Perioperative warming therapy for preventing surgical site infection in adults undergoing surgery (Protocol)

Ousey KJ, Edward KL, Lui S, Stephenson J, Duff J, Walker KN, Leaper DJ

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[Intervention Protocol]

Perioperative warming therapy for preventing surgical site infection in adults undergoing surgery

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ABSTRACT

This is the protocol for a review and there is no abstract. The objectives are as follows:

To evaluate the effects and safety of active and passive perioperative warming interventions for the prevention of SSI**,** when compared with standard care and other interventions**.**

BACKGROUND

Description of the condition

Surgical site infections (SSI) are infections that occur in any part of the operative field following a surgical procedure and are one of the most common causes of postoperative morbidity (Alexander 2011). A European Union (EU) audit of healthcare-associated infections (HCAIs) identified an overall point prevalence of 5.7% (95% confidence interval (CI) 4.5% to 7.4%) with SSIs being the third most common (19.6%; ECDC 2013), and probably the most preventable type of HCAI. In 2002, the estimated incidence rate of HCAI in the USA was 4.5%, corresponding to 9.3 infections per 1000 patient-days or 1.7 million affected patients (Klevens 2007).

The development of an SSI is an undesirable variable in successful surgical treatment and has implications for associated costs to the healthcare system, as well as patient morbidity and mortality. There is a lack of prospective cost-benefit analysis of SSIs, but retrospective analyses clearly identify that the economic costs are substantial (Fry 2002). Apart from the unrecorded indirect costs related to loss of productivity, reduced quality of life, and substantial costs of litigation, the actual cost of an SSI can involve additional inpatient treatment and procedures that can significantly increase healthcare expenditure (Leaper 2013; Strecker 2007). Whilst SSIs can be difficult to define (one review identified 41 different definitions and 13 SSI grading scales (Bruce 2001)) the Centers for Disease Control and Prevention (CDC) guidelines classify SSIs as superficial (in the skin and subcutaneous tissue); deep incisional (within fascia and muscle); or organ space infections (such as intraperitoneal or intrahepatic) (Appendix 1; CDC 1999).

Regulation of normothermia

Normothermia (homeostasis) is the maintenance of the internal environment of a human for a free and independent life; thermal homeostasis is just one aspect of this in which a constant internal temperature is maintained for optimal physiological performance (Sessler 2000). Human beings have evolved to be homeothermic and temperature regulation is a complex balance of heat production (food ingestion and metabolism; and skeletal muscle contraction such as shivering); and heat loss (conduction, convection, or radiation) that is mediated through conscious behavioural responses, and neurological and endocrine pathways. These effects are stimulated by environmental cold or heat with the hypothalamus acting as the thermostat (Vander 1998). Thermoregulation ensures that the core temperature remains constant at or around 37 °C (range 36.5 °C to 37.5 °C) but this can vary depending on the method of measurement used (Sund-Levander 2002).

Perioperative hypothermia

Perioperative hypothermia is defined as a core temperature of less than 36.0 °C (The NICE Guideline Development Group 2008a; Denzl 1994). Unplanned perioperative hypothermia is common and estimated to occur in approximately half of all patients undergoing operative procedures (Hendolin 1982; Slottman 1985; Knaepel 2012). The perioperative period encompasses the pre-, intra- and postoperative phases of surgical care. The definitions used for this review include the following:

Preoperative phase: the period from the time of preparation for surgery/administration of premedication to the time of first anaesthetic intervention.

Intraoperative phase: the period from the time of anaesthetic induction to leaving the operating theatre.

Postoperative phase: this relates to the first 24 hours postoperatively, commencing from transfer from the operating theatre to the recovery room and including the clinical area thereafter (e.g. ward, intensive care unit [ICU]).

Causes of perioperative hypothermia

Patients undergoing surgery, particularly under general or regional anaesthesia are at risk of hypothermia during the perioperative visit (Leslie 2003). Perioperative hypothermia is caused by a combination of factors including the impairment of thermoregulation resulting from a core to periphery thermal redistribution; a reduction in metabolic heat production due to the effects of anaesthetic agents; and significant heat loss precipitated by the exposure of the body surface to the cold environment (Kurz 2008). There are a number of patient and procedure specific characteristics which are known to increase a patient's risk of perioperative hypothermia. These include an American Society of Anaesthesiologists (ASA) physical status grade II-IV (mild systemic disease to moribund); preoperative hypothermia (temperature 36°C in the hour prior to anaesthesia); undergoing combined general and regional (central neuraxial block) anaesthesia; undergoing intermediate (e.g. repair of inguinal hernia) or major (e.g. joint replacement) surgery; and being at-risk of cardiac complications (The NICE Guideline Development Group 2008a).

Effects of perioperative hypothermia

The evidence that perioperative hypothermia contributes to serious adverse surgical complications is almost 20 years old (Kiekkas 2005). A 1996 prospective study reported that a 1.6°C drop in core temperature increased blood loss by 30% and significantly increased transfusion requirements (Schmied 1996), while the same year Kurz and colleagues found that a 2°C drop tripled the incidence of surgical site infection (Kurz 1996). In the following year, an RCT demonstrated that patients assigned to experience 1.4°C core hypothermia were twice as likely to experience adverse myocardial outcomes (Frank 1997). Adverse complications associated with perioperative hypothermia have been shown to prolong hospital stay and increase overall healthcare costs (Lenhardt 1997; Kurz 1996).

It should be noted, however, that under certain circumstances, particularly in relation to ischaemia-reperfusion injury (damage caused when blood supply returns after a period of restricted blood supply), perioperative hypothermia may have a tissue-protective effect due to the reduction in basal metabolic rate (the rate at which the body uses energy to maintain vital functions when at rest) (Sessler 1994).

Description of the intervention

Methods available for the avoidance of perioperative hypothermia

Perioperative hypothermia may be prevented by passive or active warming methods. Passive warming supports heat retention by providing insulation and preventing heat loss, whereas active warming increases the total heat content of the body by increasing heat production (e.g. giving an IV amino acid infusion), or through the net transfer of heat from an external source (Putzu 2007). Heat delivery systems can be classified as either systemic (whole body) or local (delivering to a specific area) and depending on the mechanism of heat generation and transfer they may be further classified into mechanical, chemical or electrical systems (Urrútia 2011). In general surgical patients, passive warming with blankets; active external warming with forced air (FAW); circulating water blankets or mattresses; mattresses or blankets with electrical heating elements; and warming of infusions can be used.

Active warming techniques: techniques that provide heat gain to a patient undergoing surgery via convection, conduction or radiation that include, but are not limited to, the use of one or

more of the following active warming mechanisms (Putzu 2007; Urrútia 2011):

- **Forced air warming devices**: a temperature management unit where heated air is used to warm patients through convection. The warming unit draws ambient air through a filter and warms the air to a specified temperature. The warmed air is delivered through a hose to a blanket or gown placed over the patient. This is the most widely used system.
- **Conductive resistive polymer mattresses and overblankets:** a conductive polymer sheet that goes under and over the patient produces heat safely and controllably throughout the perioperative period. This is the second most widely used system.
- **Electric blankets:** a blanket with an integrated electrical heating device.
- **Radiant heaters:** an electric heater that generates heat using infrared radiation.
- **Water mattresses:** a thermostatically controlled water-filled mattress placed under a patient providing warming through conduction.
- **Warmed cotton blankets:** cotton blankets warmed in a thermostatically controlled incubator.
- **Heating gel pads:** a thermostatically controlled malleable pad/mattress placed under a patient providing warming through conduction.
- **Exothermic pads:** pads exposed to air to allow an exothermic heat-releasing warmth for three to four hours and placed locally or in jackets to allow systemic (whole body) warming.
- **Heated-humidifiers:** machines that warm and moisten gases by passing air over the surface of a heated water reservoir attached to a ventilator.
- **Fluid warmers:** devices that allow the infusion of warm fluids set to a specified temperature.

Passive warming mechanisms: use insulation techniques to prevent or minimise heat loss from a patient via convection, conduction, radiation or evaporation and include, but are not limited to, the following passive warming mechanisms (Sessler 1997):

- **Reflective blankets/ clothing:** low-weight, low-bulk blanket/clothing made of heat-reflective thin plastic sheeting.
- **Fluid warming cabinets:** A thermostatically controlled cabinet for warming
- **Ambient temperature control:** maintenance of operating room temperature within set parameters as an intervention to prevent hypothermia.

Surgical doses of anaesthetics decrease vasoconstriction, which has an impact on the thermoregulatory control known as redistribution hypothermia. Preoperative warming for one to two hours is effective in reducing the initial redistribution hypothermia during anaesthesia (Just 1993), and combined preoperative and intraoperative surface warming is better than intraoperative warming alone in preventing hypothermia in the first two hours of anaesthesia (Vanni 2003). In many cases, warming is instigated on the ward to maintain normothermia from the ward via the anaesthetic room to the operating theatre through to leaving the recovery room (Andrzejowski 2008). FAW has been shown to be superior to passive warming and warming with water flow systems or radiant heat. Heating with resistive polymer-incorporated blankets is as effective as FAW (Negishi 2003). Passive and active warming interventions can have both systemic and local effects, preventing and/or reversing the consequences of hypothermia in particular.

How the intervention might work

Perioperative hypothermia is an adverse surgical event associated with SSI and other serious complications (The NICE Guideline Development Group 2008a). The use of perioperative warming to maintain normothermia has been shown to reduce the incidence of surgical site infection significantly (Kurz 1996). The proposed mechanism of action for the beneficial effect of warming is tissue oxygenation: thermoregulatory vasoconstriction reduces the levels of oxygen in tissues and results in subcutaneous hypoxia (Grief 2000; Sessler 1997). This hypoxia is a potential infection risk that impairs the oxidative killing capacity of neutrophils and weakens the healing wound by reducing deposition of collagen (Sheffield 1996; Van Oss 1980). Perioperative warming maintains tissue oxygenation by preventing or reducing thermoregulatory vasoconstriction.

Why it is important to do this review

Research on the effective management of perioperative temperature homeostasis recognises the pathophysiological adverse effects that hypothermia can have on surgical patients (Kumar 2005). Maintenance of normothermia has been shown to be an effective way of avoiding or treating many of these complications and improving outcomes in a variety of clinical contexts, for example in patients who experience large burns (Davies 2013) or in controlling fever in patients with a brain injury (Bohman 2014). In addition perioperative normothermia may reduce the incidence of surgical-wound infection and shorten hospital stay and morbid cardiac events (Bohman 2014). There are a range of patient warming devices available that can be used for prevention of hypothermia, however, The NICE Guideline Development Group 2008a concluded that evidence for many of these methods was too limited for clear recommendations to be made. Nevertheless, NICE did report that there was sufficient evidence of clinical effectiveness and cost-effectiveness for recommendations to be made on the use of FAW to prevent and treat perioperative hypothermia. Avoidance of hypothermia is now a component of many care bundles, not just to reduce the risk of SSIs, but it may also help to reduce the overuse of antibiotics (Anthony 2011).

There has been further research published in this field since the NICE guideline was released, however, to date there has been no systematic review or meta-analysis that has reported on the use of passive and active warming perioperative interventions in the prevention of surgical site infection. Kumar 2005 was a narrative literature review that concentrated on the effects of perioperative hypothermia and warming in surgical practice; while relevant, this review did not focus specifically on SSI and was published a while ago. This review will explore all warming interventions and explore the effect on the prevention of SSI. The findings will enhance our knowledge of the most effective way to warm patients in the perioperative period with systematic evaluation of the costs and benefits or disadvantages.

OBJECTIVES

To evaluate the effects and safety of active and passive perioperative warming interventions for the prevention of SSI**,** when compared with standard care and other interventions**.**

METHODS

Criteria for considering studies for this review

Types of studies

We will include randomised controlled trials (RCTs) and include cluster RCTs.

Types of participants

We will include adult patients undergoing any elective or emergency surgery under general anaesthesia. However, patients undergoing surgery requiring therapeutic hypothermia (such as certain cardiac and neurosurgical procedures) will not be included.

Types of interventions

For the purpose of this review we will include any active or passive warming intervention used perioperatively, that is during the pre-, intra- and postoperative period (up to 24 hours post-surgery) for the prevention or treatment of hypothermia.The comparisons of interest are:

- any warming (active or passive) versus no warming;
- active warming versus passive warming.

Types of outcome measures

Primary outcomes

- The status (presence or absence) of superficial, deep incisional and organ/space SSI at discharge and 30 days, 90 days and one year post-discharge. For the purposes of this review we will accept the definition of SSI used in the trial
- Adverse reactions relating to the use of warming devices (such as burns) at any time point.

Secondary outcomes

- Patient-reported outcomes (thermal comfort, satisfaction, and anxiety) measure at any time point postoperatively
- Inpatient mortality (all-cause)
- Length of hospital stay
- Rate of hospital re-admission with a 30 day re-admission rate for soft tissue surgery and one year re-admission rate for prosthetic surgery (considered as a binary variable, with no distinction being made between single and multiple re-admissions).

Search methods for identification of studies

Electronic searches

We will search the following databases to identify reports of relevant RCTs:

- Cochrane Wound Group's Specialised Register;
- Cochrane Central Register of Controlled Trials (CENTRAL; *The Cochrane Library,* latest issue);
- Ovid MEDLINE (1946 to present);
- Ovid EMBASE (1974 to present);
- EBSCO CINAHL (1982 to present).

We will combine the Ovid MEDLINE search with the Cochrane Highly Sensitive Search Strategy for identifying randomised trials in MEDLINE: - sensitivity and precision-maximising version (2008 revision; Lefebvre 2011). We will combine the EMBASE search with the Ovid EMBASE filter developed by the UK Cochrane Centre (Lefebvre 2011). We will combine the CINAHL searches with the trial filters developed by the Scottish Intercollegiate Guidelines Network (SIGN 2011). There will be no restrictions with respect to language, date of publication or study setting. We will search the following clinical trial registries:

- ClinicalTrials.gov (http://www.clinicaltrials.gov/);
- WHO International Clinical Trials Registry Platform (http://apps.who.int/trialsearch/Default.aspx);
- EU clinical trials register platform (ICTRP) (https://www.clinicaltrialsregsiter.eu/).

We will search the registers and databases using adapted phrases as recommended by (Moola 2011; Urrútia 2011).
Our search strategy will use free text and controlled language (MeSH terms) for those terms and descriptors concerning interventions (warming systems) and indications (surgery, hypothermia),
The provisional CENTRAL search strategy is:
#1 MeSH descriptor Body Temperature, this term only
#2 MeSH descriptor Heating, this term only
#3 MeSH descriptor Rewarming explode all trees
#4 (Active warming system*) or ((Mattress* or blanket*) near (warm water or Electric)) or Forced-air warming or (((Intravenous or irrigation) near fluid*) and warming) or (CO2 near warming) or (an?esthetic near warming) or ((thermal or temperature) near manag*) or (warming or blanket*):ti,ab
#5 (#1 OR #2 OR #3 OR #4)
#6 MeSH descriptor Surgical Procedures, Operative, this term only
#7 MeSH descriptor Operating Rooms explode all trees
#8 MeSH descriptor Recovery Room explode all trees
#9 ((operat* or recovery) near room*):ti,ab
#10 MeSH descriptor General Surgery, this term only
#11 MeSH descriptor Intraoperative Complications explode all trees
#12 MeSH descriptor Postoperative Complications, this term only
#13 MeSH descriptor Preoperative Care explode all trees
#14 MeSH descriptor Postoperative Care explode all trees
#15 MeSH descriptor Intraoperative Care explode all trees
#16 MeSH descriptor Surgical Site Infection explode all trees
#17 ((operat* or surg*) near complic*):ti,ab or (surg* or operat*):ti,ab or (post?operativ* or pre?operativ* or peri?operativ*):ab
#18 (#6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17)
#19 (#5 AND #18)
#20 BairHugger OR Bair Hugger OR ThermaCare OR Gaymar OR Optisan OR WarmAir OR FilteredFlow OR WarmTouch OR CareDrape OR Life-Air OR Snuggle Warm OR Warm-Gard
#21 (#19 OR #20)

Searching other resources

We will explore sources of unpublished data in order to maximise identification of data during the search stage. We will also contact manufacturers of warming devices we are evaluating for any data they may have.

Reference searching

We will inspect references of all identified studies and relevant systematic reviews for further relevant studies. We will also examine conference proceedings and systematic reviews in the field that might refer to unpublished data.

Personal contact

We will contact the first author of each included study for information regarding unpublished trials, and key opinion leaders in the field.

Data collection and analysis

Selection of studies

Two pairs of review authors (KLE and DJL; JD and KW) will independently assess the study titles and abstracts against the review inclusion criteria. We will obtain full copies of all studies felt to be potentially relevant. Two pairs of review authors (KLE and DJL; JD and KW) will independently apply the inclusion criteria to the full papers. Where disagreement occurs during the selection processes, we will resolve this by discussion between the pairs of review authors. Studies published in duplicate will be included once, but we will extract the maximum amount of data from the papers. Authors of primary studies will be contacted for clarification if necessary. We will complete a PRISMA flow chart to summarize the selection of studies (Liberati 2009).

Data extraction and management

Data extraction will be completed independently by two pairs of review authors (KLE and DJL; JD and KW) using a standardised data extraction form. Again, we will discuss any disagreement, document our decisions and, if necessary, we will contact the study authors for clarification. We will extract data presented in graphs and figures when alternative routes have been exhausted, but we will include such data only if two review authors independently reach the same result and if further statistical manipulation of data would not be required as a result of this process. We will extract information on:

- patient characteristics - gender, age, type of surgery, type of anaesthesia, duration of surgery and American Society of Anesthesiologists (ASA) grade;
- study details, including study dates, design, country in which the study was conducted and sample size;
- intervention details, including type/description of warming therapy, duration and frequency of intervention, body site covered, and temperature settings;
- comparators - no warming devices versus passive warming device; no warming versus active warming; any standard care versus active or passive warming; and any alternate form of warming versus standard care;
- outcome data by group, relating to both primary and secondary outcomes (using outcomes as defined above).

Assessment of risk of bias in included studies

Two pairs of review authors (KLE and DJL; JD and KW) will independently assess risk of bias, using the Cochrane risk of bias tool (Higgins 2011). If the raters disagree, the final rating will be made by consensus. This set of criteria is based on evidence of associations between an overestimation of effect and high risk of bias of the article, that may be caused by the way in which sequence generation, allocation concealment, blinding, incomplete outcome data, selective reporting and other issues (e.g. extreme baseline imbalance, issues with unit of investigation) are handled. We will provide an overall risk of bias assessment for the identified outcomes across all studies. We will judge each outcome as being at low or high risk of bias. We will complete a 'Risk of bias' table for each eligible study; we will combine these data into a 'Risk of bias' summary figure where judgements for each domain are tabulated by study.

Where possible, when a lack of reported information results in an 'unclear' decision, study authors will be contacted for clarification. The level of risk of bias will be noted in both the text of the review and in the 'Summary of findings' table. Consideration will be given to how the potential study bias might affect the conclusions of our review.

Measures of treatment effect

We will analyse the results of the trials using RevMan 5.3 (RevMan 2014), following the recommendations set out by the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). We will express the primary outcome of the trial and some of the secondary outcomes as dichotomous variables. In these cases we will calculate an estimation of the risk ratio (RR) and an associated 95% confidence interval (CI). For secondary outcomes expressed as continuous measures we will estimate the mean difference (MD) between groups with 95% CIs. For the secondary outcome 'length of stay' we will use median values if, as expected, this variable exhibits the skewness expected; we will also consider this variable for log transformation. We may calculate measures of effect size based on pooled estimates of variability, if appropriate. Forest plots will be used to present outcome measures and associated 95% CIs. Overlapping CIs will be considered to indicate compatible results (statistical homogeneity). We will record the adverse events reported and present this information narratively, we will report the data as count data if available. Where multiple trial arms are reported in a single trial, we will include only the relevant arms. If two interventions or more interventions are compared with control and are eligible for the same meta analysis, we will pool the intervention arms and compare that with control.

Unit of analysis issues

Cluster trials

We will check trials involving hierarchical data structures for adequacy of analysis: for example, whether or not the 'clustering effect' has been accounted for in a random-effects or fixed-effect model. Failure to account for hierarchical data structures is known to lead to potentially spurious indications of significance due to inflation of standard errors (Armitage 2005).

Where clustering is not accounted for in primary studies, we will seek to contact first authors of studies to obtain intra-class correlation coefficients (ICCs) for their clustered data and to adjust for this using accepted methods. We will not combine cluster trials with non-cluster trials in which the ICC is not available. Where clustering has been incorporated into the analysis of primary studies, we will present these data as if from a non-cluster randomised study, but adjust for the clustering effect.

Dealing with missing data

The problem of missing data is common in trials, especially those of poor quality. Excluding participants from the analysis after randomisation, or ignoring participants lost to follow-up can, in effect, undermine the process of randomisation and thus, potentially, introduce bias into the trial. If possible we will contact study authors for clarifications regarding studies with missing data. For our primary outcome, incidence of postoperative SSI, we will follow procedures outlined by Miller 1995 to assess the effect of such potential bias by bivariate and multivariate comparisons of 'stayers and leavers'.

Where a trial does not specify participant group numbers prior to dropout, we will only present complete case data. We will present data for all secondary outcomes as complete case analyses.

Assessment of heterogeneity

A standard test of heterogeneity (Cochrane's Q test) will be conducted to investigate whether the variation in individual effects is compatible with chance alone. However, it is recognised that this test is susceptible to the number of trials included in the meta-analysis and is known to be poor at detecting true heterogeneity among studies as significant (Higgins 2003). Hence we will additionally calculate the I^2 statistic (Higgins 2003), which provides an estimate of the percentage of inconsistency thought to be due to chance. An I^2 estimate of around 75%, accompanied by a statistically significant Chi^2 statistic will be interpreted as evidence of substantial levels of heterogeneity (Section 9.5.2 of the *Cochrane Handbook for Systematic Reviews of Interventions*; Higgins 2011).

Assessment of reporting biases

To assess for publication bias, we will construct funnel plots (described in Section 10 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011), subject to a suitable number (a minimum of 10) of included studies being identified.

Data synthesis

In the absence of clinical and methodological heterogeneity, we will perform a meta-analysis using a fixed-effect model. Where there is clinical heterogeneity, we will use a random-effects model (taking account of between-study variability by including it as a component of error in the model) applied to the effect indicators (primarily odds ratios and mean differences), subject to a sufficient number of studies being available. This approach leads to a reduction in the probability of spurious inferences of significance compared to the fixed-effect approach, due to the wider confidence intervals and higher P values arising from the random-effects approach.

Due to the relative rarity of the primary outcome, small numbers of events may be anticipated and Peto's method may be used to pool ORs in this instance (fixed-effect models only); otherwise the Mantel-Haenszel method will be used for this purpose. For continuous secondary outcomes, the inverse variance method will be used, based on the effect measure of mean differences, for either random-effects or fixed-effect analyses.

We will perform the analyses using the Cochrane Review Manager software (RevMan 2014).

Subgroup analysis and investigation of heterogeneity

Where possible we will undertake subgroup analyses comparing emergency surgery versus elective surgery, and clean, clean contaminated, contaminated and dirty surgery.

'Summary of findings' tables

We will present the main results of the review in 'Summary of findings' tables, providing key information concerning quality of evidence, the magnitude of the effect of the interventions examined, and the sum of the available data on the main outcomes, as recommended by the Cochrane Collaboration (Schünemann 2011a). We plan to include the main outcome (incidence of postoperative SSI) and adverse reactions, and secondary outcomes (patient acceptability of the warming intervention, mortality, length of stay,) in the 'Summary of findings' tables, which will also include an overall grading of the evidence related to each of the main outcomes, using the GRADE approach (Schünemann 2011b).

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* *Indicates the major publication for the study*

APPENDICES

Appendix 1. Centers for Disease Control and Prevention Surgical Site Infection Definition

Superficial incisional infection: is defined as a SSI that occurs within 30 days of surgery and involves only the skin or subcutaneous tissue of the incision, and meets at least one of the following criteria:

- *Criterion 1:* purulent (pus-filled) drainage from the superficial incision.
- *Criterion 2:* the superficial incision yields organisms from the culture of aseptically aspirated (drawn under sterile conditions using a needle or cannula) fluid or tissue, or from a swab, and pus cells are present.
- *Criterion 3:* at least two of the following clinical symptoms or signs are present: pain or tenderness; localised swelling; redness; or heat,

and either the superficial incision is deliberately opened by a surgeon to manage the infection (unless the incision is culture-negative) or the clinician diagnoses a superficial incisional infection.

Deep incisional infection: is defined as a SSI involving the deep tissues (i.e. fascial and muscle layers) that occurs within 30 days of surgery if no implant (an orthopaedic or vascular graft) is in place, or within a year if an implant is in place, and the infection appears to be related to the surgical procedure, and meets at least one of the following criteria:

- *Criterion 1:* purulent drainage from the deep incision but not from the organ/space component of the surgical site.
- *Criterion 2:* the deep incision yields organisms from the culture of aseptically aspirated fluid or tissue, or from a swab, and pus cells are present.
- *Criterion 3:* a deep incision that spontaneously dehisces (bursts open) or is deliberately opened by a surgeon when the patient has at least one of the following symptoms or signs (unless the incision is culture-negative): fever (temperature over 38°C); localized pain or tenderness.
- *Criterion 4:* an abscess or other evidence of infection involving the deep incision that is found by direct examination during re-operation, or by histopathological (microscopical examination) or radiological examination.
- *Criterion 5:* diagnosis of a deep incisional surgical site infection by an attending clinician.

An infection involving both superficial and deep incision is classified as deep incisional SSI unless there are different organisms present at each site.

Organ/space infection: is defined as a SSI involving any part of the anatomy (i.e. organ/space), other than the incision, opened or manipulated during the surgical procedure, that occurs within 30 days of surgery if no implant is in place, or within one year if an implant is in place and the infection appears to be related to the surgical procedure, and meets at least one of the following criteria:

- *Criterion 1:* purulent drainage from a drain that is placed through a stab wound into the organ/space.
- *Criterion 2:* the organ/space yields organisms from the culture of aseptically aspirated fluid or tissue, or from a swab, and pus cells are present.
- *Criterion 3:* an abscess or other evidence of infection involving the organ/space that is found by direct examination, during re-operation, or by histopathological or radiological examination.
- *Criterion 4:* diagnosis of an organ/space infection by an attending clinician.

CONTRIBUTIONS OF AUTHORS

Karen Ousey: conceived the review question. Developed and co-ordinated the protocol. Wrote and edited the protocol. Approved the final version of the protocol prior to submission.

Karen-Leigh Edward: conceived the review question. Developed and co-ordinated the protocol. Wrote and edited the protocol. Approved the final version of the protocol prior to submission.

Steve Lui: conceived the review question. Developed, wrote and edited the protocol.

John Stephenson: completed the first draft of the protocol and edited the protocol. Gave statistical advice on the protocol.

Jed Duff: conceived the review question. Developed, wrote and edited the protocol.

Kim Walker: advised on part of the protocol.

David Leaper: completed the first draft of the protocol and edited the protocol.

Contributions of the editorial base:

Kurinchi Gurusamy edited the protocol; advised on methodology, interpretation and protocol content. Approved the final protocol prior to submission.
Sally Bell-Syer: coordinated the editorial process. Advised on methodology, interpretation and content. Edited the protocol.
Amanda Bryant: designed the search strategy and edited the search methods section.

DECLARATIONS OF INTEREST

Karen Ousey: Provides consultancy work for a range of wound care companies with the University of Huddersfield including URGO partnership, Coloplast, Smith and Nephew, 3M Healthcare, KCI. None of the consultancy work focusses or investigates perioperative warming. As such there are no conflicts of interest.

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