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Systematic Review

Topical antibiotic prophylaxis for surgical wound infections in clean and clean-contaminated surgery: a systematic review and meta-analysis

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Abstract

Background: Topical antibiotics are widely prescribed as prophylaxis for surgical site infection (SSI). Despite giving high drug concentrations at local wound sites, their efficacy remains controversial. This study is a systematic review and meta-analysis designed to compare the efficacy and safety of topical antibiotics with non-antibiotic agents in preventing SSI.

Methods: Randomized controlled trials (RCTs) comparing topical antibiotics in patients with clean and clean-contaminated postsurgical wounds were included. Relevant trials published before 30 September 2020, were searched in the PubMed, Embase, and Cochrane databases, without language restrictions. The primary outcome was the incidence of SSIs, presented as the event rate. The secondary outcome was the incidence of contact dermatitis (safety outcome). Data were synthesized using the random-effects model, with the results expressed as risk ratio (RR) with 95 per cent confidence intervals (c.i.).

Results: Thirteen RCTs were included. The incidence of SSIs and contact dermatitis showed no significant difference between topical antibiotics and non-antibiotic agents (RR 0.89, 95 per cent c.i. 0.59 to 1.32 ($P = 0.56$, $I^2 = 48$ per cent); and RR 2.79, 95 per cent c.i. 0.51 to 15.19 ($P = 0.24$, $I^2 = 0$ per cent), respectively). In the subgroup analyses, a reduction in SSIs was also not observed in dermatological (RR 0.77, 95 per cent c.i. 0.39 to 1.55; $P = 0.46$, $I^2 = 65$ per cent), ocular (RR 0.08, 95 per cent c.i. 0.00 to 1.52; $P = 0.09$), spinal (RR 1.34, 95 per cent c.i. 0.65 to 2.77; $P = 0.43$, $I^2 = 0$ per cent), orthopaedic (RR 0.69, 95 per cent c.i. 0.37 to 1.29; $P = 0.25$, $I^2 = 0$ per cent), or cardiothoracic surgeries (RR 1.60, 95 per cent c.i. 0.79 to 3.25; $P = 0.19$).

Conclusion: Given the current evidence, the routine application of topical antibiotics to surgical wounds did not reduce the incidence of SSI. Further trials are needed to assess their effectiveness in high-risk surgeries or in selected patient groups.

Introduction

Surgical site infection (SSI) is a common postoperative com plication and a substantial cause of morbidity, prolonged hospitalization, and death[1]. Of note, SSI was the most common healthcare-associated infection from 2015 to 2017, followed by catheter-associated urinary tract infection and central line-associated bloodstream infection[2]. As such, SSI remains one of the most common preventable infections today[3]. Based on the concept that infection impairs the process of wound healing, prophylactic antibiotics play an essential role in wound management[4].

Preoperatively, prophylactic antibiotics are primarily administered intravenously (i.v.). Extensive studies of the preoperative i.v. administration of antibiotic prophylaxis have shown it to be effective in reducing SSIs[5]. However, with the rise of *Staphylococcus aureus*-related healthcare infections[2], the preoperative administration of intranasal mupirocin has also been suggested, owing to its role in the decolonization of methicillin-resistant *S. aureus* (MRSA), thereby decreasing SSIs[6].

The evidence for using topical antibiotics intraoperatively has been a matter of debate. A meta-analysis demonstrated that the use of topical antibiotic agents before wound closure could not be recommended[7]. According to recent guidelines, the irrigation of incisional wounds with antibiotic agents before closure should not be performed owing to the risk of multiple drug resistance[3,8,9]. However, the question over the intraoperative administration of vancomycin powder remains unsolved owing to the growing number of cases of MRSA infection in recent years[10].

Postoperatively, topical antibiotics are an option with several advantages, including a high drug concentration at the application site, a low incidence of systemic side effects, and good

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patient compliance[11]. Nevertheless, there is still controversy over their use owing to possible detrimental effects, such as local allergic reactions, poor skin penetration, and the emergence of resistant organisms with antibiotic exposure[11]. The Centers for Disease Control and Prevention 2017 guideline for the prevention of SSI states that additional prophylactic antibiotics should not be administered after the closure of the surgical incision in clean and clean-contaminated procedures[3]. Furthermore, despite the low-quality evidence, it also recommended against the administration of antimicrobial agents into surgical incisions for the prevention of SSIs.

Although there is no robust evidence of whether topical antibiotic prophylaxis is beneficial in patients undergoing clean and clean-contaminated surgery, it remains common practice during postsurgical wound care. The aim of this systematic review and meta-analysis was to compare the efficacy and safety of topical antibiotics with non-antibiotic agents for the prevention of SSI.

Methods

Inclusion and exclusion criteria

Surgical wounds were grouped into four classes, according to the National Academy of Sciences and the National Research Council: clean (I); clean-contaminated (II); contaminated (III); and infected/dirty (IV) (*Table S1*)[12]. The prophylaxis strategy was defined as the administration of topical antibiotics to wounds before the development of infection. Randomized controlled trials (RCTs) evaluating the outcome of using prophylactic topical antibiotics in patients undergoing surgery specifically classified as clean (I) or clean-contaminated (II) were included. Trials that contained other classes of wounds were included if the data from individual classes could be extracted. Additionally, trials were required to document their inclusion and exclusion criteria.

Different forms of topical antibiotics were included, such as ointment, cream, lotion, and powder. Trials that used antiseptic agents were also included. Studies of the use of irrigation solutions during surgery, the use of antibiotic dressings for wounds, and other delivery forms (e.g. collagen implants and antibiotic-impregnated sponges) were excluded. Observational and duplicate studies were excluded from this study. In addition, trials regarding catheter infection, therapeutic and decolonization effects, and the use of polypropylene mesh were also excluded.

Search strategy and study selection

Relevant trials published up to 30 September 2020 were identified from the PubMed, Cochrane, and Embase databases. Unpublished trials were collected from the ClinicalTrials.gov registry (http://clinicaltrials.gov/). The following medical subject headings terms were used: surgical wound; surgical wound infection; wound healing; antibacterial agents; antibiotic prophylaxis; administration; topical; staphylococcal infections; topical anti-infective agent; local topical anti-infective agent; bacterial infection; postoperative complications; surgical wound dehiscence; dermatitis; and allergic contact (*Table S2*). All retrieved abstracts, trials, and citations were reviewed. In addition, other trials were identified using the reference sections of relevant papers and through correspondence with subject experts. No language restrictions were imposed.

Methodological quality appraisal

Two reviewers (Y.M.H. and M.C.L.) independently assessed the methodological quality of each trial by using the risk of bias method, as recommended by the Cochrane Collaboration[13]. Several domains were evaluated, including the adequacy of randomization, concealment of allocation, blinding of the patients and the outcome assessors, follow-up duration, the information provided to the patients regarding study withdrawals, whether an intention-to-treat (ITT) analysis was performed, and freedom from other biases.

Data and outcome extraction

Baseline and outcome data were independently extracted by two reviewers (Y.M.H. and M.C.L.). The trial design, population characteristics, inclusion and exclusion criteria, surgery type, patient source, regimen of drug administration, and postsurgical wound infection rates were extracted. Disagreements were resolved by a third reviewer (P.J.C.).

The primary outcome was the incidence of SSI, presented as the event rate. The secondary outcome was the incidence of contact dermatitis, which represents the safety outcome.

Statistical analyses

Data were entered and analysed using Review Manager (version 5.4; The Cochrane Collaboration, Oxford, UK). The meta-analysis was performed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines[14]. Standard deviations were estimated from the provided confidence interval (c.i.) limits or standard error. Furthermore, dichotomous outcomes were analysed using risk ratios (RRs) as the summary statistics. The precision levels of the effect sizes are reported as 95 per cent confidence intervals. A pooled estimate of the RR and weighted mean difference was computed using the DerSimonian and Laird random-effects model[15].

To evaluate the statistical heterogeneity and inconsistency of prophylaxis effects across the trials, the Cochrane Q tests and I^2 statistics were used. Statistical significance was set at $P < 0.10$ for the Cochrane Q tests. Statistical heterogeneity across the trials was assessed using I^2 statistics, which quantified the outcome variability across the trials. Heterogeneity was categorized as low ($I^2 \leq 25$ per cent), moderate (25 per cent $< I^2 <$ 75 per cent) or high ($I^2 \geq 75$ per cent). Additionally, a sensitivity analysis was performed to strengthen the robustness of the results when $I^2 > 50$ per cent. A one-by-one exclusion method was applied for analysis, and subgroup analyses were performed to investigate the effect of the different types and phases of surgery (preoperative, intraoperative, and postoperative).

Results

Characteristics of the included trials and patients

Figure 1 shows the PRISMA flow diagram. The initial search strategy yielded 7157 studies, and after removing the duplicates and non-RCTs, 5057 studies were eligible for title and abstract screening. Seventy-two full-text articles were retrieved and, after further exclusions, 13 trials with complete data were included in the meta-analysis[16–28].

Twelve trials compared topical antibiotics to placebo, paraffin, petrolatum, and other non-antibiotic ingredients[16–26,28], and one trial compared topical antibiotics to placebo and antiseptic agents[27]. Regarding type of surgery, there were five trials in dermatological surgery[16–20], one in abdominal surgery[21], two in orthopaedic surgery[22,23], two in spinal surgery[24,25], one in ocular surgery[26], and two in cardiothoracic surgery[27,28]. Most trials enrolled clean (I) wounds (12 of 13)[16–20,22–28], and only one trial enrolled clean-contaminated (II) wounds[21] . The administration of topical antibiotics included a nasal administration with

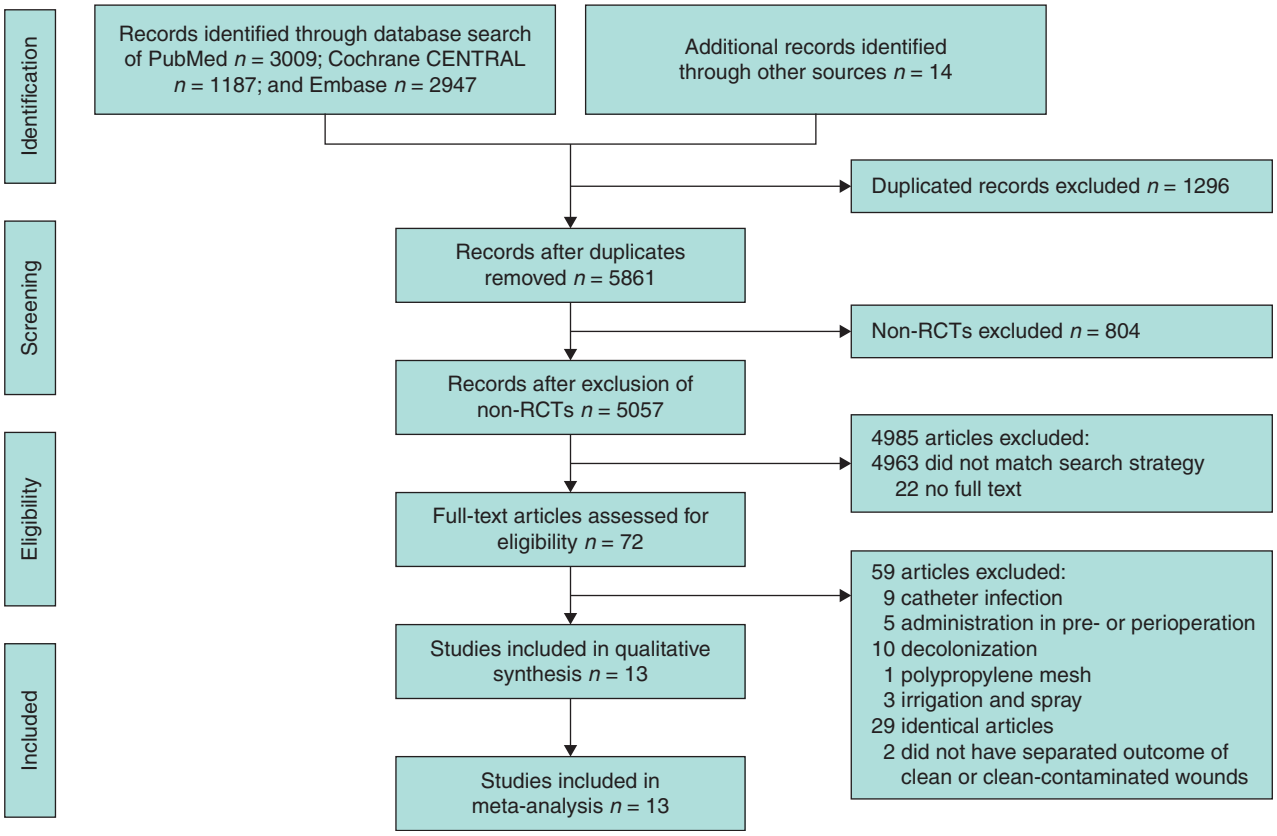

Fig. 1 Flowchart of study selection for systematic review and meta-analysis

RCT, randomized controlled trial.

mupirocin preoperatively[22,28], vancomycin powder intraoperatively[24,25] and other topical applications postoperatively[16–21,23,26,27]. The use of prophylactic antibiotics before surgery in the included trials was inconsistent, and only seven used i.v. prophylactic antibiotics[21–25,27,28] (*Table 1*). Other perioperative management related to SSI and definition of outcomes varied among these trials (*Tables S4* and *S5*).

Quality of the trials

Table S3 summarizes the results of the trial quality assessment. Most trials (10 of 13) had adequate randomization and sequence descriptions, but only six utilized allocation concealment. In the blinding domains, five of 13 had a high risk of bias in participant blinding. In some trials, blinding could not be done completely owing to limitations in drug application; however, there were no deviations from the intended intervention. The risk of bias of assessor blinding was unclear in most trials (nine of 13). Nine of 13 used the ITT analytical method, and eight had a low risk of bias in the selective reporting domain.

Efficacy outcomes

Ten of the included trials[16–19,22–26,28] were pooled to compare the prophylactic effect of topical antibiotics to a placebo in clean post-surgical wounds. *Figure 2* demonstrates the RR and incidence of SSI in both groups for each type of surgery. The total incidence of SSI was 100 of 2833 in the topical antibiotics group and 132 of 3502 in the non-antibiotic group. Compared with non-antibiotic agents, the use of topical antibiotics did not result in a statistically significant difference in SSI reduction in all populations (RR 0.89, 95 per cent c.i. 0.59 to 1.32; $P = 0.56$, $I^2 = 48$ per cent). The use of topical antibiotics in all types of surgery was not associated with a reduction in SSI, including dermatological surgery (four trials; RR 0.77, 95 per cent c.i. 0.39 to 1.55 ($P = 0.46$, $I^2 = 65$ per cent)), ocular surgery (one trial; RR 0.08, 95 per cent c.i. 0.00 to 1.52 ($P = 0.09$)), spinal surgery (two trials; RR 1.34, 95 per cent c.i. 0.65 to 2.77 ($P = 0.43$, $I^2 = 0$ per cent)), orthopaedic surgery (two trials; RR 0.69, 95 per cent c.i. 0.37 to 1.29 ($P = 0.25$, $I^2 = 0$ per cent)), and cardiothoracic surgery (one trial; RR 1.60, 95 per cent c.i. 0.79 to 3.25 ($P = 0.19$)).

Safety outcomes

Five trials collected data on contact dermatitis (*Fig. 3*)[16,17,20,26,27]. The overall RR of contact dermatitis was not statistically significantly different between topical antibiotics and non-antibiotic agents (RR 2.79, 95 per cent c.i. 0.51 to 15.19 ($P = 0.24$, $I^2 = 0$ per cent)). In dermatological (RR 5.40, 95 per cent c.i. 0.63 to 46.13 ($P = 0.12$, $I^2 = 0$ per cent)) and ocular surgeries (RR 0.93, 95 per cent c.i. 0.06 to 14.77; $P = 0.96$), the risk of contact dermatitis with topical antibiotics was not statistically significant different compared with non-antibiotic agents.

Sensitivity analysis

The subgroup analyses of administration according to the different operative phases are presented in *Fig. 4*. In the preoperative phase, nasal mupirocin did not reduce SSI *versus* non-antibiotic agents (RR 1.16, 95 per cent c.i. 0.60 to 2.24 ($P = 0.67$, $I^2 = 39$ per cent)). Similarly, topical vancomycin did not reduce SSI *versus* non-antibiotic agents (RR 1.34, 95 per cent c.i. 0.65 to 2.77 ($P = 0.43$, $I^2 = 0$ per cent)) in the intraoperative phase. Moreover, topical antibiotics did not reduce SSI *versus* non-antibiotic agents

Table 1 Study baseline ($n = 13$)

Study	Type of surgery	Wound classification	Regimen	Administrated route
Dermatologic surgery				
Dixon 2006	Skin lesion excision	I	Mupirocin ointment	Topical
Smack 1996	Ambulatory surgery	I	Bacitracin	Topical
Taylor 2011	Remove dermatosis papulosa nigra	I	Polymyxin B sulfate/bacitracin zinc	Topical
Heal 2009	Minor skin excision	I	Chloromycetin ointment	Topical
Draelos 2011	Remove seborrheic keratoses	I	Polymyxin B sulfate/bacitracin zinc bid	Topical
Abdominal surgery				
Neri 2008	Laparoscopic cholecystectomy	II	Rifamycin	Topical
Orthopaedic surgery				
Kalmeijer 2002	Prosthetic implant material	I	Mupirocin ointment bid	Nasal
Kamath 2005	Femur fracture	I	Chloramphenicol	Topical
Spinal surgery				
Mirzashahi 2018	Open spine surgery	I	1-2 g vancomycin powder	Topical
Tubaki 2013	Open spine surgery	I	1 g vancomycin powder	Topical
Ocular surgery				
Ashraf 2020	Periocular surgery	I	Erythromycin, bacitracin zinc, or bacitracin zinc plus polymyxin B sulfate ophthalmic ointment	
Cardiothoracic surgery				
Khalighi 2014	Cardiac electronic implantable device procedure	I	Povidone iodine or neomycin ointment	Topical
Konvalinka 2006	Elective open-heart surgery	I	2% mupirocin ointment bid	Nasal

Study	Comparison	Number	Prophylactic systematic antibiotics	Prophylactic timing
Dermatologic surgery				
Dixon 2006	Placebo or sterile paraffin	Abx:262; placebo:247; paraffin:269	None	After surgery
Smack 1996	Petrolatum	Abx:444; placebo:440;	None	After surgery
Taylor 2011	Aquaphor Healing Ointment	Abx:20; placebo:20	None	21 days after surgery
Heal 2009	Paraffin ointment	Abx:488; placebo:484;	None	After suturing
Draelos 2011	Petrolatum-based ointment	Abx:30; placebo:30	None	7 days after surgery
Abdominal surgery				
Neri 2008	Placebo	Abx:24; placebo:24	Ceftriaxone	3 days after surgery
Orthopaedic surgery				
Kalmeijer 2002	Placebo	Abx:315; placebo:299;	Cefamandole or clindamycin	At least 2 doses before surgery
Kamath 2005	Placebo	Abx:47; placebo:45	Cefuroxime	3 days after surgery
Spinal surgery				
Mirzashahi 2018	Placebo	Abx:193; placebo:187;	Cefazolin or clindamycin	Before surgery
Tubaki 2013	Placebo	Abx:433; placebo:474	Cefuroxime	Before surgery
Ocular surgery				
Ashraf 2020	Ophthalmic lubricant ointments, mineral oil and petrolatum	Abx:201; placebo:187	None	On the surgical site(s) 4 times daily for 7 days after surgery
Cardiothoracic surgery				
Khalighi 2014	Povidone iodine sterile non-adherent pad or placebo	Povidone iodine:257; neomycin:263; sterile non-adherent pad:240; placebo:248	Gentamicin, cefazolin or vancomycin	3 days after surgery
Konvalinka 2006	Placebo	Abx:130; placebo:127	Cefazolin or clindamycin	7 days before surgery

Abbreviation: ABx, antibiotics.

in the postoperative phase (RR 0.65, 95 per cent c.i. 0.36 to 1.18 ($P = 0.16$, $I^2 = 52$ per cent)).

In addition, a sensitivity analysis was performed using the one-by-one exclusion method (*Table S6*). After combining the RR values of the remaining trials, no significant impact was found by excluding any individual trial from the final results. Furthermore, no individual trial was found to have a significant impact on the heterogeneity, based on I^2.

Discussion

In the general population, topical antibiotics did not contribute to a reduction in SSIs, compared to non-antibiotics, during the perioperative period. There was also no benefit found in dermatological, spinal, orthopaedic, and cardiothoracic surgery. Regarding safety, the risk of contact dermatitis did not increase with the use of topical antibiotics in dermatological, cardiothoracic, or ocular surgery.

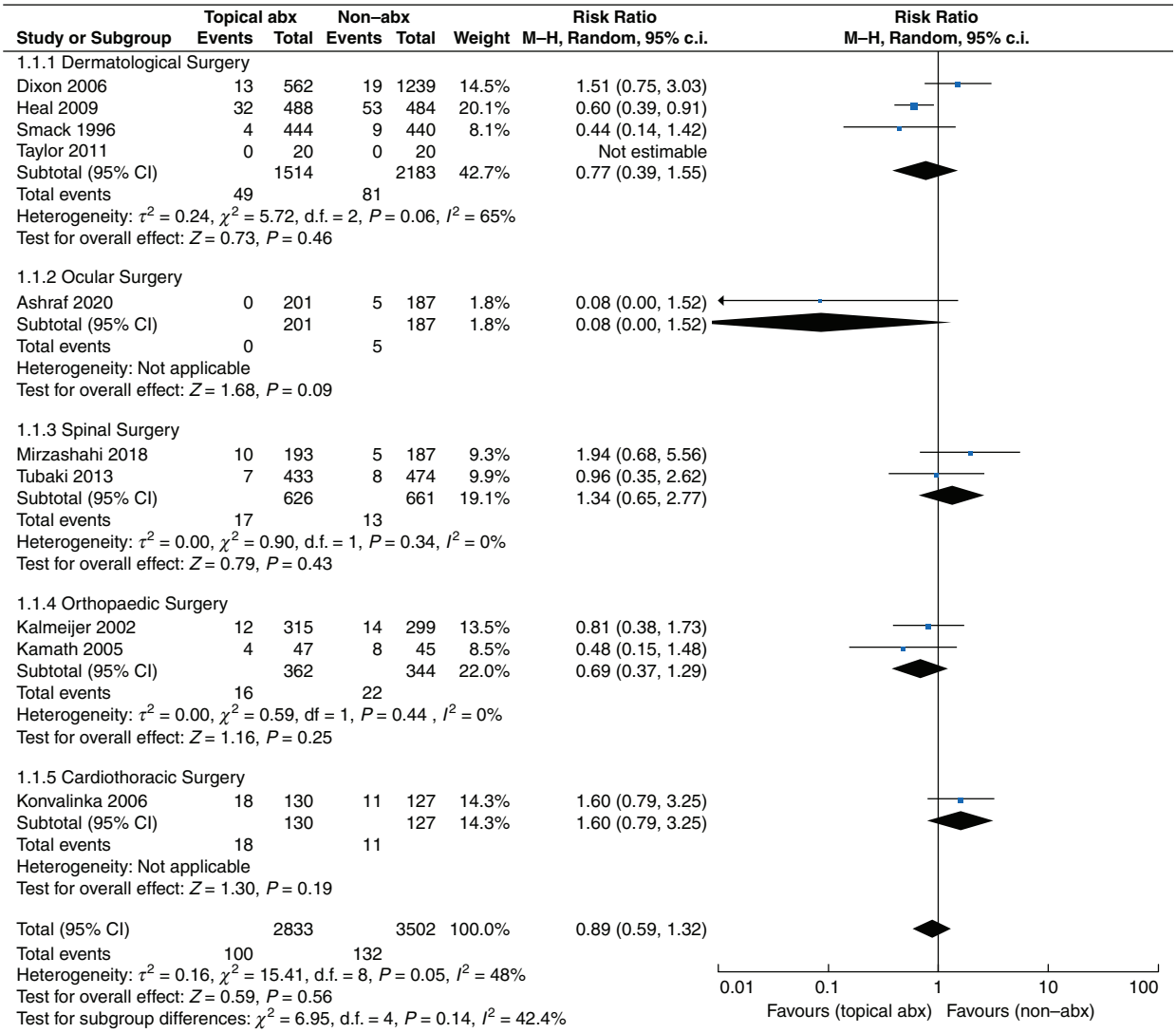

Fig. 2 Forest plot of surgical site infection

Abx, antibiotics; c.i., confidence interval.

A previous guideline[29] suggested that the use of topical antibiotics should be limited because of the unclear evidence and the potential adverse effects. Several meta-analyses have been performed to evaluate the effect of topical antibiotics. According to the meta-analysis conducted by Heal *et al.*[30], topical antibiotics reduced the risk of SSI *versus* placebo (RR 0.61, 95 per cent c.i. 0.42 to 0.87). This effect remained when compared to antiseptics (RR 0.49, 95 per cent c.i. 0.30 to 0.80). Similar findings were reported in the study by Tong *et al.*[11], where topical antibiotics were found to reduce the risk of SSI *versus* antiseptics or placebo (RR 0.56 (95 per cent c.i. 0.34 to 0.91) and RR 0.57 (95 per cent c.i. 0.37 to 0.86), respectively)[11].

In contrast, the pooled results of this study showed that topical antibiotics tended to decrease the risk of an SSI, although these were not statistically significantly different. Compared to the previously mentioned meta-analyses, more recent RCTs were included in the current study, while quasi-randomized study designs were excluded to reduce the risk of selection bias.

In addition, to clarify the prophylactic effect of the topical antibiotics, the focus was only on clean and clean-contaminated wounds. In contrast, Heal *et al.*[30] included clean, clean-contaminated, and contaminated wounds. In addition, the current study assessed the three phases of surgery (preoperative, intraoperative, and postoperative), while previous studies mainly focused on wounds after primary wound closure. Furthermore, subgroup and sensitivity analyses were carried out to assess the heterogeneity and efficacy in specific conditions.

The rates of SSIs in the modern-day outpatient dermatological setting are low, typically ranging from 0.7–4.0 per cent[31]. However, the prescription of topical antibiotics by dermatologists remains ubiquitous. Statistics show that dermatologists in the USA alone wrote three to four million prescriptions of topical antibiotics in 2003[31]. Nevertheless, the current evidence supporting their use in patients undergoing clean dermatological surgery is conflicting. The current study did not support the use of topical antibiotics compared with placebo in the dermatological field (RR 0.77, 95 per cent c.i. 0.39 to 1.55). Another meta-analysis[31] had a similar finding, and also highlighted the advantages of petrolatum-based management, suggesting that the moist environment provided by the ointment may benefit wound healing, rather than the bactericidal actions of the antibiotic[32].

In addition to wounds in patients with diabetes, wounds located in the groin or below the knees, basal cell carcinoma and

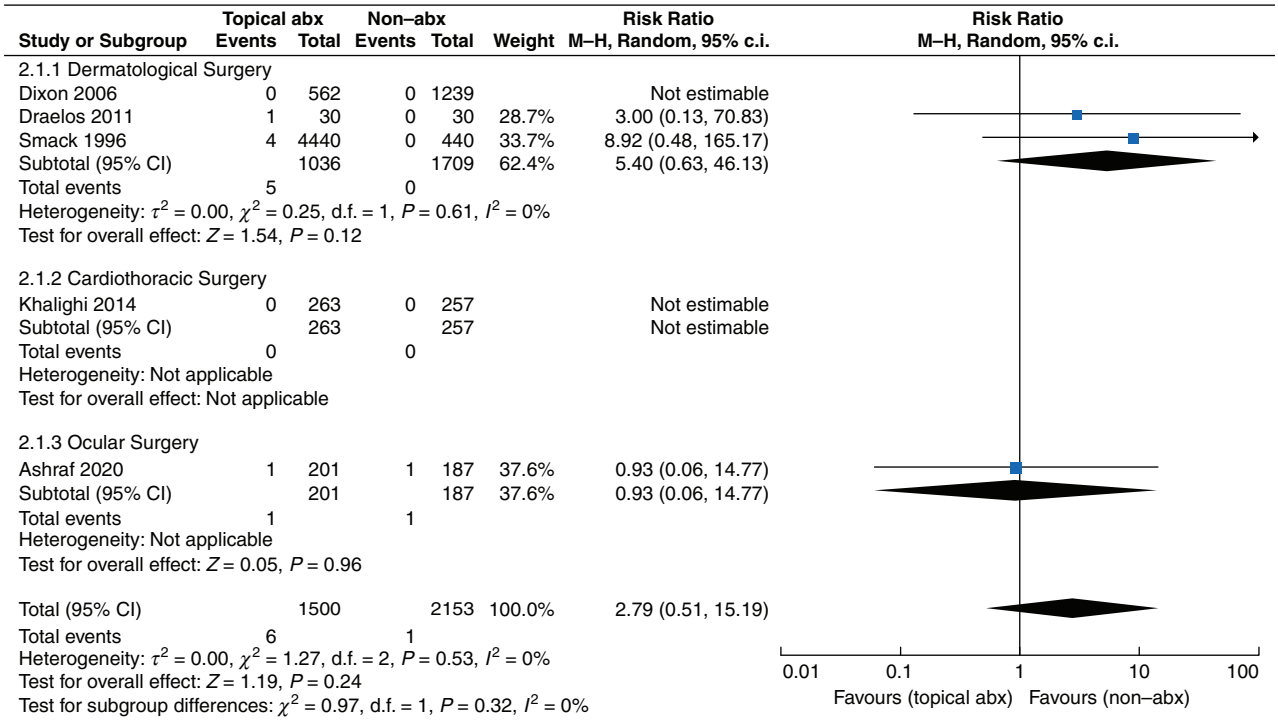

Fig. 3 Forest plot of contact dermatitis

Abx, antibiotics; CI, confidence interval.

squamous cell carcinoma excisions, skin grafts, flaps on the nose or ears, and wedge resections of the ears or lip are associated with higher rates of SSI[31]. Even in wounds with a higher risk of developing an infection, petrolatum is equally efficacious in preventing postoperative wound infections as topical antibiotics, based on the study's results[31]. Furthermore, oral prophylactic antibiotics might be another option for patients at high risk of infection[31].

In intraocular surgery, topical antibiotics are regularly administered owing to the restricted effect of systemic antibiotics caused by the blood–ocular barriers, such as the blood–aqueous barrier and the blood–retinal barrier[33]. Hence, intracameral or subconjunctival administration of topical antibiotics for surgical prophylaxis has been advocated to achieve adequate tissue drug concentration. However, a recent review on infection prophylaxis for periorbital Mohs surgery and reconstruction contradicted the recommendation of antibiotic ointment use[34]. Although the rate of SSI in oculoplastic surgery is low, typically between 0.04 and 1.7 per cent[26,35], the related complications of SSI can be devastating, possibly even vision-threatening. The included RCT of periocular surgery demonstrated that postoperative SSI was more common in the non-antibiotic group (5 *versus* 0 in the antibiotics group), although this did not reach statistical significance[26]. There is an overall trend toward increased prescription of topical antibiotics during intraorbital or oculofacial surgery by ophthalmologists.

For spinal surgery, the rate of SSI is approximately 0.7–10 per cent, despite appropriate antibiotic prophylaxis; this can cause severe complications, such as spinal instability and neurological deficit[36]. SSIs are often caused by common skin flora, mainly staphylococci. In addition, there have been growing cases of MRSA infection in recent years[10]. Therefore, vancomycin has been postulated to decrease the rates of SSI. Intravenous vancomycin was initially espoused by investigators but was later proven to be of no benefit in postoperative wound infection, compared to intravenous cephalosporins[37]. However, the intraoperative administration of vancomycin powder has gradually gained attention from researchers because of its high concentration levels at the site of operative wounds without causing any systemic side effects[24].

According to a recent guideline, for patients undergoing complicated spinal surgery, especially those with comorbidities, alternative prophylactic regimens such as intrawound vancomycin could be considered[36]. A meta-analysis, which pooled two RCTs and 19 retrospective cohort studies, found that vancomycin powder reduced SSI caused by Gram-positive bacilli and polymicrobial infections[38]. The current study only included two RCTs on spinal surgery[24,25], and pooled analysis failed to show any difference in the reduction of SSI rates *versus* placebo. The difference in results, compared to the previous meta-analysis[38], might be due to the potential confounding factors inherent to cohort studies.

Staphylococcus aureus is a leading cause of postoperative wound infections, and studies regarding orthopaedic and cardiothoracic surgery have explicitly shown that nasal colonization by *S. aureus* is a notable risk factor in the development of an SSI[6,12,39,40]. Of note, nasal decolonization has been shown to decrease the risk of *S. aureus*-related healthcare-associated infections in patients with known nasal carriage of *S. aureus*[22,28]. The evidence is particularly robust for patients undergoing cardiothoracic and orthopaedic surgery. Considering the high risk of SSI in cardiac surgery, reportedly up to 33 per cent[41], and the possible need for implant removal if SSI occurs in orthopaedic procedures[22], the preoperative intranasal application of mupirocin 2 per cent ointment for known *S. aureus* carriers is beneficial in decolonization and is highly supported by current evidence[6,9,42,43].

A meta-analysis conducted by the WHO Guidelines Development Group concluded that nasal decolonization using mupirocin ointment, with or without the combination of

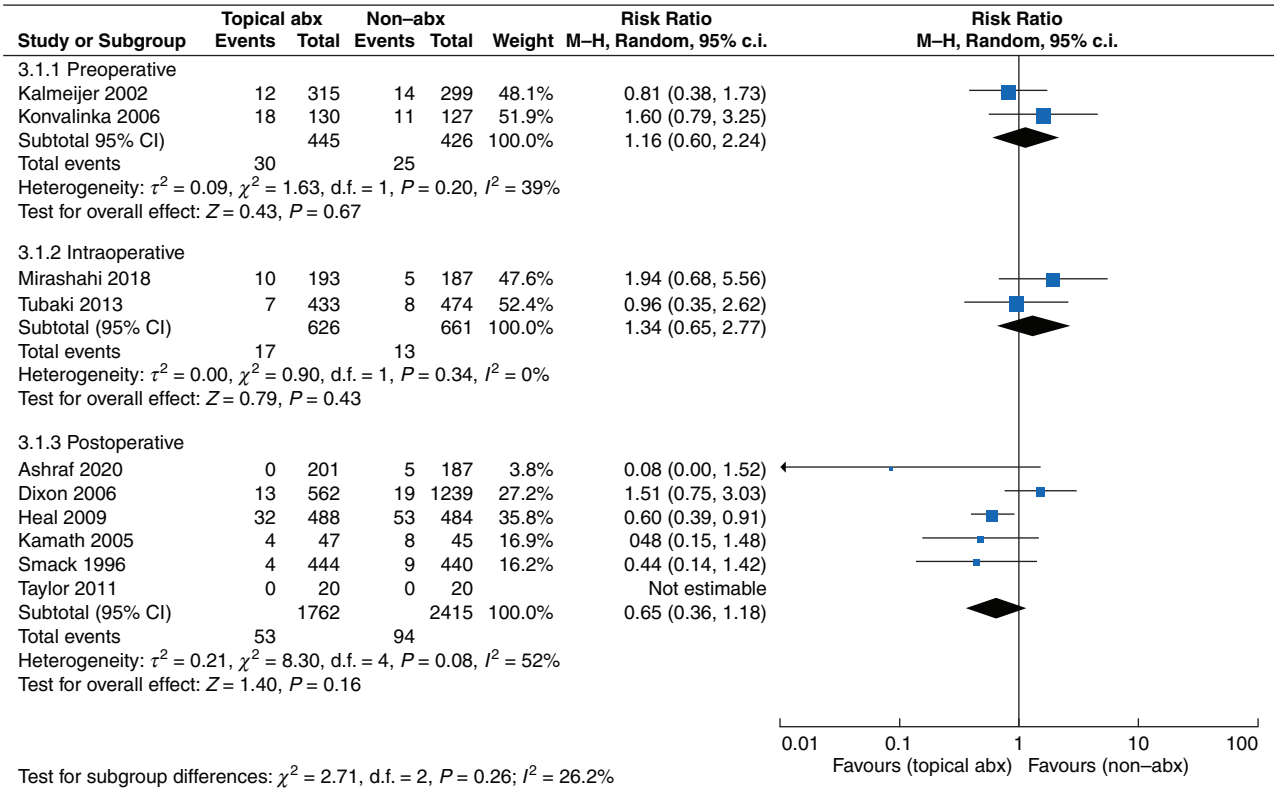

Fig. 4 Forest plot of different operative phases of administration

Abx, antibiotics; c.i., confidence interval.

chlorhexidine gluconate soap body wash preoperatively, had a significant benefit in reducing the incidence of *S. aureus* SSI in patients with known *S. aureus* carriage compared with placebo or no treatment (odds ratio 0.46, 95 per cent c.i. 031 to 069)[6].

In the current meta-analysis, trials evaluating the efficacy of preoperative nasal mupirocin administration were also included. The two included RCTs demonstrated that prophylactic intranasal mupirocin did not decrease the overall SSI or *S. aureus*-related infection rate[22,28]. Therefore, there is no clear evidence that routine nasal decolonization with mupirocin in all patients resulted in a reduction of SSIs *versus* placebo. The different results obtained by this study and the published evidence may lie in the enrolled patient groups (whether there was nasal carriage of *S. aureus* or not). The current study included patients who underwent surgery and were noticeably distinct from the WHO study groups, which consisted mainly of *S. aureus* carriers.

The strengths of the current study are that only RCTs were included in the meta-analysis to minimize selection bias and confounding factors. Further, more trials were included and provided additional results from the different types and different phases of surgery were provided. Furthermore, the sensitivity analysis strengthened the robustness of the primary outcome. Nevertheless, there are several limitations. Firstly, heterogeneity could not be avoided because the study design, perioperative management related to SSI, definition of outcomes, and enrolled patients varied among the trials. Although a subgroup and sensitivity analysis was performed, moderate heterogeneity still existed. Secondly, not all surgical wounds were included and therefore the results are not applicable to other patient groups. Finally, the number of trials in each subgroup was still insufficient, and patients at a high risk of infection were not discussed separately. Further RCTs are required to resolve these clinical problems.

Overall, this study does not support the routine use of topical antibiotics to prevent SSIs in patients undergoing clean surgeries, especially dermatological procedures. However, there is a potential benefit during ocular surgery because of the devastating outcomes of SSIs in these scenarios. In other types of surgery, the number of enrolled trials was limited and thus no conclusions concerning clean-contaminated surgical wounds can be made.

Supplementary material

Supplementary material is available at *BJS Open* online.

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PCJ and YMH contributed equally to this study, including the conception or design of the work and drafting of the manuscript. MCL and HST contributed to the acquisition, analysis, and interpretation of the data for this study. All authors critically revised the manuscript, gave final approval, agreed to be accountable for all aspects of work, and ensured its integrity and accuracy. Po-Jung Chen and Yi-Ming Hua had an equal contribution to the present study.

Disclosure. The authors declare no conflicts of interest.

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