BMJ Open

Surgical site infection prevention in abdominal surgery: is intraoperative wound irrigation with antiseptics effective? Protocol for a systematic review and meta-analysis

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To cite: Mueller T, Dimpel R, Kehl V, *et al*. Surgical site infection prevention in abdominal surgery: is intraoperative wound irrigation with antiseptics effective? Protocol for a systematic review and meta-analysis. *BMJ Open* 2023;**13**:e066140. doi:10.1136/bmjopen-2022-066140

► Prepublication history and additional supplemental material for this paper are available online. To view these files, please visit the journal online (http://dx.doi.org/10.1136/bmjopen-2022-066140).

Received 28 June 2022
Accepted 29 January 2023

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ABSTRACT

Introduction Surgical site infection (SSI) after laparotomy still represents the most frequent postoperative complicationin abdominal surgery. The effectiveness of reducing SSI rates by intra-operative irrigation of the incisional wound with antiseptic solutions or saline has been much debated, and recommendations on its use are divergent. Therefore, we aim to conduct a systematic review and meta-analysis, focusing specifically on procedures by laparotomy and considering recent evidence only.

Methods and analysis The systematic review and meta-analysis were conducted in accordance with the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P) statement. On 1 July 2022, PubMed/MEDLINE, Cochrane, Central Register of Controlled Trials and EMBASE were searched for the following predefined terms: (Surgical site infection) AND ((irrigation) OR (wound irrigation) OR (lavage)) AND ((abdominal surgery) OR (laparotomy). The search was limited to peer-revied publications, dating after 1 January 2000 in English or German language. Systematic reviews and meta-analyses were included for reference screening. Case reports, case series, non-systematic reviews and studies without follow-up information were excluded. The primary outcome is the rate of postoperative SSI after abdominal surgery by laparotomy. Meta-analysis is pooled using the Mantel-Haenszel method for random effects. The risk of bias in randomised studies will be assessed using the Cochrane developed RoB 2-tool, and the ROBINS-I tool for non-randomised studies. Completion of the analysis and publication is planned in March 2023.

Ethics and dissemination Ethical approval is not necessary for this study, as no new data will be collected. The results of the final study will be published in a peer-reviewed open-access journal.

PROSPERO registration number CRD42022321458.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ This study will provide a comprehensive analysis of the efficacy of prophylactic intra-operative wound irrigation with antiseptics to reduce SSI rates in the field of abdominal surgery, including the results of the most recent multicentre randomised clinical trial in the field (IOWISI trial, DRKS00012251).
⇒ The included data will be thoroughly analysed applying all current recommendations by the PRISMA-P statement and the Cochrane group, to maximise transparency, accuracy and significance.
⇒ Only publications after 1 January 2000 were considered to avoid redundant and repetitive analysis of out-of-date evidence that does not longer reflect today's clinical standards.
⇒ Limitations of this study will be the rareness of high-level evidence on the subject and the heterogeneity of study designs and interventions between trials.

INTRODUCTION

Rationale

Postoperative wound complications following procedures by laparotomy remain one of the big problems in modern abdominal surgery. Randomised controlled multicentre trials report surgical site infections (SSIs) rates from up to 25%.[1 2] While superficial incisional SSIs (class I) can often be treated conservatively, infections of the deeper muscular layers (class II) or within the peritoneal cavity (class III) often require reoperations and are potentially life-threatening for patients. Prophylactic intra-operative wound irrigation (IOWI) to reduce SSI rates is a widespread practice but remains of uncertain evidence and thus recommendations on its use are divergent. Several international organisations have published guidelines on SSI prevention, that is, WHO in 2016,[3] the Centers for Disease Control and Prevention (CDC) updated in 2017[4] and the National Institute for Health and Care Excellence (NICE) updated in 2020.[5] While the CDC guideline recommends IOWI with diluted iodophor solution (grade 2, weak) the WHO only suggest considering it, and the NICE guideline recommends not to do it due to

the lack of evidence.[6 7] However, these guidelines do not specifically address abdominal surgery, nor do they take other antiseptic solutions than povidone-iodine into account (as there is a lack of evidence for other irrigation solutions). They do agree, however, 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 and narrative reviews, as well as meta-analyses have already been published on the subject. However, they all included trials of low methodological quality, dating from the 1980s or even earlier, and most of them also mixed different types of surgeries (neurosurgery, orthopaedic surgery, gynaecological surgery, etc.) and various no longer recommended irrigation solutions (eg. antibiotic solutions).[8–17] In conclusion, although IOWI remains a very popular procedure among surgeons, the lack of its standardisation leads to heterogeneous clinical trials with controversial results, which is why definite recommendations on its use are still lacking.[8 11 12 18 19] Consequently, we recently conducted a large multicentre randomised controlled surgical trial (IOWISI trial, DRKS00012251) investigating if the prophylactic irrigation of the laparotomy-wound before skin closure using antiseptic polyhexanide solution or saline can reduce postoperative SSI rates after clean-contaminated, contaminated or septic abdominal procedures, the results of which will provide high-quality evidence regarding this practice.[20]

Hypothesis and objectives

To put the up-coming results of the IOWISI trial into perspective, we will systematically search the literature to conduct a systematic review and meta-analysis including only high quality and recent (published after 1999) trials, exclusively in the field of open abdominal surgery. The hypothesis is that IOWI with antiseptic solutions can effectively reduce SSI rates after abdominal surgery by laparotomy compared with irrigation with simple saline or no irrigation. Secondary objectives are to determine if there is a benefit of IOWI with saline compared with no irrigation, and to perform subgroup analysis to investigate if specific procedures or specific antiseptic agents show a more pronounced effect than others.

METHODS AND ANALYSIS

Design and amendments

This protocol systematic review and meta-analysis is designed following the recommendations of the PRISMA-P statement 2015.[21] Any amendments of the protocol that might become necessary will be registered with date and description of changes and reasons.

Eligibility criteria

Eligibility criteria are summarised in table 1. Using the recommended PICOS approach, the following inclusion criteria were defined:

Table 1 Eligibility criteria

Inclusion criteria	Exclusion criteria
Publication date after 1 January 2000	Publication date before 1 January 2000
Language English or German	All other languages
Prospective, randomised clinical trials (RCTs) and quasi-RCTs	Case reports, case series, narrative reviews, letters
Retrospective and prospective observational studies	Non-peer-reviewed publications
Systematic reviews, meta-analyses and clinical guidelines for reference screening	Insufficient reporting of methods or follow-up
Primary outcome of study: SSI within 30 days postoperatively, irrespective of the used SSI definition	Other outcomes such as bacterial counts or cost-effectiveness analyses
Comparison of prophylactic wound irrigation after closure of the peritoneum using antiseptic solutions with saline or no irrigation	► 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 ► Skin re-disinfection before closure
Comparison of prophylactic wound irrigation after closure of the peritoneum using saline with no irrigation	Comparison of saline pressure/pulsatile irrigation with normal saline irrigation
Abdominal surgery by laparotomy	Non-abdominal surgery
Visceral surgery (eg, gastrointestinal, hepatobiliary or colorectal surgery)	Gynaecological, urological or vascular abdominal procedures
Elective and emergency procedures	Paediatric population, age <18 years
Patient age >17 years	

- P (population): adult subjects (age >17 years) undergoing abdominal surgery/laparotomy for visceral surgery (elective or emergency).
- I (intervention): prophylactic IOWI after closure of the abdominal fascia using antiseptic solutions.
- C (comparison): saline irrigation OR no irrigation.
- O (outcome): SSI within 30 days postoperatively.
- S (study design): prospective, randomised clinical trials (RCTs) and quasi-RCTs, retrospective and prospective observational studies. Guidelines, systematic reviews and meta-analyses will be included for background information and reference screening.

The exclusion criteria were:

- Non-abdominal surgery (orthopaedics, neurosurgery, etc).
- Different other fields of surgery, such as gynaecological, urological or vascular abdominal procedures.
- 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), skin re-disinfection before closure.
- Different outcomes such as bacterial counts or cost-effectiveness.
- Insufficient reporting of methods or follow-up.
- Non-peer-reviewed publications.
- Case reports, case series, narrative reviews, letters.
- Publication date before 1 January 2000.
- Publications in languages other than English or German.

Information sources

The following databases were searched on the 1 July 2022: EMBASE (Scopus), MEDLINE (Pubmed), Google Scholar and the Cochrane library (CENTRAL).[22] In addition, the reference lists of all included trials, systematic reviews and the above-mentioned guidelines on SSI prevention were screened.

Search strategy

The databases were searched using the following restrictions if applicable: human subjects or medicine; Language: English or German; Publication date starting from 1 January 2000to 1 July 2022. Two reviewers (TM and RMD) performed the search independently. The following search terms were entered in a database-specific syntax: (Surgical site infection) AND ((irrigation) OR (wound irrigation) OR (lavage)) AND ((abdominal surgery) OR (laparotomy). To avoid double-publication, the PROSPERO-Database and the WHO-Trials Database will be regularly checked for ongoing or finalised but unpublished systematic reviews on the subject. The full search strategy can be found in online supplemental material 1.

Selection process and data management

The selection process is shown in figure 1. All search results were prescreened to identify clearly irrelevant articles by title and abstract. Potentially relevant records were imported into the EndNote reference manager ((Computer program), V.20, Clarivate, 2013, Philadelphia, Pennsylvania, USA). Duplicates and records in languages other than German or English as well as conference programmes, letters or commentaries were removed. The remaining articles were classified as relevant, possibly relevant or irrelevant by two reviewers independently (TM and RD), applying the inclusion and exclusion criteria. In addition, the reference lists of all included guidelines and systematic reviews were cross-checked and screened for additional reports by the two reviewers separately. All articles classified as relevant or possibly relevant were recorded in a database (Microsoft Excel (Computer Program), V 16.69.1, Microsoft Corporation, 2022) and retrieved as full-text versions. In case of exclusion after full-text retrieval, reasons were attributed and any disagreements were resolved by discussion with a third author (DR).

Data collection process/data items

From the included records, data were extracted in the predefined database (Microsoft Excel (Computer Program), V 16.69.1, Microsoft Corporation, 2022). by two reviewers independently (TM and RD). The data items include: title, author, year and country of study conduct, details on study design, inclusion and exclusion criteria, number of patients, type of surgical procedure and level of contamination, type of intervention (specifically the active antiseptic agent of irrigation solution and irrigation technique) and type of control. Furthermore, the definition of the primary outcome SSI, the results (rates of SSI in each treatment group) and the duration of follow-up were recorded. In addition, details of methods (randomisation, blinding, etc) were extracted for the quality assessment of individual trials. No automation tools were used in the data collection process and any disagreements were resolved by discussion with a third author (DR) and re-extraction if necessary.

Risk of bias assessment

Data on methodological quality of RCTs were assessed by examination of the allocation sequence, allocation concealment and blinding. The Cochrane Collaboration's Rob2 (Risk of Bias in Randomised Studies) tool for assessing risk of bias[23] was used by two reviewers (TM and RD) independently. Methodological quality of non-RCTs was assessed using the ROBINS-I (Risk of Bias in Non-randomised Studies of Interventions) tool.[24] These tools are using signalling questions and algorithm based judgement of the individual risk of bias as 'low', 'unclear' or 'high'. Any disagreements were resolved after discussion with the senior authors (DR and HF). In addition, the risk of publication bias will be investigated by means of a funnel plot.

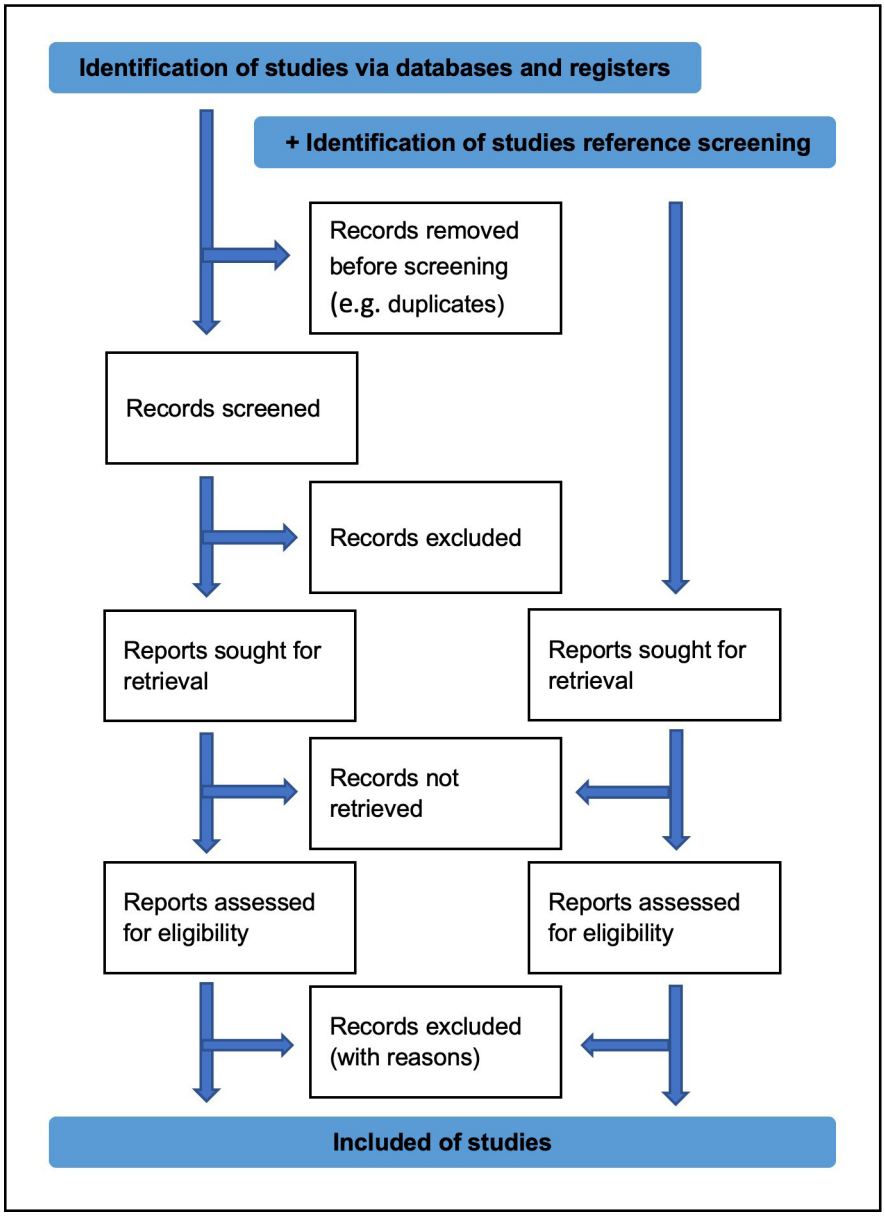

Figure 1 Study selection process.

Effect measures and synthesis methods

Trials will be grouped in comparisons according to intervention and control arm (comparison 1: antiseptic vs saline irrigation; comparison 2: antiseptic vs no irrigation; comparison 3; saline vs no irrigation). Of each comparison, meta-analysis will be performed using Review Manager (RevMan (Computer program), V.5.4.1, The Cochrane Collaboration, 2020). Furthermore, subgroup analyses will be performed for level of contamination, colorectal versus non-colorectal procedures and for each antiseptic agent. Depending on the heterogeneity regarding the used definition of SSI and the irrigation technique, additional subgroup analyses might be performed comparing CDC definition of SSI versus other definitions of SSI and different irrigation techniques (eg. soaking vs. lavage vs. pressure irrigation). Absolute numbers of patients and events will be presented for each trial incorporated in the meta-analyses and the corresponding subgroups. ORs with 95% CIs will be estimated for each trial from the numbers of events and patients treated. Due to the naturally expected heterogeneity, a random effect models with Mantel-Haenszel weights will be used to estimate the average treatment effect and a corresponding 95% CI. Forest plots will be shown to illustrate treatment effects estimated for each trial and the estimated average treatment effect for all investigated subgroups. For each analysis, τ^2 will be 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. In addition, the results of a χ^2 test for heterogeneity will be presented. A two-sided level of significance of less than 5.0% will be considered for all tests.

Confidence in cumulative evidence

The quality of evidence for all outcomes will be assessed using the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) criteria.[25]

Patient and public involvement

Patients and/or the public were not directly involved in the design, or conduct, or reporting, or dissemination plans of this research.

DISCUSSION

This systematic review and meta-analysis will provide an up to date, comprehensive overview of the evidence for efficacy of IOWI with antiseptics to prevent SSI following laparotomy for general abdominal surgery. Since SSI rates in this field are especially high and current official recommendations on the use of IOWI are divergent, this analysis will help surgeons to guide decision making and potentially influence future clinical guideline development.

Contributors TM wrote the manuscript, TM, DR and RD developed the search strategy, HF supervised and reviewed design of the protocol, all authors contributed to inclusion and exclusion criteria, VK is responsible for the statistical analysis plan, all authors read and critically revised the manuscript before submission.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

Provenance and peer review Not commissioned; externally peer reviewed.

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