Intraoperative interventions for preventing surgical site infection: An overview of Cochrane Reviews

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TABLE OF CONTENTS

[Overview of Reviews]

Intraoperative interventions for preventing surgical site infection: an overview of Cochrane Reviews

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ABSTRACT

Background

Surgical site infection (SSI) rates vary from 1% to 5% in the month following surgery. Due to the large number of surgical procedures conducted annually, the costs of these SSIs can be considerable in financial and social terms. Many interventions are used with the aim of reducing the risk of SSI in people undergoing surgery. These interventions can be broadly delivered at three stages: preoperatively, intraoperatively and postoperatively. The intraoperative interventions are largely focused on decontamination of skin using soap and antiseptics; the use of barriers to prevent movement of micro-organisms into incisions; and optimising the patient's own bodily functions to promote best recovery. Both decontamination and barrier methods can be aimed at people undergoing surgery and operating staff. Other interventions focused on SSI prevention may be aimed at the surgical environment and include methods of theatre cleansing and approaches to managing theatre traffic.

Objectives

To present an overview of Cochrane Reviews of the effectiveness and safety of interventions, delivered during the intraoperative period, aimed at preventing SSIs in all populations undergoing surgery in an operating theatre.

Methods

Published Cochrane systematic reviews reporting the effectiveness of interventions delivered during the intraoperative period in terms of SSI prevention were eligible for inclusion in this overview. We also identified Cochrane protocols and title registrations for future inclusion into the overview. We searched the Cochrane Library on 01 July 2017. Two review authors independently screened search results and undertook data extraction and 'Risk of bias' and certainty assessment. We used the ROBIS (risk of bias in systematic reviews) tool to assess the quality of included reviews, and we used GRADE methods to assess the certainty of the evidence for each outcome. We summarised the characteristics of included reviews in the text and in additional tables.

Main results

We included 32 Cochrane Reviews in this overview: we judged 30 reviews as being at low risk of bias and two at unclear risk of bias. Thirteen reviews had not been updated in the past three years. Two reviews had no relevant data to extract. We extracted data from 30 reviews with 349 included trials, totaling 73,053 participants. Interventions assessed included gloving, use of disposable face masks, patient oxygenation protocols, use of skin antiseptics for hand washing and patient skin preparation, vaginal preparation, microbial sealants, methods of surgical incision, antibiotic prophylaxis and methods of skin closure. Overall, the GRADE certainty of evidence for outcomes was low or very low. Of the 77 comparisons providing evidence for the outcome of SSI, seven provided high- or moderate-certainty evidence, 39 provided low-certainty evidence and 31 very low-certainty evidence. Of the nine comparisons that provided evidence for the outcome of mortality, five provided low-certainty evidence and four very low-certainty evidence.

There is high- or moderate-certainty evidence for the following outcomes for these intraoperative interventions. (1) Prophylactic intravenous antibiotics administered before caesarean incision reduce SSI risk compared with administration after cord clamping (10 trials, 5041 participants; risk ratio (RR) 0.59, 95% confidence interval (CI) 0.44 to 0.81; high-certainty evidence - assessed by review authors). (2) Preoperative antibiotics reduce SSI risk compared with placebo after breast cancer surgery (6 trials, 1708 participants; RR 0.74, 95% CI 0.56 to 0.98; high-certainty evidence - assessed by overview authors). (3) Antibiotic prophylaxis probably reduce SSI risk in caesarean sections compared with no antibiotics (82 relevant trials, 14,407 participants; RR 0.40, 95% CI 0.35 to 0.46; moderate-certainty evidence; downgraded once for risk of bias - assessed by review authors). (4) Antibiotic prophylaxis probably reduces SSI risk for hernia repair compared with placebo or no treatment (17 trials, 7843 participants; RR 0.67, 95% CI 0.54 to 0.84; moderate-certainty evidence; downgraded once for risk of bias - assessed by overview authors); (5) There is currently no clear difference in the risk of SSI between iodine-impregnated adhesive drapes compared with no adhesive drapes (2 trials, 1113 participants; RR 1.03, 95% CI 0.66 to 1.60; moderate-certainty evidence; downgraded once for imprecision - assessed by review authors); (6) There is currently no clear difference in SSI risk between short-term compared with long-term duration antibiotics in colorectal surgery (7 trials; 1484 participants; RR 1.05 95% CI 0.78 to 1.40; moderate-certainty evidence; downgraded once for imprecision - assessed by overview authors). There was only one comparison showing negative effects associated with the intervention: adhesive drapes increase the risk of SSI compared with no drapes (5 trials; 3082 participants; RR 1.23, 95% CI 1.02 to 1.48; high-certainty evidence - rated by review authors).

Authors' conclusions

This overview provides the most up-to-date evidence on use of intraoperative treatments for the prevention of SSIs from all currently published Cochrane Reviews. There is evidence that some interventions are useful in reducing SSI risk for people undergoing surgery, such as antibiotic prophylaxis for caesarean section and hernia repair, and also the timing of prophylactic intravenous antibiotics administered before caesarean incision. Also, there is evidence that adhesive drapes increase SSI risk. Evidence for the many other treatment choices is largely of low or very low certainty and no quality-of-life or cost-effectiveness data were reported. Future trials should elucidate the relative effects of some treatments. These studies should focus on increasing participant numbers, using robust methodology and being of sufficient duration to adequately assess SSI. Assessment of other outcomes such as mortality might also be investigated as part of non-experimental prospective follow-up of people with SSI of different severity, so the risk of death for different subgroups can be better understood.

PLAIN LANGUAGE SUMMARY

Overview of Cochrane Reviews of interventions used during surgery for preventing surgical site infection

What is the aim of this overview of reviews?

To identify and summarise all evidence from Cochrane Reviews on interventions to prevent surgical site infections (SSIs) that are delivered while surgery is taking place (during the intraoperative period).

Key messages

We cannot be certain about the effectiveness in preventing SSI of the majority of intraoperative interventions, as we judged the certainty of the evidence to be generally low or very low. In some circumstances (listed below), antibiotics were effective for the prevention of SSI. There is no high- or moderate-certainty evidence for the relative effects of intraoperative interventions on mortality, and no data at all for quality of life or costs. For these reasons, we cannot be certain whether these antibiotics, which are effective at preventing SSI, have any negative effects on mortality or quality of life. Larger trials with appropriate methods are needed to measure the outcomes that are important to both patients and health professionals.

What was studied in the overview?

If bacteria get into a surgical cut during surgery, this can result in a wound infection commonly called an SSI. SSIs are one of the most common forms of healthcare-associated infections, with around 1 in 20 surgical patients developing an SSI in hospital. SSIs can also develop after people have left hospital. SSIs can result in delayed wound healing, increased hospital stays, increased use of antibiotics, unnecessary pain and, in extreme cases, death. Their prevention is therefore a key aim for health services. Many interventions are used to reduce the risk of SSI in people having surgery. These interventions can be delivered at three stages: before, during and after the operation.

It is therefore important to identify interventions that can reduce the incidence of SSIs. This overview focuses only on interventions delivered during surgery.

What are the main results of the overview?

In July 2017 we searched for Cochrane Reviews involving interventions for preventing SSIs during surgery. We found a total of 32 Cochrane Reviews that could be included in this overview. Two reviews had no relevant data to extract so we extracted data from 30 reviews with 349 included trials, totaling 73,053 participants. Interventions assessed included use of disposable face masks and surgical gloves, the use of oxygen during surgery, antiseptics for hand washing, patient skin preparation and cleaning the vagina before caesarean section, methods of surgical incision and skin closure and use of antibiotics to prevent infection.

Evidence of at least moderate certainty indicates that the following interventions reduce SSI risk: (1) antibiotics administered via drip before caesarean incision reduce SSI risk compared with administration after cord clamping (high-certainty evidence); (2) giving antibiotics before surgery reduces SSI risk compared with placebo after breast cancer surgery (high-certainty evidence); (3) antibiotics used to prevent wound infections probably reduce SSIs for caesarean section compared with no antibiotics (moderate-certainty evidence); (4) antibiotics used to prevent wound infections probably reduce SSI risk for hernia repair compared with placebo or no treatment (moderate-certainty evidence); (5) iodine-impregnated adhesive drapes probably make no difference to SSI risk compared with no adhesive drapes (moderate-certainty evidence); (6) there is probably no difference in SSI risk when antibiotics are given in the short-term compared to the long-term during colorectal surgery (moderate-certainty evidence). One comparison showed that adhesive drapes increase the SSI risk compared with no drapes (high-certainty evidence). Overall, we judged the certainty of evidence for our primary outcomes (SSIs and death) to be low or very low.

Clinicians can use the evidence summarised in this overview to choose the best intervention for people having surgery. However, many of the comparisons were supported by low- or very low-certainty evidence and so require further evidence to support future decision making. This overview can also be used by policymakers in developing local and regional protocols or guidelines and can reveal knowledge gaps for future research.

How up to date is this overview?

We searched for reviews that had been published up to July 2017. Of the 32 reviews included in this overview, 13 reviews had not been updated in the past three years.

BACKGROUND

Description of the condition

Millions of surgical procedures are conducted around the world each year. Most procedures result in surgical wounds that heal by primary intention, where wound edges are re-approximated using sutures, staples, clips or glue. Some surgical wounds are left open to heal (where closure is not appropriate because of infection, physical impossibility of approximating wound edges or because of the need to allow drainage) and some wounds break down following closure; these open wounds heal from the 'bottom-up' (known as 'healing by secondary intention').

Surgical wounds are at risk from microbial contamination and thus possible infection. Contamination may originate from the patient, for example when microbes on the skin enter a wound, or from the surrounding environment, for example from operating staff, the theatre, or wider hospital and home environments. SSIs are relatively common: a recent US study with assessment in 183 hospitals involving 11,282 patients found that 452 people (4%) developed hospital-acquired infection; of these, 21.8% were SSIs (Magill 2014). Similar SSI incidence estimates have been reported in France (Astagneau 2009). In the UK around 2% to 5% of surgical patients develop SSIs (NICE 2008; Public Health England 2014) although the percentage varies greatly depending on the circumstances, including the contamination level of the surgery. In England, a 2006 survey of hospital-acquired infections reported that 8% of patients in hospitals had an infection while an inpatient, of which 14% were considered SSIs (Hospital Infection Society 2007; Smyth 2008). Many quoted incidence estimates for SSI are likely to be underestimates because infections that developed outside hospitals were not considered (Bruce 2001; Gibbons 2011). While more data are available for Western healthcare settings, SSI was identified as the leading cause of hospital-acquired infection in a systematic review of studies in low- and middle-income countries (Allegranzi 2010).

SSI is a serious global issue that can lead to significant morbidity, need for re-intervention and treatment (including antibiotic use), delayed wound healing, and in very serious infections, the possibility of death (Awad 2012; Brown 2014; CDC 2017). SSIs also increase consumption of healthcare resources. Recent figures from the UK suggest that SSIs lead to a median increased hospital stay of 10 days (95% confidence interval (CI) 7 to 13 days) with an associated median additional cost attributed to SSI of GBP 5239 (95% CI GBP 4622 to 6719) (Jenks 2014). The UK National Institute for Health and Care Excellence (NICE) identified that an SSI increased the costs of surgery by two to five times (NICE 2008). In the USA, De Lissovoy 2009 estimated that the extended length of stay and increased treatment costs associated with SSIs over a one-year period led to approximately 1 million additional inpatient-days, costing an additional USD 1.6 billion.

SSI risk

A patient's overall physical health can predict the risk of SSI, as can the type of surgical procedure (in terms of potential for contamination) and duration of surgery. These factors are collectively included in the National Nosocomial Infections Surveillance risk index (Gaynes 2001; SWI Task Force 1992), which proposes three criteria to assess risk: American Society of Anesthesiologists (ASA) score of 3, 4, or 5 (ASA 2014); wound class (see below); and duration of surgery. Other risk factors for SSI are suggested; such as if surgery is elective or emergency, but supporting data for these risk factors are more limited.

Wound class

Wound class is assessed using the classification system adopted by the Centres for Disease Control and Prevention (HICPAC 1999).

- Clean: non-infective operative wounds in which no inflammation is encountered, and neither the respiratory, alimentary, genito-urinary tract nor the oropharyngeal cavity is entered. In addition these cases are elective, have primary closure, and wounds are drained with closed drainage systems when required.
- Clean/contaminated: operative wounds in which the respiratory, alimentary, genital or urinary tract is entered under controlled conditions and without unusual contamination. Specifically, operations involving the biliary tract, appendix, vagina and oropharynx are included in this category, provided no evidence of infection or a major break in sterile technique is encountered.
- Contaminated: fresh, accidental wounds, operations with major breaks in sterile technique or gross spillage from the gastro-intestinal tract, and incisions in which acute, non-purulent inflammation is encountered.
- Dirty: old traumatic wounds with retained devitalised (dead) tissue and those that involve existing clinical infection or perforated viscera (internal organs or gut). This definition suggests that organisms causing postoperative infection were present in the operative field before the operation.

In the UK data from 232 NHS hospitals on 620,535 surgical procedures reported SSI rates of: 0.5% for knee prosthesis; 1% for cardiac surgery (non-coronary artery bypass graft); 0.6% for hip prosthesis and 5% for limb amputation (all clean surgery) (Health Protection Agency 2015). This is in contrast to the incidence of SSI following surgery on the large bowel (contaminated surgery) of 9.7% (Health Protection Agency 2015). Europe-wide surveillance also reports higher incidence of SSI in colon surgery (9.5% of surgeries resulting in SSI) (ECDC 2013).

Definition of SSI

Although there is no single agreed diagnostic tool or protocol to confirm the presence of an SSI, (Bruce 2001 identified 41 different definitions for SSI and 13 grading scales), the Centers for Disease Control and Prevention (CDC) definition is commonly used (Horan 1992).

A superficial SSI is defined as: "an infection occurring within 30 days after the operation and only involving the skin and subcutaneous tissue of the incision that is associated with at least one of the following:

- purulent drainage, with or without laboratory confirmation, from the surgical site;
- organisms isolated from an aseptically-obtained culture of fluid or tissue from the surgical site;
- 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 the surgeon and is

culture-positive or not cultured. A culture-negative finding does not meet this criterion;
- diagnosis of SSI by the surgeon or attending physician."

A deep incisional SSI is defined as: "infection that occurs within 30 days after the operative procedure if no implant is left in place, or within one year if an implant is left in place, and the infection appears to be related to the operative procedure *and* involves deep soft tissues (e.g. fibrous connective tissues and muscle layers) of the incision associated with one of the following:

- purulent drainage from the deep incision, but not from the organ/space component of the surgical site;
- a deep incision spontaneously dehisces (opens up) or is deliberately opened by the surgeon and is culture-positive or not cultured when the patient has at least one of the following symptoms: fever or localised pain or tenderness;
- an abscess, or other evidence of infection involving the deep incision is found on direct examination, during re-operation, or by histopathologic or radiologic examination;
- diagnosis of a deep incisional SSI by a surgeon or attending physician."

Description of the interventions

Many interventions are used with the aim of reducing the risk of SSI in people undergoing surgery. These interventions can be delivered at three stages: preoperatively, intraoperatively and postoperatively (Goodman 2017). For the purpose of this review we define:

- the preoperative phase as the time period between the decision for the need for surgery and when everything is ready for the operation to start, that is, the patient is on the operating table (for this review we have assumed that staff are ready to proceed with surgery at this point - thus the preparation of operative staff occurs in this preoperative period);
- the intraoperative phase is the time period from when the patient is on the operating table to when the operation has finished and the wound is closed (if relevant). We consider any activity taking place after induction of anaesthesia to be in this phase because this starts in the operating theatre itself. For this review, where it is clear that antibiotics were given very soon before the incision, we consider this to be intraoperative, that is, prophylactic intravenous antibiotics administered less than 60 minutes before surgery;
- the postoperative phase as the time period from the end of the intraoperative phase to resolution of surgical procedure (which we acknowledge could take several, weeks or months for some patients). We note that whilst dressings, wound drains and negative pressure wound therapy are often placed over wounds at the end of surgery, their use is predominantly outside of theatre, so they are considered in the postoperative phase.

Table 1 details key intervention types used at each stage of the operative pathway, but is not an exhaustive list. Most interventions listed are probably independent of each other and would generally be delivered concurrently. However, the interventions listed could also be grouped together as a care bundle, where a care bundle is defined as a group of three to five evidence-based interventions that are delivered together.

This overview of reviews will focus on interventions delivered in the intraoperative phase.

How the intervention might work

See Table 1. The interventions are largely focused on decontamination of skin using soap and antiseptics; the use of barriers to prevent movement of micro-organisms into wounds; and optimising the patient's own bodily functions to promote best recovery. Both decontamination and barrier methods can be aimed at people undergoing surgery and operating staff. Other interventions focused on SSI prevention may be aimed at the surgical environment and include methods of theatre cleansing and approaches to theatre traffic (i.e. how the movement of staff in and out of theatre is managed).

Why it is important to do this overview

The *Cochrane Handbook for Systematic Reviews of Interventions* describes a Cochrane overview of reviews as being "intended primarily to summarize multiple Cochrane Intervention reviews addressing the effects of two or more potential interventions for a single condition or health problem" (Becker 2011).

SSIs are a prevalent problem for global healthcare and their prevention is a major focus for healthcare providers internationally. There are several Cochrane Reviews that draw together randomised controlled trial evidence for individual interventions for the prophylaxis of SSIs along the preoperative, intraoperative and postoperative pathway. Findings from these reviews have not been collated, so a transparent and usable synthesis of this evidence is required. This overview will aid decision makers aiming to draw together Cochrane evidence that spans the SSI prevention pathway. It will also be a useful resource for guideline developers, especially for the key NICE guidelines, which have not been fully updated for several years (NICE 2008). (A planned update of the guidelines was announced in 2017.) This overview will also complement other guidelines such as those produced by the World Health Organization (Allegranzi 2016a; Allegranzi 2016b).

OBJECTIVES

To present an overview of Cochrane Reviews of the effectiveness and safety of interventions delivered during the intraoperative period aimed at preventing SSIs in all populations undergoing surgery in an operating theatre.

METHODS

Criteria for considering reviews for inclusion

Types of studies

We included reviews published in the *Cochrane Database of Systematic Reviews* that examine the effectiveness of interventions aimed at preventing SSIs. We did not consider non-Cochrane reviews. We only included systematic reviews of randomised controlled trial (RCT) evidence for patient-focused interventions. If reviews included other study designs alongside RCTs (e.g. controlled clinical trials, quasi-randomised controlled trials, or both) we only investigated if RCT evidence was presented separately for relevant analyses (e.g. as sensitivity analyses). If so, these RCT data were included. If there were no separate data for RCTs in a review of patient-focused interventions we did not include

that review in analyses. Primary RCTs published since the included reviews, but not yet included in reviews, were excluded in line with Cochrane guidance.

Where studies evaluated service-level interventions e.g. protective staff coverings, theatre traffic and environmental cleansing, designs such as interrupted time series and controlled before and after studies were more feasible and we also extracted data from these study designs as well as from RCTs (including cluster RCTs).

Types of participants

We included reviews of studies involving adults or children or both. We excluded reviews where inclusion criteria specified that study participants had infected wounds at baseline (i.e. treatment rather than prevention reviews). Reviews that considered both treatment and prevention studies were examined in detail to isolate relevant comparisons.

We included reviews of participants undergoing surgery of any contamination level (clean, clean/contaminated, contaminated and dirty). Reviews focused solely on graft sites and wounds of the mouth and eye were excluded. We included reviews looking at surgical wounds planned to heal by primary intention (closed wounds) and secondary intention (open wounds). Given their specialist nature, we excluded eye and oral surgeries and studies looking at infection prevention in pin sites.

Types of interventions

We included reviews that assessed the following interventions aimed at preventing SSIs during the intraoperative period of the patient care pathway (regardless of comparator - all were eligible):

- decontamination of patients' skin at site of surgery incision;
- use of intraoperative prophylactic antibiotics;
- skin sealants;
- use of standard and incise drapes;
- use of masks, hair covers, overshoes, gowns and other protective coverings for theatre staff;
- different glove protocols;
- use of electrosurgery for surgical incisions;
- maintaining patient homoeostasis (warming);
- maintaining patient homoeostasis (oxygenation);
- maintaining patient homoeostasis (blood glucose control);
- wound irrigation and intracavity lavage (including use of intraoperative topical antiseptics before wound closure);
- closure methods;
- theatre traffic (protocols for managing the movement of people in theatre).

We excluded reviews focusing on comparisons of different surgical approaches for the same surgery (e.g. different techniques for inguinal surgical repair; open versus closure of perianal wounds) or other interventions specific to certain types of surgery or procedures. We also excluded studies comparing different anaesthesiology regimens and those investigating the use of implants or internal devices.

Where interventions were delivered at multiple time periods in the same studies, such as for assessment of antibiotics where treatment was started in one phase and continued through multiple phases (e.g. antibiotics started preoperatively and continued postoperatively), data are presented in the overview that correspond with the start of the treatment. Thus this intraoperative overview includes reviews where the start of treatment was in the intraoperative phase. Where a review contained trials that variously delivered interventions at different starting phases, we aimed to extract and present data only for those trials relevant to the intraoperative phase (that is where the treatment started in the intraoperative phase).

Types of outcomes

We present data according to the time points used in reviews (if reported). Where possible, we grouped data into follow-up of 30 days or less and follow-up of more than 30 days. If a review presented data at many different time points, the overview authors reported data from the time points closest to 30 days and one year, noting where other time point data were available in the original review.

Primary outcome

SSIs

Occurrence of postoperative SSI as defined by the CDC criteria (Horan 1992), or the study authors' definition of SSI. Where available we present data that differentiated between superficial and deep-incisional infection.

Secondary outcomes

Mortality

All cause-postoperative mortality (e.g. we did not differentiate between infection-related mortality and other mortality from other causes).

Health-related quality of life

We included quality-of-life assessments where they were reported using a validated scale that presents a single global score (e.g. SF-12, SF-36 or EQ-5D) or a validated, disease-specific questionnaire. Ideally, reported data were adjusted for baseline scores. We did not include ad hoc measures of quality of life that were not likely to be validated and would not be common to more than one trial. We did not plan to report multiple domain scores from the same measure but rather to report only overall scores for instruments e.g. physical component summary score and mental component summary score for the SF-36.

Cost-effectiveness

Findings that considered relative costs and benefits simultaneously.

Search methods for identification of reviews

We searched the *Cochrane Database of Systematic Reviews* (CDSR) using the search strategy presented in Appendix 2. Given the large number of interventions relating to the review, the search terms focused on identification of reviews linked to SSI rather than to specific interventions. The search was undertaken on 01 July 2017 (CDSR 2017, Issue 7), after which we tracked any included reviews for updates, and followed protocols in case of full review publication until 25 July 2017 (CDSR 2017, Issue 7).

Data collection and analysis

Selection of reviews

Two overview authors independently screened review titles and abstracts to identify potentially relevant inclusions. We obtained the full text of all reviews thought to be potentially eligible for further investigation. The same two overview authors independently screened the full text of all potentially relevant resources for inclusion in the overview. We recorded reasons for exclusion of any reviews excluded at this stage. Any disagreements were resolved through discussion with a third overview author. Where overview authors were also authors of included reviews we sought to avoid bias by ensuring that decisions were made by two other overview authors.

Data extraction and management

We extracted data into a predefined and piloted data extraction form to ensure consistent data capture from each resource. Data were extracted by one overview author and independently checked by a second, with a third acting as arbiter where required. We extracted the following data for each included resource:

- study identification, review authors' details;
- review objectives;
- review inclusion and exclusion criteria;
- included settings;
- included populations, including types of surgery or procedure and depth of incision;
- all relevant comparisons and associated time points;
- concurrent intervention types that were the same for all intervention arms;
- numbers of relevant included RCTs;
- outcomes reported and details of reported outcome values;
- method and results of risk of bias and evidence quality assessment;
- GRADE assessments;
- details of any subgroup and sensitivity analyses.

Where a comparison was included in more than one review, we recorded the details multiple times (because it was relevant to each review in which it was contained). However, we reported the comparison only once for the review with the lowest risk of bias, or the most recent review if there was no difference in risk of bias assessment. We extracted meta-analysed data where possible and single study data when pooled data were not available: we extracted effect sizes with 95% confidence intervals where possible. We also extracted contextual information to enable narrative descriptions of how data were pooled (or not) presented per comparison (e.g. if some trials had been pooled for a comparison and some had not). If any information from a review was unclear or missing, we accessed the published reports of the individual trials. We did not contact study authors for details of missing data, but rather assumed that review authors had done all they could to retrieve data. We entered data into Review Manager 5 software (RevMan 2014).

Assessment of methodological quality of included reviews

Quality of included Cochrane Reviews

We used the risk of bias in systematic reviews (ROBIS) tool (Whiting 2016) to assess the risk of bias in systematic reviews. ROBIS assesses reviews in three phases: first, assessing relevance (optional); second, identifying concerns with the review process; and third, forming an overall judgement of the risk of bias. In the second phase, concerns with the review process fall into four domains: (1) study eligibility criteria; (2) identification and selection of studies; (3) data collection and study appraisal; and (4) synthesis and findings. Each domain contains a list of signalling questions to guide the bias assessment process. The signalling questions can be answered yes, probably yes, probably no, no or no information. Questions are worded so that a yes response relates to low concerns about the review e.g. "Did the review adhere to pre-defined objectives and eligibility criteria? and were the eligibility criteria appropriate for the review question?" At the end of each domain the assessor draws together their appraisal to indicate their concerns regarding: specification of study eligibility (domain 1); methods used to identify and select studies, or both (domain 2); methods used to collect data and appraise studies (domain 3); and the synthesis and findings (domain 4). Concerns can be graded low, high or unclear. We recorded the rationale or reasoning for decisions at each stage, that is for the signalling questions and the level of concern rated, in a table for each domain. As this overview only included Cochrane Reviews and relevance was considered as part of our screening and selection process, we did not assess relevance using the ROBIS tool (an optional first phase). Two reviewers (ZL and JD) assessed each review independently, without blinding, using a previously piloted standardised form based on the ROBIS Guidance Document and consulted each other to resolve any discordance and to compile a consensus judgment for each domain. We presented a summary of ROBIS results for each review using table format, which lent itself to presentation of data for a large number of reviews.

Quality or certainty of evidence extracted from included reviews

It is important to present the quality or certainty of evidence from each review. We present a GRADE assessment for each eligible outcome and comparison. Where GRADE assessment was conducted in the review we extracted this assessment; however, where GRADE assessments were not available, the overview authors undertook assessment (making it clear that they had conducted the GRADE assessment post hoc).

When making decisions for the risk of bias domain, we downgraded one level when studies had been classified at high risk of bias for one or more domains and where they were classified at unclear risk of bias for both domains that contributed to selection bias, or both.

In assessing the precision of effect estimates for SSI we followed GRADE guidance (GRADE 2013; Schünemann 2011a; Schünemann 2011b). We planned to take a conservative approach and calculated an optimal information size (OIS) for the SSI outcome using conventional sample size calculation methods and assuming a relative risk reduction of between 20% and 30% (Guyatt 2011). The OIS is summarised below but should not be treated as an optimal sample size for any future research. In GRADE assessments, the OIS is used to assess the stability of confidence intervals (CI) rather than to assess the appropriateness of a sample size to detect a difference *per se*.

Reduction in SSI from 14% to 10% (80% power; alpha 5%) = 2070 participants overall. Although on average, SSI rates are lower than 14% in many high-income countries, they can be higher in some countries and figures vary by SSI risk of the patient. We took 14% as a conservative upper estimate of SSI incidence and calculated 40% relative risk reduction.

We used the GRADE default minimum overall sample size for dichotomous outcomes of 300 in lieu of the OIS to assess precision for mortality.

If the OIS was not met we downgraded one level. We downgraded two levels if there were very few events (or very few participants for continuous outcomes). If the OIS was met we downgraded one level if the 95% CI failed to exclude important benefits and harms, which we considered as a relative risk reduction or increase of 25%.

Judgement of GRADE certainty was agreed through discussion involving at least two overview authors and involving additional overview authors where there were disagreements.

Data synthesis

The aim of this review is to present a detailed summary of treatment-effect data for interventions aimed at SSI prevention. We present all relevant comparisons grouped by intervention type (including details of co-interventions when recorded). We also considered data according to the contamination level of surgery where possible. We use tabular formats to present summaries of treatment effects with a corresponding GRADE assessment for each comparison. Where possible we extracted meta-analysed data, along with details of model type and measures of statistical heterogeneity. Where data had not been meta-analysed we report study-level treatment effects. Results from review subgroup and sensitivity analyses are also presented. We present all data in tabular, meta-analysis or narrative formats.

Where applicable, we converted available data to risk ratios (RR). Where this was not possible we present original data. We had planned not to undertake re-analysis of data beyond conversions to RR. However, due to the inclusion of multi-stage reviews (reviews that evaluated interventions at different points on the care pathways, i.e. pre-, intra- or postoperative, or a combination of these) we extracted data on only trials where the intervention was started in the intraoperative phase. Where it seemed appropriate for each comparison, the overview authors meta-analysed these subsets of trials. We have cautiously pooled these data into a new meta-analysis relevant to this overview of reviews, reporting the results as RR with 95% CI (again, if the subsets of trials were reported as odds ratios (OR), we converted available data to RR). We did not plan to undertake a network meta-analysis within given intervention types.

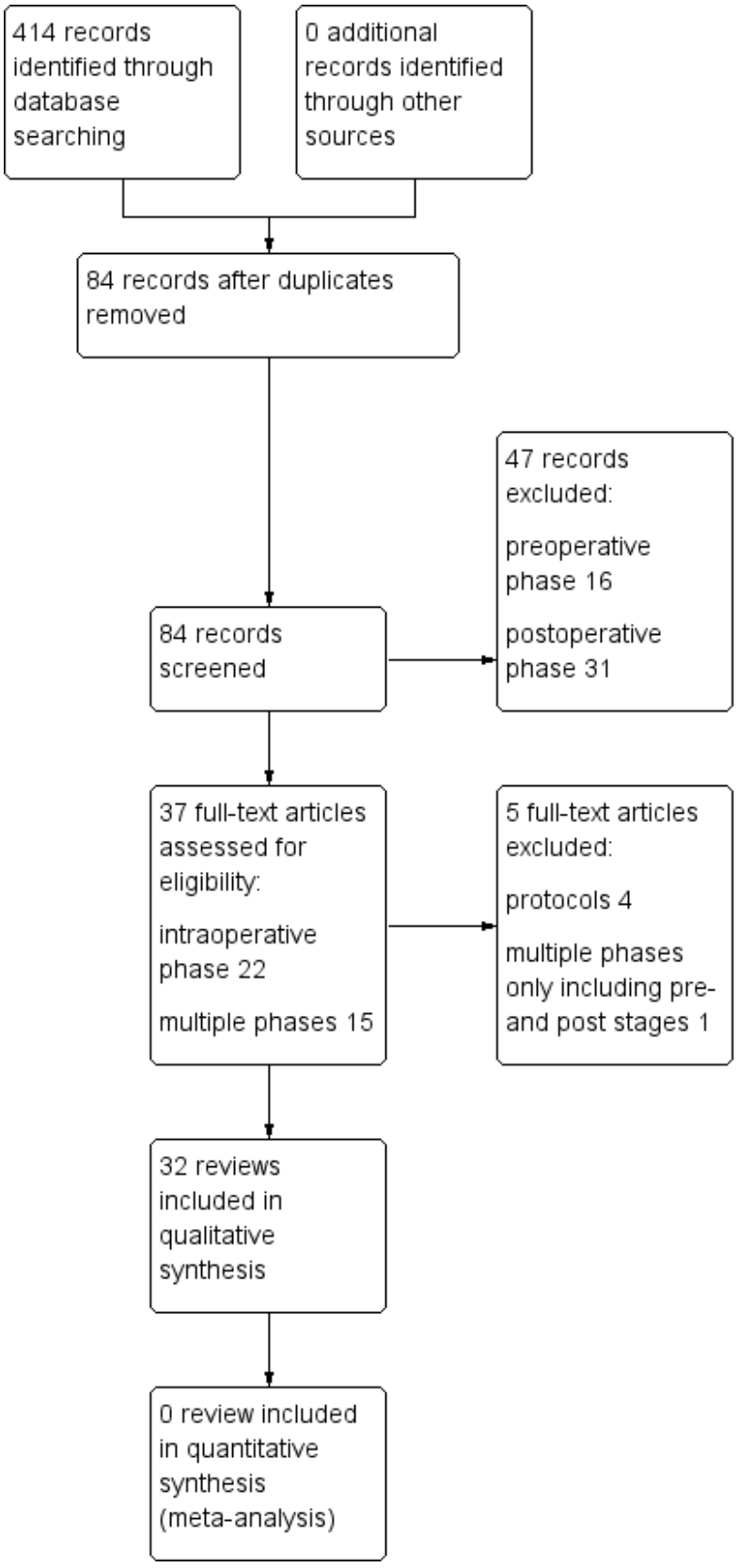
RESULTS

See Characteristics of included reviews Table 2; Characteristics of excluded reviews Table 3.

Description of included reviews

The search generated 414 records 330 of which we excluded based on the title and abstract, and 84 of which we assessed as full text. Of these, 32 reviews were eligible for this review (See Table 2; Figure 1). Of the included reviews:

Figure 1. Study flow diagram



- two focused on theatre staff attire (Tanner 2006; Vincent 2016);

- five focused on the preparation of the surgical site (Dumville 2015; Hadiati 2014; Haas 2014; Webster 2015; Wood 2016).
- two focused on the method of surgical incision (Charoenkwan 2017; Cook 2014).
- five focused on patient homeostasis during surgery (Buchleitner 2012; Campbell 2015; Grocott 2012; Kao 2009; Wetterslev 2015). Of these, two were multi-stage reviews (that is they included trials evaluating intraoperative interventions as well as pre- or postoperative interventions, or both). In these reviews we extracted the relevant trials focusing on intraoperative intervention delivery for this review) (Buchleitner 2012; Grocott 2012).
- 12 reviews focused on the use of intraoperative prophylactic antibiotics for preventing SSIs (Gurusamy 2011; Gurusamy 2013; Gyte 2014; Jones 2014; Lipp 2013; Low 2012; Mackeen 2014; Nabhan 2016; Nelson 2014;Sanabria 2010; Sanchez-Manuel 2012; Smaill 2014). Most of these were multi-stage reviews and again, we extracted only data from trials delivering interventions that started in the intraoperative phase.
- six reviews focused on interventions for wound closure (AL-Khamis 2010; Biancari 2010; Dumville 2014; Gurusamy 2014a; Gurusamy 2014b; Mackeen 2012).

SSI was reported in 75% (24/32) of the included reviews; mortality was reported in 19% (6/32) and health-related quality of life or cost-effectiveness were not reported in any included review. Six per cent (2/32) of the reviews, reported no outcome data relevant to this overview (Campbell 2015; Low 2012). In total we extracted data from 30 reviews with 349 included trials, totaling 73,053 participants. We present SSI outcome data for 77 comparisons and mortality data for nine comparisons.

Of the 52 excluded full-text reviews, 48 focused on interventions only relating to the pre- or postoperative phase (or both) and four titles were at the protocol stage only (see Table 3; Figure 1).

Methodological quality of included reviews

ROBIS quality of included reviews

We rated the quality of included reviews using the ROBIS tool signalling questions (Table 4; detailed assessments by signalling questions are shown in Appendix 3) presenting the overall 'Risk of bias' assessment results for each review in Table 4.

Our judgements of the four domain assessment findings were as follows:

- we judged study eligibility to be at low concern for all included reviews;
- we judged the process of study identification and selection to be at low concern for all included reviews;
- for data collection and study appraisal, we judged 91% of included reviews to be at low concern. We deemed study quality not fully assessed in four studies (Cook 2014; Low 2012; Tanner 2006; Vincent 2016) and we judged these as unclear;
- for synthesis and findings, we judged 97% (31/32) of included reviews to be at low concern due to the synthesis being unlikely to produce biased results. Only one review (Cook 2014) did not consider clinical diversity across studies and bias was not explicitly addressed in the synthesis; we judged this review at high concern.

Overall risk of bias

We considered issues around risk of bias in all reviews. In terms of the overall 'Risk of bias' assessment, we judged 94% (30/32) of reviews to be at low risk of bias.

Quality of evidence in included reviews

Of the 32 included reviews, 31% (10/32) reported a GRADE assessment for the SSI outcome, whilst only one review (3%) reported a GRADE assessment for the mortality outcome. No other GRADE assessments were reported in the included reviews.

The overview authors undertook GRADE assessment of relative treatment-effect data where no review-level GRADE assessment was available. Overall, the GRADE certainty of evidence was low or very low, as summarised in Table 5. Of the 77 comparisons presenting SSI data, we judged 51% (39/77) as low certainty and 40% (31/77) as very low certainty. Of the nine comparisons presenting mortality data, we judged 56% (5/9) as being at low certainty and 44% (4/9) as very low. Common reasons for downgrading the certainty of evidence were risk of bias of included studies, imprecision and inconsistency.

Effect of interventions

Analysis of results

A detailed presentation of relative treatment-effect data and GRADE assessments for all individual comparisons are in Table 5 and Table 6. Below we present a narrative summary of key findings in an order of the process of the surgery.

Where included reviews contained trials investigating only intraoperative phase interventions, we interpreted results using data reported in the review, and did not return to the original studies. Where data were reported as RR, with or without 95% CIs, we used the results directly from the reviews. Where data were reported as OR, we converted data to RR if appropriate. When the evidence was of very low certainty, we did not report RR in the main text but we did clarify RR (or original OR) in Table 5 and Table 6.

When reviews were multi-stage, that is they contained studies that variously started interventions at the pre-, intra- or postoperative stage (e.g. Antimicrobial prophylaxis for colorectal surgery (Nelson 2014)) we extracted data only for the trials relevant to this overview and reported cautious re-analysis of these extracted trials (see Data synthesis). Such re-analyses have been clearly marked in Table 5 and Table 6.

We present results by review, following an order relevant to the clinical pathway. We have made it clear that where general details of surgery were available we have reported these. Where there is a lack of detail this reflects the lack of information in the initial review. Further, we did not group the outcomes into follow-up of 30 days or less and follow-up of more than 30 days, as these time points were not recorded by the original reviews when the review authors did the meta-analysis.

1. Theatre staff attire

Two reviews investigated theatre staff attire interventions:

1.1. Double gloving for preventing SSIs

Tanner 2006 included two trials (125 participants) that compared double latex gloving with double latex gloving with a liner in a single comparison, however neither trial reported any SSI events (low-certainty evidence; downgraded twice for imprecision - assessed by overview authors).

No other outcome data relevant to the overview were reported.

1.2. Disposable face masks for preventing SSIs

Vincent 2016 included three trials (2106 participants) that compared disposable face mask use with no mask in a single comparison. Due to clinical heterogeneity, the review did not pool data.

SSI

Available trial evidence reports no clear difference in SSI risk following use of disposable face masks compared with no mask (low-certainty evidence; downgraded for once for imprecision and once for inconsistency - assessed by overview authors).

No other outcome data relevant to the overview were reported.

2. Preparation of the surgical site

Six reviews reported interventions used to prepare the surgical site.

2.1. Skin antiseptics for preventing SSIs after clean surgery

Dumville 2015 included 13 trials (2623 participants in total) and evaluated a large number of different interventions , resulting in 12 comparisons of different types of skin antiseptic solutions and scrubs on SSI risk.

SSI

Available evidence largely reports no clear difference between different types of skin antiseptics on SSI risk. The certainty of evidence for the majority of these comparisons was low or very low. Data from one trial (542 participants) suggested that 0.5% chlorhexidine in methylated spirit may reduce SSI risk compared with povidone iodine paint (RR 0.47, 95% CI 0.27 to 0.82; low-certainty evidence; downgraded once for risk of bias and once for imprecision - assessed by overview authors). The review also grouped interventions together in an analysis based on whether treatments were aqueous or alcoholic. Data from six trials (1400 participants) showed no clear difference between aqueous solutions and alcoholic solutions (RR 0.77, 95% CI 0.51 to 1.17; low-certainty evidence; downgraded once for risk of bias and once for imprecision - assessed by overview authors).

No other outcome data relevant to the overview were reported.

2.2. Skin preparation following caesarean section for preventing SSIs

Hadiati 2014 included five trials (1466 participants in total) and presented four different comparisons: one comparing drapes with no drapes (two trials with 1294 participants) and three (172 participants) comparing different skin antiseptics.

SSI

Available trial evidence reports no clear difference between compared treatments on SSIs risk (low- and very low-certainty evidence; variously downgraded once for risk of bias and once or twice for imprecision - assessed by overview authors).

No other outcome data relevant to the overview were reported.

2.3. Vaginal preparation with antiseptic solutions for preventing SSIs

Haas 2014 included six trials (2205 participants) that compared antiseptic solutions with placebos in a single comparison.

SSI

Available trial evidence reports no clear difference between compared treatments on SSI risk (low-certainty evidence; downgraded once for risk of bias and once for imprecision - assessed by review authors).

No other outcome data relevant to the overview were reported.

2.4. Plastic adhesive drapes for preventing SSIs

Webster 2015 included seven trials (4195 participants in total) and presented two comparisons.

SSI

The first comparison compared adhesive drapes with no drapes (five trials, 3082 participants) and found that use of adhesive drapes was associated with an increase in SSI risk (RR 1.23, 95% CI 1.02 to 1.48; high-certainty evidence - assessed by review authors). The second comparison compared iodine-impregnated adhesive drapes with no adhesive drapes (two trials; 1113 participants). Available trial evidence reports no clear difference in SSI risk (RR 1.03, 95% CI 0.66 to 1.60; moderate-certainty evidence; downgraded once for imprecision - assessed by review authors).

No other outcome data relevant to the overview were reported.

2.5. Microbial sealants for preventing SSIs

Wood 2016 included seven trials (859 participants in total) that compared application of cyanoacrylate microbial sealants with no microbial sealant in a single comparison.

SSI

Available trial evidence shows no clear difference in SSI risk between treatments (RR 0.53, 95% CI 0.24 to 1.18; low-certainty evidence; downgraded once for risk of bias and once for imprecision - assessed by overview authors).

No other outcome data relevant to the overview were reported.

3. Making the surgical incision

3.1. Scalpel versus electrosurgery for major abdominal incisions

Charoenkwan 2017 included 11 trials (2178 participants) comparing scalpel with electrosurgery in a single comparison.

SSI

Available trial evidence reports no clear difference between compared treatments on SSI risk (RR 1.07, 95% CI 0.74 to 1.54; low-certainty evidence; downgraded for risk of bias and imprecision - assessed by review authors).

No other outcome data relevant to the overview were reported.

3.2. Scalpel versus no-scalpel incision for vasectomy

Cook 2014 included two trials (1182 participants in total) that compared scalpel versus no-scalpel incision for vasectomy. As these two trials differed in their duration of follow-up and the level of operator experience with the no-scalpel technique, the review did not pool data.

SSI

It is uncertain whether no-scalpel incision reduces SSI risk (very low-certainty evidence; downgraded once for risk of bias, once for imprecision and once for heterogeneity - assessed by overview authors). Based on ROBIS, we assessed this review as being at unclear risk of bias because it used a limited 'Risk of bias' assessment process; and also due to the lack of information about data synthesis. The review authors did not state why synthesis was done for only some of their outcomes.

No other outcome data relevant to the overview were reported.

4. Treatment of the patient during surgery

4.1. Warming of intravenous and irrigation fluids

Campbell 2015 included 24 studies (1250 participants in total). No outcome data relevant to the overview were reported.

4.2. Intensive glycaemic control for preventing SSIs

Buchleitner 2012 included 12 trials (1403 participants in total). We categorised only two included trials (105 participants) as delivering interventions that started in the intraoperative phase.

SSI

We considered the reported outcome, 'infectious complications' to be synonymous with SSIs and pooled the data from these two trials (105 participants). It is uncertain whether intensive glycaemic control reduces SSI risk when compared with conventional glycaemic control (RR 0.71, 95% CI 0.22 to 2.26; very low-certainty evidence; downgraded twice for imprecision and once for inconsistency - assessed by overview authors).

Mortality

We pooled the data from two trials (105 participants). It is uncertain whether intensive glycaemic control reduces mortality risk compared with conventional glycaemic control (RR 1.23, 95% CI 0.18 to 8.43; very low-certainty evidence; downgraded twice for imprecision, once for inconsistency - assessed by overview authors).

No other outcome data relevant to the overview were reported.

4.3. Perioperative glycaemic control regimens for preventing SSIs

Kao 2009 included five trials (743 participants in total). We categorised only three included trials (589 participants) as delivering interventions that started in the intraoperative phase.

SSI

Evidence from one trial (78 participants) showed no clear difference in SSI risk when applying intra- and postoperative strict glycaemic control (using intravenous insulin) compared with conventional glycaemic control (RR 0.48, 95% CI 0.04 to 5.03; low-certainty evidence; downgraded twice for imprecision - assessed by overview authors). One trial (371 participants) showed no clear difference when applying strict intraoperative glycaemic control (using insulin infusion) with conventional glycaemic control (RR 0.86, 95% CI 0.30 to 2.52; low-certainty evidence; downgraded twice for imprecision - assessed by overview authors). Another trial (140 participants) reported outcomes for pneumonia and wound infections and we did not consider these data. Due to variation in SSI outcomes we did not pool these trials in this overview.

Mortality

Evidence from 1 trial (78 participants) showed no clear difference in overall mortality risk when applying intra- and postoperative strict compared with conventional glycaemic control (RR 0.81, 95% CI 0.30 to 2.20; low-certainty evidence; downgraded twice for imprecision - assessed by overview authors). Similarly, another trial (371 participants) showed no clear difference when applying intraoperative strict compared with conventional glycaemic control (RR 9.05, 95% CI 0.49 to 166.88; low-certainty evidence; downgraded twice for imprecision - assessed by overview authors). The potential for harm represented in the imprecision reported is important to acknowledge here.

No other outcome data relevant to the overview were reported.

4.4. Increased global blood flow for preventing SSIs

Grocott 2012 included 31 trials (5292 participants in total). We categorised 15 included trials (1202 participants) as delivering interventions that started in the intraoperative phase.

SSI

Five included trials (353 participants) reported SSI data, which we pooled. Increased global blood flow (e.g. fluids and/or inotrope; oesophageal doppler) may reduce SSI risk compared with no treatment (RR 0.40, 95% CI 0.19 to 0.82; low-certainty evidence; downgraded once for imprecision and once for inconsistency - assessed by overview authors).

Mortality

Fifteen relevant trials (1202 participants) reported mortality and we pooled these data. There was no clear difference in mortality risk following interventions to increase global blood flow compared with no treatment (RR 0.67, 95% CI 0.40 to 1.13; low-certainty evidence; downgraded twice for imprecision - assessed by overview authors).

No other outcome data relevant to the overview were reported.

4.5. High perioperative inspiratory oxygen fraction for preventing SSIs

Wetterslev 2015 included 28 trials (9330 participants in total). Of these, we categorised 15 included trials (7219 participants) as delivering interventions that started in the intraoperative phase.

SSI

Fifteen relevant trials (7219 participants) reported SSI data, which we pooled. There was no clear difference in SSI risk following use of 60% to 90% oxygen compared with 30% to 40% oxygen (RR 0.87, 95% CI 0.71 to 1.07; low-certainty evidence; downgraded once for risk of bias and once for inconsistency - assessed by overview authors).

Mortality

Eight relevant trials (4918 participants) in this review found no clear difference in mortality risk following use of 60% to 90% oxygen compared with 30% to 40% oxygen (RR 1.07, 95% CI 0.87 to 1.33; low-certainty evidence; downgraded once for imprecision and once for heterogeneity - assessed by overview authors).

No other outcome data relevant to the overview were reported.

5. Use of antibiotics

5.1. Antibiotic prophylaxis versus no prophylaxis for preventing infection after caesarean section

Smaill 2014 included 95 trials (more than 15,000 women). We categorised all the included trials as delivering interventions that started in the intraoperative phase. In these trials antibiotic treatment was continued postoperatively.

SSI

Eighty-two relevant trials (14,407 participants in total) reported SSI data presenting a single comparison of antibiotics with no antibiotics. Available trial evidence reports that antibiotic prophylaxis probably reduces SSIs (RR 0.40, 95% CI 0.35 to 0.46; moderate-certainty evidence; downgraded once for risk of bias - assessed by review authors).

No other outcome data relevant to the overview were reported.

5.2. Different classes of antibiotics given to women routinely for preventing SSI at caesarean section

Gyte 2014 included 31 RCTs (7697 participants in total).

SSI

There were 19 relevant included trials (3559 participants in total). Of these 17 trials specified the timing of administration, which we categorised as the intraoperative phase, while two trials did not specify the timing of administration. These trials reported SSI data presenting four comparisons of different antibiotic prophylaxis regimes, including single cephalosporin, cephalosporin drug combination, single penicillin and penicillin drug combinations. All comparisons found no clear difference in SSI risk between the different regimes used (low- or very low-certainty evidence; variously downgraded once or twice for risk of bias and imprecision - assessed by overview authors).

No other outcome data relevant to the overview were reported.

5.3. Antibiotic prophylaxis for the prevention of methicillin-resistant *Staphylococcus aureus* (MRSA)-related complications in surgical patients

Gurusamy 2013 included 12 trials (4704 participants in total). Of these, we categorised seven trials (3393 participants) as delivering interventions that started in the intraoperative phase. All these trials continued antibiotic treatment postoperatively.

SSI

Six trials (3294 participants in total) presented 11 comparisons of different prophylactic antibiotic regimens with each other, including pefloxacin, cefazolin, ertapenem, cefotetan, cefamendole, gentamycin, vancomycin, daptomycin, and cefuroxime. For all 11 comparisons there was no clear difference in SSI risk from use of one antibiotic prophylaxis regime compared with another (low- or very low-certainty evidence; variously downgraded for risk of bias and imprecision - assessed by overview authors). One trial (99 participants) compared antibiotic prophylaxis (co-amoxiclav or cefotaxime) with no antibiotic prophylaxis and showed that receiving antibiotic prophylaxis with co-amoxiclav (or cefotaxime if allergic to penicillin) may reduce SSI risk (RR 0.26, 95% CI 0.11 to 0.65; low-certainty evidence; downgraded twice for imprecision - assessed by overview authors).

Mortality

Two relevant trials reported mortality. One trial (99 participants) found no clear difference in mortality risk when using co-amoxiclav or cefotaxime compared with no antibiotic prophylaxis (RR 0.54, 95% CI 0.17 to 1.72; low-certainty evidence; downgraded twice for imprecision - assessed by overview authors). A second trial (884 participants) found no clear difference when using vancomycin compared with cefuroxime (RR 2.02, 95% CI 0.18 to 22.18; very low-certainty evidence; downgraded once for risk of bias and twice for imprecision - assessed by overview authors).

No other outcome data relevant to the overview were reported.

5.4. Prophylactic antibiotics for preventing SSIs after breast cancer surgery

Jones 2014 included 11 RCTs (2867 participants). Of these we categorised nine trials as delivering interventions that started in the intraoperative phase.

SSI

Nine trials (2739 participants in total) presented three comparisons of different prophylactic antibiotic regimens. For the comparison of antibiotics delivered immediately prior to surgery compared with placebo, we pooled data from six trials (1708 participants): the use of antibiotic reduced SSI risk (RR 0.74, 95% CI 0.56 to 0.98; high-certainty evidence - assessed by overview authors). We also pooled the data from two trials (987 participants) and the use of antibiotics immediately prior to surgery may reduce the risk of SSIs compared with no treatment (RR 0.48, 95% CI 0.28 to 0.82; low-certainty evidence; downgraded once for imprecision and once for inconsistency - assessed by overview authors). One trial (44 participants) compared perioperative antibiotics with no antibiotic and found that it is uncertain whether perioperative antibiotics reduce SSI risk (very low-certainty evidence; downgraded once for risk of bias and twice for imprecision - assessed by overview authors).

No other outcome data relevant to the overview were reported.

5.5. Systemic antimicrobial prophylaxis for preventing SSIs after percutaneous endoscopic gastrostomy (PEG)

Lipp 2013 included 13 RCTs (1637 participants in total) and we categorised all trials as delivering interventions that started in the intraoperative phase.

SSI

All trials reported peristomal infection as an outcome. A pooled analysis (by review authors) of 12 trials (1271 participants) found that prophylactic antibiotics may reduce the incidence of peristomal infection (RR 0.39, 95% CI 0.30 to 0.51; low-certainty evidence, downgraded twice for risk of bias - assessed by overview

authors). Another trial (334 participants) compared intravenous (IV) antibiotics with antibiotics via PEG but the review authors could not included it in the meta-analysis. The evidence reported that it was uncertain whether there was a difference in peristomal infection risk following treatment with systemic antibiotic (PEG) compared with systemic antibiotic (IV) (RR 0.70, 95% CI 0.30 to 1.65 very low-certainty evidence; downgraded once for risk of bias and twice for imprecision - assessed by overview authors).

No other outcome data relevant to the overview were reported.

5.6. Timing of intravenous prophylactic antibiotics for preventing SSIs undergoing caesarean delivery

Mackeen 2014 included 10 trials (5041 participants in total) and we categorised all trials as delivering interventions that started in the intraoperative phase.

SSI

This review compared prophylactic intravenous antibiotics administered before caesarean incision with administration after cord clamping in a single comparison. Available trial evidence reports caesarean antibiotic prophylaxis administered intraoperatively prior to incision reduced maternal SSIs (RR 0.59, 95% CI 0.44 to 0.81; high-certainty evidence - assessed by review authors).

No other outcome data relevant to the overview were reported.

5.7. Routes of administration of antibiotic prophylaxis for preventing infection after caesarean section

Nabhan 2016 included 10 trials (1354 participants in total). Of these we categorised seven trials (859 participants in total) as delivering interventions that started in the intraoperative phase.

SSI

Seven relevant trials (859 participants) reported SSI data. It is uncertain whether IV antibiotics reduce SSIs risk compared with irrigation (very low-certainty evidence; downgraded once for risk of bias and twice for imprecision - assessed by review authors).

No other outcome data relevant to the overview were reported.

5.8. Antibiotic prophylaxis for preventing SSIs in patients undergoing elective laparoscopic cholecystectomy

Sanabria 2010 included 11 trials (1664 participants in total). We categorised all included trials as delivering interventions that started in the intraoperative phase.

SSI

Eleven trials (1664 participants) reported SSI data presenting a single comparison of antibiotic prophylaxis with placebo or no prophylaxis. It is uncertain whether antibiotic prophylaxis reduces SSI risk in this comparison (very low-certainty evidence; downgraded twice for risk of bias and once for imprecision - assessed by overview authors).

No other outcome data relevant to the overview were reported.

5.9. Antibiotic prophylaxis for hernia repair

Sanchez-Manuel 2012 included 17 trials (7843 participants in total). We categorised all included trials as delivering interventions that started in the intraoperative phase.

SSI

Seventeen trials (7843 participants) reported SSI data presenting a single comparison of antibiotic prophylaxis with placebo or no treatment. Available trial evidence reports that antibiotic prophylaxis probably reduces SSI risk (RR 0.67, 95% CI 0.54 to 0.84; moderate-certainty evidence; downgraded once for risk of bias - assessed by overview authors). Based on ROBIS, however, we assessed this review as being at unclear risk of bias due to a limited risk of bias assessment processes being used. This means that the overview authors were unable to fully assess the risk of bias for all domains recognised in the current version of the Cochrane 'Risk of bias' tool. We have not downgraded further for this review-level issue.

No other outcome data relevant to the overview were reported.

5.10. Antimicrobial prophylaxis for preventing SSIs in colorectal surgery

Nelson 2014 included 260 trials (43,451 participants in total) and 68 different antibiotics. Of these, we categorised 22 included trials (3604 participants in total) as delivering interventions that started in the intraoperative phase.

SSI

Twenty-two trials (3604 participants) presented six comparisons of different antibiotic regimens or different routes of administration of antibiotic prophylaxis. For the comparison of antibiotic with no antibiotic/placebo, we pooled the data from five trials (405 participants) and found that antibiotic may reduce SSI risk (RR 0.25, 95% CI 0.16 to 0.41; low-certainty evidence; downgraded once for risk of bias and once for imprecision - assessed by overview authors).

For the comparison of duration of therapy, we pooled data from seven trials (1484 participants) and found probably no difference in SSI risk with short-term compared with long-term duration antibiotic (RR 1.05, 95% CI 0.78 to 1.40; moderate certainty evidence; downgraded once for imprecision - assessed by overview authors).

For the comparison of additional aerobic coverage, we pooled data from four trials (230 participants) and found that, with added aerobic coverage, an antimicrobial prophylaxis regimen may slightly reduce SSI risk compared with no additional aerobic coverage (RR 0.38, 95% CI 0.16 to 0.96; low-certainty evidence; downgraded once for risk of bias and once for imprecision - assessed by overview authors).

For the comparison of additional anaerobic coverage, we pooled data from four trials (1098 participants) and found that, with added anaerobic coverage, an antimicrobial prophylaxis regimen may slightly reduce SSI risk compared with no additional anaerobic coverage (RR 0.65, 95% CI 0.47 to 0.90; low-certainty evidence; downgraded once for risk of bias and once for imprecision - assessed by overview authors).

For the comparisons of the different routes of administration of antibiotics from one trial (72 participants), it is uncertain whether oral antibiotics reduce SSI risk compared with intravenous routes (RR 2.11, 95% CI 0.20 to 22.29; very low-certainty evidence, downgraded once for risk of bias and twice for imprecision - assessed by overview authors). Evidence from one trial (310 participants) showed no clear difference when applying combined oral and intravenous antibiotics compared with oral or intravenous antibiotics alone (RR 0.50, 95% CI 0.23 to 1.11; low-certainty evidence, downgraded once for risk of bias and once for imprecision - assessed by overview authors).

No other outcome data relevant to the overview were reported.

5.11. Methods of decreasing infection to improve outcomes after liver resections

Gurusamy 2011 included seven trials (521 participants in total). Only two included trials reported mortality data, which we categorised as delivering interventions that started in the intraoperative phase.

Mortality

One trial (180 participants) compared long-duration antibiotics with short-duration antibiotics; however there were no events in either arm in this trial (very low-certainty evidence; downgraded once for risk of bias, once for imprecision and once for publication bias - assessed by review authors). Another trial (59 participants) compared topical povidone iodine gel with no topical povidone iodine gel. It is uncertain whether topical povidone iodine gel reduces mortality risk (very low-certainty evidence; downgraded once for risk of bias, once for imprecision and once for publication bias - assessed by review authors).

No other outcome data relevant to the overview were reported.

5.12. Perioperative antibiotics to prevent infection after first-trimester abortion

Low 2012 included 19 trials (9715 participants in total). No outcome data relevant to the overview were reported.

6. Management of theatre traffic

No reviews examined management of theatre traffic.

7. Wound irrigation

No reviews examined wound irrigation.

8. Wound closure

8.1. Continuous versus interrupted skin sutures for non-obstetric surgery

Gurusamy 2014a included five trials (827 participants in total) and of these, four trials (602 participants in total) reported SSI data.

SSI

Evidence from four trials (602 participants) showed that it is uncertain whether continuous skin sutures reduce SSI risk compared with interrupted skin sutures (very low-certainty evidence; downgraded once for risk of bias and twice for imprecision - assessed by review authors).

No other outcome data relevant to the overview were reported.

8.2. Subcutaneous closure versus no subcutaneous closure after non-caesarean surgical procedures

Gurusamy 2014b included six trials (815 participants in total) that compared subcutaneous closure with no subcutaneous closure in a single comparison.

SSI

Evidence showed that it is uncertain whether subcutaneous closure reduces SSI risk (very low-certainty evidence; downgraded once for risk of bias and twice for imprecision - assessed by review authors).

No other outcome data relevant to the overview were reported.

8.3. Techniques and materials for skin closure in caesarean section for preventing SSIs

Mackeen 2012 included seven trials (1104 participants in total) and presented two comparisons reporting SSI risk.

SSI

For the comparison of staples with absorbable subcuticular suture, data from six trials (916 participants) were pooled and there was no clear difference in SSI risk following use of absorbable subcuticular suture (RR 0.85, 95% CI 0.43 to 1.71; low-certainty evidence; downgraded once for risk of bias and once for inconsistency - assessed by overview authors). For the comparison of barbed suture with polydiaxanone suture, data from one trial (188 participants) showed no clear difference in SSI risk when using the different types of sutures (RR 0.96, 95% CI 0.18 to 5.10; low-certainty evidence; downgraded twice for imprecision - assessed by overview authors).

No other outcome data relevant to the overview were reported.

8.4. Healing by primary versus secondary intention after surgical treatment for pilonidal sinus

AL-Khamis 2010 included 26 trials (2530 participants in total) and of these, 17 trials (1940 participants) reported SSI data.

SSI

Data from 10 trials (1231 participants) showed that it is uncertain whether open healing reduces SSI risk compared with midline closure (RR 1.31, 95% CI 0.93 to 1.85; very low-certainty evidence; downgraded once for risk of bias, once for imprecision and once for inconsistency - assessed by overview authors). Data from five trials (541 participants) showed midline closure may increase the rate of SSIs compared with other closure (RR 3.72, 95 5 CI 1.86 to 7.42; low-certainty evidence; downgraded for risk of bias and imprecision - assessed by overview authors). Evidence from one trial (68 participants) showed that it is uncertain whether classic Limberg reduces SSI risk compared with modified Limberg (very low-certainty evidence; downgraded once for risk of bias, twice for imprecision - assessed by overview authors). Similarly, evidence from another trial (100 participants) showed that it is uncertain whether classic Limberg reduces SSI risk compared with Karydakis (very low-certainty evidence; downgraded once for risk of bias and twice for imprecision - assessed by overview authors).

No other outcome data relevant to the overview were reported.

8.5. Staples versus sutures for closing leg wounds after vein graft harvesting for coronary artery bypass surgery

Biancari 2010 included three trials (322 participants in total) that compared staple closure with suture closure in a single comparison.

SSI

It is uncertain whether staples reduce SSI risk compared with sutures (very low-certainty evidence; downgraded once for risk of bias and twice for imprecision - assessed by overview authors).

No other outcome data relevant to the overview were reported.

8.6. Tissue adhesives for closure of surgical incisions

Dumville 2014 included 33 trials (2793 participants in total) and of these, 22 trials (1731 participants in total) reported SSI data.

SSI

Twenty-two trials (1731 participants in total) presented six comparisons of tissue adhesives with different wound-closing technologies. There was no clear difference in SSI risk between wounds closed with tissue adhesives and wounds closed using other methods reported (sutures, adhesive tape, staples or others) (low- or very low-certainty evidence; variously downgraded for risk of bias and imprecision - assessed by review authors).

No other outcome data relevant to the overview were reported.

9. Theatre cleansing

No reviews examined theatre cleansing.

DISCUSSION

Summary of main results

We have summarised the main results of the included reviews by categorising their findings and GRADE assessment (GRADE 2013) (Table 7).

The relative effects of majority of included interventions are inconclusive due to the low or very low certainty evidence. Exceptions to this are listed below. All data listed relate to SSI. There was no high or moderate certainty evidence for the relative effects of intra-operative interventions on mortality and no outcome data at all for quality of life or costs.

High quality evidence

- Prophylactic intravenous antibiotics administered before caesarean incision reduce SSI risk compared with after neonatal umbilical cord clamping (RR 0.59, 95% CI 0.44 to 0.81; high-certainty evidence - rated by review authors).
- Adhesive drapes increase SSI risk compared with no drapes (RR 1.23, 95% CI 1.02 to 1.48; high-certainty evidence - rated by review authors) (negative effects).
- Preoperative antibiotics reduce SSI risk compared with placebo after breast cancer surgery (RR 0.74, 95% CI 0.56 to 0.98; high-certainty evidence - assessed by overview authors).

Moderate quality evidence

- Antibiotic prophylaxis probably reduce SSI risk after caesarean section compared with no prophylaxis (RR 0.40, 95% CI 0.35 to 0.46; moderate-certainty evidence - rated by review authors).
- Antibiotic prophylaxis probably reduce SSI risk compared with placebo for hernia repair (RR 0.67, 95% CI 0.54 to 0.84; moderate-certainty evidence - rated by overview authors).
- Iodine-impregnated adhesive drapes (compared with no adhesive drapes); and duration of the use of antimicrobial prophylaxis for colorectal surgery (short-term compared with long-term duration antibiotic) probably lead to little difference in SSI risk (moderate-certainty evidence - rated by overview authors).

Overall completeness and applicability of evidence

The evidence included in this overview covers all eligible Cochrane Reviews. Of the 32 included reviews, seven could be considered up-to-date as they were published within the last two years (Cochrane recommends updating reviews every two years) (Campbell 2015; Dumville 2015; Nabhan 2016; Vincent 2016; Webster 2015; Wetterslev 2015; Wood 2016).

In keeping with the nature of a Cochrane overview, this body of work does not cover non-Cochrane reviews. Alternative or emerging strategies for prevention of SSIs may not yet have been covered in a Cochrane Review and thus these data are not included here, for example, use of Triclosan-containing sutures in children or laminar airflow ventilation systems. Once such strategies have been assessed in new reviews, we can and will update this overview accordingly.

Quality of the evidence

In assessing the quality of the evidence, we employed the ROBIS tool to examine the reviews, and evaluated the authors' conclusions to ensure that they were appropriate based on the available data.

All 32 included reviews scored well across the ROBIS assessment, likely due to the stringent reporting guidelines implemented by Cochrane prior to publication.

We used GRADE to assess the quality of the evidence reported by primary studies in the included reviews. The evidence presented in the majority of comparisons (91%) was rated either low- or very low-quality/certainty. The main reasons for downgrading the certainty of evidence included bias in the primary trials and imprecision, the latter caused by small sample sizes or low event rates, or both. It must be noted that the overview authors might have used different criteria to make GRADE assessments to the review authors. For example in our process we used an OIS (optimal information size) and this informed our decisions on downgrading for precision - this may not have been the case in other reviews. For transparency, we have reported review authors' GRADE decisions but these may not calibrate well with our assessments.

Potential biases in the overview process

By only searching the Cochrane Library, and including only current Cochrane Reviews we may have missed some key literature. However, previous publications have referred to the higher-quality grading (high ROBIS score) in Cochrane Reviews due to the basic criteria necessary for publication at any stage (protocol or full review), suggesting that they may be the most reliable source of evidence (Pollock 2017).

We have employed a standard GRADE process on the included studies in reviews (Schünemann 2011a; Schünemann 2011b). In one case we considered how a review-level issue of sub-optimal risk of bias assessment affected the GRADE assessment (Sanchez-Manuel 2012). In this case we did not alter the level of GRADE certainty given, but uncertainty on the quality of the review providing the evidence that was graded must be recognised.

Agreements and disagreements with other studies or reviews

Over the years, as new evidence from RCTs continues to emerge, a steady stream of publications aim to provide a comprehensive overview on the prevention of SSIs. This is a summary overview of current Cochrane Reviews, we are not aware of any similar overviews of prevention for SSIs.

World Health Organization (WHO) guidelines on SSI prevention have recently been published (WHO 2016). The WHO reviews that underpin these guidelines (WHO 2016) were also split by operative phase: preoperative, intraoperative and postoperative. The methods used to conduct the systematic reviews that underpin these guidelines were, in some cases, different to those of the corresponding Cochrane Reviews included in this overview of reviews, which means direct comparison between overview and guidelines findings is not appropriate. The WHO reviews are standard systematic reviews, more recent ones, in some cases, include observational as well as randomised controlled trial data and have review questions that, in some cases, differ in scope to corresponding Cochrane Reviews (as do related alibility criteria). Focusing on the respective findings of the guidelines and the overview for the intraoperative phase, the guidelines include topics not covered by Cochrane Reviews, such as maintenance of body temperature, maintenance of adequate circulating volume control, discontinuation of immunosuppressive agents and use of laminar airflow ventilation systems. Additionally, intraoperative antibiotic prophylaxis, considered as part of this overview, were only considered as pre- or postoperative interventions in the guidelines. Four further interventions were considered in both the guidelines and this overview: patient oxygenation, use of microbial sealants, blood glucose control and use of drapes. The WHO guidelines (WHO 2016) make a strong recommendation with moderate-quality evidence for use of 80% inspired oxygen intraoperatively and into the postoperative period for adult patients under general anaesthesia with endotracheal intubation. Our overview found low-certainty evidence from one review (Wetterslev 2015) with 15 RCTs reporting no clear difference in SSI risk following use of high perioperative inspiratory oxygen fraction for adult surgical patients. Although similar data were used in the analysis performed, unlike Wetterslev 2015, WHO 2016 conducted a subgroup analysis based on the type of anaesthesia, and it is this subgroup analysis that informs the recommendation made (on oxygenation). Use of surgical drapes was also considered by both guidelines and our overview. This overview considers two more RCTs than WHO guidelines, but both sources report similar findings in that adhesive drapes appear to increase the SSI risk compared with no drapes. Again, there were no key differences in findings reported for microbial sealant and blood glucose control.

AUTHORS' CONCLUSIONS

Implications for practice

This overview provides the most up-to-date evidence on prevention of SSIs from currently published Cochrane Reviews (intraoperative phase). Generally, we found insufficient or low-certainty evidence for the effect of most interventions for preventing SSIs. This comprehensive overview of Cochrane Reviews highlights the current uncertainty regarding the effectiveness of the intraoperative phase interventions as preventions for SSIs. It is important to note that one review with high-certainty evidence showed harms associated with the use of adhesive drapes; and another review also with high-certainty evidence showed benefit when using prophylactic intravenous antibiotics administered before caesarean incision. As there remains uncertainty on the use of a number of prophylactic SSI prevention options, health professionals are likely to follow local and national guidelines until more information becomes available.

Implications for research

The individual reviews and this overview have highlighted the lack of good evidence for intraoperative interventions for SSI prevention. Included reviews in this category focused on interventions administered during the procedure (e.g. prophylactic antibiotics, patient warming) and methods to reduce bacterial contamination (e.g. glove changes, incise drapes). Just a few interventions altered the surgical approach itself (e.g. closure methods, the use of electrosurgical incisions). It is possible that different surgical techniques may influence SSI and this may be an area in need of more research. Most of the trials and the participants included in them did not contribute to any reliable assessment of efficacy or harm, which may lead to research waste. Robust randomised controlled trials with good internal validity from use of appropriate methods of randomisation, blinding and analysis are required. Studies also need to have carefully considered sample size calculations and recruitment strategies to ensure that they are not underpowered. It is also important that the outcomes that are important to patients and health professionals are measured. Future studies should use appropriate outcome measures that are consistent, reliable, have internal and external validity, and are sensitive to change in what is being measured. Consistent use of outcomes and related definitions would maximise the value of data from across multiple studies. Improving measurement of SSI, especially after hospital discharge, is warranted to improve data collection in this phase using validated patient-reported outcome (PRO) measures or methods for wound photography, or both, to complement these. A core outcome set focused on surgical wounds may be considered by developing and applying agreed, standardised sets of outcomes in this area. Trials should also collect quality-of-life data and consider incorporating cost-effectiveness analysis. Whilst adverse events should be collected as part of a trial, additional data on mortality and other rare events might be better collected as part of observational, prospective studies - perhaps using routinely collected data if possible. Crucially it is important to understand the risk of death as a function of SSI severity and these data are unlikely to be obtained from trials. This research also highlights the need for review authors to update existing reviews to ensure that new studies are incorporated into existing reviews so that Cochrane Reviews remain contemporary and relevant.

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ADDITIONAL TABLES

Table 1. Interventions aimed at preventing surgical site infections

Intraoperative intervention types	Details	Theories on how the intervention type might work
For the patient		
Decontamination of patients' skin at site of surgery incision	Before surgery, patients' skin is disinfected using antiseptic solutions such as povidone-iodine or chlorhexidine at varying concentrations.	The aim of preoperative skin antisepsis is to reduce the risk of SSIs by reducing the number of micro-organisms on the skin (ACORN 2012; Mangram 1999).
Skin sealants	Microbial sealants are liquids that are applied to the patient's skin before surgery and left to dry forming a protective film over the planned incision site. Cyano-	As with other barrier methods, the use of skin sealants is focused on preventing contamination of the surgical wound with micro-organ-

Table 1. Interventions aimed at preventing surgical site infections *(Continued)*

	acrylate, which is also used as a tissue adhesive, can be used as a skin sealant.	isms from the patient's skin. It is proposed that skin sealant use before surgery prevents any remaining micro-organisms from migrating into the surgical wound following skin decontamination (Singer 2008).
Incise drapes	Before a surgical incision is made, sterile plastic adhesive (incise) drapes can be placed onto cleansed skin. The surgical incision is then made through the drape. Drapes can be plain or impregnated with antimicrobial products.	Drapes are used as a barrier between the incision and the patient's skin, which, although cleansed may harbour micro-organisms, such as at deeper levels of the skin that cleansing cannot reach (Swenson 2008).
Use of electrosurgery for surgical incisions	In electrosurgery, an electric current is used to generate heat, which vaporises cellular material, cutting the skin in place of a scalpel. This can be used to cut skin from the top surface down or used on deep skin layers once an incision has been made with a scalpel (Soderstrom 2003).	It has been suggested that using heat to make a surgical incision may reduce the risk of SSI.
Maintaining patient homoeostasis (warming)	During surgery the patient's bodily functions need to be optimised to promote recovery; it is further postulated this may also reduce the risk of SSI. Under general anaesthetic it is harder for the body to regulate its own temperature and this can increase the risk of perioperative hypothermia. Warming can be achieved using thermal insulation such as blankets, or active methods of warming that use machines to transfer heat to the patient, and use of heated intravenous fluids (NICE 2016; Whitney 2015).	Undertaking warming aims to maintain body temperature and prevent the development of perioperative hypothermia, which can lead to negative postoperative outcomes, which potentially include SSI. These interventions can also be used postoperatively to mitigate the impact of perioperative hypothermia when it has not been prevented.
Maintaining patient homoeostasis (oxygenation)	During surgery under general anaesthetic patients are intubated and supplied with oxygen to maintain adequate oxygen perfusion to all tissues.	It is suggested that the risk of SSI is higher when tissue oxygenation is not optimised during surgery. Some surgical protocols use higher saturation levels of oxygen during intubation to increase tissue oxygenation levels with the aim of reducing wound complications such as SSI. High oxygen levels have been linked to serious adverse events such as blindness and death (Al-Niaimi 2009).
Maintaining patient homoeostasis (blood glucose control)	Use of strict glycaemic control using medications to maintain glucose levels during surgery.	Hyperglycaemia after surgery is postulated to lead to increased risk of surgical complications including infection (Ljungqvist 2005; Stephan 2002).
Wound irrigation and intracavity lavage (including use of intraoperative topical antiseptics before wound closure)	Surgical irrigation and intracavity lavage use fluids to wash out the surgical cavity at the end of the surgical procedure before the wound is closed. Both wound irrigation and intracavity lavage can be altered by: volume of irrigation fluid; mechanism or timing of delivery; or solution composition (Barnes 2014).	The theoretical advantage of surgical wound irrigation is to reduce the bacterial load in a surgical wound, and thus the risk of SSI, through a combination of water pressure, dilution, or the application of antimicrobial agents.
Closure methods	Surgical wounds can be closed using sutures (absorbable or not) staples, adhesive strips or tissue adhesives. Some closure methods can make use of sutures that are coated in antimicrobial products.	There is a view that the method of surgical wound closure may impact on SSI risk. There is limited background evidence on mechanisms for SSI prevention, although it has been suggested that the better the seal the closure method obtains, the better the barrier to microbial contamination (Gurusamy 2014a).

Table 1. Interventions aimed at preventing surgical site infections *(Continued)*

	The timing of closure can also vary; some wounds can be left open for a period following surgery and then closed (delayed closure).	
For staff		
Use of masks, hair covers, overshoes, gowns and other protective coverings for theatre staff	Protective coverings worn in theatre by staff to limit the movement of micro-organisms in theatre (Cooper 2003). For example: masks over the face; disposable shoe covers worn over standard footwear and changed as required; disposable or reusable gowns worn over standard scrub outfits and changed as required.	There are various coverings used in surgery that are designed to act as a barrier between the environment and the patient's wound to maintain a sterile operative field, such as masks that aim to capture water droplets being expelled. Masks contain one or two very finely woven filters that can inhibit bacteria. Masks cover the nose and mouth, but there is concern that masks may be worn incorrectly and allow air leaks from the sides of the mask. Shoe coverings aim to limit the transfer of external material in and out of theatres. Gowns cover standard surgical attire and can be removed when contaminated and replaced.
Different glove protocols	Surgical staff wear disposable gloves during surgery. Gloves are used in a number of ways intended to minimise microbial contamination from staff to patients, including double gloving (using two pairs of gloves), the use of glove liners or cloth outer gloves (Kovavisarach 2002; Laine 2004).	Gloves are a barrier intervention that aim to prevent transfer of micro-organisms from the staff member's skin to the patient's skin or wound. Gloves also act as a barrier to prevent staff from infection by patients.
For the environment		
Theatre cleansing	The theatre environment needs to be cleaned regularly with detergents to disinfect surfaces. Daily deep cleaning is likely to occur using various protocols for cleaning surfaces between patient surgeries, especially areas that are contaminated with bodily fluid, or that are frequently touched by staff. Recent technologies used for theatre cleansing include UVC light decontamination and hydrogen peroxide vapour treatment. Surgical instruments are also sterilised to decontaminate them after use. Various protocols are used including steam sterilisation and chemical sterilisation, which is used when steam sterilisation is not feasible. Theatre cleaning can also involve the use of ventilation systems, such as laminar airflow systems, which supply filtered air into the environment to limit numbers of airborne micro-organisms. To avoid cross-infection, special protocols may be developed for cleansing when surgical patients are known to have specific infections.	All aspects of theatre cleansing aim to minimise numbers of micro-organisms present in the theatre environment with the aim of reducing the risk of SSI. (Spagnolo 2013).
Theatre traffic	A surgical theatre can be a busy working environment with people moving in and out. This movement can be managed, for example limiting the entrance and exit of staff during surgery, and minimising visitors into the theatre (e.g. partners of women undergoing caesarean sections) (Spagnolo 2013).	A key aim in the prevention of SSI is to limit numbers of micro-organisms in the operative environment. People moving in and out of the operative field may increase the risk of contamination. Visitors to the theatre who have not

Table 1. Interventions aimed at preventing surgical site infections *(Continued)*

	undergone full hand scrubbing protocols and so forth could also potentially increase SSI risk.

Table 2. Characteristics of included reviews

Review no.	First review author + year	Review title	Total number of included RCTs (and participants)	Review objective	Population, including types of surgery/ procedure and depth of incision	Main intervention e.g. nasal decontamination	Comparator(s)	Relevant review outcomes		Review limitations	Note
								Primary	Secondary		
CD006213	AL-Khamis 2010	Healing by primary versus secondary intention after surgical treatment for pilonidal sinus	26 studies (n = 2530)	To determine the relative effects of open compared with closed surgical treatment for pilonidal sinus on the outcomes of time to healing, infection and recurrence rate	Any participants (over 14 years of age) undergoing surgery to treat pilonidal sinus disease; surgical treatment for pilonidal sinus; variations of depth of incision (no details)	Any surgical intervention where the wound was left open to heal or closed by sutures	Another surgical intervention	Time to healing SSI Recurrence	Time to return to work Other complications and morbidity Participant (patient) satisfaction Cost Length of hospital stay Pain Quality of life Rate of change of wound volume Wound healing rate Operative time	Variations in the surgical techniques included in each group when conducting meta-analysis	They also compared different closed surgical treatments (midline vs off-midline wound closure. Within each group there were variations in the surgical techniques used: for example, the amount of tissue excised, depth of incision, type of suture material and suturing technique used
CD008057	Biancari 2010	Staples versus sutures for closing leg	4 studies (n = 839 leg wounds	To compare the rates of SSI and wound dehiscence of staples and sutures for skin closure after saphenous vein	People undergoing saphenous vein graft har-	Suture	Staples	Rates of SSI Severity of SSI Time to	Rate of wound dehiscence Length of hospital stay		Only 3 studies included (322 legs) were pooled

Table 2. Characteristics of included reviews *(Continued)*

		wounds after vein graft harvesting for coronary artery bypass surgery	in 581 participants)	graft harvesting for coronary artery bypass graft surgery	vesting for CABG; minimally invasive vein harvesting was excluded			wound healing	Pain Cost Patient comfort Lower limb revascularization	into meta-analysis. 1 study was excluded from the pooled analysis because each wound experienced both methods of closure and there was the risk of a unit of analysis error. However there was no statistically significant difference between the groups in this study.
CD007315	Buchleitner 2012[a]	Perioperative glycaemic control for diabetic patients undergoing surgery	12 studies (n = 1403)	To assess the effects of perioperative glycaemic control for people with diabetes undergoing surgery	Participants of any age, sex or ethnicity with previously diagnosed type 1 or 2 diabetes mellitus and submitted to perioperative glycaemic control	Perioperative glycaemic control protocol proposed by study authors that involves a more intensive control than the conven-	Perioperative glycaemic control protocol defined as standard or conventional care by the study authors	Any kind of infectious complication All-cause mortality Hypoglycaemic episodes	Cardiovascular events Renal failure Length of ICU and hospital stay Health-related quality of life Economical costs Weight gain	

Table 2. Characteristics of included reviews *(Continued)*

						tional care			Mean blood glucose during intervention		
CD009891	Campbell 2015	Warming of intravenous and irrigation fluids for preventing inadvertent perioperative hypothermia	24 studies (n = 1250)	To estimate the effectiveness of preoperative or intraoperative warming, or both, of intravenous and irrigation fluids in preventing perioperative hypothermia and its complications during surgery in adults	Adults undergoing elective or emergency surgery (including surgery for trauma) under general or regional (central neuraxial block) anaesthesia, or both	Warmed intravenous fluids including all methods of warming fluids before administration to the patient Warmed irrigation fluids including any irrigation fluids administered to a body cavity that is warmed by any method	Other warmed fluid interventions Standard care Thermal insulation or passive warming Active warming Preoperative or intraoperative warming, or both, of inspired and insufflated gases Preoperative and intraoperative pharmacological interventions	Risk of hypothermia at any point during surgery and temperature at the end of surgery or on admission to postanaesthesia care; Major cardiovascular complications	Infection and complications of the surgical wound Pressure ulcers Bleeding complications Other cardiovascular complication Patient-reported outcomes All-cause mortality Length of stay Unplanned high dependency or intensive care admission Adverse effects		No data of interest to overview authors reported
CD005987	Charoenkwan 2017	Scalpel versus electrosurgery for ma-	16 studies (n = 2769)	To assess the effects of electrosurgery compared with scalpel for major abdominal incisions	People undergoing major open abdominal	Wound creation using electrosurgery	Wound creation using a scalpel	Wound infection Time to wound healing	Wound incision time Wound-related blood loss		Subgroup analysis was planned but not possible to carry out

Table 2. Characteristics of included reviews *(Continued)*

		jor abdominal incisions			surgery, regardless of the orientation of the incision (vertical, oblique, or transverse) and surgical setting (elective or emergency)			Wound dehiscence	Postoperative pain Adhesion or scar formation	due to interventions being insufficiently homogeneous and badly reported. Sensitivity analysis was planned by excluding studies at high or unclear risk of bias. However, this was not possible as none of the included studies were at low risk of bias.
CD004112	Cook 2014	Scalpel versus no-scalpel incision for vasectomy	2 studies (n = 1529)	To compare the effectiveness, safety, and acceptability of the incisional versus no-scalpel approach to the vasectomy	Men of reproductive age undergoing vasectomy for sterilisation	No-scalpel	Scalpel	Post-vasectomy adverse events (including wound infection)	Operating time Pain Time to resumption of intercourse Rates for azoospermia Time to azoospermia Pregnancy Incidence of recanalization Incidence of repeat vasectomy	

Table 2. Characteristics of included reviews *(Continued)*

									Cost analysis Consumer acceptability measures Provider acceptability measures	
CD004287	Dumville 2014	Tissue adhesives for closure of surgical incisions	33 studies (n = 2793)	To determine the effects of various tissue adhesives compared with conventional skin closure techniques for the closure of surgical wounds	People of any age and in any setting requiring closure of a surgical skin incision of any length	Tissue adhesive	Another tissue adhesive or alternative conventional closure device	Wound dehiscence	Proportion of infected wounds Cosmetic appearance Patient satisfaction Surgeon satisfaction Cost Time taken to wound closure	
CD003949	Dumville 2015	Preoperative skin antiseptics for preventing surgical wound infections after clean surgery	13 studies (n = 2623)	To determine whether preoperative skin antisepsis immediately prior to surgical incision for clean surgery prevents SSI and to determine the comparative effectiveness of alternative antiseptics	People of any age undergoing clean surgery	Antiseptic solutions or powders	A control; another type of antiseptic or different dose	SSI	Quality of life Adverse events Resource use	
CD004082	Grocott 2012[a]	Perioperative increase in global blood flow to	31 studies (n = 5292)	To describe the effects of increasing perioperative blood flow using fluids with or without inotropes or vasoactive drugs. Outcomes were	Adults (aged ≥ 16 years) undergoing surgery in	Perioperative administration (initiated within 24	Control	Mortality (at longest available follow-up)	Mortality: all reported time frames Morbidity	Subgroup analysis and sensitivity analysis were done

Table 2. Characteristics of included reviews *(Continued)*

		explicit defined goals and outcomes following surgery		mortality, morbidity, resource utilization and health status.	an operating theatre	h before surgery and lasting up to 6 h after surgery) of fluids, with or without inotropes or vasoactive drugs to increase global blood flow against explicit measured goals			Resource utilisation Health status	
CD008726	Gyte 2014[a]	Different classes of antibiotics given to women routinely for preventing infection at caesarean section	31 studies (n = 7697 women) 35 studies included in the review but only 31 provided data	To determine, from the best available evidence, the balance of benefits and harms between different classes of antibiotic given prophylactically to women undergoing caesarean section	Women undergoing caesarean section, both elective and non-elective	Prophylactic antibiotic regimens	Different classes of antibiotics (≥ 2 antibiotics from the different classes of antibiotics)	Maternal: maternal sepsis (suspected or proven); endometritis Infant: infant sepsis (suspected or proven);	Maternal: fever (febrile morbidity); wound infection; urinary tract infection; thrush; serious infectious complication; adverse effects of treatment on the woman; maternal lengths of hospital stay; infections - post-hospital	Subgroup analyses were carried out by type of surgery; by time of administration; by route of administration Sensitivity analysis was not performed

Table 2. Characteristics of included reviews *(Continued)*

								oral thrush	discharge to 30 days postoperatively; readmissions Infant: immediate adverse effects of antibiotics on the infant; infant length of hospital stay; long-term adverse effects; infant's immune system development Additional outcomes: development of bacterial resistance; costs	
CD006933	Gurusamy 2011[a]	Methods of decreasing infection to improve outcomes after liver resections	7 studies (n = 521)	To determine the benefits and harms of different interventions in decreasing the infectious complications and improving the outcomes after liver resection	Peopleundergoing liver resection	Antibiotics Prebiotics or probiotics Immunomodulation-Topical antibiotic or antiseptic	No antibiotics or placebo; no probiotics or probiotics or placebo; no immunomodulation; no topical antibiotic or antiseptic or saline or	Mortality Serious adverse events Quality of life	Hospital stay Number of unplanned visits to the doctor Return to work Costs	The unit of analysis was the aggregate data on participants undergoing liver resection according to randomised group Sensitivity analysis and subgroup analysis were not conducted

Table 2. Characteristics of included reviews *(Continued)*

							placebo before wound closure; another of the included interventions				
CD010268	Gurusamy 2013[a]	Antibiotic prophylaxis for the prevention of methicillin-resistant Staphylococcus aureus (MRSA) related complications in surgical patients	12 studies (n = 4704)	To compare the benefits and harms of all methods of antibiotic prophylaxis in the prevention of postoperative MRSA infection and related complications in people undergoing surgery	People undergoing surgery, irrespective of age, type of surgery, whether surgery was elective or emergency, and whether MRSA colonisation was identified by routine screening	Antibiotic prophylaxis	Placebo (or no treatment); different antibiotic prophylaxis (and regimens)	All-cause mortality Other serious adverse events Quality of life	Total length of hospital stay Use of health care resources Rates of SSIs Rates of SSIs due to MRSA Rates of infections due to MRSA		No subgroup analysis performed. Sensitivity analysis was done
CD010365	Gurusamy 2014a	Continuous versus interrupted skin sutures for non-obstetric surgery	5 studies (n = 827)	To compare the benefits and harms of continuous compared with interrupted skin closure techniques in participants undergoing non-obstetric surgery	People, of any age and sex, undergoing non-obstetric surgery	Continuous sutures	Interrupted sutures	SSI Wound dehiscence Quality of life	Hypertrophic scarring Keloid scarring Incisional hernia Hospital stay Impact to the patient and to the healthcare funder		No subgroup analysis performed; sensitivity analysis was done

Table 2. Characteristics of included reviews *(Continued)*

CD010425	Gurusamy 2014b	Subcutaneous closure versus no subcutaneous closure after non-caesarean surgical procedures	6 studies (n = 815) 8 studies (n = 1318) included in the review but only 6 contributed data	To compare the benefits (such as decreased wound-related complications) and consequences (such as increased operating time) of subcutaneous closure compared with no subcutaneous closure in participants undergoing non-caesarean surgical procedures	People, of any age and sex, undergoing non-caesarean surgery	Subcutaneous closure	No subcutaneous closure, irrespective of the suture material	SSI Wound dehiscence Quality of life	Hypertrophic scarring Keloid scarringIncisional herniaHospital stayImpact to the patient and to the healthcare funder		No subgroup analysis performed; sensitivity analysis was done
CD007892	Haas 2014	Vaginal preparation with antiseptic solution before cesarean section for preventing postoperative infections	7 studies (n = 2816; 2635 analysed)	To determine if cleansing the vagina with an antiseptic solution before a caesarean delivery decreases the risk of maternal infectious morbidities, including endometritis and wound complications	Pregnant women who received a caesarean delivery	Vaginal cleansing with any type of antiseptic solution	Placebo solution/standard care	Postpartum endometritis	Wound infection; fever; wound seroma or hematoma Composite wound complications Side effects of vaginal preparation		Subgroup analysis was done
CD007462	Hadiati 2014	Skin preparation for preventing infection following caesarean section	6 studies (n = 1522)	To compare the effects of different agent forms and methods of preoperative skin preparation for preventing post caesarean infection	Pregnant women undergoing elective or emergency caesarean section	Antiseptic agents used for caesarean section skin preparation	Different antiseptic agents, forms or methods of application.	SSI Metritis or endometritis	Length of stay Maternal mortality Repeat surgery Re-admission resulting from infection Reduction of skin bacteria colony count		No subgroup analysis performed; sensitivity analysis was not done

Table 2. Characteristics of included reviews *(Continued)*

									Adverse events	
CD005360	Jones 2014[a]	Prophylactic antibiotics to prevent surgical site infection after breast cancer surgery	11 studies (n = 2867)	To determine the effects of prophylactic (pre- or perioperative) antibiotics on the incidence of surgical site infection (SSI) after breast cancer surgery	People with breast cancer undergoing breast surgery with or without immediate reconstruction as part of their treatment	Any pre- or perioperative antibiotic used as prophylaxis where there was no known infection	No antibiotic; placebo; another antibiotic only if there was a control or placebo arm	SSI Adverse reactions	Death Delay in adjuvant cancer treatment because of breast wound infection Time to wound healing Time to infection Readmission to hospital Cost of care (should be a comparison between the treatment and control group)	Sensitivity analysis was performed
CD006806	Kao 2009[a]	Perioperative glycaemic control regimens for preventing surgical site infections in adults	5 studies (n = 773)	To summarise the evidence for the impact of glycaemic control in the perioperative period on the incidence of surgical site infections, hypoglycaemia, level of glycaemic control, all-cause and infection-related mortality, and hospital length of stay and to investigate for differences of effect between different levels of glycaemic control.	People aged ≥ 18 years , regardless of diabetes status, who underwent a surgical procedure	1 glycaemic control regimen	At least 1 other glycaemic control regimen pre-, intra-, and/or postoperatively	SSI	Incidence and severity of hypoglycaemia Level of glycaemic control All-cause and infection-related mortality Length of hospital stay	Subgroup analysis was performed (people with and without diabetes); sensitivity analyses were not undertaken
CD005571	Lipp 2013[a]	Systemic antimicrobial	13 studies	To establish whether prophylactic use of systemic antimicrobials re-	People of any age, gender or	Antimicrobial	Placebo or usual care and	Peristomal	Identification of bacteria causing infection	

Table 2. Characteristics of included reviews *(Continued)*

		prophylaxis for percutaneous endoscopic gastrostomy	(n = 1637)	duces the risk of peristomal infection in people undergoing placement of percutaneous endoscopic gastrostomy tubes	diagnosis, undergoing placement of a PEG tube	prophylaxis	comparisons between different antimicrobial regimens	site infection	Peritonitis Adverse effects Mortality Removal of PEG tube because of infection Length of hospital stay	
CD005217	Low 2012[a]	Perioperative antibiotics to prevent infection after first-trimester abortion	19 studies (n = 9715)	To determine: 1. the effectiveness of antibiotic prophylaxis in preventing post-abortal upper genital tract infection; 2. the most effective antibiotic regimen; 3. the most effective strategy	All women undergoing induced first trimester surgical or medical abortion with or without a history of pelvic inflammatory disease, or a pre-abortion diagnosis of bacterial vaginosis, N. gonorrhoeae or C. trachomatis	Any antibiotic regimen; universal antibiotic prophylaxis	A placebo or nothing; or another antibiotic regimen; a screen-and-treat strategy and/or a combination of screen-and-treat and antibiotic prophylaxis	The proportion of women diagnosed with post-abortal upper genital tract infection	Other antibiotic treatments provided in the 6 weeks following the abortion Hospitalisation due to infectious complications Adverse effects of antibiotic prophylaxis or screening Proportion of women undergoing the screen-and-treat strategy who were re-infected with C. trachomatis	Subgroup analyses were not performed; sensitivity analyses were not undertaken. No data of interest to overview authors reported
CD003577	Mackeen 2012	Techniques and materials for skin closure in caesarean section	11 studies (n = 1554)	To compare the effects of skin closure techniques and materials on maternal outcomes and time taken to perform a caesarean	Women undergoing a caesarean	Various closure techniques and materials	Different closure techniques and materials	Wound infection	Wound complications Presence of hematoma Presence of seroma Skin separation	Only 8 (n = 1166) of the 11 included trials contributed data: 2 studies did not report

Table 2. Characteristics of included reviews *(Continued)*

									Reclosure Readmission Length of stay Pain perception Cosmesis Patient satisfaction Length of scar Total operative time Cost Maternal length of hospital stay Presence of hypertrophic scar	sufficiently on prespecified outcomes on which this review was focused; and 1 study did not report outcomes separately for women undergoing caesarean. Subgroup analysis was performed; sensitivity analysis was done too
CD009516	Mackeen 2014[a]	Timing of intravenous prophylactic antibiotics for preventing postpartum infectious morbidity in women undergoing cesarean delivery	10 studies (n = 5041)	To compare the effects of caesarean antibiotic prophylaxis administered preoperatively versus after neonatal cord clamp on postoperative infectious complications for both the mother and the neonate	Pregnant women who have undergone caesarean delivery and received prophylactic antibiotics	Prophylactic intravenous (IV) antibiotic administration for caesarean birth 0-30 and 30-60 minutes prior to skin incision	Prophylactic antibiotic administration for caesarean birth after neonatal umbilical cord clamping	Composite maternal postpartum infectious morbidity (including serious infectious complications, endomyometritis, wound infection, or death at-	Maternal mortality Maternal postpartum infection Placental transfer of antibiotics Breastfeeding	Subgroup analyses were not performed; sensitivity analyses were not undertaken

Table 2. Characteristics of included reviews *(Continued)*

								tributed to infection)			
CD011876	Nabhan 2016[a]	Routes of administration of antibiotic prophylaxis for preventing infection after caesarean section	10 studies (n = 1354)	To assess the benefits and harms of different routes of prophylactic antibiotics given for preventing infectious morbidity in women undergoing caesarean section	Women undergoing elective or emergency caesarean section	Prophylactic antibiotic regimens	Different route(s) of antibiotic administration	Maternal: endometritis; wound infection Infant: infant sepsis (suspected or proven)	Maternal: postpartum febrile morbidity; urinary tract infection; serious infectious complication; adverse effects of treatment on the woman; maternal length of hospital stay; readmissions Infant: oral thrush; infant length of hospital stay; immediate adverse effects of antibiotics on the infant	Combined groups of similar routes to create a single pair-wise comparison	Subgroup analysis was carried out by dosage; Sensitivity analysis was performed
CD001181	Nelson 2014[a]	Antimicrobial prophylaxis for colorectal surgery	260 trials (n = 43,451) 68 different antibiotics	To establish the effectiveness of antimicrobial prophylaxis for the prevention of surgical wound infection in people undergoing colorectal surgery	Patients (adults and children) undergoing either elective or emergency colorectal	All antimicrobial prophylaxis regimens delivered orally, intra-	No treatment control/placebo Regimen differing in duration,	SSI (abdominal wound)			

Table 2. Characteristics of included reviews *(Continued)*

					surgery, in which sepsis was not suspected preoperatively	venously or by intramuscular injection used to prevent postoperative infection	timing, use of aerobic/anaerobic coverage, route of administration A published gold standard regimen			
CD005265	Sanabria 2010[a]	Antibiotic prophylaxis for patients undergoing elective laparoscopic cholecystectomy	11 studies (n = 1664)	To assess the beneficial and harmful effects of antibiotic prophylaxis versus placebo or no prophylaxis for people undergoing elective laparoscopic cholecystectomy	Adult patients (> 17 years) undergoing laparoscopic cholecystectomy with preoperative clinical diagnosis of cholelithiasis without acute cholecystitis or other benign, non-acute inflammatory disease of the gallbladder. Jaundiced patients were excluded	Antibiotic prophylaxis, administered intravenously or orally, prior to elective laparoscopic surgery	Placebo or no antibiotic	All-cause mortality SSI Extra-abdominal infections Adverse events Quality of life		A sensitivity analysis using worst-best case and best-worst case analyses

Table 2. Characteristics of included reviews *(Continued)*

CD003769	Sanchez-Manuel 2012[a]	Antibiotic prophylaxis for hernia repair	17 studies (n = 7843)	To clarify the effectiveness of antibiotic prophylaxis in reducing postoperative wound infection rates in elective open inguinal hernia repair	Adult patients undergoing open elective inguinal or femoral hernia repair, with or without the use of prosthetic material	Administration of prophylactic antibiotics	Placebo or no treatment	Wound infection rate assessed at least at 30 days after the prophylactic antibiotic treatment was given		Sensitivity analysis and subgroup analysis were conducted
CD007482	Smaill 2014[a]	Antibiotic prophylaxis versus no prophylaxis for preventing infection after cesarean section	95 studies (> 15,000 women)	To assess the effects of prophylactic antibiotics compared with no prophylactic antibiotics on infectious complications in women undergoing caesarean section	Women undergoing caesarean section, both elective (planned) and non-elective/emergency	Any prophylactic antibiotic regimen administered for caesarean section	Placebo or no treatment	Maternal: febrile morbidity; wound infection; endometritis; serious infectious complication Infant: immediate adverse effects of antibiotics on the infant; oral thrush	Maternal: urinary tract infection; adverse effects of treatment on the woman; length of stay in hospital Infant: length of stay in hospital; long-term adverse effects; immune system development Additional outcomes: development of bacterial resistance; cost	A sensitivity analysis was undertaken on the primary outcomes by study quality, omitting the 9 quasi-RCTs; subgroup analyses were carried out by antibiotic regimen, type of surgery and time of administration

Table 2. Characteristics of included reviews *(Continued)*

CD003087	Tanner 2006	Double gloving to reduce surgical cross-infection	31 studies (n = not reported) Unit of analysis varied, gloves were collected)	To determine if additional glove protection reduces the number of surgical site or bloodborne infections in patients or the surgical team; to determine if additional glove protection reduces the number of perforations to the innermost pair of surgical gloves	All members of the surgical team practising in a designated surgical theatre	Single gloves Double gloves Glove liners Coloured perforation indicator systems Cloth outer gloves Steel outer gloves Triple gloves	Another/different type	Rates of SSI in surgical patients	Rates of perforations in innermost surgical gloves Rates of bloodborne infections in postoperative patients or the surgical team		2 trials were found that addressed surgical site infections in patients. Both trials reported no infections. No subgroup analysis performed; sensitivity analysis was not done.
CD002929	Vincent 2016	Disposable surgical face masks for preventing surgical wound infection in clean surgery	3 studies (n = 2106)	To determine whether the wearing of disposable surgical face masks by the surgical team during clean surgery reduces postoperative surgical wound infection	Adults and children undergoing clean surgery	The wearing, by the surgical team (scrubbed and not scrubbed), of disposable surgical face masks	No masks	The incidence of postoperative surgical wound infection	Costs Length of hospital stay Mortality rate		No subgroup analysis performed
CD006353	Webster 2015	Use of plastic adhesive drapes during surgery	7 studies (n = 4195)	To assess the effect of adhesive drapes used during surgery on surgical site infection, cost, mortality and morbidity	People of any age or gender, undergoing any type of in-	Plastic adhesive drapes through which an incision	No plastic adhesive drapes; other drapes	SSI	Mortality Length of hospital stay Costs		The only subgroup analysis that was possible, based on available

Table 2. Characteristics of included reviews *(Continued)*

		for preventing surgical site infection			patient or outpatient surgery	is made (used alone or in combination with other drapes and any antiseptic skin preparation)	(e.g. woven (material) or disposable (paper) drapes)		Hospital readmissions Adverse reactions Other serious infection or infectious complication such as septicaemia or septic shock	data, was of clean compared with contaminated surgery (wound classification). Sensitivity analyses were carried out by excluding trials most susceptible to bias: those with inadequate allocation concealment and uncertain or unblinded outcome assessment. It was not possible to undertake a planned sensitivity analysis based on the type of material the drape was made from due to insufficient detail about the products.
CD008884	Wetterslev 2015[a]	The effects of high pe-	28 studies	To assess the benefits and harms of an $FIO_2 \geq 60\%$ compared with a	Surgical patients ≥ 18	A high FIO_2 of ≥ 60%	A control FIO_2 of ≤ 40%	All-cause mortality	All-cause mortality within	Subgroup and sensitivity analy-

Table 2. Characteristics of included reviews *(Continued)*

		rioperative inspiratory oxygen fraction for adult surgical patients	(n = 9330)	control $FIO_2 \leq 40\%$ in the perioperative setting in terms of mortality, surgical site infection, respiratory insufficiency, serious adverse events and length of stay during the index admission for adult surgical patients	years who were undergoing elective or emergency surgery			SSI within 30 days of follow-up after surgery	30 days of follow-up Respiratory insufficiency Serious adverse event Duration of postoperative hospitalisations Quality of life as measured by the included trials	ses were conducted, the role of bias was examined and trial sequential analysis (TSA) was applied to examine the level of evidence supporting or refuting a high FIO_2 during surgery, anaesthesia and recovery
CD008062	Wood 2016	Cyanoacrylate microbial sealants for skin preparation prior to surgery	7 studies (n = 859)	To assess the effects of the preoperative application of microbial sealants (compared with no microbial sealant) on rates of SSI in people undergoing clean surgery	Participants undergoing any type of clean surgery in an operating theatre	Microbial sealant applied to the surgical incision site immediately before surgery	No application of microbial sealant, with or without the use of traditional preoperative preparation solutions such as povidone iodine or chlorhexidine	Rates of SSI	All-cause mortality Adverse reactions Other serious infection or infectious complication Length of hospital stay Rates of hospital re-admissions Costs Postoperative antibiotic use	No subgroup nor sensitivity analysis was not done

[a]This is a multi-stage review. We only extracted data from trials delivering interventions that started in the intraoperative phase

Table 3. Characteristics of excluded reviews

First review author + year	Reasons for exclusion
Cirocchi 2014	Protocol
McCallum 2016	Protocol
Ousey 2016	Protocol
Smith 2016	Protocol (ongoing)
Verschuur 2004	Only included pre- and postoperative stages

Table 4. Assessment of results by ROBIS (risk of bias in systematic reviews)

Review title	Phase 2 (identifying concerns with the review process)				Phase 3 (forming an overall judgement of the risk of bias)
	Study eligibility criteria	Identification and selection of studies	Data collection and study appraisal	Synthesis and findings	Risk of bias in the review
Healing by primary versus secondary intention after surgical treatment for pilonidal sinus (AL-Khamis 2010)	☺	☺	☺	☺	☺
Staples versus sutures for closing leg wounds after vein graft harvesting for coronary artery bypass surgery (Biancari 2010)	☺	☺	☺	☺	☺
Perioperative glycaemic control for diabetic patients undergoing surgery (Buchleitner 2012)	☺	☺	☺	☺	☺
Warming of intravenous and irrigation fluids for preventing inadvertent perioperative hypothermia (Campbell 2015)	☺	☺	☺	☺	☺
Scalpel versus electrosurgery for abdominal incisions (Charoenkwan 2017)	☺	☺	☺	☺	☺
Scalpel versus no-scalpel incision for vasectomy (Cook 2014)	☺	☺	?	☹	?
Tissue adhesives for closure of surgical incisions (Dumville 2014)	☺	☺	☺	☺	☺
Preoperative skin antiseptics for preventing surgical wound infections after clean surgery (Dumville 2015)	☺	☺	☺	☺	☺

Table 4. Assessment of results by ROBIS (risk of bias in systematic reviews) *(Continued)*

Perioperative increase in global blood flow to explicit defined goals and outcomes following surgery (Grocott 2012)	☺	☺	☺	☺	☺
Different classes of antibiotics given to women routinely for preventing infection at caesarean section (Gyte 2014)	☺	☺	☺	☺	☺
Methods of decreasing infection to improve outcomes after liver resections (Gurusamy 2011)	☺	☺	☺	☺	☺
Antibiotic prophylaxis for the prevention of methicillin resistant Staphylococcus aureus (MRSA) related complications in surgical patients (Gurusamy 2013)	☺	☺	☺	☺	☺
Continuous versus interrupted skin sutures for non-obstetric surgery (Gurusamy 2014a)	☺	☺	☺	☺	☺
Subcutaneous closure versus no subcutaneous closure after non-caesarean surgical procedures (Gurusamy 2014b)	☺	☺	☺	☺	☺
Vaginal preparation with antiseptic solution before cesarean section for preventing postoperative infections (Haas 2014)	☺	☺	☺	☺	☺
Skin preparation for preventing infection following caesarean section (Hadiati 2014)	☺	☺	☺	☺	☺
Prophylactic antibiotics to prevent surgical site infection after breast cancer surgery (Jones 2014)	☺	☺	☺	☺	☺
Peri-operative glycaemic control regimens for preventing surgical site infections in adults (Kao 2009)	☺	☺	☺	☺	☺
Systemic antimicrobial prophylaxis for percutaneous endoscopic gastrostomy (Lipp 2013)	☺	☺	☺	☺	☺
Perioperative antibiotics to prevent infection after first-trimester abortion (Low 2012)	☺	☺	?	☺	☺
Techniques and materials for skin closure in caesarean section (Mackeen 2012)	☺	☺	☺	☺	☺
Timing of intravenous prophylactic antibiotics for preventing postpartum infectious morbidity in women undergoing cesarean delivery (Mackeen 2014)	☺	☺	☺	☺	☺
Routes of administration of antibiotic prophylaxis for preventing infection after caesarean section (Nabhan 2016)	☺	☺	☺	☺	☺

Table 4. Assessment of results by ROBIS (risk of bias in systematic reviews) *(Continued)*

Antimicrobial prophylaxis for colorectal surgery (Nelson 2014)	☺	☺	☺	☺	☺
Antibiotic prophylaxis for patients undergoing elective laparoscopic cholecystectomy (Sanabria 2010)	☺	☺	☺	☺	☺
Antibiotic prophylaxis for hernia repair (Sanchez-Manuel 2012)	☺	☺	?	☺	?
Antibiotic prophylaxis versus no prophylaxis for preventing infection after cesarean section (Smaill 2014)	☺	☺	☺	☺	☺
Double gloving to reduce surgical cross-infection (Tanner 2006)	☺	☺	?	☺	☺
Disposable surgical face masks for preventing surgical wound infection in clean surgery (Vincent 2016)	☺	☺	☺	☺	☺
Use of plastic adhesive drapes during surgery for preventing surgical site infection (Webster 2015)	☺	☺	☺	☺	☺
The effects of high perioperative inspiratory oxygen fraction for adult surgical patients (Wetterslev 2015)	☺	☺	☺	☺	☺
Cyanoacrylate microbial sealants for skin preparation prior to surgery (Wood 2016)	☺	☺	☺	☺	☺

☺ = low risk; ☹ = high risk; and ? = unclear risk

Table 5. 'Summary of findings' table - Outcome: Surgical Site Infections (SSIs)

Intervention and comparison intervention	Meta-analysis results						Narrative results					Comments
	Illustrative comparative risks (95% CI) CI = confidence interval		**Risk Ratio (RR) (95% CI)** # random-effects, all other RR = fixed-effect	**Number of participants (studies)**	**Quality/certainty of the evidence (GRADE)** * assessed by overview authors § assessed by review authors	**GRADE Footnote**	**Reported outcome values** **Results in brackets are RR with 95% CIs unless otherwise indicated** # random-effects, all other RR = fixed-effect	**Number of participants (studies)**	**Quality/certainty of the evidence (GRADE)** * assessed by overview authors	**Quality/certainty of the evidence (GRADE)** * assessed by overview authors	**GRADE Footnote**	†meta-analysis by overview author Odd Ratio (OR)
	Assumed risk **With comparator**	**Corresponding risk** **With intervention**										
1. Theatre staff attire												
1.1. Double gloving to reduce surgical cross-infection (Tanner 2006) Double latex versus double latex with liner	0 per 1000	0 per 1000 (0 to 0)	Not estimable	125 (2)	Low*[1]	[1]Downgraded twice due to imprecision (very small numbers of participants with no events)	N/A	N/A	N/A	N/A	N/A	Both trials reported no SSI; both trials were underpowered for this outcome.
1.2. Disposable surgical face masks for preventing surgical wound infec-	N/A	N/A	N/A	N/A	N/A	N/A	RR 0.10 (0.01 to 1.83);	2106 (3)	Low*[1,2]		[1]Downgraded once due to imprecision	OR reported by review authors and con-

Table 5. 'Summary of findings' table - Outcome: Surgical Site Infections (SSIs) *(Continued)*

tion in clean surgery (Vincent 2016) Mask versus no mask			RR 1.33 (0.59 to 3.02); RR 1.16 (0.73 to 1.84)							(small numbers of events; wide confidence intervals that include the possibility of both benefit and harm for the intervention) [2]Downgraded due to inconsistency (direction of intervention effect varied between studies)	verted to RR by overview authors: OR 0.07 (0.00 to 1.63); OR 1.34 (0.58 to 3.07); OR 1.17 (0.70 to 1.97) Data not pooled due to clinical heterogeneity
2. Preparation of the surgical site											
2.1. Preoperative skin antiseptics for preventing surgical wound infections after clean surgery (Dumville 2015)											
a) 2% iodine in 90% alcohol versus 70% alcohol	13 per 1000	12 per 1000 (1 to 194)	RR 0.94 (0.06 to 14.74)	157 (1)	Very low*[1,2]	[1]Downgraded once due to risk of bias [2]Downgraded twice due to imprecision (small numbers of events;	N/A	N/A	N/A	N/A	

Table 5. 'Summary of findings' table - Outcome: Surgical Site Infections (SSIs) *(Continued)*

						wide confidence intervals that include the possibility of both benefit and harm for the intervention)					
b) Povidone-iodine (PI) paint versus soap scrub and application of methylated spirit	51 per 1000	59 per 1000 (18 to 187)	RR 1.15 (0.36 to 3.66)	200 (1)	Low*[1,2]	[1]Downgraded once due to risk of bias [2]Downgraded once due to imprecision (small numbers of events; wide confidence intervals that include the possibility of both benefit and harm for the intervention)	N/A	N/A	N/A	N/A	
c-1) 7.5% aqueous PI scrub/10% aqueous PI paint versus 10% aqueous PI paint	140 per 1000	106 per 1000 (48 to 236)	RR 0.76 (0.34 to 1.69)	178 (2)	Low*[1,2]	[1]Downgraded once due to risk of bias [2]Downgraded once due to imprecision (small numbers of events; wide confidence intervals that include the possibility of both benefit and harm for the intervention)	N/A	N/A	N/A	N/A	
c-2) 7.5% aqueous PI scrub/10% aqueous PI paint versus iodophor in alcohol paint	41 per 1000	60 per 1000 (30 to 120)	RR 1.47 (0.73 to 2.94)	621 (6)	Low*[1,2]	[1]Downgraded once due to risk of bias [2]Downgraded once due to imprecision (small numbers of events; wide confidence intervals that include the possibility of both	N/A	N/A	N/A	N/A	2 studies had no events in either group (n = 160)

Table 5. 'Summary of findings' table - Outcome: Surgical Site Infections (SSIs) *(Continued)*

						benefit and harm for the intervention)					
c-3) 10% aqueous PI paint versus iodophor in alcohol paint	20 per 1000	125 per 1000 (16 to 981)	RR 6.25 (0.80 to 49.05)	106 (1)	Low*[1]	[1]Downgraded twice due to imprecision (small numbers of events; wide confidence intervals that include the possibility of both benefit and harm for the intervention)	N/A	N/A	N/A	N/A	
d-1) 7.5% aqueous PI scrub/10% aqueous PI paint versus 2% chlorhexidine in 70% alcohol paint	N/A	N/A	N/A	N/A	N/A	N/A	N/A	100 (1)	Very low*[1,2]	[1]Downgraded once due to risk of bias [2]Downgraded twice due to imprecision (small numbers of events; wide confidence intervals that include the possibility of both benefit and harm for the in-	Not estimable due to no reported SSI events in either group

Table 5. 'Summary of findings' table - Outcome: Surgical Site Infections (SSIs) *(Continued)*

										terven-tion)	
d-2) 10% aqueous PI paint versus 2% chlorhexidine in 70% alcohol paint	63 per 1000	66 per 1000 (35 to 125)	RR 1.06 (0.56 to 2.00)	556 (1)	Low*[1,2]	[1]Downgraded once due to risk of bias [2]Downgraded once due to imprecision (small numbers of events; wide confidence intervals that include the possibility of both benefit and harm for the intervention)	Not estimable	100 (1)	N/A	N/A	No events in either group
d-3) Iodophor in alcohol (film-forming) paint versus 2% chlorhexidine in 70% alcohol paint	N/A	N/A	N/A	N/A	N/A	N/A	Not estimable	100 (1)	Very low*[1,2]	[1]Downgraded once due to risk of bias [2]Downgraded twice due to imprecision (small numbers of events; wide confidence intervals that include the possibility of both benefit and harm for	No events in either group

Table 5. 'Summary of findings' table - Outcome: Surgical Site Infections (SSIs) *(Continued)*

										the intervention)	
d-4) 7.5% aqueous PI scrub followed by 10% aqueous PI paint versus 4% chlorhexidine in 70% alcohol scrub	21 per 1000	57 per 1000 (11 to 289)	RR 2.76 (0.55 to 13.86)	183 (1)	Low*[1,2]	[1]Downgraded once due to risk of bias [2]Downgraded once due to imprecision (small numbers of events; wide confidence intervals that include the possibility of both benefit and harm for the intervention)	Not estimable	127 (1)	N/A	N/A	No events in either group
d-5) 0.5% chlorhexidine in methylated spirit versus PI paint	133 per 1000	62 per 1000 (36 to 109)	RR 0.47 (0.27 to 0.82)	542 (1)	Low*[1,2]	[1]Downgraded once due to risk of bias [2]Downgraded once due to imprecision (small numbers of events)	N/A	N/A	N/A	N/A	
e) 0.75% Cholorhexidine and 1.5% cetrimide scrub versus 0.75% chlorhexidine and 1.5% cetrimide paint	44 per 1000	44 per 1000 (6 to 296)	RR 0.98 (0.14 to 6.65)	91 (1)	Low*[1,2]	[1] Downgraded once due to risk of bias [2] Downgraded once due to imprecision (small numbers of events; wide confidence intervals that include the possibility of both benefit and harm for the intervention)	N/A	N/A	N/A	N/A	
f) Alcoholic solutions versus aqueous solutions	53 per 1000	41 per 1000	RR 0.77 (0.51 to 1.17)	1400 (6)	Low*[1,2]	[1]Downgraded once due to risk of bias	N/A	N/A	N/A	N/A	

Table 5. 'Summary of findings' table - Outcome: Surgical Site Infections (SSIs) *(Continued)*

		(27 to 62)				[2]Downgraded once due to imprecision (small numbers of events; wide confidence intervals that include the possibility of both benefit and harm for the intervention)					
2.2. Skin preparation for preventing infection following caesarean section (Hadiati 2014)											
a). Drape versus no drape	112 per 1000	144 per 1000 (109 to 191)	RR 1.29 (0.97 to 1.71)	1294 (2)	Low[§]	[§]Wide confidence interval crossing the line of no effect.	N/A	N/A	N/A	N/A	
b) 1-minute alcohol scrub with iodophor drape versus 5-minute iodophor scrub without drape	N/A	N/A	N/A	N/A	N/A	N/A	Not estimable	79 (1)	Low*[1,2]	[1]Downgraded once due to risk of bias [2]Downgraded once due to imprecision (small numbers of events; wide confidence intervals that include the possibility of both bene-	No events in either group

Table 5. 'Summary of findings' table - Outcome: Surgical Site Infections (SSIs) *(Continued)*

										fit and harm for the intervention)
c) Parachlorometaxylenol with iodine versus iodine alone	120 per 1000	40 per 1000 (5 to 359)	RR 0.33 (0.04 to 2.99)	50 (1)	Low§	§Wide confidence interval crossing the line of no effect & small sample size	N/A	N/A	N/A	N/A
d) Chlorhexidine gluconate versus povidone iodine	45 per 1000	95 per 1000 (9 to 974)	RR 2.10 (0.20 to 21.42)	43 (1)	Very low§	§One study with design limitations Wide confidence interval crossing the line of no effect, few events & small sample size	N/A	N/A	N/A	N/A
2.3. Vaginal preparation with antiseptic solution before cesarean section for preventing postoperative infections (Haas 2014) Vaginal preparation versus control	33 per 1000	29 per 1000 (18 to 45)	RR 0.86 (0.54 to 1.36)	2205 (6)	Low§	§Most studies contributing data had design limitations Wide confidence interval crossing the line of no effect	N/A	N/A	N/A	N/A
2.4. Use of plastic adhesive drapes during surgery for preventing surgical site infection (Webster 2015)										
a) Adhesive drapes versus no adhesive drapes	112 per 1000	138 per 1000 (114 to 166)	RR 1.23 (1.02 to 1.48)	3082 (5)	High§	§The total sample met requirements for optimal information size, and the total number	N/A	N/A	N/A	N/A

Table 5. 'Summary of findings' table - Outcome: Surgical Site Infections (SSIs) *(Continued)*

						of events exceeded 300					
b) Iodine-impregnated adhesive drapes versus no adhesive drapes	65 per 1000	67 per 1000 (43 to 104)	RR 1.03 (0.66 to 1.60)	1113 (2)	Moderate§	§There was imprecision on at least 2 counts; the total sample size was too small to meet optimal information size, and the total number of events was less than 300	N/A	N/A	N/A	N/A	
2.5. Cyanoacrylate microbial sealants for skin preparation prior to surgery (Wood 2016) Microbial sealant versus no microbial sealant	111 per 1000	59 per 1000 (27 to 130)	RR 0.53 (0.24 to 1.18)#	859 (7)	Low*1,2	1Downgraded once due to risk of bias 2Downgraded once due to imprecision (small numbers of events; wide confidence intervals that include the possibility of both benefit and harm for the intervention)	N/A	N/A	N/A	N/A	One study had no events in either group (n = 96)
3. Making the surgical incision											
3.1. Scalpel versus electrosurgery for major abdominal incisions (Charoenkwan 2017) Electrosurgery versus scalpel	74 per 1000	79 per 1000 (55 to 114)	RR 1.07 (0.74 to 1.54)	2178 (11)	Low§	§Serious limitation due to lack of information on randomisation and allocation concealment in three studies contributing more than 50% to the analysis Serious imprecision as 95% CIs around the estimate were wide ranging including	N/A	N/A	N/A	N/A	

Table 5. 'Summary of findings' table - Outcome: Surgical Site Infections (SSIs) *(Continued)*

						the probability of a reduction as well as an increase in wound infection					
3.2. Scalpel versus no-scalpel incision for vasectomy (Cook 2014) No-scalpel versus standard incision	22 per 1000	7 per 1000 (2 to 21)	RR 0.31 (0.10 to 0.94)	1182 (2)	Very Low*[1,2,3]	[1]Downgraded once due to risk of bias [2]Downgraded once due to imprecision (small numbers of events) [3]Downgraded once due to heterogeneity	N/A	N/A	N/A	N/A	2 studies differed in their timing and nature of postoperative evaluations, including the evaluation of sterility; and in operator experience with the no-scalpel technique Peto OR reported by review authors and converted to RR by overview authors: Peto OR 0.34 (0.13 to 0.90)

Table 5. 'Summary of findings' table - Outcome: Surgical Site Infections (SSIs) *(Continued)*

4. Treatment of patient during surgery

4.1. Warming of intravenous and irrigation fluids for preventing inadvertent perioperative hypothermia (Campbell 2015)	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	No SSI data provided
4.2. Perioperative glycaemic control for diabetic patients undergoing surgery (Buchleitner 2012) Intensive versus conventional glycaemic control	N/A	N/A	N/A	N/A	N/A	N/A	1/10 vs. 6/22: RR 0.37 (0.05, 2.66)#	32 (1)	Very low*[1,2]	[1]Downgraded twice due to imprecision (small numbers of events; wide confidence intervals that include the possibility of both benefit and harm for the intervention) [2]Downgraded due to inconsistency	Only 2 included trials were categorised in intraop phase; Outcome for Infectious complications rather than SSIs RR 0.71 (0.22 to 2.26)†
							3/37 vs. 1/36; RR 2.92 (0.32, 26.77)#	73 (1)			

Table 5. 'Summary of findings' table - Outcome: Surgical Site Infections (SSIs) *(Continued)*

										(direction of intervention effect varied between studies)	
4.3. Peri-operative glycaemic control regimens for preventing surgical site infections in adults (Kao 2009)											
a) Intra- and postoperative strict versus conventional glycaemic control with intravenous insulin	N/A	N/A	N/A	N/A	N/A	N/A	1/40 vs. 2/38; RR 0.48 (0.04 to 5.03)	78 (1)	Low*[1]	[1]Downgraded twice due to imprecision (small numbers of events; wide confidence interval that include the possibility of both benefit and harm for the intervention)	
b) Intraoperative strict versus conventional glycaemic control with insulin infusion	N/A	N/A	N/A	N/A	N/A	N/A	6/185 vs. 7/186; RR 0.86 (0.30 to 2.52)	371 (1)	Low*[1]	[1]Downgraded twice due to imprecision (small num-	Outcome for deep wound infection

Table 5. 'Summary of findings' table - Outcome: Surgical Site Infections (SSIs) *(Continued)*

										bers of events; wide confidence intervals that include the possibility of both benefit and harm for the intervention)	
c) Intra- and postoperative strict glycaemic control with intravenous glucose insulin-potassium infusion (GIK) versus conventional glycaemic control with subcutaneous insulin	N/A	N/A	N/A	N/A	N/A	N/A	0/72 vs. 9/68; RR 0.05 (0.00 to 0.84)	140 (1)	Low*[1,2]	[1]Downgraded once due to risk of bias [2]Downgraded once due to imprecision (small numbers of events; small sample size)	Outcome for pneumonia and wound infections
4.4. Perioperative increase in global blood flow to explicit defined goals and	N/A	N/A	N/A	N/A	N/A	N/A	4/50 vs. 5/50; RR 0.80 (0.23 to 2.81)	100 (1)	Low*[1]	[1]Downgraded once due to imprecision (small	RR 0.40 (0.19 to 0.82)†

Table 5. 'Summary of findings' table - Outcome: Surgical Site Infections (SSIs) *(Continued)*

outcomes following surgery (Grocott 2012) Increased global blood flow versus control							0/19 vs. 2/18; RR 0.19 (0.01 to 3.71)	37 (1)			sample size) [2]Downgraded once due to inconsistency	
							3/30 vs. 8/30: RR 0.38 (0.11 to 1.28)	60 (1)				
							2/32 vs. 10/34; RR 0.21 (0.05 to 0.90)	66 (1)				
							0/30 vs. 2/60; RR 0.39 (0.02 to 7.95)	90 (1)				
4.5. The effects of high perioperative inspiratory oxygen fraction for adult surgical patients (Wetterslev 2015) 60% to 90% oxygen versus 30% to 40% oxygen perioperatively	129 per 1000	112 per 1000 (92 to 138)	RR 0.87 (0.71 to 1.07)#	7219 (15)	Low*[1,2]	[1]Downgraded once due to risk of bias [2]Downgraded once due to heterogeneity	N/A	N/A	N/A	N/A	Review authors obtained data on (SF)-36 from the Greif 1999 trial through Daniel Sessler, who was a co-author of this trial report.	

Table 5. 'Summary of findings' table - Outcome: Surgical Site Infections (SSIs) *(Continued)*

5. Use of antibiotics

5.1. Antibiotic prophylaxis versus no prophylaxis for preventing infection after caesarean section (intra and post) (Smaill 2014) Antibiotic versus no antibiotics	89 per 1000	36 per 1000 (31 to 41)	RR 0.40 (0.35 to 0.46)#	14,407 (82)	Moderate§	§ In most studies the assessment of bias was judged as unclear. In a third of studies the control group did not receive a placebo and lack of blinding could have influenced the assessment of outcomes. In less than 20% of studies was there an adequate description of sequence generation	N/A	N/A	N/A	N/A	2 studies had no event in either arm (n = 182) 6 out of 82 were quasi-RCTs
			RR 0.40 (0.35 to 0.46)#	12,669 (76)	N/A	N/A	N/A	N/A	N/A	N/A	Sensitivity analysis excluded the 6 quasi-RCTs; no further details available
5.2. Review: Different classes of antibiotics given to women routinely for preventing infection at caesarean section (Gyte 2014) Cephalosporins versus penicillins - all women											
a) Single cephalosporin versus single penicillin	33 per 1000	27 per 1000 (12 to 59)	RR 0.83 (0.38 to 1.81)#	1497 (9)	Low§	§Most studies contributing data had design limitations. Wide confidence interval crossing the line of no effect & small sample size	N/A	N/A	N/A	N/A	

Table 5. 'Summary of findings' table - Outcome: Surgical Site Infections (SSIs) *(Continued)*

b) Single cephalosporin versus penicillin drug combination	33 per 1000	23 per 1000 (13 to 42)	RR 0.72 (0.40 to 1.30)#	1608 (7)	Low*[1,2]	[1]Downgraded once due to risk of bias [2]Downgraded once due to imprecision (small numbers of events; wide confidence intervals that include the possibility of both benefit and harm for the intervention)	N/A	N/A	N/A	N/A
c) Cephalosporin drug combination versus single penicillin	32 per 1000	65 per 1000 (14 to 311)	RR 2.02 (0.42 to 9.63)#	139 (1)	Very low*[1,2]	[1]Downgraded once due to risk of bias [2]Downgraded twice due to imprecision (small numbers of events; wide confidence intervals that include the possibility of both benefit and harm for the intervention)	N/A	N/A	N/A	N/A
d) Cephalosporin drug combination versus penicillin drug combination	37 per 1000	46 per 1000 (16 to 133)	RR 1.23 (0.42 to 3.58)#	315 (2)	Very low*[1,2]	[1]Downgraded once due to risk of bias [2]Downgraded twice due to imprecision (small numbers of events; wide confidence intervals that include the possibility of both benefit and harm for the intervention)	N/A	N/A	N/A	N/A

5.3. Antibiotic prophylaxis for the prevention of methicillin-resistant Staphylococcus aureus (MRSA) related complications in surgical patients (Gurusamy 2013)

Table 5. 'Summary of findings' table - Outcome: Surgical Site Infections (SSIs) *(Continued)*

a) Pefloxacin versus cefazolin and oxacillin (tibial fracture requiring external fixation)	90 per 1000	67 per 1000 (39 to 115)	RR 0.74 (0.43 to 1.28)	616 (1)	Very low§	§The risk of bias in the trial was high The confidence intervals overlapped 1 and/or 0.75 and 1.25. There were fewer than 300 events in total in the intervention and control groups	N/A	N/A	N/A	N/A	Overall SSIs; Group 1: intra Group 2: intra and post
b) Ertapenem versus cefotetan	15 per 1000	9 per 1000 (2 to 37)	RR 0.59 (0.14 to 2.46)	672 (1)	Very low*1,2	1Downgraded once due to risk of bias 2Downgraded twice due to imprecision (small numbers of events; wide confidence intervals that include the possibility of both benefit and harm for the intervention)	N/A	N/A	N/A	N/A	MRSA SSIs; over 30 min within 60 min prior to the initial incision
c) Cefamandole versus cefamandole and gentamycin	0 per 1000	0 per 1000 (0 to 0)	RR 5.08 (0.24 to 105.24)	522 (1)	Very low*1,2	1Downgraded once due to risk of bias 2Downgraded twice due to imprecision (small numbers of events; wide confidence intervals that include the possibility of both benefit and harm for the intervention)	N/A	N/A	N/A	N/A	Overall SSIs One study with 4 arms

Table 5. 'Summary of findings' table - Outcome: Surgical Site Infections (SSIs) *(Continued)*

d) Cefazolin and gentamycin versus cefamandole and gentamycin	0 per 1000	0 per 1000 (0 to 0)	RR 17.67 (1.03 to 304.54)	516 (1)	Very low*[1,2]	[1]Downgraded once due to risk of bias [2]Downgraded twice due to imprecision (small numbers of events; wide confidence intervals that include the possibility of both benefit and harm for the intervention)	N/A	N/A	N/A	N/A	
e) Cefazolin versus cefamandole	8 per 1000	27 per 1000 (6 to 131)	RR 3.55 (0.75 to 16.95)	514 (1)	Very low*[1,2]	[1]Downgraded once due to risk of bias [2]Downgraded twice due to imprecision (small numbers of events; wide confidence intervals that include the possibility of both benefit and harm for the intervention)	N/A	N/A	N/A	N/A	
f) Cefazolin versus cefazolin and gentamycin	32 per 1000	28 per 1000 (10 to 75)	RR 0.87 (0.32 to 2.36)	508 (1)	Very low*[1,2]	[1]Downgraded once due to risk of bias [2]Downgraded twice due to imprecision (small numbers of events; wide confidence intervals that include the possibility of both benefit and harm for the intervention)	N/A	N/A	N/A	N/A	
g) Co-amoxiclav or cefo-	375 per 1000	98 per 1000	RR 0.26 (0.11 to 0.65)	99 (1)	Low*[1]	[1]Downgraded twice due to imprecision (small	N/A	N/A	N/A	N/A	Overall SSIs

Table 5. 'Summary of findings' table - Outcome: Surgical Site Infections (SSIs) *(Continued)*

taxime versus placebo		(41 to 244)				numbers of events; small sample size)					
h) Vancomycin and cefazolin versus cefazolin (open fractures)	87 per 1000	87 per 1000 (23 to 327)	RR 1.00 (0.27 to 3.76)	92 (1)	Very low*[1,2]	[1]Downgraded once due to risk of bias [2]Downgraded twice due to imprecision (small numbers of events; wide confidence intervals that include the possibility of both benefit and harm for the intervention)	N/A	N/A	N/A	N/A	Overall SSIs
i) Daptomycin and cefazolin versus cefazolin	129 per 1000	39 per 1000 (9 to 177)	RR 0.30 (0.07 to 1.37)	113 (1)	Very low*[1,2]	[1]Downgraded once due to risk of bias [2]Downgraded twice due to imprecision (small numbers of events; wide confidence intervals that include the possibility of both benefit and harm for the intervention)	N/A	N/A	N/A	N/A	Overall SSIs; one study with 3 arms
j) Vancomycin and cefazolin versus cefazolin (vascular surgery)	129 per 1000	125 per 1000 (49 to 323)	RR 0.97 (0.38 to 2.50)	118 (1)	Very low*[1,2]	[1]Downgraded once due to risk of bias [2]Downgraded twice due to imprecision (small numbers of events; wide confidence intervals that include the possibility of both benefit and harm for the intervention)	N/A	N/A	N/A	N/A	

Table 5. 'Summary of findings' table - Outcome: Surgical Site Infections (SSIs) *(Continued)*

k) Vancomycin and cefazolin versus daptomycin and cefazolin	39 per 1000	125 per 1000 (27 to 575)	RR 3.19 (0.69 to 14.65)	107 (1)	Very low*[1,2]	[1]Downgraded once due to risk of bias [2]Downgraded twice due to imprecision (small numbers of events; wide confidence intervals that include the possibility of both benefit and harm for the intervention)	N/A	N/A	N/A	N/A	
l) Vancomycin versus cefuroxime	32 per 1000	34 per 1000 (17 to 70)	RR 1.08 (0.53 to 2.21)	884 (1)	Low*[1,2]	[1]Downgraded once due to risk of bias [2]Downgraded once due to imprecision (small numbers of events; wide confidence intervals that include the possibility of both benefit and harm for the intervention)	N/A	N/A	N/A	N/A	
5.4. Prophylactic antibiotics to prevent surgical site infection after breast cancer surgery (Jones 2014)											
a) Preoperative antibiotic versus placebo	N/A	N/A	N/A	N/A	N/A	N/A	3/69 vs 10/72; RR 0.31 (0.09 to 1.09) 17/110 vs 19/108; RR 0.88 (0.48 to 1.60) 29/164 vs	1708 (6)	High*		RR 0.74 (0.56 to 0.98)†

Table 5. 'Summary of findings' table - Outcome: Surgical Site Infections (SSIs) *(Continued)*

							32/169; RR 0.93 (0.59 to 1.47)				
							8/144 vs 13/148; RR 0.63 (0.27 to 1.48)				
							17/303 vs 26/303; RR 0.65 (0.36 to 1.18)				
							3/59 vs 5/59; RR 0.60 (0.15 to 2.40)				
b) Preoperative antibiotic versus none	N/A	N/A	N/A	N/A	N/A	N/A	9/187 vs 25/182; RR 0.35 (0.17 to 0.73)	987 (2)	Low*[1,2]	[1]Downgraded once due to imprecision (small numbers of events) [2]Downgraded due to inconsistency (direction of intervention effect var-	RR 0.48 (0.28 to 0.82)†
							10/311 vs 14/307; RR 0.71 (0.32 to 1.56)				

Table 5. 'Summary of findings' table - Outcome: Surgical Site Infections (SSIs) *(Continued)*

										ied between studies)	
c) Perioperative antibiotics versus no antibiotic	182 per 1000	20 per 1000 (2 to 355)	RR 0.11 (0.01 to 1.95)	44 (1)	Very low*[1,2]	[1]Downgraded once due to risk of bias [2]Downgraded twice due to imprecision (small numbers of events; wide confidence intervals that include the possibility of both benefit and harm for the intervention)	N/A	N/A	N/A	N/A	
5.5. Systemic antimicrobial prophylaxis for percutaneous endoscopic gastrostomy (Lipp 2013) Systemic antibiotic (IV) versus placebo/no intervention/skin antiseptic	242 per 1000	94 per 1000 (73 to 123)	RR 0.39 (0.30 to 0.51)	1271 (12)	Low*[1]	[1]Downgraded twice due to risk of bias	N/A	N/A	N/A	N/A	OR reported by review authors and converted to RR by overview authors: OR 0.36 (0.26 to 0.50)
5.6. Timing of intravenous prophylactic antibiotics for preventing postpartum infectious morbidity in women undergoing cesarean deliv-	41 per 1000	24 per 1000 (17 to 33)	RR 0.59 (0.44 to 0.81)[#]	5041 (10)	High[§]		N/A	N/A	N/A	N/A	

Table 5. 'Summary of findings' table - Outcome: Surgical Site Infections (SSIs) *(Continued)*

ery (Mackeen 2014) Prophylactic intravenous antibiotics administered before cesarean incision versus after neonatal umbilical cord clamping (maternal outcomes)											
5.7. Routes of administration of antibiotic prophylaxis for preventing infection after caesarean section (Nabhan 2016) Intravenous (IV) versus irrigation	21 per 1000	10 per 1000 (4 to 30)	RR 0.49 (0.17 to 1.43)#	859 (7)	Very low§	§Studies with design limitations Studies include relatively few patients and few events and have a wide 95% CI that includes both appreciable benefit and appreciable harm	N/A	N/A	N/A	N/A	Intra or intra & post
5.8. Antibiotic prophylaxis for patients undergoing elective laparoscopic cholecystectomy (Sanabria 2010) Antibiotic prophylaxis versus placebo	33 per 1000	27 per 1000 (15 to 46)	RR 0.81 (0.47 to 1.42)#	1664 (11)	Very low*1,2	1Downgraded twice due to risk of bias 2Downgraded once due to imprecision (small numbers of events; wide confidence intervals that include the possibility of both benefit and harm for the intervention)	N/A	N/A	N/A	N/A	Intra or intra & post OR reported by review authors and converted to RR by overview authors:

Table 5. 'Summary of findings' table - Outcome: Surgical Site Infections (SSIs) *(Continued)*

or no-prophylaxis												OR 0.87 (0.49 to 1.54)#
5.9. Antibiotic prophylaxis for hernia repair (Sanchez-Manuel 2012) Antibiotic prophylaxis versus placebo	46 per 1000	31 per 1000 (25 to 38)	RR 0.67 (0.54 to 0.84)#	17 (7843)	Moderate*1	1 Downgraded once due to risk of bias	N/A	N/A	N/A	N/A	Intra or intra & post OR reported by review authors and converted to RR by overview authors: OR 0.64 (0.50 to 0.82)#
5.10. Antimicrobial prophylaxis for colorectal surgery (Nelson 2014)												
a) Antibiotic versus no antibiotic/placebo	N/A	N/A	N/A	N/A	N/A	N/A	5/49 vs 16/50; RR 0.32 (0.13 to 0.80)# 2/30 vs 11/27; RR 0.16 (0.04 to 0.67)# 7/108 vs 8/49; RR 0.40 (0.15 to 1.03)#	405 (5)	Low*1,2	1Downgraded once due to risk of bias 2Downgraded once due to inconsistency	RR 0.25 (0.16 to 0.41)†

Table 5. 'Summary of findings' table - Outcome: Surgical Site Infections (SSIs) *(Continued)*

							3/13 vs 11/19; RR 0.40 (0.14 to 1.16)#				
							2/29 vs 12/31; RR 0.18 (0.04 to 0.73)#				
b) Duration of therapy (short-term versus long-term duration antibiotic)	N/A	N/A	N/A	N/A	N/A	N/A	2/31 vs 0/27; RR 4.38 (0.22 to 87.32)#	1484 (7)	Moderate*[1]	[1]Downgraded once due to imprecision (small numbers of events; wide confidence intervals that include the possibility of both benefit and harm for the intervention)	RR 1.05 (0.78 to 1.40)† Short-term: participants who received only a single preoperative dose; long-term: those who received at least a second intraoperative dose of antibiotic or postoperative dosing (or both)
							14/100 vs 12/104; RR 1.21 (0.59 to 2.49)#				
							9/149 vs 8/145; RR 1.09 (0.43 to 2.76)#				
							23/113 vs 22/114; RR 1.05 (0.62 to 1.78)#				

Table 5. 'Summary of findings' table - Outcome: Surgical Site Infections (SSIs) *(Continued)*

							8/65 vs 8/70; RR 1.08 (0.43 to 2.70)#				
							5/71 vs 7/67; RR 0.67 (0.22 to 2.02)#				
							22/209 vs 23/219; RR 1.00 (0.58 to 1.74)#				
c) Additional aerobic coverage versus no aerobic coverage	N/A	N/A	N/A	N/A	N/A	N/A	0/13 vs 3/11; RR 0.12 (0.01 to 2.14)#	230 (4)	Low*[1,2]	[1]Downgraded once due to risk of bias [2]Downgraded once due to imprecision (small numbers of events)	RR 0.38 (0.16 to 0.96)†#
							3/47 vs 0/50; RR 7.44 (0.39 to 140.25)#				
							0/26 vs 6/23; RR 0.07 (0.00 to 1.15)#				
							3/27 vs 7/33;				

Table 5. 'Summary of findings' table - Outcome: Surgical Site Infections (SSIs) *(Continued)*

							RR 0.52 (0.15 to 1.83)#				
d) Additional anaerobic coverage versus little anaerobic coverage	N/A	N/A	N/A	N/A	N/A	N/A	19/287 vs 44/280; RR 0.42 (0.25 to 0.70)# --- 18/121 vs 16/116; RR 1.08 (0.58 to 2.01)# --- 7/89 vs 9/85; RR 0.74 (0.29 to 1.91)# --- 9/36 vs 17/84; RR 1.24 (0.61 to 2.51)#	1098 (4)	Low*[1,2]	[1]Downgraded once due to risk of bias [2]Downgraded once due to inconsistency	RR 0.65 (0.47 to 0.90)†#
e) Oral versus intravenous	N/A	N/A	N/A	N/A	N/A	N/A	2/35 vs 1/37; RR 2.11 (0.20 to 22.29)#	72 (1)	Very low*[1,2]	[1]Downgraded once due to risk of bias [2]Downgraded twice due to impre-	

Table 5. 'Summary of findings' table - Outcome: Surgical Site Infections (SSIs) *(Continued)*

										cision (small numbers of events; wide confidence intervals that include the possibility of both benefit and harm for the intervention)
f) Combined oral and intravenous versus oral or intravenous alone	N/A	N/A	N/A	N/A	N/A	N/A	9/169 vs 15/141; RR 0.50 (0.23 to 1.11)#	310 (1)	Low*[1,2]	[1]Downgraded once due to risk of bias [2]Downgraded once due to imprecision (small numbers of events; wide confidence intervals that include the possibility of both

Table 5. 'Summary of findings' table - Outcome: Surgical Site Infections (SSIs) *(Continued)*

										bene-fit and harm for the in-terven-tion)	
5.11. Meth-ods of de-creasing in-fection to im-prove out-comes af-ter liver re-sections (Gu-rusamy 2011)	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	No SSI data provided
5.12. Peri-operative antibiotics to prevent infection after first-trimester abortion (Low 2012)	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	No SSI data provided
6. Management of theatre traffic (no reviews)											
7. Wound irrigation (no reviews)											
8. Wound closure											
8.1. Contin-uous ver-sus inter-rupted skin sutures for non-obstet-ric surgery (Gurusamy 2014a) Continuous versus inter-	71 per 1000	52 per 1000 (29 to 95)	RR 0.73 (0.40 to 1.33)	602 (4)	Very low[§]	[§]High risk of bias; the confidence in-tervals overlapped 1 and either 0.75 or 1.25, or both. The number of events in the intervention and control group was fewer than 300	N/A	N/A	N/A	N/A	

Table 5. 'Summary of findings' table - Outcome: Surgical Site Infections (SSIs) *(Continued)*

rupted skin sutures											
8.2. Subcutaneous closure versus no subcutaneous closure after non-caesarean surgical procedures (Gurusamy 2014b) Subcutaneous versus no subcutaneous closure	84 per 1000	71 per 1000 (44 to 112)	RR 0.84 (0.53 to 1.33)	815 (6)	Very low§	§The trial(s) was (were) of high risk of bias The confidence intervals overlapped 1 and either 0.75 or 1.25 or both. The number of events in the intervention and control group was fewer than 300	N/A	N/A	N/A	N/A	
8.3. Review: Techniques and materials for skin closure in caesarean section (Mackeen 2012)											
a) Staples versus absorbable subcuticular suture	31 per 1000	26 per 1000 (13 to 52)	RR 0.85 (0.43 to 1.71)	916 (6)	Low*1,2	1Downgraded once due to risk of bias 2Downgraded once due to inconsistency (direction of intervention effect varied between studies)	N/A	N/A	N/A	N/A	
	13 per 1000	10 per 1000 (2 to 40)	RR 0.72 (0.17 to 3.01)	400 (4)	Low*1,2	1Downgraded once due to imprecision (small numbers of events; wide confidence intervals that include the possibility of both benefit and harm for the intervention) 2 Downgraded once due to incon-	N/A	N/A	N/A	N/A	Sensitivity analysis: Staples (1/177) versus absorbable subcuticular suture (3/223)

Table 5. 'Summary of findings' table - Outcome: Surgical Site Infections (SSIs) *(Continued)*

						sistency (direction of intervention effect varied between studies)					
b) Barbed suture versus PDS suture	33 per 1000	31 per 1000 (6 to 167)	RR 0.96 (0.18 to 5.10)	188 (1)	Low*[1]	[1]Downgraded twice due to imprecision (small numbers of events; wide confidence intervals that include the possibility of both benefit and harm for the intervention)	N/A	N/A	N/A	N/A	
8.4. Healing by primary versus secondary intention after surgical treatment for pilonidal sinus (AL-Khamis 2010)											
primary versus secondary intention											
a) Open versus closed (all)	77 per 1000	100 per 1000 (71 to 142)	RR 1.31 (0.93 to 1.85)	1231 (10)	Very low*[1,2,3]	[1]Downgraded once due to risk of bias [2]Downgraded once due to imprecision (small numbers of events; wide confidence intervals that include the possibility of both benefit and harm for the intervention) [3]Downgraded once due to inconsistency (direction of intervention effect varied between studies)	N/A	N/A	N/A	N/A	
b) Closed (midline) versus closed (other)	33 per 1000	124 per 1000 (62 to 246)	RR 3.72 (1.86 to 7.42)	541 (5)	Low*[1,2]	[1]Downgraded once due to risk of bias	N/A	N/A	N/A	N/A	1 study out of 5 had no event

Table 5. 'Summary of findings' table - Outcome: Surgical Site Infections (SSIs) *(Continued)*

						[2]Downgraded once due to imprecision (small numbers of events; wide confidence intervals that include the possibility of both benefit and harm for the intervention)					in both arms
c) Classic Limberg versus modified Limberg	30 per 1000	228 per 1000 (30 to 1000)	RR 7.54 (1.00 to 57.07)	68 (1)	Very low*[1,2]	[1]Downgraded once due to risk of bias [2]Downgraded twice due to imprecision (small numbers of events; wide confidence intervals that include the possibility of both benefit and harm for the intervention)	N/A	N/A	N/A	N/A	
d) Karydakis versus classic Limberg	80 per 1000	260 per 1000 (91 to 743)	RR 3.25 (1.14 to 9.29)	100 (1)	Very low*[1,2]	[1]Downgraded once due to risk of bias [2]Downgraded twice due to imprecision (small numbers of events; wide confidence intervals that include the possibility of both benefit and harm for the intervention)	N/A	N/A	N/A	N/A	
8.5. Staples versus sutures for closing leg wounds after vein graft	80 per 1000	97 per 1000 (48 to 192)	RR 1.20 (0.60 to 2.39)	322 (3)	Very low*[1,2]	[1]Downgraded once due to risk of bias [2]Downgraded twice due to imprecision (small	No statistically significant difference: P = 0.99	258 participants with 516 leg segments	N/A	N/A	One study was excluded from the pooled

Table 5. 'Summary of findings' table - Outcome: Surgical Site Infections (SSIs) *(Continued)*

harvesting for coronary artery bypass surgery (Biancari 2010) Staples versus sutures						numbers of events; wide confidence intervals that include the possibility of both benefit and harm for the intervention)					analysis due to the risk of a unit of analysis error
8.6. Tissue adhesives for closure of surgical incisions (Dumville 2014)											
a) Tissue adhesives versus sutures	23 per 1000	40 per 1000 (22 to 73)	RR 1.72 (0.94 to 3.16)	1239 (18)	Very low§	§Study 95% CI is wide; Possible unit of analysis issues	N/A	N/A	N/A	N/A	Eight studies had no events in either group (n = 495) Sensitivity analysis was conducted due to the unit of analysis issues in 3 studies; showing similar results
b) Tissue adhesives versus adhesive tape	43 per 1000	60 per 1000 (17 to 209)	RR 1.37 (0.39 to 4.81)#	190 (3)	Low§	§Study 95% CIs are very wide Evidence of inconsistency in point estimates. With the point estimate from one study lying outside the 95% CIs of another	N/A	N/A	N/A	N/A	

Table 5. 'Summary of findings' table - Outcome: Surgical Site Infections (SSIs) *(Continued)*

c) Tissue adhesives versus staples	71 per 1000	99 per 1000 (21 to 463)	RR 1.39 (0.30 to 6.54)#	320 (4)	Very low§	§Study 95% CIs are very wide Evidence of point estimates lying in opposite directions with the estimate for one study lying outside the 95% CI of another	N/A	N/A	N/A	N/A	One study had no events in either group (n = 70)
d) Tissue adhesives versus other techniques	66 per 1000	27 per 1000 (7 to 105)	RR 0.41 (0.11 to 1.60)#	249 (2)	Low§	§Study 95% CIs are very wide Single study with low event rate	N/A	N/A	N/A	N/A	One study had no events in either group (n = 40)
e) Adhesives versus adhesives: high viscosity versus low viscosity	47 per 1000	38 per 1000 (7 to 200)	RR 0.82 (0.16 to 4.31)	148 (1)	Very low§	§Study 95% CIs are very wide Single study with low event rate	N/A	N/A	N/A	N/A	
f) Adhesives versus adhesives: octylcyanoacrylate versus butylcyanoacrylate	333 per 1000	210 per 1000 (70 to 627)	RR 0.63 (0.21 to 1.88)	80 (2)	Low§	§The 95% CI estimate around the RR of 1.46 is very wide	N/A	N/A	N/A	N/A	One study had no events in either group (n = 43)
9. Theatre cleansing (no reviews)											

Table 6. 'Summary of findings' table - Outcome: Mortality

Intervention and comparison intervention	Meta-analysis results					Narrative results				Comments†
	Illustrative comparative risks (95% CI)	Risk Ratio (RR) (95% CI)	Number of partic-	Quality/certainty of	GRADE Footnote	Reported out-	Number of partic-	Quality/certainty of	GRADE Footnote	meta-analysis by

Table 6. 'Summary of findings' table - Outcome: Mortality *(Continued)*

	CI = confidence interval **Assumed risk** **With comparator**	**Corresponding risk** **With intervention**	#random-effects, all other RR = fixed-effect	**ipants (studies)**	**the evidence (GRADE)** * assessed by overview authors § assessed by review authors		**come values** **Results in brackets are RR with 95% CIs unless otherwise indicated** # random-effects, all other RR = fixed-effect	**ipants (studies)**	**the evidence (GRADE)** *assessed by overview authors		overview authorOdd Ratio (OR)	
4.2. Perioperative glycaemic control for diabetic patients undergoing surgery (Buchleitner 2012) Intensive versus conventional glycaemic control	N/A	N/A	N/A	N/A	N/A	N/A	0/10 vs. 2/22: RR 0.42 (0.02 to 7.99)#	32 (1)	Very low*1,2	1Downgraded twice due to imprecision (small numbers of events; wide confidence intervals that include the possibility of both benefit and harm for the intervention) 2Downgraded once due	RR 1.23 (0.18 to 8.43)†	
							2/37 vs. 0/36: RR 4.87 (0.24 to 98.02)#	73 (1)				

Table 6. 'Summary of findings' table - Outcome: Mortality *(Continued)*

										to inconsistency
4.3. Peri-operative glycaemic control regimens for preventing surgical site infections in adults (Kao 2009)										
Intra- and post-operative strict versus conventional glycaemic control with intravenous insulin	N/A	N/A	N/A	N/A	N/A	N/A	6/40 vs. 7/38; RR 0.81 (0.30 to 2.20)	78 (1)	Low*[1]	[1]Downgraded twice due to imprecision (small numbers of events; wide confidence intervals that include the possibility of both benefit and harm for the intervention)
Intra-operative strict versus conventional glycaemic control with insulin infusion	N/A	N/A	N/A	N/A	N/A	N/A	4/185 vs. 0/186; RR 9.05 (0.49 to 166.88)	371 (1)	Low*[1]	[1]Downgraded twice due to imprecision (small numbers of events; wide confidence intervals that include the possibility of both benefit and harm for the intervention)

Table 6. 'Summary of findings' table - Outcome: Mortality *(Continued)*

4.4. Perioperative increase in global blood flow to explicit defined goals and outcomes following surgery (Grocott 2012) Increased global blood flow versus control	66 per 1000	44 per 1000 (26 to 74)	RR 0.67 (0.40 to 1.13)	1202 (15)	Low*[1]	[1] Downgraded twice due to imprecision (small numbers of events; wide confidence intervals that include the possibility of both benefit and harm for the intervention)	N/A	N/A	N/A	N/A	Time intervention started - Intra-operative; 3 studies have no events in either group (n=177)
4.5. The effects of high perioperative inspiratory oxygen fraction for adult surgical patients (Wetterslev 2015) 60% to 90% oxygen versus 30% to 40% oxygen perioperatively	164 per 1000	137 per 1000 (89 to 212)	RR 1.07 (0.87 to 1.33) #	4918 (8)	Low*[1,2]	[1] Downgraded once due to imprecision (small numbers of events; wide confidence intervals that include the possibility of both benefit and harm for the intervention) [2] Downgraded once due to heterogeneity	N/A	N/A	N/A	N/A	2 studies have no events in either group (n=393)
5.1. Antibiotic prophylaxis for the prevention of methicillin-resistant Staphylococcus aureus (MRSA) related complications in surgical patients (Gurusamy 2013)											
Co-amoxiclav or cefotaxime versus placebo	146 per 1000	79 per 1000 (25 to 251)	RR 0.54 (0.17 to 1.72)	99 (1)	Low*[1]	[1]Downgraded twice due to imprecision (small numbers of events; wide confidence intervals that include the possibility of	N/A	N/A	N/A	N/A	

Table 6. 'Summary of findings' table - Outcome: Mortality *(Continued)*

						both benefit and harm for the intervention)					
Vancomycin versus cefuroxime	2 per 1000	5 per 1000 (0 to 50)	RR 2.02 (0.18 to 22.18)	884 (1)	Very low*[1,2]	[1]Downgraded once due to risk of bias [2]Downgraded twice due to imprecision (small numbers of events; wide confidence intervals that include the possibility of both benefit and harm for the intervention)	N/A	N/A	N/A	N/A	
5.11. Methods of decreasing infection to improve outcomes after liver resections (Gurusamy 2011)											
Long duration antibiotics versus short duration antibiotics	Not estimable	Not estimable	Not estimable	180 (1)	Very low[§]	[§]High risk of bias The number of trials were too few to assess inconsistency The confidence intervals of risk ratio overlapped 0.75 and 1.25 Publication bias could not be assessed because of the few trials	N/A	N/A	N/A	N/A	Not estimable due to no event in either group
Topical povidone iodine gel versus no topical povidone iodine gel	71 per 1000	96 per 1000 (17 to 538)	RR 1.35 (0.24 to 7.53)	59 (1)	Very low[§]	[§]High risk of bias The number of trials were too few to assess inconsistency	N/A	N/A	N/A	N/A	

Table 6. 'Summary of findings' table - Outcome: Mortality *(Continued)*

				The confidence intervals of risk ratio overlapped 0.75 and 1.25	
				Publication bias could not be assessed because of the few trials	

Table 7. GRADE interventions according to outcomes

Outcome	High-certainty evidence		Moderate-certainty evidence		Low-certainty evidence		Very low-certainty evidence/no studies
	What works (Important/less important benefit/harm)	**What doesn't work (no important benefit/harm)**	**What probably works (Important/less important benefit/harm)**	**What probably doesn't work (no important benefit/harm)**	**What may work (Important/less important benefit/harm)**	**No current evidence of clear difference (no important benefit/harm)**	**Uncertainty**
SSI	Adhesive drape (**harm**)	N/A	Antibiotic prophylaxis (hernia repair)	Iodine-impregnated adhesive drapes	Intra- and postoperative strict glycaemic control with intravenous glucose insulin-potassium infusion	Aqueous solutions	2% iodine in 90% alcohol
	Prophylactic intravenous antibiotics administered before caesarean incision	N/A	Antibiotic prophylaxis (caesarean section)	Duration of therapy (antimicrobial prophylaxis for colorectal surgery)	Increased global blood flow	Double gloving	Iodophor-in-alcohol paint
	Preoperative antibiotic (breast cancer surgery)	N/A		N/A	Antibiotic prophylaxis (co-amoxiclav or cefotaxime)	Disposable surgical face masks	Chlorhexidine gluconate

Table 7. GRADE interventions according to outcomes *(Continued)*

N/A	N/A	N/A	N/A	N/A	PI paint	Scalpel versus electrosurgery
N/A	N/A	N/A	N/A	Systemic antibiotic (IV)	Aqueous PI scrub	No-scalpel
N/A	N/A	N/A	N/A	Antibiotic prophylaxis (colorectal surgery)	Cholorhexidine and cetrimide scrub	Warming of IV and irrigation fluids
N/A	N/A	N/A	N/A	Additional aerobic coverage (colorectal surgery)	Vaginal preparation	Intensive glycaemic control
N/A	N/A	N/A	N/A	Additional anaerobic coverage (colorectal surgery)	Skin preparation (drape; alcohol scrub with iodophor drape; parachlorometaxylenol with iodine)	Antibiotic prophylaxis (pefloxacin; ertapenem; cefamandole; cefazolin and gentamycin; cefazolin; vancomycin and cefazolin; daptomycin and cefazolin; vancomycin and cefazolin; daptomycin and cefazolin; cephalosporin drug combination)
N/A	N/A	N/A	N/A	N/A	Techniques and materials for skin closure	IV versus irrigation
N/A	N/A	N/A	N/A	N/A	Microbial sealant	Antibiotic prophylaxis (elective laparoscopic cholecystectomy)
N/A	N/A	N/A	N/A	N/A	Intra- and postoperative strict glycaemic control	Oral versus intravenous (antimicrobial prophylaxis for colorectal surgery)
N/A	N/A	N/A	N/A	N/A	High perioperative inspiratory oxygen	Methods of decreasing infection to improve outcomes after liver resections
N/A	N/A	N/A	N/A	N/A	Antibiotic prophylaxis (vancomycin; single cephalosporin)	Perioperative antibiotics to prevent infection after first-trimester abortion
N/A	N/A	N/A	N/A	N/A	Combined oral and IV versus alone (antimicrobial	Continuous compared with interrupted skin sutures

Table 7. GRADE interventions according to outcomes *(Continued)*

						prophylaxis for colorectal surgery)	
	N/A	N/A	N/A	N/A	N/A	Intraoperative strict glycaemic control	Subcutaneous closure
	N/A	N/A	N/A	N/A	N/A	N/A	Open versus closed (primary versus secondary intention)
	N/A	N/A	N/A	N/A	N/A	N/A	Staples versus sutures
	N/A	N/A	N/A	N/A	N/A	N/A	Tissue adhesives for closure
Mortality	N/A	N/A	N/A	N/A	N/A	Increased global blood flow	Intensive glycaemic control
	N/A	N/A	N/A	N/A	N/A	Intra- and postoperative strict or Intraoperative strict glycaemic control	Long-duration antibiotics versus short-duration antibiotics
	N/A	N/A	N/A	N/A	N/A	High perioperative inspiratory oxygen	Topical PI gel
	N/A	N/A	N/A	N/A	N/A	Antibiotic prophylaxis (coamoxiclav or cefotaxime)	Antibiotic prophylaxis (vancomycin and cefuroxime)

IV: intravenous; **NA**: not applicable; **PI**: povidone iodine; **SSI**: surgical site infection

APPENDICES

Appendix 1. Summary of common topical antiseptics used in preoperative skin decontamination

Antiseptic agents

Alcohol

Alcohol denatures the cell wall proteins of bacteria. Alcohol rubs are usually available in preparations of 60% to 90% strength and are effective against a wide range of gram-positive and gram-negative bacteria, *Mycobacterium tuberculosis*, and many fungi and viruses. The three main alcohols used are ethanol, isopropanol and n-propanol, and some rubs may contain a mixture of these. Alcohol-based solutions usually (but not always) contain additional active ingredients to combine the rapid bacteriocidal effect of alcohol with more persistent chemical activity.

Iodine and iodophors

Iodine and iodophors are iodine solutions that are effective against a wide range of gram-positive and gram-negative bacteria, the tubercle bacillus (TB), fungi and viruses. These penetrate cell walls, then oxidise and substitute the microbial contents with free iodine (Hardin 1997; Mangram 1999; Warner 1988). Iodophors contain a surfactant or stabilising agent that liberates the free iodine (Wade 1980). Iodophor has largely replaced iodine as the active ingredient in antiseptics. Iodophor comprises free iodine molecules bound to a polymer such as polyvinyl pyrrolidine (i.e. povidone), so is often termed povidone iodine (PI) (Larson 1995). Typically, 10% PI formulations contain 1% available iodine (Larson 1995; Reichman 2009). PI is soluble in both water and alcohol, and available preparations include aqueous iodophor scrub and paint, aqueous iodophor one-step preparation with polymer (3M), and alcoholic iodophor with water insoluble polymer (DuraPrep).

Chlorhexidine

Chlorhexidine is a biguanide. It is effective against a wide range of gram-positive and gram-negative bacteria, lipophilic viruses and yeasts. Although its immediate antimicrobial activity is slower than alcohols, it is more persistent because it binds to the outermost layer of skin.

Triclosan

Triclosan (2,4,4'–trichloro-2'-hydroxydiphenyl ether) has been incorporated in detergents (0.4% to 1%) and alcohols (0.2% to 0.5%) used for hygienic and surgical hand antisepsis or preoperative skin disinfection. It inhibits *Staphylococci*, coliforms, enterobacteria and a wide range of gram-negative intestinal and skin flora.

Appendix 2. Search strategy

#1MeSH descriptor: [Surgical Wound Infection] explode all trees
#2MeSH 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{or #1-#11}
#13 {or #1-#11} in Cochrane Reviews (Reviews and protocols)

Appendix 3. Assessment by ROBIS signalling questions

Review	Study eligibility criteria	Identification and selection of studies	Data collection and study appraisal					Synthesis and finding						Risk of bias in the review		
	Primary study eligibility criteria were prespecified, clear, and appropriate to the review question	Were all primary studies that would have met the inclusion criteria included in the review?	Efforts were made to minimise error in data collection	Sufficient study characteristics available	All relevant study results were collected	Appropriate criteria to assess risk of bias	Efforts made to minimise error in risk of bias assessment	Synthesis included all studies	All predefined analyses followed	Synthesis was appropriate	Heterogeneity was addressed	Robust findings e.g. assessed with funnel plot or sensitivity analyses	Addressed biases in the synthesis	Interpretations of findings addressed all of the concerns identified	Relevance of identified studies to the review's research question was appropriately considered	Reviewers avoided emphasising results on the basis of their statistical significance
AL-Khamis 2010	Y	Y	Y	Y	Y	Y	Y	Y	Y	PY	PY	PN	Y	PY	Y	Y
Biancari 2010	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	PN	Y	PY	Y	Y
Buchleitner 2012	Y	Y	Y	Y	Y	Y	Y	Y	Y	PY	Y	Y	PY	PY	Y	Y
Campbell 2015	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	Y	PN	Y	Y
Charoenkwan 2017	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y

(Continued)

Cook 2014	Y	Y	Y	Y	Y	N	Y	PN	PN	PN	PN	PN	PN	PN	PY	PN
Dumville 2014	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Dumville 2015	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Grocott 2012	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Gyte 2014	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Gurusamy 2011	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Gurusamy 2013	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Gurusamy 2014a	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Gurusamy 2014b	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Haas 2014	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	Y	PY	Y	Y
Hadiati 2014	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	PN	PY	PY	Y	Y
Jones 2014	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Kao 2009	Y	Y	Y	Y	Y	Y	Y	Y	Y	PY	PY	PN	PY	PY	Y	Y
Lipp 2013	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Low 2012	Y	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Mackeen 2012	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Mackeen 2014	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Nabhan 2016	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	PY	Y	Y	Y	Y
Nelson 2014	Y	Y	Y	Y	Y	PY	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Sanabria 2010	Y	Y	Y	Y	Y	PY	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Sanchez-Manuel 2012	Y	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y

(Continued)

Smaill 2014	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Tanner 2006	Y	Y	Y	Y	Y	N	Y	Y	Y	PY	PY	N	PY	PY	Y	Y
Vincent 2016	Y	Y	Y	Y	Y	Y	Y	Y	Y	PY	PY	PN	PY	PY	Y	Y
Webster 2015	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Wetterslev 2015	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Wood 2016	Y	Y	Y	Y	Y	Y	Y	Y	Y	PY	Y	N	PY	PY	Y	Y

Footnotes

Y = yes; PY = probably yes; N = no; and PN = probably no

CONTRIBUTIONS OF AUTHORS

Zhenmi Liu: conceived, designed and coordinated the overview; extracted data; analysed and interpreted data; undertook and checked quality assessment; performed statistical analysis; produced the first draft of the overview; contributed to writing and editing the overview; performed previous work that was the foundation of the current overview; wrote to study authors / experts / companies; approved the final overview prior to submission and is a guarantor of the overview.

Jo Dumville: conceived, designed and coordinated the overview; extracted data; checked the quality of data extraction; analysed and interpreted data; checked the quality of the statistical analysis; produced the first draft of the overview; contributed to writing and editing the overview; made an intellectual contribution to the overview; advised on the overview; secured funding; performed previous work that was the foundation of the current overview; wrote to study author / experts / companies; and approved the final overview prior to submission.

Gill Norman: advised on the overview; and approved the final overview prior to submission.

Maggie Westby: advised on the overview; and approved the final overview prior to submission.

Jane Blazeby: advised on the overview; secured funding; and approved the final overview prior to submission.

Emma McFarlane: advised on the overview; and approved the final overview prior to submission.

Nicky Welton: advised on the overview; and approved the final overview prior to submission.

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Julie Cawthorne: advised on the overview; and approved the final overview prior to submission.

Ryan George: advised on the overview; and approved the final overview prior to submission.

Emma Crosbie: advised on the overview; and approved the final overview prior to submission.

Amber Rithalia: advised on the overview; and approved the final overview prior to submission.

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Contributions of the editorial base:

Nicky Cullum (Co-ordinating Editor): edited the overview; advised on methodology, interpretation and overview content; approved the final overview prior to publication.

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

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

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