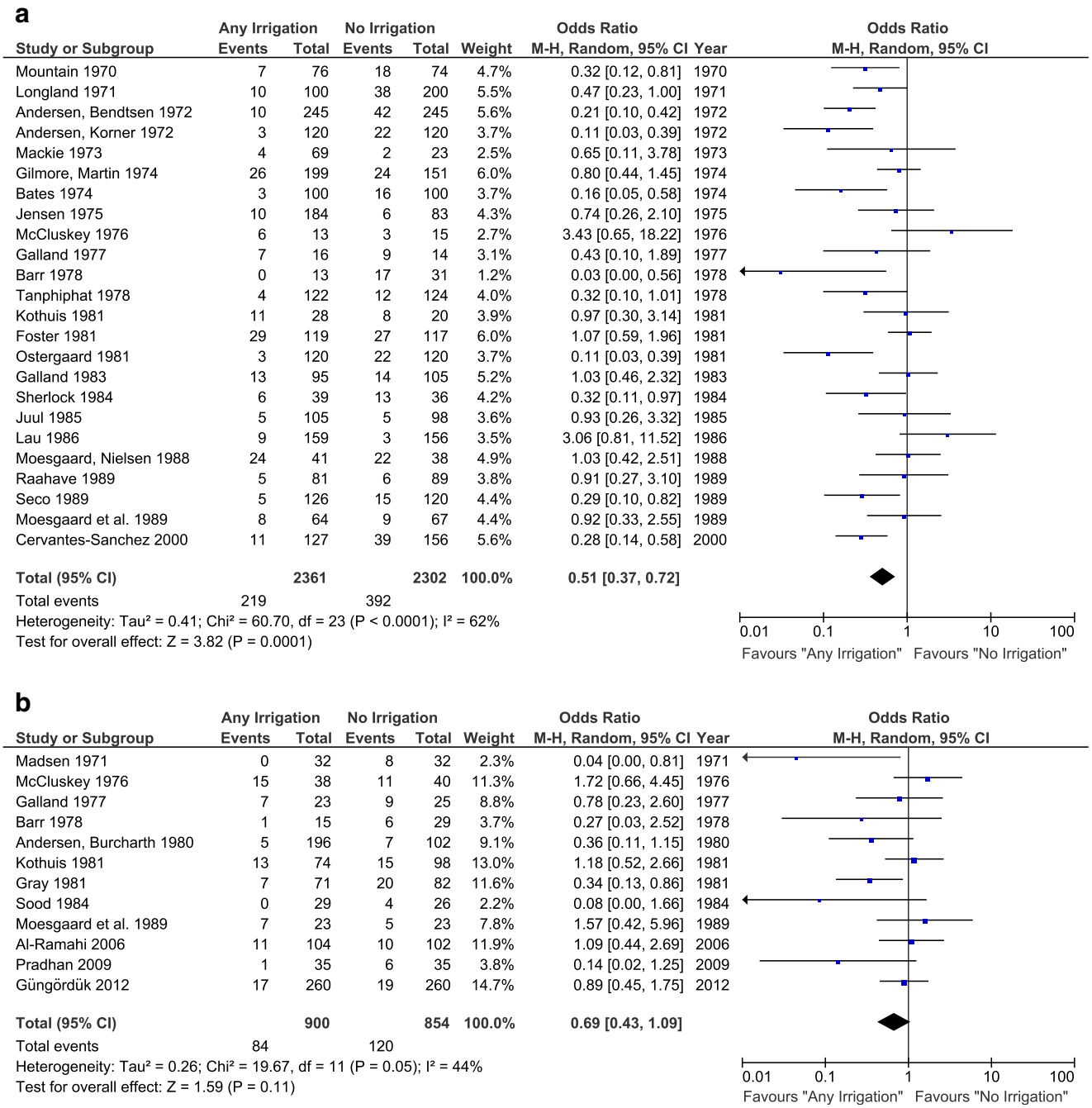


Fig. 3 **a** Subgroup analysis of any irrigation vs. no irrigation in colorectal surgeries. **b** Subgroup analysis of any irrigation vs. no irrigation in non-colorectal surgeries

was more effective than irrigation with saline (OR=0.44, 95 % CI [0.21; 0.96], p=0.04) (Fig. 5a). Inclusion of the additional trial (Sindelar et al. 1979) in this analysis did not change the results significantly (OR=0.37, 95 % CI [0.18; 0.75], p=0.006).

Further, subgroup analysis showed that the estimated effect for IOWI with antibiotics vs. saline (OR=0.32, 95 % CI [0.12; 0.84], p=0.02) (Fig. 5b) was larger than for IOWI with PVP-I vs. saline (OR=0.72, 95 % CI [0.24; 2.16], p=0.56). This result was also not significantly changed when the Sindelar trial [24] was added to the analysis (OR=0.42, 95 % CI [0.13; 1.40], p=0.16).

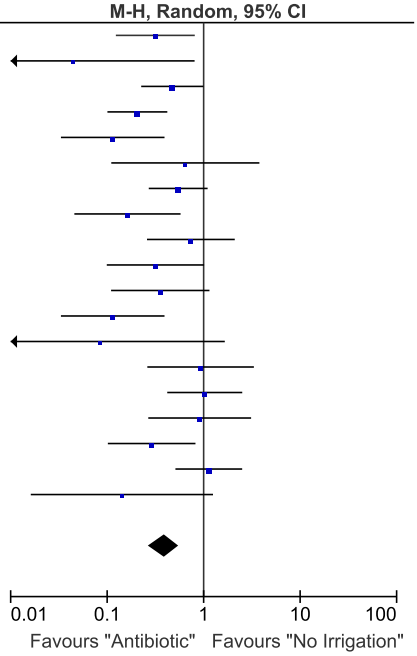
Discussion

Intra-operative wound irrigation with antibiotics, PVP-I, or saline is currently not recommended in the NICE guideline

a

Study or Subgroup	Antibiotic Events	Antibiotic Total	No Irrigation Events	No Irrigation Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
Mountain 1970	7	76	18	74	6.6%	0.32 [0.12, 0.81]	1970
Madsen 1971	0	32	8	32	1.4%	0.04 [0.00, 0.81]	1971
Longland 1971	10	100	38	200	7.9%	0.47 [0.23, 1.00]	1971
Andersen, Bendtsen 1972	10	245	42	245	8.1%	0.21 [0.10, 0.42]	1972
Andersen, Korner 1972	3	120	22	120	5.0%	0.11 [0.03, 0.39]	1972
Mackie 1973	4	69	2	23	3.1%	0.65 [0.11, 3.78]	1973
Gilmore, Martin 1974	14	150	24	151	8.2%	0.54 [0.27, 1.10]	1974
Bates 1974	3	100	16	100	4.8%	0.16 [0.05, 0.58]	1974
Jensen 1975	10	184	6	83	5.9%	0.74 [0.26, 2.10]	1975
Tanphiphat 1978	4	122	12	124	5.3%	0.32 [0.10, 1.01]	1978
Andersen, Burcharth 1980	5	196	7	102	5.3%	0.36 [0.11, 1.15]	1980
Ostergaard 1981	3	120	22	120	5.0%	0.11 [0.03, 0.39]	1981
Sood 1984	0	29	4	26	1.3%	0.08 [0.00, 1.66]	1984
Juul 1985	5	105	5	98	4.8%	0.93 [0.26, 3.32]	1985
Moesgaard, Nielsen 1988	24	41	22	38	6.8%	1.03 [0.42, 2.51]	1988
Raahave 1989	5	81	6	89	5.0%	0.91 [0.27, 3.10]	1989
Seco 1989	5	126	15	120	5.9%	0.29 [0.10, 0.82]	1989
Moesgaard et al. 1989	15	87	14	90	7.5%	1.13 [0.51, 2.51]	1989
Pradhan 2009	1	35	6	35	2.2%	0.14 [0.02, 1.25]	2009
Total (95% CI)		**2018**		**1870**	**100.0%**	**0.39 [0.27, 0.55]**	
Total events	128		289				

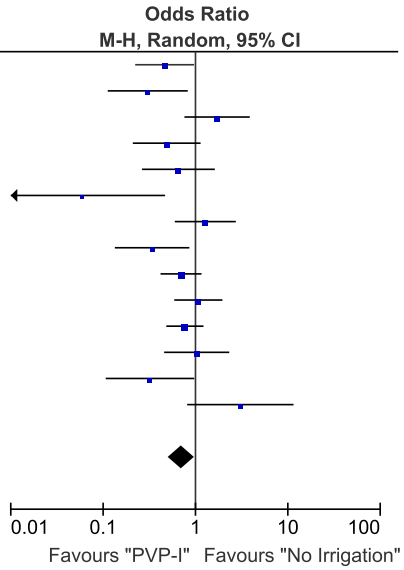
Heterogeneity: Tau² = 0.29; Chi² = 35.40, df = 18 (P = 0.008); I² = 49%
Test for overall effect: Z = 5.16 (P < 0.00001)



b

Study or Subgroup	PVP-I Events	PVP-I Total	No Irrigation Events	No Irrigation Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
Gilmore, Martin 1974	12	149	24	151	8.2%	0.46 [0.22, 0.97]	1974
Gilmore, Sanderson 1975	6	63	18	70	6.0%	0.30 [0.11, 0.82]	1975
McCluskey 1976	21	56	14	54	7.5%	1.71 [0.76, 3.87]	1976
Stokes 1977	11	55	21	62	7.2%	0.49 [0.21, 1.14]	1977
Galland 1977	14	39	18	39	6.7%	0.65 [0.26, 1.62]	1977
Barr 1978	1	28	23	60	2.1%	0.06 [0.01, 0.47]	1978
Kothuis 1981	16	102	15	118	7.9%	1.28 [0.60, 2.73]	1981
Gray 1981	7	71	20	82	6.5%	0.34 [0.13, 0.86]	1981
Walsh 1981	28	308	40	319	10.5%	0.70 [0.42, 1.16]	1981
Foster 1981	29	119	27	117	9.5%	1.07 [0.59, 1.96]	1981
de Jong 1982	39	303	45	279	11.0%	0.77 [0.48, 1.22]	1982
Galland 1983	13	95	14	105	7.5%	1.03 [0.46, 2.32]	1983
Sherlock 1984	6	39	13	36	5.3%	0.32 [0.11, 0.97]	1984
Lau 1986	9	159	3	156	4.2%	3.06 [0.81, 11.52]	1986
Total (95% CI)		**1586**		**1648**	**100.0%**	**0.70 [0.51, 0.97]**	
Total events	212		295				

Heterogeneity: Tau² = 0.19; Chi² = 29.03, df = 13 (P = 0.006); I² = 55%
Test for overall effect: Z = 2.16 (P = 0.03)



c

Study or Subgroup	Saline Events	Saline Total	No Irrigation Events	No Irrigation Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
Cervantes-Sanchez 2000	11	127	39	156	34.5%	0.28 [0.14, 0.58]	2000
Al-Ramahi 2006	11	104	10	102	30.0%	1.09 [0.44, 2.69]	2006
Güngördük 2012	17	260	19	260	35.5%	0.89 [0.45, 1.75]	2012
Total (95% CI)		**491**		**518**	**100.0%**	**0.64 [0.28, 1.46]**	
Total events	39		68				

Heterogeneity: Tau² = 0.38; Chi² = 7.13, df = 2 (P = 0.03); I² = 72%
Test for overall effect: Z = 1.07 (P = 0.29)

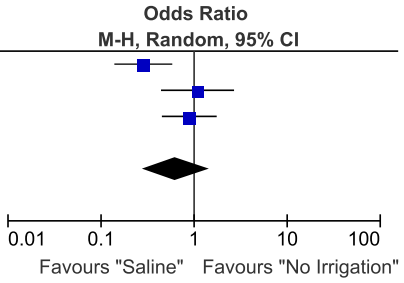


Fig. 4 **a** Subgroup analysis of topical antibiotic wound irrigation vs. no irrigation. **b** Subgroup analysis of PVP-I wound irrigation vs. no irrigation. **c** Subgroup analysis of saline wound irrigation vs. no irrigation

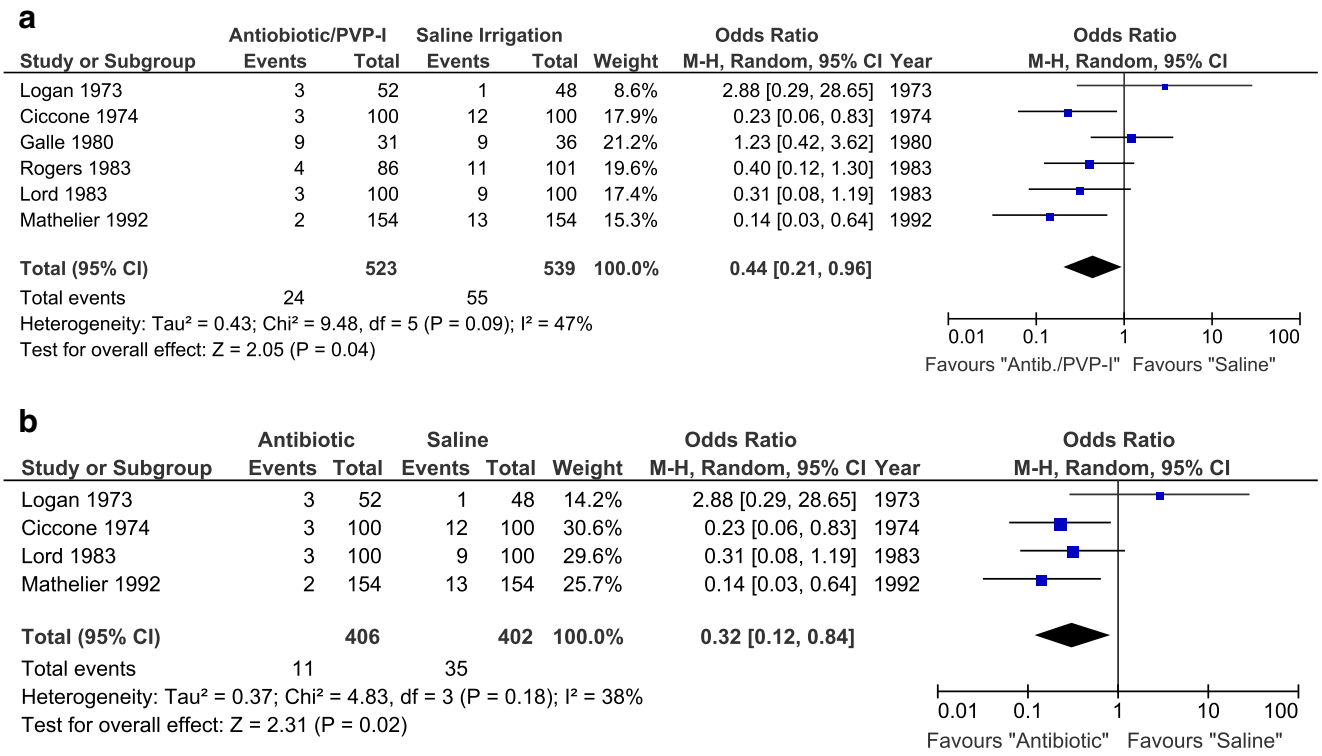


Fig. 5 **a** Forrest plot of RCTs comparing IOWI with topical antibiotics or PVP-I vs. saline irrigation (group B). **b** Subgroup analysis of RCTs comparing IOWI with topical antibiotics vs. saline irrigation

[5]. Despite these recommendations, many abdominal surgeons still use IOWI to prevent postoperative wound infections [13, 66, 67]. For example, in a survey of Swiss surgeons, roughly 80 % of clinicians stated that they rinse the operation site with saline and only 4–9 % reported to never use any deep or subcutaneous irrigation [13]. In contrast to previous reviews, all of the IOWI solutions mentioned in the NICE guideline (topical antibiotics, saline, and PVP-I solutions), all types of open abdominal surgeries and RCTs only were included in this systematic review. Meta-analysis showed a significant benefit of IOWI with any solution in comparison to no irrigation (Fig. 2). Subgroup analysis showed that the estimated effect was significant only in colorectal surgeries and not in non-colorectal surgeries (Fig. 3a, b). Further, subgroup analysis showed that the estimated effect in reduction of postoperative SSI was significant only for IOWI with topical antibiotics or PVP-I but not for saline (Fig. 4a–c). This was confirmed in the analysis of group B, where IOWI with topical antibiotics/PVP-I was compared to saline irrigation.

Limitations of available data

The majority of trials have been published from 1970 to 1990, and their results might not reflect current clinical practice. Furthermore, the quality assessment (supplement 2) revealed that most of the trials are at a high risk of bias, mainly because of insufficient data reported and also because of methodological flaws. Methods of sequence generation, allocation concealment, and blinding were often inadequate or not reported. In addition, interventions, follow-up times, and definitions of SSI varied widely between studies which might explain the large variance in overall SSI rates between 3.0 [40] and 58.2 % [52]. Most studies used a non-standardized definition of SSI, based on the presence of a purulent discharge from the wound or a sero-sanguinous discharge that gave a positive bacteriological culture result [68]. Three studies did not specify the definition criteria for SSI [38, 58, 63]. The current internationally accepted Centers for Disease Control (CDC) SSI definition, however, was not published until 1999 [69]. This problem was addressed by a systematic review of SSI definitions used in clinical trials between 1993 and 1999. It was shown that within 90 trials, as much as 41 distinct SSI definitions had been used [70]. Likewise, while current CDC criteria recommend a follow-up time for SSIs of at least 30 days, the reported length of follow-up in the included trials was 30 days or more in only 21 out of 41 trials. The remaining trials reported follow-up times of as short as 5–10 days or did not specify the follow-up time at all. In addition, the number and frequency of follow-up visits varied largely, as did the type and blinding status of the primary outcome assessor. Moreover, a number of trials did not clearly specify inclusion and exclusion criteria (supplement 1). Furthermore, the

concentration, application volume and duration of application of irrigation solutions were frequently not specified and might vary between trials. Finally, although a number of risk factors for SSI have been well established, including patient-related factors such as obesity, smoking, ASA status, diabetes mellitus, as well as surgery-related risk factors like preoperative skin/bowel preparation, level of contamination, and the duration of the operation [69]. Most of the included trials did not accurately report the presence of these risk factors. Hence, adjustment of our analysis for those risk factors was not possible.

IOWI with saline

Plain saline is a widely used irrigation solution, as it is isotonic and does not interfere with wound healing [71]. Furthermore, it is generally used to clear wounds from blood clots and necrotic tissue. However, evidence for IOWI with saline to prevent SSI is scarce. Only three RCTs comparing saline with no irrigation were identified [56, 57, 59], and meta-analysis showed no statistically significant effect on the rate of SSIs (Fig. 4c, OR=0.64, 95 % CI [0.28; 1.46], p=0.29). However, two of the trials that did not report any significant effect of IOWI with saline were performed in gynecological surgery [57, 59]. In contrast, the third trial investigated the effectiveness of syringe pressure irrigation of subcutaneous tissue with saline following appendectomy and found that the rate of postoperative SSI was significantly reduced in complicated (perforated) cases within the saline group [56]. Compared to gynecological surgery, bacterial contamination of the wound during surgery is more likely to occur during perforated appendectomy, where irrigation with saline did reduce the SSI rate. This evidence is clearly not sufficient to give a definite clinical recommendation on the use of IOWI with saline.

IOWI with PVP-I

Much debate has also surfaced over the use of PVP-I, and the use of this solution has been removed from many wound management regimes because of a putative negative effect on tissue regeneration. PVP-I demonstrates dose-dependent levels of tissue toxicity but is still better tolerated than preparations containing chlorhexidine or octenidine [14]. However, when studied in a clinical context, a recent evidence-based review of the effects of PVP-I solutions on wound healing failed to show a negative effect [72]. Consequently, the majority of high-quality trials analyzed in that review supported the use of PVP-I for IOWI. Nevertheless, the NICE guidelines do not recommend the use of IOWI or intra-operative skin re-disinfection with PVP-I products [5, 15]. However, only a limited number of available trials was considered for these recommendations [15]. In this meta-analysis, IOWI with PVP-I was shown to significantly reduce SSI rates when compared to no irrigation (Fig. 4b; OR=0.70, 95 % CI [0.51; 0.97], p=0.03). Unfortunately, negative effects on tissue regeneration have not been evaluated in the included trials. A meta-analysis of 24 RCTs, by Fournel et al., also found that IOWI with PVP-I reduced the incidence of postoperative SSI in the main analysis and in the subgroup analyses of the method of PVP-I administration (spray or irrigation), its timing (before or after closure) and the type of surgery (clean or contaminated) [12]. In contrast to our analysis, however, the authors included abdominal as well as neurosurgical and orthopedic procedures, which differ drastically in terms of contamination level and microbiological spectrum. In line with our data, systematic reviews by Chundamala [16] and Pattana-Arun [17] also showed a trend toward reduction of SSI rates after PVP-I irrigation in abdominal surgery, despite limitations regarding trial methodology and heterogeneity. In accordance with our findings of a more pronounced effect of IOWI in the colorectal subgroup, Pattana-Arun et al. concluded that PVP-I irrigation might be more useful in dirty or contaminated operations [17]. In summary, the majority of existing evidence suggests a beneficial effect of PVP-I irrigation but is not sufficient for definite recommendations.

IOWI with topical antibiotics

Observations from animal models suggest that topical application of antibiotics to the surgical incision could significantly reduce postoperative SSI rates and is equally effective as systemic antibiotics [15]. Furthermore, it has been shown that by local application, higher concentrations of the antibiotic were achieved in the wound for a longer period of time. However, combining topical and systemic application of antibiotics was of no additional benefit in these models [73, 74]. In clinical practice, IOWI with solutions containing antibiotics used to be widespread in the 1980s, especially in dirty-contaminated abdominal or trauma/orthopedic surgery [75]. Currently, guidelines do not support the use of antibiotic IOWI anymore, due to the lack of evidence for their benefit and the potential enhancement of microbial resistance [5]. In contrast, a recent review by Alexander et al. recommends the use of topical antibiotics by repeated irrigation during an operation and before skin closure based on the analysis of clinical and experimental studies [15, 76]. Especially in obese patients, who are predisposed to develop SSI, infusion of topical antibiotics to the wound allowed to achieve higher local concentrations in the poorly perfused subcutaneous adipose tissue then by intravenous application [76]. Others have evaluated pre- or intra-incisional infiltration of the subcutaneous tissue with antibiotics and also found significant beneficial effects in the prevention of SSI after contaminated abdominal surgery [77]. Similarly, a number of older reviews support the use of topical antibiotics for prophylaxis of SSI in certain indications including general abdominal surgery and appendectomies [19, 78].

In line with this data, we found a significant reduction of SSIs in the subgroup analysis of 19 trials comparing IOWI with antibiotic solutions vs. no irrigation (Fig. 4a; OR=0.39, 95 % CI [0.27; 0.55], $p<0.0001$). However, different antibiotics, concentrations, and applications were used meaning that heterogeneity was high and no regime can currently be recommended unequivocally. Furthermore, future clinical trials on the subject should focus on the ideal timing of application and measures to prevent development or selection of drug-resistant bacterial strains.

Conclusions

Based on this systematic review, IOWI has a significant beneficial effect on the reduction of postoperative SSI following open abdominal surgery. The estimated effect was most pronounced in colorectal surgeries and for IOWI with antibiotic solutions. However, given the methodological flaws and the large heterogeneity of the analyzed trials, the clinical relevance has to be balanced against the risk of impaired wound healing and the potential raise of resistant microbiological stains. Therefore, no single regime can be recommended unequivocally at this moment. High-quality evidence from future RCTs using standardized outcome parameters is awaited urgently to clearly establish the role of IOWI in abdominal surgery on an evidence-based level in order to encounter the substantial problem of this huge health care burden worldwide.

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Conflicts of interest None.

Authors' contributions T. Mueller: Conception and design of study, literature review, data extraction, risk of bias evaluation, statistical analyses, draft of manuscript, writing and editing and submission of manuscript, and corresponding author

M. Loos: Conception and design of study, literature review, data extraction, risk of bias evaluation, statistical analyses, draft of manuscript, critical revision, and approval of final version

B. Haller: Conception and design of study, statistical analyses, revision and editing of manuscript, and approval of final version

A. Mihaljevic: Conception and design of study, consensus if TM and ML disagreed during literature review, data extraction or risk of bias evaluation, statistical analyses, draft of manuscript, revision and editing of manuscript, and approval of final version

U. Nitsche: Conception and design of study, revision and editing of manuscript draft, consensus if TM and ML disagreed during literature review, and approval of final version

H. Friess: Conception and design of study, critical revision and editing of manuscript draft, and approval of final version

J. Kleeff: Conception and design of study, critical revision and editing of manuscript draft, and approval of final version

F. Bader: Conception and design of study, revision and editing of manuscript, consensus during data extraction and risk of bias evaluation, and revision and approval of final manuscript version

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