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Intracavity lavage and wound irrigation for prevention of surgical site infection (Review)

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[Intervention Review]

Intracavity lavage and wound irrigation for prevention of surgical site infection

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ABSTRACT

Background

Surgical site infections (SSIs) are wound infections that occur after an operative procedure. A preventable complication, they are costly and associated with poorer patient outcomes, increased mortality, morbidity and reoperation rates. Surgical wound irrigation is an intraoperative technique, which may reduce the rate of SSIs through removal of dead or damaged tissue, metabolic waste, and wound exudate. Irrigation can be undertaken prior to wound closure or postoperatively. Intracavity lavage is a similar technique used in operations that expose a bodily cavity; such as procedures on the abdominal cavity and during joint replacement surgery.

Objectives

To assess the effects of wound irrigation and intracavity lavage on the prevention of surgical site infection (SSI).

Search methods

In February 2017 we searched the Cochrane Wounds Specialised Register; the Cochrane Central Register of Controlled Trials (CENTRAL); Ovid MEDLINE; Ovid Embase and EBSCO CINAHL Plus. We also searched three clinical trials registries and references of included studies and relevant systematic reviews. There were no restrictions on language, date of publication or study setting.

Selection criteria

We included all randomised controlled trials (RCTs) of participants undergoing surgical procedures in which the use of a particular type of intraoperative washout (irrigation or lavage) was the only systematic difference between groups, and in which wounds underwent primary closure. The primary outcomes were SSI and wound dehiscence. Secondary outcomes were mortality, use of systemic antibiotics, antibiotic resistance, adverse events, re-intervention, length of hospital stay, and readmissions.

Data collection and analysis

Two review authors independently assessed studies for inclusion at each stage. Two review authors also undertook data extraction, assessment of risk of bias and GRADE assessment. We calculated risk ratios or differences in means with 95% confidence intervals where possible.

Main results

We included 59 RCTs with 14,738 participants. Studies assessed comparisons between irrigation and no irrigation, between antibacterial and non-antibacterial irrigation, between different antibiotics, different antiseptics or different non-antibacterial agents, or between different methods of irrigation delivery. No studies compared antiseptic with antibiotic irrigation.

Surgical site infection

Irrigation compared with no irrigation (20 studies; 7192 participants): there is no clear difference in risk of SSI between irrigation and no irrigation (RR 0.87, 95% CI 0.68 to 1.11; I^2 = 28%; 14 studies, 6106 participants). This would represent an absolute difference of 13 fewer SSIs per 1000 people treated with irrigation compared with no irrigation; the 95% CI spanned from 31 fewer to 10 more SSIs. This was low-certainty evidence downgraded for risk of bias and imprecision.

Antibacterial irrigation compared with non-antibacterial irrigation (36 studies, 6163 participants): there may be a lower incidence of SSI in participants treated with antibacterial irrigation compared with non-antibacterial irrigation (RR 0.57, 95% CI 0.44 to 0.75; I^2 = 53%; 30 studies, 5141 participants). This would represent an absolute difference of 60 fewer SSIs per 1000 people treated with antibacterial irrigation than with non-antibacterial (95% CI 35 fewer to 78 fewer). This was low-certainty evidence downgraded for risk of bias and suspected publication bias.

Comparison of irrigation of two agents of the same class (10 studies; 2118 participants): there may be a higher incidence of SSI in participants treated with povidone iodine compared with superoxidised water (Dermacyn) (RR 2.80, 95% CI 1.05 to 7.47; low-certainty evidence from one study, 190 participants). This would represent an absolute difference of 95 more SSIs per 1000 people treated with povidone iodine than with superoxidised water (95% CI 3 more to 341 more). All other comparisons found low- or very low-certainty evidence of no clear difference between groups.

Comparison of two irrigation techniques: two studies compared standard (non-pulsed) methods with pulsatile methods. There may, on average, be fewer SSIs in participants treated with pulsatile methods compared with standard methods (RR 0.34, 95% CI 0.19 to 0.62; I^2 = 0%; two studies, 484 participants). This would represent an absolute difference of 109 fewer SSIs occurring per 1000 with pulsatile irrigation compared with standard (95% CI 62 fewer to 134 fewer). This was low-certainty evidence downgraded twice for risks of bias across multiple domains.

Wound dehiscence

Few studies reported wound dehiscence. No comparison had evidence for a difference between intervention groups. This included comparisons between irrigation and no irrigation (one study, low-certainty evidence); antibacterial and non-antibacterial irrigation (three studies, very low-certainty evidence) and pulsatile and standard irrigation (one study, low-certainty evidence).

Secondary outcomes

Few studies reported outcomes such as use of systemic antibiotics and antibiotic resistance and they were poorly and incompletely reported. There was limited reporting of mortality; this may have been partially due to failure to specify zero events in participants at low risk of death. Adverse event reporting was variable and often limited to individual event types. The evidence for the impact of interventions on length of hospital stay was low or moderate certainty; where differences were seen they were too small to be clinically important.

Authors' conclusions

The evidence base for intracavity lavage and wound irrigation is generally of low certainty. Therefore where we identified a possible difference in the incidence of SSI (in comparisons of antibacterial and non-antibacterial interventions, and pulsatile versus standard methods) these should be considered in the context of uncertainty, particularly given the possibility of publication bias for the comparison of antibacterial and non-antibacterial interventions. Clinicians should also consider whether the evidence is relevant to the surgical populations under consideration, the varying reporting of other prophylactic antibiotics, and concerns about antibiotic resistance.

We did not identify any trials that compared an antibiotic with an antiseptic. This gap in the direct evidence base may merit further investigation, potentially using network meta-analysis; to inform the direction of new primary research. Any new trial should be adequately powered to detect a difference in SSIs in eligible participants, should use robust research methodology to reduce the risks of bias and internationally recognised criteria for diagnosis of SSI, and should have adequate duration and follow-up.

PLAIN LANGUAGE SUMMARY

'Washout' during surgery for prevention of surgical site infection

What is the aim of this review?

The aim of this review was to find out whether intracavity lavage and wound irrigation (washing out a wound during surgery) can help to prevent surgical site infection (SSI). Researchers from Cochrane collected and analysed all relevant studies (randomised controlled trials) to answer this question and found 59 relevant studies.

Key messages

The certainty of all the evidence we gathered on the effect of washing out wounds on SSIs was low or very low. This was due to problems with how results were reported, some small sample sizes and concern that not all relevant evidence was published. This means that the true effects of treatments may be substantially different from our results. Washing out surgical wounds may make no clear difference to SSI rates compared with not washing out. Using antibacterial solutions to wash out wounds may reduce infection rates compared with non-antibacterial products. Pumping the washing solution into the wound may reduce infections compared with other methods of washing out. Side effects were not well reported.

What was studied in the review?

Infections can often develop in wounds following surgery. This can prevent the wound from healing and can lead to infection spreading through the body. People with SSIs spend longer in hospital and are more likely to need a repeat operation. Techniques used to reduce the risk of infection include intracavity lavage or wound irrigation (washing out the wound during surgery using water or medicated solutions). We wanted to find out if this reduced SSI rates, and improved wound healing. We also wanted to find out about serious consequences such as severe infections that cannot be treated with antibiotics, abscesses, and lengthy hospital stays.

What are the main results of the review?

We found 59 studies involving 14,738 participants (both adults and children). Some studies enrolled only women because of the type of surgery (e.g. caesarean sections). The studies compared washing out wounds with no treatment, antibacterial and non-antibacterial washing solutions, and different methods of washing. Follow-up times ranged from a few days to several months but most were between two and eight weeks. Most studies did not state how they were funded, but when funding was reported it was mostly non-commercial.

Twenty studies involving 7192 participants compared washing out with no washing. The results showed no clear difference in SSI rates (low-certainty evidence). Antibacterial washing solutions may reduce infection rates compared with non-antibacterial solutions (low-certainty evidence from 36 trials involving 6163 participants). Two studies involving 484 participants compared standard washing methods (pouring using a jug or a syringe) with pumping or pulsing the washing solution. There may be fewer SSIs when the solution is pumped into the wound (low-certainty evidence). There may be fewer SSIs when a solution of povidone iodine is used compared with an alternative antiseptic (superoxidised water, Dermacyn) (low-certainty evidence from 1 trial with 190 participants). The results for all other comparisons showed no clear differences or were very uncertain. Wound reopening (dehiscence), infections, which are hard to treat with antibiotics, and deaths were not widely reported. Washing out wounds may not affect the length of time people stay in hospital (low- or moderate-certainty evidence).

How up to date is this review?

We searched for studies that had been published up to February 2017.

SUMMARY OF FINDINGS

Summary of findings for the main comparison. All irrigation compared with no irrigation for prevention of surgical site infection

All irrigation compared with no irrigation for prevention of surgical site infection

Patient or population: participants undergoing clean, clean-contaminated, contaminated or dirty surgical procedures

Setting: hospitals
Intervention: irrigation of any type
Comparison: no irrigation

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with no irrigation	Risk with irrigation				
SSI	Study population: participants undergoing clean-contaminated, contaminated or dirty surgical procedures		RR 0.87 (0.68 to 1.11)	6106 (14 RCTs)	⊕⊕⊖⊖ Low[1]	On the basis of the included studies there is no clear difference between the intervention and comparison groups in the incidence of SSI.
	98 per 1000	85 per 1000 (67 to 108)				
	Risk difference: 13 fewer SSI occur per 1000 with irrigation than with no irrigation (31 fewer to 10 more)					
Wound dehiscence	Study population: participants undergoing clean procedures (split-body design)		RR 1.17 (0.44 to 3.06)	30 (1 RCT)	⊕⊕⊖⊖ Low[2]	There is no clear difference between surgical sites treated with irrigation and those in the control condition. This is based on a single split-body design with small numbers of participants.
	200 per 1000	234 per 1000 (88 to 612)				
	Risk difference: 34 more wound dehiscences occur per 1000 with irrigation than with no irrigation (112 fewer to 412 more)					
Adverse events	Study population: participants undergoing clean-contaminated or dirty surgical procedures		RR 1.05 (0.76 to 1.44)	403 (3 RCTs)	⊕⊕⊖⊖ Low[3]	There is no clear difference in the number of adverse events between participants treated with irrigation and those in the control condition.
	247 per 1000	259 per 1000 (187 to 355)				
	Risk difference: 12 more per 1000 (from 59 fewer to 108 more)					

Adverse events: abscess formation	Study population: participants undergoing dirty or contaminated surgical procedures 149 per 1000 136 per 1000 **Risk difference:** 13 fewer per 1000 (from 69 fewer to 80 more)	RR 0.91 (0.54 to 1.54)	331 (3 RCTs)	⊕⊕⊕⊖ Moderate[4]	There is no clear difference in the number of adverse events between participants treated with irrigation and those in the control condition.

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the __relative effect__ of the intervention (and its 95% CI).

CI: confidence interval; **RR:** risk ratio; **SSI:** surgical site infection

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect

[1]Downgraded once for risk of bias in one or more domains other than performance bias in studies that account for more than 50% of the analysis weight; downgraded once for imprecision because confidence intervals include both benefit and harm. Publication bias could not be clearly ruled out but was not additionally downgraded for as the evidence was unclear.
[2]Downgraded twice for imprecision because confidence intervals are wide and fragile and include the possibility of both benefit and harm. There is also uncertainty as to whether the analysis was correctly adjusted for a split-body design.
[3]Downgraded once for imprecision and once for high risk of detection bias in the study with 77% of the analysis weight.
[4]Downgraded once for imprecision.

Summary of findings 2. Irrigation with antibacterial solution compared with irrigation with non-antibacterial solution for prevention of surgical site infection

Irrigation with antibacterial compared with non-antibacterial solution for prevention of surgical site infection

Patient or population: participants undergoing clean, clean-contaminated, contaminated or dirty surgical procedures
Setting: hospitals
Intervention: irrigation with antibacterial solution (antiseptic or antibiotic)
Comparison: irrigation with solution without antibacterial properties

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with non-antibacterial	Risk with antibacterial				

SSI	Study population: participants undergoing clean-contaminated, contaminated or dirty surgical procedures		RR 0.57 (0.44 to 0.75)	5141 (30 RCTs)	⊕⊕⊖⊖ Low[1]	The included studies found that there may be fewer SSIs in participants treated with antibacterial irrigation compared with those treated with non-antibacterial irrigation.
	140 per 1000	80 per 1000 (62 to 105)				
	Risk difference: 60 fewer SSI occur per 1000 with antibacterial irrigation than with non-antibacterial (78 to 35 fewer)					
Wound dehiscence	Study population: participants undergoing clean or clean-contaminated surgical procedures		RR 1.26 (0.65 to 2.45)	660 (3 RCTs)	⊕⊖⊖⊖ Very low[2]	The effect of antibacterial compared with non-antibacterial irrigation on wound dehiscence is very uncertain.
	45 per 1000	56 per 1000 (29 to 109)				
	Risk difference: 11 more wound dehiscences occur per 1000 with antibacterial irrigation than with non-antibacterial (16 fewer to 64 more)					
Adverse events	Study population: participants undergoing clean, clean-contaminated or dirty surgical procedures		RR 0.55 (0.22 to 1.34)	178 (3 RCTs)	⊕⊕⊖⊖ Low[3]	It is unclear whether there is a difference in the incidence of all adverse events between participants treated with antibacterial irrigation compared with those treated with non-antibacterial irrigation.
	67 per 1000	37 per 1000 (15 to 90)				
	Risk difference: 30 fewer adverse events occur per 1000 with antibacterial irrigation than with non-antibacterial (53 fewer to 23 more)					
Adverse events: abscess formation	Study population: participants undergoing clean-contaminated, contaminated or dirty surgical procedures		RR 0.82 (0.42 to 1.62)	1309 (9 RCTs)	⊕⊖⊖⊖ Very low[4]	The effect of antibacterial compared with non-antibacterial irrigation on abscess formation is very uncertain
	31 per 1000	25 per 1000 (13 to 50)				
	Risk difference: 6 fewer abscesses form per 1000 with antibacterial irrigation than with non-antibacterial (18 fewer to 19 more)					

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: confidence interval; **RR:** risk ratio; **SSI:** surgical site infection

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect

Moderate quality: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low quality: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect
Very low quality: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect

[1]Downgraded once for risk of bias due to high risk of bias for at least one domain in studies contributing over 50% of the weight and once for probable publication bias. We did not further downgrade for inconsistency because the inconsistency present appeared due to the difference between larger and smaller studies and hence was accounted for by the downgrade for potential publication bias.
[2]Downgraded once for inconsistency due to study with highest weight showing effect in opposite direction to other included studies, once for high risk of bias and twice for imprecision, due to confidence intervals being wide and fragile, and including both benefit and harm.
[3]Downgraded twice for imprecision due to wide and fragile confidence intervals, which included both benefit and harm, as well as no difference between interventions.
[4]Downgraded once for risk of bias in studies with the majority of the weight and twice for imprecision due to wide and fragile confidence intervals, which included both benefit and harm, as well as no difference between interventions.

Summary of findings 3. Standard irrigation compared with pulsatile irrigation for prevention of surgical site infection

Standard irrigation compared with pulsatile irrigation for prevention of surgical site infection

Patient or population: participants undergoing clean, clean-contaminated, contaminated or dirty surgical procedures
Setting: hospital
Intervention: standard irrigation with saline
Comparison: pulsatile irrigation with saline

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with standard irrigation	Risk with pulsatile irrigation				
SSI	Study population: participants undergoing clean or clean-contaminated surgical procedures		RR 0.34 (0.19 to 0.62)	484 (2 RCTs)	⊕⊕⊖⊖ Low[1]	Included studies show that there may be fewer SSIs in participants treated with pulsatile saline irrigation compared with standard techniques; the evidence is low certainty due to high risk of biases in the study contributing the majority of participants and weight to the analysis.
	165 per 1000	56 per 1000 (31 to 103)				
	Risk difference: 109 fewer SSI occur per 1000 with pulsatile irrigation than with standard (134 fewer to 62 fewer)					
Wound dehiscence	Study population: participants undergoing clean-contaminated surgical procedures		RR 0.31 (0.01 to 7.55)	128 (1 RCT)	⊕⊕⊖⊖ Low[2]	There is no clear difference in the incidence of wound dehiscence between groups treated with standard or pulsatile techniques of saline irrigation.
	16 per 1000	5 per 1000				

	(0 to 122)				Confidence intervals include both benefit and harm and are wide and fragile.
	Risk difference: 11 fewer wound dehiscences occur per 1000 with pulsatile irrigation than with standard (16 fewer to 106 more)				
Adverse events	Study population: participants undergoing clean-contaminated surgical procedures	RR 1.31 (0.87 to 1.97)	128 (1 RCT)	⊕⊕⊖⊖ Low[2]	There is no clear difference in the incidence of adverse events between groups treated with standard or pulsatile techniques of saline irrigation. Confidence intervals include both benefit and harm and are wide and fragile.
	486 per 1000 371 per 1000				
	Risk difference: 115 fewer adverse events occur per 1000 with pulsatile irrigation (360 fewer to 48 more)				
Adverse events: abscess formation	There were no reported data on abscess formation				

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: confidence interval; **RR:** risk ratio; **SSI:** surgical site infection

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect

[1]Downgraded twice for high risk of bias in multiple domains for study contributing most of the weight.
[2]Downgraded twice for imprecision due to wide and fragile confidence intervals, which include both benefit and harm.

BACKGROUND

Description of the condition

Surgical site infections (SSIs) encompass a range of superficial to deep wound infections that can occur after an operative procedure. SSIs are a preventable complication, responsible for substantial financial burden to health services that can result in poorer patient outcomes, increased mortality, morbidity and reoperation rates. A 2006 prevalence survey in the UK National Health Service (NHS) indicated that approximately 8% of all patients (5743/75,694 patients over a four-month period) admitted to hospital suffer healthcare-associated infections, with 15% of these infections being SSIs (Smyth 2008). A US study found that in over 750,000 episodes of surgical hospitalisation, 1% resulted in a SSI, and similar estimates have been found in France (Astagneau 2009; De Lissovoy 2009). However, such values are known to underestimate the levels of SSI by not considering those that develop outside hospitals (Bruce 2001; Gibbons 2011), as most SSIs present within the first 30 days following a procedure, although commonly between the fifth and tenth postoperative day (NICE 2008). Patients who develop SSIs have longer hospital stays and incur higher treatment costs than other patients; in some types of surgery they also have higher mortality rates (Coello 2005; Jenks 2014). Diagnosis with a SSI after hospital discharge is associated with a greater number of healthcare visits, higher resource use, and more readmissions (Perencevich 2003). While more data are available for Western healthcare settings, SSI was the leading cause of hospital-acquired infection in a systematic review of studies in low- and middle-income countries (Allegranzi 2010). Surgical site infection can also contribute to wound dehiscence, which is also a primary outcome of this review; such wounds may then convert to healing by secondary intention with a resultant increased healing time and impact on the individual and on costs to the health service.

While the cause of SSIs is multifactorial, recognised risk factors include: length of hospital stay, obesity, patient co morbidities, duration and complexity of surgery, and degree of wound contamination (Anderson 2008; Chemaly 2010; Edwards 2008; Korol 2013; Omran 2007). Using the classification system adopted by the Centers for Disease Control and Prevention (CDC; HICPAC 1999), wounds can be classified by their level of contamination as follows.

- Clean (Class 1): noninfective operative wounds in which no inflammation is encountered, with no involvement of respiratory, gastrointestinal, genitourinary tract, and oropharyngeal cavity.
- Clean-contaminated (Class 2): operative wounds in which either the respiratory, gastrointestinal, or genitourinary tract is entered under controlled conditions and with only minor contamination. This category specifically includes wounds as a result of operations involving the biliary tract, appendix, and oropharynx, provided no evidence of infection or a major break in sterile technique is encountered.
- Contaminated (Class 3): fresh, accidental wounds, resulting from operations with major breaks in sterile technique or gross spillage from the gastrointestinal tract, and incisions in which acute, nonpurulent (free from pus) inflammation is encountered. This category includes traumatic lacerations.
- Dirty (Class 4): old traumatic wounds with retained devitalised tissue and those that involve existing clinical infection or perforated viscera. Organisms causing postoperative infection are likely to be present in the operative field before the operation.

The risk of developing a SSI is related to the level of contamination of the wound. Higher classifications of contamination are associated with higher risks of a SSI, as demonstrated in recent surveillance of surgical infections in NHS hospitals in England, which showed that gastrointestinal procedures, especially large bowel surgery, carry the highest risk of bacterial contamination (10.2%) (Public Health England 2014). Conversely, hip and knee prosthesis surgeries were shown to carry the lowest risk of infection, with an occurrence rate of 0.7% and 0.6%, respectively (Public Health England 2014).

Standard definitions of SSIs exist, as described by the CDC, the Surgical Site Infection Surveillance Service, the Southampton wound scoring system, and the ASEPSIS score (Bailey 1992; Horan 1992; Ridgeway 2005; Wilson 1986). The most commonly applied definition by the CDC describes three levels of SSI (Horan 1992). The lowest level of SSI can be defined as '*superficial incisional*' infections. These are limited to the skin and subcutaneous tissue. Such infections are identified by localised clinical (Celsian) signs such as redness, pain, heat, swelling, or the drainage of pus. '*Deep incisional*' infections affect the fascial and muscular layers and are identified by the presence of pus, abscess, fever, localised tenderness, or the separation of incision edges. Finally, 'cavity space' infection is considered the most severe level of SSI. Such infections can be identified by the drainage of pus, formation of an abscess or histological, radiological, or visual signs during reoperation. These involve anatomical parts of the body that have been manipulated during a surgical procedure, for example, a joint cavity or the peritoneum. Visceral infection is not included within the scope of the CDC guidelines.

SSIs are not restricted to these definitions and are often accompanied by microbiological evidence from microscopy and culture of infection tissue and fluid. However, it is important to note that normal flora may colonise superficial skin sites, and therefore positive microbiological growth in the absence of clinical signs is rarely indicative of SSIs.

Description of the intervention

Surgical wound irrigation is an intraoperative surgical technique, which may reduce the rate of SSIs by the removal of debris (dead or damaged tissue), metabolic waste, and wound exudate. It aims to create the optimal environment for wound healing, and is used with variable uptake among surgical practitioners (Barnes 2014). The theoretical advantage of surgical wound irrigation is to reduce the bacterial load in a surgical or traumatic wound by a combination of water pressure, dilution, or the application of antimicrobial agents. Usually, irrigation is undertaken at the end of an operative procedure, prior to wound closure, however postoperative wound irrigation may also be applied.

Intracavity lavage is another intraoperative surgical technique, which utilises similar principles to surgical wound irrigation with the aim of reducing SSI risk. It can be adopted during any operation that exposes a bodily cavity, but is most commonly used for procedures on the abdominal (peritoneal) cavity and during joint replacement surgery. Both wound irrigation and intracavity lavage can be altered by three basic variables: volume of irrigation

fluid; mechanism/timing of delivery; or solution composition. We use the terms 'irrigation' and 'lavage' separately in this review, however they do not necessarily describe distinctly separate surgical techniques, and may often refer to similar methods of washout for a cavity or a wound.

How the intervention might work

The aim of wound irrigation and lavage is to reduce the bacterial load in a surgical or traumatic wound by a combination of water pressure, dilution, or the application of antimicrobial agents. Usually, this is undertaken at the end of an operative procedure, prior to wound closure, to reduce the likelihood of the introduction of bacteria.

Both wound irrigation and intracavity lavage can be achieved using various solutions. Normal saline is commonly used along with antimicrobial agents for intracavity lavage. However, there is concern that antimicrobial agents may damage tissue and prevent normal healing. It is thought that the introduction of large volumes of fluid into a cavity or wound could wash away inflammatory cells vital to the host defence (Schultz 2011).

Why it is important to do this review

National Institute for Care and Health Excellence (NICE) guidelines reviewed evidence from 20 randomised controlled trials (RCTs) and concluded that the use of surgical wound irrigation or intracavity lavage could not be recommended to reduce the risk of SSIs (NICE 2008). The search used to inform this guideline is now almost 10 years old, making it likely that a number of additional trials will be available. In some areas of surgical practice this is likely to lead to changes in conclusions; we are aware of a recent systematic review which found a benefit to intraoperative irrigation over no irrigation in abdominal surgery (Mueller 2015); this included both RCTs and studies that we consider to be quasi-RCTs. A recent review restricted to prophylactic wound irrigation (excluding surgeries with high levels of contamination) has just been published (De Jonge 2017), which informed recent WHO guidance (WHO 2016) A recent expert consensus paper also identified the need for more evidence on several of the questions in this review (Barnes 2014). This review aims to update this evidence base.

OBJECTIVES

To assess the effects of wound irrigation and intracavity lavage on the prevention of surgical site infection (SSI).

METHODS

Criteria for considering studies for this review

Types of studies

We included published and unpublished randomised controlled trials (RCTs), including cluster-RCTs, irrespective of language of report. We excluded studies using quasi-randomisation (i.e. a method of allocating participants to different forms of care that is not truly random, for example, allocation by date of birth, day of the week, medical record number, month of the year, or the order in which participants are included in the study (alternation)).

Types of participants

All patients undergoing elective or emergency surgery, where surgery was defined as a procedure involving: (1) an incision being made into the skin forming an open wound; or (2) an operative procedure to treat an existing traumatic wound/injury. We included studies including either, or both, adults and children. Only studies focusing on wounds intended to heal by primary intention (i.e. where wound edges are held together after surgery) were included in this review. This included interventions for open fractures or operated traumatic wounds if the aim of the procedure was to heal the wound by primary intention. We excluded surgery intended to create wounds with planned healing by secondary intention (i.e. left open to heal through the formation of new tissues) or wounds healing by delayed primary/tertiary intention (wounds which are intentionally initially left open for a period of time, but then have the edges brought together for the rest of the healing process).

Types of interventions

We included studies where the type or schedule of intraoperative washout (either wound irrigation or intracavity lavage) was the only systematic difference between study arms.

Surgical wound irrigation may occur as a singular event during wound closure, or involve the irrigation of a wound continuously/repeatedly during surgery, or in the postoperative period. Types of surgical wound irrigation may vary by volume of irrigation fluid, mechanism of delivery, or solution composition. We did not include studies where the irrigation was confined solely to the interior of internal organs (e.g.) the uterus, bowel or bladder, but did include studies in which (e.g.) the peritoneum was irrigated in addition to such procedures. We did not include studies of surgery in the oral or aural cavities or in the eyes.

Intracavity lavage may also occur as a singular event during surgery, which exposes a body cavity, or involve the irrigation of a cavity continuously/repeatedly during surgery, or in the postoperative period. Types of intracavity lavage again may vary by volume of irrigation fluid, mechanism of delivery, or solution composition.

In practice we found that the terms 'irrigation' and 'lavage' are often used interchangeably. We included all studies in which a washout procedure was conducted and we have used the term 'irrigation' throughout the review. Where the term 'lavage' was used in the included studies, this is reflected in the Characteristics of included studies tables; this section also details all available information on the point(s) at which irrigation occurred during surgery. We did not pre-specify any subgrouping based on the use of irrigation or lavage or the level at which it was conducted; we have not conducted any post-hoc analysis based on this but have followed the protocol and grouped all forms of intraoperative washout. The only exception was where one study used procedures which were so different from the other studies in the comparison that we treated this separately.

We anticipated that likely comparisons in this review may include:

- comparison of wound irrigation/intracavity lavage with no washout;
- comparison of different solutions used for wound irrigation or intracavity lavage;
- comparison of different volumes of fluid used for wound irrigation or intracavity lavage;

- comparison of different mechanisms of delivery used for wound irrigation or intracavity lavage; and
- comparison of different schedules/timings of wound irrigation or intracavity lavage.

Types of outcome measures

We list primary and secondary outcome measures below. If a trial was otherwise eligible (correct study design, population, and intervention/comparator) but did not report a listed outcome, then we attempted to contact the study authors, in order to establish whether a relevant outcome was measured but not reported. However, we did not plan to exclude otherwise eligible studies solely on the basis of reported outcomes. In several instances author contact was not immediately successful and we recorded these studies as Studies awaiting classification.

Where possible, we anticipated grouping outcomes by the following time points; the review authors used their judgement as to whether statistical pooling within these time categories was appropriate:

- short-term: 30 days
- medium-term: more than 30 days to 12 months
- long-term: more than 12 months.

In practice we found that the overwhelming majority of the data reported were for time points of between two and eight weeks postoperatively, with the majority being at either four or six weeks, sometimes with interim but unreported follow-up points. We therefore decided that we would group all the data together for the outcomes reported; we did not consider dividing data reported at points that narrowly spanned 30 days to be informative.

Primary outcomes

- Surgical site infection measured as: occurrence of postoperative surgical site infection (SSI) as defined by the CDC criteria (Horan 2008), or the study authors' definition of SSI. We did not differentiate between superficial and deep incisional infection. We planned to document septicaemia or septic shock under this outcome.
- Wound dehiscence within 30 days of operation. This included both superficial dehiscence (involving skin and subcutaneous tissues) or deep dehiscence (burst abdomen or dehiscence of fascia). Postoperative wound dehiscence refers to wound disruption resulting from poor wound healing. This may be caused by various factors, including infection, as well as the type of incision and patient characteristics, such as diabetes or smoking (Sandy-Hodgetts 2015).

Secondary outcomes

- 30-day mortality/in-hospital mortality
- Proportion of participants with postoperative SSI using systemic antibiotics within 30 days of surgery
- Occurrence of infections that show antibiotic resistance
- Adverse events including postoperative abscess formation; we planned to include these, where reported, as total number of individuals with an adverse event in each intervention group
- Surgical re-intervention rates (including the placement of radiologically-guided drains and joint revision surgery)
- Mean length of hospital stay
- Number of hospital readmissions.

Search methods for identification of studies

Electronic searches

We searched the following electronic databases for randomised controlled trials:

- the Cochrane Wounds Specialised Register (searched 1 February 2017);
- the Cochrane Central Register of Controlled Trials (CENTRAL; 2017, issue 1) in the Cochrane Library (searched 1 February 2017);
- Ovid MEDLINE (1946 to 1 February 2017);
- Ovid MEDLINE (In-Process & Other Non-Indexed Citations) (searched 1 February 2017);
- Ovid Embase (1974 to 1 February 2017);
- EBSCO CINAHL Plus (1937 to 1 February 2017).

The search strategies for the Cochrane Wounds Specialised Register, CENTRAL, Ovid MEDLINE, Ovid Embase and EBSCO CINAHL Plus are available in Appendix 1. We combined the Ovid MEDLINE search with the Cochrane Highly Sensitive Search Strategy for identifying randomised trials in MEDLINE: sensitivity- and precision-maximising version (2008 revision) (Lefebvre 2011). We combined the Embase search with the Ovid Embase randomised trials filter terms developed by the UK Cochrane Centre (Lefebvre 2011). We combined the CINAHL Plus searches with the randomised trials filter terms developed by the Scottish Intercollegiate Guidelines Network (SIGN 2017). We did not impose any restrictions with respect to language, date of publication, or study setting.

We also searched the following clinical trials registries for ongoing studies in March 2017:

- ClinicalTrials.gov (searched 7 March 2017);
- World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP) (searched 7 March 2017);
- EU Clinical Trials Register (searched 7 March 2017).

Search strategies for the clinical trials registries are available in Appendix 1.

Searching other resources

We sought to identify other potentially eligible trials or ancillary publications by searching the reference lists of retrieved included trials as well as relevant systematic reviews, meta-analyses, and health-technology assessment reports.

Data collection and analysis

Selection of studies

Two review authors (CR and either TS or GN) independently assessed the titles and abstracts of the citations retrieved by the searches for relevance. After this initial assessment, we obtained full-text copies of all studies considered to be potentially relevant. Two review authors (GN and either CR or TS) independently checked the full papers for eligibility; disagreements were resolved by discussion and, where required, the input of a third review author (CR, TS, JD or RA as appropriate). Where required and

possible, we contacted study authors where the eligibility of a study was unclear. We recorded all reasons for exclusion of studies for which we had obtained full copies, where it was not immediately obvious that the study was ineligible after being ordered due to a very sparse citation record. We completed a PRISMA flowchart to summarise this process (Liberati 2009); Figure 1.

Figure 1. Study flow diagram

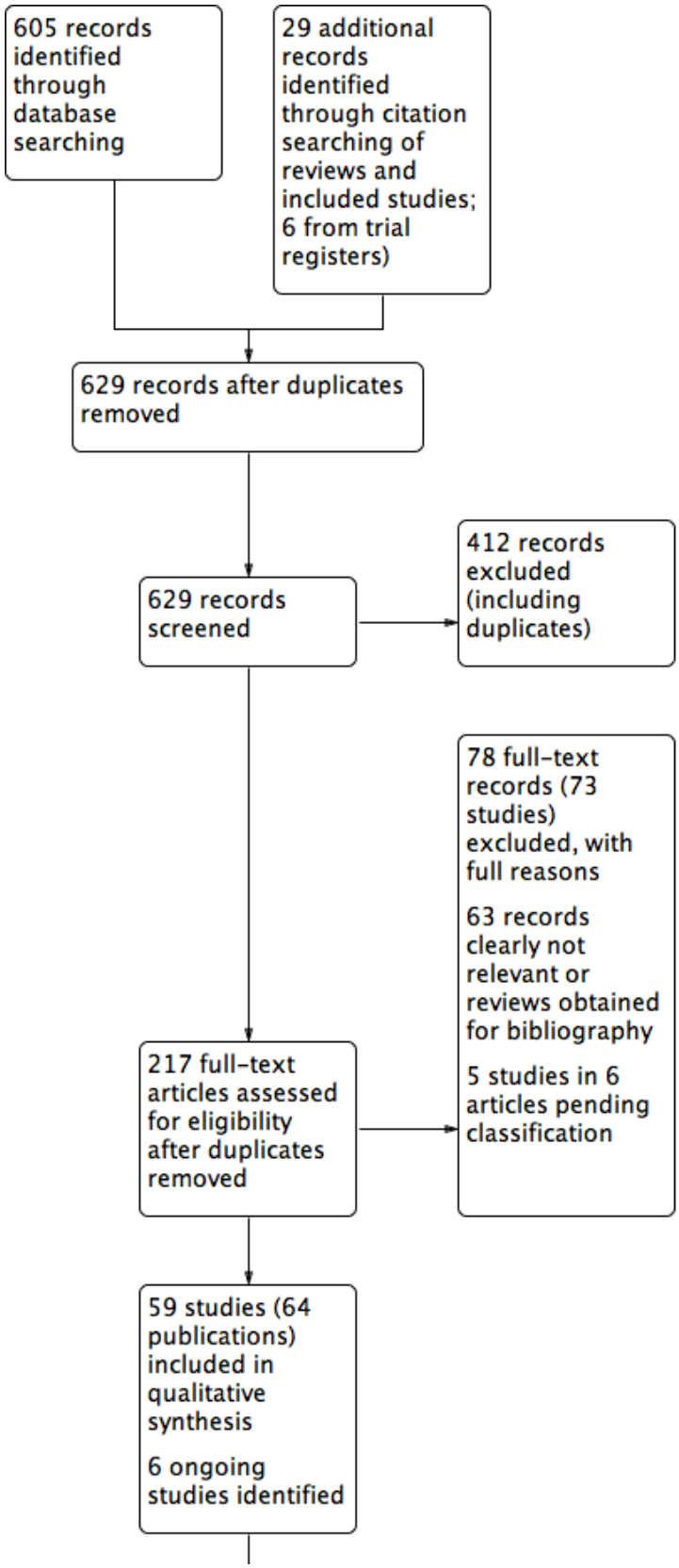
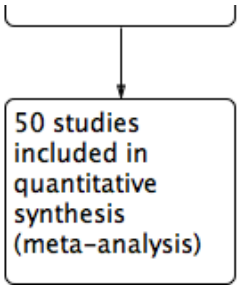


Figure 1. (Continued)



Where studies were reported in multiple publications/reports, we obtained all publications. Whilst we included the study only once in the review, we extracted data from all reports to ensure maximal relevant data were obtained. Where it was unclear whether publications referred to the same study we attempted to contact the authors for clarification.

Data extraction and management

We extracted and summarised details of the eligible studies using a data extraction sheet. Two review authors (two of CR,TS, GN, RA and AR) extracted data independently and resolved disagreements by discussion, drawing on a third review author (JD) where required. Where key data were missing from reports, we attempted to contact the study authors to obtain this information. Where a study with more than two intervention arms was included, we only extracted data from intervention and control groups that met the eligibility criteria.

We extracted the following data, where possible, by treatment group for the prespecified interventions and outcomes in this review. We planned to collect outcome data for relevant time points, as described in Types of outcome measures; in practice most studies reported only one time point.

- Country of origin
- Type of wound and surgery
- Unit of randomisation (e.g. participant or wound)
- Unit of analysis (e.g. participant or wound)
- Trial design (e.g. parallel; cluster)
- Number of participants/wounds randomised to each trial arm
- Eligibility criteria and key baseline participant data
- Details of treatment regimen received by each group
- Duration of treatment
- Details of any co-interventions
- Primary and secondary outcome(s) (with definitions and time points)
- Outcome data for primary and secondary outcomes (by group)
- Duration of follow-up.
- Number of withdrawals (by group)
- Publication status of study
- Source of funding for trial.

Assessment of risk of bias in included studies

Two review authors (two of CR, TS, GN, RA or AR) independently assessed included studies using the Cochrane approach for assessing risk of bias as detailed in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011a). We resolved disagreements through discussion or by consulting a third review author (typically JD). The tool addresses specific domains: sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessors, incomplete data, selective outcome reporting, and other issues – in this review we planned to record issues with unit of analysis, for example, where a cluster trial had been undertaken but analysed at the individual level in the study report (Appendix 2). We recorded issues with adjustment for paired data in split-body designs and with early stopping in this domain. We assessed blinding and completeness of outcome data for each of the review outcomes separately. In this review we anticipated that blinding of participants and personnel may not be possible. For this reason the assessment of the risk of detection bias focused on whether blinded outcome assessment was reported (because assessment of wound outcomes, such as breakdown and healing, can be subjective and at high risk of detection bias when outcome assessment is not blinded). We used blinding of outcome assessment to determine risk of bias from blinding in these instances. Although we recorded risk of bias from blinding of personnel and participants, we did not downgrade the certainty of the evidence for this alone, where the nature of the comparison made it highly likely. We presented our assessment of risk of bias using two 'Risk of bias' summary figures; one that is a summary of bias for each item across all studies, and a second that shows a cross-tabulation of each trial by all of the risk of bias items (Figure 2; Figure 3).

Figure 2. Risk of bias summary: review authors' judgements about each risk of bias item for each included study

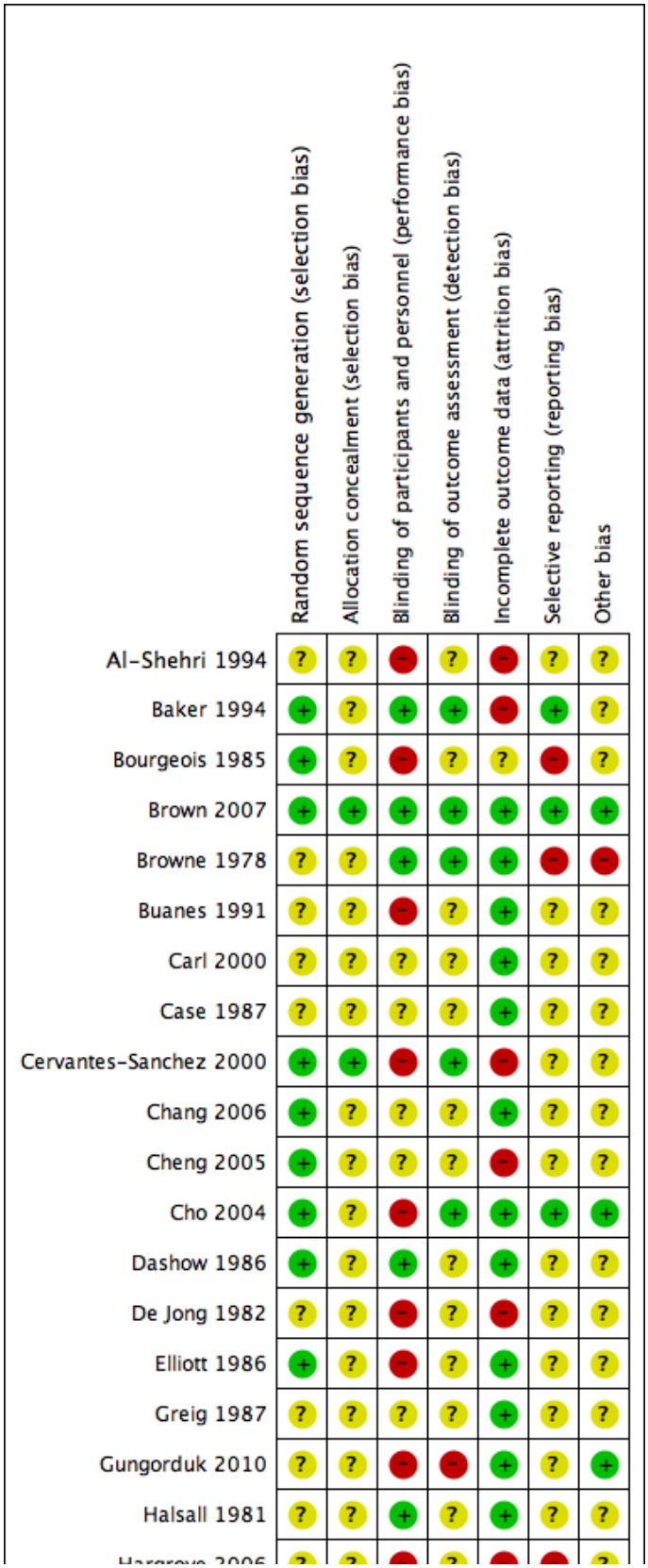


Figure 2. (Continued)

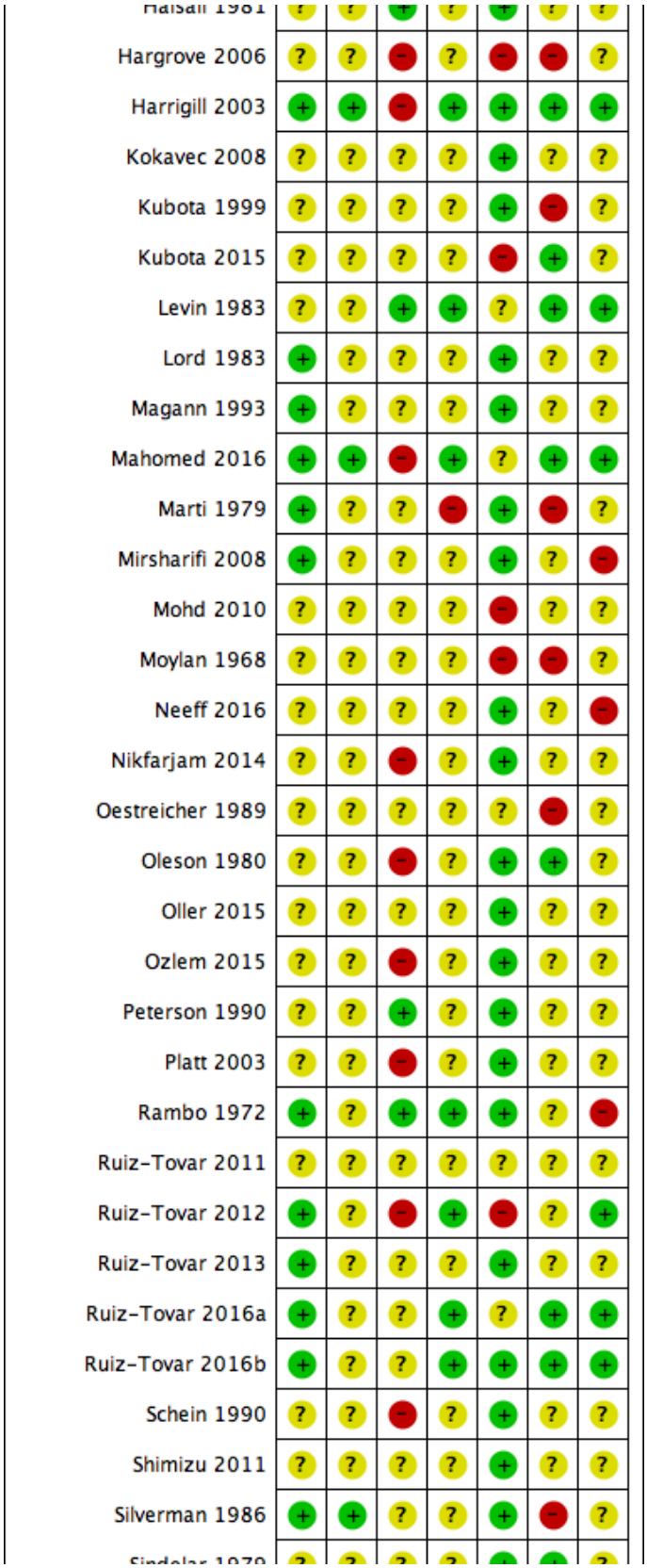


Figure 2. (Continued)

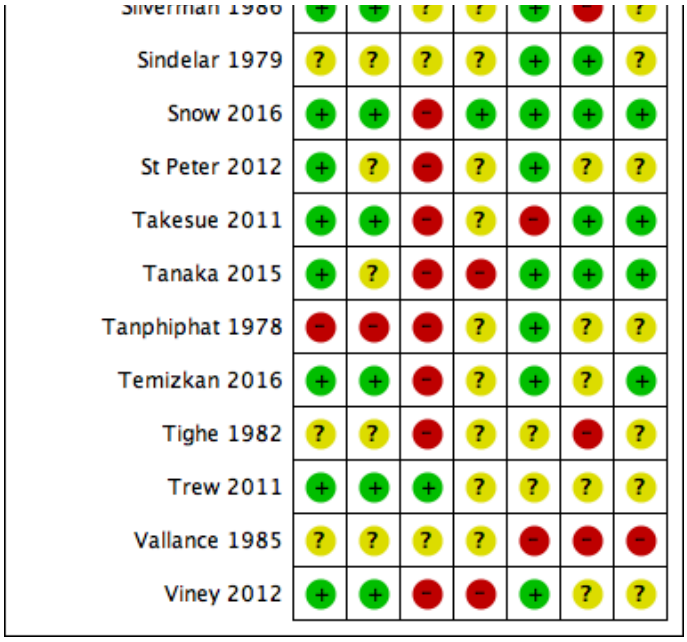
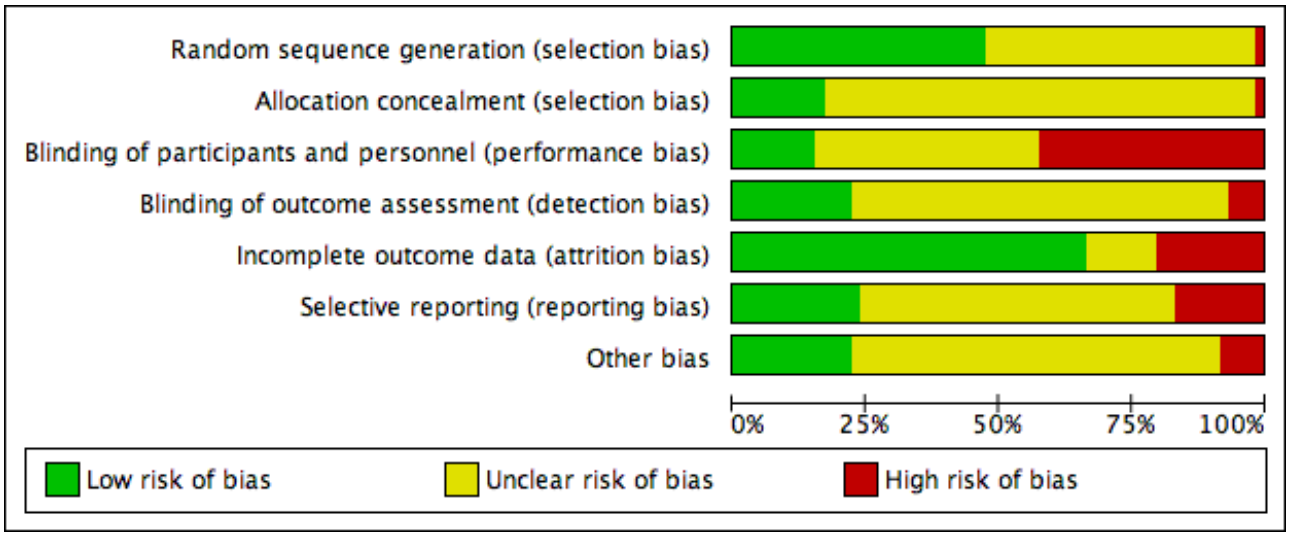


Figure 3. Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies



For trials using cluster-randomisation, we also planned to consider the risk of bias considering: recruitment bias, baseline imbalance, loss of clusters, incorrect analysis, and comparability with individually randomised trials (Higgins 2011b; Appendix 3).

Measures of treatment effect

For dichotomous outcomes, we calculated the risk ratio (RR) with 95% confidence intervals (CIs). For continuous outcomes we used the difference in means with 95% CIs, if all trials used the same or similar assessment scale. If trials had used different assessment scales, we planned to use the standardised difference in means with 95% CIs.

Unit of analysis issues

If included studies had randomised at the participant level and measured outcomes at the wound level, we planned to treat the participant as the unit of analysis when the number of wounds assessed appeared equal to the number of participants (e.g. one wound per person).

Particular unit of analysis issues in wound care trials can occur when: (1) studies randomise at the participant level, use the allocated treatment on multiple wounds per participant, and then analyse outcomes per wound; or (2) studies undertake multiple assessments of an outcome over time per participant. These approaches should be treated as cluster trials, alongside more

standard cluster designs – such as delivery of interventions at an organisational level.

Where a cluster trial had been conducted and correctly analysed we planned to meta-analyse effect estimates and their standard errors using the generic inverse-variance method in Review Manager 5 (RevMan 2014).

We planned to record where a cluster-randomised trial had been conducted, but incorrectly analysed as part of the 'Risk of bias' assessment. If possible, we planned to approximate the correct analyses based on guidance from the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011b), using information on:

- the number of clusters (or groups) randomised to each intervention group; or the average (mean) size of each cluster;
- the outcome data ignoring the cluster design for the total number of individuals (for example, number or proportion of individuals with events, or means and standard deviations); and
- an estimate of the intra cluster (or intra class) correlation coefficient (ICC).

If we had been unable to analyse the study data correctly, we planned to extract and present outcome data but not analyse it further.

We did not identify any cluster randomised studies, but did identify a split-body design in which two incisions on each participant were randomised to different treatment groups. This represented paired data and it was unclear that this had been adjusted for. Unadjusted paired data will generate confidence intervals wider than the true ones for the effect estimate. We presented the results of the single study with this design in narrative form, but did not include data from the study in any meta-analysis.

Dealing with missing data

It is common to have data missing from trial reports. Excluding participants post-randomisation from the analysis, or ignoring those participants who are lost to follow-up compromises the randomisation, and potentially introduces bias into the trial. Where there were missing data that we thought should be included in the analyses, or where data were unclear, we attempted to contact relevant study authors to request or clarify these data.

Where data remained missing for the proportion of participants with dehisced wounds or participants with SSI, we assumed that if randomised participants were not included in the results section of the paper, their wound did not show dehiscence or they did not have a SSI (i.e. in the analysis, missing participants were considered in the denominator but not the numerator). When appropriate, we planned to conduct a completed case analysis as a sensitivity analysis and also planned to explore alternative scenarios using different assumptions about missing cases. In the event only one trial had very substantive numbers of participants who were absent from the reported results and, because of clinical considerations we considered an ITT analysis non-conservative. We therefore conducted a completed case analysis and conducted a sensitivity analysis to explore the impact of excluding this trial from the meta-analysis.

For continuous variables, for example, length of hospital stay, and for all secondary outcomes, we presented available data from the study reports/study authors, but we did not impute missing data. Where measures of variance were missing, we planned to calculate these if this were possible. When calculation was not possible, we attempted to contact study authors. Where these measures of variation were not available, we excluded the study from any relevant meta-analyses that we conducted.

Assessment of heterogeneity

Assessment of heterogeneity can be a complex, multifaceted process. Firstly, we considered clinical and methodological heterogeneity: that is, the degree to which the included studies varied in terms of participant, intervention, outcome, and characteristics such as duration of follow-up. We supplemented this assessment of clinical and methodological heterogeneity with information regarding statistical heterogeneity - assessed using the Chi^2 test (we considered a significance level of $P < 0.10$ to indicate statistically significant heterogeneity) in conjunction with the I^2 statistic (Higgins 2003). The I^2 statistic examines the percentage of total variation across RCTs that is due to heterogeneity rather than chance (Higgins 2003). In general, I^2 values of 25%, or less, can be interpreted as a low level of heterogeneity (Higgins 2003), and values of 75%, or more, indicate very high heterogeneity (Deeks 2011). However, these figures are only a guide, and it has been recognised that statistical tests and metrics may miss important heterogeneity - thus, whilst these were assessed, the overall assessment of heterogeneity used these measures in combination with the methodological and clinical assessment of heterogeneity: see Data synthesis for further information about how we dealt with potential heterogeneity in the data analyses.

Assessment of reporting biases

Reporting biases arise when the dissemination of research findings is influenced by the nature and direction of results. Publication bias is one of a number of possible causes of 'small study effects', that is, a tendency for estimates of the intervention effect to be more beneficial in smaller RCTs. Funnel plots allow a visual assessment of whether small study effects may be present in a meta-analysis. A funnel plot is a simple scatter plot of the intervention effect estimates from individual RCTs against some measure of each trial's size or precision (Sterne 2011). We presented funnel plots for meta-analyses comprising 10 RCTs or more using Review Manager 5 (RevMan 2014). We also conducted Egger's test as a post-hoc measure on the advice of peer reviewers.

Data synthesis

We combined details of included studies in narrative review according to type of comparator and contamination level of wound. We planned to group outcomes by time period but in practice found that this was not helpful (see Differences between protocol and review). We considered clinical and methodological heterogeneity, and undertook pooling when studies appeared appropriately similar in terms of wound type, intervention type, duration of follow-up, and outcome type.

In terms of meta-analytical approach, our default approach was to use the random-effects model. We planned to only use a fixed-effect approach if clinical heterogeneity was thought to be minimal and statistical heterogeneity was not statistically significant for the Chi^2 value and 0% for the I^2 assessment (Kontopantelis 2013). We adopted this approach as it is recognised that statistical assessments can miss potentially important between-

study heterogeneity in small samples, hence the preference for the more conservative random-effects model (Kontopantelis 2012). Since either clinical or statistical heterogeneity indicated that a random-effects analysis was appropriate in all cases, we did not use any fixed-effect analyses. Where clinical heterogeneity was thought to be acceptable, or of interest, we planned that we would meta-analyse even when statistical heterogeneity was high, but would have attempted to interpret the causes behind this heterogeneity. We planned to consider using meta-regression for that purpose, if possible (Thompson 1999). In the event, heterogeneity was not sufficiently high to require this approach but we used some exploratory subgroup analyses to confirm that lower levels of heterogeneity were not a consequence of particular differences between interventions.

We presented data using forest plots, where possible. For dichotomous outcomes, we presented the summary estimate as a RR with 95% CI. If continuous outcomes were measured in the same way across studies, we presented a pooled difference in means with 95% CI; we had planned to pool standardised difference in means estimates where studies measured the same outcome, but use different methods. However the studies that reported continuous data all used the same unit of measurement. For time to event data, we planned to plot (and, if appropriate, pool) estimates of hazard ratios and 95% CIs, as presented in the study reports, using the generic inverse variance method in Review Manager 5 (RevMan 2014), however no time-to event data were reported in included studies.

We obtained pooled estimates of treatment effect using Cochrane Review Manager 5 software (RevMan 2014).

'Summary of findings' tables

We presented the main results of the review in 'Summary of findings' tables. These tables present key information concerning the quality of the evidence, the magnitude of the effects of the interventions examined, and the sum of the available data for the main outcomes (Schünemann 2011a). The 'Summary of findings' tables also include an overall grading of the evidence related to each of the main outcomes using the GRADE (Grades of Recommendation, Assessment, Development and Evaluation) approach. The GRADE approach defines the quality of a body of evidence as the extent to which one can be confident that an estimate of effect or association is close to the true quantity of specific interest. The quality of a body of evidence involves consideration of within-trial risk of bias (methodological quality), directness of evidence, heterogeneity, precision of effect estimates, and risk of publication bias (Schünemann 2011b). GRADE was undertaken for all outcomes where it was possible to calculate an estimate of effect. We planned to present the following primary outcomes in the 'Summary of findings' tables:

- surgical site infection (SSI);
- wound dehiscence within 30 days of operation.

In addition we also included adverse events in the 'Summary of findings' tables; this was at the suggestion of peer reviewers as noted in Differences between protocol and review.

We did not produce a 'Summary of findings' table for comparisons where the data were limited. Instead we summarised the specified outcomes together with their GRADE assessment in an additional table, Table 1. This was done in order to make the 'Summary of findings' tables manageable and improve the readability of the review.

Subgroup analysis and investigation of heterogeneity

Where feasible, we planned to explore the effects of interventions in children (aged under 18) and adults separately. We also planned in advance, and conducted (where possible) an exploration of the effects of interventions according to classification of wound contamination (clean, clean-contaminated, contaminated, dirty). We used a post-hoc exploratory sub-group analysis to confirm the appropriateness of combining studies that used different types of lavage solution.

Sensitivity analysis

Where possible, we planned and conducted sensitivity analyses to explore the effect of the following criteria:

- studies at high risk of bias for any domain compared with other studies with no domain classed at high risk of bias;
- studies at high risk of detection bias compared with other studies.

Elements of this Methods section are based on the standard Cochrane Wounds Protocol Template. The published protocol is archived in the Cochrane Library (Smith 2016).

RESULTS

Description of studies

Results of the search

The electronic searches identified 605 records. Of these we obtained 182 full-text records. Citation searching identified a further 29 records, which were thoroughly assessed as full texts. An additional six records of relevant ongoing studies were identified from searches of trials registers. The results of the search and assessment process are shown in Figure 1.

Included studies

We included 59 RCTs reported in 64 publications and together involving 14,738 participants.

Most included studies assessed the following comparisons.

- Use of irrigation compared with no irrigation (20 studies) (Bourgeois 1985; Buanes 1991; Cervantes-Sanchez 2000; Cho 2004; De Jong 1982; Elliott 1986; Gungorduk 2010; Harrigill 2003; Mahomed 2016; Oleson 1980; Ozlem 2015; Platt 2003; Schein 1990; Snow 2016; St Peter 2012; Tanaka 2015; Tanphiphat 1978; Temizkan 2016; Tighe 1982; Viney 2012)
- Use of an antibacterial (antibiotic or antiseptic) solution compared with a non-antibacterial irrigant such as saline (36 studies) (Al-Shehri 1994; Baker 1994; Bourgeois 1985; Browne 1978; Carl 2000; Case 1987; Chang 2006; Cheng 2005; Dashow 1986; Greig 1987; Halsall 1981; Kokavec 2008; Kubota 1999; Kubota 2015; Levin 1983; Lord 1983; Magann 1993; Marti 1979; Mirsharifi 2008; Moylan 1968; Neeff 2016; Oleson 1980; Oller 2015; Oestreicher 1989; Rambo 1972; Ruiz-Tovar 2011; Ruiz-Tovar 2012; Ruiz-Tovar 2013; Ruiz-Tovar 2016a; Ruiz-Tovar

2016b; Schein 1990; Silverman 1986; Sindelar 1979; Takesue 2011; Tighe 1982; Vallance 1985)

- Different methods of irrigation delivery (standard or pulsatile) compared (two studies) (Hargrove 2006; Nikfarjam 2014)
- Different antibacterial irrigants compared (six studies) (Dashow 1986; Mohd 2010; Oller 2015; Peterson 1990; Tighe 1982; Vallance 1985)
- Different non-antibacterial irrigants compared (three studies) (Brown 2007; Shimizu 2011; Trew 2011)

No studies compared an antibiotic solution with an antiseptic and no studies compared different volumes of irrigation.

There were eleven studies with more than two relevant arms (Bourgeois 1985; Dashow 1986; Elliott 1986; Levin 1983; Magann 1993; Marti 1979; Oleson 1980; Oller 2015; Tighe 1982; Schein 1990; Vallance 1985); where appropriate to the comparison we combined data from two or more arms.

A majority of included studies enrolled adult participants. A small number (Kokavec 2008; Kubota 1999; Kubota 2015; St Peter 2012) included only children, and in several others there were a mixture of adult and paediatric participants or it was unclear whether children, adults or a mixture were included. More information on study participants is given for each comparison (see Effects of interventions). Because of the nature of the surgeries assessed (e.g. caesarean sections), many studies enrolled only women.

A wide range of surgical operations and all classes of surgery (clean, clean-contaminated, contaminated, dirty) were represented in the review. Use of prophylactic antibiotics varied but was, as anticipated, more likely to be reported for studies enrolling participants undergoing surgeries with higher levels of contamination. For further details of the operations and surgical category represented in each comparison (see Effects of interventions).

Ongoing or pending assessment studies

Five studies (reported in six publications) are pending assessment (De Cicco 2015; De Kok 1998; Kosuş 2010; Munoz-Mahamud 2011; Taylor 1999). In each case there were no relevant review outcomes reported; we have attempted to contact study authors without success to date in four cases. In the case of De Cicco 2015 a further publication with relevant data is pending but the corresponding author was unable to supply this in advance of publication. We were able to exclude a further study after author contact confirmed that the purpose of the study was outside the scope of this review and no relevant outcome data were available (Keblawi 2006) (see Excluded studies).

Searching of trial registers identified six additional studies, which appeared to meet inclusion criteria but which were either still ongoing or which were completed but had no available outcome data or related publications. See Ongoing studies for details of these trials.

Excluded studies

We excluded 141 papers after appraisal of the full text. We ordered many of these because the initial records contained so little information, and upon obtaining full texts it was immediately evident that many studies were not eligible; others were reviews obtained solely in order to screen the bibliography. We noted more nuanced reasons for exclusion for 73 studies reported in 78 records; these studies are detailed here (see Characteristics of excluded studies).

We excluded studies for the following reasons: use of quasi-randomisation (14 studies: Al-Ramahi 2006; Bertheussen 1980; Bhargava 2006; Geraghty 1984; Iqbal 1998; Kellum 1985; Ko 1992; Makvandi 2014; Nachamie 1968; Nomikos 1986; Noon 1967; Rogers 1983; Salvati 1988; Sood 1985); or lack of randomisation only apparent after translation or study author contact (two studies: Terzi 2015; Wu 1992); use of perioperative irrigation was not the only systematic difference between groups (20 studies: Alcantara 2011; Badia 1994; Bennett-Guerrero 2016; Boothby 1984; Donnenfeld 1986; Ducharme 1986; Fountas 1999; Freischlag 1984; Garg 2013; Gonen 1986; Kothuis 1981; Mathelier 1992; Pollock 1978; Sarr 1988; Sauven 1986; Scheuerlein 2000; Shapiro 1986; Toki 1995; White 2008; Xiao 2010); the study enrolled participants from a different patient population - some or all participants did not undergo surgery (eight studies: Chisholm 1992; Ghafouri 2016a; Ghafouri 2016b; Granick 2007; Longmire 1987; Morse 1998; Rosen 1985; Weiss 2013) or there was healing by delayed primary or secondary intention in some or all wounds (12 studies: Akay 2006; Anglen 2005; Angobaldo 2008; FLOW 2011; Galle 1980; Hesami 2014; Hunt 1982; Martins 2012; Plaumann 1985; Scammell 1985; Sherman 1976; Sindelar 1985); the study assessed an ineligible intervention including irrigation conducted as a method of analgesia only, volumes of liquid used being too low to be considered irrigation, or irrigation was not the intervention of interest (17 studies: Cherian 2000; Dwivedi 2009; Everett 1969; Georgiadis 2013; Givens 2002; Horn 1999; Iqbal 2015; Keblawi 2006; Lau 1986; Lavery 1986; Logan 1973; Mohamed 2017; Pitt 1982; Pobereskin 2000; Sarzaeem 2014; Seco 1990; Yarussi 1999).

Risk of bias in included studies

A minority of studies were at high risk of avoidable bias in one or more domains. Many more were at risk of performance bias because of the nature of the comparison evaluated, and in more still there was a lack of clarity about the risk of bias across many or even all domains. The risk of bias for each study and a summary across all studies is shown in Figure 2 and Figure 3.

Allocation

About half of the included studies reported appropriate methods of generating a randomisation sequence. The others had an unclear risk of bias with the exception of one where it appeared that an otherwise acceptable method was likely not to have been implemented and the authors noted concern that randomisation may have been compromised (Tanphiphat 1978). Fewer studies reported adequate concealment of allocation; in a majority this was unclear.

Blinding

Many of the studies assessed a comparison between lavage/irrigation and no lavage/irrigation. In these cases personnel could not be blinded and the studies were therefore at high risk of performance bias. Because of this we focused on blinding of outcome assessment (risk of detection bias) when performing the GRADE assessment for these comparisons and did not downgrade because of high risk of performance bias. Where blinding was more feasible it often remained unclear whether personnel and participants were aware of the treatment groups. Blinding of

outcome assessors was reported for a minority of studies. While only a few studies were clearly at high risk of detection bias many more had an unclear risk as the assessment was poorly described.

Incomplete outcome data

Almost two-thirds of studies were classed as being at low risk of bias for this domain. However a minority of studies were at high risk of bias with exclusions from analyses representing a serious threat to the validity of the result.

Selective reporting

A minority of studies showed clear evidence of reporting bias. A somewhat greater number clearly reported full details of all specified outcomes, but many more were poorly reported and it was unclear whether all planned outcomes were fully reported.

Other potential sources of bias

There were few additional sources of bias which were evident from the trial reports but many studies were poorly or very briefly reported and it was difficult to determine whether there were additional factors that we may have considered to pose a serious risk of bias.

Effects of interventions

See: **Summary of findings for the main comparison** All irrigation compared with no irrigation for prevention of surgical site infection; **Summary of findings 2** Irrigation with antibacterial solution compared with irrigation with non-antibacterial solution for prevention of surgical site infection; **Summary of findings 3** Standard irrigation compared with pulsatile irrigation for prevention of surgical site infection

We assessed the following types of comparisons.

- Comparison of irrigation with no irrigation
- Comparisons of different types of irrigation solution
  - antibacterial (antibiotic or antiseptic) versus non-antibacterial
  - comparisons of different antibacterial solutions - either two antibiotics or two antiseptics
  - comparisons of different non-antibacterial solutions
- Comparisons of different methods of lavage delivery.

Comparison 1: comparison of irrigation with no irrigation

Summary of findings for the main comparison

Twenty studies (7192 participants) compared the use of some form of wound irrigation with no irrigation.

Types of surgery represented in this comparison include breast surgery (reduction), caesarean sections, appendicitis surgery, gastrectomy, uterine surgery, liver resection and various abdominal procedures and cover clean, clean-contaminated, contaminated and dirty surgical classifications. One study was classed as clean (Platt 2003); nine as clean-contaminated (Bourgeois 1985; Cho 2004; Elliott 1986; Gungorduk 2010; Harrigill 2003; Mahomed 2016; Tanaka 2015; Temizkan 2016; Viney 2012); three as contaminated (Cervantes-Sanchez 2000; Tanphiphat 1978; Tighe 1982) and five as dirty (Buanes 1991; Oleson 1980; Ozlem 2015, Schein 1990; St Peter 2012). Two studies included surgical procedures in several categories (De Jong 1982; Snow 2016).

One of the studies enrolled only children (St Peter 2012); 11 enrolled only adults (Bourgeois 1985; Elliott 1986; Gungorduk 2010; Harrigill 2003; Mahomed 2016; Platt 2003; Schein 1990; Snow 2016; Tanaka 2015; Temizkan 2016; Viney 2012) and in eight studies the population was mixed or unclear (Buanes 1991; Cervantes-Sanchez 2000; Cho 2004; De Jong 1982; Oleson 1980; Ozlem 2015; Tanphiphat 1978; Tighe 1982).

The type of solution used for irrigation varied and included saline (15 studies, 2667 participants Bourgeois 1985; Buanes 1991; Cervantes-Sanchez 2000; Cho 2004; Gungorduk 2010; Harrigill 2003; Oleson 1980; Ozlem 2015, Platt 2003; Schein 1990; Snow 2016; St Peter 2012; Tanaka 2015; Temizkan 2016; Viney 2012), an alternative without antibacterial properties (1 study, 131 participants Tighe 1982), different antiseptic solutions (4 studies, 4367 participants De Jong 1982; Mahomed 2016; Tanphiphat 1978; Tighe 1982), and solutions containing various antibiotics or combinations of antibiotics (4 studies, 501 participants Bourgeois 1985; Elliott 1986; Oleson 1980; Schein 1990). Antiseptics used included povidone iodine, chlorhexidine and cetrimide (Savlon) and super-oxidised water (Dermacyn); antibiotics used were cefoxitin, cefamandole, ampicillin or chloramphenicol. Doses and concentrations of both antibiotics and antiseptics varied; full details are given in Characteristics of included studies.

Three three-arm studies randomised participants to no treatment, antibiotic irrigation or saline irrigation (Bourgeois 1985; Oleson 1980; Schein 1990); another randomised participants to no treatment, antiseptic irrigation or sterile water irrigation (Tighe 1982). In each case we combined the antibiotic or antiseptic and non-antibacterial interventions and compared them with 'no irrigation'. One four-arm study (Elliott 1986) used a factorial design to assess antibiotic irrigation and intravenous antibiotics; we combined the arms that used antibiotic irrigation and compared them with the combined arms that used no irrigation.

One study Buanes 1991 compared additional postoperative irrigation with no additional treatment following intraoperative irrigation in both arms. We considered this intervention to be substantively different from the comparisons assessed in the other studies and did not include it in the meta-analyses conducted. One study (Platt 2003) used a 'split-body' or intra-individual design, where the two operative sites on each participant were randomised to the two intervention groups. We also excluded this study from the meta-analysis because it was unclear whether the analysis adjusted for the use of paired data.

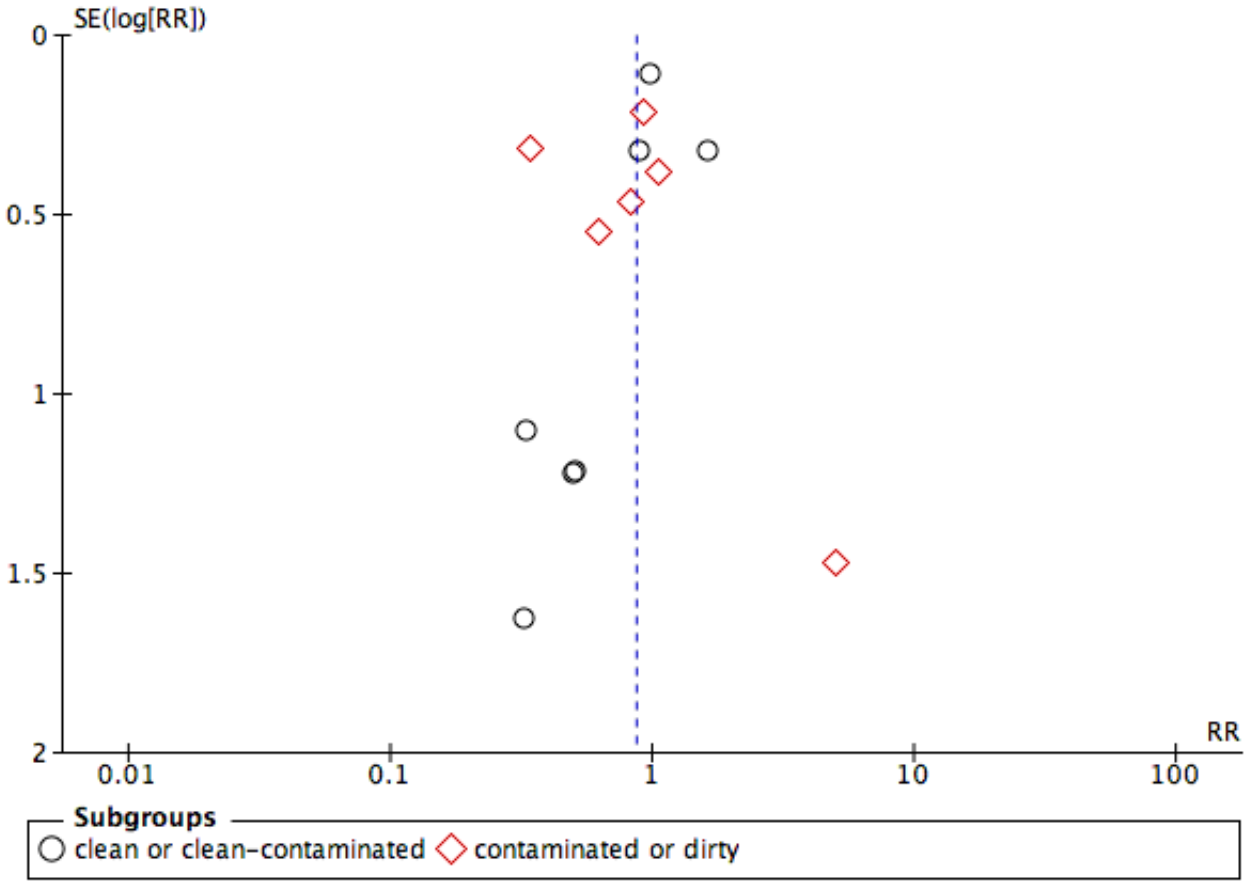
Primary outcome: SSI

Fifteen studies with 6297 participants reported analysable data for the outcome of SSI, which was variously defined (some studies did not provide a definition) (Cervantes-Sanchez 2000; Cho 2004; De Jong 1982; Elliott 1986; Gungorduk 2010; Harrigill 2003; Mahomed 2016; Oleson 1980; Ozlem 2015; Platt 2003; Schein 1990; Snow 2016; Tanaka 2015; Tanphiphat 1978; Temizkan 2016). Tighe 1982 did not report the number of events in each group and Platt 2003 was not included in the analysis because of the split-body design employed. Details for all studies are given in Table 2.

There is, on average, no clear difference in the incidence of SSI between groups treated with irrigation of any type and those not treated with irrigation. The overall RR was 0.87 (95% CI 0.68 to 1.11; I^2 = 28%) Analysis 1.1. This was based on 14 trials with 6106 participants. This was low-certainty evidence downgraded once for risk of bias across various domains in studies that contributed almost half the weight of the analysis, and once for imprecision because confidence intervals included both no effect and values suggesting both harm and benefit. In absolute terms this equates to 13 fewer SSIs per 1000 with irrigation than with no irrigation, with 95% CI from 31 fewer to 10 more SSIs.

We assessed whether the analysis may be affected by publication bias; it was not clear that this was the case although we considered it to be possible, but did not downgrade for this (Figure 4).

Figure 4. Funnel plot of comparison 1: all irrigation versus no irrigation, outcome: 1.1 surgical site infection



We conducted planned subgroup analysis based on the category of surgery, grouping the studies with a mixture of surgery categories (De Jong 1982; Snow 2016) with the most high-risk category represented; in this case, this was dirty surgery. There was only one study of participants undergoing clean surgery, Platt 2003, which was excluded from the analysis due to the 'split-body' design used. There were also only three studies of participants undergoing dirty surgery, one of which was extremely small (Ozlem 2015; 14 participants). Because of this, we decided to group clean and clean-contaminated studies together, and similarly to group contaminated, dirty and mixed studies together. The RR for SSI for the clean-contaminated sub-group was 1.00 (95% CI 0.82 to 1.21). The RR for SSI for contaminated or dirty surgeries was 0.74 (95% CI 0.47 to 1.16). Category of surgery may explain some differences between estimates of effect in the included studies; the I^2 for subgroup differences was 29.1%.

We could not carry out planned subgroup analysis for this comparison, based on whether participants were adults or children, as only one study (St Peter 2012) enrolled only children, and it did not report SSI data.

We undertook an exploratory post-hoc subgroup analysis of the type of irrigation solution (non-antibacterial, antiseptic, antibiotic) to test the rationale for combining all studies comparing irrigation with no irrigation in the same comparison. This analysis did not explain the heterogeneity (I^2 for subgroup differences = 0%), supporting the analysis plan employed. The results of this exploratory analysis are shown in Table 3.

We conducted a planned sensitivity analysis excluding studies at high risk of bias. All studies were at high risk of bias for blinding of personnel so we excluded studies at high risk of bias in additional domains. Excluding five studies gave an overall effect estimate of RR 0.94 (95% CI 0.77 to 1.16), which is not materially different to the main analysis. Results for the two subgroups were,

respectively, clean-contaminated: RR 0.95 (95% CI 0.77 to 1.19) and contaminated/dirty/mixed: RR 0.82 (95% CI 0.42 to 1.61). We conducted another planned sensitivity analysis excluding studies at high risk of detection bias; this excluded only one study in the clean-contaminated group and also did not materially change the estimate of effect RR 0.79 (95% CI 0.61 to 1.04); the RR for the clean-contaminated group was 0.95 (95% CI 0.76 to 1.17).

We had decided to exclude Platt 2003 from the analysis because of the split-body design; however the study reported no events in either arm so no estimate of effect could be calculated and no weight would have been contributed to the analysis. In one study (De Jong 1982), there was more than one wound per person in some cases and wounds rather than participants were the unit of analysis. There were also a substantial number of post-randomisation exclusions due to death or need for reoperation. Because we were uncertain about the number of wounds in the excluded participants, and because the reasons for exclusion made an assumption that these participants did not have an SSI doubtful, we have reported the completed case analysis for this study and examined the impact of excluding it from the meta-analysis in a post-hoc sensitivity analysis. Excluding De Jong 1982 made little difference to the estimate of effect, either overall (RR 0.84, 95% CI 0.62 to 1.14) or in the subgroup of contaminated, dirty or mixed surgeries (RR 0.69, 95% CI 0.38 to 1.25).

Buanes 1991 compared additional postoperative irrigation with no additional treatment following intraoperative irrigation in both arms in 83 participants with generalised peritonitis; we analysed this trial separately as a substantively different clinical comparison and showed an increased rate of SSI in the group given additional postoperative irrigation: RR of 5.08 (95% CI 1.17 to 22.09). This was low-certainty evidence, which was downgraded twice for imprecision due to small numbers of participants and very wide confidence intervals.

Primary outcome: wound dehiscence

Only Platt 2003 reported data on wound dehiscence. This split-body design study conducted in 30 women undergoing clean breast surgery did not clearly adjust for the use of paired data; unadjusted paired data may produce wider confidence intervals than should be the case. There may be little or no difference in the incidence of wound dehiscence (RR 1.17, 95% CI 0.44 to 3.06). This was low-certainty evidence downgraded twice for imprecision due to small numbers, wide confidence intervals and uncertainty about the analysis.

Secondary outcome: adverse events

Three studies reported analysable data on overall adverse events (Harrigill 2003; Ozlem 2015; Tanaka 2015). Three other studies focused specifically on abscess formation, which we had prespecified as a specific event of interest (Oleson 1980; Snow 2016; St Peter 2012); Ozlem 2015 reported one abscess but did not state in which group it occurred. Other studies reported only specific additional complications (Bourgeois 1985; Elliott 1986) or information that was not group-specific (Cervantes-Sanchez 2000). Current trial evidence shows that, on average, there is no clear difference in the total number of adverse events between groups treated with irrigation and those treated with no irrigation (RR 1.05, 95% CI 0.76 to 1.44, I^2 = 0%; 403 participants) (low-certainty evidence downgraded once for imprecision and once for high risk of detection bias in the study with 78% of the analysis weight) Analysis 1.2. There is also no clear difference in the number of participants with abscess formation (RR 0.91, 95% CI 0.54 to 1.54, I^2 = 0%, 331 participants) (moderate-certainty evidence downgraded once for imprecision) Analysis 1.3.

Secondary outcome: mortality

Two studies reported data on mortality explicitly (Schein 1990; Tanaka 2015). On average, there is no clear difference in mortality between the irrigation and no irrigation groups in these studies; the confidence intervals are wide and likely to be fragile, they also span both benefit and harm (RR 0.86, 95% CI 0.36 to 2.04, I^2 = 0%, 280 participants). This was low-certainty evidence downgraded twice for imprecision Analysis 1.4.

Secondary outcome: hospital stay

Nine studies with 1949 participants reported some data on hospital stay. Seven (1597 participants) reported data on mean length of stay (Bourgeois 1985; Elliott 1986; Gungorduk 2010; Harrigill 2003; Schein 1990; St Peter 2012; Tanaka 2015) and three (352 participants) reported median length of stay (Oleson 1980; Snow 2016; Viney 2012). There is, on average, little or no difference in the length of stay between the irrigation and no irrigation groups; the difference in means was -0.13 days (95% CI -0.38 to 0.12; I^2 = 82%) Analysis 1.5. This was moderate-certainty evidence, downgraded once for risk of bias in one or more domains (other than performance bias) in studies accounting for more than 50% of the analysis weight. The studies reporting medians did not demonstrate differences between the groups either (Table 4).

The study that we considered too clinically dissimilar to be included in meta-analysis (Buanes 1991) reported median length of stay as 5 days in both groups with ranges of 3 to 11 days with postoperative irrigation compared with 4 to 12 days without.

Secondary outcome: reoperation (return to theatre)

One large study, Mahomed 2016, reported the proportion of participants returned to theatre after irrigation with povidone iodine compared with no irrigation in women undergoing caesarean sections; a smaller study reported this in children with appendicitis and used saline irrigation compared with no irrigation (St Peter 2012). There were a total of 3490 randomised participants but a completed case analysis was reported for Mahomed 2016 so 3247 were analysed. Event rates were low and evidence from these studies was that, on average, there is no clear difference between the groups (RR 0.72, 95% CI 0.28 to 1.84; I^2 = 0%) Analysis 1.6. This was low-certainty evidence downgraded twice for imprecision due to the very low event rates that led to wide confidence intervals, which included both no effect and values suggesting both harm and benefit.

Secondary outcome: readmission to hospital

Mahomed 2016 and St Peter 2012 (total of 3490 randomised participants with 3247 included in the completed case analysis) reported the proportion of participants re-admitted to hospital. From these studies it is uncertain whether there is a difference between the groups on this measure: RR 0.70 (95% CI 0.10 to 4.90 ; I^2 = 53%) Analysis 1.7. This was very low certainty evidence downgraded twice for imprecision due to the low event rates, which led to wide confidence intervals (despite including 3247

participants) and because the 95% CIs span both benefit and harm as well as no effect, and once for inconsistency between the study estimates.

Secondary outcome: systemic antibiotics within 30 days

Only Tighe 1982 reported this outcome and the data were not reported by treatment group so no estimate of effect was possible and no full GRADE assessment could be performed (Table 4); the certainty of this evidence is affected by risk of bias as well as imprecision.

Other secondary outcomes

No studies reported the occurrence of wound infections with antibiotic resistance.

Summary of comparison

Twenty studies assessed a comparison of irrigation and no intervention; 15 of these, with over 6000 participants, reported SSI outcome data. Based on the included trial evidence there is currently no clear difference in incidence of SSI between participant groups treated with irrigation and those given no irrigation. Planned subgroup analysis found that this was the case in each of the surgical contamination subgroups we were able to assess (clean-contaminated versus contaminated or dirty). Exploratory analysis supported our clinical opinion that it was reasonable to group irrigation solutions with different antibacterial properties together. This was low-certainty evidence, which was downgraded once due to relevant risks of bias and once due to imprecision. There were no studies included in the analysis that had been conducted in clean surgeries therefore the results may be only indirectly relevant to these operations. A single, small, split-body design study in clean surgery was the only study to report wound dehiscence: this single study provides low-certainty evidence reporting no clear difference between groups; downgrading was due to very serious imprecision.

Comparison 2: comparison of antibacterial irrigation with non-antibacterial irrigation

Summary of findings 2

Thirty-six studies (6163 participants) compared the use of an antibacterial irrigation with non-antibacterial irrigation solution.

The specific surgery types represented included appendicitis surgery, including perforated appendices; breast surgery (mastectomy or other); cardiac (pacemaker pocket) surgery; gastrointestinal and colorectal surgeries; caesarean sections; surgery for peritonitis; spinal surgery; orthopaedic (hip, pelvic and femoral) surgery; various abdominal procedures; uterine surgery; and general (mixed) surgical populations. All categories of surgery (clean, clean-contaminated, contaminated, dirty) were represented. We classed eight studies as clean (Case 1987; Chang 2006; Cheng 2005; Dashow 1986; Kokavec 2008; Magann 1993; Oller 2015; Ruiz-Tovar 2013); 12 as clean-contaminated (Bourgeois 1985; Baker 1994; Carl 2000; Levin 1983; Mirsharifi 2008; Moylan 1968; Neeff 2016; Ruiz-Tovar 2011; Ruiz-Tovar 2012; Ruiz-Tovar 2016a; Ruiz-Tovar 2016b; Takesue 2011); three as contaminated (Al-Shehri 1994; Marti 1979; Tighe 1982) and six as dirty (Browne 1978; Kubota 1999; Kubota 2015; Oleson 1980; Rambo 1972; Schein 1990). Seven studies included surgeries in several categories (Greig 1987; Halsall 1981; Lord 1983; Oestreicher 1989; Silverman 1986; Sindelar 1979; Vallance 1985). We grouped these with the most contaminated class represented in each study (dirty in each case).

Three of the studies enrolled only children (Kokavec 2008; Kubota 1999; Kubota 2015); 19 enrolled only adults Baker 1994; Bourgeois 1985; Carl 2000; Case 1987; Dashow 1986; Chang 2006; Cheng 2005; Levin 1983; Lord 1983; Magann 1993; Mirsharifi 2008; Oller 2015; Ruiz-Tovar 2012; Ruiz-Tovar 2013; Ruiz-Tovar 2016a; Ruiz-Tovar 2016b; Schein 1990; Silverman 1986; Takesue 2011) and in 13 studies the population was mixed or unclear (Al-Shehri 1994; Browne 1978; Greig 1987; Marti 1979; Moylan 1968; Neeff 2016; Oestreicher 1989; Oleson 1980; Rambo 1972; Ruiz-Tovar 2011; Sindelar 1979; Tighe 1982; Vallance 1985).

In all except two studies the non-antibacterial irrigant was saline; one study used sterile water (Tighe 1982) and one used Ringer's solution (Neeff 2016). Fourteen studies (3261 participants) used an antiseptic solution (Baker 1994; Browne 1978; Chang 2006; Cheng 2005; Halsall 1981; Kokavec 2008; Kubota 1999; Kubota 2015; Neeff 2016; Oestreicher 1989; Sindelar 1979; Takesue 2011; Tighe 1982; Vallance 1985). Vallance 1985 was a three-armed study that randomised participants to saline or one of two different antiseptic solutions; for this comparison we combined the two antiseptic groups and compared them with saline; the comparison between the two antiseptics is assessed in comparison 5. Antiseptic agents used included povidone iodine (Betadine), chlorhexidine, polyhexanide, taurolidine (Taurolin), and acidic electrolysed water. Twenty-two studies (2902 participants) used an antibiotic solution (Al-Shehri 1994; Bourgeois 1985; Carl 2000; Case 1987; Dashow 1986; Greig 1987; Levin 1983; Lord 1983; Magann 1993; Marti 1979; Mirsharifi 2008; Moylan 1968; Oleson 1980; Oller 2015; Rambo 1972; Ruiz-Tovar 2011; Ruiz-Tovar 2012; Ruiz-Tovar 2013; Ruiz-Tovar 2016a; Ruiz-Tovar 2016b; Schein 1990; Silverman 1986). Levin 1983; Marti 1979 and Oller 2015 were all three-arm trials assessing saline and two different antibiotic solutions; for this comparison we combined the two antibiotic groups and compared them with saline. Magann 1993 used a factorial design to also assess skin preparation regimens; we combined arms as appropriate. Dashow 1986 was a five-arm trial assessing saline and four different antibiotic solutions; we combined the antibiotic groups here. Comparisons between the different antibiotics are assessed in comparison 5. Antibiotics used included: gentamicin, clindamycin (alone or in combination), ampicillin, tetracycline, cefotetan, cephapirin or cefoxitin, cefazolin, kanamycin, epicillin or lincomycine, cephalothin, chloramphenicol, cefamandole and moxalactam. Doses and concentrations of both antibiotics and antiseptics varied; full details are given in Characteristics of included studies. Bourgeois 1985; Oleson 1980 and Tighe 1982 were three-arm studies that also randomised participants to no irrigation; these groups are included in comparison 1.

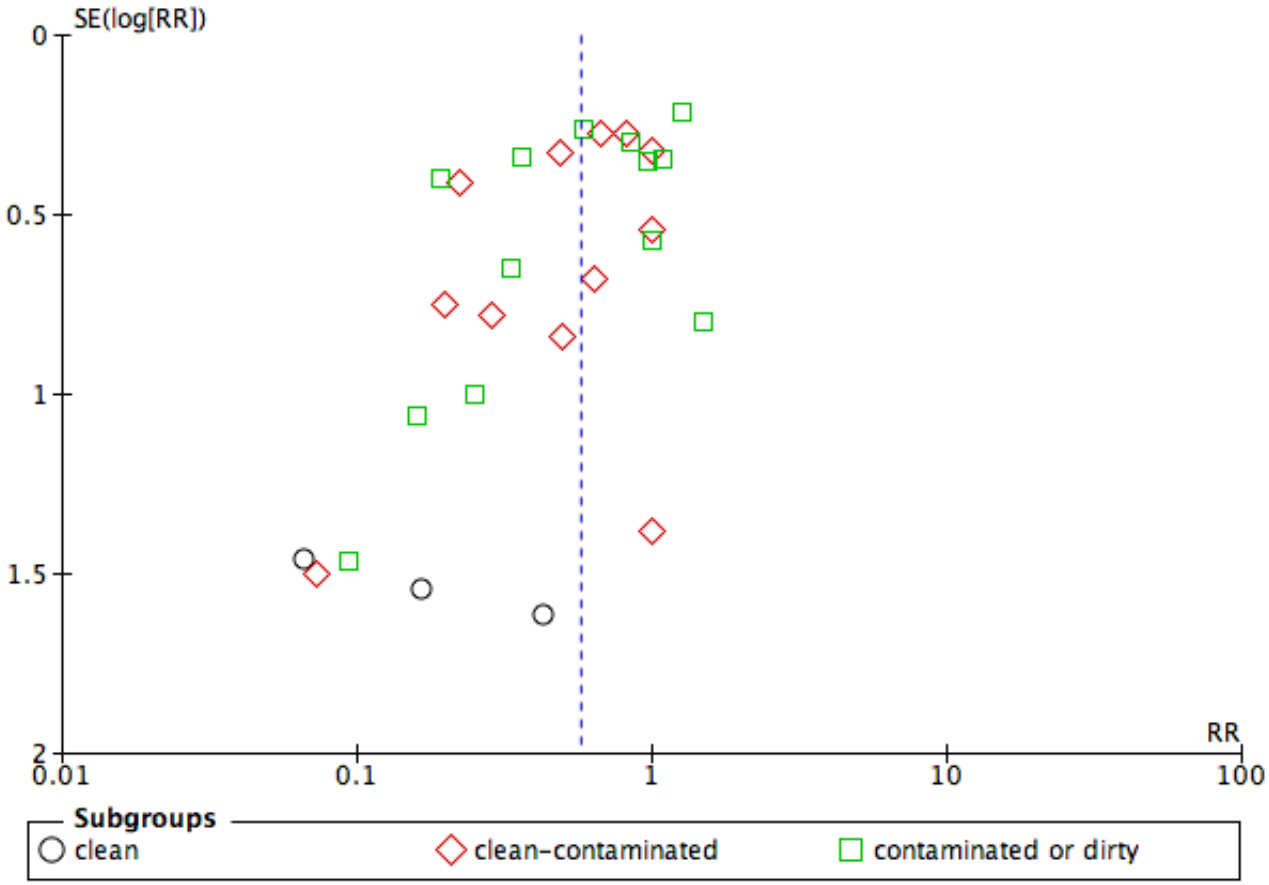
In one case we were unsure whether two study reports included some of the same participants (Chang 2006; Cheng 2005). Attempts to contact the authors for clarification were unsuccessful so we have included only data from the larger of the two studies (Cheng 2005) in our an analysis for the primary outcome of SSI and conducted a sensitivity analysis to explore the impact of including both data sets independently; only one of these studies reported secondary outcomes so the issue did not impact these analyses.

Primary outcome: SSI

Thirty-one studies (5141 randomised participants) reported analysable data for the outcome of SSI, which was variously defined (some studies did not provide a definition) (Al-Shehri 1994; Baker 1994; Carl 2000; Case 1987; Chang 2006; Cheng 2005; Dashow 1986; Greig 1987; Halsall 1981; Kokavec 2008; Kubota 1999; Kubota 2015; Levin 1983; Lord 1983; Magann 1993; Mirsharifi 2008; Moylan 1968; Neeff 2016; Oestreicher 1989; Oleson 1980; Oller 2015; Rambo 1972; Ruiz-Tovar 2011; Ruiz-Tovar 2012; Ruiz-Tovar 2013; Ruiz-Tovar 2016a; Schein 1990; Silverman 1986; Sindelar 1979; Takesue 2011; Vallance 1985). Details for all studies are given in Table 2. However, Chang 2006 was included only for a sensitivity analysis (see below). Two studies (Marti 1979; Tighe 1982) reported data which could not be included in the analysis as events were not attributable to groups.

There may be, on average, a benefit to the use of some form of antibacterial irrigation compared with non-antibacterial irrigation. The pooled RR for SSI was 0.57 (95% CI 0.44 to 0.75; I^2 = 53%) Analysis 2.1. This was low-certainty evidence downgraded once because 54% of the analysis weight was contributed by studies at high risk of bias in one or more domains, and once because publication bias was considered likely to have affected the result (Figure 5). We conducted an exploratory post-hoc Egger test on the advice of peer-reviewers. The P value for small study effects was 0.073. The RR equates to an absolute difference in risk of 60 (95% CI 35 to 78) fewer SSIs per 1000 participants with antibacterial irrigation than with non-antibacterial irrigation.

Figure 5. Funnel plot of comparison 2: antibacterial versus non-antibacterial irrigation, outcome: 2.1 surgical site infection



We also undertook planned subgroup analysis based on the category of surgery. Because only one study that we classed as contaminated reported analysable data, we grouped this together with the studies of dirty or mixed surgical populations. The estimates of effect for the groups were as follows: clean RR 0.16 (95% CI 0.03 to 0.89); clean-contaminated RR 0.57 (95% CI 0.40 to 0.79) and contaminated, dirty or mixed RR 0.61 (95% CI 0.40 to 0.92). It was not clear that these subgroupings explained much of the heterogeneity between studies; the I^2 for between-group differences was 9.7%. The result for the clean subgroup is fragile as it is based on very low event rates in small studies, with a zero event rate in one intervention group.

We did not carry out planned subgroup analysis for the comparison of antibacterial and non-antibacterial irrigants for adults and children; only three studies (Kokavec 2008; Kubota 1999; Kubota 2015), representing 3% of the analysis weight, enrolled only children, so meaningful results were unlikely. One of these studies enrolled children undergoing clean, orthopaedic surgeries (Kokavec 2008); this reported 0 out of 79 participants with SSI in

the antibacterial group compared with 2 out of 83 in the non-antibacterial group.

The other two studies (Kubota 1999; Kubota 2015) enrolled children undergoing surgeries for appendicitis, classed as dirty. The two studies reported a total of 1 out of 32 participants with SSI in the antibacterial groups compared with 8 out of 28 in the non-antibacterial group; both studies were at high risk of bias in one domain.

We undertook an exploratory post-hoc subgroup analysis of the type of antibacterial irrigation (antiseptic or antibiotic) to test the rationale for combining all studies comparing irrigation with no irrigation in the same comparison. This analysis did not explain the heterogeneity, supporting the analysis plan employed, also based on clinical assessment. The results of this exploratory analysis are shown in Table 3.

As noted we were unsure whether two study reports included some of the same participants (Chang 2006; Cheng 2005). Attempts to contact the study authors for clarification were unsuccessful so we have included only data from the larger of the two studies (Cheng 2005) in our an analysis. A sensitivity analysis to explore the impact of including both data sets independently did not materially change the estimate of effect (RR 0.56, 95% CI 0.43 to 0.74; I^2 = 51%).

We conducted a planned sensitivity analysis to look at the impact of excluding studies at high risk of bias in one or more domains. This had the effect of excluding half of the studies and the majority of participants with reported data and produced a larger estimate of effect than the main analysis (RR 0.38 95% CI 0.25 to 0.58). Because so many participants were excluded we do not place any emphasis on this analysis. No studies were at high risk of detection bias so we did not perform this planned sensitivity analysis.

Primary outcome: wound dehiscence

Three studies (Case 1987; Chang 2006; Takesue 2011) with 660 participants reported wound dehiscence and the impact of antibacterial irrigation on dehiscence is very uncertain (RR 1.26; 95% CI 0.65 to 2.45, I^2 = 0%) Analysis 2.2. This was very low-certainty evidence downgraded once for risk of bias in the study with the great majority of weight in the analysis, once for imprecision and once for inconsistency.

Secondary outcome: adverse events

Three studies with 202 participants reported analysable data on overall adverse events that could be clearly determined to represent all participants with an adverse event (Ruiz-Tovar 2013; Ruiz-Tovar 2016b; Schein 1990). There is no clear difference between the groups (RR 0.55, 95% CI 0.22 to 1.34, I^2 = 0%; 178 participants); this was low-certainty evidence downgraded twice for imprecision Analysis 2.3.

Ten studies focused specifically on abscess formation, which we had prespecified as a specific event of interest (Al-Shehri 1994; Baker 1994; Dashow 1986; Kubota 1999; Kubota 2015; Oleson 1980; Rambo 1972; Ruiz-Tovar 2012; Schein 1990; Silverman 1986). Rambo 1972 grouped abscesses together with another type of event so could not be included in the analysis. Therefore nine studies were included in the analysis, three of which reported no events in either arm (Al-Shehri 1994; Dashow 1986; Oleson 1980). It is uncertain whether there is a difference in abscess formation between antibacterial and non-antibacterial irrigation; the pooled RR was 0.82, 95% CI 0.42 to 1.62, I^2 = 0%; 1309 participants); this is very low-certainty evidence downgraded once for risk of bias and twice for imprecision Analysis 2.4.

A further eight studies reported additional specific types of adverse events that we had not prespecified, such as respiratory distress or endometritis, or made general non-group specific statements about events (Bourgeois 1985; Levin 1983; Lord 1983; Magann 1993; Marti 1979; Moylan 1968; Ruiz-Tovar 2016a; Silverman 1986); several of the studies included in analyses of abscess also specified such events. Details are provided in Characteristics of included studies but these data are not further analysed.

Secondary outcome: mortality

Eleven studies (1121 participants) reported data on mortality for antibacterial vs. non-antibacterial irrigation (Baker 1994; Browne 1978; Lord 1983; Oller 2015; Rambo 1972; Ruiz-Tovar 2012; Ruiz-Tovar 2013; Ruiz-Tovar 2016a; Ruiz-Tovar 2016b; Schein 1990; Vallance 1985). It is uncertain whether there is a difference in mortality between the treatment groups (RR 0.81, 95% CI 0.48 to 1.36) Analysis 2.5. This was very low-certainty evidence downgraded once for risk of bias in studies contributing 64% of the weight in the analysis and twice for imprecision.

Secondary outcome: hospital stay

Fifteen studies reported some data on length of hospital stay (Al-Shehri 1994; Baker 1994; Bourgeois 1985; Halsall 1981; Kubota 1999; Kubota 2015; Levin 1983; Oleson 1980; Oller 2015; Ruiz-Tovar 2012; Ruiz-Tovar 2013; Ruiz-Tovar 2016a; Schein 1990; Tighe 1982; Vallance 1985). Three studies did not report data separately for the intervention groups (Al-Shehri 1994; Baker 1994; Tighe 1982). Seven studies reported mean length of stay although two (Halsall 1981; Schein 1990) did not report measures of variance. There may, on average, be a very slightly shorter length of stay in participants treated with antibacterial irrigation. The difference in means was -0.85 days (95% CI -1.60 to -0.09; I^2 = 55%; 635 participants) Analysis 2.6. Five studies reported median length of stay (Oleson 1980; Oller 2015; Ruiz-Tovar 2012; Ruiz-Tovar 2013; Ruiz-Tovar 2016a); in each case the median lengths of stay were very similar for the two groups. This was low-certainty evidence downgraded for risks of bias across multiple domains.

Secondary outcome: systemic antibiotics

Two studies with a total of 375 participants reported some data on use of systemic antibiotics (Chang 2006; Tighe 1982). Tighe 1982 did not report the data based on treatment group allocation (they noted 53 of 131 participants receiving antibiotics "distributed evenly across the groups"); while Chang 2006 reported that all six of the participants with SSI received systemic antibiotics up to six weeks postoperatively (there were no infections in the povidone iodine group). Calculating an RR for this outcome would not produce a meaningful result since the data merely duplicate the results for the primary outcome of SSI; consequently no independent GRADE assessment is possible.

Secondary outcome: antibiotic-resistant infection

Five studies with 1198 participants reported some information about antibiotic resistance in organisms sampled (Chang 2006; Lord 1983; Moylan 1968; Rambo 1972; Takesue 2011). Chang 2006

reported that 5 out of 6 infections in participants treated with saline tested positive for methicillin-resistant *Staphylococcus aureus* (MRSA) (there were no infections in the povidone iodine group). Takesue 2011 also focused on *S. Aureus* resistance and reported data for a majority of the participants with infection; however, the data could not be linked to the proportion of participants with or without resistance. Both studies used antiseptic rather than antibiotic irrigations. Moylan 1968 reported tests for resistance to kanamycin (the antibiotic used in the study) in all wound cultures but provided specific results on the proportion with resistance for only one group. Lord 1983 and Rambo 1972 reported data for resistance for specific organisms but these data were incomplete and could not be linked to participant-level infections. We were not able to calculate any meaningful estimate of effect for the proportion of participants with antibiotic-resistant infection and therefore no GRADE assessment was possible.

Secondary outcome: reoperation

Two studies with 403 participants reported data on reoperation (Chang 2006; Silverman 1986). There were low numbers of events. It is uncertain if there is a difference between the treatment groups. The RR was 1.26 (95% CI 0.12 to 13.60) Analysis 2.7. This was very low-certainty evidence downgraded once for inconsistency and twice for imprecision.

Other secondary outcomes

No study reported on readmission to hospital.

Summary of comparison

Thirty-six studies compared irrigation with antibacterial and non-antibacterial irrigants and 33 reported the outcome of SSI; data from 30 studies with over 5000 participants could be included in the analysis. There may be a lower incidence of SSI in participants treated with antibacterial irrigation solutions compared with non-antibacterial irrigants. This was low-certainty evidence downgraded once for risk of bias in varying domains affecting studies that account for over half the weight of the analysis and once because publication bias is suspected. A pre-planned subgroup analysis showed that the possible benefit was present in each of the surgical contamination subgroups that we were able to assess (clean versus clean-contaminated versus contaminated or dirty) although the results in the clean group were based on small numbers of participants and very low numbers of events. Exploratory subgroup analysis confirmed that it was reasonable to combine different types of antibacterial solution in a single analysis. It is very uncertain whether there is a difference in the incidence of wound dehiscence between the treatment groups; this was very low-certainty evidence based on three studies.

Comparison 3: comparison of two non-antibacterial irrigation solutions

Table 1

One study (20 participants) compared irrigating with saline and artifical cerebrospinal fluid (CSF) in 20 participants undergoing clipping of cerebral aneurysms (classed as clean) (Shimizu 2011).

Two studies compared irrigation with icodextrin and Ringer's solution. One enrolled 426 women undergoing primary removal of myomas or endometriotic cysts (Trew 2011); a second study enrolled 449 women undergoing laparoscopic gynaecological surgery for a range of diagnoses (Brown 2007). Both these studies involved surgeries classed as clean-contaminated.

Primary outcome: SSI

Saline versus artificial CSF

Shimizu 2011 did not report SSI.

Icodextrin versus Ringer's solution

The RR for Trew 2011 was 2.89 (95% CI 0.30 to 27.56; 426 participants). In Brown 2007 it was not clear that the infection data reported referred to SSI; attempts to clarify this with the study authors have not been successful so far. There is no clear evidence of a difference. This was low-certainty evidence downgraded twice for imprecision based only on the data from the trial where we were confident this was SSI data (Trew 2011).

Primary outcome: wound dehiscence

This was not reported by either study.

Secondary outcome: mortality

Icodextrin versus Ringer's solution

Both Brown 2007 and Trew 2011 reported no deaths in either intervention group (total of 875 participants). Since no estimate of effect was therefore calculable no full GRADE assessment was made; the evidence is affected by imprecision however Analysis 3.1.

Secondary outcome: adverse events

Saline versus artificial CSF

Shimizu 2011 reported the number of participants with postoperative events; this included neurological events and events visualised on CT or MRI scans. There were two participants with events in each group (total of 20 participants); because of the inclusion of imaging results in these data we have not reported an effect estimate and have not undertaken a GRADE assessment.

Icodextrin versus Ringer's solution

Both Brown 2007 and Trew 2011 reported total number of participants with adverse events and the number with events that were considered to be related to treatment. There was, on average, no difference in the number of participants with an adverse event (RR 0.99, 95% CI 0.96, 1.02; I^2 = 0%; 875 participants) Analysis 3.2. The effect estimate for events considered to be related to treatment may be a more meaningful measure; this also showed no clear difference, on average, with confidence intervals that included the possibility of a small benefit from icodextrin as well as harm: RR 1.35 (95% CI 0.98 to 1.86; I^2 = 0%; 875 participants) Analysis 3.3. This was moderate-certainty evidence downgraded once for imprecision. Brown 2007 also reported the proportions of participants with serious adverse events (RR 1.20, 95% CI 0.80 to 1.78; 426 participants) and serious events that were considered to be treatment-related (RR 0.71, 95% CI 0.29 to 1.73; 449 participants). In both cases there may be little or no difference between the treatment groups (low-certainty evidence).

Other secondary outcomes

No studies reported data for other secondary outcomes.

Summary of comparison

There were two comparisons where both arms involved a solution without antibacterial properties. A single study comparing saline with artifical CSF in brain surgery (clean) did not report either SSI or wound dehiscence. Two studies compared icodextrin with Ringer's solution in gynaecological surgery (clean-contaminated) but only one clearly reported SSI and neither reported wound dehiscence. There is no clear difference in SSI incidence between the treatment groups. This was low-certainty evidence downgraded twice for imprecision.

Comparison 4: comparison of povidone iodine with alternative antiseptic

Table 1

One study compared povidone iodine with superoxidised water irrigation (Dermacyn) in 190 participants undergoing coronary artery bypass graft (CABG) (classed as clean) (Mohd 2010).

One three-armed study compared povidone iodine with chlorhexidine in 53 adults undergoing surgery for peritonitis (classed as dirty) (Vallance 1985); a third group were randomised to saline irrigation (see comparison 2). The number of participants relevant to this comparison was 33.

Primary outcome: SSI

Povidone iodine versus superoxidised water (Dermacyn)

There may be more infections in wounds irrigated with povidone iodine compared with Dermacyn. The RR for Mohd 2010 was 2.80 (95% CI 1.05 to 7.47; 190 participants). This would represent an absolute difference of 95 more SSIs per 1000 people treated with povidone iodine than with superoxidised water (95% CI 3 more to 341 more). This was low-certainty evidence downgraded once for risk of bias and once for imprecision.

Povidone iodine versus chlorhexidine

It is uncertain whether there is a difference between the groups. The RR in Vallance 1985 was 1.13 (95% CI 0.78 to 1.63; 29 participants). This represents a completed case analysis, as early mortality cases were excluded from the analysis and could not be accurately assigned to groups. This was very low-certainty evidence downgraded twice for risks of bias across multiple domains and twice for imprecision.

Details for both studies are given in Table 2; GRADE judgements are summarised in Table 1.

Primary outcome: wound dehiscence

This was not reported by any of the studies.

Secondary outcome: mortality

Povidone iodine versus superoxidised water (Dermacyn)

Mohd 2010 reported deaths together with the need for reopening of the chest due to bleeding. There were four deaths in total but it was not clear in which group they occurred. A full GRADE assessment was not possible but certainty would be affected by risk of bias as well as imprecision.

Povidone iodine versus chlorhexidine

It is uncertain whether there is a difference between the groups. The RR in Vallance 1985 was 0.45 (0.05 to 3.90; 33 participants). These data refer to deaths within four days of surgery; later mortality was recorded but was not reported separately for the treatment groups. This was very low-certainty evidence downgraded twice for risks of bias across multiple domains and twice for imprecision.

Secondary outcome: hospital stay

Povidone iodine versus chlorhexidine

It is uncertain whether there is a difference between the groups.The difference in means in Vallance 1985 was 3.30 days more in the povidone iodine group (95% CI 0.53 to 6.07; 33 participants). This was very low-certainty evidence downgraded twice for risks of bias across multiple domains and twice for imprecision.

Secondary outcome: reoperation (return to theatre)

Povidone iodine versus Dermacyn

It is uncertain whether there is a difference between the groups. The RR in Mohd 2010 was 8.80 (95% CI 0.48 to 161.11; 178 participants) based on four events, all in the povidone iodine group. This was very low-certainty evidence downgraded once for risk of bias and twice for imprecision.

Other secondary outcomes

No studies reported data for other secondary outcomes.

Summary of comparison

There were two studies where one arm was povidone iodine and the other was another antiseptic solution. Each study undertook a different comparison. Numbers of participants were low. The comparison with superoxidised water (Dermacyn) was undertaken in clean cardiac operations while the comparison with chlorhexidine was in dirty operations for peritonitis. There may be more infections in wounds treated with povidone iodine compared with superoxidised water; low-certainty evidence downgraded once for risk of bias and once for imprecision. It is very uncertain whether there is a difference in SSI incidence between povidone iodine and chlorhexidine; very low-certainty evidence downgraded twice for risk of bias across multiple domains and twice for imprecision. Neither study reported wound dehiscence.

Comparison 5: comparisons of different antibiotic irrigation solutions

Table 1

One three-arm study compared use of cephapirin with cefoxitin in 132 women undergoing caesarean sections (classed as clean-contaminated) (Levin 1983); a third group were randomised to saline irrigation (see comparison 2). The number of participants relevant to this comparison was 85.

One three-arm study compared the use of clindamycin with gentamicin in 51 women undergoing planned axillary node dissection (Oller 2015); a third group of women were randomised to saline (see comparison 2). The number of participants relevant to this comparison was 34. All participants received an initial saline irrigation, women in the two antibiotic groups received a second

irrigation with either gentamicin or clindamycin solution. This surgery was classed as clean.

One three-arm study compared the use of epicillin with lincomycine in a group of 162 adults and children undergoing surgery for appendicitis (classed as contaminated) (Marti 1979); a third group of participants were randomised to saline irrigation (see comparison 2).

One five-arm study assessed irrigation with four different antibiotic solutions (cephapirin, cefamandole, moxalactam or ampicillin) or saline in 360 women undergoing caesarean section (Dashow 1986). The comparison of antibiotic irrigation versus saline is included in comparison 2; we were also able to assess six comparisons involving the individual antibiotics.

One study assessed irrigation with either cefazolin of cefamandole in women undergoing caesarean section. Peterson 1990 enrolled 207 women and randomised 113 to groups relevant to this review.

Primary outcome: SSI

Cephapirin versus cefoxitin

The RR for Levin 1983 was not estimable because there were no SSI events in either treatment group (85 participants). Therefore no full GRADE assessment was possible but the certainty of the evidence would be affected by risks of bias as well as imprecision.

Epicillin versus lincomycine

Marti 1979 did not specify the number of participants relevant to this comparison (162 total participants) and did not report any outcome data by the intervention group in which the event occurred, instead reporting only the total number of events in all three intervention groups for both SSI and adverse events. We could not analyse these data further and no full GRADE assessment was possible, but the certainty of the evidence would be affected by risks of bias as well as imprecision.

Clindamycin versus gentamicin

The RR for Oller 2015 was not estimable because there were no SSI events in either treatment group (34 participants relevant to this comparison). Therefore no full GRADE assessment was possible; the certainty of this evidence would be affected by imprecision.

Cephapirin versus cefamandole

The RR for Dashow 1986 was 1.37 (95% CI 0.24 to 7.95; 134 participants) based on 3 out of70 participants with SSI in the cephapirin group and 2 out of 64 in the cefamandole group.

Cephapirin versus moxalactam

The RR for Dashow 1986 was 1.69 (95% CI 0.29 to 9.84; 149 participants) based on 3 out of 70 participants with SSI in the cephapirin group and 2 out of 79 in the moxalactam group.

Cephapirin versus ampicillin

The RR for Dashow 1986 was 7.00 (95% CI 0.37 to 133.06; 140 participants) based on 3 out of 70 participants with SSI in the cephapirin group and 0 out of 70 in the ampicillin group.

Cefamandole versus moxalactam

The RR for Dashow 1986 was 1.23 (95% CI 0.18 to 8.52; 143 participants) based on 2 out of 64 participants with SSI in the cefamandole group and 2 out of 79 in the moxalactam group.

Cefamandole versus ampicillin

The RR for Dashow 1986 was 5.46 (95% CI 0.27 to 111.65; 134 participants) based on 2 out of 64 participants with SSI in the cefamandole group and 0 out of 70 in the ampicillin group.

moxalactam versus ampicillin

The RR for Dashow 1986 was 4.44 (95% CI 0.22 to 90.88; 149 participants) based on 2 out of 79 participants with SSI in the moxalactam group and 0 out of 70 in the ampicillin group.

Cefazolin versus cefamandole

The RR for (Peterson 1990) was 4.58 (95% CI 0.22 to 93.38; 113 participants) based on 2 out of 59 participants with SSI in the cefazolin group and 0 out of 54 in the cefamandole group.

Where a full GRADE assessment was possible, in each case we judged these estimates to represent low-certainty evidence, which was downgraded twice for serious imprecision. Details for all studies are given in Table 2; GRADE judgements are summarised in Table 1.

Primary outcome: wound dehiscence

This was not reported by any of the studies.

Secondary outcome: adverse events

Cephapirin versus cefoxitin

Levin 1983 reported only a single type of adverse event (endometritis); these data were not further analysed.

Epicillin versus lincomycine

Marti 1979 reported that one abscess occurred in the groups treated with antibiotics but did not report in which group the event occurred therefore no full GRADE assessment was possible although the certainty of the evidence would be affected by risks of bias as well as imprecision.

Dashow 1986 reported that there were no occurrences of abscess in any group; because there were zero events in every group (total 360 participants), no estimates of effect could be calculated for any comparison. The study also reported the proportion of participants with infection-related morbidity; these data did not clearly represent all participants with adverse events and were not further analysed for any of the six comparisons of antibiotics.

No full GRADE assessment was possible for any of the comparisons but any assessment of the certainty of the evidence would be affected by imprecision.

Secondary outcome: mortality

Clindamycin versus gentamicin

The RR for Oller 2015 was not estimable because there were no events in either treatment group (34 participants relevant to this comparison). Therefore no GRADE assessment was possible.

No other studies reported this outcome.

Secondary outcome: length of stay:

Cephapirin versus cefoxitin

There may be little or no difference between the groups; the difference in means in Levin 1983was 0.10 days (lower for the cephapirin group) (95% CI -0.78 to 0.58; 85 participants). This was low-certainty evidence downgraded twice for imprecision.

Clindamycin versus gentamicin

Oller 2015 reported a median length of stay of 3 days (range 1 to 3) in each group (total 34 relevant participants) suggesting that there may be little difference between the groups. This was low-certainty evidence downgraded twice for imprecision.

No other studies reported this outcome.

Other secondary outcomes

No studies reported data for other secondary outcomes.

Summary of comparison

There were 10 comparisons of different antibiotic solutions. Each comparison was assessed in a single study; six comparisons were represented by the same trial that randomised participants to saline or one of four different antibiotic solutions. Numbers of participants were low. All of the comparisons reported SSI as an outcome and none reported wound dehiscence. For three comparisons we could not calculate an estimate of effect, either because there were no events (cephapirin versus cefoxitin and clindamycin versus gentamicin) or because no group data were reported (epicillin versus lincomycine). In each of the other comparisons (cephapirin versus cefamandole; cephapirin versus moxalactam; cephapirin versus ampicillin; cefamandole versus moxalactam; cefamandole versus ampicillin; moxalactam versus ampicillin; cefazolin versus cefamandole) there was low-certainty evidence of no clear difference between the groups, downgraded twice for imprecision because of wide confidence intervals, which included the possibility of no effect and both benefit and harm for each treatment. All except the last of these comparisons were represented by the single, multi-arm trial. Although all classes of surgery were represented, effect estimates were only calculable for those comparisons assessed in clean-contaminated surgery.

Comparison 6: comparison of two different methods of irrigation delivery

Summary of findings 3

Comparison of standard (non-pulsed) saline irrigation using a jug or a syringe with pulsatile saline irrigation was assessed by two studies (Hargrove 2006; Nikfarjam 2014) with a total of 484 participants. Hargrove 2006 enrolled 356 people (ages not reported clearly) having surgery for displaced neck of femur (classed as clean). Nikfarjam 2014 enrolled 137 adults undergoing open elective abdominal surgery scheduled to last at least two hours (classed as clean-contaminated).

Primary outcome: SSI

Both Hargrove 2006 and Nikfarjam 2014 assessed SSI. There may, on average, be a lower incidence of SSI in participants treated with pulsatile irrigation compared with standard irrigation. There were 13 cases of SSI in the 230 participants in the pulsatile groups compared with 42 out of 254 in the standard groups. The pooled RR was 0.34 (95% CI 0.19, 0.62; I^2 = 0%; 484 participants) Analysis 4.1. This was low-certainty evidence, which was downgraded twice for multiple additional risks of bias in Hargrove 2006, which contributed 69% of the weight in the analysis; both studies were necessarily at high risk of performance bias due to the nature of the comparison. The RR equates to an absolute risk difference of 109 (95% CI 62 to 134) fewer SSIs per 1000 participants with pulsatile irrigation than with standard irrigation.

Because there was only a single study in each surgical class and populations were mixed or adult we were unable to conduct pre-planned subgroup analyses on the basis of either surgical category or adult/paediatric populations.

Primary outcome: wound dehiscence

Nikfarjam 2014 reported that there was one incidence of wound dehiscence in the standard irrigation group. The RR for this was 0.31 (95% CI 0.01 to 7.55; 128 participants). This was low-certainty evidence downgraded twice for imprecision.

Secondary outcome: mortality

Hargrove 2006 reported that there were 25 deaths among the 356 participants but did not state in which treatment group they occurred; Nikfarjam 2014 did not report mortality. No GRADE assessment was possible.

Secondary outcome: adverse events

Nikfarjam 2014 reported the number of participants with complications that were not wound infections. The RR was 1.31 (95% CI 0.87 to 1.97; 128 participants). This was low-certainty evidence downgraded twice for imprecision.

Secondary outcome: use of systemic antibiotics

Nikfarjam 2014 reported that 14 of the 16 participants with wound infection were treated with systemic antibiotics but did not report data by treatment group; no GRADE assessment was possible.

Secondary outcome: antibiotic resistance

Hargrove 2006 reported that "half" of the wound infections tested positive for MRSA but did not report data by treatment group. Nikfarjam 2014 reported some qualitative data on the organisms isolated. No GRADE assessment was possible.

Secondary outcome: length of stay

Nikfarjam 2014 reported the median length of stay as 9 days in both groups, the range in the pulsatile group was 5 to 45 days compared with 4 to 71 days in the standard group. This suggested that there may be little difference between the groups. This was moderate-certainty evidence downgraded once for imprecision.

Secondary outcome: reoperation

Nikfarjam 2014 reported the need for reoperation for two specific reasons: major debridement and relaparotomy. The effect estimate for all reintervention showed no clear difference between the groups (RR 0.56, 95% CI 0.14 to 2.26; 128 participants). This was low-certainty evidence downgraded twice for imprecision.

Secondary outcome: hospital readmission

Nikfarjam 2014 reported readmissions to hospital; there is no clear difference between the groups. The RR was 1.41 (95% CI 0.53 to 3.73; 128 participants). This was low-certainty evidence downgraded twice for imprecision.

Summary of comparison

Two studies assessed pulsatile versus standard techniques of irrigation using saline. One was conducted in clean and one in clean-contaminated surgeries. There may be fewer incidences of SSI in participants treated with pulsatile irrigation compared with normal irrigation. This was low-certainty evidence downgraded twice for multiple additional risks of bias in the study with the majority of the weight in the analysis; both studies were also at high risk of performance bias. There is no clear difference between the groups in the incidence of wound dehiscence; low-certainty evidence downgraded twice for imprecision.

DISCUSSION

Summary of main results

We identified a total of 59 studies involving 14,738 participants. Most included studies had a parallel-group design (there was one split-body design and two factorial designs that assessed, respectively, skin preparation and intravenous antibiotics as well as wound irrigation). Most studies reported the primary review outcome (SSI), with other outcomes of interest sparsely reported. Key results for each comparison and outcome are summarised below.

Surgical site infection

Comparison with no intervention

Twenty studies with 7192 participants compared some form of irrigation with no irrigation, The irrigation fluid was either non-antibacterial (typically saline) or an antiseptic or antibiotic solution. The majority of these studies reported analysable SSI data, which contributed to a pooled analysis, and we were able to carry out one of the prespecified subgroup analyses based on surgical classification. We also undertook an exploratory analysis on the basis of type of irrigation solution, which supported our informed decision to conduct a single analysis that included studies that used different types of irrigation solution. Based on available data there was, on average, no clear difference between the groups in incidence of SSI, and this was also the case in the two subgroups (clean-contaminated versus contaminated or dirty). This was low-certainty evidence downgraded for risk of bias and imprecision; although fewer infections were reported in the groups treated with irrigation, confidence intervals included both benefit and harm despite large numbers of participants.

Comparison of antibacterial irrigation with non-antibacterial irrigation

Thirty-six studies (6163 participants) compared a non-antibacterial (typically saline) irrigation with either an antiseptic (14 studies) or an antibiotic solution (22 studies). The majority of these studies reported analysable SSI data, which contributed to a pooled analysis, and we were able to carry out one of the prespecified subgroup analyses based on surgical classification. We also undertook an exploratory analysis, which confirmed that it was reasonable to conduct a single analysis that included studies that used different types of antibacterial irrigation solution. There may, on average, be a lower incidence of SSI in participants treated with antibacterial irrigation compared with non-antibacterial irrigation. This was low-certainty evidence, which was downgraded once due to risk of bias across multiple domains in studies accounting for much of the analysis weight, and once due to the probability of publication bias.

Comparisons between interventions of the same class

Several single studies compared two different irrigants without antibacterial properties or compared two different antiseptic agents or two different antibiotics. No studies compared antibiotics with antiseptics. The great majority of these studies were underpowered and had limited reporting of methodology. Only one comparison was represented by more than one study (icodextrin versus lactated Ringer's solution) and this was also the only comparison of this nature with adequately powered and well-reported studies; however SSI was not the primary outcome of either study and in one study we were not clear that ambiguous data actually represented this outcome.

As a consequence of the poor reporting and small numbers of participants, events or both, all of the comparisons between agents of the same class represented low-certainty evidence. Only one comparison found that there may be a difference between the groups: there may be more SSI in participants treated with povidone iodine compared with superoxidised water (downgraded for risk of bias as well as imprecision); in all other cases, based on available evidence, there is no clear difference between the treatment groups. Individual studies represented particular classes of surgical contamination and the applicability of the evidence from the comparisons to participants in other surgical classes may be reduced by indirectness.

Comparison of pulsatile irrigation with standard irrigation

There was low-certainty evidence from two studies that, on average, there may be fewer SSIs in participants treated with pulsatile compared with standard (non-pulsed - pouring method) irrigation. This was based on participants undergoing clean or clean-contaminated surgery and may therefore be only indirectly relevant to participants undergoing more contaminated surgeries. We downgraded this evidence twice for risk of bias across multiple domains in the study with the greatest weight in the analysis.

Wound dehiscence

Only a minority of studies reported wound dehiscence across all comparisons. For no comparison where this was reported is there a clear difference between the groups. This was low- or very low-certainty evidence in each case. Imprecision was a factor in all comparisons, inconsistency or high risk of bias were also present in some cases.

Secondary outcomes

Many studies did not report any of the secondary outcomes we specified for this review. Those that did often only reported one or two and these were most often length of hospital stay or adverse event data. We pooled data that reported mean lengths of stay and provided narrative summaries where medians were reported. With adverse event data we pooled studies that reported the number of participants in each group with an event. We documented reports

of specific types of adverse events but did not analyse these with the exception of abscess formation, which we had prespecified as being of particular interest to the review; we analysed this separately. Mortality was reported in only a minority of studies; in many instances this is likely to be a consequence of there being zero events in low-risk participants undergoing clean or clean-contaminated procedures. Outcomes related to antibiotic resistance – proportion of participants on systemic antibiotics in the 30-day postoperative period and incidence of antibiotic-resistant infection were especially poorly reported. There were few data and the data that were reported were often incomplete. The evidence for the impact of interventions on length of hospital stay was low or moderate certainty; where differences were seen they were too small to be clinically important.

Overall completeness and applicability of evidence

A wide range of types of surgery is included in this review and all four categories of surgery (clean, clean-contaminated, contaminated and dirty) were represented. However, as might be anticipated, only small numbers of participants undergoing clean operations were identified. Therefore, although we did not identify a material difference between subgroups in our planned analyses based on surgical category, it should be emphasised that most of the data relate to clean-contaminated, contaminated or dirty surgeries. Only one very small study assessed the comparison of no intervention with intervention in participants undergoing clean surgery and numbers were low for the comparison between antibacterial and other solutions too.

A substantial number of studies included only women because of the nature of the surgery undertaken (e.g. caesarean sections), although we do not believe this would impact on the relevance of the results to all surgical patients. Few studies included only children although many included both adults and children.

Publication dates of included studies ranged from 1968 to 2016. This is likely to be a source of considerable differences between participants and surgical techniques, while the development of antibiotic resistance over time may also make results from early studies less directly relevant to current practice. Twenty of the 59 studies - approximately one third - were published before 1990. There were variations in the use of prophylactic antibiotics, as would be anticipated given the different types and contamination levels of surgery involved and the time span across which studies were conducted and published. This may affect the applicability of some of the evidence.

We did not include studies that compared irrigation with another intervention, so can present no evidence for the value of irrigation compared with, for example, antibiotics delivered by another method. This represents a gap in the comprehensive evidence synthesis but other reviews have included these studies (see Agreements and disagreements with other studies or reviews). We would have included any studies that compared the use of an antibiotic solution with an antiseptic solution but none were identified. This is a clear gap in the evidence and possible methods for dealing with this are discussed in Implications for research. We also did not identify any studies that compared the use of different volumes of the same solution.

Although the great majority of included studies reported the primary outcome of SSI, few reported wound dehiscence and participant numbers were such that there was insufficient power for a difference between groups to be detected. Key secondary outcomes such as adverse events and antibiotic resistance were poorly and inconsistently assessed and reported in most trials and for most comparisons. Mortality was reported in only a minority of studies, although we believe that this is at least partially explained by a zero incidence in many studies not being formally reported. Although we planned to look at the time points of outcome assessment, in practice the overwhelming majority of data related to short-term post-surgical assessment at between two and eight weeks. Long-term follow-up was rare and limited to a small number of orthopaedic or spinal operations, which followed participants for several months, but even in these cases they reported limited data beyond the initial postoperative period. This is unlikely to be a serious threat to the applicability of the results for SSI but it may have implications for other outcomes such as mortality.

Despite searching multiple databases and extensive citation checking we are not confident that we have identified all extant studies although we believe we are likely to have identified the great majority of published studies. Analysis of funnel plots for comparisons of intervention versus no intervention and for antibacterial versus non-antibacterial interventions suggested that publication bias was possible or likely. The implications of this are explored in Potential biases in the review process.

Quality of the evidence

In studies that compare irrigation with no irrigation or compare different irrigation techniques it is difficult or impossible for personnel to be blinded to treatment allocation. Since none of these studies explicitly reported doing so, we classified them all as being at high risk of performance bias. However we did not downgrade for this risk of performance bias if no other domain was classed as posing a high risk of bias. Blinding of outcome assessment is a more important risk of bias and this was reported to be low for only a minority of studies; in many more it was unclear whether this was undertaken for the key outcomes of SSI and wound dehiscence. Just under half of studies were at risk of bias other than inherent performance bias, and the great majority were poorly reported in multiple domains, placing them at unclear risk of bias on many factors.

Where possible we conducted preplanned sensitivity analyses, which looked at the impact of removing studies at a high risk of bias in one or more domains; we were able to do this for the outcome of SSI for the comparisons between irrigation and no irrigation and between antibacterial and non-antibacterial irrigation. When we performed the sensitivity analysis for the comparison of no irrigation with irrigation we did not remove studies which were only at high risk in the domain of performance bias, because all studies necessarily had a high risk in this domain. The results of these sensitivity analyses suggested that data from studies with a high risk of bias were not acting to increase an estimate of effect, although such studies included large numbers of participants.

Poor reporting means that we are not confident that most of the studies that did not show a clear high risk of bias in any domain are free from such a risk; it is likely that many are but that this is not evident from the limited reporting of the study.

Finally as noted in Overall completeness and applicability of evidence and Potential biases in the review process, we are

concerned that the certainty of the evidence may be compromised by selective incompleteness - a pattern of missingness which may serve to increase the estimates of effect.

Potential biases in the review process

We believe that this review is unlikely to be affected by language bias; it includes studies in Slovak, Korean, Persian, French and Danish. Studies in other languages, including Chinese and German were also identified and considered for inclusion at full text (see Excluded studies).

We identified a substantial number of trials through citation searching in addition to those found through database and trial registry searches. However, while we have some confidence that we are likely to have identified the great majority of relevant published studies, we cannot rule out the possibility that there are unpublished studies which are not included in the review and which may have affected the results. We were able to construct funnel plots for the primary outcome of SSI for both the comparison of irrigation with no treatment and the comparison of antibacterial with non-antibacterial solutions. In the latter case there was a strong suggestion that there may be small studies with negative results that were absent from the evidence identified and we downgraded the certainty of the evidence once because of this. The appearance of the funnel plot for the comparison with no treatment was ambiguous, while we could not rule this out there was no clear suggestion of a publication bias effect. There were too few trials in the other analyses to permit funnel plot analyses so we are unable to assess the likelihood of publication bias in these sections of the review; it is nevertheless possible that it may be present. The impact of publication bias of the type we may have identified is to increase the estimate of effect relative to the true effect of the intervention.

The exploratory subgroup analysis, which we used to confirm our strategy of comparing any type of irrigation with no irrigation, suggested that none of the heterogeneity in that analysis was explained by whether the solution used was antibiotic, antiseptic or antibacterial. However, we have identified that there may be fewer SSIs in participants treated with antibacterial (antiseptic or antibiotic) irrigation compared with no irrigation. The fact that we found no evidence of a differential effect of solution type in the comparison with no irrigation may represent an additional reason for caution in the interpretation of this data, alongside the noted risks of bias and publication bias. Equally, however, it is important not to over interpret subgroup analyses, particularly when these are not prespecified. We should also note that the two analyses (irrigation versus no irrigation; antibacterial versus non-antibacterial) contained different proportions of participants in the different surgical categories, meaning that baseline incidence of SSI will differ.

In the majority of the included studies the source of funding was not reported and where it was reported it was mostly non-commercial. Whilst it is possible that funding may play a role in the potential differential absence of small negative trials, it may be more likely due to the other factors including the reluctance of both journals and authors to pursue publication in such cases. We identified only one completed study that was without extant publication in our search or trial registers, this had only recently passed its completion date; we also identified one study that had passed the planned completion date but that did not have an identified publication.

Agreements and disagreements with other studies or reviews

We identified a number of reviews as being relevant to this synthesis; these proved extremely helpful to our citation searching although none had the same scope as our review in all respects. Existing reviews fell into the following classes: reviews focusing on a particular type of surgery (e.g. Mueller 2015); and reviews focusing on a particular agent or class of agents (e.g. Fournel 2010 and Oliveira 2008, which look at the use of intraoperative povidone iodine); in some cases they focused even more narrowly on a specific intervention for a specific operation (e.g. Eke 2016; Smaill 2014).

Some reviews differed from our work in that they included studies other than RCTs - either quasi-RCTs (some of which were classed as RCTs) or even less rigorous research methodologies. Some also used a very wide definition of irrigation or had a broader objective and included any method of topical application of their agent of interest to the wound, including, for example, assessments of aerosols, dry powder or very low volumes of liquid. There were also broader definitions of the area irrigated; we did not include studies where only internal (e.g.) uterine, bladder or bowel irrigation was reported. We have employed a narrower definition of irrigation but adopted a much broader approach to the types of agents and classes of surgery which were of interest. Several reviews also considered comparisons that were outside the scope of our review because the use of irrigation of a particular type was not the only systematic difference between the treatment groups. Finally our review has a much more recent search than many of these and, while many studies in the review were old, over a third of the included studies - including many of those with large numbers of participants and stronger methodologies - were published from 2010 onwards, with a significant number having 2015 and 2016 publication dates.

The most recent review, and the one with the closest scope to ours is De Jonge 2017, which focuses on prophylactic irrigation; this review supported the recent recommendations of the World Health Organization on prevention of SSI (WHO 2016). For a number of reasons De Jonge 2017 included fewer studies than our review as it excluded studies where wounds could already be considered to be infected (and where treatment was therefore not considered prophylactic) and was restricted to irrigation at the level of the wound rather than deeper (e.g. peritoneal) irrigation. The authors also required that there be a description of appropriate antibiotic prophylaxis, which we did not; many of the studies included here had very limited reporting of co-interventions and reporting of antibiotic use varied. There were other variations in the inclusion criteria - including a restriction by De Jonge to four, widely spoken European languages whereas we applied no language restrictions. A combination of these factors accounts for many of the differences between their review and ours. One principal result of the differing inclusion criteria is that our review includes many studies in obstetric surgery, which are not included in theirs. A small number of trials, which were included in their review, were excluded from ours based on differing interpretation of adequate randomisation or volume of liquid required for irrigation.

AUTHORS' CONCLUSIONS

Implications for practice

The evidence base identified by this review was generally of low certainty, which means that the true effects may be substantially different to the estimates of effect. Therefore where we have identified a difference in surgical site infection (SSI) incidence - as with the comparisons of antibacterial and non-antibacterial interventions and pulsatile versus standard methods - these should be considered in the context of uncertainty. This is particularly the case as we suspect that the evidence base may have been affected by the tendency for small studies with negative results to remain unpublished and absent from meta-analyses. Clinicians should also consider whether the evidence is relevant to the surgical populations under consideration, for instance where the surgery is considered to be a clean procedure. They should also take into consideration the limited data available on wound dehiscence. They may also wish to consider the varying reporting of prophylactic antibiotic use delivered by other means (e.g. oral, intramuscular etc); in some of the studies in the review no such prophylaxis was reported whereas their practice may be to routinely use this for the procedure under consideration - or vice-versa. They may wish to consider this in conjunction with the evidence of this review on the efficacy of different types of irrigation solutions. The limited reporting of many relevant outcomes should also be considered.

Finally, while many studies in the review are recent, others are old and predate current levels of, and concern over, the development of antibiotic resistance.

Implications for research

We did not identify any trials that compared antibiotic irrigation with antiseptic irrigation; this represents a gap in the direct evidence base, which may merit further investigation. If the possible benefit of antibacterial irrigation treatment represents a true effect this is particularly worth investigating, given growing concerns over antibiotic resistance.

The evidence base we have identified means that this gap in the evidence could be investigated using a network meta-analysis; an analysis of the indirect evidence for the comparison could then inform a decision as to whether new primary research was warranted.

There was a considerable amount of heterogeneity between the studies we identified and this was not explicable by surgery class in prespecified analyses. Exploratory analyses also confirmed that this was not explained by our decision to combine studies using different types of irrigation fluids. We did not pre-specify the operative point of irrigation as being a factor of interest (i.e. at what level of wound closure it was undertaken); this did vary between studies and is a factor that may benefit from investigation. Future trials should also carefully consider how prophylactic antibiotics would be used and documented.

Any future network analysis could also consider indirect evidence for comparisons of different volumes of particular solutions. Any further research, whether primary or secondary should also take account of the level of contamination of procedures under consideration although we have not identified this as an effect modifier.

Finally pulsatile irrigation should be explored further in primary research. The authors of one of the included studies Nikfarjam 2014 suggest that pulsatile irrigation may reduce bacterial counts and help to remove tissue that could otherwise act as a focus for infection but the mechanism for its possible benefit is not clear and would require further research.

Any new primary research should use this systematic review and meta-analysis as a guide for calculating sample sizes, in order to have sufficient power to detect a difference in SSIs, particularly if undertaken in participants undergoing clean or clean-contaminated surgery where event rates are low.

Any such trial should use appropriate and robust research methodology to reduce the risks of bias, should use internationally recognised criteria for the diagnosis of SSI and should have adequate follow-up procedures and duration to ensure that SSIs occurring after hospital are recorded. Other outcomes such as wound dehiscence - a primary review outcome for which there was little evidence - and health-related quality of life should also be considered. In view of the limited reporting of relevant outcomes that this review has identified, consideration should be given to the development and use of core outcome sets defined using transparent and rigorous methodology.

We identified a number of ongoing trials and the completion dates of these should be taken into consideration in the planning of a network meta-analysis.

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Al-Shehri 1994

Methods	2-arm RCT Setting: NR; appears to be single hospital in Saudi Arabia Participants reportedly followed up for 1 month, no additional details
Participants	254 adults and children (aged 5-80 years, mean age 21 (Group I) and 24 years (Group II)) undergoing appendectomy for acute appendicitis were randomised; 249 analysed Inclusion criteria: people undergoing appendectomy through gridiron incision for clinically suspected acute appendicitis Exclusion criteria: allergy to ampicillin; systemic diseases requiring systemic antibiotic administration
Interventions	Group I: (saline): wound irrigation with 100 mL normal sterile saline at closure (134 participants randomised; 132 analysed; 2 participants withdrawn post-randomisation) Group II: (Ampicillin): wound irrigation with 1 g Ampicillin powder dissolved in 100 mL normal sterile saline (120 participants randomised; 117 analysed; 3 participants withdrawn post-randomisation) Co-interventions: IV metronidazole (500 mg for adults; 15 mg/kg for children) and gentamicin (75 mg for adults and 1.5 mg/kg for children) 1 h before surgery. If appendix was found to be gangrenous or perforated antibiotics were continued for 5 ds postoperatively.
Outcomes	**Primary outcome: SSI** (defined as presence of purulent discharge in wound, regardless of culture results, or as occurrence of serous discharge with a positive culture) within 1 month Group I (Saline): 7/132 (134 randomised) Group II (Ampicillin): 1/117 (120 randomised) **Secondary outcome: adverse events including abscess:** Abscess Group I (saline): 0/132 Group II (Ampicillin): 0/117 Other specific post-operative complications were reported but total number of participants with adverse events was not clear. **Secondary outcome: hospital stay:** reported to be reduced by 2.5 d by avoidance of wound infection. Median reported for participants with (5.5, range 3-11 d) and without infection (3.0, range 2-11 d) but not for each treatment group.
Notes	Funding: NR

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "254 patients fulfilled the criteria and were randomized into two groups using sealed envelopes" Comment: no information on how the randomisation sequence was generated.

Al-Shehri 1994 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	Quote: "254 patients fulfilled the criteria and were randomized into two groups using sealed envelopes that were opened intraoperatively" Comment: although sealed envelopes were used it is not clear that they were opaque or that the allocation sequence was fully concealed at all times.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Comment: no direct quote but it is clear that personnel were made aware of allocation once the envelopes were opened. Unclear if participants were aware
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: no direct quote but it is unclear whether the outcome assessment was performed by individuals aware of group allocation.
Incomplete outcome data (attrition bias) All outcomes	High risk	Comment: there were a small number of post-randomisation exclusions for protocol violations described. However there were low numbers of events relative to these exclusions, increasing the risk of attrition bias impacting the results.
Selective reporting (reporting bias)	Unclear risk	Comment: rhe data for one of the secondary outcomes (bed-stay) were not reported on a per-group base making this outcome difficult to evaluate.
Other bias	Unclear risk	Comment: there was no evidence of other sources of bias but reporting was not clear enough to be certain.

Baker 1994

Methods	2-arm RCT Setting: single centre; 1 surgical unit in UK Follow-up: close monitoring during hospital stay; full inquiry into possible infection signs at 6-week outpatient clinic follow-up
Participants	330 participants undergoing elective colorectal surgery (mean ages 61 (Group I) and 63 years (Group II)); 300 analysed Inclusion criteria: participants undergoing elective colorectal surgery Exclusion criteria: NR
Interventions	Group I (taurolidine PVP): peritoneal lavage in 2 stages with 250 mL 2% taurolidine in 5% PVP (150 participants) Group II (saline): peritoneal lavage in 2 stages with 250 mL normal saline (150 participants) In each group 250 mL lavage solution diluted in a further 250 mL normal saline was placed in the abdomen as a washout and then removed with suction. This was followed by instillation of a second 250 mL undiluted lavage solution, which was left in the abdomen. If abdominal drains were present these were clamped for at least 20 min. Cointerventions: all participants (except 11 who had severe constricting colonic lesions and were in imminent danger of bowel obstruction) received up to 8 doses of magnesium sulphate (4 g by mouth) for 48 h starting 72 h before surgery followed by 2 sachets of sodium picosulphate (Picolax; Fering Pharmaceutical, Feltham, UK) given in the 24 h immediately before surgery. Participants with severe constricting colonic lesions were prepared according to the wishes of the surgeon; 8 received Klean-Prep (Norgine, Oxford, UK) in place of Picolax and 3 no preparation. All participants received cefotaxime 1

Baker 1994 *(Continued)*

	g and metronidazole 500 mg IV at induction of anaesthesia, and 8 h and 16 h later. 5 participants with penicillin allergy received gentamicin 160 mg on induction, and 120 mg at 8 h and 16 h after induction; doses were individually adjusted according to body mass, renal function and age.
Outcomes	**Primary outcome: SSI** (defined as spontaneous or incisional discharge from the wound, either of pus or serous fluid, with an infective organism positively identified on culture) Group I (taurolidine PVP): 17/150 (10 superficial, 7 deep) Group II (saline): 17/150 (12 superficial, 5 deep) **Secondary outcome: 30-day mortality** Group I (taurolidine PVP): 4/150 Group II (saline): 4/150 **Secondary outcome: adverse events including abscess**: Pelvic abscess Group I (taurolidine PVP): 2/150 Group II (saline): 1/150 Other specific post-operative complications were reported but total number of participants with adverse events was not clear. **Secondary outcome: length of hospital stay** Group I (taurolidine PVP): median 11 d for 133 participants without infection; 18 d for 17 with infection (paper reports N = 134, error suspected) Group II (saline): median 11 d for 133 participants without infection; 18 d for 17 with infection (mean NR, range NR)
Notes	Funding: NR

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "This paper reports a randomized controlled trial.....Bottles of lavage fluid were dispensed in identical containers according to a computer-generated randomized code held by the hospital pharmacy with no stratification for severity of contamination or procedure. " Comment: appears there was a computer-generated randomisation sequence
Allocation concealment (selection bias)	Unclear risk	Quote: "Bottles of lavage fluid were dispensed in identical containers according to a computer-generated randomized code held by the hospital pharmacy with no stratification for severity of contamination or procedure." Comment: although the allocation sequence was held by the hospital pharmacy it is not clear whether it was adequately concealed.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "Bottles of lavage fluid were dispensed in identical containers according to a computer-generated randomized code held by the hospital pharmacy... The trial and control solutions were indistinguishable to users." Comment: personnel appear to have been blinded; although there is no direct information on participants it is likely that they were also blinded.

Baker 1994 *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "All patients were monitored closely after operation until hospital discharge for clinical signs of abdominal sepsis and wound infection by an independent (non-operating) trained assessor (J.AJ.)." Comment:
Incomplete outcome data (attrition bias) All outcomes	High risk	Quote: "Sixteen patients were withdrawn from the trial after consent because the operative procedure performed did not constitute elective colorectal surgery ..... A further eight patients were withdrawn as lavage was not undertaken for logistical reasons, such as breakage of solution bottles. A further six patients were withdrawn at the time of surgery because of overt sepsis or severe faecal spillage, which rendered the intraoperative lavage a therapeutic rather than a prophylactic measure. Thus 300 patient reports were available for analysis." Comment: almost 10% of randomised participants were not included in the analysis. Although full reasons are given for this the number of withdrawals is almost equivalent to the number of events.
Selective reporting (reporting bias)	Low risk	Comment: the data for one of the secondary outcomes (bed-stay) were not fully reported (measure of variance lacking) but no other evidence of selective reporting
Other bias	Unclear risk	Comment: there was no evidence of other sources of bias but reporting was not clear enough to be certain.

Bourgeois 1985

Methods	Parallel-group RCT Setting: single hospital in USA Follow-up: 6 weeks (review of records after discharge)
Participants	223 women undergoing cesarean section Inclusion criteria: women delivered by caesarean section Exclusion criteria: allergy to penicillin or cephalosporins, taken an antibiotic within 7 d of surgery or required antibiotics around time of surgery for other reasons. Participants with temperature elevated to 38ºC or with foul amniotic fluid prior to or immediately after surgery were considered to have infection and excluded. High risk and low risk participants were separated according to duration of labor prior to cesarean section, with 6 h arbitrarily chosen as the division point. Each group contained both high risk (more than 6 h labour) and low risk (less than 6 h labour) participants
Interventions	Group I: irrigation with 2 g cefamandole in 1000 mL normal saline (73 participants) Group II: irrigation with 1000 mL normal saline (75 participants) Group III: no irrigation (75 participants)
Outcomes	**Secondary outcome: length of stay** Group I: low risk: 5.2 (0.3) d (N = 46); high risk: 5.3 (0.2) (N = 27) Group II: low risk: 5.9 (0.4) d (N = 40); high risk 6.8 (0.6) (N = 35)

Bourgeois 1985 *(Continued)*

	Group III: low risk 5.8 (0.3) d (N = 44); high risk: 6.9 (0.4) (N = 31) **Secondary outcome: adverse events** Only a specific event (metritis) was reported Group I: low risk: 2 (4.3% of 46); high risk: NR Group II: low risk: 4 (10% of 40); high risk: NR Group III: low risk: 9 (20.5% of 44); high risk: NR Infection data were also reported but were not clearly SSI and were not reported for all participants Group I: low risk: NR; high risk: 3 (11.1% of 27) Group II: low risk: NR; high risk: 17 (48.6% of 35) Group III: low risk: NR; high risk: 17 (54.8% of 31)
Notes	Funding: NR

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "members of each group were then assigned to a cohort according to a computer-generated table of random numbers under the direction of the hospital pharmacy" Comment: appropriate method used to generate randomisation sequence; randomisation stratified by duration of labour: > 6 h vs < 6 h
Allocation concealment (selection bias)	Unclear risk	Quote: "under the direction of the hospital pharmacy" Comment: unclear whether adequate methods were used to conceal allocation
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "Physicians who performed the operation and provided postoperative care were unaware of the type of irrigation provided" Comment: physicians were unaware of the type of irrigation used but are likely to have been aware of whether irrigation was used or not. It is unclear whether participants were aware of treatment allocation.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "Patients were followed postoperatively by the resident and attending physicians on service" Comment: not clear whether outcomes were determined by personnel blinded to treatment allocation.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Quote: "of all 451 patients who had cesarean sections during the study period, 223 were included" Comment: it appears that the 223 participants described as included were all included in the analyses but it's not completely clear that this is the total number who were randomised.
Selective reporting (reporting bias)	High risk	Comment: not all data relating to outcomes of infection, adverse events and postoperative hospitalisations were reported.

Bourgeois 1985 *(Continued)*

Other bias	Unclear risk	Comment: no obvious source of additional bias but reporting insufficient to be certain

Brown 2007

Methods	Parallel-group RCT Setting: 16 referral centres in the USA Follow-up: 28-56 d
Participants	449 women (age 32.6 years in Adept group vs 32.3 in lactated Ringer's solution group) undergoing laparoscopic gynaecological surgery. Primary diagnoses included pelvic pain, infertility endometriosis and known adhesions. Inclusion criteria: aged > 18 years and in good health. Laparoscopic surgery was planned for a gynaecologic procedure that included adhesiolysis followed by a second follow-up laparoscopy 4–8 weeks later. Exclusion criteria: preoperative: the use of concomitant systemic corticosteroids, antineoplastic agents, and/or radiation; pregnancy; diagnosis of an active pelvic or abdominal infection, or cancer; and a known allergy to starch-based polymers. Intraoperative exclusion criteria included women requiring an additional non obstetric/gynaecologic surgical procedure to be performed during the laparoscopic procedure; unplanned surgery necessitating opening the bowel (excluding appendectomy); any laparotomy procedure; and use of another adhesion reduction agent. Adhesion site exclusion criteria included women having < 3 of the available anatomical study sites with adhesions or, if fewer than three were lysed, removal of any anatomical sites being scored for the purposes of the study; and an inability to visualise clearly all available anatomical score sites.
Interventions	Group I: irrigated with a minimum 100 mL Adept (icodextrin 4% solution) solution every 30 min during surgery; any remaining solution at end of surgery was aspirated and then 1 L instilled from a fresh supply of solution (227 ITT, 205 PP participants) Group II: irrigated with a minimum 100 mL lactated Ringer's solution every 30 min during surgery; any remaining solution at end of surgery was aspirated and then 1 L instilled from a fresh supply of solution (222 ITT 205 PP participants)
Outcomes	**Postoperative infections** were reported but unclear whether these referred to SSI Group I (icodextrin): 1% of 227 calculated as 2 Group II (Ringer's solution): 3% of 222 calculated as 7 **Secondary outcome: adverse events** Group I (icodextrin): 221/227 of which 44 serious; 55 considered related, reported as serious 8 participants (25 events) Group II (Ringer's solution): 218/222 of which 36 serious; 38 considered related, reported as serious 11 participants (19 events) **Secondary outcome: mortality** Group I (icodextrin): 0/227 Group II (Ringer's solution): 0/222
Notes	Funding: Innovata Limited, Vectura Group
Risk of bias	

Brown 2007 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Treatment was randomized by computer-generated randomization on a 1:1 basis" Comment: an appropriate method of generating the randomisation sequence was reported.
Allocation concealment (selection bias)	Low risk	Quote: "Patient numbers were allocated to treatment group before labelling of the blinded study treatment bags. The study solutions were presented in identical 1 L infusion bags, and each bag had an outer wrap that contained the study code and patient number on an identification label" Comment: adequate method for concealment of treatment allocation reported
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "Double-blinding was possible because Adept and LRS are both clear and odourless solutions with similar viscosities to water." Comment: blinding appears to have been undertaken for personnel and participants.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "Safety was assessed by serious adverse events (SAEs), adverse events, and changes in laboratory values. Patients completed diary cards between initial surgery and follow-up surgery. At postoperative checkup (visits 3 and 4), cards were assessed to monitor progress. They allowed the patient to record their well-being and all concomitant medications. All adverse events whether they were considered related to study solutions or not, were investigated, and the details of nature, severity, duration, outcome, and relationship to study device were recorded" Comment: safety outcomes were assessed by participants who were blinded to treatment allocation.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "Safety was assessed in the intent-to-treat (ITT) population, which included all patients who had the study solution instilled. Efficacy results are presented for the per protocol (PP) population. These patients were those who had completed both first- and second-look laparoscopies without major protocol violations." Comment: the outcomes relevant to this review were assessed using the ITT population so almost all randomised participants were included in the analyses.
Selective reporting (reporting bias)	Low risk	Comment: outcomes were prespecified; all planned outcomes appeared fully reported.
Other bias	Low risk	Comment: no evidence of other sources of bias and reporting is sufficient to be reasonably confident that this is the case

Browne 1978

Methods	Parallel-group RCT

Browne 1978 *(Continued)*

	Setting: single hospital in UK Follow-up: NR
Participants	35 participants with gross peritonitis or frank fecal soiling and a positive culture swab at operation Inclusion criteria: gross peritonitis or frank fecal soiling and a positive culture swab at operation Exclusion criteria: NR
Interventions	Group I: 2% taurolin in 5% PVP solution (normal saline) up to 200 mL instilled prior to closure of abdomen or afterwards through a tube drain. Additional 200 mL could be instilled daily if required for 7 d (17 participants) Group II: 5% PVP solution (normal saline) to 200 mL instilled prior to closure of abdomen or afterwards through a tube drain. Additional 200 mL could be instilled daily if required for 7 d (18 participants) Additional antibiotic use was documented as including gentamycin, lincomycin, cephalosporin [cephalosporine], ampicillin
Outcomes	**Secondary outcome: mortality** Group I (taurolin): 3/17 Group II (PVP): 0/18
Notes	Outcome was classed as "good" or "bad" where a normal recovery with normal wound healing and no sepsis was a good result and all other outcomes were bad Funding NR

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Envelopes containing cards, previously randomly arranged were available in theatre for selection of solution A or solution B" Comment: no information on how the random sequence arrangement was generated
Allocation concealment (selection bias)	Unclear risk	Quote: "Envelopes containing cards, previously randomly arranged were available in theatre for selection of solution A or solution B" Comment: no information on whether or how the random sequence arrangement was concealed.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "Two solutions were prepared ....in identical bottles labelled A and B" Comment: it appears that measures were taken to blind personnel and participants.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "Thirty-five patients entered the trial. It was intended to include a much larger number but at this stage there was a marked difference in results which was statistically significant..... so the code was broken" Comment: it appears that measures were taken to ensure blinded outcome assessment
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: it appears that all randomised participants were included in the analysis. However many fewer participants than planned were randomised (see other sources of bias).

Browne 1978 *(Continued)*

Selective reporting (reporting bias)	High risk	Outcomes were not prespecified and "a good result" was defined only in the results section.
Other bias	High risk	Quote: "For ethical reasons it was decided the trial should be stopped as soon as a statistically significant difference between the two groups emerged.....Thirty-five patients entered the trial. It was intended to include a much larger number but at this stage there was a marked difference in results which was statistically significant..... so the code was broken." Trial was stopped very early (a long way short of planned recruitment). Although this was preplanned this approach to early stopping is highly likely to produce an artefactual difference between groups

Buanes 1991

Methods	Parallel-group RCT Setting: single hospital in Norway Follow-up: 6 weeks postoperatively
Participants	85 participants with perforated appendicitis and generalised peritonitis Inclusion criteria: diagnosis of perforated appendicitis and generalised peritonitis verified at laparotomy Exclusion criteria: age < 6 years; known allergy to ampicillin or tinidazole, localised infiltration or abscess around the appendix.
Interventions	Group I: 24 hs postoperative lavage with 0.9% saline 1 L x 20 for adults, 0.5 L for children (39 participants) Group II: no postoperative lavage (44 participants) Cointerventions: intra-operative peritoneal lavage with 2 L of saline; 2 g ampicillin every 6 hs and 800 mg tinidazole daily until oral fluids commenced then pivampicillin 500 mg 3/d and 1 g tinidazole daily orally; children received pivampicillin 100 mg/kg/d and tinidazole 400 mg daily (rectal) for 5 d
Outcomes	**Primary outcome: SSI** (wound infection defined as temperature > 38.5 C for > 24 h plus localised, drainage-confirmed accumulation of fluid in the abdominal incision Group I (postoperative lavage): 9/39 Group II (no postoperative lavage): 2/44 **Secondary outcome: length of stay** Group I (postoperative lavage): median 5 d (range 3-11) 39 participants Group II (no postoperative lavage): median 5 d (range 4 -12) 44 participants
Notes	Treatment (postoperative lavage) was discontinued early in 10/39 participants

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "As soon as the diagnosis of perforated appendicitis with generalized peritonitis was verified at laparotomy, the patient was randomized..."

Buanes 1991 *(Continued)*

		Comment: no information on how the randomisation sequence was produced.
Allocation concealment (selection bias)	Unclear risk	Quote: "As soon as the diagnosis of perforated appendicitis with generalized peritonitis was verified at laparotomy, the patient was randomized..." Comment: no information as to whether allocation was adequately concealed.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Comment: allocation to postoperative lavage versus no postoperative lavage would be evident to both personnel and participants.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: unclear whether outcome assessment was performed by blinded individuals
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: 2/85 randomised participants were withdrawn for a documented reason (ampicillin allergy); although both were in the same group the number is low and is unlikely to have been a source of bias.
Selective reporting (reporting bias)	Unclear risk	Comment: outcomes were not all prespecified in the methods although a priori definitions for intra-abdominal and wound infection were given.
Other bias	Unclear risk	Comment: no evidence of other source of bias but reporting insufficient to be certain

Carl 2000

Methods	Parallel-group RCT Setting: appears to be single hospital in USA Follow-up: 4-6 weeks postoperatively
Participants	40 women undergoing caesarean section at high risk of infection
Interventions	Group I: irrigation with cefazolin; 2 g in 1000 cc normal saline; 700 cc intrauterine 100 cc in each gutter and 100 cc subcutaneously (20 participants) Group II: irrigation with 1000 cc normal saline 700 cc; intrauterine 100 cc in each gutter and 100 cc subcutaneously (20 participants) Cointerventions: none reported
Outcomes	**Primary outcome: SSI** (defined only as "wound infection") Group I (cefazolin): 1/20 Group II (saline): 1/20
Notes	Abstract only. Funding NR

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote: "Patients at high risk of infection were randomly placed in two groups"

Carl 2000 *(Continued)*

		Comment: no information as to how the randomisation sequence was generated
Allocation concealment (selection bias)	Unclear risk	Quote: "Patients at high risk of infection were randomly placed in two groups" Comment: no information as to whether there was adequate concealment of allocation
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Comment: no specific quote, no information as to whether these groups were blinded to treatment allocation
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: there is no information as to who performed the outcome evaluation or whether they were blinded to treatment allocation
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "Only 2 of 40 high risk patients who received prophylactic irrigation developed...." Comment: it appears that all randomised participants were included in the analysis.
Selective reporting (reporting bias)	Unclear risk	Quote: "The objective of this study is to determine the impact of copious antibiotic irrigation versus normal saline (ns) on the incidence of post-cesarean wound infections" Comment: the primary outcome was specified and reported but it is not clear from the abstract which other outcomes the study may have planned to assess.
Other bias	Unclear risk	Comment: there were no additional sources of bias noted but the abstract reporting was insufficient to be certain.

Case 1987

Methods	2-arm RCT Setting: single centre; 1 surgical unit in the UKm Follow-up: included outpatient assessment 6 weeks post-surgery
Participants	54 women undergoing planned Patey mastectomy for carcinoma of the breast (mean age 56; range 32-75 years) randomised (52 women and 53 breasts analysed) Inclusion criteria: Patey mastectomy Exclusion criteria: participants with allergy to tetracycline
Interventions	Group I (tetracycline): lavage of 1 g tetracycline in 100 mL saline (23 women) Group II (saline): lavage of 100 mL saline (30 women) Lavage was given at wound closure and was contained within the axilla and skin flaps as much as possible during closure. Cointerventions: drainage was standardised to Vygon suction drains to axilla and skin flaps; drains removed at request of surgical staff when drainage for previous 24 hs appeared minimal

Case 1987 *(Continued)*

Outcomes	**Primary outcome: SSI** (not defined) Group I (tetracycline): 0/23 Group II (saline): 1/30 **Primary outcome: wound dehiscence** Group I (tetracycline): 0/23 Group II (saline): 1/30 (described as "minor")
Notes	One woman underwent bilateral mastectomy and was randomised for each breast. Funding: NR

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "....were randomized to receive at wound closure" Comment: no information on how the randomisation sequence was generated
Allocation concealment (selection bias)	Unclear risk	Quote: "....were randomized to receive at wound closure" Comment: no information on whether allocation was adequately concealed
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Comment: no direct quote but no information on whether participants and personnel were blinded
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "Records were kept on a standard form by the nursing staff, who were unaware of the patient's randomization." Comment: no information on whether the blinded nursing staff performed outcome assessment at follow-up.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "Two women were excluded after randomization because they subsequently did not undergo Patey mastectomy" Comment: the number of exclusions was very small and both were accounted for by a substantive operative protocol deviation
Selective reporting (reporting bias)	Unclear risk	Comment: there is no evidence of selective reporting but because most outcomes were not specified in the methods section it is not clear whether it may have occurred
Other bias	Unclear risk	There may be a minor unit of analysis issue due to the randomisation of one woman twice for each breast. Otherwise there is no evidence of other bias but the reporting is not full enough to be sure.

Cervantes-Sanchez 2000

Methods	2-arm RCT Setting: single centre, Emergency Department in Mexico

Cervantes-Sanchez 2000 *(Continued)*

	Follow-up: 2 and 4 weeks after operation
Participants	350 participants entered into study; 283 considered evaluable (mean age of 27.99 years (SD 12.81 years), range from 9-82 years); (67 rejected from final analysis due to finding of another pathology different from appendix) Inclusion criteria: adults and children of both sexes admitted with a clinical diagnosis of acute abdomen suggestive of acute appendicitis with aid of laboratory and X-ray, confirmed during operation and by histopathologic study Exclusion criteria: age < 5 years, allergy to metronidazole or aminoglycosides, antibiotic therapy within 72 h preceding operation, pregnancy, those with other intraperitoneal bacterial infection not originating from the appendix, and those with any immune deficiency (diabetes mellitus, chronic renal insufficiency, malnourishment, chemotherapy, radiotherapy, corticosteroid therapy, asplenism)
Interventions	Group I: no irrigation (156 participants) Group II: syringe pressure irrigation with saline: after closure of the fascial planes, subcutaneous fat tissue irrigated with 300 mL of normal saline solution, delivered with a 20-mL syringe with a 19-gauge IV catheter, applying to the embolus the force of one hand, at a distance of 2 cm from the wound tissues, aspirating the fluid collected in the wound with a bulb syringe (127 participants) Cointerventions: each participant was administered metronidazole (30 mg/kg/day) 3/d, plus amikacin (15 mg/kg/d) once daily IV 30–45 min before skin incision. In cases of uncomplicated appendicitis they were stopped within the first 24 h, whereas in cases of complicated appendicitis they were maintained for a minimum of 7 d
Outcomes	**Primary outcome: SSI** (Definition: "A wound was considered to be infected...when there was a collection of pus or a positive bacteriologic culture from a wound discharge") Group I: (no irrigation): 39/156 Group II: (syringe pressure irrigation): 11/127 **Secondary outcome: adverse events**. The authors stated that "Antibiotics used for prophylaxis were well tolerated without any case of allergy or intolerance." The proportion of participants with any adverse event was not reported.
Notes	Funding: NR

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "All patients included were randomly assigned by a computerized assignment system into 2 groups of the trial." Comment: randomisation sequence generated by computer
Allocation concealment (selection bias)	Low risk	Quote: "The randomization chart was kept by our statistician, who was blind to the follow-up, until June 1995." Comment: appears that allocation sequence was concealed from trial personnel
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "Statistical analysis of the results...was conducted by our statistician who was blind to the surgical procedures and follow-up." Comment: control arm did not include comparator intervention and so unable to conceal allocation to staff present at operation. Study design indicated as "double blind," so assumption that participants were not told of their treatment allocation

Cervantes-Sanchez 2000 *(Continued)*

		High risk of physicians not being blinded; unclear or low risk for participants
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "...sought by daily examination of all patients by one of the members of the research team who was blind to the random allocation and the surgical procedures, until discharge." Quote: "...reevaluated at the outpatient consultation 2 and 4 weeks after operation by the responsible author who was blind to the random assignment and the surgical procedures." Comment: appears that outcome assessment for SSI was conducted by blinded assessor
Incomplete outcome data (attrition bias) All outcomes	High risk	Quote: "A total of 350 patients were entered into the study, and 283 (80.9%) were considered evaluable. The reason for rejection of the 67 (19.1%) patients from the final analysis was the finding of another pathology different from the appendix." Comment: the number of exclusions was high and the study did not achieve its aim of including 133 participants in each arm. Therefore confirmation of appendicitis during surgery appears to be an inclusion criterion and so exclusions based on pathology do not violate inclusion criteria. There was a high rate of exclusion relative to event rate for the primary outcome.
Selective reporting (reporting bias)	Unclear risk	Comment: main end point (defined surgical wound infection) was reported overall and for complicated and uncomplicated types of appendicitis. It is unclear whether there were any other end points specified in the study protocol.
Other bias	Unclear risk	Comment: there was no evidence of other sources of bias but reporting was insufficient to be certain.

Chang 2006

Methods	2-arm RCT Setting: single centre at hospital in Taiwan Follow-up: at 2 weeks, 1 month and 3 months after operation, and then every 3 months until end of study (approximately 19 months)
Participants	244 participants (age range 20-89 years; Group I: average 67.1 years, (range 20-82 years); Group II: average 65.4 years (range 22-89 years)). Inclusion criteria: primary instrumented lumbosacral posterolateral fusion for degenerative spinal disorder with lumbar or lumbosacral segmental instability defined by chronic back, buttock and/or leg pain and degenerative spondylolisthesis, degenerative scoliosis or isthmic spondylolisthesis Exclusion criteria: prior spinal surgery, spinal trauma, malignant tumour, infectious spondylitis, rheumatoid arthritis, ankylosing spondylitis, metabolic bone disease, skeletal immaturity or immunosuppressive treatment
Interventions	Group I (povidone-iodine): wounds irrigated with 0.35% povidone-iodine solution to soak for 3 min, followed by irrigation with 2000 cc normal saline to remove povidone-iodine solution (120 participants) Group II (saline): wounds irrigated with only 2000 cc normal saline (124 participants) Cointerventions: wound closure by layer after suction drainage applied; drain removed 48 h or 72 h post-operatively. Routine analgesic pain control applied for 3 d. Pre-operative IV bolus injection of cefa-

Chang 2006 *(Continued)*

	zolin (1000 mg) and gentamicin (60 mg); additional cefazolin (1000 mg/6 h) and gentamicin (60 mg/12 h) also given for 48 hs after surgery, and then oral cefazolin (500 mg/6 h) for 3 d
Outcomes	**Primary outcome: SSI** (Definition: "Infections were classified as superficial (above lumbosacral fascia) or deep (below lumbosacral fascia), and as early onset (within 2 weeks postoperatively) or late onset (otherwise). All deep infections were confirmed by laboratory parameters including erythrocyte sedimentation rate (ESR) and level of C-reactive protein (CRP) and a positive culture of biopsy." Group I (povidone-iodine): 0/120 Group II (saline): 6/124 (2 early onset; 4 late onset) **Primary outcome: wound dehiscence within 30 d** (time NR but it says all others healed with sutures removed on day 14 so can presume < 30 d. No infection found in wounds) Group I: 1/120 Group II: 2/124 **Secondary outcome: proportion of participants with postoperative SSI using systemic antibiotics within 30 d of surgery** Group II: (saline): "After radical debridement and parenteral antibiotics (according to sensitivities) for 6 weeks and oral antibiotics for 2 months, a satisfactory outcome has been reached except in two cases." **Secondary outcome: occurrence of infections showing antibiotic resistance** Group II: (saline): MRSA cultured from 5/6 cases **Secondary outcome: surgical re-intervention rates** Group I: (povidone-iodine): 3 participants underwent exploration of the non-union site and re-arthrodesis with autogenous bone graft Group II: (saline): 4 participants underwent exploration of the non-union site and re-arthrodesis with autogenous bone graft Group II: (saline): "After radical debridement and parenteral antibiotics (according to sensitivities) for 6 weeks and oral antibiotics for 2 months, a satisfactory outcome has been reached except in two cases." These 2 cases had implants removed 4 months post-operatively as infection could not be eradicated
Notes	Interventions: no information given on duration of irrigation of wounds with normal saline for either group. Funding: Quote: "No funds were received in support of this work. No benefits in any form have been received or will be received from a commercial party related directly or indirectly to the subject of this manuscript."

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Patients...were randomly assigned to either treatment group. An independent person unaware of the subject characteristics and the study design delivered pre-coded sealed enveloped randomly (containing serial numbers from 1 to 300) to the assignment of the subjects into the two groups." Comment: clearly states how sequence was generated
Allocation concealment (selection bias)	Unclear risk	Quote: "An independent person unaware of the subject characteristics an the study design delivered pre-coded sealed enveloped randomly (containing serial numbers from 1 to 300) to the assignment of the subjects into the two

Chang 2006 *(Continued)*

		groups. The sealed envelope was not opened until the middle of the surgery before wound irrigation." Comment: although sealed envelopes were used it is not clear that they were opaque or that the allocation sequence was fully concealed at all times.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Comment: no direct quote, but no information on how personnel might have been blinded to the treatment performed. Unclear whether participants were blinded, but report states it was "single blind"
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "All clinical and radiographic assessments were made by independent observers other than the treating surgeons." Comment: unclear whether observers were aware of treatment group
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: no direct quote, but no evidence of attrition
Selective reporting (reporting bias)	Unclear risk	Comment: no evidence of selective reporting but not enough information to be certain
Other bias	Unclear risk	Comment: there was no evidence of other sources of bias but reporting was insufficient to be certain

Cheng 2005

Methods	2-arm RCT Setting: single centre at hospital in Taiwan Follow-up: at 2 weeks, 4 weeks and 2 months after operation, and then every 3 months until end of study (mean follow-up 15.5 months for both groups)
Participants	417 consecutive eligible participants enrolled. 3 who died during the follow-up period were excluded (1 case in Group I and 2 cases in Group II); 414 were included (average age 64 years (Group I) and 61 years (Group II)) Inclusion criteria: pre-operative diagnosis of degenerative scoliosis or stenosis; degenerative disc disease; disc prolapse; traumatic spinal fracture; spinal metastasis lesion. Undergoing procedure such as decompression for degenerative stenosis; decompression, fusion and fixation for degenerative scoliosis or stenosis; fixation of traumatic spinal fracture; discectomy for disc prolapse; excision with fixation for spinal metastatic lesions. Exclusion criteria: those with overt or suspected pyogenic vertebral osteomyelitis, discitis, or any form of pre-operative spinal infection were excluded. Those with fever or other suspected sources of infection also excluded
Interventions	Group I (povidone-iodine): surgical wound soaked with dilute povidone-iodine solution for 3 min after operation. Commercially available Betadine solution used had a concentration of 10% povidone-iodine (100 mg povidone-iodine per 1 mL solution). Approximately 5 mL povidone-iodine was diluted with normal saline to achieve a 0.35% povidone-iodine (3.5% Betadine) solution for use during the operation. The wound was irrigated with copious amounts of normal saline (2000 mL) after Betadine solution irrigation (208 participants) Group II (saline): irrigation with copious normal saline (2000 mL) performed alone (206 participants)

Cheng 2005 *(Continued)*

	Cointerventions: each participant received 1 dose of parenteral cefazolin (1000 mg) and gentamicin (60 mg) 1 h before surgery. Cefazolin (1000 mg) every 6 hs and gentamicin (60 mg) every 12 hs were then given for 48 hs after surgery. Additional doses of antibiotics were given to maintain antibiotics levels during prolonged surgery. Following IV antibiotics, cefazolin (500 mg every 6 hs) was continued orally for 3 d. Drains were retained until < 100 mL of output was observed.
Outcomes	**Primary outcome: SSI** (Definition: "Infection was suspected when unusual pain, tenderness, erythema, induration, fever, or wound drainage was noted. Such findings were investigated with measurement of erythrocyte sedimentation rate, C-reactive protein, and bacteriological cultures from the operative site or blood. Cultures were obtained from blood and wound discharge by aseptic methods.") Group I (povidone-iodine): 0/208 Group II (saline): 7/206 (one superficial and 6 deep) **Secondary outcome: occurrence of infections which show antibiotic resistance** Group II (saline): MRSA cultured from 5/7 cases **Secondary outcome: surgical re-intervention rates** Group II (saline): 7/206 (all those with highly suspected wound infection underwent surgical debridement)
Notes	Funding: Quote: "No funds were received in support of this work. No benefits in any form have been received or will be received from a commercial party related directly or indirectly to the subject of this manuscript."

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Patients were randomly assigned to two groups, using pre-coded sealed envelopes containing serial numbers from 1 to 500. Patients with odd serial numbers were group 1 (study group) and those with even serial number were group 2 (controls)." Comment: clearly states how sequence was generated
Allocation concealment (selection bias)	Unclear risk	Quote: "Patients were randomly assigned to two groups, using pre-coded sealed envelopes containing serial numbers from 1 to 500. Envelopes were not opened until the end of surgery, before wound irrigation. Patients with odd serial numbers were group 1 (study group) and those with even serial number were group 2 (controls) Comment: although sealed envelopes were used it is not clear that they were opaque or that the allocation sequence was fully concealed at all times.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Comment: no direct quote, but no information on how personnel might have been blinded to the treatment performed. Unclear whether participants were blinded, but report states it was "single blind"
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: no direct quote; no information given regarding who collected outcome assessment data
Incomplete outcome data (attrition bias) All outcomes	High risk	Quote: "Three patients who died during the follow-up period were excluded (one case in group 1 and two cases in group 2)."

Cheng 2005 *(Continued)*

		Comment: number of exclusions is low but similar to number of events
Selective reporting (reporting bias)	Unclear risk	Comment: no evidence of selective reporting but not enough information to be certain
Other bias	Unclear risk	Comment: there was no evidence of other sources of bias but reporting was not clear enough to be certain

Cho 2004

Methods	Parallel RCT Setting: single centre in Republic of Korea Follow-up: 2 weeks
Participants	34 patients undergoing gastrectomy Inclusion criteria: naive stomach cancer patients Exclusion criteria: history of diabetes, pneumonia, urinary tract infection, chemotherapy
Interventions	Group I: saline exchange after gastrectomy (17 participants) Group II: no saline exchange during surgery (17 participants) Co-interventions: preoperative cefametazol 1 g
Outcomes	**Primary outcome: SSI** Superficial, deep SSI defined by Horan 1992 Group I (saline exchange): 1/17 Group II (no saline exchange): 3/17
Notes	Funding: NR Reported in Korean. Data extraction and risk of bias assessment performed by translator

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Comment: random number table was used
Allocation concealment (selection bias)	Unclear risk	Comment: method of allocation concealment was not described
Blinding of participants and personnel (performance bias) All outcomes	High risk	Comment: personnel were blinded because they were under anaesthesia but personnel would have been aware of the allocation due to the nature of the comparison
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Comment: outcome assessors were blinded

Cho 2004 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: all participants were included
Selective reporting (reporting bias)	Low risk	Comment: pre-specified outcomes were reported
Other bias	Low risk	Comment: not detected

Dashow 1986

Methods	Parallel-group, 5-arm RCT Setting: single hospital in USA Follow-up: unclear
Participants	360 women undergoing caesarean section. Both caesareans in labour and without labour were included. Mean ages between 24.59 and 27.52 years. Gestational ages between 37.85 and 39.31 weeks Inclusion criteria: women undergoing caesarean section Exclusion criteria: history of penicillin or cephalosporin allergy, taking antibiotics, known infectious process (e.g. chorioamnionitis or urinary tract infection)
Interventions	Group 1: saline lavage (800 mL) Group 2: 2 g cephapirin sodium lavage Group 3: 2 g cefamandole nafate lavage Group 4: 2 g moxalactam disodium lavage Group 5: 2 g ampicillin sodium lavage Inferred that each antibiotic lavage used 800 mL Cointerventions: none reported
Outcomes	**Primary outcome: SSI** (wound breakdown with positive culture or presence of cellulitis) Group 1 (saline): 3/77 Group 2 (cephapirin): 3/70 Group 3 (cefamandole): 2/64 Group 4 (moxalactam): 2/79 Group 5 (ampicillin): 0/70 **Secondary outcome: adverse events including abscess** There were 0 abscess events; other adverse events reported were infection-related morbidity as follows Group 1 (saline): 22/77 Group 2 (cephapirin): 17/70 Group 3 (cefamandole): 8/64

Dashow 1986 *(Continued)*

	Group 4 (moxalactam): 19/79 Group 5 (ampicillin): 10/70
Notes	Funding NR

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "A computer-generated table of pseudo-random numbers.... was used by the pharmacy to assign each patient to one of five groups" Comment: an acceptable method of sequence generation was reported.
Allocation concealment (selection bias)	Unclear risk	Quote: "A computer-generated table of pseudo-random numbers.... was used by the pharmacy to assign each patient to one of five groups" Comment: there was no information on how allocation concealment was undertaken.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "A vitamin .... was added to each solution for disguise" "The patients and physicians were unaware of the group assignment until after completion of the study and chart review by the authors" Comment: blinding of both participants and physicians was undertaken.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: no specific quote but it was unclear who performed the outcome assessments and hence whether they were blinded to group allocation.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: all randomised participants were included in the analyses.
Selective reporting (reporting bias)	Unclear risk	Comment: the outcomes were not defined in the methods section so it is unclear whether all planned outcomes were fully reported.
Other bias	Unclear risk	Comment: no apparent sources of additional bias but reporting insufficient to be certain

De Jong 1982

Methods	2-arm RCT with 2 phases Setting: NR, but appears to be a general surgery department at a hospital in the Netherlands Follow-up: at 4, 8 and 14 d, and 4 weeks after surgery
Participants	592 participants, of which 34 excluded (18 in the control group and 16 in the povidone-iodine group) because they died before the end of the control period or had to be operated upon again through the same wound during this period. 2 wounds were present in 21 participants (9 in the control group and 12 in the povidone-iodine group). A total of 582 wounds were evaluated in 558 participants. Inclusion criteria: all elective and acute patients who underwent intra-abdominal operations or operations for inguinal hernia

De Jong 1982 *(Continued)*

	Exclusion criteria: children < five years of age and those undergoing vascular reconstruction.
Interventions	Group I (control): quote "No special measures were taken" Group II (povidone-iodine): carried out in 2 phases. Subcutaneous tissues irrigated with a povidone-iodine solution at the end of the operation. Lavage with an ample amount of 1% aqueous povidone-iodine solution (Phase 1) or 10% aqueous povidone-iodine solution (Phase 2). Lavage was performed after closure of the fascia with interrupted polyglactin 910 sutures. After lavage for 1 min, excess fluid was aspirated and skin closed with interrupted with nylon sutures. If present, drains were brought out through a second wound.
Outcomes	**Primary outcome: SSI** (Definition: "Diagnosis of wound infection made if a purulent discharge form the wound was seen within a period of four weeks after the operation or if culturing of fluid from the wound was positive.") Group I (control): Phase 1: 21/142 wounds Phase 2: 15/137 wounds (270 participants? - participant numbers unclear) Group II (povidone-iodine): Phase 1: 17/154 wounds Phase 2: 22/149 wounds (291 participants? - participant numbers unclear)
Notes	Participants: age NR Outcomes: these appear to refer to number of wounds, not participants Funding: NR

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "The patients were divided at random into two groups." Comment: it is unclear how randomisation was performed.
Allocation concealment (selection bias)	Unclear risk	Quote: "The patients were divided at random into two groups." Comment: no information on whether the randomisation sequence was concealed
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "In the first group, no special measures were taken." Comment: the control arm did not involve an intervention as a comparator, and so unable to conceal allocation to staff present at the operation. Unclear whether all staff were aware of the different phases of the study (and concentrations of solution used as the intervention). Unclear whether participants were aware of treatment allocation
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "Postoperatively, all wounds were assessed by the same investigator..." Comment: unclear as to whether the investigator was blinded to the treatment allocation
Incomplete outcome data (attrition bias) All outcomes	High risk	Quote: "34, 18 in the control group and 16 in the povidone-iodine group, were excluded because they either died before the end of the control period or had to be operated upon again through the same wound during this period." Comment: number of exclusions is high. No reasons given for cause of death or re-operations

De Jong 1982 *(Continued)*

Selective reporting (reporting bias)	Unclear risk	No evidence of reporting bias, but report is not complete enough to be sure
Other bias	Unclear risk	Comment: there was no evidence of other sources of bias but reporting was not clear enough to be certain

Elliott 1986

Methods	4-arm RCT Setting: 2 hospitals in USA Follow-up: 6 weeks
Participants	'High risk' patients (for developing post operative febrile morbidity) undergoing cesarean section for a variety of reasons 158 women included in study Inclusion criteria: women in active labour or with ruptured membranes, at least one digital vaginal examination (i.e. high risk from developing postoperative febrile morbidity) Exclusion criteria: allergy to cephalosporins or penicillin, presence of fever ≥ 37.8 C during labour with suspicion of chorioamnionitis, maternal use of antibiotics in 2-week period before delivery
Interventions	Group I: 8 doses of IV cefoxitin 2 g (1st dose after umbilical cord clamp, then every 6 hs) (39 participants) Group II: irrigation of uterus and peritoneum with 2 g cefoxitin (in 1000 mL of normal saline). After delivery of the placenta, the fundus of the uterus was irrigated with 300 mL, the uterine incision with 150 mL, after closure of the first layer 150 mL, bladder flap 150 mL, remainder used to irrigate peritoneal cavity and excess suctioned away before closure of the abdomen (42 participants) Group III: combination of IV antibiotic (8 doses of 2 g cefoxitin) and irrigation with cefoxitin (in 1000 mL of normal saline) i.e. treatments of groups I and II combined (38 participants) Group IV: control group who received no prophylactic antibiotics (39 participants)
Outcomes	**Primary outcome: SSI (wound infection)** Group I (IV antibiotics only): 0/39 Group II (irrigation with antibiotics only): 0/42 Group III (IV antibiotics plus irrigation with antibiotics): 0/38 Group IV (no IV and no irrigation):1/39 **Secondary outcome: hospital stay (mean (SD) d)** Group I: 4.8 (1.1) Group II: 4.9 (1.0) Group III 4.9 (1.2) Group IV: 5.4 (1.4) **Secondary outcome: adverse events**

Elliott 1986 *(Continued)*

	Infectious (endomyometritis, urinary tract infection, wound infection (1 case, see above), pulmonary infection, septicaemia) Group I: 2/39 Group II: 3/42 Group III: 2/38 Group IV: 14/39 Non-infectious (seroma, transfusion reaction, atelectasis) Group I: 1/39 Group II: 1/42 Group III: 1/38 Group IV: 0/39
Notes	Funding: NR

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Randomization into one of four treatment groups was performed by using a table of random numbers" Comment: an appropriate method appears to have been used
Allocation concealment (selection bias)	Unclear risk	Comment: there is no information about allocation concealment
Blinding of participants and personnel (performance bias) All outcomes	High risk	Comment: there is no information about blinding. It is possible that participants were blinded, but personnel would be aware of treatment as the protocols are quite different.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: there is no information about blinding or who performed outcome assessment
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: all participants are accounted for in the results
Selective reporting (reporting bias)	Unclear risk	Comment: the outcomes do not appear to have been pre-specified, although febrile morbidity was extensively defined
Other bias	Unclear risk	Comment: there is no evidence of additional sources of bias but the reporting is insufficient to be confident that there were none.

Greig 1987

Methods	2-arm RCT Setting: single hospital in UK

Greig 1987 *(Continued)*

	Follow-up: 1 month
Participants	129 patients undergoing elective and emergency colorectal surgery Age: unknown; Type of operations: unknown Inclusion criteria: NR Exclusion criteria: NR
Interventions	Group I: 1000 mL saline lavage at the end of the operation (65 participants) Group II: 1000 mL saline lavage with 1 g cefotetan at the end of the operation (64 participants) Co-interventions: Groups I and II both received 500 mg metronidazole and 120 mg gentamicin IV at anaesthesia induction
Outcomes	Primary outcome: **SSI** (defined as discharge of pus from the wound "wound sepsis") Group I (saline): 18/65 Group II (cefotetan): 15/64
Notes	Funding: NR Limited information from paper

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Patients were randomly allocated to receive either 1 liter of saline lavage or 1 liter of saline containing 1g of cefotetan..." Comment: the method of randomisation is not described
Allocation concealment (selection bias)	Unclear risk	Comment: there is no mention of allocation concealment
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Comment: there is no mention of blinding of participants or personnel
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "Post-operatively, patients were assessed regularly by a single observer for the development of wound sepsis..." Comment: there is no mention of blinding of the observer
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: participants are all accounted for in the outcome data of interest
Selective reporting (reporting bias)	Unclear risk	Comment: the outcome of interest (SSI) is reported but it is not clear that related results are fully reported

Greig 1987 *(Continued)*

Other bias	Unclear risk	Comment: there is not enough methodological information to judge whether there were any additional sources of bias

Gungorduk 2010

Methods	2-arm RCT Setting: single hospital in Turkey Follow-up: participants were examined at 2 and 6 weeks after surgery. Wounds examined twice daily during hospitalisation. After discharge, women were instructed to contact investigators immediately if any of the listed symptoms appeared. Women who contacted the investigators were examined within 12 h
Participants	520 women with indications for elective or emergency caesarean section (incidence of emergency surgery (45.5 vs 51.5%; P = 0.53)) Inclusion criteria: past 37 weeks' gestation and required a caesarean section (elective or emergency). Exclusion criteria: anaemia (haemoglobin: < 7 g/dL), chorioamnionitis and fever on admission
Interventions	Group I: underwent wound irrigation before wound closure with 100 mL of sterile saline with a 30–60 mL syringe (260 participants) Group II: no wound irrigation before wound closure (260 participants)
Outcomes	**Primary outcomes: SSI** (wound drained purulent material or serosanguineous fluid in association with induration, warmth and tenderness) Group I (saline): 17/260 Group II (no irrigation): 19/260 **Secondary outcomes: mean length of hospital stay** Group I (saline): 2.05 (0.21) d Group II (no irrigation): 2.04 (0.20)
Notes	Funding: NR

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Consenting patients were preoperatively randomised using numerically ordered cards in sealed envelopes" Comment: method of sequence generation is not reported
Allocation concealment (selection bias)	Unclear risk	Quotes: "Consenting patients were preoperatively randomised using numerically ordered cards in sealed envelopes" "The investigator was not blinded to the procedure allocation" "The allocated envelope was opened by the clinician just before surgery" Comment: the use of sealed envelopes suggests an attempt to conceal some aspect of allocation but the authors state that the investigator was not blinded to allocation; envelopes are not stated to be opaque

Gungorduk 2010 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "The allocated envelope was opened by the clinician just before surgery. The procedure allocation was recorded in the women's charts" Comment: personnel and participants were both aware of treatment
Blinding of outcome assessment (detection bias) All outcomes	High risk	Quote: "The procedure allocation was recorded in the women's charts" "The investigator was not blinded to the procedure allocation" Comment: it is not explicitly stated but the report suggests the outcome assessors were not blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: data are reported for all participants
Selective reporting (reporting bias)	Unclear risk	Comment: apart from SSI, it is unclear which outcomes were prespecified
Other bias	Low risk	Comment: there is no evidence of other bias

Halsall 1981

Methods	Parallel-group RCT Setting: single hospital in UK Follow-up: 4 weeks postoperatively
Participants	192 participants undergoing appendectomy via grid iron incision Inclusion criteria: appendectomy via a right iliac fossa incision Exclusion criteria: female participants of child bearing age not adequately protected by contraceptive practice
Interventions	Group I: 50 mL 2% taurolin in 5% PVP in "saline sufficient to produce solutions of equal tonicity"; wound irrigated for 2 min; then 10 mL instilled through a quill after closure of the skin Group II 50 mL of 5% PVP in "saline sufficient to produce solutions of equal tonicity" wound irrigated for 2 min; then 10 mL instilled through a quill after closure of the skin Cointerventions: antibiotics and drains as required
Outcomes	**Primary outcome: SSI** (wound sepsis) defined as a wound discharging pus Group I (taurolin): 18/99 Group II (placebo): 29/93 **Secondary outcome: length of stay** Group I (taurolin): 6.4 d (mean, no SD) Group II (placebo): 6.6 d (mean, no SD)
Notes	Funding: NR
Risk of bias	

Halsall 1981 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "the taurolin and placebo being randomly allocated to sequential numbers 1 to 200" Comment: no information on how the randomisation sequence was generated
Allocation concealment (selection bias)	Unclear risk	Quote: "the taurolin and placebo being randomly allocated to sequential numbers 1 to 200" Comment: no information on whether allocation was adequately concealed
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "neither solution was distinguishable to users" Comment: it appeared that personnel (and participants) were blinded
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote:"During the hospital stay the wound was observed be a member of the medical staff participating in trial" Comment: it was unclear whether the individual who assessed the outcomes was blinded to treatment group
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: the 8 participants who were not included in the analyses were clearly documented. Although 7 of these were placebo group-allocated participants it appears unlikely that these exclusions would have affected the results.
Selective reporting (reporting bias)	Unclear risk	Comment: the primary outcome was specified but it was unclear which other outcomes were planned to be recorded
Other bias	Unclear risk	Comment: there is no evidence of other sources of bias but reporting was insufficient to be certain.

Hargrove 2006

Methods	2-arm RCT Setting: multicentre trial: 4 UK hospitals in the "South of England" Study period: 18-months Follow-up: 30 d post surgery or discharge from unit (1 assessor in each hospital reviewed participants' wounds twice a week until discharge)
Participants	356 participants with a displaced intracapsular fractured neck of femur, due to be treated with a hemiarthroplasty, were randomised into 2 groups Inclusion criteria: displaced intracapsular fractured neck of femur, due to be treated with a hemiarthroplasty Exclusion criteria: NR
Interventions	Group I: the 'pulse lavage' group had a 2-L normal saline wash delivered via pulsatile lavage in stages throughout the procedure (164 participants) Group II: the control group had a 2-L normal saline wash delivered by a jug or a syringe according to the surgeon's preference with 1 L being given before prosthesis insertion and 1 L after insertion (192 participants)

Hargrove 2006 *(Continued)*

	Co-interventions: NR
Outcomes	**Primary outcome: SSI** Wound infections were diagnosed using criteria from the Nosocomial Infection National Surveillance Survey and graded as superficial or deep. Group I (pulse lavage): 9/164 (3/164 'deep') Group II (control): 30/192 (10/192 'deep') **Secondary outcome: occurrence of infections with antibiotic resistance** No group data but quote: "Half of the deep space infections were due to methicillin-resistant Staphylococcus aureus" **Secondary outcome: mortality** NR by group. There were 25 deaths within the study period (7%); 18 of these were associated with American Society of Anaesthesiologists (ASA) scores of 3 or below
Notes	Funding: no records

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "...all patients... were randomized into two groups" Comment: no details about method
Allocation concealment (selection bias)	Unclear risk	Comment: no mention of allocation concealment
Blinding of participants and personnel (performance bias) All outcomes	High risk	Comment: no mention of blinding, but nature of intervention and control means personnel would not be blind to treatment
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "One assessor in each hospital reviewed patients' wounds twice a week until discharge" Comment: no mention of blinding and it is unclear if the assessor would have been aware of treatment
Incomplete outcome data (attrition bias) All outcomes	High risk	Quote: "the difference in size between the two groups was due to 'start up' problems within the hospitals where pulse lavage had not been previously associated with hemiarthroplasty operations" "In cases where hemiarthroplasties were due to have pulse lavage but this was forgotten, the cases were struck from the study" Comment: the authors describe issues with implementing the pulse lavage intervention and although they describe participants being excluded at some point for this reason (presumably post-randomisation) there are no details about them. It is probable that this introduced bias to the study.
Selective reporting (reporting bias)	High risk	Comment: data are fully reported for some outcomes but others are not reported by group
Other bias	Unclear risk	Comment: there is insufficient information to judge

Harrigill 2003

Methods	2-arm, parallel-group RCT Setting: single centre in USA Follow-up: NR
Participants	196 women undergoing caesarean delivery. 94 were elective repeat procedures, age 27.5 vs 28.2 years Inclusion criteria: women presenting with term (> 37 weeks) singleton pregnancies undergoing routine caesarean delivery for arrest of dilation, arrest of descent, foetal malpresentation or as an elective repeat procedure Exclusion criteria: women diagnosed with chorioamnionitis, type I diabetes, placenta previa, placenta accreta, maternal coagulopathy, multiple gestation, HIV–positive status, prior severe gastrointestinal disease, or non-reassuring fetal monitoring requiring immediate delivery
Interventions	Group I: irrigation with 500-1000 mL warm saline after closure of the uterine incision but before closure of the abdominal wall (97 participants) Group II: no irrigation (99 participants)
Outcomes	**Primary outcome: SSI** (undue tenderness, erythema, discharge, or separation of the incision accompanying maternal fever) Group I (saline irrigation): 1/97 Group II (no irrigation): 2/99 **Secondary outcome: length of stay (d)** Group I (saline irrigation): 2.9 (1.0) Group II (no irrigation): 2.8 (0.9) **Secondary outcome: adverse events** (postpartum complications including SSI) Group I (saline irrigation): 14/97 Group II (no irrigation): 13/99
Notes	Funding: NR

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Assignment was performed by pulling sequentially numbered opaque envelopes containing computer-randomized individual allocations." Comment: an appropriate method of random sequence generation was reported
Allocation concealment (selection bias)	Low risk	Quote: "Assignment was performed by pulling sequentially numbered opaque envelopes containing computer-randomized individual allocations." Comment: an appropriate method of allocation concealment was reported
Blinding of participants and personnel (performance bias)	High risk	Quote: "This randomization was carried out by research staff before initiation of the study, and the patients were blinded to treatment once assigned."

Harrigill 2003 *(Continued)*

All outcomes		Comment: although participants were blinded to treatment allocation it is unclear whether personnel were also blinded, the nature of the intervention groups suggests that they were not.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "Postoperative care providers were blinded to group assignment to minimize potential bias. .... The randomizing physician collected the initial data. Data entry was performed by data technicians who did not participate in the design or execution of the study; these technicians also reviewed the charts of each randomized patient to assess the accuracy of information provided by the treating physician. The senior investigator performed periodic reviews of data entry to ensure completeness and accuracy of information in the computer database. The data analysis was performed by an investigator blinded to group assignment." Comment: blinded outcome assessment was conducted
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: all randomised participants were included in the analyses
Selective reporting (reporting bias)	Low risk	Quote: "The primary outcome measure was the incidence of maternal morbidity, defined as the presence of at least one of the following:..." Comment: primary and secondary outcomes were clearly specified and fully reported.
Other bias	Low risk	Comment: there were no other sources of bias evident and reporting was sufficient to be reasonably confident that this was the case.

Kokavec 2008

Methods	2-arm RCT Setting: single hospital in Slovakia Follow-up: 7.8 months (mean) 2-14 months (range): follow-up at 2 weeks, 6 weeks and then 3-monthly
Participants	162 children (undergoing 182 surgical procedures on soft and bone tissues in the proximal femur, hip and pelvic regions. mean age was 7.9 vs 7.5 years Types of procedures: adductor tenotomy, femoral or pelvic osteotomy, extraction of metal materials, open reductions, epiphysiodesis, resection or biopsy. Children had the following long-term conditions: developmental dysplasia of the hip, cerebral palsy, tumours, Perthes disease Inclusion criteria: children undergoing surgery of the femur, hip or pelvis Exclusion criteria: NR
Interventions	Group I: lavage with 3.5% Betadine solution (0.35% povidone iodine) diluted in 30 mL sterile saline Group II: lavage with 30 mL sterile saline Cointerventions: antibiotic prophylaxis begun preoperatively in participants with femoral or pelvic osteotomy or massive surgery of soft tissues and continued for 48-72 hs postoperatively (dose determined by weight). Drains left in until second postoperative day where necessary
Outcomes	**Primary outcome: SSI** (positive bacteriological examination) Group I (Betadine lavage): 0/89

Kokavec 2008 *(Continued)*

	Group II (saline lavage): 2/73
Notes	Funding: NR Slovak; data entry and risk of bias based on information provided by translator

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Comment: no information about the sequence generation process but stated that the participants were allocated to 2 groups randomly
Allocation concealment (selection bias)	Unclear risk	Comment: no information on whether the allocation was adequately concealed
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Comment: no information on whether personnel or participants were blinded to the interventions
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: no information on who assessed the presence of SSI or whether they were blinded to treatment allocation
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote "In the first group (89 patients) [we] found no peri- or post-operative infection. In the second group of patients (73) [we] brought to light two surface infection[s] (2.7%)" Comment: it appears that all participants were included in the analysis
Selective reporting (reporting bias)	Unclear risk	Comment: outcomes were not specified in the methods section so difficult to be certain whether all planned outcomes were assessed
Other bias	Unclear risk	No evidence of additional bias but reporting insufficient to be certain

Kubota 1999

Methods	2-arm RCT Setting: NR, appears to be single centre in Japan Follow-up: NR
Participants	16 children (aged 2-12 years) undergoing appendectomy for perforated appendicitis Inclusion criteria: generalised peritonitis or nonlocalised abscess Exclusion criteria: NR
Interventions	After appendectomy, the peritoneal cavity was lavaged with 100 mL/kg (1500-4000 mL) of the following warmed lavage solutions: Group I : normal saline (8 participants) Group II: acidic oxidative water (AOPW), a strong acidic water produced by the electrolysis of tap water containing 10% W/V sodium chloride (8 participants)

Kubota 1999 *(Continued)*

	Co-interventions: antibiotics moxalactam [reported as LMOX] (100 mg/kg/d) or cefazolin [reported as CEZ] (50 mg/kg/d) were given in both groups for 5 d or until serum C-reactive protein was at a normal level
Outcomes	**Primary outcome: SSI** No definition given for wound infection Group I (saline): 4/8 Group II (APOW): 1/8 **Secondary outcome: adverse events: abscess formation** Group I (saline): 1/8 Group II (APOW): 0/8 **Secondary outcome: length of hospital stay (mean (SD) d)** Group IS (saline): 22.7 (11.1) Group II (APOW): 12.1 (5.1)
Notes	Funding: NR

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "They were randomly divided into two groups" Comment: no details of randomisation method
Allocation concealment (selection bias)	Unclear risk	Comment: no mention of allocation concealment
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Comment: no mention of blinding
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: no mention of who performed the assessment of outcomes or whether blinding occurred
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: all participants are included in the results
Selective reporting (reporting bias)	High risk	Comment: outcomes were not prespecified beyond "effectiveness and safety"
Other bias	Unclear risk	Comment: there is not enough methodological detail to judge

Kubota 2015

Methods	2-arm RCT

Kubota 2015 *(Continued)*

	Setting: appears to be multiple centres, Japan ("our affiliated hospitals") Follow-up: 30 d Duration of study: 2008-2012
Participants	44 children aged 3-14 Group I: 16 boys and 4 girls, ranging in age from 4-11 years Group II: 12 boys and 12 girls, ranging in age from 3-14 years Inclusion criteria: children (age not defined) appendectomy for perforated appendicitis with extensive or panperitonitis Exclusion criteria: pre-operative antibiotics or requirement of antibiotics due to massive abscess formation
Interventions	After appendectomy, the peritoneal cavity was lavaged with 100 mL/kg saline or SAEW (strong acid electrolysed water, generated by electrolysis of tap water containing 0.2% NaCl), in Groups I and II, respectively. After closure of the fascial layer, the wound was washed out with 200 mL same solution before skin suture Group I: 100 mL/kg saline (20 participants) Group II: 100 mL/kg SAEW (24 participants) Co-intervention: cefmetazole, 100 mg/kg/d, was given initially to both groups, which was replaced by the most sensitive antibiotics after identification of causative pathogens for 5 or 7 d depending on response. The abdominal wall was disinfected with povidone iodine, and laparotomy was performed via a pararectal incision, saving the muscle layers, followed by appendectomy, carried out in the same manner in both groups.
Outcomes	**Primary outcome: SSI** Defined as infection at the operation site, occurring up to 30 d after surgery, with confirmed causative pathogen(s) identical to those of the appendicitis. Group I (saline): 4/20 Group II (SAEW): 0/24 **Secondary outcome: adverse events (intraperitoneal abscess)** Group I (saline): 1/20 Group II (SAEW): 1/24 **Secondary outcome: length of hospital stay (mean (SD) d)** Group I (saline): 9.4 (4.7) Group II (SAEW): 8.7 (4.0)
Notes	34 participants were excluded from the study because some had received antibiotics before the operation and some had required antibiotics for massive abscess formation to be resected primarily with appendectomy Funding: NR

Risk of bias

Bias	Authors' judgement	Support for judgement

Kubota 2015 *(Continued)*

Random sequence generation (selection bias)	Unclear risk	Quote: "Patients were allocated randomly to one of two treatment groups" Comment: no details about method of randomisation
Allocation concealment (selection bias)	Unclear risk	Comment: no mention of allocation concealment
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Comment: no mention of blinding
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: no mention of who performed the outcome assessment or whether blinding occurred
Incomplete outcome data (attrition bias) All outcomes	High risk	Quote: "34 patients were excluded from the study..." Comment: it is unclear if the exclusions were before or after randomisation
Selective reporting (reporting bias)	Low risk	Comment: all outcomes of interest appear to be reported
Other bias	Unclear risk	Comment: there is not enough methodological information to judge

Levin 1983

Methods	3-arm RCT Setting: Kaiser-Permanente Medical Center - Santa Clara, USA Follow-up: at least 8 weeks
Participants	128 women undergoing cesarean section for various indications including repeat, breech and cephalopelvic disproportion. (132 entered study but 4 were excluded for irrigation protocol deviation and data are only presented for 128) Inclusion criteria: undergoing cesarean section Exclusion criteria: fever or other evidence of infection in labour, history of sensitivity to cephapirin or cefoxitin
Interventions	Group I: following delivery of the placenta, the uterine cavity and incision, bladder flap, pelvic gutters, and subcutaneous tissue were irrigated with 2 mg cephapirin in 1000 mL normal saline (44 participants) Group II: irrigation with 2 mg cefoxitin in 1000 mL normal saline (41 participants) Group III: irrigation with 1000 mL normal saline only (43 participants)
Outcomes	**Primary outcome: SSI (**defined as purulent wound discharge with or without wound separation) Group I (cephapirin): 0/44 Group II (cefoxin): 0/41 Group III (saline): 3/43

Levin 1983 *(Continued)*

	Secondary outcome: endometritis (defined as persistent fever, uterine tenderness, foul-smelling lochia, with no other obvious source of infection) Group I (cephapirin):4/44 Group II (cefoxin): 1/41 Group III (saline): 5/43 (one of these also had wound infection) **Secondary outcome: length of hospital stay (mean (SD) d)** Group I (cephapirin): 4.8 (1.2) Group II (cefoxin): 4.9 (1.9) Group III (saline): 5.2 (2.1)
Notes	4 excluded from the analysis for protocol deviation Funding: NR

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "... bags were sequenced randomly by a lottery method and used in numerical order" Comment: the method is not explained in enough detail to know whether it was appropriate
Allocation concealment (selection bias)	Unclear risk	Quote: "... bags were sequenced randomly by a lottery method and used in numerical order" Comment: there is not enough detail about the method of randomisation and allocation concealment to judge
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "...bags of irrigant were prepared by pharmacy personnel" "One millilitre of multivitamin infusion was added to create an identical appearance of all solutions" "Patients, physicians, operating room personnel, and data collectors were thus blinded to the group assignment." Comment: steps were have been taken to ensure blinding of participants and personnel
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "Patients, physicians, operating room personnel, and data collectors were thus blinded to the group assignment." Comment: steps appear to have been taken to ensure blinding of outcome assessors
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Quote: "One hundred thirty-two patients were entered in the study. Four patients were eliminated from the statistical analysis because of deviations from the protocol of irrigation technique" Comment: there are only a few participants lost during the study but no details of these participants are reported and since numbers of events are small this could potentially have an impact.
Selective reporting (reporting bias)	Low risk	Comment: the outcomes of interest appear to be fully reported

Levin 1983 *(Continued)*

Other bias	Low risk	Comment: there is no evidence of other bias

Lord 1983

Methods	2-arm RCT Setting: NR; appears to be single hospital in USA Follow-up: NR
Participants	200 participants undergoing elective and emergency gastrointestinal surgery (procedures on biliary tract 63/100 vs 57/100; gastroduodenal 14 vs 19 and colon 23 vs 24). Mean age was 61.7/61.6 years (range 17-93). Malignancy present in 29/100 versus 25/100; diabetes 6/100 vs 8/100; obesity 30/100 vs 18/100 Inclusion criteria: elective or emergency procedures on the gastrointestinal tract Exclusion criteria: parenteral antibiotics had been administered preoperatively or intraoperatively; a colostomy was required; if frank pus was encountered at operation
Interventions	Group I (kanamycin sulphate and cephalothin sodium): operative site was irrigated intermittently from the beginning to completion of the operation with a solution containing 1 g of kanamycin sulphate and 1 g of cephalothin sodium in 1000 mL of normal saline solution (100 participants) Group II (saline): operative site was irrigated intermittently from the beginning to completion of the operation with a solution of normal saline (100 participants) Cointerventions: the average volume of irrigant used for each operation was 750 mL. No cointerventions were reported
Outcomes	**Primary outcome: SSI (postoperative wound infection)** Group I (kanamycin sulphate and cephalothin sodium): 3/100 Group II (saline): 9/100 **Secondary outcome: mortality (postoperative deaths- last recorded 43 d post-op)** Group I (kanamycin sulphate and cephalothin sodium): 5/100 Group II (saline): 3/100 Note: 2 participants who died had wound infections but sepsis was not the cause of the deaths **Secondary outcome: antibiotic resistance** Details of individual species recovered from wounds of participants with SSI were reported together with their sensitivity or resistance where this was tested for. Multiple species reported for each participant **Secondary outcome: adverse events** Postoperative peritonitis: Group I (kanamycin sulphate and cephalothin sodium): 0/100 Group II (saline): 1/100 **Secondary outcome: antibiotic resistance**

Lord 1983 *(Continued)*

	Resistance of specific organisms to kanamycin sulphate and cephalothin sodium reported for each type of surgery. Large numbers of samples reported as not tested
Notes	Funding: NR

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Designation was made by computer-generated listing using a standard table of random numbers." Comment: sequence generation used an appropriate method
Allocation concealment (selection bias)	Unclear risk	Quote: "Designation was made by computer-generated listing using a standard table of random numbers." Comment: no indication as to whether allocation was adequately concealed
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "a prospective, randomized, double-blind study" Comment: it was unclear who was blinded; while participants would probably be blinded it is unclear if personnel were
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "a prospective, randomized, double-blind study" Comment: it was unclear whether the double-blinding referred to outcome assessors
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: all randomised participants were included in the analyses
Selective reporting (reporting bias)	Unclear risk	Comment: outcomes were not defined in the methods section so it is difficult to be sure whether all planned outcomes were fully reported.
Other bias	Unclear risk	Comment: no evidence of other sources of bias but reporting insufficient to be certain

Magann 1993

Methods	Parallel-group RCT (factorial) Setting: single hospital in the USA Follow-up: NR
Participants	100 women undergoing caesarean section Inclusion criteria: women undergoing caesarean section; indications for surgery included elective repeat caesarean, failed trial of labour after prior caesarean, abnormal presentation, failure to progress, cephalopelvic disproportion, and severe pre-eclampsia without thrombocytopenia or coagulopathy Exclusion criteria: chorioamnionitis at caesarean, emergency caesarean for foetal distress with inadequate time for skin preparation
Interventions	Group I: saline irrigation (500 mL) of pelvis and subcutaneous tissue at uterine and fascial closure (50 participants)

Magann 1993 *(Continued)*

	Group II: cefazolin irrigation (1 g in 500 mL saline) of pelvis and subcutaneous tissue at uterine and fascial closure (50 participants) Cointerventions: factorial randomisation to 2 alternative skin preparations: povidone iodine 7.5% scrub followed by povidone iodine 10% solution (standard skin preparation) versus 5-min scrub with parachlorometaxylenol followed by povidone iodine scrub and solution (special skin preparation). No additional interventions were reported.
Outcomes	**Primary outcome: SSI** (hyperemic skin incision and fluctuant mass which when opened contained purulent material) Group I (saline): 4/50 (3/25 with standard skin preparation; 1/25 with special skin preparation) Group II (cefazolin): 2/50 (2/25 with standard skin preparation) **Secondary outcome: adverse events** (endometritis) Group I (saline): 30/50 (16/25 with standard skin preparation; 14/25 with special skin preparation) Group II (cefazolin): 11/50 (8 with standard skin preparation; 3/25 with special skin preparation)
Notes	Funding: supported in part by the Vicksburg Hospital Medical Foundation

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Random assignment was achieved by card selection from sealed opaque envelopes with group appointment derived from a random number table" Comment: it appeared that an appropriate method was used to generate the randomisation sequence
Allocation concealment (selection bias)	Unclear risk	Quote: "Random assignment was achieved by card selection from sealed opaque envelopes with group appointment derived from a random number table" Comment: it was not clear that enough measures were taken to ensure adequate concealment of allocation
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Comment: there was no information on whether personnel and participants were blinded to treatment allocation
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: there was no information on who performed the outcome assessment or whether they were blinded to treatment allocation
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: all randomised participants were included in the analyses
Selective reporting (reporting bias)	Unclear risk	Comment: outcomes were not clearly prespecified so difficult to determine if all planned outcomes were fully assessed
Other bias	Unclear risk	Comment: no obvious additional sources of bias but reporting insufficient to be certain

Mahomed 2016

Methods	2-arm RCT Setting: single hospital in Australia Follow-up: letter or text message 4 weeks after surgery (following discharge from hospital)
Participants	3270 women undergoing caesarean section. Of those followed up 1508 had elective surgery and 1519 had surgery during labour. Mean age was 28.5 years in the Betadine group vs 28.6 years in the no Betadine group. 13.8% versus 12.9% had diabetes Inclusion criteria: women undergoing caesarean section either elective or during labour (stratified randomisation) Exclusion criteria: suspected or known allergy to iodine
Interventions	Group I: wound irrigation with 50 mL of 10% aqueous povidone iodine (Betadine) solution just before skin closure (1634 participants randomised; 1634 received allocated intervention; 1520 analysed) Group II: no irrigation (1636 participants randomised; 1636 received allocated intervention; 1507 analysed) Cointerventions: alcoholic povidone iodine for skin preparation unless an allergy to iodine present, in which case chlorhexidine was used. Prophylactic cephalothin administered to all women soon after spinal anaesthesia
Outcomes	**Primary outcome: SSI** (wound abscess or wound draining pus or sero-sanguinous fluid, or redness, induration, warmth and tenderness or if woman's general practitioner had seen her and prescribed antibiotics for presumed infection) Group I (povidone iodine irrigation): 144/1520 Group II (no irrigation): 147/1507 **Secondary outcome: return to theatre** Group I (povidone iodine irrigation): 7/1520 Group II (no irrigation): 9/1507 **Secondary outcome: hospital readmission** Group I (povidone iodine irrigation): 39/1520 Group II (no irrigation): 30/1507 Completed case analyses reported here: ITT population 1634 vs 1636 - used in analyses for SSI
Notes	Funding: states "we had no funding for this study..."

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "The allocation was prepared using computer generated list of random numbers using a variable block of 10 and performed by a staff member not part of the clinical team" Comment: acceptable method of sequence generation; randomisation also stratified by elective versus non-elective procedure

Mahomed 2016 *(Continued)*

Allocation concealment (selection bias)	Low risk	Quote: "Women were randomised to 'Betadine' or 'no Betadine' group using sequentially numbered sealed opaque envelopes that contained the allocation..... After all layers were sutured and just prior to starting skin closure, the envelope with the allocation was opened by one of the theatre nurse[sic]" Comment: appropriate measures appear to have been taken to ensure allocation concealment.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote "In the control group (no Betadine group), layers would be sutured in exactly the same manner right up to the point of skin closure as it was only at this point that the allocation was revealed to the surgical team." Comment: surgical personnel were aware of group allocation; unclear whether participants were blinded
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "Information on outcome measures was obtained by the research team blinded to the allocation and also not involved in clinical care of the women" Comment: blinded outcome assessment for all outcomes
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Quote: "Of the total number randomised, 243 women were inadequately followed up either due to change of address, wrong telephone number or just not receiving the text messages" Comment: 7% of women were lost to follow-up; this was balanced between the arms (114 versus 129) and between the types of surgery (elective versus non-elective) undertaken. Although this is close to the wound infection rate it does not appear likely to have impacted on the risk ratio of infection.
Selective reporting (reporting bias)	Low risk	Quote "Primary outcome was the incidence of SSI as a whole but also specifically readmission for intravenous antibiotics and/ or return to theatre for wound infection" Comment: The outcomes were specified in the methods section and then fully reported
Other bias	Low risk	Comment: no specific quote but no evidence of other bias and reporting sufficient to be reasonably confident.

Marti 1979

Methods	Three-arm RCT Setting NR; appears to be single hospital in Switzerland Follow-up: not clear beyond 4 d/discharge from hospital
Participants	162 participants with appendicitis Inclusion criteria: people undergoing appendectomy carried out through an incision at McBurney's point, without the use of drains and without the use of pre-, peri- or post-operative systemic antibiotics Exclusion criteria: people with perforated or gangrenous appendices or with peritonitis
Interventions	Group I (saline): irrigation with 500 mL saline (0.9%) after the closure of the peritoneum. The liquid was re-aspirated and the wound was not swabbed. The skin was then closed. Group II: (epicillin): irrigation with 500 mL saline with 1 g epicillin (Spectacilline) in solution as for Group I

Marti 1979 *(Continued)*

	Group III: (lincomycine): irrigation with 500 mL saline with 600 mL lincomycine (Lincocin) in solution as for Group I Cointerventions: NR
Outcomes	**Primary outcome: SSI** (septic complications with spontaneous or induced purulent discharge): results only reported for all groups together (1/162) compared with a non-randomised group without irrigation (7/158) **Secondary outcome: adverse events including abscess**: results only reported for all groups together: 1/162 abscess from one of the antibiotic groups
Notes	Funding: NR Paper in French; data extracted by one review author, checked by a fluent speaker

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "162 appendicectomies were randomised to treatment by blindly drawn lots" Comment: acceptable method of sequence generation
Allocation concealment (selection bias)	Unclear risk	Quote: "162 appendicectomies were randomised to treatment by blindly drawn lots" Comment: unclear whether there was adequate concealment of allocation
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	No direct quote; no information on whether any personnel were blinded after the treatment allocation
Blinding of outcome assessment (detection bias) All outcomes	High risk	Quote "In the irrigated groups a questionnaire was sent to the treating physician to establish whether postoperative wound infections developed" Comment: no information as to whether the physicians were aware of treatment allocation
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: all randomised participants appeared in the analysis
Selective reporting (reporting bias)	High risk	Comment: the results for the three randomised groups were reported together and contrasted only with a non-randomised comparison group
Other bias	Unclear risk	No other sources of bias were apparent but reporting insufficient to be certain

Mirsharifi 2008

Methods	2-arm RCT Setting: a single hospital in Iran Follow-up: 1, 2, 4 and 6 weeks post surgery

Mirsharifi 2008 *(Continued)*

Participants	102 participants (mean age: Group I: 50.63 years, Group II: 50.28 years) undergoing open cholecystectomy surgery Inclusion criteria: cholecystitis diagnosed by surgeon Exclusion criteria: age > 80 years, diabetes, immunosuppression (acquired or hereditary), history of immunosuppressive therapy, use of antibiotics during referral time for other reasons, history of recurrent cholecystitis, laparoscopic cholecystectomy, limitation for follow up [sic]
Interventions	Group I: open cholecystectomy, then before wound closure irrigation with 1 g cefazolin IV [sic] antibiotics (51 participants) Group II: open cholecystectomy with no antibiotic irrigation before wound closure (51 participants) Co-interventions: same surgery and general anaesthesia
Outcomes	**Primary outcome: SSI** Signs of infection included erythema, induration, tenderness, warmth, suppurative discharge Group I: 6/51 Group II: 6/51
Notes	Funding: none reported Reported in Persian. Data extraction and 'Risk of bias' assessment performed by translator

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Comment: they used a random number table
Allocation concealment (selection bias)	Unclear risk	Translator did not identify any information
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Translator did not identify any information
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Translator did not identify any information
Incomplete outcome data (attrition bias) All outcomes	Low risk	Translator judged all randomised participants included in analysis
Selective reporting (reporting bias)	Unclear risk	Translator did not identify any information
Other bias	High risk	Comment: had a potential source of bias related to the specific study design used, they did not have well-defined outcome, the evaluation of some participants by telephone!

Mohd 2010

Methods	2-arm RCT Setting: NR; appears to be single hospital in Malaysia Follow up at 2, 4 and 6 weeks post-operatively for wound infection and adverse events
Participants	190 participants (178 analysed) undergoing CABG surgery. Mean age was 61.6 (7.6) years. Comorbidities documented were diabetes (44.4%), chronic obstructive pulmonary disease (37.1%), end stage renal failure (18%) and obesity (11.2%) Inclusion criteria: scheduled for elective CABG Exclusion criteria: emergency cases, those who underwent other surgical procedures in addition to CABG, those allergic to Dermacyn, and those who had infective or other skin lesions over anterior chest wall area
Interventions	Group I (Dermacyn): Dermacyn wound irrigation (15-min soak) upon chest closure and after insertion of sternal wires before subcutaneous tissue and skin closure (88 participants analysed) Group II (povidone-iodine): povidone-iodine would irrigation (15-min soak) upon chest closure and after insertion of sternal wires before subcutaneous tissue and skin closure (90 participants analysed) Cointerventions: IV prophylaxis with 1.2 g Augmentin (amoxicillin and clavulanate) at induction. 2 drains were normally left in the mediastinal cavity.
Outcomes	**Primary outcome: SSI** (sternotomy wound infection, which was defined according to the Centers for Disease Control and Prevention system. Wound infections were graded as superficial (involving the skin and subcutaneous tissue of the incision), deep (involving fascia, muscle layers, and sternum), or deep organ space. Group I (Dermacyn): 5/88 (5 superficial; 0 deep) Group II (povidone-iodine): 14/90 (10 superficial; 4 deep) **Secondary outcome: need for reoperation** Group I (Dermacyn): 0/88 Group II (povidone-iodine): 4/90 (sternal dehiscence requiring surgical debridement and repair) **Secondary outcome: mortality** 12 participants were described as having "dropped out"; 4 owing to postoperative mortality and 8 dropped for re-opening of chest due to bleeding Group I (Dermacyn): 7/95 Group II (povidone iodine): 5/95
Notes	Funding: NR

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "patients were consecutively randomized into 2 groups" Comment: no information on how the randomisation sequence was generated
Allocation concealment (selection bias)	Unclear risk	Quote: "patients were consecutively randomized into 2 groups"

Mohd 2010 *(Continued)*

		Comment: no information on whether allocation concealment was adequate
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Comment: no information on whether the participants or personnel were blinded
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "The sternotomy wounds were inspected on postoperative day 2 and daily until discharge. Patients were then followed up at 2, 4, and 6 weeks postoperatively to assess for the presence of wound infection and Dermacyn side effects." Comment: no information on whether the inspections and follow-up were carried out by blinded assessors
Incomplete outcome data (attrition bias) All outcomes	High risk	Quote: "We recruited 190 patients for this trial, 95 patients in each group. Twelve patients, however, dropped out owing to postoperative mortality (4 cases, 2 deaths due to poor left ventricular function of < 20% and 2 deaths due to cerebrovascular accident) and chest re-opened for bleeding (8 cases)" Comment: the number of dropouts (exclusions) was close to the number of primary outcome events. The outcome of mortality can be assessed using the ITT population so is at low risk but the SSI outcome is at high risk.
Selective reporting (reporting bias)	Unclear risk	Quote: "The primary outcome was the presence of sternotomy wound infection," Comment: only the primary outcome was prespecified and it is difficult to be certain whether other planned outcomes were fully reported.
Other bias	Unclear risk	Comment: no evidence of other bias but reporting insufficient to be certain

Moylan 1968

Methods	2-arm RCT Setting: single hospital in USA Follow-up: carried out daily until discharge
Participants	260 randomised participants undergoing enterotomy during abdominal surgery. No further information on participant characteristics. Inclusion criteria: enterotomy during abdominal surgery Exclusion criteria: NR
Interventions	Group I (kanamycin): lavage prior to closure of the abdominal incision with 100 mL of 1% kanamycin; excess allowed to enter the peritoneal cavity (124 analysed participants; number randomised unclear) Group II (saline): lavage prior to closure of the abdominal incision with 100 mL of saline; excess allowed to enter the peritoneal cavity (116 analysed participants; number randomised unclear) Cointerventions: concomitant systemic antibiotics in approximately one fifth of wounds
Outcomes	**Primary outcome: SSI** (not defined) Group I (kanamycin): 12/124

Moylan 1968 *(Continued)*

Group II (saline): 23/116

Secondary outcomes: mortality, reoperation

20 participants were excluded for early postoperative death, reoperation or delayed primary closure. Group allocations and numbers excluded for each reason were not reported

Secondary outcome: antibiotic resistance to kanamycin in wound culture

Group I (kanamycin): 12/12

Group II (saline): "over half" of 23

Secondary outcome: adverse events

Respiratory depression was only event reported on:

Group I (kanamycin): 2/124

Group II (saline):4/116

Notes	Funding: NR

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "The solution, either 1% kanamycin or saline, was administered according to an established randomized schedule" Comment: no information on how the randomisation schedule was generated
Allocation concealment (selection bias)	Unclear risk	Quote: "The solution, either 1% kanamycin or saline, was administered according to an established randomized schedule" Comment: no information on whether the allocation was adequately concealed
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "an established randomized schedule under a double-blind protocol" Comment: unclear who was blinded to the allocations
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "The appearance of the wound was graded daily until discharge by a single observer and any deviation from optimal healing was documented serially with photographs" Comment: unclear whether the single observer was blinded to treatment allocation
Incomplete outcome data (attrition bias) All outcomes	High risk	Quote: "of the 260 patients admitted to the study, 20 were excluded for reasons of early postoperative death, reoperation or delayed primary wound closure" Comment: the number of exclusions was comparable to the numbers of infections in each group; the group allocation of excluded participants was not reported.
Selective reporting (reporting bias)	High risk	Comment: outcomes were not defined in the methods section so it is difficult to be sure whether all planned outcomes were fully reported. Some outcomes were not fully reported with data for each treatment group.

Moylan 1968 *(Continued)*

Other bias	Unclear risk	Comment: no evidence of other sources of bias but reporting insufficient to be certain

Neeff 2016

Methods	2-arm RCT Setting: unclear but appears to be a single centre in Germany Follow up: NR
Participants	197 participants undergoing elective colorectal resection Inclusion criteria: NR Exclusion criteria: NR
Interventions	Group I: irrigation with polyhexanide 0.04% solution before final wound closure (101 participants) Group II: irrigation with Ringer's solution before final wound closure (concentration not given) (96 participants) Cointerventions: NR
Outcomes	**Primary outcome:** SSI (not defined) Group I (polyhexanide): 19/101 Group II (Ringer's solution): 22/96
Notes	Funding: NR Abstract only States "interim analysis was done after 250 patients were screened and is presented here."

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote "This study was conducted as a double blind, randomized, single center study" Comment: no information on how the randomisation sequence was generated
Allocation concealment (selection bias)	Unclear risk	Quote: "This study was conducted as a double blind, randomized, single center study" Comment: no information on whether the allocation sequence was adequately concealed
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote "This study was conducted as a double blind, randomized, single center study" Comment: although described as double-blind it is unclear who was blinded and whether the blinding was adequate
Blinding of outcome assessment (detection bias)	Unclear risk	Quote "This study was conducted as a double blind, randomized, single center study"

Neeff 2016 *(Continued)*

All outcomes		Comment: although described as double-blind it is unclear who was blinded and whether the blinding was adequate
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "A total number of 197 elective colorectal resections were randomized. 101 patients received verum. Univariate analysis was followed by multivariate analysis where appropriate. Results: There were 41 wound infections in 197 patients (20.8%). 19 in the verum group, 22 in the control group (p=0.478)." Comment: it appeared that all randomised participants were included in the analysis.
Selective reporting (reporting bias)	Unclear risk	Quote: "Primary endpoint was the rate of SSI in each group" Comment: there is too little information to be sure if all planned outcomes were assessed and reported.
Other bias	High risk	Comment: an interim analysis. This is an abstract and there is too little information to determine if there were other additional sources of potential bias.

Nikfarjam 2014

Methods	Setting: 2 tertiary hepatobiliary and pancreatic surgery units in Australia Follow-up: at 1 and 2 weeks following surgery, and thereafter as indicated. Minimum follow-up 1 month after surgery
Participants	137 consecutive participants enrolled, undergoing major elective open abdominal operative procedures; 128 assigned to treatment (median age 63 years, range 18-86 years) Inclusion criteria: adults undergoing an elective open abdominal operation anticipated to extend beyond 2 h Exclusion criteria: those undergoing laparoscopic procedures
Interventions	In all cases, prior to abdominal closure, the peritoneal cavity was irrigated with least 3 L of warm saline without any added antibiotics. participants then received the following treatment after randomisation: Group I (pulse irrigation): surgical irrigation device (Stryker Instruments, Portage, MI) used after fascia closure to irrigate the surgical wound with 2 L of normal saline at room temperature; pressure close to (but not exceeding) 15 psi delivered through cone-shaped applicator Group II (saline): following closure of the fascia in the standard group, 2 L of normal saline at room temperature was poured into the subcutaneous tissue without any agitation Excess fluid was removed from the subcutaneous tissue with application of a dry pack. Subcutaneous drainage or closure was not undertaken. The skin was reapproximated with continuous subcuticular 3/0 Monocryl sutures. Skin staples were not used in any case. A Duoderm dressing was applied to the wound. Cointerventions: all participants received dexamethasone phosphate 8 mg IV as part of routine antiemetic prophylaxis. At induction of anaesthesia all participants received ampicillin 1 g IV, gentamicin IV (2 mg/kg), and metronidazole 500 mg IV. Antibiotics were continued for 24 h postoperatively. In cases of penicillin allergy, vancomycin 1 g IV or cefazolin [cephazolin] 1 g IV was administered according to the particular sensitivity reaction.
Outcomes	**Primary outcome: SSI**

Nikfarjam 2014 *(Continued)*

Wound infection defined as: (1) purulent drainage, with or without laboratory confirmation, from the superficial incision; (2) organisms isolated from an aseptically obtained culture of fluid or tissue from the superficial incision; (3) at least one of the following signs or symptoms of infection: pain or tenderness, localised swelling, redness, or heat and superficial incision is deliberately opened by surgeon, unless the incision was culture-negative; (4) diagnosis of superficial incisional SSI by the surgeon or the attending physician

Group I (pulse irrigation): 4/66 (all superficial)

Group II (saline): 12/62 (2 required major debridement with prolonged course of dressings; one had partial abdominal wall dehiscence)

Primary outcome: wound dehiscence within 30 d of operation

Group I (pulse irrigation): 0/4

Group II (saline): 1/12

Secondary outcome: participants with postoperative SSI using systemic antibiotics within 30 d of surgery

14/16 participants; no data regarding which treatment group these were associated with

Secondary outcome: antibiotic-resistant infections

Details of organisms isolated but not of resistance were reported, this was not group data

Secondary outcome: adverse events

Cellulitis (without wound cultures): 1/16; no data regarding which treatment group this was associated with

Any non-wound-related complication

Group I (pulse irrigation): 32/66

Group II (saline): 23/62

Secondary outcome: surgical reintervention

Relaparotomy

Group I (pulse irrigation): 3/66

Group II (saline): 3/62

Debridement of wounds with SSI

Group I (pulse irrigation): 0/4

Group II (saline): 2/12

Secondary outcome: length of stay

Group I (pulse irrigation): median 9 (range 4-71) d

Group II (saline): median 9 (range 5-45) d

Secondary outcome: hospital readmissions

Group I (pulse irrigation): 9/66

Group II (saline): 6/62

Notes	Funding: supported by a University of Melbourne, Early Career Development Grant, awarded to lead author. No supplementary support was provided by Stryker

Nikfarjam 2014 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Grouping allocation was determined by a sealed envelope selection. Blocks of 20 patients were randomized at one time. Diabetic patients were randomized separately to achieve close to even distribution in each group." Comment: no information on how randomisation schedule was generated.
Allocation concealment (selection bias)	Unclear risk	Quote: "Grouping allocation was determined by a sealed envelope selection." Comment: unclear whether opaque envelopes were used
Blinding of participants and personnel (performance bias) All outcomes	High risk	No direct quote; no information on blinding Comment: it is unclear whether participants and personnel were blinded; personnel unlikely to be blinded after randomisation due to difference in intervention procedures between arms
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "Patients were monitored by a dedicated acute pain service and reviewed daily for any complications arising from their analgesic regime." Comment: unclear whether personnel were blind to treatment allocation
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "A total of 137 patients were enrolled, as 8 cases did not reach the 2 h duration required for randomization." Comment: study flow diagram indicates that 9 were excluded because they did not conform to inclusion criterion of needing to be > 2 h in duration; there is a discrepancy in the report text stating 8 were excluded for this reason. Attrition bias judged to be low risk given that all others conforming to inclusion criteria were analysed
Selective reporting (reporting bias)	Unclear risk	Comment: unclear whether all prescribed outcomes were reported
Other bias	Unclear risk	Comment: no evidence of other sources of bias but reporting insufficient to be certain

Oestreicher 1989

Methods	2-arm RCT Setting: single hospital in Switzerland Follow-up: NR
Participants	540 randomised participants undergoing surgery Inclusion criteria: participants undergoing surgery Exclusion criteria: oto-rhino-laryngeal surgical cases; thyroid surgeries; day-case surgeries
Interventions	Group I (saline): irrigation with saline. 2 rinses were performed; the first of the operative site, and the second performed before skin closure (273 participants - information derived from graph)

Oestreicher 1989 *(Continued)*

	Group II (povidone-iodine): irrigation with Betadine-R solution (10% PVP-iodine with 1% available iodine, diluted in a 1/10 solution). 2 rinses were performed; the first of the operative site, and the second performed before skin closure. (267 participants - information derived from graph) Cointerventions: after 1 min the excess liquid was re-aspirated. In all participants skin disinfection was carried out using a standard Betadine-R solution.
Outcomes	**Primary outcome: SSI** (not defined) Group I (saline): 15/273 Group II (Betadine): 16/267
Notes	Paper in French; data extracted by one review author, checked by a fluent speaker SSI data presented graphically across 2 figures; these data extracted using graph-reader software Funding: NR

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote "A prospective randomized study was undertaken.....a draw of two groups on the basis of a pre-established list, was carried out at entrance to theatre" Comment: not clear how the randomisation sequence was established
Allocation concealment (selection bias)	Unclear risk	Quote "A prospective randomized study was undertaken.....a draw of two groups on the basis of a pre-established list, was carried out at entrance to theatre" Comment: not clear whether allocation sequence was adequately concealed
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote " all information about the participant, the type of interventions, the personnel, the bacteriological findings and the antibiotic therapies was stored on a computer" Comment: no information as to whether personnel were blinded to interventions
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No direct quote but no information as to who determined the presence of SSI or whether they were blinded to treatment allocation
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	No direct quote: no attrition is reported but results are presented only graphically and it is difficult to determine whether all randomised participants were represented in the results.
Selective reporting (reporting bias)	High risk	No direct quote: results are not adequately reported for each group and it is very unclear if all outcome data are fully reported.
Other bias	Unclear risk	No other source of bias was apparent but the reporting was insufficient to be certain.

Oleson 1980

Methods	Parallel-group RCT Setting: single hospital in Denmark Follow-up: mean 8 d (5-16 d)
Participants	33 participants undergoing surgery for perforated appendix Inclusion criteria: all patients admitted for surgery for perforated appendix with diffuse peritonitis. Visible perforation of appendix with free pus in peritoneum, verified by microbiological culture of extracted peritoneal material. Normal function of kidneys in serum-creatinin concentration demanded. Exclusion criteria: pregnant women, < 15 and > 75 years, with malignant disorders and known allergy to penicillin
Interventions	Group I: no irrigation Group II: postoperative peritoneal flushing with 1 g ampicillin per L flushing fluid Group III: postoperative peritoneal flushing without ampicillin in the flushing fluid Cointerventions: all participants had systemic antibiotics: ampicillin 2 g 4/d IV, gentamycin 1.5 mg/kg weight as the first dose – then 1 mg/kg weight 3/d IM, and clindamycin 600 mg 3/d IM
Outcomes	**Primary outcome: SSI** Group I (no irrigation): 4/10 Group II (ampicillin irrigation): 3/10 Group III (saline irrigation): 2/10 **Secondary outcome: adverse events (intra-abdominal abscess)** Group I (no irrigation): 1/10 Group II (ampicillin irrigation): 010 Group III (saline irrigation): 0/10 **Secondary outcome: length of stay** Group I (no irrigation): 14 d (8-22) Group II (ampicillin irrigation): 13 d (9-20) Group III (saline irrigation): 13 d (10-22)
Notes	Funding: NR Data extraction and 'Risk of bias' assessment performed by translator from the Danish; some aspects discussed with a review author

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Comment: described by one Danish word; the envelope system
Allocation concealment (selection bias)	Unclear risk	Comment: described by one Danish word; the envelope system

Oleson 1980 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	High risk	Comment: Groups II and III had additional catheter added for flushing fluids. Group II also had ampicillin added to the flushing fluid. Personnel would therefore be aware of allocation, unclear if participants were also aware
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: no description of whether assessors were the same as the personnel
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: all 30 participants were included in analysis
Selective reporting (reporting bias)	Low risk	Comment: all outcomes mentioned in the methods section were reported. In the discussion they reported that no kidney or liver dysfunction was observed
Other bias	Unclear risk	Comment: none identified

Oller 2015

Methods	Three-arm RCT Setting: single hospital in Spain Follow-up: unclear
Participants	51 women undergoing axillary lymph node dissection for breast neoplasm. Mean age 55.6 years Inclusion criteria: diagnosis of breast neoplasm and plans to undergo an elective axillary lymph node dissection of Berg's levels I and II because of axillary metastases determined pre-operatively by core biopsy or evidence of metastasis in the sentinel lymph node biopsy (SLNB) in the intra-operative or differential analysis Exclusion criteria: allergy to any of the antibiotic drugs to be used, chronic renal failure secondary to possible toxicity of gentamicin, and planned modified radical mastectomy
Interventions	Group I: 2 lavages with 500 mL of physiologic saline (17 participants) Group II: lavage with 500 mL of saline followed by lavage with 500 mL of a 240-mg gentamicin solution (17 participants) Group III: lavage with 500 mL of saline followed by lavage with 500 mL of a 600-mg clindamycin solution (17 participants) Cointerventions: pre-operative systemic antibiotics (amoxicillin-clavulanic acid 2 g IV; a single dose within 30 min of incision) were employed in all groups. Once the dissection was finished, a Redon drain was placed and connected to a low-pressure vacuum device (primary closure was undertaken)
Outcomes	**Primary outcome: SSI** (incisional, not further defined) Group I (2 x saline lavages) 0/17 Group II (saline then 240 mg gentamicin lavages) 0/17 Group III (saline then 600 mg clindamycin lavages) 0/17 **Secondary outcome: mortality** Group I (2 x saline lavages) 0/17

Oller 2015 *(Continued)*

	Group II (saline then 240 mg gentamicin lavages) 0/17 Group III (saline then 600 mg clindamycin lavages) 0/17 **Secondary outcome: length of hospital stay** Group I (2 x saline lavages) median 3 d (range 1-3) Group II (saline then 240 mg gentamicin lavages) median 3 d (range 1-3) Group III (saline then 600 mg clindamycin lavages) median 3 d (range 1-3)
Notes	Funding: NR

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote "The patients were randomized by means of an Internet module into three groups" Comment: mechanism of the internet module used for randomisation unclear
Allocation concealment (selection bias)	Unclear risk	Quote "The patients were randomized by means of an Internet module into three groups" Comment: no information as to whether the allocation was adequately concealed
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "The patients were blinded as to whether they received saline, gentamicin, or clindamycin." Comment: participants were blinded but unclear whether personnel were also blinded
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: there is insufficient information to determine who performed the assessment of outcomes and whether they were blinded to treatment allocation.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: it appears that all the randomised participants were included in the analyses.
Selective reporting (reporting bias)	Unclear risk	Comment: the outcomes reported were not prespecified in the methods so it is difficult to determine whether all planned outcomes were fully reported.
Other bias	Unclear risk	Comment: there is no evidence of other sources of bias but reporting is insufficiently detailed to be sure.

Ozlem 2015

Methods	2-arm RCT Setting: NR but appears to be a hospital in Turkey Follow-up: NR
Participants	14 participants with perforated appendix (among 279 undergoing appendectomy for acute appendicitis)

Ozlem 2015 *(Continued)*

	Inclusion criteria: perforated appendix, undergoing appendectomy for acute appendicitis Exclusion criteria: appendix not perforated
Interventions	Group I: peritoneal lavage with irrigation and aspiration (7 participants) Group II: aspiration alone (7 participants) Co-interventions: NR
Outcomes	**Primary outcome: SSI** Wound infection Group I (lavage): 2/7 Group II (aspiration only): 0/7 **Secondary outcome: adverse events** (1 intra-abdominal abscess, 1 postoperative ileus) Group I (lavage): 1/7 Group II (aspiration only): 1/7
Notes	Abstract only but further information received via study author correspondence Funding: NR

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote (via correspondence): "The randomisation method is envelope method" Comment: unclear how the randomisation sequence was generated
Allocation concealment (selection bias)	Unclear risk	Comment: insufficient information on use of envelopes to be sure whether allocation was adequately concealed
Blinding of participants and personnel (performance bias) All outcomes	High risk	Comment: no information on whether participants or personnel were blinded but personnel must have been aware due to differences in intervention
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: no information on who performed the assessment or whether they were blinded to treatment allocation
Incomplete outcome data (attrition bias) All outcomes	Low risk	It appears that all randomised participants were included in the analysis.
Selective reporting (reporting bias)	Unclear risk	It is unclear whether all planned outcomes were fully reported; we contacted the study author in order to fully report SSI outcome on a per-group basis.
Other bias	Unclear risk	Abstract only and reporting insufficient to be certain there were no other sources of bias.

Peterson 1990

Methods	Parallel-group RCT Setting: single medical centre in USA Follow-up: at least 2 weeks postoperatively
Participants	207 women undergoing caesarean section Inclusion criteria: non elective caesarean section Exclusion criteria: allergic to penicillin or cephalosporins, already on antibiotics, ongoing infection, requiring bacterial endocarditis prophylaxis
Interventions	Group I: cefazolin lavage; 2 g in 1000 mL saline administered to the uterine incision (300 mL), bladder flap (200 mL), abdominal gutters (200 mL) and abdominal incision (remaining fluid) Group II: cefamandole lavage; 2 g in 1000 mL saline administered to the uterine incision (300 mL), bladder flap (200 mL), abdominal gutters (200 mL) and abdominal incision (remaining fluid) 2 additional groups were included in the trial using the same antibiotics delivered IV with saline lavage. These groups are not relevant to this review and we did not extract any data relating to them. Cointerventions: normal saline bolus IV after cord clamped
Outcomes	**Primary outcome: SSI (presence of cellulitis and/or purulent exudate)** Group I (cefazolin): 2/59 Group II (cefamandole) 0/54
Notes	Funding: NR

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Patients were randomly assigned to one of four treatments" Comment: no information on how the randomisation sequence was generated or whether an appropriate method was used.
Allocation concealment (selection bias)	Unclear risk	Quote: "Patients were randomly assigned to one of four treatments" Comment: no information on whether there was adequate allocation concealment.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "The operating-room nurses prepared the 1000 mL lavage solutions, to which all surgeons and patients were blinded" Comment: participants and personnel were blinded to treatment allocation.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: no specific quote but it was not clear who performed the outcome assessment and whether they were blinded to treatment allocation.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: all 207 randomised participants were included in the analyses.

Peterson 1990 *(Continued)*

Selective reporting (reporting bias)	Unclear risk	Comment: outcomes were not clearly specified in the methods so it is unclear whether all planned outcomes were fully reported.
Other bias	Unclear risk	Comment: no obvious sources of additional bias but reporting insufficient to be certain

Platt 2003

Methods	Within-subject design - all participants received both treatment and control Setting: single hospital in UK Follow-up: 1, 4 and 8 weeks
Participants	30 women undergoing bilateral breast reduction. Participants had breasts randomised to the 2 treatment groups. Mean age 33 years (range 18-65), mean BMI 26.3 Inclusion criteria: BMI ≤ 30, undergoing bilateral breast reduction Exclusion criteria: NR
Interventions	Group I (saline): breast washed out with saline for approximately 2 min just prior to wound closure (30 participants, 30 breasts) Group II (control): no wash out with saline (same 30 participants as Group I, 30 breasts) Co-interventions: each breast was preinfiltrated with 300 mL saline containing adrenaline diluted to 1:500,000, lignocaine and hyaluonidase. Infiltration was performed uniformly through the breast using a spinal needle and syringe, sparing the pedicle. All wounds were closed over corrugated drains which were removed 24 hs after surgery.
Outcomes	**Primary outcome: SSI** Wound discharge, invasive infection Group I (saline): 0/30 Group II (control): 0/30 **Primary outcome: wound dehiscence** Minor wound breakdown in 13/60 breasts (7 < 1 cm wide, 6 > 1 cm) 11/60 participants affected, 9 unilaterally, 2 bilaterally Group I (saline): 7/30 Group II (control): 6/30
Notes	Generalisability: outcomes were related to BMI and this group were preselected based on BMI Some methodological details were provided via study author correspondence Funding: NR

Risk of bias

Bias	Authors' judgement	Support for judgement

Platt 2003 *(Continued)*

Random sequence generation (selection bias)	Unclear risk	Quote (from text): "The side to be washed out with normal saline was randomised so that the contralateral breast acted as each patient's own control" Quote (from author correspondence): "I think we used sealed envelopes" Comment: not enough detail about the method to judge whether appropriate method of sequence generation was used.
Allocation concealment (selection bias)	Unclear risk	Quote (from author correspondence): "I think we used sealed envelopes" Comment: not enough detail about the method to judge whether there was adequate allocation concealment.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Comment: there is no mention of blinding. The participants may have been blinded but the personnel would be aware of the different treatments.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote (from author correspondence): "Assessors were blind to the side washed out but could include the surgeons." Comment: although some assessors were blind to treatment, they could also have included the surgeons who were not blinded.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote (from author correspondence): "All people enrolled were included in the study." Comment: all participants accounted for in the results
Selective reporting (reporting bias)	Unclear risk	Comment: there is insufficient information to judge whether all planned outcomes were appropriately assessed.
Other bias	Unclear risk	Comment: the study design means that the 2 groups are not independent. It's not clear whether the analysis was adjusted for paired data.

Rambo 1972

Methods	2-arm RCT Setting: single hospital in USA Follow-up: NR
Participants	94 patients undergoing surgery for peritonitis. Mean age Group I: 40.1 years, Group II: 40.3 years Inclusion criteria: participants deemed by surgeon, at time of operation, that irrigation would be helpful for mechanical cleansing of peritoneal cavity or for direct application of an antibiotic to a grossly contaminated peritoneum. Exclusion criteria: NR
Interventions	Group I (cephalothin): irrigation with solution containing 4 g/L cephatholin (43 participants irrigated with 4 L of solution, 1 participant irrigated with 2 L of solution) Group II (saline and multivitamin): irrigation with 0.9% saline solution containing 0.25 mL/L of IV multivitamin solution (Betalin, Eli Lilly, Indiana) (48 participants irrigated with 4 L of solution, 2 participants irrigated with 2 L of solution)

Rambo 1972 *(Continued)*

	Cointerventions: use of concomitant antibiotics (cephaolthin; cephalothin plus other antibiotic; penicillin and streptomycin; miscellaneous) was at surgeon's discretion
Outcomes	**Primary outcome: SSI** (no definition provided) Group I (cephalothin): 11/44 Group II (saline and multivitamin): 13/50 **Secondary outcome: mortality** Group I (cephalothin): 5/44 Group II (saline and multivitamin): 8/50 **Secondary outcome: antibiotic-resistant infections** Group I (cephalothin): 7 organisms reported to be resistant; 28 to be sensitive Group II (saline and multivitamin): 12 organisms reported to be resistant; 49 to be sensitive It was not clear how this related to participant-level data; individual organism types were reported **Secondary outcome: adverse events** Abscess/peritonitis: Group I (cephalothin): 8/44 Group II (saline and multivitamin): 10/50
Notes	Participants: "Two patients had irrigation of the peritoneal cavity on two separate occasions, each of which was counted as a distinct clinical entity unto itself" Funding: NR Time points for all assessments unknown

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Patients were assigned by the pharmacy to the cephalothin or to the control group by use of a table of random numbers." Comment: sequence generation used an appropriate method.
Allocation concealment (selection bias)	Unclear risk	Quotes: "Patients were assigned by the pharmacy to the cephalothin or to the control group by use of a table of random numbers;" "The study was double blind, and the charts were fully evaluated prior to breaking the code, which was kept by the pharmacy;" Comment: participants allocated to treatment group by pharmacy who held the randomisation schedule, but unknown whether pharmacy staff were blinded to the allocation sequence
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quotes: "The study was double blind, and the charts were fully evaluated prior to breaking the code, which was kept by the pharmacy." Comment: appears that treating staff and participants were unaware of treatment allocation until after data collection
Blinding of outcome assessment (detection bias)	Low risk	Quote: "The study was double blind, and the charts were fully evaluated prior to breaking the code, which was kept by the pharmacy."

Rambo 1972 *(Continued)*

All outcomes		Comment: appears that staff were unaware of the allocation until after data collection
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: no evidence of attrition, as data reported for all randomised patients
Selective reporting (reporting bias)	Unclear risk	Comment: all outcomes specified in study methods are reported in the results, but not enough information to determine whether all outcomes in the study protocol are reported
Other bias	High risk	Quote: "Patients were admitted to the study if their surgeon, at the time of operation, believed that irrigation would be helpful for mechanical cleansing of the peritoneal cavity or for direct application of an antibiotic to a grossly contaminated peritoneum." Comment: potential bias relating to participant selection, based on subjective rather than objective criteria.

Ruiz-Tovar 2011

Methods	2-arm RCT Setting: single hospital in Spain Follow-up: NR
Participants	128 participants Inclusion criteria: colorectal surgery for neoplasms Exclusion criteria: NR
Interventions	Group I: intraperitoneal irrigation with normal saline (64 participants) Group II: intraperitoneal irrigation with solution containing gentamicin (240 mg) and clindamycin [clindamicin] (600 mg) (64 participants)
Outcomes	**Primary outcome: SSI** (not defined) Wound infection (unsure of calculation to numbers as whole numbers/64 do not round to these %) Group I (saline): 41.9%; 27/64 (extrapolated from percentage and rounded to nearest whole number) Group II (antibiotic): 9.5%; 6/64 (extrapolated from percentage and rounded to nearest whole number) Intra-abdominal infection (excluding 5% cases diagnosed with anastomotic leak) (intra-abdominal abscess?) Group I (saline): 16.3%; 10/64 (extrapolated from percentage and rounded to nearest whole number) Group II (antibiotic): 0%; 0/64
Notes	Abstract only Funding: NR
Risk of bias	

Ruiz-Tovar 2011 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote "A prospective randomized study of all the patients undergoing colorectal surgery for neoplasms at Hospital General Universitario de Elche during 2010 was performed. Patients were divided in 2 groups..." Comment: not clear how the randomisation sequence was generated
Allocation concealment (selection bias)	Unclear risk	Quote "A prospective randomized study of all the patients undergoing colorectal surgery for neoplasms at Hospital General Universitario de Elche during 2010 was performed. Patients were divided in 2 groups..." Comment: not clear whether allocation was adequately concealed
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Comment: no direct quote but no information on blinding of either participants or personnel
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: no direct quote but no information on how the outcomes were assessed or whether the assessors were blinded to treatment allocation
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Quote: "128 patients were analyzed, 64 in each group." Comment: the number of participants randomised is not stated, only the number analysed
Selective reporting (reporting bias)	Unclear risk	Quote: "Wound infection and intrabdominal abscess were investigated." Comment: both these outcomes were reported but it is not clear whether they were the only planned outcomes
Other bias	Unclear risk	Comment: no evidence of other bias but reporting insufficient to be confident (abstract only)

Ruiz-Tovar 2012

Methods	2-arm RCT Setting: single hospital in Spain Follow-up: 30 d after discharge
Participants	108 participants with adenocarcinoma (5 excluded postoperatively due to anastomotic leak). Mean (SD) age 69.9 (11.3) years. Comorbidities: diabetes mellitus (34%), high blood pressure (48%), dyslipedaemia (32%), cardiopathies (21%), chronic obstructive pulmonary diseases (11%), nondecompensated liver cirrhosis (1%). Inclusion criteria: diagnosis of colorectal neoplasms and due to undergo elective operation with curative aims Exclusion criteria (preoperative): diagnosis of chronic renal failure Exclusion criteria (postoperative): anastomotic leak identified by computed tomography (CT) scan with rectal contrast enema

Ruiz-Tovar 2012 *(Continued)*

Interventions	Group I (saline): irrigation of entire abdominal cavity with 500 mL normal saline, followed by aspiration of the liquid and abdominal wall closure (54 participants) Group II (antibiotics): irrigation with 500 mL normal saline, aspiration, then lavage with antibiotic solution (gentamicin 240 g and clindamycin 600 mg dissolved in 500 mL normal saline) for 3 min, aspiration and abdominal wall closure (54 participants) Co-interventions: perioperative antibiotics given to all (ciprofloxacin 400 mg and metronidazol 1500 mg, single dose within 30 min of incision with redose after 4 h if surgery prolonged)
Outcomes	**Primary outcome: SSI** Wound infection defined as presence of purulent discharge from the surgical wound, confirmed with microbiologic culture Group I (saline): 14% (calculated as**7/51** analysed participants) Group II (antibiotic): 4% (calculated as **2/52** analysed participants) **Secondary outcome: mortality** Group I (saline): 2 (unclear whether this is out of 51 analysed or 54 randomised participants) [we will assume completed case here] Group II (antibiotic): 1 (unclear whether this is out of 52 analysed or 54 randomised participants) **Secondary outcome: intra-abdominal abscess** Defined as the presence of a fluid collection at CT scan in symptomatic participant (fever, abdominal pain, prolonged postoperative ileus or septic status) Group I (saline): 6% (calculated as **3/51** analysed participants) Group II (antibiotic): 0 (presumably **0/52** analysed participants) **Secondary outcome: length of hospital stay (median (range) d)** Group I (saline): 6 (5-32) Group II (antibiotic): 6.5 (5-14)
Notes	Funding: financial support provided by Fundacion Navarro Tripodi

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "The patients were randomized by means of an Internet randomization module" Comment: **a**ppropriate method of sequence generation appears to have been used
Allocation concealment (selection bias)	Unclear risk	Comment: no mention of allocation concealment
Blinding of participants and personnel (performance bias) All outcomes	High risk	Comment: there is no mention of blinding participants or personnel but differences in treatment mean personnel would not have been blinded

Ruiz-Tovar 2012 *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "Wound infection was determined by an epidemiology nurse blinded to treatment groups" "The diagnosis of intra-abdominal abscess was determined by a radiologist blinded to the treatment groups" Comment: outcome assessors were blinded
Incomplete outcome data (attrition bias) All outcomes	High risk	Quote: "Exclusion criteria were... or an anastomotic leak in the postoperative course, which would represent a bias in the diagnosis of intra-abdominal infection" Comment: 5 participants were excluded from the analysis as they were considered to be at high risk of infection and represent a bias - however it is not clear what bias they would introduce as their results are not reported.
Selective reporting (reporting bias)	Unclear risk	Comment: outcomes are not clearly reported as they are presented as percentages and do not clarify participant numbers.
Other bias	Low risk	Comment: there is no evidence of other bias.

Ruiz-Tovar 2013

Methods	2-arm RCT Setting: single breast unit at hospital in Spain Follow-up: 2 weeks after surgery
Participants	40 female participants (mean age 54.8 (SD 13.7) years) undergoing axillary lymph node dissection Inclusion criteria: diagnosis of breast neoplasms and plans to undergo elective axillary lymph node dissection (ALND) of Berg's levels I and II due to axillary metastasis determined preoperatively by core biopsy or evidence of metastasis in the sentinel lymph node biopsy (SLNB) in the intraoperative or in the differed analysis. Exclusion criteria: chronic renal failure due to possible toxicity of gentamicin and participants undergoing a modified radical mastectomy.
Interventions	Group I (saline): lavage performed immediately prior to closure, after placement of drain and a first swab for microbiological culture. First lavage with 500 mL normal saline, which was aspirated and a second swab for culture obtained. Second lavage with 500 mL normal saline, which was aspirated prior to third swab for culture Group II (gentamicin): lavage performed immediately prior to closure, after placement of drain and a first swab for microbiological culture. First lavage with 500 mL normal saline, which was aspirated and a second swab for culture obtained. Second lavage with 240 mg gentamicin dissolved in 500 mL normal saline, which was aspirated prior to third swab for culture. Cointerventions: perioperative systemic antibiotics (single dose amoxicillin/clavulanic acid 2 g IV, within 30 min of incision) were administered in both groups. Redon drain was left in place and connected to a low pressure vacuum device, and removed when drainage volume was < 30 mL/d
Outcomes	**Primary outcome: SSI** ("wound infection" - not defined) Group I (saline): 0/20 Group II (gentamicin): 0/20 **Secondary outcome: length of hospital stay (median (range) d)**

Ruiz-Tovar 2013 *(Continued)*

	Group I: 3 (1-3) Group II: 3 (1-3) **Secondary outcome: mortality** Group I (saline): 0/20 Group II (gentamicin): 0/20 **Secondary outcome: adverse events (all types)** Group I (saline): 0/20 Group II (gentamicin): 0/20
Notes	Funding: Fundación Navarro Tripodi

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Patients were randomized by means of an Internet randomization module into 2 groups." Comment: sequence generation used an appropriate method
Allocation concealment (selection bias)	Unclear risk	Quote: "Patients were randomized by means of an Internet randomization module into 2 groups." Comment: unclear whether randomisation schedule was concealed from staff
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "Patients were blinded as to whether they received gentamicin or not." Comment: unclear whether staff were blinded to treatment allocation
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: no direct quote; no information on who performed outcome assessment or whether they were blinded to treatment allocation
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: no evidence of attrition bias
Selective reporting (reporting bias)	Unclear risk	Comment: no evidence of selective reporting but not enough information to be certain
Other bias	Unclear risk	Comment: no evidence of other sources of bias, but reporting is not sufficient to be certain

Ruiz-Tovar 2016a

Methods	2-arm RCT Setting: several hospitals in Spain and 1 hospital in UK ("at our institutions" - not stated how many - it isn't clear from authorship) Follow-up: minimum 42 months post surgery (infection surveillance was for 30 d following discharge)

Ruiz-Tovar 2016a *(Continued)*

Participants	106 participants undergoing elective surgery for colon neoplasms (data only presented for 104 as 2 who died perioperatively were excluded). Mean (SD) age: Group I 69.1 (10.2) years, Group II 68.5 (10.2) years. Co-morbidities included diabetes mellitus (Group I 33%, Group II 29%), high blood pressure (Group I 46%, Group II 50%), dyslipidemia (Group I 33%, Group II 29%), cardiopathy (Group I 23%, Group II 27%). Groups were balanced in terms of tumour stage and surgical technique used. Inclusion criteria: diagnosis of colon neoplasms, undergoing elective surgery with curative aims Exclusion criteria: pre-operative diagnosis of renal failure, allergy to gentamicin or clindamycin, diagnosis of rectal cancer
Interventions	Group I: immediately prior to closure of the abdominal wall, lavage was performed with an antibiotic solution (gentamicin 240 mg and clindamycin 600 mg dissolved in 500 mL normal saline). The solution was allowed to sit in the abdominal cavity for 3 min, then aspirated (53 participants) Group II: as above but with 500 mL normal saline (53 participants) Co-interventions: perioperative systemic antibiotics (ciproflaxin 400 mg and metronidazole 1500 mg, single dose given within 30 min of incision, additional dose after 4 h if surgery prolonged)
Outcomes	**Primary outcome: SSI** Incisional SSI (defined as the presence of a purulent discharge from the surgical incision and confirmed with microbiological culture) Group I (antibiotic): 3.8% (calculated as 2/52) Group II (saline): 13.5% (calculated as 7/52) Organ-space SSI Group I (antibiotic): 0% (0/52) Group II (saline): 5.8% (calculated as 3/52) **Secondary outcome: length of hospital stay (median (range) d)** Group I (antibiotic): 6.5 (5-14) Group II (saline): 6 (5-32) **Secondary outcome: adverse events** Anastomotic leak Group I (antibiotic): 2/52 Group II (saline): 3/52 **Secondary outcome: mortality** 1 participant from each group died perioperatively and was excluded from the analysis. Survival analysis is reported for remaining participants as the primary outcome of the study was disease-free survival, but 30-day survival is not reported. 30-day mortality Group I (antibiotic): 1/53 Group II (saline): 1/53
Notes	Funding: NR

Risk of bias

Ruiz-Tovar 2016a *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Patients were randomly assigned using a random number table" Comment: appropriate method used
Allocation concealment (selection bias)	Unclear risk	Comment: no mention of allocation concealment
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Comment: There is no mention of blinding of participants and personnel. It is unlikely that personnel were blinded but possible
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "Incisional SSI was determined by an epidemiology nurse blinded to the treatment groups" Comment: outcome assessor was blinded (for SSI)
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Comment: 1 participant in each group died perioperatively and was excluded from analysis. This is unlikely to have biased results but no details about these participants are included so it is difficult to judge.
Selective reporting (reporting bias)	Low risk	Comment: there does not appear to have been selective outcome reporting and the primary outcomes of the study are reported in detail
Other bias	Low risk	Comment: there is no evidence of other bias

Ruiz-Tovar 2016b

Methods	Parallel-group RCT Setting: single hospital in Spain Follow-up: 30 d after discharge
Participants	80 participants undergoing laparoscopic sleeve gastrectomy (LSG) as a bariatric procedure. Mean age 43.1 years; mean BMI 47.8 kg/m^2 Inclusion criteria: BMI either > 40 kg/m2 or > 35 kg/m2 with comorbidities associated with obesity and undergoing laparoscopic sleeve gastrectomy (LSG) as a bariatric procedure. Exclusion criteria (preoperative): documented gastroesophageal reflux (these underwent laparoscopic Roux-en-Y gastric bypass), uncontrolled psychiatric disorders, active infection or malignant disease, and any other concomitant pathology considered to be a contraindication to bariatric surgery diagnosis of chronic renal failure. Post-operative complications were also excluded from the analysis.
Interventions	Group I: intra-abdominal lavage with 500 mL saline (40 participants) Group II: intra-abdominal lavage with a gentamicin–clindamycin solution: gentamicin (240 mg) and clindamycin (600 mg) dissolved in 500 mL (40 participants) Cointerventions: Peri-operative systemic antibiotics (cefuroxime 3 g; single dose pre-operatively within 30 min of incision, repeated after 4 h when the surgery exceeded that time)
Outcomes	**Secondary outcome: mortality** Group I (saline): 1/40

Ruiz-Tovar 2016b *(Continued)*

	Group II (clindamycin-gentamicin): 0/40 **Secondary outcome: adverse events - complications of surgery** Group I (saline): 2/40 Group II (clindamycin-gentamicin): 1/40
Notes	Declaration of no competing financial interests, funding otherwise NR

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "The patients were randomized by means of an Internet randomization module into two groups" Comment: appropriate means of randomisation sequence generation reported
Allocation concealment (selection bias)	Unclear risk	Quote: "The patients were randomized by means of an Internet randomization module into two groups" Comment: unclear if appropriate measures were taken to conceal allocation
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Comment: there was no information on whether personnel and participants were blinded to group allocation
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "Incisional SSI was determined by an epidemiology nurse blinded to the treatment groups. Infection surveillance was extended for 30 d after discharge. The diagnosis of organ-space SSI and leak was determined by a radiologist blinded to the treatment group." Comment: outcome assessment was performed in a blinded manner
Incomplete outcome data (attrition bias) All outcomes	Low risk	Exclusions due to postoperative complications (3 participants) from some analyses were fully reported and accounted for; all participants could be included in analysis of SSI
Selective reporting (reporting bias)	Low risk	Outcomes were clearly predefined and appeared to be fully reported
Other bias	Low risk	No evidence of other sources of bias and reporting sufficient to suggest there were none

Schein 1990

Methods	3-arm RCT Setting: 1 surgical unit in South Africa Follow-up: at least 2 weeks after operation
Participants	87 participants undergoing surgery for peritonitis (mean age 53 years, range 18-91 years) Inclusion criteria: confirmed diffuse or localised intra-abdominal infection

Schein 1990 *(Continued)*

	Exclusion criteria: those with nonruptured, localised abscesses and those participants undergoing appendectomy through right iliac fossa incisions; those with diffuse fecal peritonitis, infected pancreatic necrosis, or postoperative peritonitis
Interventions	Group I (control): all peritoneal contamination was sucked out or picked out manually; the peritoneal cavity was then swabbed gently with large abdominal swabs (29 participants) Group II (saline): all peritoneal contaminants were sucked out, and the peritoneal cavity was generously irrigated with no less than 5 L of saline solution (29 participants) Group III (chloramphenicol succinate): all peritoneal contaminants were sucked out, and the peritoneal cavity was generously irrigated with no less than 5 L of saline solution; 2 g of chloramphenicol succinate was added to the last L of the lavage fluid (29 participants) Cointerventions: all participants received systemic antibiotics penicillin G potassium, amikacin sulfate and metronidazole. Therapy with antibiotics was started preoperatively and continued after operation for 24 hs and more, depending on the operative finding and each participant's clinical course. Intraperitoneal drains were placed only when abscesses were found.
Outcomes	**Primary outcome: SSI** "Wound infection" defined as a discharge of pus from the wound; considered to be minor in cases where no early removal of sutures was necessary and primary healing was achieved; considered to be major when wounds required premature removal of sutures and drainage of pus and that healed by secondary intention. Group I (control): 6/29 (4 minor, 2 major) Group II (saline): 5/29 (3 minor, 2 major) Group III (chloramphenicol succinate): 5/29 (3 minor, 2 major) **Secondary outcome: mortality** Group I (control): 6/29 Group II (saline): 6/29 Group III (chloramphenicol succinate): 3/29 **Secondary outcome: adverse events** Surgical complications Group I (control): 3/29 (one pelvic abscess) Group II (saline): 7/29 (one pelvic abscess) Group III (chloramphenicol succinate): 2/29 Medical complications Group I (control): 8/29 Group II (saline): 9/29 Group III (chloramphenicol succinate): 5/29 **Secondary outcome: mean length of hospital stay** Group I (control): 13 d Group II (daline): 13 d Group III (chloramphenicol succinate): 10 d

Schein 1990 *(Continued)*

Notes	Funding: NR

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Patients were randomized into one of the following three treatment groups..." Comment: unclear how randomisation was performed
Allocation concealment (selection bias)	Unclear risk	Quote: "Patients were randomized into one of the following three treatment groups..." Comment: unclear whether randomisation schedule was concealed
Blinding of participants and personnel (performance bias) All outcomes	High risk	Comment: no direct quote; no information on whether participants or personnel were blinded to treatment
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "Patients were monitored closely after operation and followed up in the outpatient clinic for at least 2 weeks after the operation." Comment: Nno information on whether personnel performing outcome assessments were blinded to treatment
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: no evidence of attrition bias
Selective reporting (reporting bias)	Unclear risk	Comment: no evidence of selective reporting, but not enough information to be certain
Other bias	Unclear risk	Comment: no evidence of other sources of bias, but reporting not sufficient to be certain

Shimizu 2011

Methods	2-arm RCT Setting: neurosurgical department in Japan Follow up: 10 d post surgery
Participants	20 participants (mean age 60 years) admitted for clipping surgery for unruptured cerebral aneurysms; indications for clipping surgery are age < 70 years, no significant systemic risk for general anaesthesia, and aneurysm size > 5 mm. In 2 participants, 2 aneurysms were clipped in one surgery. Inclusion criteria: age between 20 and 70 years; planned surgery for aneurysm(s) of the internal carotid artery territory through a unilateral pterional approach; no steno-occlusive lesions (> 50%) in cerebral arteries as evaluated by magnetic resonance (MR) angiography and/or conventional angiography; and aneurysms that presented no significant surgical difficulty Exclusion criteria: aneurysms presenting more surgical difficulty than usual; aneurysms suitable for approaches other than the pterional approach; aneurysms suitable for intravascular surgery; history of

Shimizu 2011 *(Continued)*

	cerebrovascular diseases causing any disability (modified Rankin scale score 1 or worse); and significant medical problems
Interventions	Group I (artificial CSF): brain surfaces and basal and sylvian cisterns irrigated during surgery with Artcereb, an artificial CSF (10 participants) Group II (saline): brain surfaces and basal and sylvian cisterns irrigated during surgery with physiological saline (10 participants)
Outcomes	**Primary outcome: SSI** NR **Secondary outcome: adverse events: (postoperative, all types, includes MRI findings)** Group I (artificial CSF): 2/10 Group II (saline): 2/10 (2/10 participants with 2 events each)
Notes	Published paper does not report any of specified primary outcomes for this review Funding: Nihon Medi-Physics Co, Ltd, Tokyo, Japan, provided N-isopropyl-p-[123I]iodoamphetamine and Otsuka Pharmaceutical Co., Tokyo, Japan, provided Artcereb. The study did not receive any other financial support. **Contacted lead study author to find out if there are any further data relating to our outcomes**

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "The patient was randomly assigned to irrigation fluid A or B during surgery to irrigate the basal and sylvian cisterns and the brain surface." Comment: unclear how randomisation was performed
Allocation concealment (selection bias)	Unclear risk	Quote: "A total of 20 bottles each containing 500 mL of Artcereb (Artcereb group, n = 10) or physiological saline (saline group, n = 10) were prepared. The bottles of Artcereb were labelled A, and those of physiological saline were labelled B, without the knowledge of the study participants. The assignment was kept in a shielded envelope and only opened after all study data were collected." Comment: unclear whether allocation sequence was concealed
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "The bottles of Artcereb were labelled A, and those of physiological saline were labelled B, without the knowledge of the study participants. The assignment was kept in a shielded envelope and only opened after all study data were collected." Comment: unclear whether personnel were blind to treatment allocation
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "All 20 patients were serially evaluated on postoperative days 1, 3 to 5, and 7 to 10." Potentially amend this after obtaining more information from study authors, as it may not specifically relate to assessment of wound. Comment: study author contacted to determine if this relates to wound assessment
Incomplete outcome data (attrition bias)	Low risk	Comment: no evidence of attrition

Shimizu 2011 *(Continued)*
All outcomes

Selective reporting (reporting bias)	Unclear risk	Comment: no evidence of selective reporting, but not enough information to be certain
Other bias	Unclear risk	Comment: no evidence of other sources of bias, but reporting not sufficient to be certain

Silverman 1986

Methods	2-arm RCT Setting: a general hospital, UK Follow-up: 6 weeks post surgery (close monitoring in post-operative period, then outpatient review at 6 weeks) Also a 1-year follow-up (see notes)
Participants	159 patients undergoing elective or emergency transperitoneal intestinal surgery of various types and for a range of conditions (e.g. colorectal neoplasm, inflammatory bowel disease, diverticular disease). Mean (range) age: Group I (saline): 51 (16-89) years, Group II (tetracycline): 50 (19-85) years. Stratification 1) high risk and low risk operation category 2) IV antibiotic used (three regimes) Inclusion criteria: elective or emergency transperitoneal intestinal surgery (small bowel, colon and rectum) Exclusion criteria: allergy to penicillin or cephalosporins
Interventions	Group I (saline): prior to closing the abdomen at the conclusion of the operation, peritoneal lavage was performed with 2 L 0.9% sterile saline. The lavage fluid was washed around the peritoneal cavity for at least 2 min and then sucked out with a sump sucker (74 participants) Group II (tetracycline): same method as above but with lavage fluid 2 L 0.9% sterile saline containing 2 g tetracycline (85 participants) Co-interventions: all participants received IV antibiotic at the beginning of the operation (metronidazole 1.5 g and either gentamicin 120 mg (55 participants), ceftriaxone 2 g (55 participants), or mezlocillin 5 g (49 participants)). All participants had abdomen closed with a mass suture technique and primary skin closure with suction drainage to the pelvis
Outcomes	**Primary outcome: SSI** Wound infection was defined as a discharge of pus from the wound. (Abdominal minor/major and perineal infection, and IV antibiotic groups also reported separately) Group I (saline): 24/74 Group II (tetracycline): 10/85 **Secondary outcome: adverse events** Intra-abdominal abscess Group I (saline): 10/74 Group II (tetracycline): 11/85 Septicemia Group I (saline): 0/74

Silverman 1986 *(Continued)*

	Group II (tetracycline): 2/85 **Secondary outcome: surgical re-intervention rate** Reoperation for adhesive obstruction within 1 year of surgery (reported in the discussion rather than results) Group I (saline): 0/74 Group II (tetracycline): 3/85
Notes	Surgical re-intervention rate was reported in the discussion rather than the results and is from 1-year follow-up. Funding: NR

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Each patient was assigned a study number on a consecutive basis. The hospital pharmacist then dispensed... according to a computed-generated randomization code." "Randomization was stratified so that patients classified as 'high risk' or 'low risk' were distributed equally between the two lavage groups and also among the three intravenous antibiotic regimens" Comment: appropriate methods used to generate the sequence
Allocation concealment (selection bias)	Low risk	Quote: "The hospital pharmacist then dispensed the intravenous antibiotics and the lavage fluid according to a computer-generated randomization code. All drugs were in numbered ampoules, the pharmacist being the sole possessor of the code" Comment: the allocation sequence appears to have been concealed
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "The hospital pharmacist then dispensed the intravenous antibiotics and the lavage fluid according to a computer-generated randomization code. All drugs were in numbered ampoules, the pharmacist being the sole possessor of the code" Comment: suggests that there may have been blinding of participants and personnel but not explicitly stated
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "All patients were monitored... by assessors independent of the surgical team" Comment: suggests they may have been blind to treatment but not explicitly stated
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: all participants are included in the results
Selective reporting (reporting bias)	High risk	Comment: some outcomes were NR by group, or were only reported in the discussion (re-operation rate) and it is not clear which outcomes were decided prospectively
Other bias	Unclear risk	Comment: no evidence of other bias but reporting insufficient to be certain

Sindelar 1979

Methods	2-arm RCT Setting: single hospital in USA Follow-up: 12 weeks post surgery (daily examination for 7 d, then at least weekly)
Participants	500 patients undergoing operative procedures (age reported as groups rather than mean - there are participants of all age groups from < 9 years to > 80 years). Surgery categories included clean, potentially contaminated, contaminated and dirty. Inclusion criteria: elective or emergency surgery, abdominal and gastrointestinal procedures, oncologic procedures, vascular reconstructions, head and neck operations, thoracic procedures, genitourinary procedures, trauma operations Exclusion criteria: amputations for ischaemic disease, drainage of subcutaneous abscesses, skin grafting, anorectal procedures, a history of iodine sensitivity, thyroid disease or significant renal impairment
Interventions	Group I (povidone-iodine): following closure of the fascia, subcutaneous tissues were irrigated for 60 s with 10% povidone-iodine solution (242 participants) Group II (saline): following closure of the fascia, subcutaneous tissues were irrigated for 60 s with saline solution (258 participants) Co-interventions: wounds categorised as dirty had close system suction wound catheters placed in the subcutaneous space, which were removed 48 h postoperatively. Systemic antibiotics (clindamycin and gentamycin, or doxycycline for those with a history of allergy or suspected early impaired renal function) were given preoperatively to participants in potentially contaminated, contaminated, and dirty wound categories. If there were clinical indications of sepsis, systemic antibiotics were continued in some participants beyond 48 h postoperatively.
Outcomes	**Primary outcome: SSI** An incision was considered infected if any amount of pus was discharged within 12 weeks of operation. Serous drainage from questionable wounds was cultured and the wound was classified as infected if any bacterial growth was recovered. Group I (povidone-iodine): 7/242 Group II (saline): 39/258 Results also reported by wound category (clean, potentially contaminated, contaminated, dirty) for both groups
Notes	Funding: NR

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "...eligible patients...were randomly allocated into treatment and control groups" Comment: there are no details on how participants were randomly allocated
Allocation concealment (selection bias)	Unclear risk	Comment: there is no information about allocation concealment

Sindelar 1979 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Comment: there is no mention of blinding
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "All wounds were examined daily by a single observer" Comment: there is no mention of blinding
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: data from all randomised participants are included in the analysis
Selective reporting (reporting bias)	Low risk	Comment: the only outcome of interest was SSI and these data are fully reported
Other bias	Unclear risk	Comment: there is not enough methodological detail to judge

Snow 2016

Methods	2-arm equivalence RCT Setting: single hospital (2 sites) in Australia Follow-up: 6 weeks by phone call and state-wide record searching
Participants	83 adults with intraoperative finding of acutely inflamed appendix undergoing laparoscopy for suspected appendicitis. Mean age 20 years (suction only group) versus 32 years (irrigation and suction group) Inclusion criteria: adult patients (English-speaking), > 18 years, undergoing laparoscopy for clinically or radiologically suspected appendicitis meeting the following intra-operative case definition: "Intra-operative finding of an acutely inflamed appendix, with suppuration or perforation localized to the right iliac fossa, paracolic gutter or pelvis, and when the surgery is completed via a laparoscopic approach." Exclusion criteria: pathology not satisfying the case definition, pregnant, interval appendectomy, appendectomy following percutaneous drainage for abscess, appendectomy for reasons other than appendicitis (for example, tumour)
Interventions	Group I: saline irrigation and suction. Median volume 675 mL (minimum 500 mL); irrigation deployment to contaminated areas at surgeon's discretion (41 participants allocated; 40 received intervention; 40 analysed) Group II: suction only (no irrigation) (42 participants allocated; 41 received intervention; 41 analysed) Cointerventions: all participants were treated with pre-operative, IV, broad-spectrum antibiotics. Continuation post-operatively for purulent or perforated appendicitis, with transition to oral antibiotics recommended for 5 d but at the discretion of the treating surgeon: 17/41 vs 21/40 received these
Outcomes	**Primary outcome: SSI** Group I (saline irrigation): 0/40 Group II (no irrigation): 0/41 **Secondary outcome: length of stay** Group I (saline irrigation): 2.0 (1 - 3)

Snow 2016 *(Continued)*

	Group II (no irrigation): 2.0 (1 - 2.25) **Secondary outcome: adverse events - abscess formation** Group I (saline irrigation): 2/40 Group II (no irrigation): 2/41
Notes	Funding: no funding was received

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Following enrolment, patients underwent simple randomization to either “suction only” (SO) or “irrigation and suction” (IS), with the use of computer-generated random number sequencing." Comment: it appears that an appropriate method was used to generate the randomisation sequence.
Allocation concealment (selection bias)	Low risk	Quote: "Group allocation and data-collection forms were stored in identical, opaque sealed envelopes" Comment: it appears that an appropriate method was used to conceal the allocation sequence.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Comment: personnel (surgeons) were aware of the allocation to intervention groups. It is unclear if participants were also aware of allocation.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote "Data collection was performed by an individual not involved in clinical treatment of enrolled patients." Comment: it appears that blinded outcome assessment was undertaken
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "All enrolled patients were accounted for in follow-up through hospital medical records and searching the statewide admission database" Comment: 1 participant in each group converted to open surgery and therefore did not receive the intended intervention. All other participants were included in the analysis.
Selective reporting (reporting bias)	Low risk	Comment: both primary and secondary outcomes were predefined and appear to be fully reported
Other bias	Low risk	There were no other sources of bias apparent, and reporting was sufficiently detailed to be reasonably confident that this was the case.

St Peter 2012

Methods	2-arm RCT Setting: single study in USA Follow-up: early follow-up by clinic follow-up or phone call at 2-4 weeks
Participants	220 children < 18 years with perforated appendicitis undergoing laparoscopic appendectomy

St Peter 2012 *(Continued)*

	Inclusion criteria: children < 18 years who were found to have perforated appendicitis. Perforation was defined as a hole in the appendix or fecalith in the abdomen Exclusion criteria: NR
Interventions	Group I: saline irrigation, minimum 500 mL volume plus suction, mean volume 867 (327) (110 participants) Group II: no irrigation, suction only (110 participants) Cointerventions: 50 mg/kg dose of ceftriaxone (maximum dose 2 g) and 30 mg/kg dose of metronidazole (maximum dose 1 g) before the operation. Once daily dosing of ceftriaxone and metronidazole continued postoperatively
Outcomes	**Secondary outcome**: **adverse events - abscess formation** Group I (saline irrigation): 20/110 (calculated from 18.3% of 110) Group II (no irrigation): 21/110 (calculated from 19.1% of 110) **Secondary outcome: length of stay** Group I (saline irrigation): 5.4 (2.7) Group II (no irrigation): 5.5 (3.0) **Secondary outcome: readmission** Group I (saline irrigation): 0/110 Group II (no irrigation): 3/110 **Secondary outcome: reoperation** Group I (saline irrigation): 0/110 Group II (no irrigation): 1/110
Notes	Funding: NR

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "A computer-generated individual unit of randomization was utilized in a nonstratified sequence in blocks of 10" Comment: an appropriate method was used to generate the randomisation sequence.
Allocation concealment (selection bias)	Unclear risk	Quote: "After consent for study enrolment was obtained, the randomization sequence was accessed to identify the next allotment. The attending surgeon did not obtain consent and was blind to the allotment throughout the enrolment process." Comment: it seems that allocation concealment was used but procedures are not clear enough to be sure it was adequate.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Comment: no specific quote but it appears that personnel could not be blinded; it is unclear whether participants were blinded.

St Peter 2012 *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: no specific quote; no information on whether outcome assessors were blinded to treatment allocation. It is stated that "Surgeons were not blinded during the postoperative course" but it is unclear if they were performing the outcome assessment.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: all eligible randomised participants were included in the analysis. There were a large number of participants who consented but were excluded because of the intraoperative inclusion criterion. As this was prespecified this is unlikely to be a source of bias.
Selective reporting (reporting bias)	Unclear risk	Quote: "This was a definitive trial design using postoperative abscess as the primary outcome variable." Comment: only the primary outcome was prespecified in the methods so it is difficult to determine if all planned outcomes were fully reported.
Other bias	Unclear risk	Comment: there is no evidence of other sources of bias but the reporting is insufficiently detailed to be certain.

Takesue 2011

Methods	2-arm RCT Setting: a single centre in Japan Follow-up: 3 months post surgery. (After the operation, there was wound inspection daily by nurses, once a week by an infection control nurse and surgeon during hospital stay, and at 4 week and 3 month post operative visits)
Participants	400 participants undergoing elective colorectal surgery for a variety of conditions (e.g. colorectal cancer, ulcerative colitis and Crohn's disease). 37 randomised participants were excluded for protocol violations (e.g. inappropriate bowel preparation, inappropriate antimicrobial prophylaxis, colon was not opened) therefore baseline data include 363 participants. Mean (SD) age: Group I (ESAAS) 51.8 (17.4) years, Group II (saline) 51.9 (17.7) years; diabetes 14/180 vs 13/183; colorectal cancer 82/180 vs 90/183 Inclusion criteria: participants undergoing elective colorectal surgery Exclusion criteria: dirty/infected wound, emergency surgery, laparoscopic surgery, stoma creation without bowel resection, transrectal operation, use of antibiotics within 10 d preceding surgery
Interventions	Group I (ESAAS): the surgical wound was irrigated with at least 500 mL of ESAAS (electrolysed strongly acidic aqueous solution, produced by the electrolysis of tap water containing 0.12% NaCl) after the completion of fascial suture (200 participants, of whom 20 excluded due to protocol violation) Group II (saline): the surgical wound was irrigated with at least 500 mL of saline solution after the completion of fascial suture (200 participants, of whom 17 excluded due to protocol violation) Co-interventions: all participants received Magcorol P (68 g magnesium citrate) for bowel preparation, antimicrobial prophylaxis 30 min before surgery with 1 g of second generation cephalosporins IV. If surgery was > 3 h, these were redosed. The same antibiotics were continued for 24 h after the operation (3-4 doses). Povidone-iodine was used for skin preparation.
Outcomes	**Primary outcome: SSI** Diagnosis based on guidelines issued by the National Nosocomial Infections Surveillance system. Infection had to occur within 30 d of the operation. Group I (ESAAS): 19/180

Takesue 2011 *(Continued)*

	Group II (saline): 29/183 Incisional SSI Group I (ESAAS): 11/180 Group II (saline): 21/183 Organ/space SSI Group I (ESAAS): 8/180 Group II (saline): 8/183 **Primary outcome: wound dehiscence** Superficial wound dehiscence defined as > 1 cm separation of the incision above the fascia with or without infection that required packing and healing by secondary intention. Fascial dehiscence involved disruption of the fascia. (Superficial incisions deliberately opened to treat SSI were excluded.) Group I (ESAAS): 17/180 (15 superficial; 2 fascial) Group II (saline): 12/183 (10 superficial; 2 fascial) **Secondary outcome: antibiotic resistance** MRSA Group I (ESAAS): 4/14 Group II (saline): 8/24 MSSA Group I (ESAAS): 0/14 Group II (saline): 3/24 (other organisms are reported but without sensitivity)
Notes	Funding: none reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Computer generated sequence allocation was used" Comment: approriate methods appear to have been used
Allocation concealment (selection bias)	Low risk	Quote: "concealment was achieved by use of opaque envelopes opened at operating room by a third party" Comment: appropriate steps were taken to conceal allocation with opaque envelopes and third party
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "some surgeons could make the distinction between ESAAS and saline solution during application to the wound" Comment: authors state that personnel were not blinded
Blinding of outcome assessment (detection bias)	Unclear risk	Quote: "the diagnosis of SSI was made by our infection control team" Comment: it is not clear whether personnel knew treatment allocation

Takesue 2011 *(Continued)*
All outcomes

Incomplete outcome data (attrition bias) All outcomes	High risk	Comment: 37/400 randomised participants were excluded at baseline due to protocol violation. This is a large number and it is possibly biased as personnel were not blinded, even though reasons for exclusion appear similar in the 2 treatment groups. No participants were lost to follow-up.
Selective reporting (reporting bias)	Low risk	Comment: all results are reported for the stated outcomes of interest
Other bias	Low risk	Comment: there is no evidence for other sources of bias

Tanaka 2015

Methods	2-arm RCT Setting: single centre in Japan Follow-up: 4 weeks post surgery
Participants	193 participants undergoing elective liver resection surgery (200 randomised, 7 excluded due to complications during surgery). Median age 68.5 years (range 21-87 years), mean age 66.4 (11.2) vs 66.8 (11.3) years. Diabetes mellitus co-morbidity: Group I 24.0%, Group II 19.6%. Hepatocellular carcinoma: Group I 35/96, Group II 37/97. Cholangiocellular carcinoma: Group I 3/96. Group II 2/97. Liver metastases: Group I 45/96, Group II 52/96 Inclusion criteria: elective liver resection without resection/reconstruction of the bile duct or intestine Exclusion criteria: resection/reconstruction of the bile duct and/or intestine, an operation designated Class III or higher according to CDC guidelines, detection of peritoneal dissemination of cancer
Interventions	Group I (lavage): after removal of resected liver and confirmation of haemostasis, irrigation with sterile saline (37° C) directed at the dissected area. 3000 mL was used in open surgery and 1000 mL in laparoscopic surgery (96 participants) Group II (no lavage): no intraoperative lavage performed (97 participants) Co-interventions: prophylactic antibiotic (flomoxef sodium) 1 g IV 30 mins before surgery, 1 g every 3 h during surgery, 1 g 2h after surgery, then 2 g daily for 4 d. A closed suction drain was placed near the transection plane of the liver parenchyma for all participants, and wound washout was performed using sterile saline after fascial closure but before skin closure
Outcomes	**Primary outcome: SSI** Incisional infection (either superficial or deep) or organ/space infection. Incisional infection defined by clinically apparent cellulitis, induration, or purulent discharge from the closure site. Organ/space infection defined by radiologic evidence of a fluid collection necessitating drainage or antibiotic therapy. Total SSI Group I (lavage): 21/96 Group II (no lavage): 13/97 Superficial/deep SSI Group I (lavage): 7/96 Group II (no lavage): 6/97

Tanaka 2015 *(Continued)*

	Organ/space SSI Group I (lavage): 16/96 Group II (no lavage): 7/97 **Secondary outcome: mortality (90 d)** Group I (lavage): 2/96 Group II (no lavage): 1/97 **Secondary outcome: morbidity (post-operative complications)** Group I (lavage): 37/96 Group II (no lavage): 36/97 **Secondary outcome: hospital stay (mean (SD) d)** (median (range) also reported) Group I (lavage): 15.2 (13.4) Group II (no lavage): 15.2 (13.1)
Notes	Funding: NR

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "..simple randomization was carried out by comparing a number within a sealed envelope with numbers in a computer-generated random number table" Comment: use of a random number table
Allocation concealment (selection bias)	Unclear risk	Quote: "...a number within a sealed envelope.." Comment: it appears that steps were taken to conceal allocation in some way, but it is not known if envelopes were opaque and consecutively numbered
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "By its nature this study was unblinded" Comment: no blinding of personnel, appears to state that participants were also unblinded
Blinding of outcome assessment (detection bias) All outcomes	High risk	Quote: "By its nature this study was unblinded" Comment: no blinding of personnel, appears to state that outcome assessors were also unblinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: all participants reported at baseline accounted for in analysis (but 7 excluded during surgery; probably too few to impact analysis
Selective reporting (reporting bias)	Low risk	Comment: all outcomes of interest appear to have been reported for all participants
Other bias	Low risk	Comment: there is no evidence of other sources of bias

Tanphiphat 1978

Methods	3-arm RCT Setting: a single hospital in Thailand Follow-up: minimum 2 weeks post surgery
Participants	374 participants randomised in total, 252 in the 2 arms of interest. Mean age (range): Group I (control) 27 (15-65) years, Group II (Savlon) 24.5 (15-55) years Inclusion criteria: > 15 years of age with acute appendicitis requiring emergency operation Exclusion criteria: known penicillin sensitivity, preoperative antibiotics received, microscopically normal appendices, periappendicitis due to inflammation elsewhere
Interventions	Group I (control): no local treatment during operation (124 participants) Group II (Savlon): each layer was irrigated with 1% solution of cetyl trimethyl ammonium bromide (Savlon) and possibly also chlorhexidine, but this is unclear; and swabbed dry before closure (128 participants) Co-interventions: "The use of peritoneal drainage and postoperative antibiotics was left to the surgeon's discretion" drains were used for 4 participants in group I (control) and 8 in group II (Savlon), all but 1 were for participants with a perforated appendix
Outcomes	**Primary outcome: SSI** "A wound was considered to be infected when there was a collection of pus which emptied itself spontaneously or after incision" Group I (control): 3/108 participants with non-perforated appendix, 9/16 participants with perforated appendix Total 12/124 Group II (Savlon): 5/111 participants with non-perforated appendix, 8/17 participants with perforated appendix Total 13/128
Notes	There is an additional trial arm in which ampicillin powder is applied to wounds. Funding: NR

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Quote: "At operation patients were randomly allocated into three groups by drawing cards" "randomisation may not have been adequate because more perforated appendices were found in the ampicillin group, which suggests that a large number of junior staff on rotation may have disregarded randomisation in what they took (rightly) to be the patient's interest" Comment: it is not clear whether allocation was random, the study authors express doubt
Allocation concealment (selection bias)	High risk	Quote: "At operation patients were randomly allocated into three groups by drawing cards" "randomisation may not have been adequate because more perforated appendices were found in the ampicillin group, which suggests that a large number of junior staff on rotation may have disregarded randomisation in what they took (rightly) to be the patient's interest"

Tanphiphat 1978 *(Continued)*

		Comment: it is not clear whether allocation was random, the study authors express concern
Blinding of participants and personnel (performance bias) All outcomes	High risk	Comment: there is no information about blinding. The participants may have been blinded to treatment, but it is clear the personnel were not.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: there is no information about blinding of outcome assessment
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: all randomised participants are accounted for in the results
Selective reporting (reporting bias)	Unclear risk	Comment: there is not enough information to judge
Other bias	Unclear risk	Comment: there is not enough information to judge

Temizkan 2016

Methods	2-arm RCT Setting: single hospital in Turkey Follow up: NR
Participants	430 women undergoing elective caesarean section. Mean age was 27.7 years (irrigation group) vs 28.2 years (mean number of previous births was 1)39% vs 36% had a comorbidity such as asthma or thyroid dysfunction. Inclusion criteria: women with gestational age > 38 weeks and elective cesarean delivery. Elective caesarean was defined as being performed before the presence of labour with or without previous history of caesarean delivery Exclusion criteria: women with emergency cesarean delivery, chorioamnionitis, type I diabetes, placenta previa, placenta accreta, maternal coagulopathy, or prior severe gastrointestinal disease
Interventions	Group I: saline irrigation of the abdominal cavity using 500 mL of warm normal saline after closure of the uterine incision but before closure of the abdominal wall. All blood clots, vernix, and other debris were evacuated from the paracolic gutters, anterior and posterior cul-de sacs, and under the bladder flap when employed. Group II: no irrigation; all clots, vernix and other debris were left in place. Cointerventions: 5 IU IV bolus of oxytocin over 5–10 s when the umbilical cord was clamped. Then, 30 IU of oxytocin in 500 mL lactated Ringer solution administered at a rate of 125 mL/h, and continued for 4 h. A total of 1 g cefazolin diluted in 20 mL normal saline administered over a 5-min period
Outcomes	**Primary outcome: SSI** (partial or total separation of the incision, as well as the presence of purulent or serous wound discharge with induration, warmth, and tenderness) Group I (saline irrigation): 1/215 Group II (no irrigation): 2/215

Temizkan 2016 *(Continued)*

Notes	Funding: Departmental funds only

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "The participants were randomized to either an irrigation group or a control group. Assignment to one of the two treatment groups was determined using a random number table." Comment: an appropriate method was used to generate the randomisation sequence
Allocation concealment (selection bias)	Low risk	Quote: "The assigned treatments were written on cards and sealed in secure opaque envelopes numbered in sequence." Comment: appropriate measures to ensure allocation concealment appear to have been followed.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "The surgeons were not blinded to the procedure allocation. The allocated envelope was opened by the surgeon just before surgery, and the procedure allocation was recorded on each woman's chart." Comment: personnel were not blinded; unclear if participants were blinded
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quotes: "Postoperative physicians were blinded to group assignment to avoid any potential bias; however, the surgeon who performed the operative procedure cared for the patient in the postoperative period, thus, was not blinded to the study group." "All data were recorded and analyzed by another researcher, who was blinded to the group assignments." Comment: some elements of outcome assessment were undertaken by a blinded assessor but it's not clear whether all assessment was.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: all randomised participants were included in the analysis.
Selective reporting (reporting bias)	Unclear risk	Quote: "The primary outcome measured was the rate of antiemetic drugs required in the postoperative period following cesarean delivery. Secondary outcome measures included the rate of PIM. Other outcomes evaluated were nausea and emesis occurring during the postoperative hospitalization." Comment: additional outcomes to those specified were also reported so it is difficult to determine whether all planned outcomes were assessed and reported.
Other bias	Low risk	Comment: there is no evidence of any other bias and reporting is detailed.

Tighe 1982

Methods	3-arm RCT Setting: a single hospital in Ireland Follow-up: not stated

Tighe 1982 *(Continued)*

Participants	131 participants undergoing appendectomy (age range 3.5-74 years) Inclusion criteria: all participants undergoing appendectomy over a stated time period Exclusion criteria: NR
Interventions	Group I (Betadine): following appendectomy, participants were irrigated with 150 mL 1% Betadine (main constituent povidone iodine) solution intraperitoneally and 50 mL to the wound following closure of the peritoneum (49 participants) Group II (sterile water): participants were irrigated with approximately 150 mL sterile water intraperitoneally and 50 mL to the wound following closure of the peritoneum (31 participants) Group III (no irrigation): no irrigation following appendectomy (51 participants)
Outcomes	**Primary outcome: SSI** "Wound infection was defined as the presence of pus either spontaneously or on probing. All infections were confirmed bacteriologically" There were 17 wound infections among the 131 participants. Results are not given by trial arm. The authors state "when broken down according to type of irrigation, there was no significant difference between the three groups" **Secondary outcome: systemic antibiotic use** 53/131 participants "distributed evenly across the groups" **Secondary outcome: length of hospital stay** Participants with infection: 10 d Participants without infection 6 d Results NR by group
Notes	Results are only provided for the whole group, by appendix histology or for participants with infected wounds vs uninfected, not by treatment group. Funding: NR

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "The randomization took place in theatre following induction of anaesthesia by selecting a disc from a box" Comment: not enough information to judge whether this method was adequate
Allocation concealment (selection bias)	Unclear risk	Quote: "The randomization took place in theatre following induction of anaesthesia by selecting a disc from a box" Comment: not enough information to judge whether this method was adequate
Blinding of participants and personnel (performance bias) All outcomes	High risk	Comment: no information provided about blinding. The participants may have been blinded but personnel would be aware of treatment

Tighe 1982 *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: no information provided about who performed outcome assessment
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Comment: no participants appear to have dropped out of the study
Selective reporting (reporting bias)	High risk	Comment: results are not reported for study arms so there are no data provided to back up authors' claim of no difference between groups.
Other bias	Unclear risk	Comment: not enough information to judge

Trew 2011

Methods	2-arm RCT Setting: 25 centres in Europe Follow-up: 4-16 weeks post surgery (follow-up laparoscopy)
Participants	498 participants randomised, of whom 72 were excluded from study before or during surgery due to failure to meet pre-operative or intra-operative inclusion criteria Inclusion criteria: female, aged 18-45 years, undergoing primary removal of myomas or endometriotic cysts, using adequate contraceptive and not pregnant (negative test and agreement to use adequate contraception) Exclusion criteria (pre-operative): pregnancy, serum glutamic oxaloacetic transaminase, serum glutamic pyruvic transaminase and/or bilirubin > 20% above normal range and considered clinically significant; blood urea nitrogen and creatinine > 30% above normal range and considered clinically significant; systemic corticosteroids, antineoplastic drugs and/or radiation; gonadotropin-releasing hormone agonist/antagonist (except oral contraceptive) in 4 weeks prior to study; active pelvic/abdominal infection; known allergy to starch polymers; known/suspected intolerance to study materials; prior surgery for endometriotic cysts or myomas; non-gynaecological surgical procedure planned during laparoscopic procedure; > 4 myomas, largest myoma < 2 or > 8 cm diameter, or endometriotic cysts < 3 or > 7 cm on pre-operative ultrasound; history of alcohol or other substance abuse within last year; use of another investigational agent; participation in another clinical trial within last 30 d; (at centres in France, diabetes mellitus was also an exclusion criterion) Exclusion criteria (intra-operative and post-operative): clinical evidence of cancer, pregnancy, rectovaginal endometriosis, endometriosis class III or IV other than endometrial cysts (American Fertility Society (AFS) classification), conversion to laparotomy, unplanned surgery involving opening of the bowel (excluding appendectomy), extensive pelvic adhesions (AFS scores moderate or severe), use during procedure of any anti-adhesion agent, use of O_2 enhanced insufflation, adhesions requiring lysing during planned myomectomy or planned endometrial cyst removal (other than those around the ovarian fossa), endometriotic cysts not removed and ovary not left open, suturing the ovarian capsule, pedunculated cysts, use of glue, peritoneum sutured to fascia, use of drains, and post-operative ovarian histology consistent with a non-endometriotic cyst
Interventions	At surgery, the abdomen was washed with warm study solution and this washing/irrigation of the abdominal cavity was repeated/continued with a minimum of 100 mL at intervals of at least once every 30 min. At the end of surgery, after a final irrigation with a minimum of 100 mL and evacuation of intraoperative solution, a final 1000 mL was instilled from a fresh treatment bag. Group I (Adept): study solution was Adept, a 4% icodextrin solution (217 participants) (non-antibacterial)

Trew 2011 *(Continued)*

	Group II (LRS): study solution was lactated Ringer's solution (209 participants) (non-antibacterial) Co-interventions: none specifically mentioned. There was standardised surgical management and all trocar ports ≥ 10 mm were double sutured to the fascia to help minimise any leakage.
Outcomes	**Primary outcome: SSI** 'Wound infection' listed in treatment-related adverse events table VII Group I (Adept): 1/217 Group II (LRS): 1/209 'Wound infection and vomiting' listed in adverse events designated serious table VIII (none deemed treatment-related) Group I (Adept): 2/217 (1 with faecal impaction) Group II (LRS): 0/209 **Secondary outcome: mortality** Mentioned within adverse events section Group I (Adept): 0/217 Group II (LRS): 0/209 **Secondary outcome: adverse events** Group I (Adept): 71/217 of which 18 considered treatment-related Group II (LRS):72/209 of which 15 considered treatment-related
Notes	Outcomes: the objective of the study was to examine the effect of irrigation on adhesion formation hence this was the primary outcome and infection and mortality were only mentioned among adverse events and are reported for the designated safety population Funding: Shire Pharmaceutical Development Ltd was the original study sponsor, providing research funding to all hospital departments involved, and funding was also provided by Baxter BioSurgery (Shire and Baxter are the previous and current distributors of Adept)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Treatment was randomized through a 24-h central randomisation telephone system" "Patients were stratified according to their diagnosis of either myomas or endometriotic cysts and were randomised in a 1:1 ratio to separate randomisation lists" "The system was administered by the study Clinical Research Organisation" Comment: method of sequence generation is not explicitly stated but appropriate service and method for stratification appear to have been used
Allocation concealment (selection bias)	Low risk	Quote: "The system was administered by the study Clinical Research Organisation" "the treatment pack assigned was not permitted for allocation to any other patient in the study" Comment: use of 3rd party and other steps to conceal allocation

Trew 2011 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "Double-blinding was possible as both fluids are clear and odourless solutions with similar viscosities to water and they were packaged identically" Comment: adequate methods used to blind participants and personnel
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: (referring to primary outcome) "Reviewers were blinded to the study treatment assignment" Comment: it appears steps were taken to blind outcome assessors for the primary outcome however blinding is not mentioned for safety assessment (our outcomes of interest)
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Quote: "The safety population consisted of all consenting patients who received randomized treatment" Comment: 72/498 randomised participants were excluded from the study before (27) or during (45) surgery. There does not appear to be any bias in this exclusion but it is possible.
Selective reporting (reporting bias)	Unclear risk	Comment: our primary outcome of interest (infection) is not clearly defined or reported as it not a primary outcome of the study.
Other bias	Unclear risk	Comment: the study was funded by pharmaceutical companies which may have influenced reporting of safety data.

Vallance 1985

Methods	3-arm RCT Setting: 2 hospitals in the UK Follow-up: 3, 7, 10 d, and 1 month post-surgery
Participants	53 participants undergoing operations for generalised purulent or faecal peritonitis. Mean (range) age: Group I 56.1 (10-84) years, Group II 49.7 (10-83) years, Group III 56.0 (18-79) years Inclusion criteria: generalised purulent or faecal peritonitis confirmed at laparotomy Exclusion criteria: NR
Interventions	Following completion of surgical procedure, participants were given a thorough peritoneal toilet and lavage until solutions ran clear with the following protocols: Group I (saline): warm saline solution lavage, with a further 100 mL saline inserted into the abdominal cavity before wound closure (20 participants) Group II (chlorhexidine): warm chlorhexidine gluconate (Hibitane) 1:5000 solution lavage, with 100 mL inserted before wound closure (19 participants) Group III (PVP-I): warm saline solution lavage, with 100 mL PVP-I solution ('Betadine' peritoneal lavage solution) inserted before wound closure (14 participants) Co-interventions: broad spectrum antibiotics (metronidazole and either gentamicin or cefuroxime) were given pre-operatively and continued for at least 5 d postoperatively. Abdominal drains were inserted in all participants as required by the focus of primary sepsis or nature of surgery performed
Outcomes	**Primary outcome: SSI**

Vallance 1985 *(Continued)*

Wound abnormalities indicative of infection presented (can be added as each participants is only counted once)

Pus in wound

Group I (saline): 5/16

Group II (chlorhexidine): 4/16

Group III (PVP-I): 4/13

Sero-sanguinous discharge

Group I (saline): 4/16

Group II (chlorhexidine): 6/16

Group III (PVP-I): 5/13

Inflammation or induration

Group I (saline): 1/16

Group II (chlorhexidine): 2/16

Group III (PVP-I): 2/13

Summed data

Group I (saline):10/16

Group II chlorhexidine): 12/16
Group III: (PVP-I): 11/13

Secondary outcome: mortality

12 participants died, 8 within 4 d of the operation (data below), and 4 died 8-52 d postoperatively but group assignment was not reported. Authors state "all deaths were due either to the severity of the presenting disease or co-existing complicating conditions"

Mortality (within 4 d of surgery)

Group I (saline): 4/20

Group II (chlorhexidine): 3/19

Group III (PVP-I): 1/14

Secondary outcome: length of hospital stay

Mean (SD) d (unclear on numbers of participants in groups (see mortality) 41 survivors included in total)

Group I (saline): 11.4 (4.4)

Group II (chlorhexidine): 9.3 (4.3)

Group III (PVP-I): 12.6 (3.8)

Notes	Funding: NR

Risk of bias

Bias	Authors' judgement	Support for judgement

Vallance 1985 *(Continued)*

Random sequence generation (selection bias)	Unclear risk	Quote "Patients were randomized to receive..." Comment: no details about method of randomisation
Allocation concealment (selection bias)	Unclear risk	Comment: no information in report
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Comment: no information in report
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: no information in report
Incomplete outcome data (attrition bias) All outcomes	High risk	Comment: 12/53 participants died, thus removing some outcome data e.g. length of hospital stay. Causes of death were reported and there was no attrition for other reasons.
Selective reporting (reporting bias)	High risk	Comment: details of deaths are provided but it is not reported which groups some of these participants were assigned to. Outcomes are not fully reported and may have been selectively reported.
Other bias	High risk	Quote: "the random allocation of patients to the different lavage groups resulted in an uneven distribution of the causes of peritonitis between the groups" Comment: due to small numbers of participants and broad inclusion criteria the groups may be too different to demonstrate a treatment effect.

Viney 2012

Methods	Parallel-group RCT Single hospital in the USA Follow-up: NR
Participants	236 women undergoing caesarean section Inclusion criteria: "pregnant English-speaking women, ≥ 18 years, presenting for labour or scheduled cesarean delivery Exclusion criteria: "declining consent or urgent and emergent clinical situations in which the staff caring for the patient determined the time required for the consent process could adversely affect the potential participant's clinical care"
Interventions	Group I: lavage with 500-1000 mL warm saline after closure of the hysterotomy, but before the closure of the abdominal wall (110 participants) Group II: no lavage (126 participants) Cointerventions: blood clots and other debris manually evacuated. 1 g cefazolin IV as antibiotic prophylaxis before the start of surgery. Participants with cefazolin allergy received 900 mg clindamycin.
Outcomes	**Secondary outcome: length of stay** (reported as day of discharge) Group I (saline lavage): 3 d

Viney 2012 *(Continued)*

	Group II (no lavage): 3 d
Notes	Funding: NR

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Assignment was performed by opening a sequentially numbered opaque envelope containing computer-randomized individual allocations" Comment: appropriate method of sequence generation reported
Allocation concealment (selection bias)	Low risk	Quote: "Assignment was performed by opening a sequentially numbered opaque envelope containing computer-randomized individual allocations" Comment: appropriate method of allocation concealment reported
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "The original randomization was performed by research staff before the initiation of the study using a random number table generator, and the participants were blinded to treatment once assigned." "The envelope was opened by the circulation nurse in the operating room and silently viewed by the surgeons after closure of the hysterotomy." Comment: participants were blinded to the treatment allocation but personnel were not.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Quote: "This was recorded by nursing staff not blinded to the randomization....Postoperative nursing staff were blinded to group assignment to avoid any potential bias; however, the surgeon who performed the operative procedure cared for the patient in the postoperative period and, thus, was not blinded to the study group". Comment: some outcome assessors were not blinded.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: all randomised participants were included in the analysis.
Selective reporting (reporting bias)	Unclear risk	Comment: outcomes assessed were clearly prespecified and mostly fully reported but measures of variance were not given for some outcomes.
Other bias	Unclear risk	Quote "Our study was stopped halfway through to allow for planned midpoint data analysis for resident research day" Comment: unclear if the study was stopped early and if so whether this was on the basis of a specific stopping rule. No evidence of other sources of bias and reporting sufficient to be reasonably confident of this.

BMI: body mass index; CABG: coronary artery bypass graft; CDC: Centers for Disease Control and Prevention; CSF: cerebrospinal fluid; ITT: intention-to-treat; IM: intramuscular; IV: intravenous; MRI: magnetic resonance imaging; MRSA: methicillin-resistant *Staphylococcus aureus*; MSSA: methicillin-susceptible *Staphylococcus aureus*; NR: not reported; PP: per-protocol; PVP: polyvinyl pyrrolidine; RCT: randomised controlled trial; SSI: surgical site infection

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Akay 2006	Different indication: healing by delayed primary or secondary intention in some or all participants
Al-Ramahi 2006	Quasi-randomised RCT
Alcantara 2011	Use of peri-operative irrigation/lavage was not the only systematic difference between the groups
Anglen 2005	Different indication: healing by delayed primary or secondary intention in some or all participants
Angobaldo 2008	Different indication: healing by delayed primary or secondary intention in some or all participants
Badia 1994	Use of peri-operative irrigation/lavage was not the only systematic difference between the groups
Bennett-Guerrero 2016	Use of peri-operative irrigation/lavage was not the only systematic difference between the groups
Bertheussen 1980	Quasi-randomised RCT
Bhargava 2006	Quasi-randomised RCT
Boothby 1984	Use of peri-operative irrigation/lavage was not the only systematic difference between the groups
Cherian 2000	Different indication: used for anaesthesia purposes
Chisholm 1992	Ineligible population: some or all participants did not undergo surgery
Donnenfeld 1986	Use of peri-operative irrigation/lavage was not the only systematic difference between the groups
Ducharme 1986	Use of peri-operative irrigation/lavage was not the only systematic difference between the groups
Dwivedi 2009	Ineligible intervention: extremely small volume of liquid
Everett 1969	Different intervention: lavage was not the intervention of interest
FLOW 2011	Different indication: healing by delayed primary or secondary intention in some or all participants
Fountas 1999	Use of peri-operative irrigation/lavage was not the only systematic difference between the groups
Freischlag 1984	Use of peri-operative irrigation/lavage was not the only systematic difference between the groups
Galle 1980	Different indication: healing by delayed primary or secondary intention in some or all participants
Garg 2013	Ineligible intervention: differences in lavage procedure were not the only difference between the groups
Georgiadis 2013	Different indication: used for anaesthesia purposes
Geraghty 1984	Quasi-randomised RCT
Ghafouri 2016a	Ineligible population: some or all participants did not undergo surgery
Ghafouri 2016b	Ineligible population: some or all participants did not undergo surgery
Givens 2002	Different indication: used for anaesthesia purposes
Gonen 1986	Use of peri-operative irrigation/lavage was not the only systematic difference between the groups

Study	Reason for exclusion
Granick 2007	Ineligible population: some or all participants did not undergo surgery
Hesami 2014	Ineligible indication: healing by delayed primary or secondary intention in some or all participants
Horn 1999	Different indication: used for anaesthesia purposes
Hunt 1982	Ineligible indication: healing by delayed primary or secondary intention in some or all participants
Iqbal 1998	Quasi-randomised RCT
Iqbal 2015	Ineligible intervention: extremely small volume of liquid
Keblawi 2006	Different indication; study author contact confirmed that no relevant outcome data were collected and purpose of study was to evaluate pain and WBC
Kellum 1985	Quasi-randomised RCT
Ko 1992	Quasi-randomised RCT
Kothuis 1981	Use of peri-operative irrigation/lavage was not the only systematic difference between the groups
Lau 1986	Ineligible intervention: extremely small volume of liquid
Lavery 1986	Use of peri-operative irrigation/lavage was not the only systematic difference between the groups
Logan 1973	Ineligible intervention: extremely small volume of liquid
Longmire 1987	Ineligible population: some or all participants did not undergo surgery
Makvandi 2014	Quasi-randomised RCT
Martins 2012	Ineligible indication: healing by delayed primary or secondary intention in some or all participants
Mathelier 1992	Use of peri-operative irrigation/lavage was not the only systematic difference between the groups
Mohamed 2017	Different indication: used for anaesthesia purposes
Morse 1998	Ineligible population: some or all participants did not undergo surgery
Nachamie 1968	Quasi-randomised RCT
Nomikos 1986	Quasi-randomised RCT
Noon 1967	Quasi-randomised RCT
Pitt 1982	Use of peri-operative irrigation/lavage was not the difference between the groups
Plaumann 1985	Ineligible indication: healing by delayed primary or secondary intention in some or all participants
Pobereskin 2000	Different indication: used for anaesthesia purposes
Pollock 1978	Use of peri-operative irrigation/lavage was not the only systematic difference between the groups
Rogers 1983	Quasi-randomised RCT

Study	Reason for exclusion
Rosen 1985	Ineligible population: some or all participants did not undergo surgery
Salvati 1988	Quasi-randomised RCT
Sarr 1988	Use of peri-operative irrigation/lavage was not the only systematic difference between the groups
Sarzaeem 2014	Different indication: used for anaesthesia purposes
Sauven 1986	Use of peri-operative irrigation/lavage was not the only systematic difference between the groups
Scammell 1985	Ineligible indication: healing by delayed primary or secondary intention in some or all participants
Scheuerlein 2000	Use of peri-operative irrigation/lavage was not the only systematic difference between the groups
Seco 1990	Ineligible intervention: extremely small volume of liquid
Shapiro 1986	Use of peri-operative irrigation/lavage was not the only systematic difference between the groups
Sherman 1976	Ineligible indication: healing by delayed primary or secondary intention in some or all participants
Sindelar 1985	Ineligible indication: healing by delayed primary or secondary intention in some or all participants
Sood 1985	Quasi-randomised RCT
Terzi 2015	Quasi-randomised RCT
Toki 1995	Use of peri-operative irrigation/lavage was not the only systematic difference between the groups
Weiss 2013	Ineligible population: some or all participants did not undergo surgery
White 2008	Use of peri-operative irrigation/lavage was not the only systematic difference between the groups
Wu 1992	Quasi-randomised RCT
Xiao 2010	Use of peri-operative irrigation/lavage was not the only systematic difference between the groups
Yarussi 1999	Different indication: used for anaesthesia purposes

RCT: randomised controlled trial; WBC: white blood count

Characteristics of studies awaiting assessment *[ordered by study ID]*

De Cicco 2015

Methods	2-arm RCT
Participants	20 women undergoing surgery for endometriosis
Interventions	Group I: lavage performed routinely Group II: lavage performed until liquid was clear
Outcomes	Primary outcome: C-reactive protein concentration White blood cell count

De Cicco 2015 *(Continued)*

	Temperature
	Complications
Notes	We have contacted study author who confirms relevant outcome data were collected; these are currently unpublished although a publication is being prepared. Study author unable to supply data in advance of publication

De Kok 1998

Methods	2-arm RCT
Participants	80 people receiving knee or hip replacement surgery
Interventions	Group I: iodophore irrigation of wound during surgery (40 participants) Group II: physiologic salt solution irrigation of wound during surgery (40 participants)
Outcomes	Primary outcome: contamination of suction device used during surgery Group I: 13/40 Group II: 14/40
Notes	2 records for this study; one in Dutch. Notes from translator on methodology, "The authors say it is randomised, however there is no description as to how this was done and the allocation is not reported" "Very low quality, bad methodology, baseline not clearly described" Unclear whether any relevant outcomes were collected. Unable to contact study author to date

Kosuş 2010

Methods	2-arm RCT Setting: "private hospital" in Turkey Follow-up: 40 d Duration of study: 2004-2007
Participants	1272 women undergoing cesarean section Loss to follow-up: 17 participants were lost from follow-up Age range: 23.1-33.7 years Inclusion criteria: women undergoing cesarean section Exclusion criteria: coincident remote site infections or colonisation, diabetes, cigarette smoking, systemic steroid use, obesity (> 20% ideal body weight), excessive subcutaneous scar tissue due to previous operations, perioperative transfusion of blood products and altered immune response were excluded from the study (33 women). Operation time, > 2 h or blood loss > 1 L or having premature rupture of membrane > 6 hs were discharged from the study (26 women)
Interventions	Group I: povidone-iodine 10% was used for preoperative antisepsis of skin and after closure of skin (600 participants)

Kosuş 2010 *(Continued)*

	Group II: povidone-iodine was used in the same way but also subcutaneous tissue was irrigated with rifamycin SV/ 250 mg, before closure of subcutaneous tissue (596 participants) Amount of irrigation fluid: not stated Cointervention: single dose of 1 g ceftriaxone was given to all participants for prophylaxis in peri-operative period after clamping of umbilical cord
Outcomes	Primary outcome: SSI Group I: 12/600. All of them were superficial incisional SSI Group II: 0/596 Secondary outcome: cost [costs were given in dollars, we have assumed these to be USD] Group I: total cost of 12 participants with SSI was USD 5386 Group II: total cost of the rifamycin SV used for washing of subcutaneous tissue was USD 876.12 P value: not stated for cost alone When groups were compared, surgical site infection and cost were significantly lower in study group (P <0.05)
Notes	Funding: not stated Not clear whether randomisation was adequate. Study author contact attempted but so far unsuccessful

Munoz-Mahamud 2011

Methods	2-arm RCT Setting: appears to be single hospital in Spain Follow-up: 1 year
Participants	79 Participants with orthopaedic (hip and knee) implant infection undergoing surgery for the infection
Interventions	Group I: low-pressure pulsatile lavage Group II: high-pressure pulsatile lavage Cointerventions: after open debridement, a broad-spectrum intravenous antimicrobial regimen was started and maintained until obtaining definitive microbiological results. The definitive oral antibiotic treatment was selected according to the antibiogram. The duration of intravenous and oral antibiotics was not standardised and this was decided according to the clinical manifestations and the C-reactive protein values of each case
Outcomes	Remission of infection; relapse of infection; retention of prosthesis; reinfection; success rate
Notes	The source of funding did not play any role in the investigation. Unclear whether any relevant outcomes were reported. Study author contact attempted but so far unsuccessful.

Taylor 1999

Methods	2-arm RCT

Taylor 1999 *(Continued)*

	Setting: single UK hospital
	Follow-up: none reported
Participants	44 participants undergoing hip fracture fixation
	Inclusion and exclusion criteria not reported
Interventions	Group I: 0.05% chlorhexidine jet lavage (number of participants not reported)
	Group II: no intervention (number of participants not reported)
	Co-interventions: not reported
Outcomes	Air bacterial counts and mean operating times
Notes	Unclear whether any relevant outcomes were reported. Unable to contact study author to date
	No funding reported

RCT: randomised controlled trial

Characteristics of ongoing studies *[ordered by study ID]*

ACTRN12610000423011

Trial name or title	Does Peritoneal lavage influence the rate of complications in paediatric laparoscopic appendicectomy? A prospective randomised clinical trial
Methods	Parallel-group (2-arm) RCT
Participants	Children with perforated appendicitis
Interventions	Peritoneal lavage with 0.9% saline then suction
	No lavage (suction only)
Outcomes	Length of hospital stay in days, including any days of re-admission
	Intra-abdominal abscess
Starting date	20 May 2010
Contact information	Charles Keys
	Department of Paediatric Surgery
	Southern Health
	Monash Medical Centre
	246 Clayton Road
	Clayton
	Vic 3168
	Australia
Notes	No updates registered

NCT01175044

Trial name or title	Dilute Betadine lavage in the prevention of postoperative infection
Methods	Parallel-group (2-arm) RCT
Participants	People who are scheduled to undergo a revision total knee arthroplasty
Interventions	Betadine lavage: dilute Betadine lavage prior to surgical closure for 3 min followed by 2000 mL of sterile saline irrigation Saline lavage: (2000 mL) prior to closure
Outcomes	Infection
Starting date	2 August 2010
Contact information	Darren R Plummer, BBA, MBA; darren.plummer@rushortho.com Rush University Medical Center Chicago, Illinois, United States, 60612
Notes	Currently recruiting

NCT02186457

Trial name or title	Antibiotic irrigation for pancreatoduodenectomy
Methods	Parallel-group (2-arm) RCT
Participants	Adults undergoing pancreatoduodenectomy (Whipple procedure)
Interventions	Antibiotic irrigation via peritoneal lavage (polymyxin B (500,000 U) in 1 L of 0.9% normal saline) Placebo irrigation via peritoneal lavage (0.9 % normal saline)
Outcomes	Infections Fistulas
Starting date	1 July 2014
Contact information	Michael G. House, Associate Professor of Surgery, Indiana University Indianapolis, Indiana, United States, 46202 michouse@iupui.edu
Notes	Recruiting

NCT02395614

Trial name or title	Incidence of surgical site infection after irrigation of surgical pocket with 0.05% chlorhexidine compared with triple antibiotic solution in post-mastectomy breast reconstruction
Methods	Intra-individual (split-body) (2-arm) RCT
Participants	Women with breast cancer undergoing bilateral breast reconstruction
Interventions	0.05% chlorhexidine solution (IrriSept®) commercially prepared in 450 mL bottles Triple antibiotic solution will contain 1 g of cefazolin, 50,000 U of bacitracin, and 80 mg of gentamicin in 500 mL of normal saline Each participant will receive triple antibiotic solution on one breast and the chlorhexidine on the other breast
Outcomes	Surgical site infection
Starting date	17 March 2015
Contact information	Kent Higdon, MD 615-936-0160 kent.higdon@vanderbilt.edu Vanderbilt University Medical Center Nashville, Tennessee, United States, 37232
Notes	Recruiting

NCT02527512

Trial name or title	Bacterial contamination: iodine vs saline irrigation in pediatric spine surgery
Methods	Parallel (2-arm) RCT
Participants	Children aged 3-18 years undergoing surgery for diagnosis of spinal deformity
Interventions	Povidone-iodine - 0.35% povidone-iodine (Betadine) Normal saline - sterile sodium chloride (NaCl) solution
Outcomes	Postoperative infection
Starting date	7 August 2015 (received), anticipated start date February 2017
Contact information	Principal investigator: Michael Glotzbecker, MD; Boston Children's Hospital
Notes	Not yet open to recruitment

NCT02714023

Trial name or title	Water and saline head-to-head in the blinded evaluation study trial (WASHITBEST)
Methods	Parallel-group (2-arm) RCT

NCT02714023 *(Continued)*

Participants	Participants diagnosed with acute appendicitis aged at least 6 years
Interventions	Irrigation of the abdomen during surgery with normal saline Irrigation of the abdomen during surgery with sterile water
Outcomes	Postoperative deep space organ infection as defined by the Surgical Infection Society (time frame: 30 d) Infection after surgery within the peritoneal space Temperature > 38.5° C (time frame: 30 d) > 2 d to return of bowel function as evident by either flatus or bowel movement (time frame: 30 d) Length of hospital stay (time frame: 30 d)
Starting date	8 March 2016 (information received). Study start date April 2013
Contact information	Arthur Rawlings, MD University of Missouri-Columbia
Notes	Completed

RCT: randomised controlled trial

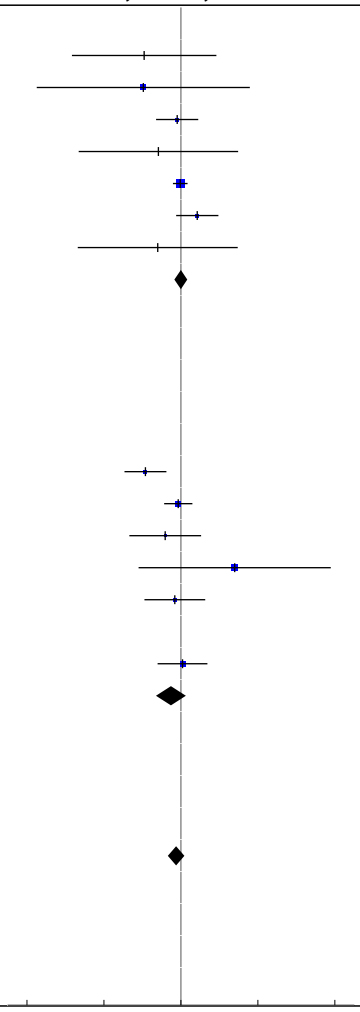
DATA AND ANALYSES

Comparison 1. All irrigation versus no irrigation

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 SSI	14	6106	Risk Ratio (M-H, Random, 95% CI)	0.87 [0.68, 1.11]
1.1 clean or clean-contaminated	7	4801	Risk Ratio (M-H, Random, 95% CI)	1.00 [0.82, 1.21]
1.2 contaminated or dirty	7	1305	Risk Ratio (M-H, Random, 95% CI)	0.74 [0.47, 1.16]
2 Adverse events	3	403	Risk Ratio (M-H, Random, 95% CI)	1.05 [0.76, 1.44]
3 Abscess	3	331	Risk Ratio (M-H, Random, 95% CI)	0.91 [0.54, 1.54]
4 Mortality	2	280	Risk Ratio (M-H, Random, 95% CI)	0.86 [0.36, 2.04]
5 Hospital stay	7	1597	Mean Difference (IV, Random, 95% CI)	-0.13 [-0.38, 0.12]
6 Return to theatre (reoperation)	2	3247	Risk Ratio (M-H, Random, 95% CI)	0.72 [0.28, 1.84]
7 Readmission to hospital	2	3247	Risk Ratio (M-H, Random, 95% CI)	0.70 [0.10, 4.90]

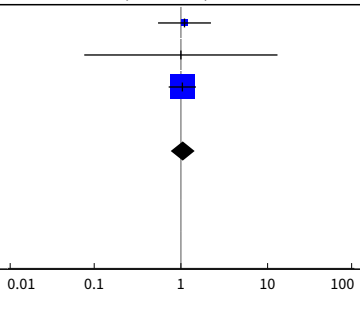
Analysis 1.1. Comparison 1 All irrigation versus no irrigation, Outcome 1 SSI.

Study or subgroup	Irrigation n/N	No irrigation n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
1.1.1 clean or clean-contaminated					
Cho 2004	1/17	3/17		1.26%	0.33[0.04,2.89]
Elliott 1986	0/80	1/78		0.59%	0.33[0.01,7.86]
Gungorduk 2010	17/260	19/260		10.61%	0.89[0.48,1.68]
Harrigill 2003	1/97	2/99		1.04%	0.51[0.05,5.54]
Mahomed 2016	144/1634	147/1636		27.19%	0.98[0.79,1.22]
Tanaka 2015	21/96	13/97		10.6%	1.63[0.87,3.07]
Temizkan 2016	1/215	2/215		1.03%	0.5[0.05,5.47]
Subtotal (95% CI)	**2399**	**2402**		**52.32%**	**1[0.82,1.21]**
Total events: 185 (Irrigation), 187 (No irrigation)					
Heterogeneity: Tau^2=0; Chi^2=4.57, df=6(P=0.6); I^2=0%					
Test for overall effect: Z=0.01(P=0.99)					
1.1.2 contaminated or dirty					
Cervantes-Sanchez 2000	11/127	39/156		10.71%	0.35[0.19,0.65]
De Jong 1982	36/279	39/279		17.23%	0.92[0.61,1.41]
Oleson 1980	5/20	4/10		4.59%	0.63[0.21,1.83]
Ozlem 2015	2/7	0/7		0.72%	5[0.28,88.53]
Schein 1990	10/58	6/29		6.08%	0.83[0.34,2.07]
Snow 2016	0/40	0/41			Not estimable
Tanphiphat 1978	13/128	12/124		8.34%	1.05[0.5,2.21]
Subtotal (95% CI)	**659**	**646**		**47.68%**	**0.74[0.47,1.16]**
Total events: 77 (Irrigation), 100 (No irrigation)					
Heterogeneity: Tau^2=0.13; Chi^2=9.41, df=5(P=0.09); I^2=46.84%					
Test for overall effect: Z=1.3(P=0.19)					
Total (95% CI)	**3058**	**3048**		**100%**	**0.87[0.68,1.11]**
Total events: 262 (Irrigation), 287 (No irrigation)					
Heterogeneity: Tau^2=0.05; Chi^2=16.58, df=12(P=0.17); I^2=27.61%					
Test for overall effect: Z=1.14(P=0.25)					
Test for subgroup differences: Chi^2=1.41, df=1 (P=0.24), I^2=29.09%					

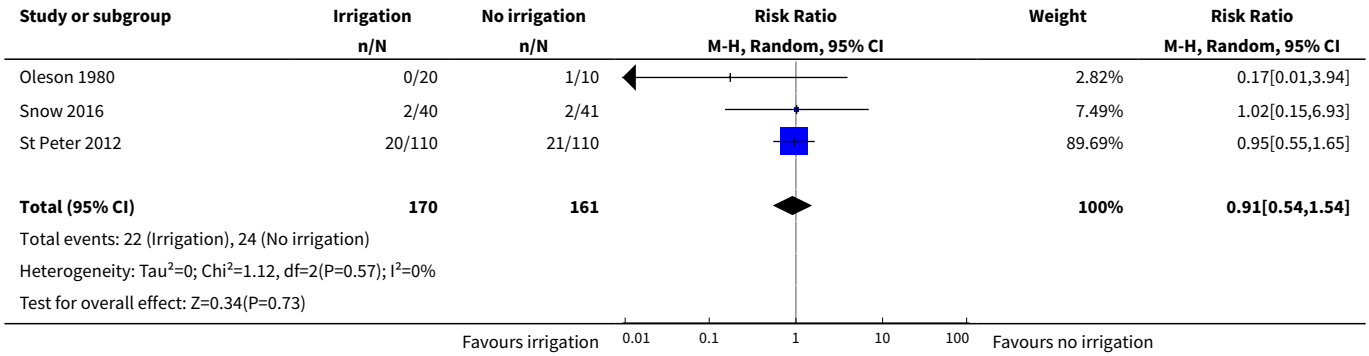


Analysis 1.2. Comparison 1 All irrigation versus no irrigation, Outcome 2 Adverse events.

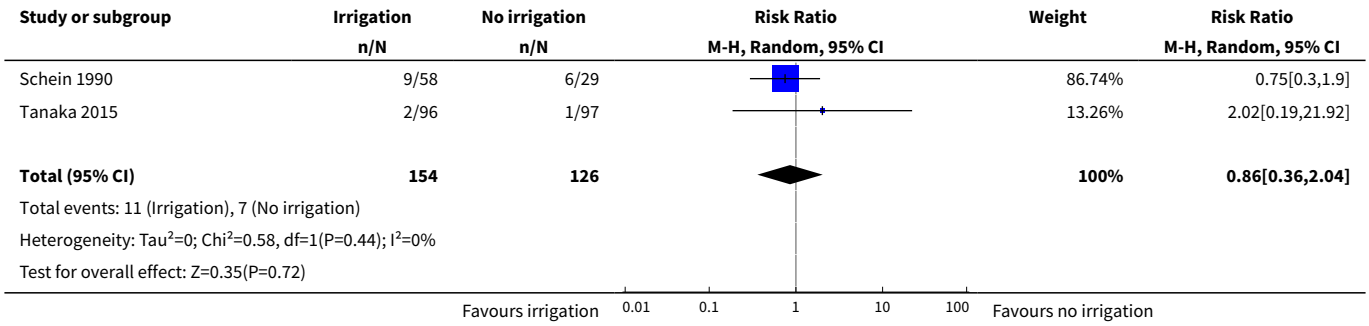
Study or subgroup	Irrigation n/N	No irrigation n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
Harrigill 2003	14/97	13/99		20.71%	1.1[0.55,2.22]
Ozlem 2015	1/7	1/7		1.55%	1[0.08,13.02]
Tanaka 2015	37/96	36/97		77.75%	1.04[0.72,1.49]
Total (95% CI)	**200**	**203**		**100%**	**1.05[0.76,1.44]**
Total events: 52 (Irrigation), 50 (No irrigation)					
Heterogeneity: Tau^2=0; Chi^2=0.02, df=2(P=0.99); I^2=0%					
Test for overall effect: Z=0.3(P=0.76)					



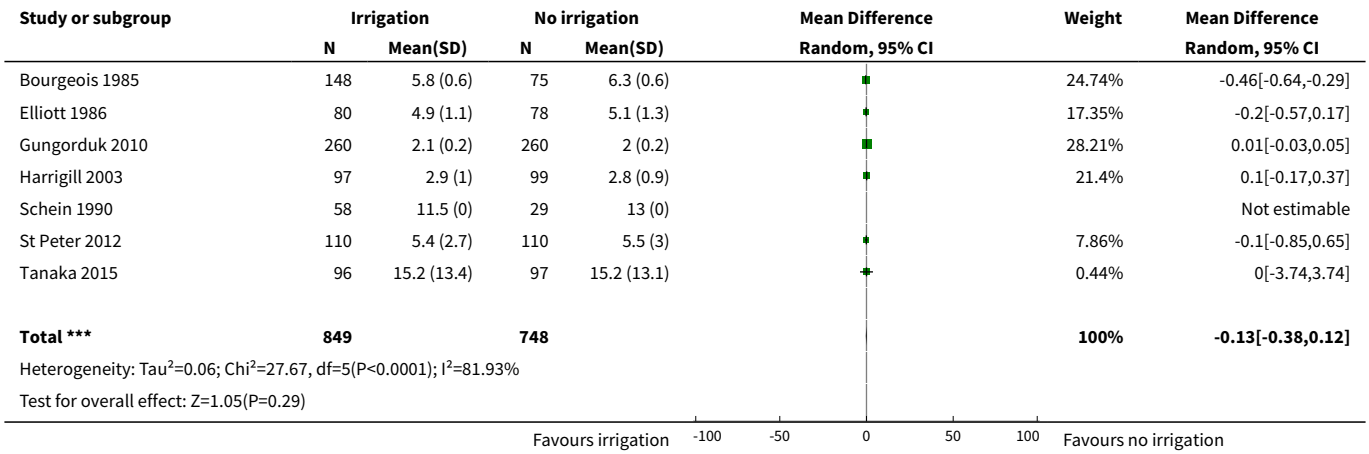
Analysis 1.3. Comparison 1 All irrigation versus no irrigation, Outcome 3 Abscess.



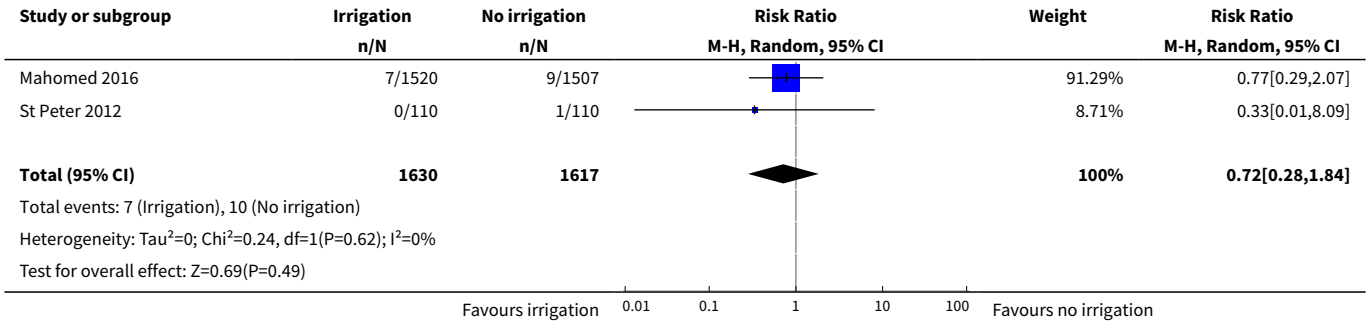
Analysis 1.4. Comparison 1 All irrigation versus no irrigation, Outcome 4 Mortality.



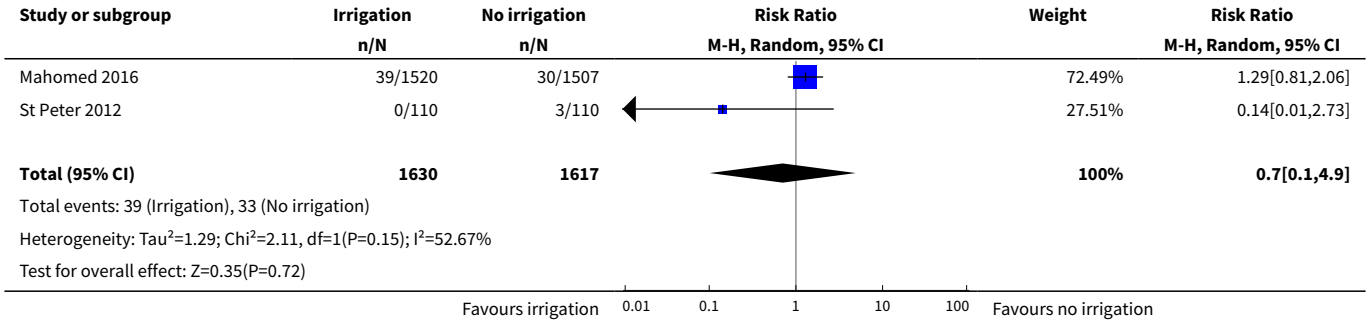
Analysis 1.5. Comparison 1 All irrigation versus no irrigation, Outcome 5 Hospital stay.



Analysis 1.6. Comparison 1 All irrigation versus no irrigation, Outcome 6 Return to theatre (reoperation).



Analysis 1.7. Comparison 1 All irrigation versus no irrigation, Outcome 7 Readmission to hospital.



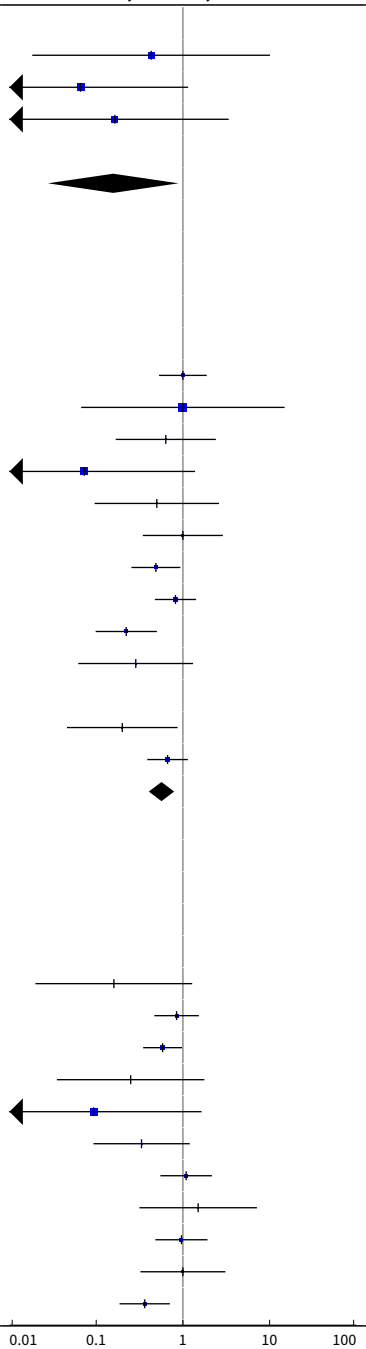
Comparison 2. Antibacterial irrigation versus non-antibacterial irrigation

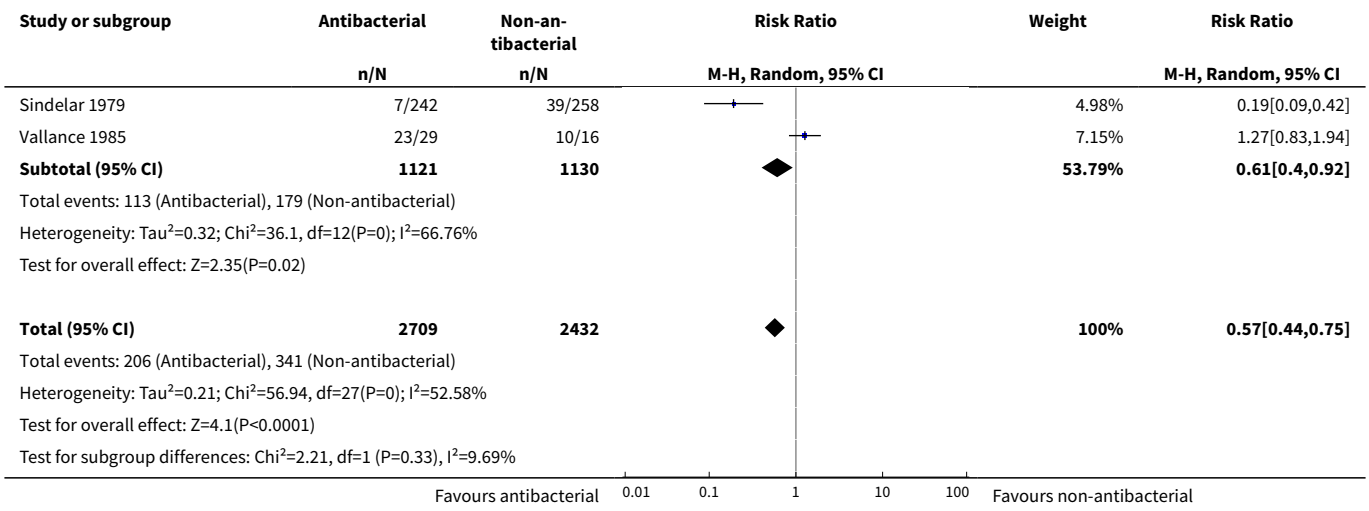
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 SSI	30	5141	Risk Ratio (M-H, Random, 95% CI)	0.57 [0.44, 0.75]
1.1 clean	4	680	Risk Ratio (M-H, Random, 95% CI)	0.16 [0.03, 0.89]
1.2 clean-contaminated	13	2210	Risk Ratio (M-H, Random, 95% CI)	0.57 [0.40, 0.79]
1.3 contaminated or dirty	13	2251	Risk Ratio (M-H, Random, 95% CI)	0.61 [0.40, 0.92]
2 Wound dehiscence	3	660	Risk Ratio (M-H, Random, 95% CI)	1.26 [0.65, 2.45]
3 Adverse events	3	178	Risk Ratio (M-H, Random, 95% CI)	0.55 [0.22, 1.34]
4 Abscess	9	1309	Risk Ratio (M-H, Random, 95% CI)	0.82 [0.42, 1.62]
5 Mortality	11	1121	Risk Ratio (M-H, Random, 95% CI)	0.81 [0.48, 1.36]
6 Hospital stay	7	635	Mean Difference (IV, Random, 95% CI)	-0.85 [-1.60, -0.09]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
7 Return to theatre (re-operation)	2	403	Risk Ratio (M-H, Random, 95% CI)	1.26 [0.12, 13.60]

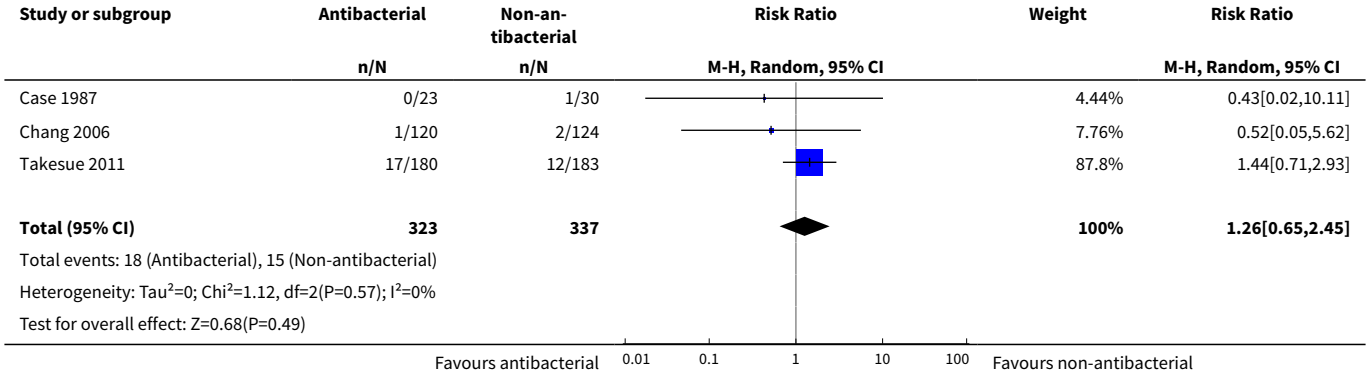
Analysis 2.1. Comparison 2 Antibacterial irrigation versus non-antibacterial irrigation, Outcome 1 SSI.

Study or subgroup	Antibacterial n/N	Non-antibacterial n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
2.1.1 clean					
Case 1987	0/23	1/30		0.67%	0.43[0.02,10.11]
Cheng 2005	0/208	7/206		0.8%	0.07[0,1.15]
Kokavec 2008	0/89	2/73		0.72%	0.16[0.01,3.37]
Oller 2015	0/34	0/17			Not estimable
Subtotal (95% CI)	**354**	**326**		**2.18%**	**0.16[0.03,0.89]**
Total events: 0 (Antibacterial), 10 (Non-antibacterial)					
Heterogeneity: Tau^2=0; Chi^2=0.79, df=2(P=0.67); I^2=0%					
Test for overall effect: Z=2.09(P=0.04)					
2.1.2 clean-contaminated					
Baker 1994	17/150	17/150		5.86%	1[0.53,1.88]
Carl 2000	1/20	1/20		0.88%	1[0.07,14.9]
Dashow 1986	7/283	3/77		2.77%	0.63[0.17,2.4]
Levin 1983	0/85	3/43		0.76%	0.07[0,1.38]
Magann 1993	2/50	4/50		2.02%	0.5[0.1,2.61]
Mirsharifi 2008	6/51	6/51		3.67%	1[0.35,2.89]
Moylan 1968	12/124	23/116		5.75%	0.49[0.25,0.94]
Neeff 2016	19/101	22/96		6.39%	0.82[0.48,1.42]
Ruiz-Tovar 2011	6/64	27/64		4.83%	0.22[0.1,0.5]
Ruiz-Tovar 2012	2/54	7/54		2.28%	0.29[0.06,1.31]
Ruiz-Tovar 2013	0/20	0/20			Not estimable
Ruiz-Tovar 2016a	2/52	10/52		2.41%	0.2[0.05,0.87]
Takesue 2011	19/180	29/183		6.43%	0.67[0.39,1.14]
Subtotal (95% CI)	**1234**	**976**		**44.03%**	**0.57[0.4,0.79]**
Total events: 93 (Antibacterial), 152 (Non-antibacterial)					
Heterogeneity: Tau^2=0.1; Chi^2=16.37, df=11(P=0.13); I^2=32.82%					
Test for overall effect: Z=3.31(P=0)					
2.1.3 contaminated or dirty					
Al-Shehri 1994	1/120	7/134		1.39%	0.16[0.02,1.28]
Greig 1987	15/64	18/65		6.11%	0.85[0.47,1.53]
Halsall 1981	18/99	29/93		6.58%	0.58[0.35,0.98]
Kubota 1999	1/8	4/8		1.54%	0.25[0.04,1.77]
Kubota 2015	0/24	4/20		0.79%	0.09[0.01,1.64]
Lord 1983	3/100	9/100		2.92%	0.33[0.09,1.2]
Oestreicher 1989	16/267	15/273		5.55%	1.09[0.55,2.16]
Oleson 1980	3/10	2/10		2.2%	1.5[0.32,7.14]
Rambo 1972	11/44	13/50		5.5%	0.96[0.48,1.92]
Schein 1990	5/29	5/29		3.42%	1[0.32,3.09]
Silverman 1986	10/85	24/74		5.64%	0.36[0.19,0.71]

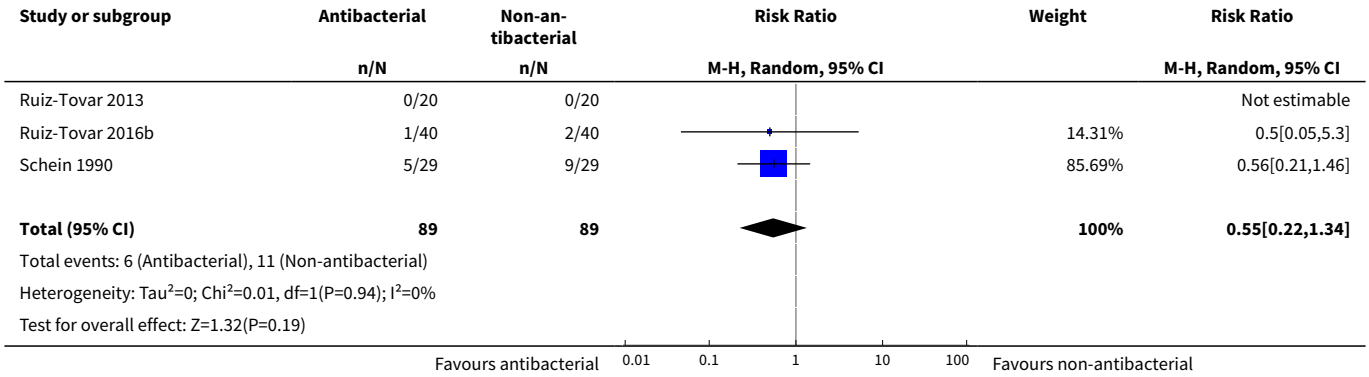




Analysis 2.2. Comparison 2 Antibacterial irrigation versus non-antibacterial irrigation, Outcome 2 Wound dehiscence.



Analysis 2.3. Comparison 2 Antibacterial irrigation versus non-antibacterial irrigation, Outcome 3 Adverse events.



Analysis 2.4. Comparison 2 Antibacterial irrigation versus non-antibacterial irrigation, Outcome 4 Abscess.

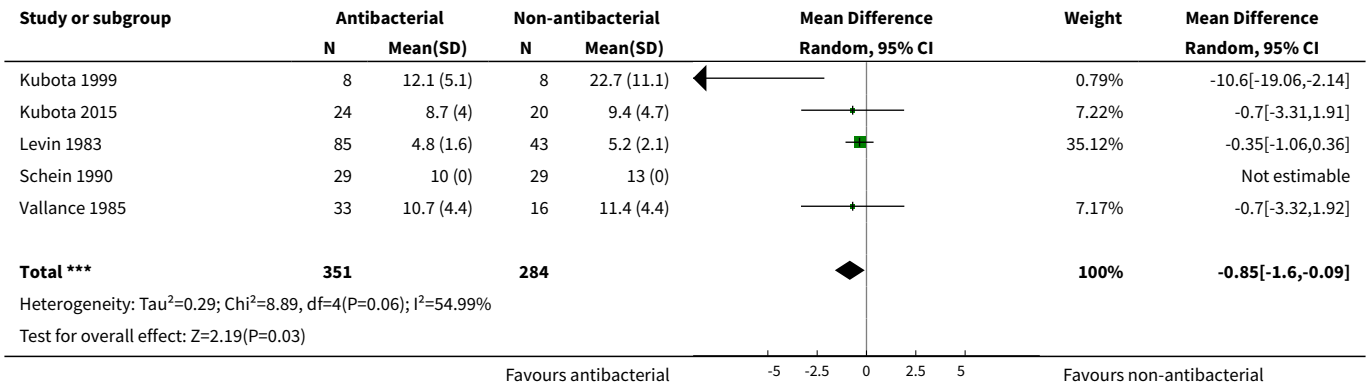
Study or subgroup	Antibacterial n/N	Non-antibacterial n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
Al-Shehri 1994	0/117	0/132			Not estimable
Baker 1994	2/150	1/150		7.94%	2[0.18,21.82]
Dashow 1986	0/283	0/77			Not estimable
Kubota 1999	0/8	1/8		4.83%	0.33[0.02,7.14]
Kubota 2015	1/24	1/20		6.18%	0.83[0.06,12.49]
Oleson 1980	0/10	0/10			Not estimable
Ruiz-Tovar 2012	0/52	3/51		5.25%	0.14[0.01,2.65]
Schein 1990	0/29	1/29		4.54%	0.33[0.01,7.86]
Silverman 1986	11/85	10/74		71.26%	0.96[0.43,2.13]
Total (95% CI)	**758**	**551**		**100%**	**0.82[0.42,1.62]**
Total events: 14 (Antibacterial), 17 (Non-antibacterial)					
Heterogeneity: Tau^2=0; Chi^2=2.77, df=5(P=0.74); I^2=0%					
Test for overall effect: Z=0.56(P=0.57)					

Analysis 2.5. Comparison 2 Antibacterial irrigation versus non-antibacterial irrigation, Outcome 5 Mortality.

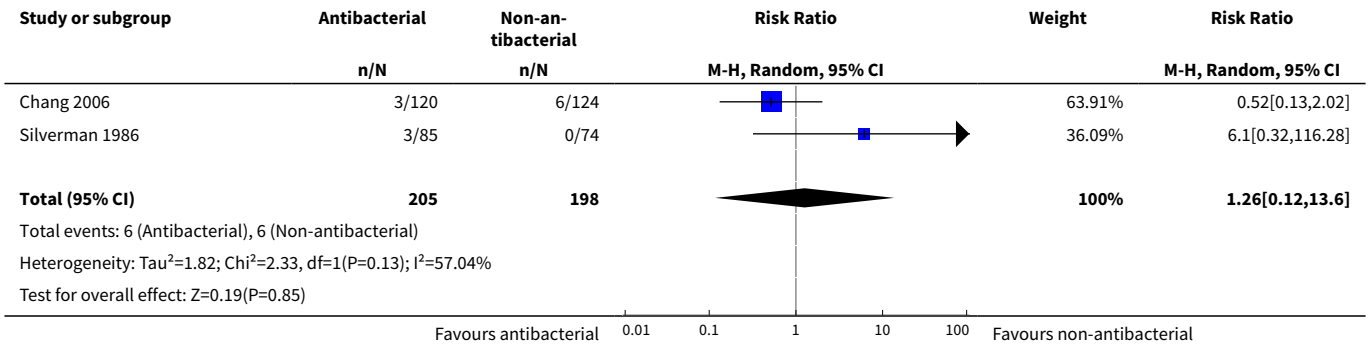
Study or subgroup	Antibacterial n/N	Non-antibacterial n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
Baker 1994	4/150	4/150		14.39%	1[0.25,3.92]
Browne 1978	3/17	0/18		3.22%	7.39[0.41,133.24]
Lord 1983	5/100	3/100		13.64%	1.67[0.41,6.79]
Oller 2015	0/34	0/17			Not estimable
Rambo 1972	5/44	8/50		24.8%	0.71[0.25,2.01]
Ruiz-Tovar 2012	1/52	2/52		4.79%	0.5[0.05,5.35]
Ruiz-Tovar 2013	0/20	0/20			Not estimable
Ruiz-Tovar 2016a	1/53	1/53		3.57%	1[0.06,15.57]
Ruiz-Tovar 2016b	0/40	1/40		2.67%	0.33[0.01,7.95]
Schein 1990	3/29	6/29		16.24%	0.5[0.14,1.81]
Vallance 1985	4/33	4/20		16.68%	0.61[0.17,2.16]
Total (95% CI)	**572**	**549**		**100%**	**0.81[0.48,1.36]**
Total events: 26 (Antibacterial), 29 (Non-antibacterial)					
Heterogeneity: Tau^2=0; Chi^2=4.7, df=8(P=0.79); I^2=0%					
Test for overall effect: Z=0.79(P=0.43)					

Analysis 2.6. Comparison 2 Antibacterial irrigation versus non-antibacterial irrigation, Outcome 6 Hospital stay.

Study or subgroup	Antibacterial N	Antibacterial Mean(SD)	Non-antibacterial N	Non-antibacterial Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
Bourgeois 1985	73	5.2 (0.3)	75	6.3 (0.7)		49.69%	-1.08[-1.25,-0.92]
Halsall 1981	99	6.4 (0)	93	6.6 (0)			Not estimable



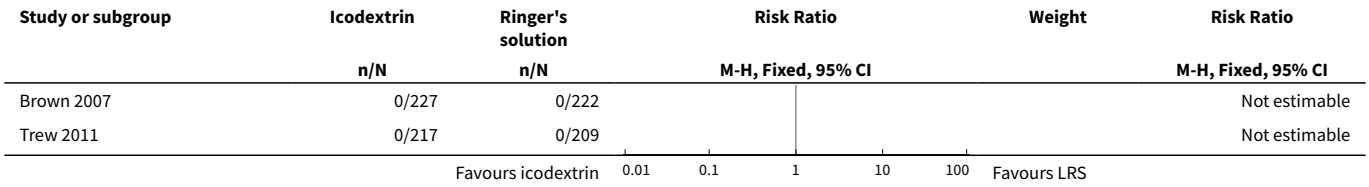
Analysis 2.7. Comparison 2 Antibacterial irrigation versus non-antibacterial irrigation, Outcome 7 Return to theatre (reoperation).

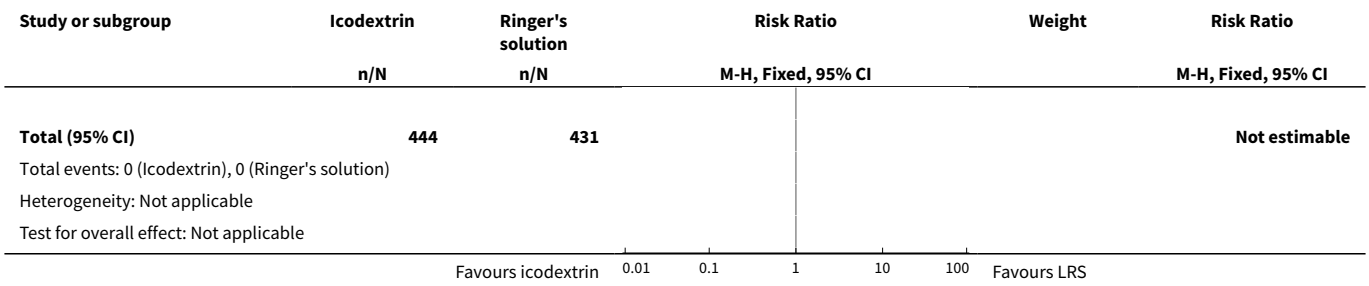


Comparison 3. Icodextrin versus lactated Ringer's solution

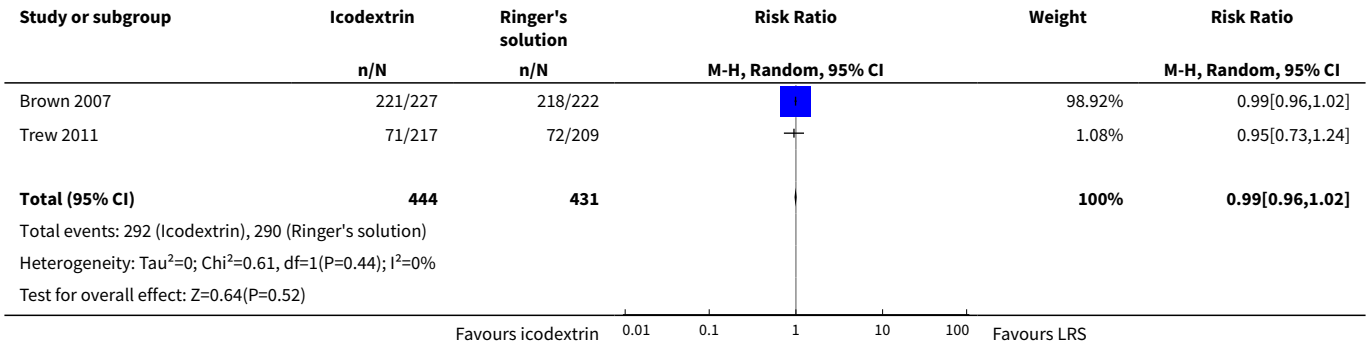
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Mortality	2	875	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
2 Adverse events	2	875	Risk Ratio (M-H, Random, 95% CI)	0.99 [0.96, 1.02]
3 Treatment-related adverse events	2	875	Risk Ratio (M-H, Random, 95% CI)	1.35 [0.98, 1.86]

Analysis 3.1. Comparison 3 Icodextrin versus lactated Ringer's solution, Outcome 1 Mortality.

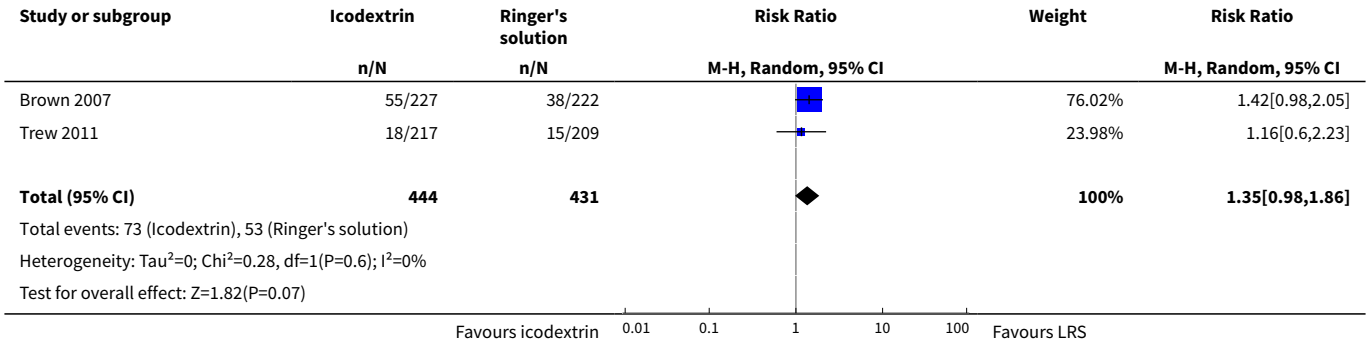




Analysis 3.2. Comparison 3 Icodextrin versus lactated Ringer's solution, Outcome 2 Adverse events.



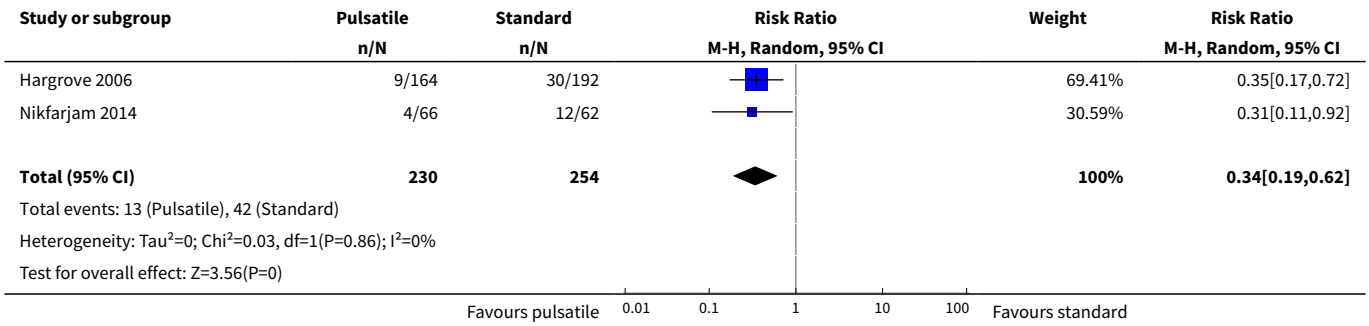
Analysis 3.3. Comparison 3 Icodextrin versus lactated Ringer's solution, Outcome 3 Treatment-related adverse events.



Comparison 4. Standard irrigation versus pulsatile irrigation

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 SSI	2	484	Risk Ratio (M-H, Random, 95% CI)	0.34 [0.19, 0.62]

Analysis 4.1. Comparison 4 Standard irrigation versus pulsatile irrigation, Outcome 1 SSI.



ADDITIONAL TABLES

Table 1. Summary of GRADE assessments for comparisons with limited data

Comparison	Surgery	Participants (studies)	SSI RR (95% CI)	GRADE judgement: certainty of the evidence	Reason for downgrading
Icodextrin vs Ringer's solution	Clean-contaminated (uterine)	426 (1 RCT) Trew 2011	2.89 (0.30 to 27.56)	Low	Downgraded twice for very serious imprecision
Povidone iodine vs Dermacyn	Clean (cardiac)	190 (1 RCT) Mohd 2010	2.80 (1.05 to 7.47)	Low	Downgraded once for high risk of bias and once for imprecision
Povidone iodine vs chlorhexidine	Dirty (peritonitis)	53 (1 RCT)[1] Vallance 1985	1.13 (0.78 to 1.63)	Very low	Downgraded twice for high risk of bias in multiple domains and once for imprecision
Cepharin vs cefoxitin	Clean-contaminated (caesarean section)	132 (1 RCT)[1] Levin 1983	Not estimable (no events in either group)	No assessment possible	-
Epicillin vs lincomycin	Contaminated (appendicitis)	162 (1 RCT)[1] Marti 1979	Not estimable (data not reported for groups)	No assessment possible	-
Gentamicin vs clindamycin	Clean (breast)	51 (1 RCT)[1] Oller 2015	Not estimable (no events in either group)	No assessment possible	-
Cephapirin versus moxalactam	Clean-contaminated (caesarean section)	149 (total 360) (1 RCT)[2] Dashow 1986	1.69 (0.29 to 9.84)	Low	Downgraded twice for very serious imprecision

Table 1. Summary of GRADE assessments for comparisons with limited data *(Continued)*

Cephapirin versus cefamandole	Clean-contaminated (caesarean section)	134 (total 360) (1 RCT)[2] Dashow 1986	1.37 (0.24 to 7.95)	Low	Downgraded twice for very serious imprecision
Cephapirin versus ampicillin	Clean-contaminated (caesarean section)	140 (total 360) (1 RCT)[2] Dashow 1986	7.00 (0.37 to 133.06)	Low	Downgraded twice for very serious imprecision
Cefamandole versus moxalactam	Clean-contaminated (caesarean section)	143 (total 360) (1 RCT)[2] Dashow 1986	1.23 (0.18 to 8.52)	Low	Downgraded twice for very serious imprecision
Cefamandole versus ampicillin	Clean-contaminated (caesarean section)	134 (total 360) (1 RCT)[2] Dashow 1986	5.46 (0.27 to 111.65)	Low	Downgraded twice for very serious imprecision
Moxalactam versus ampicillin	Clean-contaminated (caesarean section)	149 (total 360) (1 RCT)[2] Dashow 1986	4.44 (0.22 to 90.88)	Low	Downgraded twice for very serious imprecision
Cefazolin versus cefamandole	Clean-contaminated (caesarean section)	207 (1 RCT) Peterson 1990	4.58 (0.22 to 93.38)	Low	Downgraded twice for very serious imprecision

[1]Three-armed trial; not all participants relevant to this comparison.
[2]Five-armed trial; not all participants relevant to this comparison.
CI: confidence interval; RCT: randomised controlled trial; RR: risk ratio; SSI: surgical site infection

Table 2. Summary of primary outcome data: surgical site infection (SSI) and wound dehiscence

Study	Surgical category/type	Participants	Interventions	Definition of SSI	Follow-up	SSI events	Risk ratio (95% CI)	Wound dehiscence risk ratio (95% CI)
Comparison of irrigation compared with no irrigation								
Bourgeois 1985	Clean-contaminated Caeasarean section	223	Antibiotic irrigation/saline irrigation No irrigation	NR				
Buanes 1991	Dirty Perforated appendicitis	35	Saline postoperative irrigation No postoperative irrigation	Temperature > 38.5C for > 24 h plus localised, drainage-confirmed accumulation of fluid	6 weeks	9/39 2/44	5.08 (1.17 to 22.09) Not included in pooled analysis - intervention too different	NR
Cervantes-Sanchez 2000	Contaminated Appendicitis	283	Saline irrigation No irrigation	Collection of pus or positive bacteriologic culture from wound discharge	4 weeks	11/127 39/156	0.25 (0.19 to 0.65)	NR
Cho 2004	Clean-contaminated Gastrectomy	34	Saline irrigation No irrigation	Centers for Disease Control and Prevention criteria	2 weeks	1/17 3/17	0.33 (0.04 to 2.89)	NR
De Jong 1982	Mixed Abdominal/inguinal hernia	592	Antiseptic irrigation No irrigation	Purulent discharge seen within 4 weeks or culturing of fluid from the wound was positive	4 weeks	36/279 39/279	0.92 (0.61 to 1.41)	NR
Elliott 1986 [1]	Clean-contaminated Caeasarean section	158	Antibiotic irrigation No irrigation	NR	6 weeks	0/80 1/78	0.33 (0.01 to 7.86)	NR
Gungorduk 2010	Clean-contaminated	520	Saline irrigation No irrigation	Wound drained purulent material/serosanguineous fluid plus induration, warmth and tenderness	6 weeks	17/260 19/260	0.89 (0.48 to 1.68)	NR

Table 2. Summary of primary outcome data: surgical site infection (SSI) and wound dehiscence *(Continued)*

	Caeasarean section							
Harrigill 2003	Clean-contaminated Caeasarean section	196	Saline irrigation No irrigation	Undue tenderness, erythema, discharge, or separation of the incision accompanying fever	NR	1/97 2/99	0.51 (0.05 to 5.54)	NR
Mahomed 2016	Clean-contaminated Caeasarean section	3270	Antiseptic irrigation No irrigation	Abscess or wound draining pus or sero-sanguinous fluid, or redness, induration, warmth and tenderness or general practitioner prescribed antibiotics	4 weeks	144/1520 147/1507	0.97 (0.78 to 1.21)	NR
Oleson 1980	Dirty Perforated appendicitis	33	Antibiotic irrigation/saline irrigation No irrigation	NR	Mean 8 d (5-16)	5/20 4/10	0.63 (0.21 to 1.83)	NR
Ozlem 2015	Dirty Perforated appendicitis	14	Saline irrigation No irrigation	NR	NR	2/7 0/7	5.00 (0.28 to 88.53)	NR
Platt 2003	Clean Breast	30	Saline irrigation No irrigation	Wound discharge, invasive infection	8 weeks	0/30 0/30	Not estimable Not included in pooled analysis - split-body design	1.15 (0.44 to 3.06)
Schein 1990	Dirty Abdominal infection	87	Saline irrigation/ Antibiotic irrigation No irrigation	Discharge of pus	2 weeks	10/58 6/29	0.83 (0.34 to 2.07)	NR
Snow 2016	Mixed Appendix	83	Saline irrigation No irrigation	NR	6 weeks	0/40 0/41	Not estimable	NR
St Peter 2012	Dirty Appendix	220	Saline irrigation No irrigation	NR				NR

Table 2. Summary of primary outcome data: surgical site infection (SSI) and wound dehiscence *(Continued)*

Tanaka 2015	Clean-contaminated Liver resection	193	Saline irrigation No irrigation	Incisional or organ/space infection Incisional infection: clinically apparent cellulitis, induration, or purulent discharge. Organ/space infection: radiologic evidence of fluid collection necessitating drainage or antibiotic therapy	4 weeks	21/96 13/97	1.63 (0.87 to 3.07)	NR
Tanphiphat 1978	Contaminated Appendix	374	Antiseptic irrigation No irrigation	Collection of pus that emptied itself spontaneously or after incision	2 weeks	13/128 12/124	1.05 (0.50 to 2.21)	NR
Temizkan 2016	Clean-contaminated Caeasarean section	430	Saline irrigation No irrigation	Partial or total separation of incision, plus purulent or serous wound discharge with induration, warmth, and tenderness	NR	1/215 2/215	0.50 (0.05 to 5.47)	NR
Tighe 1982	Contaminated Appendix	131	Antiseptic irrigation No irrigation Non-antibacterial irrigation	Prescence of pus either spontaneously or on probing. All infections confirmed bacteriologically	NR	17/131 Results are not given by intervention group; no effect estimate calculable		NR
Viney 2012	Clean-contaminated Caeasarean section	236	Saline irrigation No irrigation	NR				NR
Comparison of antibacterial irrigationwith non-antibacterial irrigation								
Al-Shehri 1994	Mixed Appendicits	254	Antibiotic Saline	Purulent discharge in wound, regardless of culture results, or occurrence of serous discharge with positive culture	1 month	1/120 7/134	0.16 (0.02 to 1.28)	NR
Baker 1994	Clean-contaminated	330	Antiseptic	Spontaneous or incisional discharge from wound, pus or	6 weeks	17/150	1.00 (0.53 to 1.88)	NR

Table 2. Summary of primary outcome data: surgical site infection (SSI) and wound dehiscence *(Continued)*

	Colorectal		Saline	serous fluid, with infective organism identified on culture		17/150		
Bourgeois 1985	Clean-contaminated Caeasarean section	223	Antibiotic irrigation Saline irrigation (No irrigation)	NR				NR
Browne 1978	Dirty Peritonitis	35	Antiseptic irrigation Saline irrigation	NR				NR
Carl 2000	Clean-contaminated	40	Antibiotic Saline	NR	4-6 weeks	1/20 1/20	1.00 (0.07 to 14.90)	NR
Case 1987	Clean Breast	54	Antibiotic Saline	NR	6 weeks	0/23 1/30	0.43 (0.02 to 10.11)	0.43 (0.02 to 10.11)
Chang 2006	Clean Spinal	244	Antiseptic Saline	Superficial (above lumbosacral fascia) or deep (below lumbosacral fascia), early onset (within 2 weeks) or late onset (otherwise). Deep infections confirmed by laboratory parameters: erythrocyte sedimentation rate, level of C-reactive protein, and positive biopsy culture	2 weeks, long-term follow-up to 19 months	0/120 6/124	0.08 (0.00 to 1.40) Only included in sensitivity analysis due to suspected data overlap with Cheng 2005	0.52 (0.05 to 5.62)
Cheng 2005	Clean Spinal	417	Antiseptic Saline	Unusual pain, tenderness, erythema, induration, fever, or wound drainage; investigated with erythrocyte sedimentation rate, C-reactive protein, and bacteriological cultures from operative site or blood	2 weeks', long-term follow-up to mean 15.5 months	0/208 7/206	0.07 (0.00 to 1.015)	NR
Dashow 1986	Clean-contaminated Caesarean	360	4 antibiotics Saline	Wound breakdown with positive culture or presence of cellulitis	NR	7/283 3/77	0.63 (0.17 to 2.40)	NR

Table 2. Summary of primary outcome data: surgical site infection (SSI) and wound dehiscence *(Continued)*

Greig 1987	Mixed Colorectal	129	Antibiotic Saline	Discharge of pus from the wound "wound sepsis"	1 month	15/64 18/65	0.85 (0.47 to 1.53)	NR
Halsall 1981	Mixed Appendicitis	192	Antiseptic Saline	Wound discharging pus	4 weeks	18/99 29/93	0.58 (0.35 to 0.98)	NR
Kokavec 2008	Clean Orthopaedic	162	Antiseptic Saline	Positive bacteriological examination	6 weeks then mean 7.8 (2-4) months	0/89 2/73	0.16 (0.01 to 3.37)	NR
Kubota 1999	Dirty Perforated appendicitis	16	Antiseptic Saline	NR	NR	1/8 4/8	0.25 (0.04 to 1.77)	NR
Kubota 2015	Dirty Perforated appendicitis	44	Antiseptic Saline	Infection at operation site, up to 30 d after surgery; confirmed causative pathogen(s) identical to those of appendicitis	30 d	0/24 4/20	0.09 (0.01 to 1.64)	NR
Levin 1983	Clean-contaminated Caeasarean section	128	2 Antibiotics Saline	Purulent wound discharge with or without wound separation	8 weeks	0/85 3/43	0.07 (0.00 to 1.38)	NR
Lord 1983	Mixed Gastrointestinal/colorectal	200	Antibiotic Saline	NR	NR	3/100 9/100	0.33 (0.09 to 1.20)	NR
Magann 1993	Clean-contaminated Caeasarean section	100	Antibiotic Saline	Hyperemic skin incision and fluctuant mass which when opened contained purulent material	NR	2/50 4/50	0.50 (0.10 to 0.50)	NR
Marti 1979	Contaminated Appendicitis	162	2 Antibiotics Saline	Septic complications with spontaneous or induced purulent discharge	4 d; longer follow-up unclear	Results are not given by intervention group; no effect estimate calculable		NR

Table 2. Summary of primary outcome data: surgical site infection (SSI) and wound dehiscence *(Continued)*

Mirsharifi 2008	Clean-contaminated Cholecystectomy	102	Antibiotic Saline	Erythema, induration, tenderness, warmth, suppurative discharge	6 weeks	6/51 6/51	1.00 (0.35 to 2.89)	NR
Moylan 1968	Clean-contaminated Abdominal	260	Antibiotic Saline	NR, wounds were monitored with daily photographs	Until discharge	12/124 23/116	0.49 (0.25 to 0.94)	NR
Neeff 2016	Clean-contaminated Colorectal	197	Antiseptic Non-antibacterial	NR	NR	19/101 22/96	0.82 (0.48 to 1.42)	NR
Oestreicher 1989	Mixed General surgery	540	Antiseptic Saline	NR	NR	16/267 15/273	1.09 (0.55 to 2.16)	NR
Oleson 1980	Dirty Perforated appendicitis	33	Antibiotic irrigation Saline irrigation No irrigation	NR	mean 8 d (5-16)	3/10 2/10	1.50 (0.32 to 3.09)	NR
Oller 2015	Clean Breast	51	2 Antibiotics Saline	NR	NR	0/34 0/17	Not estimable	NR
Rambo 1972	Dirty Peritonitis	94	Antibiotic Saline	NR	NR	11/44 13/50	0.96 (0.48 to 1.92)	NR
Ruiz-Tovar 2011	Clean-contaminated Colorectal	128	Antibiotic Saline	NR	NR	6/64 27/64	0.22 (0.10 to 0.50)	NR
Ruiz-Tovar 2012	Clean-contaminated Colorectal	108	Antibiotic Saline	Presence of purulent discharge, confirmed with microbiologic culture	30 d	2/52 7/51	0.29 (0.06 to 1.31)	NR
Ruiz-Tovar 2013	Clean	40	Antibiotic	NR	2 weeks	0/20	Not estimable	NR

Table 2. Summary of primary outcome data: surgical site infection (SSI) and wound dehiscence *(Continued)*

	Breast		Saline			0/20		
Ruiz-Tovar 2016a	Clean-contaminated Colorectal	106	Antibiotic Saline	NR	30 d	2/52 7/52	0.20 (0.05 to 1.87)	NR
Ruiz-Tovar 2016b	Clean-contaminated Bariatric surgery	80	Antibiotic Saline	NR	30 d after discharge	NR		NR
Schein 1990	Dirty Abdominal infection	87	Antibiotic Saline (No irrigation)	Discharge of pus	2 weeks	5/29 5/29 (6/29)	1.00 (0.32 to 3.09)	NR
Silverman 1986	Mixed Gastrointestinal/colorectal	159	Antibiotic Saline	Discharge of pus	6 weeks	10/85 24/74	0.36 (0.19 to 0.71)	NR
Sindelar 1979	Mixed General Surgery	500	Antiseptic Saline	Pus discharged within 12 weeks or serous drainage from questionable wounds plus positive culture	12 weeks	7/242 39/258	0.19 (0.09 to 0.42)	NR
Takesue 2011	Clean-contaminated Colorectal	400	Antiseptic Saline	National Nosocomial Infections Surveillance system	30 d (total 3 months)	19/180 29/183	0.67 (0.39 to 1.14)	1.44 (0.71 to 2.93)
Tighe 1982	Contaminated Appendix	131	Antiseptic irrigation Non-antibacterial irrigation (No irrigation)	Prescence of pus either spontaneously or on probing. All infections confirmed bacteriologically	NR	7/131 Results are not given by intervention group; No effect estimate calculable		NR
Vallance 1985	Dirty Peritonitis	53	2 Antiseptics Saline	Pus in wound, sero-sanguinous discharge, Inflammation or induration	1 month	23/29 10/16	0.61 (0.40 to 0.92)	NR

Table 2. Summary of primary outcome data: surgical site infection (SSI) and wound dehiscence *(Continued)*

Comparisons of two different agents in the same class

Brown 2007	Clean-contaminated Uterine	449	2 non-antibacterials Icodextrin Ringer's solution	NR clearly; data on infection ambiguous				NR
Dashow 1986	Clean-contaminated Caesarean	360	4 antibiotics (Saline) Cephapirin Cefamandole Moxalactam Ampicillin	Wound breakdown with positive culture or presence of cellulitis	NR	3/70 2/64 2/79 0/70	Cephapirin: cefamandole 1.37 (0.24 to 7.95) Cephapirin: moxalactam 1.69 (0.29 to 9.84) Cephapirin: ampicillin 7.00 (0.37 to 133.06) Cefamandole: moxalactam 1.23 (0.18 to 8.52) Cefamandole: ampicillin 5.46 (0.27 to 111.65) Moxalactam: ampicillin 4.44 (0.22 to 90.88)	NR
Levin 1983;	Clean-contaminated	128	2 antibiotics (Saline)	Purulent wound discharge with or without wound separation	8 weeks	0/44 0/41	Not estimable; zero events	NR

Table 2. Summary of primary outcome data: surgical site infection (SSI) and wound dehiscence *(Continued)*

	Caesarean		Cephapirin cefoxitin					
Marti 1979	Contaminated Appendicitis	162	2 antibiotics (Saline) Epicillin Lincomycin	Septic complications with spontaneous or induced purulent discharge	4 d; longer follow-up unclear	Not estimable; number of participants and events per group not reported		NR
Mohd 2010;	Clean Cardiac	190	2 antiseptics Povidone iodine Dermacyn	Centers for Disease Control and Prevention criteria	6 weeks	14/90 5/88	2.80 (1.05 to 7.47)	NR
Oller 2015	Clean Breast	51	2 antibiotics Clindamycin Gentamicin	NR	NR	0/17 0/17	Not estimable; zero events	NR
Peterson 1990	Clean-contaminated Caesarean	207 113 in relevant groups	2 antibiotics Cefazolin Cefamandole	Presence of cellulitis and/or purulent exudate	> 2 weeks	2/59 0/54	4.58 (0.22 to 93.38)	NR
Shimizu 2011	Clean Brain	20	2 non-antibacterials Saline Artificial CSF	NR				NR
Trew 2011	Clean-contaminated Uterine	498	2 non-antibacterials Icodextrin Ringer's solution	NR	4-16 weeks	3/217 1/209	2.89 (0.30 to 27.56)	NR
Vallance 1985	Dirty Peritonitis	53	2 antiseptics (Saline)	Pus in wound, sero-sanguinous discharge, Inflammation or induration	1 month	4/16 4/13	1.13 (95% CI 0.78 to 1.63)	NR

Table 2. Summary of primary outcome data: surgical site infection (SSI) and wound dehiscence *(Continued)*

			Povidone iodine Chlorhexidine					
Comparison of pulsatile versus standard irrigation delivery								
Hargrove 2006	Clean Orthopaedic	356	Pulsatile saline Standard saline	Nosocomial Infection National Surveillance Survey	30 days or discharge	9/164 30/192	0.35 (0.17 to 0.72)	NR
Nikfarjam 2014	Clean-contaminated Abdominal	137	Pulsatile saline Standard saline	Purulent drainage, with or without laboratory confirmation; organisms isolated from aseptically obtained culture of fluid or tissue; at least 1 of the following: pain or tenderness, localised swelling, redness, or heat and incision is deliberately opened by surgeon, unless incision is culture-negative; diagnosis of superficial incisional SSI by surgeon or attending physician	1 month	4/66 12/62	0.31 (0.11 to 0.92)	0.31 (0.01 to 7.55)

[1]Elliott is a 4-armed trial with a factorial design, arms with and without intravenous antibiotics are combined
CI: confidence interval; CSF: cerebrospinal fluid; NR: not reported; RR: risk ratio

Table 3. Summary of subgroup analyses

Comparison	Subgroup basis	Pre-specified or exploratory	Subgroups used	Subgroup results RR (95% CI)	I^2 & Chi^2 subgroup differences	I^2 & Chi^2 overall
Irrigation vs no irrigation	Surgical classification	Pre-specified	Clean-contaminated	1.00 (0.82, 1.21)	I^2 = 29.1%.	I^2 = 28%
			Contaminated/Dirty/Mixed	0.74 (0.47 to 1.16)	Chi^2 = 1.41	Chi^2 = 16.58
Irrigation vs no irrigation	Type of irrigation	Exploratory	Non-antibacterial	0.80 (0.46 to 1.41)	I^2 = 0%	I^2 = 28%
			Antiseptic	0.97 (0.81 to 1.17)	Chi^2 = 0.39	Chi^2 = 16.58
			Antibiotic	0.92 (0.42 to 1.99)		
Antibacterial vs non-antibacterial	Surgical classification	Pre-specified	Clean	0.17 (0.03 to 0.89)	I^2= 9.7%	I^2 = 53%
			Clean-contaminated	0.57 (0.40 to 0.79)	Chi^2 = 2.21	Chi^2 = 56.94
			Contaminated/Dirty/Mixed	0.61 (0.40 to 0.92)		
Antibacterial vs non-antibacterial	Type of irrigation	Exploratory	Antiseptic	0.63 (0.40 to 0.95)	I^2= 0%	I^2 = 53%
			Antibiotic	0.57 (0.44 to 0.75)	Chi^2 = 0.38	Chi^2 = 56.94

CI: confidence interval; RR: risk ratio

Table 4. Summary of secondary outcomes

Study Surgical category/type	Participants (N) Follow-up	Interventions	Mortality RR (95% CI)	Systemic antibiotics RR (95% CI)	Antibiotic resistance RR (95% CI)	Adverse events RR (95% CI)	Reoperation RR (95% CI)	Readmission RR (95% CI)	Length of stay (days (95% CI))
Irrigation compared with no irrigation									
Bourgeois 1985 Clean-contaminated Caeasarean section	223 6 weeks	Antibiotic irrigation/Saline irrigation No irrigation	-	-	-	Specific complication only	-	-	Difference in means -0.46 (-0.64 to -0.29)
Buanes 1991 Dirty Perforated appendicitis	85 6 weeks	Saline postoperative irrigation No postoperative irrigation	-	-	-	-	-	-	Medians 5 (3-11) vs 5 (4-12)
Cervantes-Sanchez 2000 Contaminated Appendicitis	283 4 weeks	Saline irrigation No irrigation	-	-	-	No group data	-	-	-
Cho 2004 Clean-contaminated Gastrectomy	34 2 weeks (primary outcome)	Saline irrigation No irrigation	No secondary outcomes were reported						
De Jong 1982 Mixed Abdominal/inguinal hernia	592 4 weeks (primary outcome)	Antiseptic irrigation No irrigation	No secondary outcomes were reported						
Elliott 1986 [1] Clean-contaminated Caeasarean section	158 6 weeks	Antibiotic irrigation No irrigation	-	-	-	Specific complication only	-	-	Difference in means -0.20 (-0.57 to 0.17)

Table 4. Summary of secondary outcomes *(Continued)*

Gungorduk 2010 Clean-contaminated Caeasarean section	520 6 weeks	Saline irrigation No irrigation	-	-	-	-	-	-	Difference in means 0.01 (-0.03 to 0.05)
Harrigill 2003 Clean-contaminated Caeasarean section	196 NR	Saline irrigation No irrigation	-	-	-	Overall RR 1.10 (0.55 to 2.22)	-	-	Difference in means 0.10 (-0.17 to 0.37)
Mahomed 2016 Clean-contaminated Caeasarean section	3270 4 weeks	Antiseptic irrigation No irrigation	-	-	-	-	RR 0.77 (0.29 to 2.07)	RR 1.29 (0.81 to 2.06)	-
Oleson 1980 Dirty Perforated appendicitis	33 mean 8 days (5-16)	Antibiotic irrigation/Saline irrigation No irrigation	-	-	-	Abscess RR 0.17 (0.01 to 3.94)	-	-	Medians 14 (8-22) vs 13 (9-22)
Ozlem 2015 Dirty Perforated appendicitis	14 NR	Saline irrigation No irrigation	-	-	-	Overall RR 1.00 (0.08 to 13.02) Abscess but no group data	-	-	-
Platt 2003 Clean Breast	30 8 weeks	Saline irrigation No irrigation	-	-	-	-	-	-	-
Schein 1990 Dirty Abdominal infection	87 2 weeks	Saline irrigation Antibiotic irrigation No irrigation	RR 0.75 (0.30 to 1.90)	-	-	-	-	-	Difference in means not estimable 11.5 vs 13
Snow 2016 Mixed	83 6 weeks	Saline irrigation No irrigation	-	-	-	Abscess RR 1.02 (0.15 to 6.93)	-	-	Medians

Table 4. Summary of secondary outcomes *(Continued)*

Appendix									2.0 (1-3) vs 2.0 (1-2.25)
St Peter 2012 Dirty Appendix	220 2-4 weeks	Saline irrigation No irrigation	-	-	-	Abscess RR 0.95 (0.55 to 1.65)	RR 0.33 (0.01 to 8.09)	RR 0.14 (0.01 to 2.73)	Difference in means -0.10 (-0.85 to 0.65)
Tanaka 2015 Clean-contaminated Liver resection	193 4 weeks	Saline irrigation No irrigation	RR 2.02 (0.36 to 2.04)	-	-	Overall RR 1.04 (0.72 to 1.49)	-	-	Difference in means 0.00 (-3.74 to 3.74)
Tanphiphat 1978 Contaminated Appendix	374 2 weeks	Antiseptic irrigation No irrigation	No secondary outcomes were reported						
Temizkan 2016 Clean-contaminated Caeasarean section	430 NR	Saline irrigation No irrigation	No secondary outcomes were reported						
Tighe 1982 Contaminated Appendix	131 NR	Antiseptic irrigation No irrigation Non-antibacterial irrigation	-	53/131 participants "distributed evenly across the groups"	-	-	-	-	No group data
Viney 2012 Clean-contaminated Caeasarean section	236 NR	Saline irrigation No irrigation	-	-	-	-	-	-	Median discharge day: 3 in both groups
Antibacterial irrigation vs non-antibacterial irrigation									
Al-Shehri 1994 Mixed	254 1 month	Antibiotic Saline	-	-	-	Abscess			No group data

Table 4. Summary of secondary outcomes *(Continued)*

Appendicits						RR not estimable 0 events			
Baker 1994 Clean-contaminated Colorectal	330 6 weeks	Antiseptic Saline	RR 1.00 (0.25 to 3.92)	-	-	Abscess RR 2.0 (0.18 to 21.82)			No group data
Bourgeois 1985 Clean-contaminated Caeasarean section	223 6 weeks	Antibiotic irrigation Saline irrigation (No irrigation)	-	-	-	Specific complication only	-	-	Difference in means -1.08 (-1.25 to -0.92)
Browne 1978 Dirty Peritonitis	35 NR	Antiseptic irrigation Saline irrigation	RR 7.39 (0.41 to 133.24)	-	-	-			-
Carl 2000 Clean-contaminated Caeasarean section	40 4-6 weeks	Antibiotic Saline	-	-	-	-			-
Case 1987 Clean Breast	54 6 weeks	Antibiotic Saline	-	-	-	-			-
Chang 2006 Clean Spinal	244 2 weeks, long-term follow-up to 19 months	Antiseptic Saline	-	All 6 participants with SSI received these; all in saline group	5/6 infections positive for MRSA	-			-
Cheng 2005 Clean Spinal	417 2 weeks long -term follow -up to	Antiseptic Saline	-	-	-	-			-

Table 4. Summary of secondary outcomes *(Continued)*

	mean 15.5 months						
Dashow 1986 Clean-contaminated Caeasarean section	360 NR	4 antibiotics Saline	-	-	-	Abscess RR not estimable 0 events	-
Greig 1987 Mixed Colorectal	129 1 month	Antibiotic Saline	No secondary outcomes were reported				
Halsall 1981 Mixed Appendicitis	192 4 weeks	Antiseptic Saline	-	-	-	-	Difference in means not estimable (6.4 vs 6.6)
Kokavec 2008 Clean Orthopaedic	162 mean 7-8 months (range 2-14 months) (primary outcome)	Antiseptic Saline	No secondary outcomes were reported				-
Kubota 1999 Dirty Perforated appendicitis	16 NR	Antiseptic Saline	-	-	-	Abscess RR 0.33 (0.02 to 7.14)	Difference in means -10.60 (-19.06 to -2.14)
Kubota 2015 Dirty Perforated appendicitis	44 30 days	Antiseptic Saline	-	-	-	Abscess RR 0.83 (0.06 to 12.49)	Difference in means -0.70 (-3.31 to 1.91)
Levin 1983 Clean-contaminated	128 8 weeks	Antibiotic Saline	-	-	-	Specific complication only	Difference in means -0.35 (-1.06 to 0.36)

Table 4. Summary of secondary outcomes *(Continued)*

Caeasarean section							
Lord 1983 Mixed Gastrointestinal/colorectal	200 NR	Antibiotic Saline	RR 1.67 (0.41 to 6.79)	-	Specific organisms	Specific complication only	-
Magann 1993 Clean-contaminated Caeasarean section	100 NR	Antibiotic Saline	-	-	-	Specific complication only	-
Marti 1979 Contaminated Appendicitis	162 4 days; longer follow-up unclear	Antibiotic Saline	-	-	-	Specific complication only	-
Mirsharifi 2008 Clean-contaminated Cholecystectomy	102 6 weeks	Antibiotic Saline	No secondary outcomes were reported				
Moylan 1968 Clean-contaminated Abdominal	260 Until discharge	Antibiotic Saline	-	-	Kanamycin resistance Kanamycin: 12/12 Saline: "over half" of 23	Specific complication only	-
Neeff 2016 Clean-contaminated Colorectal	197 NR	Antiseptic Saline	No secondary outcomes were reported				
Oestreicher 1989 Mixed	540 NR	Antiseptic Saline	No secondary outcomes were reported				-

Table 4. Summary of secondary outcomes *(Continued)*

General surgery

Oleson 1980 Dirty Perforated appendicitis	33 Mean 8 days (5-16	Antibiotic irrigation Saline irrigation No irrigation	-	-	-	Abscess RR not estimable 0 events	Medians 13 (9-20 13 (10-22)
Oller 2015 Clean Breast	51 NR	Antibiotic 1/ Antibiotic 2 Saline	RR not estimable, 0 events	-	-	-	Medians 3 (1-3) 3 (1-3)
Rambo 1972 Dirty Peritonitis	94 NR	Antibiotic Saline	RR 0.71 (0.25 to 2.01)	-	Specific organisms	Abscess grouped with another event - not estimable	-
Ruiz-Tovar 2011 Clean-contaminated Colorectal	128 NR	Antibiotic Saline	No secondary outcomes were reported				
Ruiz-Tovar 2012 Clean-contaminated Colorectal	108 30 days	Antibiotic Saline	RR 0.50 (0.05 to 5.35)	-	-	Abscess RR 0.14 (0.01 to 2.65)	Medians 6 (5-32) 6.5 (5-14)
Ruiz-Tovar 2013 Clean Breast	40 2 weeks	Antibiotic Saline	RR not estimable, 0 events	-	-	Overall RR not estimable 0 events	Medians 3 (1-3) 3 (1-3)
Ruiz-Tovar 2016a Clean-contaminated Colorectal	106 30 days	Antibiotic Saline	RR 1.00 (0.06 to 15.57)	-	-	Specific complication only	Medians 6.5 (5-14) 6 (5-32)
Ruiz-Tovar 2016b Clean-contaminated	80 30 days	Antibiotic Saline	RR 0.33 (0.01 to 7.95)	-	-	Overall RR 0.50 (0.05 to 5.30)	-

Table 4. Summary of secondary outcomes *(Continued)*

Bariatric surgery

Schein 1990 Dirty Abdominal infection	87 2 weeks	Antibiotic Saline	RR 0.50 (0.14 to 1.81)	-	-	Overall RR 0.56 (0.21 to 1.46) Abscess RR 0.33 (0.01 to 7.86)			Difference in means not estimable 10 vs 13
Silverman 1986 Mixed Gastrointestinal/colorectal	159 6 weeks	Antibiotic Saline	-	-	-	Abscess RR 0.96 (0.43 to 2.13) Specific additional complication	RR 6.10 (0.32 to 116.28)		-
Sindelar 1979 Mixed General Surgery	500 12 weeks	Antiseptic Saline	No secondary outcomes were reported						
Takesue 2011 Clean-contaminated Colorectal	400 30 days (total 3 months)	Antiseptic Saline	-	-	MRSA 4/14 vs 8/24 MSSA 0/14 vs 3/24	-			-
Tighe 1982 Contaminated Appendix	131 NR	Antiseptic Non-antibacterial (No irrigation)	-	53/131 participants "distributed evenly across the groups"	-	-	-	-	No group data
Vallance 1985 Dirty Peritonitis	53 1 month	Antiseptic Saline	RR 0.61 (0.17 to 2.16)	-	-	-			Difference in means -0.70 (-3.32 to 1.92)
Comparisons of two different agents in the same class									

Table 4. Summary of secondary outcomes *(Continued)*

Brown 2007 Clean-contaminated Uterine	449 28-56 days	2 non-antibacterials Icodextrin Ringer's solution	RR not estimable - 0 events	-	-	Total: RR 0.99 (0.96 to 1.02) Treatment-related RR 1.42 (0.98 to 2.05) Serious RR 1.20 (0.80 to 1.78) Serious treatment-related RR 0.71 (0.29 to 1.73)	-	-	-
Dashow 1986 Clean-contaminated Caeasarean section	360 NR	4 antibiotics (Saline) Cephapirin Cefamandole Moxalactam Ampicillin	-	-	-	Abscess: no effect estimate calculable - 0 events Other specific events	-	-	-
Levin 1983 Clean-contaminated Caeasarean section	128 8 weeks	2 antibiotics (Saline) Cephapirin Cefoxitin	-	-	-	Specific event data only	-	-	Difference in means 0.10 (-0.78 to 0.58)
Marti 1979 Contaminated Appendicitis	162 4 days; longer follow-up unclear	2 antibiotics (Saline) Epicillin Lincomycin	-	-	-	1 abscess in antibiotic groups; no group data	-	-	-
Mohd 2010 Clean Cardiac	190 6 weeks	2 antiseptics Povidone iodine Dermacyn	4 deaths but no group data; group data for	-	-	-	RR 8.80 (0.48 to 161.11)	-	-

Table 4. Summary of secondary outcomes *(Continued)*

			composite outcome with re-opening of chest						
Oller 2015 Clean Breast	51 NR	2 antibiotics Clindamycin Gentamicin	RR not estimable, 0 events	-	-	-	-	-	Median 3 (1-3) in each group
Peterson 1990 Clean-contaminated Caeasarean section	207 113 in relevant groups 2 weeks + (primary outcome)	2 antibiotics Cefazolin Cefamandole	No secondary outcomes were reported						
Shimizu 2011 Clean Brain	20 10 days	2 non-antibacterials Saline Artificial CSF	-	-	-	2 participants in each group, included MRI data. RR not calculated	-	--	-
Trew 2011 Clean-contaminated Uterine	498 4-16 weeks	2 non-antibacterials Icodextrin Ringer's solution	RR not estimable - 0 events	-		Total: RR 0.95 (0.73 to 1.24) Treatment-related RR 1.16 (0.60 to 2.23)	-	-	-
Vallance 1985 Dirty Peritonitis	53 1 month	2 antiseptics (Saline) Povidone iodine Chlorhexidine	RR 0.45 (0.05 to 3.90) within 4 days, no group data for later events	-	-	-	-	-	Difference in means 3.30 (0.53 to 3.90)
Comparison of pulsatile versus standard irrigationdelivery									

Table 4. Summary of secondary outcomes *(Continued)*

Hargrove 2006 Clean Orthopaedic	356 30 days or discharge	Pulsatile saline Standard saline	No group data	-	No group data "half" SSI positive for MRSA	-	-	-	-
Nikfarjam 2014 Clean-contaminated Abdominal	137 1 month	Pulsatile saline Standard saline	-	No group data: 14/16 SSI treated	Qualitative data on organisms isolated	Complications, not wound infections RR 1.31 (0.87 to 1.97)	RR 0.56 (0.14 to 2.26)	RR 1.41 (0.53 to 3.73)	Median 9 (5 -45) 9 (4-71)

More details of interventions can be found in Table 1 and Characteristics of included studies
1 Elliott is a four-armed trial with a factorial design, arms with and without iv antibiotics are combined
CI: confidence interval; CSF: cerebrospinal fluid; MRI: magnetic resonance imaging; MRSA: methicillin-resistant *Staphylococcus aureus*; RR: risk ratio; SSI: surgical site infection

APPENDICES

Appendix 1. Search strategies

The Cochrane Wounds Specialised Register

1 (surg* near5 infect*) AND INREGISTER
2 ((surg* near5 wound*)) AND INREGISTER
3 ((surg* near5 site*)) AND INREGISTER
4 ((surg* near5 incision*)) AND INREGISTER
5 ((surg* near5 dehisc*)) AND INREGISTER
6 ((wound* near5 dehisc*)) AND INREGISTER
7 ((wound* near5 infect*)) AND INREGISTER
8 ((wound near5 disruption*)) AND INREGISTER
9 ("wound complication*") AND INREGISTER
10 (SSI) AND INREGISTER
11 #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 AND INREGISTER
12 ((intraoperative near3 wash*)) AND INREGISTER
13 ((intra-operative near3 wash*)) AND INREGISTER
14 (irrigat*) AND INREGISTER
15 (lavage) AND INREGISTER
16 #12 OR #13 OR #14 OR #15 AND INREGISTER
17 #11 AND #16 AND INREGISTER

The Cochrane Central Register of Controlled Clinical Trials (CENTRAL)

#1 MeSH descriptor: [Surgical Wound Infection] explode all trees
#2 MeSH descriptor: [Surgical Wound Dehiscence] explode all trees
#3 (surg* near/5 infect*):ti,ab,kw
#4 (surg* near/5 wound*):ti,ab,kw
#5 (surg* near/5 site*):ti,ab,kw
#6 (surg* near/5 incision*):ti,ab,kw
#7 (surg* near/5 dehisc*):ti,ab,kw
#8 (wound* near/5 dehisc*):ti,ab,kw
#9 (wound* near/5 infect*):ti,ab,kw
#10 (wound near/5 disruption*):ti,ab,kw
#11 (wound next complication*):ti,ab,kw
#12 SSI:ti,ab,kw
#13 {or #1-#12}
#14 MeSH descriptor: [Therapeutic Irrigation] explode all trees
#15 (intraoperative near/3 wash*):ti,ab,kw
#16 (intra-operative near/3 wash*):ti,ab,kw
#17 irrigat*:ti,ab,kw
#18 lavage:ti,ab,kw
#19 {or #14-#18}
#20 {and #13, #19} in Trials

Ovid MEDLINE

1. exp Surgical Wound Infection/
2. exp Surgical Wound Dehiscence/
3. (surg* adj5 infect*).tw.
4. (surg* adj5 wound*).tw.
5. (surg* adj5 site*).tw.
6. (surg* adj5 incision*).tw.
7. (surg* adj5 dehisc*).tw.
8. (wound* adj5 dehisc*).tw.
9. (wound* adj5 infect*).tw.
10. (wound adj5 disrupt*).tw.
11. wound complication*.tw.
12. SSI.tw.
13. or/1-12

14. (intraoperative adj3 wash*).tw.
15. (intra-operative adj3 wash*).tw.
16. exp Therapeutic Irrigation/
17. irrigat*.tw.
18. lavage.tw.
19. or/14-18
20. and/13,19
21. randomized controlled trial.pt.
22. controlled clinical trial.pt.
23. randomi?ed.ab.
24. placebo.ab.
25. clinical trials as topic.sh.
26. randomly.ab.
27. trial.ti.
28. or/21-27
29. exp animals/ not humans.sh.
30. 28 not 29
31. 20 and 30

Ovid Embase

1. exp surgical infection/
2. exp wound dehiscence/
3. (surg* adj5 infect*).tw.
4. (surg* adj5 wound*).tw.
5. (surg* adj5 site*).tw.
6. (surg* adj5 incision*).tw.
7. (surg* adj5 dehisc*).tw.
8. (wound* adj5 dehisc*).tw.
9. (wound* adj5 infect*).tw.
10. (wound adj5 disrupt*).tw.
11. wound complication*.tw.
12. SSI.tw.
13. or/1-12
14. (intraoperative adj3 wash*).tw.
15. (intra-operative adj3 wash*).tw.
16. exp lavage/
17. exp wound irrigation/
18. irrigat*.tw.
19. lavage.tw.
20. or/14-19
21. and/13,20
22. Randomized controlled trials/
23. Single-Blind Method/
24. Double-Blind Method/
25. Crossover Procedure/
26. (random* or factorial* or crossover* or cross over* or cross-over* or placebo* or assign* or allocat* or volunteer*).ti,ab.
27. (doubl* adj blind*).ti,ab.
28. (singl* adj blind*).ti,ab.
29. or/22-28
30. exp animals/ or exp invertebrate/ or animal experiment/ or animal model/ or animal tissue/ or animal cell/ or nonhuman/
31. human/ or human cell/
32. and/30-31
33. 30 not 32
34. 29 not 33
35. 21 and 34

EBSCO CINAHL Plus

S33 S19 AND S32
S32 S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12
S31 TI allocat* random* or AB allocat* random*
S30 MH "Quantitative Studies"

S29 TI placebo* or AB placebo*
S28 MH "Placebos"
S27 TI random* allocat* or AB random* allocat*
S26 MH "Random Assignment"
S25 TI randomi?ed control* trial* or AB randomi?ed control* trial*
S24 AB (singl* or doubl* or trebl* or tripl*) and AB (blind* or mask*)
S23 TI (singl* or doubl* or trebl* or tripl*) and TI (blind* or mask*)
S22 TI clinic* N1 trial* or AB clinic* N1 trial*
S21 PT Clinical trial
S20 MH "Clinical Trials+"
S19 S12 AND S18
S18 S13 OR S14 OR S15 OR S16 OR S17
S17 TI lavage OR AB lavage
S16 TI irrigat* OR AB irrigat*
S15 (MH "Therapeutic Irrigation")
S14 TI intra-operative N3 wash* OR AB intra-operative N3 wash*
S13 TI intraoperative N3 wash* OR AB intraoperative N3 wash*
S12 S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11
S11 TI SSI OR AB SSI
S10 TI wound complication* OR AB wound complication*
S9 TI wound* N5 disrupt* OR AB wound* N5 disrupt*
S8 TI wound* N5 dehisc* or AB wound* N5 dehisc*
S7 TI surg* N5 dehisc* or AB surg* N5 dehisc*
S6 TI surg* N5 incision* or AB surg* N5 incision*
S5 TI surg* N5 site* or AB surg* N5 site*
S4 TI surg* N5 wound* or AB surg* N5 wound*
S3 TI surg* N5 infection* or AB surg* N5 infection*
S2 (MH "Surgical Wound Dehiscence")
S1 (MH "Surgical Wound Infection")

Trials Registers

All trials registers were searched using the terms (lavage OR irrigation) AND surgery on 7 March 2017.

- ClinicalTrials.gov (280 total results)
- World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP) (31 records for 29 trials)
- EU Clinical Trials Register (19 results)

Appendix 2. Risk of bias assessment (individually randomised controlled trials)

1. Was the allocation sequence randomly generated?

Low risk of bias

The investigators describe a random component in the sequence generation process such as: referring to a random number table; using a computer random number generator; coin tossing; shuffling cards or envelopes; throwing dice; drawing of lots.

High risk of bias

The investigators describe a non-random component in the sequence generation process. Usually, the description would involve some systematic, non-random approach, for example: sequence generated by odd or even date of birth; sequence generated by some rule based on date (or day) of admission; sequence generated by some rule based on hospital or clinic record number.

Unclear

Insufficient information about the sequence generation process to permit judgement of low or high risk of bias.

2. Was the treatment allocation adequately concealed?

Low risk of bias

Participants and investigators enrolling participants could not foresee assignment because one of the following, or an equivalent method, was used to conceal allocation: central allocation (including telephone, web-based and pharmacy-controlled randomisation); sequentially numbered drug containers of identical appearance; sequentially numbered, opaque, sealed envelopes.

High risk of bias

Participants or investigators enrolling participants could possibly foresee assignments and thus introduce selection bias, such as allocation based on: use of an open random allocation schedule (e.g. a list of random numbers); assignment envelopes without appropriate safeguards (e.g. envelopes were unsealed, non-opaque, or not sequentially numbered); alternation or rotation; date of birth; case record number; any other explicitly unconcealed procedure.

Unclear

Insufficient information to permit judgement of low or high risk of bias. This is usually the case if the method of concealment is not described or not described in sufficient detail to allow a definite judgement, for example if the use of assignment envelopes is described, but it remains unclear whether envelopes were sequentially numbered, opaque and sealed.

3. Blinding - was knowledge of the allocated interventions adequately prevented during the study?

Low risk of bias

Any one of the following.

- No blinding, but the review authors judge that the outcome and the outcome measurement are not likely to be influenced by lack of blinding.
- Blinding of participants and key study personnel ensured, and unlikely that the blinding could have been broken.
- Either participants or some key study personnel were not blinded, but outcome assessment was blinded and the non-blinding of others unlikely to introduce bias.

High risk of bias

Any one of the following.

- No blinding or incomplete blinding, and the outcome or outcome measurement is likely to be influenced by lack of blinding.
- Blinding of key study participants and personnel attempted, but likely that the blinding could have been broken.
- Either participants or some key study personnel were not blinded, and the non-blinding of others likely to introduce bias.

Unclear

Either of the following.

- Insufficient information to permit judgement of low or high risk of bias.
- The study did not address this outcome.

4. Were incomplete outcome data adequately addressed?

Low risk of bias

Any one of the following.

- No missing outcome data.
- Reasons for missing outcome data unlikely to be related to true outcome (for survival data, censoring unlikely to be introducing bias).
- Missing outcome data balanced in numbers across intervention groups, with similar reasons for missing data across groups.
- For dichotomous outcome data, the proportion of missing outcomes compared with observed event risk not enough to have a clinically relevant impact on the intervention effect estimate.
- For continuous outcome data, plausible effect size (difference in means or standardised difference in means) among missing outcomes not enough to have a clinically relevant impact on observed effect size.
- Missing data have been imputed using appropriate methods.

High risk of bias

Any one of the following.

- Reason for missing outcome data likely to be related to true outcome, with either imbalance in numbers or reasons for missing data across intervention groups.
- For dichotomous outcome data, the proportion of missing outcomes compared with observed event risk enough to induce clinically relevant bias in intervention effect estimate.
- For continuous outcome data, plausible effect size (difference in means or standardised difference in means) among missing outcomes enough to induce clinically relevant bias in observed effect size.
- 'As-treated' analysis done with substantial departure of the intervention received from that assigned at randomisation.

- Potentially inappropriate application of simple imputation.

Unclear

Either of the following.

- Insufficient reporting of attrition/exclusions to permit judgement of low or high risk of bias (e.g. number randomised not stated, no reasons for missing data provided).
- The study did not address this outcome.

5. Are reports of the study free of suggestion of selective outcome reporting?

Low risk of bias

Either of the following.

- The study protocol is available and all of the study's prespecified (primary and secondary) outcomes that are of interest in the review have been reported in the prespecified way.
- The study protocol is not available but it is clear that the published reports include all expected outcomes, including those that were prespecified (convincing text of this nature may be uncommon).

High risk of bias

Any one of the following.

- Not all of the study's prespecified primary outcomes have been reported.
- One or more primary outcomes are reported using measurements, analysis methods or subsets of the data (e.g. subscales) that were not prespecified.
- One or more reported primary outcomes were not prespecified (unless clear justification for their reporting is provided, such as an unexpected adverse effect).
- One or more outcomes of interest in the review are reported incompletely so that they cannot be entered in a meta-analysis.
- The study report fails to include results for a key outcome that would be expected to have been reported for such a study.

Unclear

Insufficient information to permit judgement of low or high risk of bias. It is likely that the majority of studies will fall into this category.

6. Other sources of potential bias

Low risk of bias

The study appears to be free of other sources of bias.

High risk of bias

There is at least one important risk of bias. For example, the study:

- had a potential source of bias related to the specific study design used; or
- has been claimed to have been fraudulent; or
- had some other problem.

Unclear

There may be a risk of bias, but there is either:

- insufficient information to assess whether an important risk of bias exists; or
- insufficient rationale or evidence that an identified problem will introduce bias.

Appendix 3. Risk of bias assessment (cluster-randomised controlled trials)

In cluster-randomised trials, particular biases to consider include: (i) recruitment bias; (ii) baseline imbalance; (iii) loss of clusters; (iv) incorrect analysis; and (v) comparability with individually randomised trials.

(i) Recruitment bias can occur when individuals are recruited to the trial after the clusters have been randomised, as the knowledge of whether each cluster is an 'intervention' or 'control' cluster could affect the types of participants recruited.

(ii) Cluster-randomised trials often randomise all clusters at once, so lack of concealment of an allocation sequence should not usually be an issue. However, because small numbers of clusters are randomised, there is a possibility of chance baseline imbalance between the

randomised groups, in terms of either the clusters or the individuals. Although not a form of bias as such, the risk of baseline differences can be reduced by using stratified or pair-matched randomisation of clusters. Reporting of the baseline comparability of clusters, or statistical adjustment for baseline characteristics, can help reduce concern about the effects of baseline imbalance.

(iii) Occasionally, complete clusters are lost from a trial, and have to be omitted from the analysis. Just as for missing outcome data in individually randomised trials, this may lead to bias. In addition, missing outcomes for individuals within clusters may also lead to a risk of bias in cluster-randomised trials.

(iv) Many cluster-randomised trials are analysed by incorrect statistical methods, not taking the clustering into account. Such analyses create a 'unit of analysis error' and produce over-precise results (the standard error of the estimated intervention effect is too small) and P values that are too small. They do not lead to biased estimates of effect. However, if they remain uncorrected, they will receive too much weight in a meta-analysis.

(v) In a meta-analysis including both cluster and individually randomised trials, or including cluster-randomised trials with different types of clusters, possible differences between the intervention effects being estimated need to be considered. For example, in a vaccine trial of infectious diseases, a vaccine applied to all individuals in a community would be expected to be more effective than if the vaccine was applied to only half of the people. Another example is provided by a Cochrane Review of hip protectors. The cluster trials showed large positive effect, whereas individually randomised trials did not show any clear benefit. One possibility is that there was a 'herd effect' in the cluster-randomised trials (which were often performed in nursing homes, where compliance with using the protectors may have been enhanced). In general, such 'contamination' would lead to underestimates of effect. Thus, if an intervention effect is still demonstrated despite contamination in those trials that were not cluster-randomised, a confident conclusion about the presence of an effect can be drawn. However, the size of the effect is likely to be underestimated. Contamination and 'herd effects' may be different for different types of cluster.

CONTRIBUTIONS OF AUTHORS

Gill Norman: co-ordinated the review, extracted and checked data, undertook and checked quality assessment, analysed data and performed statistical analysis, contacted study authors, produced the first draft of the review and is a guarantor of the review.

Ross Atkinson: extracted and checked data, undertook and checked quality assessment, analysed data and performed statistical analysis, contacted study authors, and contributed to the writing and editing of the review.

Tanya Smith: conceived and designed the review, extracted data and undertook quality assessment, and made an intellectual contribution to the review.

Ceri Rowlands: conceived and designed the review, extracted data and undertook quality assessment, and made an intellectual contribution to the review.

Amber Rithalia: extracted and checked data, undertook and checked quality assessment and made an intellectual contribution to the review.

Emma Crosbie contributed to editing the review and made an intellectual contribution to the review.

Jo Dumville: conceived and designed the review, checked the statistical analysis, advised on the review, contributed to writing and editing the review, secured funding for the review and is a guarantor of the review.

Contributions of the editorial base

Nicky Cullum (Coordinating Editor): edited the protocol and the review; advised on methodology interpretation and review content; approved the final review prior to submission.

Gill Rizzello (Managing Editor): co-ordinated the editorial process; advised on content; edited the protocol and the review.

Reetu Child (Information Specialist) : designed the search strategy and edited the search methods section.

Naomi Shaw (Information Specialist): updated the search and edited the search methods section.

Ursula Gonthier (Editorial Assistant): edited the Abstract, the Plain Language Summary and the reference sections of the review.

DECLARATIONS OF INTEREST

Gill Norman: my employment at the University of Manchester is supported by a grant from National Institute for Health Research (NIHR), UK (NIHR Cochrane Programme Grant 13/89/08-High Priority Cochrane Reviews in Wound Prevention and Treatment).

Ross Atkinson: none known.

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Ceri Rowlands: none known.

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DIFFERENCES BETWEEN PROTOCOL AND REVIEW

We have clarified that this review does not include studies where the irrigation was confined to the interior of (e.g.) the uterus, bowel or bladder, but did include studies in which (e.g.) the peritoneum was irrigated in addition to such procedures. We also did not include studies of surgery in the oral or aural cavities or in the eyes.

The protocol did not specify methods for dealing with studies with a 'split-body' design, in which two operative sites are present on each participant and these are randomised to different treatment groups. We decided to include these studies in the review but not to include them in meta-analyses with participant-level randomisation; we included only one such study in the review and this decision did not materially affect the meta-analyses involved due to limited data.

We prespecified two subgroup analyses on the basis of the surgical category and on the basis of whether participants were adults or children. We conducted the surgical category analysis for the primary outcome of SSI for the two comparisons with the largest number of participants and studies. However, small numbers of studies enrolling only children meant that we judged that the second prespecified analysis would be uninformative. We did not carry out any subgroup analyses for the secondary outcomes because there were many fewer studies and they were not well distributed between the surgical categories. We did carry out an exploratory subgroup analysis on the basis of the type of irrigation solution used in order to check that our analysis approach was reasonable. This is clearly reported as an additional post-hoc analysis.

In addition to planned sensitivity analyses we conducted additional analyses to assess the impact of (1) including a study that we suspected contained participants also included in another study and (2) excluding a study where we had conducted a completed-case analysis because of a substantial amount of attrition and the explanation provided for this attrition.

We had planned to analyse outcomes by the time point at which they were reported based on short, medium or long term. In practice we found that the overwhelming majority of the data reported were for time points of between two and eight weeks postoperatively, with the majority being at either four or six weeks, sometimes with interim but unreported follow-up points. We therefore decided that we would group all the data together for the outcomes reported; dividing data reported at points that narrowly spanned the 30-day cut-off for short-term data was not considered informative (medium term spanned from 30 days to 12 months).

In response to suggestions from the peer reviewers we have added adverse events to the 'Summary of findings tables'; we are grateful to them for this suggestion.

INDEX TERMS

Medical Subject Headings (MeSH)

Abscess [epidemiology]; Anti-Bacterial Agents [administration & dosage]; Anti-Infective Agents, Local [administration & dosage]; Drug Combinations; Hypochlorous Acid [administration & dosage]; Incidence; Povidone-Iodine [administration & dosage]; Randomized Controlled Trials as Topic; Sodium Hypochlorite [administration & dosage]; Surgical Wound Dehiscence [epidemiology]; Surgical Wound Infection [epidemiology] [*prevention & control]; Therapeutic Irrigation [methods]

MeSH check words

Humans