



Dumville, J. C., Norman, G., Westby, M. J., Blazeby, J., McFarlane, E., Welton, N., ... Liu, Z. (2017). Intra-operative interventions for preventing surgical site infection: an overview of Cochrane reviews. *Cochrane Database of Systematic Reviews*, (5), [CD012653].
<https://doi.org/10.1002/14651858.CD012653>

Publisher's PDF, also known as Version of record

Link to published version (if available):
[10.1002/14651858.CD012653](https://doi.org/10.1002/14651858.CD012653)

[Link to publication record in Explore Bristol Research](#)
PDF-document

This is the final published version of the article (version of record). It first appeared online via Cochrane Library at <http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD012653/full>. Please refer to any applicable terms of use of the publisher.

University of Bristol - Explore Bristol Research

General rights

This document is made available in accordance with publisher policies. Please cite only the published version using the reference above. Full terms of use are available:
<http://www.bristol.ac.uk/pure/about/ebr-terms>



Cochrane
Library

Cochrane Database of Systematic Reviews

Intra-operative interventions for preventing surgical site infection: an overview of Cochrane reviews (Protocol)

Dumville JC, Norman G, Westby MJ, Blazeby J, McFarlane E, Welton NJ, O'Connor L, Cawthorne J, George RP, Liu Z, Crosbie EJ

Dumville JC, Norman G, Westby MJ, Blazeby J, McFarlane E, Welton NJ, O'Connor L, Cawthorne J, George RP, Liu Z, Crosbie EJ.

Intra-operative interventions for preventing surgical site infection: an overview of Cochrane reviews.

Cochrane Database of Systematic Reviews 2017, Issue 5. Art. No.: CD012653.

DOI: 10.1002/14651858.CD012653.

www.cochranelibrary.com

TABLE OF CONTENTS

HEADER	1
ABSTRACT	1
BACKGROUND	1
OBJECTIVES	3
METHODS	3
ACKNOWLEDGEMENTS	6
REFERENCES	7
ADDITIONAL TABLES	9
APPENDICES	13
CONTRIBUTIONS OF AUTHORS	15
DECLARATIONS OF INTEREST	15
SOURCES OF SUPPORT	16

Intra-operative interventions for preventing surgical site infection: an overview of Cochrane reviews

Jo C Dumville¹, Gill Norman¹, Maggie J Westby¹, Jane Blazeby², Emma McFarlane³, Nicky J Welton⁴, Louise O'Connor⁵, Julie Cawthorne⁵, Ryan P George⁵, Zhenmi Liu¹, Emma J Crosbie⁶

¹Division of Nursing, Midwifery & Social Work, School of Health Sciences, Faculty of Biology, Medicine & Health, University of Manchester, Manchester Academic Health Science Centre, Manchester, UK. ²NIHR Bristol Biomedical Research Centre, School of Social & Community Medicine, University of Bristol, Bristol, UK. ³Centre for Guidelines, National Institute for Health and Care Excellence, Manchester, UK. ⁴School of Social and Community Medicine, University of Bristol, Bristol, UK. ⁵Infection Prevention & Control / Tissue Viability Team, Central Manchester University Hospitals NHS Foundation Trust, Manchester, UK. ⁶Division of Molecular and Clinical Cancer Sciences, Faculty of Biology, Medicine & Health, University of Manchester, Manchester, UK

Contact address: Jo C Dumville, Division of Nursing, Midwifery & Social Work, School of Health Sciences, Faculty of Biology, Medicine & Health, University of Manchester, Manchester Academic Health Science Centre, Manchester, M13 9PL, UK. jo.dumville@manchester.ac.uk.

Editorial group: Cochrane Wounds Group.

Publication status and date: New, published in Issue 5, 2017.

Citation: Dumville JC, Norman G, Westby MJ, Blazeby J, McFarlane E, Welton NJ, O'Connor L, Cawthorne J, George RP, Liu Z, Crosbie EJ. Intra-operative interventions for preventing surgical site infection: an overview of Cochrane reviews. *Cochrane Database of Systematic Reviews* 2017, Issue 5. Art. No.: CD012653. DOI: 10.1002/14651858.CD012653.

Copyright © 2017 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

ABSTRACT

This is a protocol for a Cochrane Review (Overview). The objectives are as follows:

To present an overview of the effectiveness and safety of interventions delivered during the intra-operative period aimed at preventing surgical site infections in all populations under going surgery in operating theatre settings.

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. Surgical site infections (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 contamination level of 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 which 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 (96% 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

The 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 2017); 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 Centers 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).

Defintion 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: pre-operatively, intra-operatively and post-operatively (Goodman 2016). For the purpose of this review we define:

- the pre-operative phase as the time period between the decision for the need for surgery and when everything is ready for the operation to start i.e. 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 pre-operative period);
- the intra-operative phase as 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 listed to take place at induction of anaesthesia in this phase;
- the postoperative phase as the time period from the end of the intra-operative 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 intra-operative 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 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 over 20 Cochrane reviews that draw together randomised controlled trial evidence for individual prophylactic SSI interventions along the pre-operative, intra-operative 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 National Institute for Health and Care Excellence (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 the effectiveness and safety of interventions delivered during the intra-operative period aimed at preventing surgical site infections in all populations under going surgery in operating theatre settings.

METHODS

Criteria for considering reviews for inclusion

Types of studies

We will include reviews published in the *Cochrane Database of Systematic Reviews* that examine the effectiveness of interventions aimed at preventing surgical site infections (SSIs). We will not consider non-Cochrane reviews. We will only include systematic reviews of randomised controlled trial (RCT) evidence for patient-focused interventions. If reviews include other study designs alongside RCTs (e.g. controlled clinical trials, quasi-randomised controlled trials, or both) we will investigate if RCT evidence is presented separately for relevant analyses (e.g. as sensitivity analyses). If so, these RCT data will be included. If there are no separate data for RCTs in a review of patient-focused interventions we will not include that review in analyses. Primary RCTs published since the included reviews, but not yet included in reviews, will be excluded in line with Cochrane guidance.

Where studies evaluate 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 are more feasible and we will also extract data from these study designs as well as from RCTs (including cluster RCTs).

Types of participants

We will include reviews of studies involving adults or children or both. We will exclude 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 will be examined in detail to isolate relevant comparisons.

We will include 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 will be excluded. We will include reviews looking at surgical wounds planned to heal by primary intention (closed wounds) and secondary intention (open wounds). Given their specialist nature, we will exclude eye and oral surgeries and studies looking at infection prevention in pin sites.

Types of interventions

We will include reviews that assessed the following interventions aimed at preventing SSIs during the intra-operative period of the patient care pathway (regardless of comparator - all are eligible):

- decontamination of patients' skin at site of surgery incision;
- use of intra-operative 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 intra-operative topical antiseptics before wound closure);
- closure methods;
- theatre traffic (protocols for managing the movement of people in theatre).

We will exclude reviews focusing on comparison 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 will also exclude studies comparing different anaesthesiology regimens and those investigating the use of implants or internal devices.

Where interventions are delivered at multiple time periods in the same studies, such as for assessment of antibiotics where treatment is started in one phase and continued through multiple phases (e.g. antibiotics started pre-operatively and continued postoperatively), data will be presented in the overview that correspond with the start of the treatment. Thus this intra-operative overview will include reviews where the start of treatment is in the intra-operative phase. Where a review contains trials that variously deliver interventions at different starting phases we will aim to extract and present data for only those trials relevant to the intra-operative phase (that is where the treatment starts in the intra-operative phase).

Types of outcomes

We will present data according to the time points used in reviews (if reported). Where possible, we will group data into follow up of 30 days or less and follow up of more than 30 days. If a review presents data at many different time points, the overview authors may report data from the time points closest to 30 days and one year, noting where other time point data are 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 will present data that differentiates between superficial and deep-incisional infection.

Secondary outcomes

Mortality: postoperative mortality.

Health-related quality of life: we will include quality of life assessments where they are 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 will be adjusted for baseline scores. We will 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 will not report on multiple domain scores for validated measures.

Cost-effectiveness: findings that consider relative costs and benefits simultaneously.

Search methods for identification of reviews

We will search the *Cochrane Database of Systematic Reviews* using the search strategy presented in [Appendix 2](#). Given the large number of interventions relating to the review, the search terms focus on identification of reviews linked to surgical site infection rather than to specific interventions.

Data collection and analysis

Selection of reviews

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

Data extraction and management

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

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

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

Assessment of methodological quality of included reviews

Quality of included Cochrane reviews

We will assess the risk of bias of each included review using the ROBIS tool ([Whiting 2016](#)) which focuses on four key domains:

- study eligibility criteria;
- identification and selection of studies;
- data collection and study appraisal; and
- 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. The final phase of assessment using the ROBIS tool involves allocating an overall risk of bias judgement for the review (graded high, low or unclear) using the following signalling questions.

- Did the interpretation of findings address all of the concerns identified in domains 1 to 4?
- Was the relevance of identified studies to the review's research question appropriately considered?
- Did the reviewers avoid emphasising results on the basis of their statistical significance?

The rationale or reasoning for decisions at each stage, that is for the signalling questions and the level of concern rated, will be recorded in a table for each domain. We will aim to present a summary of ROBIS results for each review either using the suggested approach (a circle with five coloured segments per review) or coloured symbols in a table format which we think will lend itself to presentation of data for a large number of reviews.

We note that the ROBIS tool also contains an optional first phase called assessing the relevance. We do not anticipate using this phase because the relevance will be considered as part of our screening and selection process.

Quality or certainty of evidence extracted from included reviews

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

When making decisions for the risk of bias domain, we will downgrade one level when studies have 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 will follow GRADE guidance (GRADE 2013; Schünemann 2011a; Schünemann 2011b). We plan to take a conservative approach and will calculate 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 optimal sample sizes 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. Although on average, SSI rates are lower than 14% in many developed countries, they can be higher in some countries and figures vary by SSI risk of the patient. We have taken

14% as a conservative upper estimate of SSI incidence and will calculate 40% relative risk reduction.

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

If the OIS is not met we will downgrade one level. We will downgrade two levels if there are very few events (or very few participants for continuous outcomes). If the OIS is met we will downgrade one level if the 95% CI fails to exclude important benefits and harms which we will consider as a relative risk reduction or increase of 25%.

Data synthesis

The aim of this review is to present a detailed summary of treatment effect data for interventions aimed at SSI prevention. We anticipate presenting all relevant comparisons grouped by intervention type (including details of co-interventions when recorded). We will also consider data according to the contamination level of surgery where possible. We will use tabular formats to present summaries of treatment effects with a corresponding GRADE assessment for each comparison. Where possible we will extract meta-analysed data, along with details of model type and measures of statistical heterogeneity. Where data have not been meta-analysed we will report study-level treatment effects. Results from review subgroup and sensitivity analyses will also be presented. We anticipate that most, if not all, results will be presented in tabular and narrative formats. An example of the type of table we plan to use to present results is presented as Table 2.

Where applicable, we will convert available data to risk ratio (RR). Where this is not possible we will present original data. We do not plan to undertake re-analysis of data beyond conversions to RR and are not planning to undertake a network meta-analysis within given intervention types.

Elements of this protocol are drawn from related protocols and reviews by the authors (Dumville 2016; Norman 2015; Wu 2015).

ACKNOWLEDGEMENTS

The authors would like to thank peer reviewers Lawrence Best, Janet Whale, Gill Worthy, Kurinchi Gurusamy and Ros Wade and copy editor Ann Jones.

REFERENCES

Additional references

ACORN 2012

Australian College of Operating Room Nurses (ACORN). *Standards for Perioperative Nursing*. 14th Edition. Adelaide, Australia: ACORN, 2012.

Al-Niaimi 2009

Al-Niaimi A, Safdar N. Supplemental perioperative oxygen for reducing surgical site infection: a meta-analysis. *Journal of Evaluation in Clinical Practice* 2009;**15**(2):360–5.

Allegranzi 2010

Allegranzi B, Nejad SB, Combescurie C, Graafmans W, Attar H, Donaldson L, et al. Burden of endemic health-care-associated infection in developing countries: systematic review and meta-analysis. *Lancet* 2010;**377**(9761):228–41.

Allegranzi 2016a

Allegranzi B, Bischoff P, de Jonge S, Kubilay NZ, Zayed B, Gomes SM, et al. WHO Guidelines Development Group. New WHO recommendations on preoperative measures for surgical site infection prevention: an evidence-based global perspective. *Lancet Infectious Diseases* 2016;**16**(12):e276–87.

Allegranzi 2016b

Allegranzi B, Zayed B, Bischoff P, Kubilay NZ, de Jonge S, de Vries F, et al. WHO Guidelines Development Group. New WHO recommendations on intraoperative and postoperative measures for surgical site infection prevention: an evidence-based global perspective. *Lancet Infectious Diseases* 2016;**16**(12):e288–303.

ASA 2017

American Society of Anesthesiologists (ASA). ASA Physical Status Classification System. <https://www.asahq.org/resources/clinical-information/asa-physical-status-classification-system> Accessed 2nd May 2017.

Astagneau 2009

Astagneau P, L'Héritier F, Daniel F, Parneix P, Venier AG, Malavaud S, et al. Reducing surgical site infection incidence through a network: results from the French ISO-RAISIN surveillance system. *Journal of Hospital Infection* 2009;**72**(2):127–34.

Awad 2012

Awad SS. Adherence to surgical care improvement project measures and post-operative surgical site infections. *Surgical Infections* 2012;**13**(2):234–7.

Barnes 2014

Barnes S, Spencer M, Graham D, Johnson HB. Surgical wound irrigation: a call for evidence-based standardization of practice. *American Journal of Infection Control* 2014;**42**(5):525–9.

Becker 2011

Becker LA, Oxman AD. Chapter 22: Overviews of reviews. In: Higgins JP, Green S, editor(s). *Cochrane Handbook for Systematic Reviews of Interventions* Version 5.1.0

(updated March 2011). The Cochrane Collaboration, 2011. Available from handbook.cochrane.org.

Brown 2014

Brown B, Tanner J, Padley W. This wound has spoiled everything: emotional capital and the experience of surgical site infections. *Sociology of Health and Illness* 2014;**36**(8):1171–87.

Bruce 2001

Bruce J, Russell EM, Mollison J, Krukowski ZH. The measurement and monitoring of surgical adverse events. *Health Technology Assessment* 2001;**5**(22):1–194.

CDC 2017

Centers for Disease Control and Prevention (CDC). Surgical site infection (SSI) event. Procedure-associated module. January 2017. www.cdc.gov/nhsn/PDFs/pscmanual/9pscscscurrent.pdf (accessed 20 January 2017).

Cooper 2003

Cooper BS, Stone SP, Kibbler CC, Cookson BD, Roberts JA, Medley GF, et al. Systematic review of isolation policies in the hospital management of methicillin-resistant *Staphylococcus aureus*: a review of the literature with epidemiological and economic modelling. *Health Technology Assessment* 2003;**7**(39):1–194.

De Lissovoy 2009

De Lissovoy G, Fraeman K, Hutchins V, Murphy D, Song D, Vaughn BB. Surgical site infection: incidence and impact on hospital utilization and treatment costs. *American Journal of Infection Control* 2009;**37**(5):387–97.

Dumville 2016

Dumville JC, Gray TA, Walter CJ, Sharp CA, Page T, Macefield R, et al. Dressings for the prevention of surgical site infection. *Cochrane Database of Systematic Reviews* 2016, Issue 12. [DOI: 10.1002/14651858.CD003091.pub4]

ECDC 2013

European Centre for Disease Prevention and Control (ECDC). Point prevalence survey of healthcare associated infections and antimicrobial use in European acute care hospitals 2011–2012. ecdc.europa.eu/en/publications/publications/healthcare-associated-infections-antimicrobial-use-pps.pdf (accessed 12 December 2016).

Gaynes 2001

Gaynes RP, Culver DH, Horan TC, Edwards JR, Richards C, Tolson JS. Surgical site infection (SSI) rates in the United States, 1992–1998: the National Nosocomial Infections Surveillance System basic SSI risk index. *Clinical Infectious Diseases* 2001;**33**(Suppl 2):S69–77.

Gibbons 2011

Gibbons C, Bruce J, Carpenter J, Wilson AP, Wilson J, Pearson A, et al. Identification of risk factors by systematic review and development of risk-adjusted models for surgical site infection. *Health Technology Assessment* 2011;**15**(30):1–156.

Goodman 2016

Goodman T, Spry C. Introduction to perioperative nursing. *Essentials of Perioperative Nursing*. Sixth. Boston, US: Jones and Barlett Nursing, March 2016.

GRADE 2013

Schünemann H, Broz ek J, Guyatt G, Oxman A, GRADE working group. GRADE handbook. gdt.guidelinedevelopment.org/central_prod/_design/client/handbook/handbook.html (accessed 5 February 2016).

Gurusamy 2014

Gurusamy KS, Toon CD, Allen VB, Davidson BR. Continuous versus interrupted skin sutures for non-obstetric surgery. *Cochrane Database of Systematic Reviews* 2014, Issue 2. [DOI: 10.1002/14651858.CD010365.pub2]

Guyatt 2011

Guyatt GH, Oxman AD, Kunz R, Broz ek J, Alonso-Coello P, Rind D, et al. GRADE guidelines 6. Rating the quality of evidence: imprecision. *Journal of Clinical Epidemiology* 2011;**64**(12):1283-93.

Hardin 1997

Hardin W, Nichols R. Handwashing and patient skin preparation. In: Malangoni MA editor(s). *Critical Issues in Operating Room Management*. Philadelphia: Lippincott-Raven, 1997:133-49.

Health Protection Agency 2015

Health Protection Agency. Surveillance of surgical site infections in NHS hospitals in England 2014/2015. www.gov.uk/government/uploads/system/uploads/attachment_data/file/484874/Surveillance_of_Surgical_Site_Infections_in_NHS_Hospitals_in_England_report_2014-15.pdf (accessed 12 December 2016).

HICPAC 1999

Hospital Infection Control Practices Advisory Committee (HICPAC). Guideline for prevention of surgical site infection 1999. *Infection Control and Hospital Epidemiology* 1999;**20**(4):259.

Horan 1992

Horan TC, Gaynes RP, Martone WJ, Jarvis WR, Emori T. CDC definitions of nosocomial surgical site infections 1992: a modification of CDC definitions of surgical wound infections. *Infection Control and Hospital Epidemiology* 1992;**13**(10):606-8.

Hospital Infection Society 2007

Hospital Infection Society. Third prevalence survey of healthcare associated infections in acute hospitals in England 2006. webarchive.nationalarchives.gov.uk/20081105143757/dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_078388 (accessed 12 December 2016).

Jenks 2014

Jenks PJ, Laurent M, McQuarry S, Watkins R. Clinical and economic burden of surgical site infection and predicted financial consequences of elimination of SSI from an English hospital. *Journal of Hospital Infection* 2014;**86**(1):24-33.

Kovavisarach 2002

Kovavisarach E, Seedadee C. Randomised controlled trial of glove perforation in single and double-gloving methods in gynaecologic surgery. *Australia and New Zealand Journal of Obstetrics and Gynaecology* 2002;**42**(5):519-21.

Laine 2004

Laine T, Aarnio P. Glove perforation in orthopaedic and trauma surgery: a comparison between single, double indicator and double gloving with two regular gloves. *Journal of Bone and Joint Surgery* 2004;**86**(6):898-900.

Larson 1995

Larson E. APIC guideline for handwashing and hand antisepsis in health-care settings. *American Journal of Infection Control* 1995;**23**(4):251-69.

Ljungqvist 2005

Ljungqvist O, Nygren J, Soop M, Thorell A. Metabolic perioperative management: novel concepts. *Current Opinion in Critical Care* 2005;**11**(4):295-9.

Magill 2014

Magill SS, Edwards JR, Bamburg W, Beldavs ZG, Dumyati G, Kainer MA, et al. Multistate point-prevalence survey of health care-associated infections. *New England Journal of Medicine* 2014;**370**(13):1198-208.

Mangram 1999

Mangram A, Horan T, Pearson M, Silver L, Jarvis W, Hospital Infection Control Practices Advisory Committee. Guideline for prevention of surgical site infection, 1999. *Infection Control and Hospital Epidemiology* 1999;**20**(4):250-78.

NICE 2008

National Institute for Health and Care Excellence (NICE). Surgical site infections: prevention and treatment. Clinical guideline [CG74]. October 2008. www.nice.org.uk/guidance/cg74 (accessed 23 February 2017).

NICE 2016

National Institute for Health and Care Excellence (NICE). Hypothermia: prevention and management in adults having surgery. Clinical guideline [CG65]. December 2016. www.nice.org.uk/guidance/cg65 (accessed 23 February 2017).

Norman 2015

Norman G, Dumville JC, Mohapatra DP, Hassan IA, Edwards J, Christie J. Antiseptics for burns. *Cochrane Database of Systematic Reviews* 2015, Issue 8. [DOI: 10.1002/14651858.CD011821]

Public Health England 2014

Public Health England. Surveillance of surgical site infections in NHS hospitals in England: 2013 to 2014. www.gov.uk/government/uploads/system/uploads/attachment_data/file/386927/SSI_report_2013_14_final_3_.pdf (accessed 1 December 2016).

Reichman 2009

Reichman DE, Greenberg JA. Reducing surgical site infections: a review. *Reviews in Obstetrics and Gynecology* 2009;**2**(4):212-21.

RevMan 2014 [Computer program]

The Nordic Cochrane Centre. Review Manager (RevMan). Version 5.3. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration 2014.

Schünemann 2011a

Schünemann HJ, Oxman AD, Higgins JP, Deeks JJ, Glasziou P, Guyatt GH. Chapter 12: Interpreting results and drawing conclusions. In: Higgins JP, Green S, editor(s). *Cochrane Handbook for Systematic Reviews of Interventions* Version 5.1.0 (updated March 2011). The Cochrane Collaboration, 2011. Available from handbook.cochrane.org.

Schünemann 2011b

Schünemann HJ, Oxman AD, Higgins JP, Vist GE, Glasziou P, Guyatt GH. Chapter 11: Presenting results and 'Summary of findings' tables. In: Higgins JP, Green S, editor(s). *Cochrane Handbook for Systematic Reviews of Interventions* Version 5.1.0 (updated March 2011). The Cochrane Collaboration, 2011. Available from handbook.cochrane.org.

Singer 2008

Singer AJ, Quinn JV, Hollander JE. The cyanoacrylate topical skin adhesives. *American Journal of Emergency Medicine* 2008;**26**(4):490–6.

Smyth 2008

Smyth ET, McIlvenny G, Enstone JE, Emmerson AM, Humphreys H, Fitzpatrick F, et al. Four country healthcare associated infection prevalence survey 2006: overview of the results. *Journal of Hospital Infection* 2008;**69**(3):230–48.

Soderstrom 2003

Soderstrom R. Principles of electrosurgery as applied to gynaecology. In: Rock JA, Jones HW III editor(s). *Te Linde's Operative Gynecology*. 9th Edition. Philadelphia: Lippincott Williams & Wilkins, 2003:291–308.

Spagnolo 2013

Spagnolo AM, Otrria G, Amicizia D, Perdellif, Cristina ML. Operating theatre quality and prevention of surgical site infections. *Journal of Preventive Medicine and Hygiene* 2013;**54**(3):131–7.

Stephan 2002

Stephan F, Yang K, Tankovic J, Soussy CJ, Dhonneur G, Duvaldestin P, et al. Impairment of polymorphonuclear neutrophil functions precedes nosocomial infections in critically ill patients. *Critical Care Medicine* 2002;**30**(2):315–22.

Swenson 2008

Swenson BR, Camp TR, Mulloy DP, Sawyer RG. Antimicrobial-impregnated surgical incise drapes in the prevention of mesh infection after ventral hernia repair. *Surgical Infections* 2008;**9**(1):23–32.

SWI Task Force 1992

Surgical Wound Infection (SWI) Task Force. Consensus paper on the surveillance of surgical wound infections. *Infection Control and Hospital Epidemiology* 1992;**13**(10):599–605.

Wade 1980

Wade A. *Pharmaceutical Handbook*. 19th Edition. London: Pharmaceutical Press, 1980.

Warner 1988

Warner C. Skin preparation in the surgical patient. *Journal of the National Medical Association* 1988;**80**(8):899–904.

Whiting 2016

Whiting P, Savovic J, Higgins J, Caldwell D, Reeves B, Shea B, et al. ROBIS: a new tool to assess risk of bias in systematic reviews was developed. *Journal of Clinical Epidemiology* 2016; Vol. 69:225–34.

Whitney 2015

Whitney JD, Dellinger EP, Weber J, Swenson RE, Kent CD, Swanson PE, et al. The effects of local warming on surgical site infection. *Surgical Infections* 2015;**16**(5):595–603.

Wu 2015

Wu L, Norman G, Dumville JC, O'Meara S, Bell-Syer SE. Dressings for treating foot ulcers in people with diabetes: an overview of systematic reviews. *Cochrane Database of Systematic Reviews* 2015, Issue 7. [DOI: 10.1002/14651858.CD010471.pub2]

* Indicates the major publication for the study

ADDITIONAL TABLES**Table 1. Interventions aimed at preventing surgical site infections**

Intervention	Details	Theories on how the intervention type might work
Intra-operative intervention types		Intra-operative
Decontamination of patients' skin at site of surgery incision (for the patient)	Before surgery, patients' skin is disinfected using antiseptic solutions such as povidone-iodine or chlorhexidine at varying concen-	The aim of preoperative skin antisepsis is to reduce the risk of SSIs by reducing the number of microorganisms on the skin (

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

	Interventions	ACORN 2012; Mangram 1999).
Skin sealants (for the patient)	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. Cyanoacrylate, which is also used as a tissue adhesive, can be used as a skin sealant	As with other barrier methods, the use of skin sealants is focused on preventing contamination of the surgical wound with micro-organisms 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 (for the patient)	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 masks, hair covers, overshoes, gowns and other protective coverings for theatre staff (for 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 re-usable 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 (for staff)	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
Use of electrosurgery for surgical incisions (for the patient)	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	It has been suggested that using heat to make a surgical incision may reduce the risk of SSI

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

	layers once an incision has been made with a scalpel (Soderstrom 2003).	
Maintaining patient homoeostasis (warming) (for the patient)	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 peri-operative 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 peri-operative hypothermia which can lead to negative postoperative outcomes, which potentially include SSI. These interventions can also be used post-operatively to mitigate the impact of peri-operative hypothermia when it has not been prevented
Maintaining patient homoeostasis (oxygenation) (for the patient)	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) (for the patient)	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 intra-operative topical antiseptics before wound closure) (for the patient)	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 (for the patient)	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 The timing of closure can also vary; some wounds can be left open for a period follow-	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

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

	ing surgery and then closed (delayed closure)	(Gurusamy 2014).
Theatre cleansing (for the environment)	<p>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</p> <p>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</p> <p>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</p> <p>To avoid cross-infection, special protocols may be developed for cleansing when surgical patients are known to have specific infections</p>	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 (for the environment)	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 undergone full hand scrubbing protocols and so forth could also potentially increase SSI risk

Table 2. Example overview of review summary of findings table

Interventions for [condition] in [population]							Interventions for [condition] in [population]
Outcome	Intervention and Comparison intervention	Illustrative comparative risks (95% CI)	Relative effect (95% CI)	Number of participants (studies)	Quality of the evidence (GRADE)	Comments	

Table 2. Example overview of review summary of findings table (Continued)

		Assumed risk	Corresponding risk					
		With comparator	With intervention					
Outcome #1								Outcome #1
	Intervention/ comparison # 1							
	Intervention/ comparison # 2							
Outcome #2								Outcome #2
	Intervention/ comparison # 1							
	Intervention/ comparison # 2							
Outcome #3								Outcome #3
	Intervention/ Comparison # 1							
	Intervention/ Comparison # 2							

APPENDICES

Appendix 1. Summary of common topical antiseptics used in pre-operative 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 which 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 pyrrolidone (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 pre-operative skin disinfection. It inhibits *S. taphylococci*, 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 dehis*):ti,ab,kw
#8(wound* near/5 dehis*):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)

CONTRIBUTIONS OF AUTHORS

All authors approved the protocol prior to submission.

Jo Dumville: secured funding, conceived the review question, developed the protocol and co-ordinated its development, wrote the protocol edited and advised on the protocol, and is a guarantor of the protocol.

Gill Norman: edited and advised on the protocol, made an intellectual contribution to the protocol.

Maggie Westby: edited and advised on the protocol, made an intellectual contribution to the protocol.

Jane Blazeby: edited and advised on the protocol, made an intellectual contribution to the protocol.

Emma McFarlane: edited and advised on the protocol, made an intellectual contribution to the protocol.

Nicola Welton: edited and advised on the protocol, made an intellectual contribution to the protocol.

Louise O'Connor: edited and advised on the protocol, made an intellectual contribution to the protocol.

Julie Cawthorne: edited and advised on the protocol, made an intellectual contribution to the protocol.

Ryan P George: edited and advised on the protocol, made an intellectual contribution to the protocol.

Zhenmi Liu: edited and advised on the protocol, made an intellectual contribution to the protocol.

Emma Crosbie: edited and advised on the protocol, made an intellectual contribution to the protocol.

Contributions of the editorial base:

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

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

Ursula Gonthier (Editorial Assistant): edited the reference section.

DECLARATIONS OF INTEREST

Jo Dumville: I receive research funding from the National Institute for Health Research (NIHR) UK for the production of systematic reviews focusing on high priority Cochrane reviews in the prevention and treatment of wounds.

Gill Norman: my employment at the University of Manchester is funded by the National Institute for Health Research (NIHR) UK and focuses on high priority Cochrane reviews in the prevention and treatment of wounds.

Maggie Westby: my employment at the University of Manchester is funded by the National Institute for Health Research (NIHR) UK and focuses on high priority Cochrane reviews in the prevention and treatment of wounds.

Jane Blazeby: none known.

Emma McFarlane: none known.

Nicola Welton: I have received research grants from the NIHR and the MRC. Pfizer part-fund a junior researcher working on a methodology project using historical data in a clinical area unrelated to this project. I have received honoraria from ABPI for delivering masterclasses on evidence synthesis. I have delivered a short-course on network meta-analysis to ICON plc, the funds from which were paid to my institution.

Louise O'Connor: none known.

Julie Cawthorne: none known.

Ryan P George: none known.

Zhenmi Liu: my employment at the University of Manchester is supported by a grant from the National Institute for Health Research (NIHR) UK (NIHR Systematic Review Fellowships).

Emma Crosbie: I am a Scientific Editor for BJOG. I have received funding from an NIHR Clinician Scientist Award, the HTA, Wellbeing of Women/the Wellcome Trust and Central Manchester University Hospitals NHS Foundation Trust. I am an employee of the University of Manchester.

SOURCES OF SUPPORT

Internal sources

- Division of Nursing, Midwifery and Social Work, School of Health Sciences University of Manchester, UK.

External sources

- National Institute for Health Research (NIHR), UK.

This project was supported by the National Institute for Health Research, via Cochrane Infrastructure and Cochrane Programme Grant funding (NIHR Cochrane Programme Grant 13/89/08 - High Priority Cochrane Reviews in Wound Prevention and Treatment) to Cochrane Wounds. The views and opinions expressed therein are those of the authors and do not necessarily reflect those of the Systematic Reviews Programme, NIHR, NHS or the Department of Health.

- National Institute for Health Research (NIHR) Systematic Review Fellowships, UK.
- National Institute for Health Research Collaboration for Leadership in Applied Health Research and Care (NIHR CLAHRC) Greater Manchester Centre, UK.

Jo Dumville was partly funded by the National Institute for Health Research Collaboration for Leadership in Applied Health Research and Care (NIHR CLAHRC) Greater Manchester. The funder had no role in the design of the studies, data collection and analysis, decision to publish, or preparation of the manuscript. However, the review may be considered to be affiliated to the work of the NIHR CLAHRC Greater Manchester. The views expressed herein are those of the authors and not necessarily those of the NHS, NIHR or the Department of Health.