Negative pressure wound therapy for skin grafts and surgical wounds healing by primary intention (Protocol)

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[Intervention Protocol]

Negative pressure wound therapy for skin grafts and surgical wounds healing by primary intention

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ABSTRACT

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

To assess the effects of NPWT on surgical wounds that are expected to heal by primary intention, that is through primary closure or skin grafting.

BACKGROUND

Description of the condition

It is estimated that between 187 and 281 million operations are carried out annually worldwide, equating to one operation each year for every 25 people (WHO 2009). This figure is higher in developed countries. For example, in Australia in 2008/09 it can be calculated from hospital statistics that there was one elective surgery for every 12.4 people (Australian Institute of Health and Welfare 2010).

Surgical wounds generally heal by primary intention; that is, the wound heals when the wound edges are brought together so that they are adjacent to each other, including skin grafting or primary closure. Wound closure is usually assisted using sutures (stitches), staples, adhesive tape or glue (Coulthard 2010) and healing begins within hours of closure (Rodero 2010). However, some types of surgical wounds, such as skin grafts (Culliford 2007) and sternal wounds (Schimmer 2008) are more difficult to heal due to their anatomical position or an increased likelihood of infection. So too are surgical wounds in certain types of patients, such as the morbidly obese (Waisbren 2010).

Failure of a wound to heal may be due to underlying patient characteristics such as age or medical conditions, including malnutrition, obesity, uncontrolled diabetes, cardiovascular disease, compromised immunity or infection (Baronski 2008). It may also be the result of dehiscence, or separation of the wound edges. Reasons for dehiscence are either technical, such as sutures breaking, cutting through tissue or knots slipping, or inadequate splinting (Baronski 2008) or related to patient factors, such as those listed above and particularly wound infection (Ortega 2010). Chronic obstructive pulmonary disease is a major risk factor for dehiscence in sternal surgery (Olbrecht 2006). The most serious complication of dehiscence is wound evisceration, where the wound completely separates, exposing the underlying organs (Harvey 2005).

Description of the intervention

Negative pressure wound therapy (NPWT) has been used to aid healing since it was first developed in the late 1990s (Fleischmann 1997; Morykwas 1997). The treatment is recommended for a diverse range of lesions including open abdominal wounds (Stevens 2009), open fractures (Stannard 2009), skin graft donor sites (Chio 2010), acute burns (Molnar 2005), pressure ulcers (Mandal 2007), post-traumatic wounds (Kanakaris 2007), diabetic foot ulcers (Eneroth 2008), split thickness skin grafts (Blume 2010), sternal wounds (Sjogren 2010) and, more recently, for clean surgery in obese patients (Dragu 2010). When NPWT is used following skin grafts and clean surgery the intent is prophylactic: to prevent a surgical site complication. This is in contrast to the more usual application: to promote the formation of granulation tissue in chronic or infected wounds.

The treatment is based on a closed sealed system that produces negative pressure to the wound surface. The wound is covered or packed with an open-cell foam or gauze dressing and sealed with an occlusive drape. Intermittent or continuous suction is maintained by connecting suction tubes from the wound dressing to a vacuum pump and liquid waste collector. Standard negative pressure rates range between 50 and 125 mm Hg (Ubbink 2008; Vikatmaa 2008). Most of the reported studies have used a vacuum-assisted closure (VAC®) system (Morykwas 1997), however, because purchasing or renting this equipment carries a high cost, innovative alternatives are being reported (Llanos 2006; Mody 2008; Rozen 2008).

How the intervention might work

In humans, the wound healing process may be sub-divided into three consecutive and overlapping stages: inflammation, new tissue formation and remodelling (Gurtner 2008). The precise way in which NPWT may aid this process has not been clearly explained. However, experimental evidence suggests that a number of factors contribute, including increased local blood flow, increased granulation tissue, reduction in bacterial contamination, wound area reduction, reduction in oedema and exudate, and changes to the microenvironment of the wound (Banwell 2003). One of the basic theoretical principles underpinning the development of NPWT is that it increases perfusion or blood flow, but this has been recently challenged. In an experimental study, using healthy controls, a negative relationship was found between perfusion and increased topical pressure. In other words, local blood flow decreased as suction pressure increased (Kairinos 2009).

Why it is important to do this review

Wounds that fail to heal may cause considerable distress to patients and impact negatively on the physical, social, emotional and economic aspects of their life (Andersson 2010). Investigations into interventions to avoid wound breakdown are therefore important. NPWT was approved by the American Food and Drug Administration (FDA) for the treatment of non-healing wounds in 1995 (Kloth 2002). More recently, a multi-national expert working group has issued guidelines for the use of the therapy for diabetic foot ulcers, complex leg ulcers, pressure ulcers, dehisced sternal wounds, open abdominal wounds and traumatic wounds (Expert Working Group 2008). While negative pressure wound therapy has become an accepted part of modern wound healing techniques, there have also been reports of severe adverse events associated with the therapy. Problems have included stomal dehiscence (Steenvoorde 2009), extraperitoneal bladder leakage (Heuser 2005), necrotising fasciitis (Citak 2010) and bleeding after cardiac surgery (Petzina 2010). In addition, when compared to other forms of wound management, patients receiving NPWT

report higher levels of pain (Apostoli 2008) and anxiety (Keskin 2008). Communiqués issued in 2009 by the FDA reported six deaths and 77 injury reports associated with the use of NPWT. The information sheets contained warnings and recommendations for consumers and healthcare practitioners about use of the treatment in certain circumstances (FDA 2009a; FDA 2009b).

Although several reviews of NPWT have been published, none have focused specifically on postoperative wounds expected to heal by primary intention (Gregor 2008; Ubbink 2008; Vikatmaa 2008); nor have any included an economic analysis. In addition, although publication bias has been noted, both in terms of the majority of trials being funded by manufacturers (Vikatmaa 2008) and premature termination of studies (Gregor 2008), no sub-analyses to control for these potential biases have been conducted. Recent reviews have concluded that the evidence for the effectiveness of NPWT remains uncertain, however, this is an evolving therapy and the indications for its use are widening. Consequently, a Cochrane Review is required to summarise current evidence for postoperative wounds expected to heal by primary intention and to ensure that future trials are included in updates.

OBJECTIVES

To assess the effects of NPWT on surgical wounds that are expected to heal by primary intention, that is through primary closure or skin grafting.

METHODS

Criteria for considering studies for this review

Types of studies

We will include only randomised controlled trials (RCTs) that evaluate the effects of NPWT on the healing of surgical wounds. Surgical wounds may include split skin grafts, full skin grafts or any primary wound closure. This criterion encompasses comparative full and partial economic evaluations conducted within the framework of eligible RCTs (i.e. cost-effectiveness analyses, cost-utility analyses, cost-benefit analyses and cost-analyses). We will not include trials of skin graft donor sites or wounds that were unable to be closed immediately because of damaged tissue (for example in severe trauma), infection or chronicity. Cross-over trials and quasi-randomised studies, e.g. treatment allocation alternate or by date of birth, will be also be ineligible.

Types of participants

We will include trials involving people of any age, and in any care setting, involving the use of NPWT for surgical wounds.

Types of interventions

The primary intervention will be NPWT delivered by any mode (for example vacuum-assisted closure (VAC® system) or simple closed-system suction drainage) delivered continuously or intermittently over any time period. The comparison will be any standard dressing (for example gauze) or any advanced dressing (for example hydrogels, alginates, hydrocolloids).

Types of outcome measures

Primary outcomes

- Proportion of surgical wounds healing by primary intention that completely heal (surgical wounds may include split skin grafts, full skin grafts or any primary wound closure).
- Mortality.
- Adverse events.

Secondary outcomes

- Time to complete healing.
- Pain (measured by any valid pain assessment instrument).
- Wound complications (such as wound infection, dehiscence, haematoma, seroma) (we will accept any definition used by the author).
- Quality of life (measured by any valid assessment instrument).
- Patient satisfaction.

Economic outcomes

- Utility scores representing health-related quality of life
- Multi-attribute utility instrument (MAUI)
- Algorithm used for scoring the MAUI
- Other measures of utility
- Treatment costs per patient per wound
- Costs of health practitioner time or visits
- Costs of hospital stay for wound healing
- Procedure costs to treat adverse events, infections or complications
- Costs of hospital stay resulting from adverse events and complications
- Unit costs of resources required
- Indirect health resource consumption, such as the cost of additional hospital bed days
- Incremental cost per event (such as per additional wound healed)
- Incremental cost per life year gained

- Incremental cost per quality adjusted life year (QALY)
- Cost-benefit ratio

Search methods for identification of studies

Electronic searches

We will search the following electronic databases to identify reports of relevant randomised clinical trials:

- The Cochrane Wounds Group Specialised Register;
- The Cochrane Central Register of Controlled Trials (CENTRAL) (*The Cochrane Library*) (latest issue);
- Ovid MEDLINE (2005 to present);
- Ovid EMBASE (2009 to present);
- EBSCO CINAHL (1982 to present).

We will use the following search strategy in the Cochrane Central Register of Controlled Trials (CENTRAL):
#1 MeSH descriptor Negative-Pressure Wound Therapy explode all trees
#2 MeSH descriptor Suction explode all trees
#3 MeSH descriptor Vacuum explode all trees
#4 ("negative pressure" or negative-pressure or TNP):ti,ab,kw
#5 (sub-atmospheric or subatmospheric):ti,ab,kw
#6 ((seal* NEXT surface*) or (seal* NEXT aspirat*)):ti,ab,kw
#7 (wound NEAR/3 suction*):ti,ab,kw#8 (wound NEAR/3 drainage):ti,ab,kw
#9 ((foam NEXT suction) or (suction NEXT dressing*)):ti,ab,kw
#10 ((vacuum NEXT therapy) or (vacuum NEXT dressing*) or (vacuum NEXT seal*) or (vacuum NEXT assist*) or (vacuum NEAR closure) or (vacuum NEXT compression) or (vacuum NEXT pack*) or (vacuum NEXT drainage) or VAC):ti,ab,kw
#11 ("vacuum assisted closure technique" or VAC):ti,ab,kw
#12 (#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11)
#13 MeSH descriptor Surgical Wound Infection explode all trees
#14 MeSH descriptor Surgical Wound Dehiscence explode all trees
#15 surg* NEAR/5 infect*:ti,ab,kw
#16 surg* NEAR/5 wound*:ti,ab,kw
#17 surg* NEAR/5 site*:ti,ab,kw
#18 surg* NEAR/5 incision*:ti,ab,kw
#19 surg* NEAR/5 dehisc*:ti,ab,kw
#20 wound* NEAR/5 dehisc*:ti,ab,kw
#21 (#13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20)
#22 (#12 AND #21)
We will adapt this strategy to search Ovid MEDLINE, Ovid EMBASE and EBSCO CINAHL. 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 and CINAHL searches with the trial filters developed by the Scottish Intercollegiate Guidelines Network (SIGN 2011). We will also conduct supplementary searches of the NHS Economic Evaluation Database (http://www.crd.york.ac.uk/crdweb/) and the Health Economic Evaluations Database. We will not restrict studies with respect to language, date of publication or study setting.
We will search the following clinical trials registries for details of relevant protocols and will contact the relevant research team:

- Clinical trials.gov;
- World Health Organization (WHO) International Clinical Trials Registry Platform;
- Australian and New Zealand Clinical Trials Registry;
- Current Controlled Trials.

Searching other resources

We will check the citation lists of papers identified by the above strategies for further reports of eligible studies. We will contact corresponding authors of identified studies and the manufacturers and distributors of devices used to deliver negative pressure wound therapy, such as Vacuum-Assisted Closure (VAC), Kinetic Concepts, Inc (KCI USA); SNaP® Wound Care System Dressing, Spiracur Inc; Venrturi™ Avanti and Venturi™ Compact (Talley Group, England); RENASYS EZ*, Smith & Nephew. We will contact experts in the field to ask for information about any unpublished studies.

Data collection and analysis

Selection of studies

JW, WC and MS will independently review titles and abstracts identified through the search process. We will retrieve full reports of all potentially relevant trials for further assessment of eligibility based on the inclusion criteria. Differences of opinion will be settled by consensus or referral to the fourth review author. There will be no blinding of study authorship.

Data extraction and management

For eligible studies, three review authors (JW, WC and MS) will independently extract data using a pre-designed data collection sheet. Abstracted data will include the following characteristics:

- methods (number eligible and randomised, adequacy of randomisation, allocation concealment, blinding, completeness of follow up);
- participant characteristics and exclusions;
- type of surgery;
- setting;
- interventions; and
- outcomes.

We will resolve discrepancies through discussion or, if required, we will consult the fourth review author. One review author (JW) will enter data into the Review Manager software (RevMan 2011) and data will be checked for accuracy by the other review authors. If information regarding any data is unclear, we will attempt to contact study authors of the original reports to provide further details. When more than one publication has arisen from a study, we will extract data from all relevant publications but will not duplicate data.

Assessment of risk of bias in included studies

Three review authors will independently assess the quality of eligible trials (JW, WC, MS) using the Cochrane Collaboration tool for assessing risk of bias (Higgins 2011). This tool addresses six specific domains, namely sequence generation, allocation concealment, blinding, incomplete outcome data, selective outcome reporting and other issues which may potentially bias the study (see Appendix 1 for details of the criteria on which the judgement will be based). We will assess blinding and completeness of outcome data for each outcome separately. We will complete a 'Risk of bias' table for each eligible study. Disagreements between authors will be resolved by consensus or referral to the fourth author. We will contact investigators of included trials to resolve any ambiguities. We will report bias, and more generally study limitations within economic evaluations, using the checklist from the NICE Guidelines Manual (NICE 2009).

We will present assessment of risk of bias using a 'Risk of bias' summary figure, which presents all the judgements in a cross-tabulation of study by entry.

Measures of treatment effect

For individual trials, we will extract the numbers with an event for each treatment group and use them to calculate the risk ratio (RR) with its 95% confidence interval (CI). For statistically significant effects, we will calculate number needed to treat (NNT) or number needed to harm (NNH) from the risk difference. For continuous outcomes, we will extract the mean and standard deviation (SD) and calculate the mean difference (MD) or, if the scale of measurement differs across trials, the standardised mean difference (SMD), each with its 95% CI.

Economic analyses

We will present a tabled analysis of the identified economic data in accordance with current guidance on the use of economics methods in the preparation of Cochrane Reviews (Shemilt 2011). We will classify economic evaluation according to the framework in Drummond et al (Drummond 2005). We will tabulate the main characteristics and results of the identified economic evaluation studies and augment these with a narrative description. This will discuss the methods used and compare the key results of those studies.

The results of cost-effectiveness studies are likely to vary according to the particular circumstances of each study. For example, the comparator treatment, such as standard care, may differ for different types of wounds and in different settings. Our analysis will place the results of the economic studies in context and will entail a discussion of scenarios that are likely to lead to the most cost-effective use of negative pressure wound therapy as well as the least cost-effective use.

Costs

All substantial costs that are observed to differ between patients administered the negative pressure wound therapy and patients administered standard care are intended to be captured and reported as part of the economic analysis.

We will report unit costs along with the currency and price year in each original study. These costs will then be converted to 2011 values by applying implicit price deflators for GDP of that currency and then converted into the currency most frequently observed in the articles reviewed using GDP Purchasing Power Parities (Shemilt 2010). This will allow readers of the review to make meaningful comparisons between costs in studies that may have been conducted in different countries and at different times.

The main costs are likely to be those associated with the NPWT itself, specialist and other practitioner costs as measured by time or number of visits, potential cost-savings from a change in the number of bed days in hospital, and costs stemming from differing rates of adverse events and complications (including procedures initiated due to the failure of wounds to heal, such as amputation). The key cost drivers will be identified from the studies included. This will enable users of the review to gain a clear understanding of the nature of resource use associated with negative pressure wound therapy.

Outcomes

The primary trial outcome (proportion of wounds healed) and secondary outcome (time to complete healing) are relevant to the economic analysis as they may indicate a difference in the number of hospital bed days and specialist time required and a possible improvement in quality of life for the patient.

We will examine information on the change in health-related quality of life (HR-QoL) via utilities measured by a multi-attribute utility instrument (MAUI) or other approaches (such as the time trade-off, standard gamble) where possible. Ideally these data will be reported in trials for both the group treated with NPWT and a control group receiving the comparator wound care. The utility data will need to be assessed for comparability and representativeness considering issues such as the types of wounds included, the patient populations, timing of the baseline point and follow-up collection, the MAUI used and the algorithm for scoring the MAUI. We will present discussion of the potential impact on HR-QoL attributable to the intervention as part of the analysis.

If differences can be observed in the rates of adverse events, wound infections and complications resulting from the treatment of the wound, we will discuss the economic implications as part of the economic analysis.

Unit of analysis issues

We do not anticipate any unit of analysis issues. Cross-over trials are not eligible. Cluster-randomised trials are not expected in this field.

Dealing with missing data

If some outcome data remain missing despite our attempts to obtain complete outcome data from authors, we will perform an available-case analysis, based on the numbers of patients for whom outcome data are known. We will also conduct best case and worst case analysis. If standard deviations (SD) are missing, we will impute them from other studies or, where possible, compute them from standard errors (SE) using the formula SD = SE x $\sqrt{N}$, where these are available (Higgins 2011).

Assessment of heterogeneity

We will assess heterogeneity visually and by using the Chi^2 test with significance being set at $P < 0.10$. In addition, we will investigate the degree of heterogeneity by calculating the I^2 statistic (Higgins 2011). If evidence of significant heterogeneity is identified (> 30%), we will explore potential causes and use a random-effects approach to the analysis, otherwise we will use a fixed-effect method.

Assessment of reporting biases

If sufficient studies are included, we will assess reporting bias using funnel plots (Higgins 2011).

Data synthesis

Where studies are clinically similar and outcome measurements are comparable, we will pool results using a fixed-effect model and report the pooled estimate together with its 95% CI. We will estimate hazard ratios (HR) and 95% confidence intervals (CI) as relevant effect measures directly or indirectly for time-to-event data (Altman 2001). Where heterogeneity exists that cannot easily be explained by clear differences in clinical groups or outcomes, we will use a random-effects approach for data synthesis. We will conduct a narrative review of eligible studies where statistical synthesis of data from more than one study is not possible or considered not appropriate, for example if the I^2 statistic is above 60%.

Subgroup analysis and investigation of heterogeneity

We plan to analyse potential sources of heterogeneity using the following subgroup analyses:

1. type of setting (community, hospital, inpatient, outpatient);
2. type of negative pressure device (vacuum-assisted closure (KCL), RENASYS system^{TM} (Smith & Nephew, UK), Chariker-Jeter gauze-based negative pressure systems (V1STA, Versatile-1 and EZ-Care; Smith & Nephew, Inc.);
3. type of surgery (traumatic wounds, reconstructive procedures, other post-surgical wounds);
4. type of comparison dressing (saline gauze, Jelonet, hydrocolloid, foam, alginate); and
5. intermittent versus continuous negative pressure.

Sensitivity analysis

We will perform sensitivity analyses to explore the effect of the following criteria:

1. concealment of allocation (allocation adequately concealed versus not reported or inadequate);
2. duration of follow up (no stated follow up versus any follow up; follow up for < 4 weeks versus 4 weeks or greater); and
3. type of randomisation (truly randomised with adequate method of generating the randomisation sequence versus not reported).

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* *Indicates the major publication for the study*

APPENDICES

Appendix 1. Risk of bias criteria

1. Was the allocation sequence randomly generated?

Low risk of bias

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

High risk of bias

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

Unclear

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

2. Was the treatment allocation adequately concealed?

Low risk of bias

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

High risk of bias

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

Unclear

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

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

Low risk of bias

Any one of the following.

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

High risk of bias

Any one of the following.

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

Unclear

Any one of the following.

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

4. Were incomplete outcome data adequately addressed?

Low risk of bias

Any one of the following.

- No missing outcome data.

- Reasons for missing outcome data unlikely to be related to true outcome (for survival data, censoring unlikely to be introducing bias).
- Missing outcome data balanced in numbers across intervention groups, with similar reasons for missing data across groups.
- For dichotomous outcome data, the proportion of missing outcomes compared with observed event risk not enough to have a clinically relevant impact on the intervention effect estimate.
- For continuous outcome data, plausible effect size (difference in means or standardised difference in means) among missing outcomes not enough to have a clinically relevant impact on observed effect size.
- Missing data have been imputed using appropriate methods.

High risk of bias

Any one of the following.

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

Unclear

Any one of the following.

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

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

Low risk of bias

Any of the following.

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

High risk of bias

Any one of the following.

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

Unclear

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

6. Other sources of potential bias:

Low risk of bias

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

High risk of bias

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

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

Unclear

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

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

HISTORY

Protocol first published: Issue 8, 2011

CONTRIBUTIONS OF AUTHORS

Joan Webster conceived the review question, co-ordinated protocol development, completed the first draft of the protocol and approved the final version prior to submission.

Paul Scuffham performed part of the writing or editing of the protocol, made an intellectual contribution, and approved the final version of the protocol prior to submission.

Monica Stankiewicz made an intellectual contribution to the protocol and approved the final version prior to submission.

Wendy Chaboyer approved the final version of the protocol prior to submission.

Contributions of editorial base:

Nicky Cullum: edited the protocol; advised on methodology, interpretation and protocol content. Approved the final protocol prior to submission.
Sally Bell-Syer: co-ordinated the editorial process. Advised on methodology, interpretation and content. Edited and copy edited the protocol.
Ruth Foxlee: designed the search strategy and edited the search methods section.

DECLARATIONS OF INTEREST

None

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Internal sources

- School of Nursing and Midwifery, Queensland University of Technology, Australia.

Time to conduct review

- Griffith University, Australia.

Time to conduct review

External sources

- NIHR/Department of Health (England), (Cochrane Wounds Group), UK.