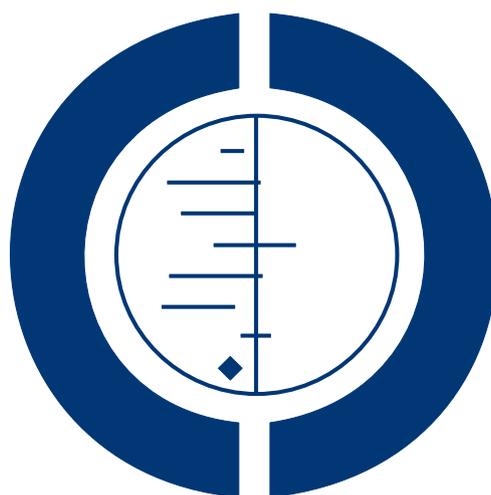


# Negative pressure wound therapy for skin grafts and surgical wounds healing by primary intention (Review)

Webster J, Scuffham P, Stankiewicz M, Chaboyer WP



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[Intervention Review]

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

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## ABSTRACT

### Background

Indications for the use of negative pressure wound therapy (NPWT) are broadening with a range of systems now available on the market, including those designed for use on clean, closed incisions and skin grafts. Reviews have concluded that the evidence for the effectiveness of NPWT remains uncertain, however, it is a rapidly evolving therapy. Consequently, an updated systematic review of the evidence for the effects of NPWT on postoperative wounds expected to heal by primary intention is required.

### Objectives

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

### Search methods

We searched the following electronic databases to identify reports of relevant randomised clinical trials: the Cochrane Wounds Group Specialised Register (searched 28 January 2014); the Cochrane Central Register of Controlled Trials (CENTRAL; 2013, issue 12); Database of Abstracts of Reviews of Effects (2013, issue 12); Ovid MEDLINE (2011 to January 2014); Ovid MEDLINE (In-Process & Other Non-Indexed Citations 24 January 2014); Ovid EMBASE (2011 to January 2014 Week 44); and EBSCO CINAHL (2011 to January 2014). We conducted a separate search to identify economic evaluations.

### Selection criteria

We included trials if they allocated patients to treatment randomly and compared NPWT with any other type of wound dressing, or compared one type of NPWT with a different type of NPWT.

### Data collection and analysis

We assessed trials for their appropriateness for inclusion and for their quality. This was done by three review authors working independently, using pre-determined inclusion and quality criteria.

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

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## Main results

In this first update, we included an additional four trials, taking the total number of trials included to nine (785 participants). Three trials involved skin grafts, four included orthopaedic patients and two included general surgery and trauma surgery patients; all the included trials had unclear or high risk of bias for one or more of the quality indicators we assessed. Seven trials compared NPWT with a standard dressing (two of these were 'home-made' NPWT devices), one trial compared one 'home-made' NPWT with a commercially available device. In trials where the individual was the unit of randomisation, there were no differences in the incidence of surgical site infections (SSI); wound dehiscence, re-operation (in incisional wounds); seroma/haematoma; or failed skin grafts. Lower re-operation rates were observed among skin graft patients in the 'home-made' NPWT group (7/65; 10.8%) compared to the standard dressing group (17/66; 25.8%) (risk ratio (RR) 0.42; 95% CI 0.19 to 0.92). The mean cost to supply equipment for VAC® therapy was USD 96.51/day compared to USD 4.22/day for one of the 'home-made' devices (P value 0.01); labour costs for dressing changes were similar for both treatments. Pain intensity score was also reported to be lower in the 'home-made' group when compared with the VAC® group (P value 0.02). One of the trials in orthopaedic patients was stopped early because of a high incidence of fracture blisters in the NPWT group (15/24; 62.5%) compared with the standard dressing group (3/36; 8.3%) (RR 7.50; 95% CI 2.43 to 23.14).

## Authors' conclusions

Evidence for the effects of negative pressure wound therapy (NPWT) for reducing SSI and wound dehiscence remains unclear, as does the effect of NPWT on time to complete healing. Rates of graft loss may be lower when NPWT is used, but hospital-designed and built products are as effective in this area as commercial applications. There are clear cost benefits when non-commercial systems are used to create the negative pressure required for wound therapy, with no evidence of a negative effect on clinical outcome. In one study, pain levels were also rated lower when a 'home-made' system was compared with a commercial counterpart. The high incidence of blisters occurring when NPWT is used following orthopaedic surgery suggests that the therapy should be limited until safety in this population is established. Given the cost and widespread use of NPWT, there is an urgent need for suitably powered, high-quality trials to evaluate the effects of the newer NPWT products that are designed for use on clean, closed surgical incisions. Such trials should focus initially on wounds that may be difficult to heal, such as sternal wounds or incisions on obese patients.

## PLAIN LANGUAGE SUMMARY

### Negative pressure wound therapy for acute surgical wounds

Negative pressure wound therapy (NPWT) is the application of suction (negative pressure) to wounds that are healing. NPWT has been used for many years for the treatment of chronic wounds, such as leg ulcers and bed sores. More recently, the system has been modified for use on clean surgical wounds, including skin grafts. We undertook a review of studies that compared NPWT with other wound treatments in order to see whether NPWT really works. We found nine trials to consider. These showed that it is still not clear whether NPWT promotes faster healing and reduces complications associated with clean surgery or skin grafts, or not.

## 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 high-income countries. For example, in Australia in 2008/09 it can be calculated from hospital statistics that there was one elective

surgical procedure for every 12.4 people (Australian Institute of Health and Welfare 2010).

Surgical wounds generally heal by primary intention during which the wound edges are brought together so that they are adjacent to each other - except in the case of skin grafts, where a larger surface area is required to allow for contraction. Wound closure is usually assisted by the use of 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 and sternal wounds (Culliford 2007; 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 (separation of the wound edges) or separation of the graft from the wound bed. 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 separates completely, exposing the underlying organs (Harvey 2005).

## Description of the intervention

Negative pressure wound therapy (NPWT) has been used to treat wounds since the late 1990s (Fleischmann 1997; Morykwas 1997). NPWT 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 2011), and, more recently, after clean surgery in obese patients (Dragu 2011). NPWT is used prophylactically following skin grafts and clean surgery to prevent a surgical site complication, in contrast to its more frequent use in wounds healing by secondary intention (left open to heal from the bottom up) such as chronic or infected wounds.

NPWT consists of a closed, sealed system that applies negative pressure (suction) 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 from - 50 mmHg to -125 mmHg (Ubbink 2008; Vikatmaa 2008). The longest established device is the vacuum-assisted closure (VAC® KCI, San Antonio, Texas) system (Morykwas 1997), however alternatives have been developed and are being used (Llanos 2006; Mody 2008; Rozen 2008). More recently, portable versions of the device have been introduced and are being used increasingly in community settings (Hurd 2014; Ousey 2014). An emerging advance has been the addition of 'intillations' of sterile water, saline or antibiotics to VAC therapy. For example the new a new NPWTi system (V.A.C. VeraFlo™

Therapy, KCI USA, Inc., San Antonio, TX) delivers controlled volumes of solution to aid wound healing (Gabriel 2014).

## How the intervention might work

In humans, the wound healing process is regarded as occurring in three consecutive and overlapping stages, namely: inflammation, new tissue formation and remodelling (Gurtner 2008). The precise way in which NPWT may aid this process is not clear. Experimental evidence suggests that NPWT may assist wound healing by increasing local blood flow and production of granulation tissue (Xia 2014), and reducing bacterial contamination, oedema and exudate. There may be other 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 challenged recently, as in an experimental study that used healthy volunteers, 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 lives (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 NPWT 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), bleeding after cardiac surgery (Petzina 2010), pain (Apostoli 2008), secondary wound formation (Karabacak 2014), 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 has 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 (Kairinos 2014; 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, an updated systematic review to summarize evidence on the effects of NPWT on the healing of surgical wounds healing by primary intention is required.

## OBJECTIVES

To assess the effects of NPWT on surgical wounds (primary closure, skin grafts or flap closure) that are expected to heal by primary intention.

## METHODS

### Criteria for considering studies for this review

#### Types of studies

We included only randomised controlled trials (RCTs) that evaluated the effects of NPWT on the healing of surgical wounds. Surgical wounds included split-skin grafts, full-skin grafts, flap closure or any other primary wound closure. This criterion encompassed 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 did 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, where, for example, treatment allocation was made through alternation or by date of birth, were also ineligible.

#### Types of participants

We included trials involving people of any age, and in any care setting, involving the use of NPWT for surgical wounds healing by primary intention.

#### Types of interventions

The primary intervention was NPWT delivered by any mode (for example vacuum-assisted closure (VAC® KCI, San Antonio, Texas) or simple closed-system suction drainage), continuously or intermittently over any time period. The comparison interventions were any standard dressing (for example gauze) or any advanced dressing (for example hydrogels, alginates, hydrocolloids); or comparisons between different negative pressure devices.

## Types of outcome measures

### Primary outcomes

- Mortality
- Adverse events (surgical site infection and dehiscence)

### Secondary outcomes

- Time to complete healing
- Re-operation
- Seroma/haematoma
- Graft failure
- Fracture blisters
- Pain (measured by any valid pain assessment instrument)
- Quality of life (measured by any valid assessment instrument)
- Cost (including: utility scores representing health-related quality of life; 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; incremental cost per life year gained; incremental cost per quality adjusted life year and cost-benefit ratio)

## Search methods for identification of studies

### Electronic searches

For an outline of the search methods used in the first publication of this review see [Appendix 1](#).

For this first update we searched the following electronic databases to identify reports of relevant randomised clinical trials:

- the Cochrane Wounds Group Specialised Register (searched 28 January 2014);
- the Cochrane Central Register of Controlled Trials (CENTRAL 2013, Issue 12);
- Database of Abstracts of Reviews of Effects (2013, Issue 12);
- Ovid MEDLINE (2011 to January Week 3 2014);
- Ovid MEDLINE (In-Process & Other Non-Indexed Citations January 24, 2014);
- Ovid EMBASE (2011 to 2014 January 24);
- EBSCO CINAHL (2011 to 28 January 2014).

We used 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 dehis\*:ti,ab,kw  
 #20 wound\* NEAR/5 dehis\*:ti,ab,kw  
 #21 (#13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20)  
 #22 (#12 AND #21)

The search strategies for Ovid MEDLINE, Ovid EMBASE and EBSCO CINAHL can be found in [Appendix 2](#); [Appendix 3](#) and [Appendix 4](#) respectively. We combined the Ovid MEDLINE search with the Cochrane Highly Sensitive Search Strategy for identifying randomised trials in MEDLINE: sensitivity- and precision-maximising version (2008 revision) ([Lefebvre 2011](#)). We combined the EMBASE and CINAHL searches with the trial filters developed by the Scottish Intercollegiate Guidelines Network ([SIGN 2011](#)).

We conducted separate searches to identify economic evaluations in the following electronic databases:

- NHS Economic Evaluation Database (2013, Issue 12);
- Ovid MEDLINE (2011 to January Week 3 2014);
- Ovid MEDLINE (In-Process & Other Non-Indexed Citations 22 January 2014);

- Ovid EMBASE (2011 to 24 January 2014);
- EBSCO CINAHL (2011 to 28 January 2014)

We used economics filters developed by Centre for Reviews and Dissemination in combination with terms to describe the condition and intervention in Ovid MEDLINE, Ovid EMBASE and EBSCO CINAHL searches ([CRD 2010](#); see [Appendix 5](#); [Appendix 6](#) and [Appendix 7](#) respectively). We did not restrict any of the above searches with respect to language, date of publication or study setting.

We searched the following clinical trials registries for details of relevant protocols and contacted the relevant research teams:

- Clinical trials.gov (<http://www.clinicaltrials.gov/>);

- World Health Organization (WHO) International Clinical Trials Registry Platform ([www.who.int/trialsearch](http://www.who.int/trialsearch));
- Australian and New Zealand Clinical Trials Registry ([www.anzctr.org.au](http://www.anzctr.org.au));
- Current Controlled Trials.

## Searching other resources

We checked the citation lists of papers identified by the above strategies for further reports of eligible studies. We contacted corresponding authors of identified studies. In the first version of this review we contacted the manufacturers and distributors of devices used to deliver NPWT, such as Vacuum-Assisted Closure (VAC@ KCI, San Antonio, Texas); SNaP<sup>®</sup> Wound Care System Dressing, Spiracur Inc; Venrturi<sup>™</sup> Avanti and Venturi<sup>™</sup> Compact (Talley Group, England); RENASYS EZ\*; and Smith & Nephew. We did not contact manufacturers or distributors for this update.

## Data collection and analysis

### Selection of studies

JW, WC and MS independently reviewed titles and abstracts identified through the search process. We retrieved full reports of all potentially relevant trials for further assessment of eligibility based on the inclusion criteria. Differences of opinion were settled by consensus. There was no blinding of study authorship.

### Data extraction and management

JW and MS independently extracted the following data using a pre-designed checklist:

- methods (number of participants eligible and randomised, adequacy of randomisation, allocation concealment, blinding, completeness of follow-up);
- participant characteristics and exclusions;
- type of surgery;
- setting;
- study dates;
- interventions;
- number of participants per group;
- information about ethics approval, consent and conflict of interest; and
- outcomes.

We resolved discrepancies through discussion. One review author (JW) entered data into the Review Manager software ([RevMan 2011](#)), and MS checked data for accuracy. If information regarding any data was unclear, we attempted to contact study authors of the original reports to ask them to provide further details.

## Assessment of risk of bias in included studies

Two review authors independently assessed the eligible trials (JW and 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 8 for details of the criteria on which the judgement was based). We assessed blinding and completeness of outcome data for each outcome separately. We completed a 'Risk of bias' table for each eligible study. We resolved disagreements between review authors by consensus. We contacted investigators of included trials to resolve any ambiguities. We were to have reported bias, and more generally study limitations within economic evaluations, using the checklist from the NICE Guidelines Manual (NICE 2009). We have presented assessment of risk of bias using a 'Risk of bias' summary figure, which shows all the judgements in a cross-tabulation of study by entry.

## Measures of treatment effect

For individual trials, we extracted the numbers with an event for each treatment group and used them to calculate the risk ratio (RR) with its 95% confidence interval (CI). For statistically significant effects, we planned to calculate the number needed to treat for an additional beneficial outcome (NNTB) or number needed to treat for an additional harmful outcome (NNTH) from the risk difference. However, based on the quality of the data, we decided not to conduct these calculations. For continuous outcomes, we extracted the mean and standard deviation (SD) and calculated the mean difference (MD) or, if the scale of measurement differed across trials, the standardised mean difference (SMD), each with its 95% CI.

## Economic analyses

We were to have undertaken the following economic analysis but no studies provided suitable data. However the methods remain detailed here in the event that future updates of this review identify economic data.

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 described by Drummond and colleagues (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 the therapy, as well as the least cost-effective use.

## Costs

All substantial costs that are observed to differ between patients administered NPWT 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 gross domestic product (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 NPWT.

## Outcomes

The primary trial outcome (adverse events) 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

It is possible that wounds rather than participants may be randomised. Where there is evidence that multiple wounds on a single person have been analysed incorrectly (that is, by considering outcomes for multiple wounds or grafts as independent), we will seek further information from the trialist. Cross-over trials were excluded and cluster-randomised trials were not expected for this type of intervention.

### Dealing with missing data

Where possible, we will perform all analyses using the intention-to-treat (ITT) principle, that is, participants will be analysed according to their allocated treatment group. Where it appears that data have been excluded from the analyses, we will contact authors for these missing data. If data remain missing, despite our best efforts to obtain them, we planned an available-case analysis, based on the numbers of patients for whom outcome data were known. We also planned best-case and worst-case analyses. In the event of missing standard deviations (SD) we planned imputation from other studies or, where possible, calculation from standard errors (SE) using the formula  $SD = SE \times \sqrt{N}$ , where these were available (Higgins 2011).

### Assessment of heterogeneity

We assessed heterogeneity visually and by using the Chi<sup>2</sup> test with significance being set at P less than 0.10. In addition, we investigated the degree of heterogeneity by calculating the I<sup>2</sup> statistic (Higgins 2011). We planned to explore potential causes of moderate to significant heterogeneity (I<sup>2</sup> > 30%) and use a random-effects approach to the analysis, but this was not necessary.

### Assessment of reporting biases

If sufficient studies had been identified (more than 10) we had planned to assess reporting bias using funnel plots (Higgins 2011).

### Data synthesis

Where studies were clinically similar and outcome measurements comparable, we pooled results using a fixed-effect model and reported the pooled estimate together with its 95% CI. We conducted a narrative review of eligible studies where statistical synthesis of data from more than one study was not possible or considered inappropriate, for example if the I<sup>2</sup> statistic was above 60%. There were no time-to-event data so estimates of hazard ratios (HR) and 95% confidence intervals (CI) were not required (Altman 2001).

### Subgroup analysis and investigation of heterogeneity

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

- type of setting (community, hospital, inpatient, outpatient);
- type of negative pressure device (such as vacuum-assisted closure (VAC® KCI, San Antonio, Texas), RENASYS system<sup>TM</sup> (Smith & Nephew, UK), Chariker-Jeter gauze-based negative pressure systems (V1STA, Versatile-1 and EZ-Care; Smith & Nephew Inc) and non-commercial systems;
- type of surgery (traumatic wounds, reconstructive procedures, other post-surgical wounds; skin grafts);
- type of comparison dressing (saline gauze, Jelonet, hydrocolloid, foam, alginate); and
- intermittent versus continuous negative pressure.

### Sensitivity analysis

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

- concealment of allocation (allocation adequately concealed versus not reported or inadequate);
- duration of follow-up (no stated follow-up versus any follow-up; follow-up for less than four weeks versus follow-up of four weeks or longer); and
- type of randomisation (truly randomised with adequate method of generating the randomisation sequence versus not reported).

## RESULTS

### Description of studies

See [Characteristics of included studies](#); [Characteristics of excluded studies](#) and [Characteristics of ongoing studies](#).

### Results of the search

#### Interventions search

For this first update, we identified 177 new, unique records through our electronic search. After reading the titles and abstracts, 166 were excluded as irrelevant. We retrieved the remaining 11 full-text papers for inspection. From these we selected an additional four papers, with results from four trials, for inclusion in the review (Crist 2014; Masden 2012; Petkar 2012; Stannard 2012), bringing the total number of included studies to nine. Additional information was sought from the correspondence author of each of the trials. Responses, with additional, useful information were received from the authors of Crist 2014 and Stannard 2012.

In the first version of this review a search of trial registry platforms identified 17 protocols related to NPWT. Eleven of these planned to investigate chronic wounds and were ineligible. Of the six remaining trials, five named investigators and one named a company (KCI) as the investigator. We attempted contact with the five study authors, three of whom did not respond. The investigator of one of the remaining protocols stated that the planned start date for the trial was in early 2011 (Chan 2011). For this update we have been unable to find any further information about this trial. We were also unable to contact the other author (Graves 2011). To our knowledge, neither trial has been published. With regard to the company trial, KCI advised us that the trial will not be conducted. No participants were enrolled in the study, all sites were closed and all site payments reconciled. No reason was provided for terminating the study. In the first version of the review, we sent emails to all the manufacturers mentioned in our search strategy. We were advised of one animal study, but identified no further human trials meeting our inclusion criteria; we did not contact manufacturers for this update. Our updated search of trial registries identified 20 protocols that potentially meet our criteria. Nine of these were actively recruiting, and five of these named a manufacturer as either a sponsor or collaborator. Two trials appear to be on-going and are classified as [Studies awaiting classification](#) (Chan 2011; Graves 2011).

#### Economic analysis search

Electronic searches yielded 115 references in the first version of our review, none of which met our economic inclusion criteria. For this update, a further 77 trials were identified. One of these trials appeared relevant, but it was an abstract from conference presentation and we were unable to extract sufficient information from the abstract for this review (see Mullins 2012 in [Studies awaiting classification](#)). Attempts to contact the author were unsuccessful. We will wait for a paper to be published.

#### Included studies

##### Types of participants

In the initial review, the five included trials enrolled a total of 280 participants (Chio 2010; Dorafshar 2011; Howell 2011; Llanos 2006; Pachowsky 2011). A further 516 participants from four trials have been added in this update (Crist 2014; Masden 2012; Petkar 2012; Stannard 2012). Participants in three trials underwent skin grafts: Chio 2010 investigated the forearm donor site in 54 participants undergoing a radial forearm free flap; Llanos 2006 enrolled 60 burn patients who had split-thickness skin grafts applied to their burn site; and Petkar 2012 recruited 71 patients deemed fit for split-skin grafting. In the other trials, Dorafshar 2011 recruited 87 patients with acute wounds resulting from trauma, surgery or dehiscence; Howell 2011 included 60 patients

undergoing a total knee arthroplasty who were obese and at risk of infection; Pachowsky 2011 enrolled 19 patients with closed surgical wounds after total hip arthroplasty; 115 participants in the Crist 2014 and 249 participants in the Stannard 2012 trials were also orthopaedic patients; and in the Masden 2012 trial, the target group was patients requiring primary closure for lower extremity or abdominal wounds, with 81 of the 93 patients randomised being available for analysis. Six trials were conducted in the USA (Chio 2010; Crist 2014; Dorafshar 2011; Howell 2011; Masden 2012; Stannard 2012), one in Chile (Llanos 2006), one in Germany (Pachowsky 2011), and one in India (Petkar 2012).

##### Types of interventions

Four trials compared the VAC® (KCI, San Antonio, Texas) negative pressure device vacuum-assisted closure, set to -125 mmHg with a standard dressing (Chio 2010; Howell 2011; Masden 2012; Stannard 2012). The comparison standard dressings varied between the trials: Chio 2010 used sterile surgical foam, cut to size and wrapped in Adaptic dressing; Howell 2011 used a sterile gauze dressing secured with a perforated, stretchable cloth tape; Masden 2012 described the control dressing as a non-adhesive silicone layer (Mepitel; Mölnlycke Health Care AB, Göteborg, Sweden) and a bacteriostatic single silver layer (Acticoat, Smith & Nephew, Hull, United Kingdom); whereas the Stannard 2012 trial described the dry dressing simply as a 'standard gauze dressing'. Crist 2014 used VAC® (KCI, San Antonio, Texas) as the intervention device and compared this to a standard gauze dressing. Pachowsky 2011 used the PREVENA™ system (KCI, San Antonio, Texas) for the intervention treatment and a dry wound dressing as the control treatment. Three trials developed non-standard negative pressure devices: Llanos 2006 used the hospital's central aspiration system at a pressure of -80 mmHg to achieve a vacuum, the comparison dressing was identical in both groups, but no pressure was applied to the aspiration tubing in the control group; Petkar 2012 also used the hospital's continuous wall suction system at -80 mmHg to create the 'vacuum' for the negative pressure dressing intervention, using Vaseline gauze and conventional cotton gauze and elastic bandages over the graft in the control group; Dorafshar 2011 compared two negative pressure systems: VAC® KCI (San Antonio, Texas) and a subatmospheric pressure wound therapy system (GSUC), which is a locally developed system based on a gauze dressing moistened with 0.9% normal saline and sealed with an occlusive cover, a red rubber catheter is placed in the middle of the dressing and attached to continuous wall suction at -75 mmHg to -80 mmHg.

##### Types of outcomes

Four treatment comparisons are included in the review. For the first, 'negative pressure closure versus standard dressing', incidence of adverse events was the only pre-specified primary outcome reported (Crist 2014; Howell 2011; Masden 2012; Stannard 2012),

with no trials reporting on mortality. Adverse events included surgical site infection (Crist 2014; Howell 2011; Masden 2012; Stannard 2012), and dehiscence (Masden 2012; Stannard 2012). Secondary outcomes for this comparison included time to complete healing (Howell 2011), reoperation (Llanos 2006; Masden 2012; Petkar 2012), seroma/haematoma (Pachowsky 2011), graft failure (Chio 2010), and fracture blisters (Howell 2011). In the Chio 2010 trial outcomes were measured two weeks after surgery; in the Crist 2014 and Howell 2011 trials participants were followed up for 12 months; Dorafshar 2011 assessed outcomes on day seven; and Llanos 2006 assessed outcomes when wounds were uncovered at four days post-surgery. The average follow-up period was 113 days in the Masden 2012 trial; Pachowsky 2011 conducted ultrasound examinations on days five and 10 post surgery; and Petkar 2012 followed participants for one month. The follow-up period was unclear in the Stannard 2012 trial.

Only one trial was included in the second treatment comparison of 'one negative pressure closure versus another negative pressure closure'. Dorafshar 2011 compared the GSUC system with VAC® (KCI, San Antonio, Texas). The trial reported on outcomes of interest to this review including adverse events, pain and cost.

Two trials investigated the third treatment comparison of 'non-commercial NPWT versus standard care', but reported only on secondary outcomes in the review, specifically: re-operation (Llanos 2006; Petkar 2012), graft loss (Llanos 2006), length of stay (Llanos 2006), and cost (Petkar 2012).

We included a fourth comparison, 'commercially funded versus non-commercially funded trials', which included all of the above outcomes (Chio 2010; Crist 2014; Dorafshar 2011; Howell

2011; Llanos 2006; Masden 2012; Pachowsky 2011; Petkar 2012; Stannard 2012).

Other outcomes, such as median graft loss, time from grafting to hospital discharge and rates of change in surface area and wound volume, were reported by trialists, but these data were not included in our pre-specified primary or secondary outcomes, so results have not been included in this review.

### Excluded studies

In the first version of this review five trials were excluded (Hu 2009; Johannesson 2008; Kim 2007; Moues 2004; Moues 2007). The intervention dressing in one trial was not a negative pressure device (Johannesson 2008); one was not a randomised controlled trial (Kim 2007); and three did not include acute wounds (Hu 2009; Moues 2004; Moues 2007). Two trials previously classified as 'Studies awaiting classification', have been re-classified as 'Excluded studies' as no further information about these studies was available (Braakenburg 2006; Moisisdis 2004). For the current update we have excluded a further five studies: Albert 2012 (no acute wounds); Banasiewicz 2013 (included participants with infected wounds); Bondoki 2011 (prospective cohort study); Eisenhardt 2012 (none of our outcomes of interest were reported); Grauhan 2013 (quasi randomised by time of operation).

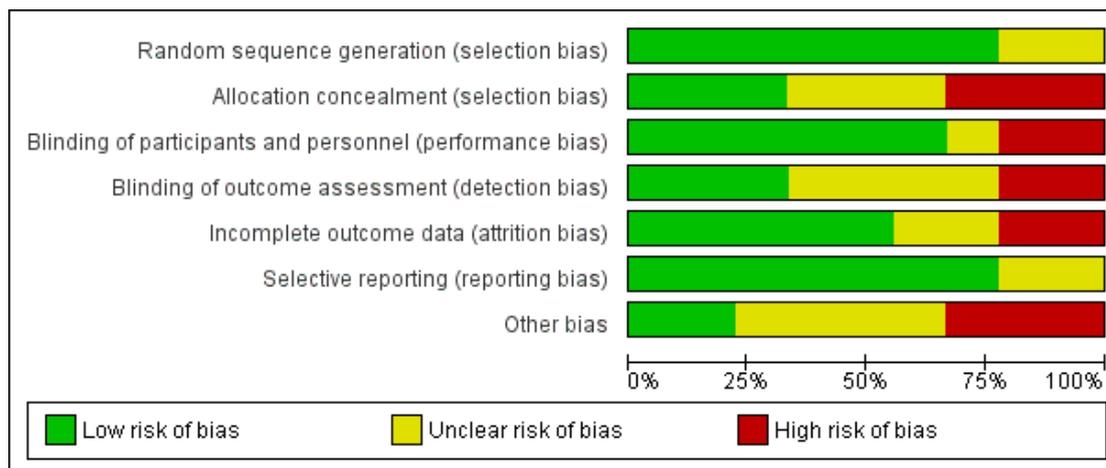
### Risk of bias in included studies

See Figure 1 and Figure 2 for the 'Risk of bias' summary.

**Figure 1. Risk of bias summary: review authors' judgements about each risk of bias item for each included study**

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Chio 2010	+	-	+	-	-	+	+
Crist 2014	+	+	+	+	-	+	?
Dorafshar 2011	+	?	+	-	+	+	?
Howell 2011	?	+	-	?	+	+	-
Llanos 2006	+	-	?	+	+	+	+
Masden 2012	+	+	+	+	?	+	-
Pachowsky 2011	?	?	-	?	+	?	?
Petkar 2012	+	-	+	?	+	?	?
Stannard 2012	+	?	+	?	?	+	-

**Figure 2. Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies**



## Allocation

### Sequence generation

Seven of the nine investigators described some process used to generate the random allocation list. A computer-based random-number generator was used in five trials (Chio 2010; Crist 2014; Llanos 2006; Petkar 2012; Stannard 2012), and a web-based random-number generator in a sixth (Dorafshar 2011). Masden 2012 used a 'block randomization protocol' but it was unclear whether this was computer generated. The two other studies did not specify how the sequence was generated (Howell 2011; Pachowsky 2011).

### Allocation concealment

The method used for allocation concealment was unclear in the Dorafshar 2011; Masden 2012; Pachowsky 2011 and Stannard 2012 trials. In the Dorafshar 2011 study, participants were allocated to their group "by drawing a previously prepared card", however, it was unclear whether cards were concealed until the point of randomisation. Opaque sealed envelopes were used by Howell 2011 and Crist 2014. Allocation in the Chio 2010, Llanos 2006 and Petkar 2012 trials was not concealed, open lists were used so the next allocation would have been predictable.

## Blinding

### Participants and personnel

The appearance of dressings was dissimilar in the Chio 2010; Crist 2014; Dorafshar 2011; Howell 2011; Masden 2012; Pachowsky 2011; Petkar 2012 and Stannard 2012 trials, so blinding was impossible. Dressings were identical in the Llanos 2006 trial, and both groups had tubing attached to a suction apparatus, however, participants and staff would almost certainly have been aware if suction was activated.

### Outcome assessment

Two trials did not blind outcome measurement (Chio 2010; Dorafshar 2011), and it was unclear in the Howell 2011; Petkar 2012, and Stannard 2012 trials whether outcome assessment had been blinded. Ultrasound was used to assess outcomes in the Pachowsky 2011 trial, but it was not stated whether the ultrasonographer was blinded to allocation. In the Llanos 2006 study, assessment was conducted via photographs and the person assessing the photographs was "masked to which intervention the patient had received". Outcome assessors were also unaware of group allocation in the Crist 2014 and Masden 2012 trials.

### Incomplete outcome data

All participants were included in the analyses of five trials (Dorafshar 2011; Howell 2011; Llanos 2006; Pachowsky 2011; Petkar 2012). In the Chio 2010 trial four (14.8%) participants in the NPWT group were unavailable for follow-up, but complete follow-up data were reported for the control group, therefore Chio 2010 was deemed to be at a high risk of attrition bias. Similarly, in the Crist 2014 trial, 10.9% of the participants in the NPWT group and 30.0% of the control group were lost to follow-up, so the trial was classified as being at high risk for this domain. In the Stannard 2012 trial, a total of 249 patients were recruited from four hospitals: results were reported for all of these participants at hospital discharge and at long-term follow-up (follow-up period not defined). Since four hospitals were involved in this study, it seems unlikely that complete follow-up would have occurred for all of those recruited, which suggests an 'available case' analysis. Consequently, we have classified this trial as being at uncertain risk of bias. In the Masden 2012 trial, 12 participants were lost to follow-up, but the numbers were equally distributed across the groups, so we assigned the study a low risk status for attrition bias.

### Selective reporting

In the Chio 2010; Crist 2014; Dorafshar 2011; Howell 2011; Llanos 2006; Masden 2012; Pachowsky 2011; Petkar 2012 and Stannard 2012 trials each of the pre-specified outcomes, as defined in the methods section of the papers, was reported in the results. No published protocol was available for six of the trials (Chio 2010; Howell 2011; Llanos 2006; Masden 2012; Pachowsky 2011; Petkar 2012). In the Dorafshar 2011 trial, assessment measures reflected the pre-defined outcomes listed in the published protocol (NCT00724750), however, the study began in 2006 but the protocol was first published in July 2008, so there was potential for study characteristics to have changed before or during the study. Similarly, the Stannard 2012 trial was registered nine months after data collection ceased. Crist 2014 was the only investigator to pre-register the trial and, while the protocol nominated one primary outcome (infection) and four secondary outcomes (wound drainage, hospital length of stay, dressing supply costs and nursing time costs), the study abstract reported only wound infection and length of stay. The full paper has not yet been published.

### Other potential sources of bias

A manufacturer funded the Howell 2011 trial, which also contained unequal numbers in each arm of the trial. This trial was stopped early due to an unacceptably higher rate of blisters among patients in the negative pressure group. The Pachowsky 2011 trial was also manufacturer-funded and one of the authors received conference funding from the manufacturer of the trial intervention. The Stannard 2012 trial was manufacturer-sponsored and the trialist is also a consultant with KCI. Two investigators in the

Masden 2012 trial are consultants for KCI. Two of the authors in the Crist 2014 trial have been consultants for KCI and have received funding from the company for previous trials. The current trial however was not company-sponsored (correspondence with the author).

A co-intervention (a bacteriostatic single silver layer) was included as part of the control group dressing in the Masden 2012 trial.

In the Stannard 2012 study, some participants had more than one wound. Data were analysed by wounds, rather than by individuals, creating the possibility of a 'unit of analysis error'. We have presented data from this study separately.

## Effects of interventions

### Comparison 1: Negative pressure wound therapy compared with standard dressing (six trials, 189 participants)

#### Primary outcomes

##### Mortality

Although not directly reported, results indicate that no participant died during any of the trials.

#### Adverse events

##### Surgical site infection

Four trials with a total of 498 participants and of variable quality reported data for this outcome (Crist 2014; Howell 2011; Masden 2012; Stannard 2012). Data from three studies (232 participants) could be combined in the meta-analyses (Crist 2014; Howell 2011; Masden 2012). No differences in the rate of surgical site infection (SSI) were noted; RR 1.02 (95% CI 0.41 to 2.54, Analysis 1.1). Stannard 2012 analysed data by wound, not by individual, and we have presented data from this study in a separate forest plot. Results favoured the NPWT group (14/144; 9.7%) compared with the standard dressing group (23/122; 18.9%) (RR 0.52, 95% CI 0.28 to 0.96, P value 0.04, Analysis 1.2).

##### Dehiscence

Two studies (203 participants) provided dehiscence rates (Masden 2012; Stannard 2012). In the Masden 2012 trial the analysis was by individual and there were no between-group differences for dehiscence outcome; RR 1.22 (95% CI 0.65 to 2.30, Analysis

1.3). [Stannard 2012](#) also assessed dehiscence, but outcomes were analysed by wound, not by individual. In the NPWT group 12/139 (8.6%) wounds dehisced compared with 20/122 (16.4%) in the standard dressing group; RR 0.48(95% CI 0.22 to 1.03, [Analysis 1.4](#)). This finding contained a 'unit of analysis' issue, which was not adjusted for, so results should be interpreted with caution. In other words, if the 'clustering effect' is not adjusted for in the analysis, the standard error of the intervention effect may be too small, which has implications for the statistical significance of the comparison.

## Secondary outcomes

### Time to complete healing

In the [Howell 2011](#) trial, there was no reported difference in time to wound closure between groups (negative pressure 4.3 days; static pressure 4.1 days). None of the other five trials provided data for this outcome ([Chio 2010](#); [Crist 2014](#); [Masden 2012](#); [Pachowsky 2011](#); [Stannard 2012](#)).

### Re-operation

There are two sub-groups for this outcome, incisional wounds and skin grafts. In the [Masden 2012](#) trial (81 participants), there was no difference between groups in the re-operation rates for incisional wounds. Whereas in two trials of uncertain to high risk of bias that assessed re-operation rates among skin graft patients, pooling of data showed that NPWT was more effective than other dressings; RR 0.42 (95% CI 0.19 to 0.92; 131 participants; [Llanos 2006](#); [Petkar 2012](#)). When data from these three trials were combined there was a 40% reduction in the re-operation rates favouring the NPWT group, but the true rate for the NPWT intervention lies somewhere between a 66% reduction and a 5% increase in re-operation rates; RR 0.60 (95% CI 0.34 to 1.05) ([Analysis 1.5](#)).

### Seroma/haematoma

The [Pachowsky 2011](#) trial, with only 19 post-arthroplasty participants, showed a lower seroma rate in the NPWT group compared to the standard dressing group RR 0.49 (95% CI 0.23 to 1.05) but confidence intervals were wide indicating that NPWT may lead to a 51% reduction or to a 5% increase in seroma rates ([Analysis 1.6](#)).

### Graft failure

[Chio 2010](#) (50 participants) reported on graft failure: there were no differences between the groups for failure rates at either two weeks or one month post surgery ([Analysis 1.7](#)).

### Fracture blisters

The [Howell 2011](#) trial was stopped early due to a high rate of fracture blisters in the NPWT group; RR 7.50 (95% CI 2.43 to 23.14; [Analysis 1.8](#)).

### Length of hospital stay

There was no reported difference in the length of hospital stay in the [Stannard 2012](#) trial (mean NPWT 2.5 days and standard dressing 3.0 days; P value 0.10)

### Pain, quality of life, cost

None of the studies included in this comparison provided measures for the outcomes of pain, quality of life or cost ([Chio 2010](#); [Crist 2014](#); [Howell 2011](#); [Masden 2012](#); [Pachowsky 2011](#); [Stannard 2012](#)).

### Comparison 2: One negative pressure closure method (GSUC) compared with another negative pressure closure method (VAC® KCI, San Antonio, Texas) (one trial, 87 participants)

## Primary outcomes

### Mortality

No deaths were reported in the trial.

### Adverse events

No data were reported for adverse events.

## Secondary outcomes

### Seroma/haematoma

[Dorafshar 2011](#) (87 participants) showed no difference in rates of haematoma between groups (VAC® 1/42; GSUC 0/45); (RR, 0.31, 95% CI 0.01 to 7.44; [Analysis 2.1](#)).

### Time to complete healing

The trial reported no data for time to complete healing.

### Pain

Pain before, during and after dressing changes was reported to be lower in the GSUC group than in the VAC® group (P value 0.02) ([Dorafshar 2011](#)).

### Quality of life

Quality of life was not measured in this trial.

### Cost

A within-trial cost analysis was undertaken by Dorafshar 2011, who reported that the mean cost of supply equipment for VAC® therapy was USD 96.51/day compared to USD 4.22/day for the GSUC therapy (P value 0.01). The daily labour costs to change the dressings were USD 21.18/day for GSUC versus USD 25.55/day for VAC® (P value 0.11). Overall, the costs in the VAC® group were more than four times as much as the costs in the GSUC group.

### Comparison 3: Non-commercial NPWT versus standard care (two trials, 131 participants)

#### Primary outcomes

#### Mortality

No deaths were reported in either trial (Llanos 2006; Petkar 2012).

#### Adverse events

No adverse events were reported in either trial (Llanos 2006; Petkar 2012).

#### Secondary outcomes

#### Re-operation

Both Llanos 2006 and Petkar 2012 used 'home-made' devices to create negative pressure over the wounds. When compared with standard care, their products were more effective at preventing re-operation; RR 0.42 (95% CI 0.19 to 0.92; Analysis 3.1). However, both trials were at uncertain or high risk of bias for important domains, such as allocation concealment.

#### Graft loss

Llanos 2006 reported lower rates of graft loss in the NPWT group compared to controls (median percent loss in NPWT 0.0%, range 0.0 to 62%; control group 12.8%, range 0 to 79.9%; P value 0.001). Petkar 2012 also reported higher rates of graft take by day 14 (NPWT 95.29%, SD 5.89; control 85.89%, SD 25.10).

### Length of hospital stay

The median length of stay in the Llanos 2006 trial was reported to be 13.5 days for the NPWT group compared with 17.0 days for the control group (P value 0.01).

### Time to complete healing

No data were reported for time to complete healing.

### Pain

No data were reported for pain.

### Quality of life

Quality of life was not measured in these trials.

### Cost

Petkar 2012 reported that the cost of their home made vacuum-closure assembly for an average size of wound was approximately GBP 6.27.

### Comparison 4: Commercially funded compared with non-commercially funded (nine trials, 785 participants)

To assess the effect of manufacturer funding we combined all outcomes from all trials (Analysis 4.1); three sub-groups were included.

- 'Manufacturer-funded' (four trials using commercial NPWT devices, 426 participants). There was a positive effect favouring commercial NPWT devices (RR 0.73, 95% CI 0.54 to 0.97; Howell 2011; Masden 2012; Pachowsky 2011; Stannard 2012).
- 'Non-manufacturer funded' (two trials using commercial NPWT devices, 141 participants). No differences between groups were found in the non-commercially funded trials that used a commercial NPWT device (Chio 2010; Crist 2014).
- 'Non-manufacturer funded, using non-commercial NPWT devices' (three trials, 218 participants). The non-commercial NPWT devices were effective in reducing the number of adverse outcomes (Dorafshar 2011; Llanos 2006; Petkar 2012); RR 0.68 (95% CI 0.52 to 0.87).

## DISCUSSION

### Summary of main results

## Wound complications

This systematic review examined the evidence from randomised controlled trials (RCTs) that focused on the effects of negative pressure wound therapy (NPWT) for acute surgical wounds. Four new trials were added to this update bringing the total number of trials to nine and total number of participants to 785. Although NPWT is widely used and is supported for use in a range of surgical applications (Krug 2011), evidence to support or refute its effects on outcomes for acute surgical wounds remains unclear.

Trials in this review included use of NPWT after orthopaedic surgery, skin grafts and general surgery. We found evidence, from three studies, which showed equivalent rates of wound infection when NPWT was compared with standard dressings. Similarly, NPWT had no effect on dehiscence rates.

Three trials suggested a benefit of NPWT for skin graft survival (Chio 2010; Llanos 2006; Petkar 2012), and one trial suggested a benefit in prevention of seroma or haematoma (Dorafshar 2011; Pachowsky 2011), but all of these trials were at unclear or high risk of bias, which reduces our confidence in the results. Conversely, there was evidence for increased harm caused by the use of NPWT in one trial, when skin blisters formed around the edge of the NPWT dressing (Howell 2011). In this trial, the dressing-associated blister rate was 63% in the NPWT group (Howell 2011), which compares poorly with the rates of 2.4% to 26.0% seen in other recent trials where modern wound dressings have been used for postoperative orthopaedic wounds (Abuzakuk 2006; Koval 2007; Ravenscroft 2006; Ravnskog 2011), and was the reason for the early termination of the trial. It is unclear why skin blisters occur after orthopaedic surgery, but this may be due to postoperative swelling, which leads to shear or friction when the tape securing the dressing is stretched (Ravenscroft 2006).

It is also unclear which NPWT system should be used to deliver the therapy. Although there is a substantial literature relating to wound healing using the vacuum-assisted closure (VAC® KCI, San Antonio, Texas) system (Morykwas 1997), our review failed to support the use of a commercial device for acute wounds. These systems are very expensive and our results suggest that alternative, cheaper methods may be as effective. For example, we have shown in Analysis 4.1 that commercial NPWT reduced the overall wound related complications by 27%, whereas hospital-devised and built systems reduced the complication rate by 63%.

## Cost

Combined equipment and labour costs were four times lower when a hospital-devised and built system was used than when a commercial system was used for delivering NPWT (USD 25.40/day compared to USD 110.06/day). This was due entirely to higher equipment cost for the commercial product, as the cost for labour to change the dressings was similar (Dorafshar 2011). A second non-commercial NPWT trial found that use of the home-made vacuum-closure assembly added only around GBP 6.27 to

the standard care costs (Petkar 2012). Although these cost data come from only two trials, additional studies are unlikely to change this finding unless equipment costs from commercial manufacturers reduce substantially. Innovative attempts to develop hospital-based systems are increasing in order to find ways around these costs (Mody 2008; Perez 2010; Rozen 2008; Shalom 2008).

## Pain

Pain levels in one study were significantly lower during and after dressing changes in the hospital-based negative pressure group (Dorafshar 2011). However, the hospital-based device used continuous suction at -75 mmHg to -80 mmHg, whereas the VAC® system was set between -75 mmHg to -125 mmHg, which may account for the reported difference.

## Overall completeness and applicability of evidence

Indications for the use of NPWT in closed surgery are broadening (DeCarbo 2010; Pachowsky 2011), with a range of new systems on the market, including those designed for use on closed clean wounds (Allen 2011). However, the studies eligible for inclusion in our review represented a relatively narrow focus; there were three on patients with skin grafts, two trials included patients with acute wounds from trauma or surgery and four recruited patients undergoing a planned total knee or hip arthroplasty. Trials were small, with the largest enrolling 249 patients; the average number of subjects amongst the other trials was 65. Negative pressure levels varied between trials and between device types, with hospital aspiration systems generally using a lower pressure than the VAC® system. Whether different pressures produce different outcomes is unclear from our results, but animal studies indicate that performance is similar across the range of pressures used in the trials we included (Morykwas 2001). Another limitation was a variation in the follow-up times, which ranged from the fourth postoperative day (Llanos 2006) to 12 months post surgery (Howell 2011). Finally, included trials were geographically limited; six were conducted in North America, one in South America, one in India and one in Germany, further restricting the external validity of results. In light of these limitations, uncertainty remains about whether NPWT should be used at all for closed surgical wounds, unless there are reasons to believe that the wound may be difficult to heal. There are also important questions about the use of NPWT for orthopaedic surgery; one trial in this category was terminated early because of high blister rates.

## Quality of the evidence

### Limitations in study design and implementation

Risk of bias was assessed according to six domains: sequence generation; allocation concealment; blinding; selective outcome reporting; incomplete follow-up and other potential biases. Our assessments of the risk of bias for a number of these domains in all the included studies showed limitations in study design and implementation, which have been reported elsewhere in the review (Figure 1). We had particular concern that for studies where blinding of the intervention is difficult or impossible, there was subsequent uncertainty about allocation concealment and blinding of outcome assessment. Accordingly, the quality of the evidence was considered to be unclear for all of the outcomes.

### Indirectness of evidence

The review was limited by a lack of conformity; in both the experimental and the control interventions. For example the negative pressure devices used varied between studies, as did the control dressings. Consequently, the evidence was restricted to indirect comparisons between these varied interventions. Additionally, the review aimed to assess NPWT for acute surgical wounds, but its use was investigated in a limited range of types of surgery. As a result, the evidence may be regarded as indirect for other types of surgery. Finally, direct evidence of the effect of the intervention on wound infection or dehiscence - arguably the most important adverse outcomes of surgery - was reported in only two trials. Taken together, these limitations restrict confident decision-making concerning the use of NPWT for acute wounds.

### Unexplained heterogeneity or inconsistency of results

Heterogeneity was 30% or less In all of the pooled outcomes, however, there was some expected heterogeneity between sub-groups, due either to different types of surgery (acute wounds versus skin grafts; Analysis 1.1) or differences in interventions (Analysis 4.1).

### Imprecision of results

Confidence intervals (CIs) were wide in the pooled outcomes, but few studies were included, so future trials may have an impact on the certainty of these results. Two of the single study outcomes showed evidence of effect. In the Stannard 2012 trial, there was some uncertainty around the effect size with CIs between 0.28 and 0.96. A much higher level of uncertainty around the effect size was apparent in the Howell 2011 trial, where NPWT was more likely to cause fracture blisters than the standard dressing. The CIs in this trial (2.43 to 23.14) indicated the high level of uncertainty around the effect size. Further research is therefore very likely to have an important impact on the confidence of the estimate of effect for most of the outcomes measured in this review.

### Publication bias

We feel confident that our comprehensive electronic searches identified all existing, published randomised controlled trials addressing the review question, helping to limit bias in the review process. However, most of the trials identified through a search of the Clinical Trial Registries have not been published and we were unable to track down any information about them. Moreover, the scant contribution of the nine included trials, in the face of such wide use of NPWT, is unusual. These two factors may or may not indicate publication bias.

### Potential biases in the review process

Clearly described procedures were followed to prevent potential bias in the review process. A careful literature search was conducted and the methods we used were transparent and reproducible. It is possible that trials published in journals that were outside our search strategy may have been missed. None of the authors of the review has any conflicts of interest or associations with manufacturers of products included in this review.

### Agreements and disagreements with other studies or reviews

Our results are consistent with the most recent evidence-based recommendations for the use of NPWT, which cover a range of applications, including NPWT for acute wounds (Krug 2011). One systematic review, Ubbink 2008, was published before seven of our included trials were undertaken and included an earlier trial that we excluded from our review (Moisidis 2004), so results are not comparable. However, our findings differ from those of two recent systematic reviews, which evaluated the effectiveness of NPWT for incisional wounds. Important differences in the inclusion criteria account for the differences: the first included 10 RCTs and five observational studies (Ingargiola 2013), and the second included 33 publications (Karlakki 2013), seven of which were RCTs, with the remaining publications consisting of a combination of non-comparative case series, comparative cohort studies and comparative laboratory studies. Neither author included trials that had used 'home-made' devices. Authors from the Karlakki 2013 trial disclosed conflicts of interest, all benefiting from funding from the manufacturer of the NPWT device. Both of these reviews found in favour of NPWT for reducing surgical site infection (SSI) and other negative wound outcomes. Consequently, the issue of manufacturer sponsorship in studies of healthcare products remains. Specifically, a review of the effect of manufacturer involvement on studies of negative pressure wound therapy showed that 19 of the 24 studies reviewed had manufacturer involvement. Importantly, 18 of the 19 studies showed a positive effect for the manufacturer's product, while one was 'impartial' (Kairinos 2014). However, our findings are in agreement with other non-randomised studies that

show that NPWT may reduce skin graft complications (Blume 2010; Kim 2007). Other randomised (Hu 2009) and non-randomised studies have also shown a marked cost benefit when non-commercial applications were compared with commercial products (Rozen 2008; Shalom 2008). In one of these studies, a net saving per patient was USD 2603 (Rozen 2008).

## AUTHORS' CONCLUSIONS

### Implications for practice

Evidence about whether negative pressure wound therapy (NPWT) reduces surgical site infection or wound dehiscence remains unclear, as does its effect on time to complete healing. Rates of graft loss may be lower when NPWT is used. Machines and systems that are designed and built within hospitals are as effective in this area as commercial products. There are clear cost benefits when non-commercial systems are used to create the negative pressure required for wound therapy, with no evidence of worsening of clinical outcome. Pain levels are also rated lower when hospital-designed systems are used compared with their commercial counterparts. The high incidence of blisters occurring when NPWT is used following orthopaedic surgery suggests that the therapy should be limited until safety in this population is established.

### Implications for research

There is an urgent need for suitably powered, high-quality trials to evaluate the effectiveness of the newer NPWT products, which are designed for use on closed clean surgical incisions. Such trials

should focus initially on wounds that may be difficult to heal, such as sternal wounds or incisions on obese patients. Given the large cost differences between products, further trials comparing different types of NPWT are also justified. Full economic evaluations, including those associated with the NPWT system 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) need to be included. This will enable users of any future review to gain a clear understanding of the nature of resource use associated with negative pressure wound therapy. To facilitate assessment, future trials that combine different types of conditions (acute, sub-acute and chronic) should present results of each condition group separately. It may also be useful to test NPWT at various pressures.

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\* Indicates the major publication for the study

## CHARACTERISTICS OF STUDIES

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

#### Chio 2010

Methods	<p><b>Study design:</b> randomised controlled trial</p> <p><b>Ethics and informed consent:</b> ethics approved and consent obtained</p> <p><b>Sample size calculation:</b> yes</p> <p><b>ITT analysis:</b> participants analysed in groups to which they were assigned but 4 participants, who did not present for follow-up, were not included in the analysis</p>
Participants	<p><b>Location:</b> Columbus, Ohio, USA</p> <p><b>Intervention group:</b> n = 27; <b>Control group 2:</b> n = 27</p> <p><b>Mean age: Intervention group</b> = 62.1 years; <b>Control Group 2</b> = 58.1 years</p> <p><b>Inclusion criteria:</b> patients scheduled to undergo radial forearm free flap</p> <p><b>Exclusion criteria:</b> none stated</p>
Interventions	<p><b>Aim/s:</b> to evaluate the effectiveness of negative pressure dressings compared with static pressure dressings in the prevention of graft failure</p> <p><b>Intervention/s in both groups:</b> <i>Quote</i> “In all subjects, iodine petroleum-impregnated gauze rolls were placed over the skin graft in the inter-tendon spaces, followed by coverage with a sheet of Adaptic nonadherent dressing (Johnson &amp; Johnson, Langhorne, PA) . Dressings in both treatment groups were left in place for a total of six days, after which all dressings were then taken down, and the donor site dressed with Adaptic and circumferential gauze roll for a total of two weeks”</p> <p><b>Group 1 (NPD) intervention:</b> <i>Quote</i> “foam specifically designed for use with the negative pressure device (V.A.C. device; KCI, San Antonio, TX) was cut and the arm covered with an occlusive dressing. The vacuum device was attached and activated intraoperatively and set to -125 mmHg with adequate seal verified. No immobilizing splint was used”</p> <p><b>Group 2 (SPD) intervention:</b> <i>Quote</i> “a piece of sterile surgical foam cut to size and wrapped in Adaptic dressing was secured over the recipient bed followed by placement of a volar wrist-immobilizing splint”</p> <p><b>Study date/s:</b> March 2007-August 2009</p>
Outcomes	<ul style="list-style-type: none"> <li>● Graft failure</li> <li>● Percentage of area of skin graft failure</li> <li>● Adverse events</li> </ul> <p><b>Validity of measure/s:</b> quantitative measurements of the donor site were accomplished with the aid of a 1 x 1 cm grid transparency, which was laid over the donor site. The exact borders of the skin graft were then traced onto the overlying grid with a permanent marker</p> <p><b>Time points:</b> follow-up at 2 weeks post surgery (NB graft failure was also measured at 1 month post surgery but it was unclear if those from the 2-week follow-up had been included in this measure)</p>
Notes	
<i>Risk of bias</i>	

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	<b>Evidence:</b> <i>Quote</i> "A randomization schedule, created by a biostatistician using a random number generator" <b>Comment:</b> blocking not mentioned
Allocation concealment (selection bias)	High risk	<b>Evidence:</b> <i>Quote</i> "We had a list of the randomization schedule, and pts [participants] were assigned to either group based on the order of their surgery" (personal, email communication) <b>Comment:</b> surgeons aware of the next assignment
Blinding of participants and personnel (performance bias) All outcomes	Low risk	<b>Evidence for participants:</b> not possible <b>Comment:</b> unlikely to affect outcomes <b>Evidence for personnel:</b> not possible <b>Comment:</b> unlikely to affect outcomes
Blinding of outcome assessment (detection bias) All outcomes	High risk	<b>Evidence:</b> <i>Quote</i> "Evaluators at the time of the postoperative visits were not blinded as to which treatment arm the subjects belonged" <b>Comment:</b> correspondence with the author confirmed that "evaluators" were investigators
Incomplete outcome data (attrition bias) All outcomes	High risk	<b>Evidence:</b> <i>Quote</i> "Four subjects 4/54 (all of whom belonged to the NPD group) were lost to the first postoperative follow-up and were thus excluded from final analysis because no postoperative data could be recorded for these subjects. Of the remaining 50 subjects, only 32 patients (16 subjects in SPD group and 16 subjects in NPD group) returned for their second postoperative visit" <b>Comment:</b> only data from the first postoperative visit have been included Unequal distribution of 'drop outs' (15% in negative pressure group; 0% in static pressure group)
Selective reporting (reporting bias)	Low risk	<b>Comment:</b> all the pre-specified clinical outcomes were presented in Table 2 of the trial report. Adverse events were reported in the Results section of the trial report.

Chio 2010 (Continued)

		Measures reflect the aims of the intervention and the pre-defined outcomes. A published protocol was not available
Other bias	Low risk	<b>Evidence:</b> the authors report: <i>Quote</i> “Competing interests: None. Sponsorships: None” <b>Comment:</b> no other potential biases were identified

Crist 2014

Methods	<p><b>Study design:</b> randomised controlled trial</p> <p><b>Ethics and informed consent:</b> ethics approved and consent obtained</p> <p><b>Sample size calculation:</b> not stated</p> <p><b>ITT analysis:</b> available case analysis</p>
Participants	<p><b>Location:</b> Columbia, USA</p> <p><b>Intervention group:</b> n = 55; <b>Control group:</b> n = 60</p> <p><b>Mean age:</b> <b>Intervention group</b> = 47.2 years (SD 19.6); <b>Control group</b> = 48.3 years (SD 20.1). Data extracted from results section of clinicaltrials.gov (NCT00635479)</p> <p><b>Inclusion criteria:</b> patients that underwent an open surgical exposure for hip, pelvis, or acetabular fracture</p> <p><b>Exclusion criteria:</b> none stated</p>
Interventions	<p><b>Aim/s</b></p> <p><b>Primary :</b> to determine the effectiveness of using NPWT over primarily closed surgical incisions used for open reduction and internal fixation of hip, pelvis, and acetabular fracture surgery</p> <p><b>Secondary :</b></p> <p><b>Group 1 (NPC) intervention:</b> <i>Quote</i> “negative pressure dressing applied over the primarily closed incision sterilely in the operating room. NPWT was left on for 2 days or longer if drainage continued.”</p> <p><b>Group 2 (Control) intervention:</b> <i>Quote</i> “standard gauze dressing”. The ‘standard dressing’ was not described</p> <p><b>Study date/s:</b> not provided</p>
Outcomes	<ul style="list-style-type: none"> <li>● Infection</li> <li>● LOS</li> <li>● Total serious adverse events</li> </ul> <p><b>Validity of measure/s:</b> not provided</p> <p><b>Time points:</b> followed for 12 months</p>
Notes	Conference abstract. Additional information provided by the investigator and from a search of clinicaltrials.gov (NCT00635479)
<b>Risk of bias</b>	

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	<b>Evidence:</b> <i>Quote</i> "Computer randomization" <b>Comment:</b> correspondence with author
Allocation concealment (selection bias)	Low risk	<b>Evidence:</b> <i>Quote</i> "Opaquesealed envelope opened in the OR" <b>Comment:</b> correspondence with author
Blinding of participants and personnel (performance bias) All outcomes	Low risk	<b>Evidence for participants:</b> not possible <b>Comment:</b> unlikely to affect outcomes <b>Evidence for personnel:</b> not possible <b>Comment:</b> unlikely to affect outcomes
Blinding of outcome assessment (detection bias) All outcomes	Low risk	<b>Evidence:</b> <i>Quote</i> "Yes" <b>Comment:</b> correspondence with author
Incomplete outcome data (attrition bias) All outcomes	High risk	<b>Evidence:</b> <i>Quote</i> "55 patients randomized to the NPWT group and 60 patients randomized to the standard dressing group. The NPWT group included 49 patients and the gauze group included 42 patients that completed the 12 month follow-up." <b>Comment:</b> 10.9% patients in NPWT group and 30.0% of control group were lost to follow-up
Selective reporting (reporting bias)	Low risk	<b>Comment:</b> protocol registered on ClinicalTrials.gov with identifier: NCT00635479. Expected outcomes were reported in the abstract, but other outcomes nominated in the protocol were not reported (such as total serious adverse events). These may be included when the full trial is published
Other bias	Unclear risk	<b>Evidence:</b> <i>Quote</i> "Two of the authors have been advisory consultants for KCI and have previously received research funding for different projects. This study was not funded by KCI." <b>Comment:</b> correspondence with author

Methods	<p><b>Study design:</b> randomised controlled trial</p> <p><b>Ethics and informed consent:</b> ethics approved and consent obtained</p> <p><b>Sample size calculation:</b> yes</p> <p><b>ITT analysis:</b> yes</p>
Participants	<p><b>Location:</b> University of Chicago Medical Center, IL, USA</p> <p><b>Intervention group:</b> n = 42; <b>Control group:</b> n = 45</p> <p><b>Mean age: Group 1 = 53 years; Group 2 = 54 years</b></p> <p><b>Inclusion criteria:</b> patients admitted to University of Chicago Medical Center, 18 years of age and over, with acute wounds resulting from trauma, dehiscence, or surgery</p> <p><b>Exclusion criteria:</b></p> <ul style="list-style-type: none"> <li>● systemic sepsis caused by wound infection;</li> <li>● grossly necrotic wounds;</li> <li>● malignancy in the wound;</li> <li>● wounds with untreated osteomyelitis;</li> <li>● patients with allergy to sulfamylon and Dakin's (sodium hypochlorite) solution;</li> <li>● patients with severe peripheral vascular disease.</li> </ul>
Interventions	<p><b>Aim/s:</b> <i>Quote</i> "The primary objective was to compare the efficacy of VAC and GSUC with respect to changes in wound size. Secondary objectives were to compare associated costs of the dressings, the ease of application, and the pain associated with each dressing change"</p> <p><b>Intervention/s in both groups:</b> <i>Quote</i> "Patients had ad lib access to analgesics administered via PCA or a nurse"</p> <p><b>Group 1 (GSUC) intervention:</b> <i>Quote</i> "In the GSUC arm, a gauze dressing (Kerlix 4.5 inch roll, Covidien, Mansfield MA) moistened with 0.9% normal saline was applied to the wounds, a red rubber catheter (CR Bard, Covington, GA) was placed in the center of the dressing, and the dressing was then sealed with an occlusive cover (Ioban Antimicrobial Incise Drape, 3M, St Paul, MN). Continuous wall suction at -75 to -80 mm Hg was applied and the dressings were changed daily"</p> <p><b>Group 2 (VAC) intervention:</b> <i>Quote</i> "In the VAC arm, GranuFoam black sponge (KCI, San Antonio, TX) was applied to the wounds and sealed with an occlusive plastic cover; continuous suction at -75 to -125 mm Hg was initiated and the dressing was changed every 48 hours, as recommended by VAC therapy guidelines. All components of the dressing were obtained from Kinetics Concepts, Inc"</p> <p><b>Study date/s:</b> October 2006-May 2008</p>
Outcomes	<ul style="list-style-type: none"> <li>● Rate of change in surface area between groups (expressed as the rate of change %/day)</li> <li>● Rate of change in wound volume between groups (expressed as the rate of change %/day)</li> <li>● Cost/day</li> <li>● Pain measured using a 0 to 10 linear analogue scale and reported as the "sum of pain intensity differences"</li> <li>● Wound complications</li> <li>● Adverse events</li> </ul> <p><b>Validity of measure/s</b></p> <ul style="list-style-type: none"> <li>● "Wound size was calculated using the Xakellis and Frantz method: wound surface area = length X width X 0.783; wound volume area = area X depth X 0.327"</li> </ul>

	<ul style="list-style-type: none"> <li>Pain was self-reported and measured "according to the 0 to 10 linear analogue scale immediately before, during, and after removal of the dressing. The sum of pain intensity differences (SPID) was used to facilitate comparison of pain levels between the 2 groups. The SPID score was calculated using the formula: (pain during - pain before) + (pain after - pain during)."</li> </ul> <p><b>Time points:</b> data collected up to day 7 were included in the analyses</p>	
Notes	The intervention was a 'home made' device.	
<b>Risk of bias</b>		
<b>Bias</b>	<b>Authors' judgement</b>	<b>Support for judgement</b>
Random sequence generation (selection bias)	Low risk	<b>Evidence:</b> <i>Quote</i> "The randomization sequence was generated from the Web site <a href="http://www.randomization.com">http://www.randomization.com</a> " <b>Comment:</b> blocking not mentioned
Allocation concealment (selection bias)	Unclear risk	<b>Evidence:</b> <i>Quote</i> "On enrolment, patients were then randomized to either GSUC or VAC therapy in a 1:1 ratio by drawing a previously prepared card" <b>Comment:</b> unclear whether the allocations on the previously prepared card were visible before allocation
Blinding of participants and personnel (performance bias) All outcomes	Low risk	<b>Evidence for participants:</b> <i>Quote</i> "The 2 methods of SAWT were obviously and visibly different, so it was impossible to blind either the therapists or the patients to the method of treatment" <b>Comment:</b> unlikely to affect outcomes <b>Evidence for personnel:</b> <i>Quote</i> "The 2 methods of SAWT were obviously and visibly different, so it was impossible to blind either the therapists or the patients to the method of treatment" <b>Comment:</b> unlikely to affect outcomes
Blinding of outcome assessment (detection bias) All outcomes	High risk	<b>Evidence:</b> <i>Quote</i> "A senior therapist who was highly experienced with both VAC and GSUC changed all of the dressings. We tried to minimize bias by using therapists who were not participating in the study to gather and record data" <b>Comment:</b> the therapist was not blinded

Incomplete outcome data (attrition bias) All outcomes	Low risk	<b>Evidence:</b> <i>Quote</i> “An intention-to-treat analysis was performed for all of the primary and secondary outcomes. Forty-five patients in the GSUC group and 42 patients in the VAC group were included in the analyses.”
Selective reporting (reporting bias)	Low risk	<b>Comment:</b> all the pre-specified clinical outcomes were presented in Tables 3 and 4 in the trial report. Complications and adverse events were reported in the results section of the trial report. We accessed the published protocol (NCT00724750) and confirmed that the aims of the study and the pre-defined outcomes listed in the protocol were the same as in the published paper
Other bias	Unclear risk	<b>Evidence:</b> the study began in 2006 but the protocol was <i>Quote</i> “First Received on July 25, 2008” at ClinicalTrials.gov <b>Comment:</b> potential for study characteristics to have changed before or during the study

**Howell 2011**

Methods	<b>Study design:</b> randomised controlled trial <b>Ethics and informed consent:</b> not reported <b>Sample size calculation:</b> yes <b>ITT analysis:</b> all participants completed the study
Participants	<b>Location:</b> NYU Hospital for Joint Disorders, New York, NY, USA <b>Intervention group:</b> n = 24; <b>Group 2:</b> n = 36 <b>Mean age:</b> not reported <b>Inclusion criteria:</b> patients undergoing unilateral or bilateral primary total knee arthroplasty who were obese (BMI > 30), who met criteria of increased risk for postoperative wound drainage and who were prescribed enoxaparin sodium for deep vein thrombosis prophylaxis <b>Exclusion criteria:</b> patient refusal to participate in the study, revision total knee replacement, prior knee surgery (except arthroscopy), and patients with documented diabetes mellitus
Interventions	<b>Aim/s:</b> to compare the number of days to dry wound in a negative pressure dressings group compared with a static pressure dressings group <b>Intervention/s in both groups:</b> <i>Quote</i> “All patients received three doses of peri-operative intravenous antibiotics and were maintained on subcutaneous DVT prophylaxis for 30 days after surgery”

	<p><b>Group 1 (NPD) intervention:</b> <i>Quote</i> "Subsequent to the closure of the surgical incision, a negative pressure dressing (VAC Therapy, Kinetic Concepts Inc., San Antonio, Texas) was applied under sterile conditions. A medical grade open cell polyurethane ether foam (pore size of 400--600 micrometers) was cut into the shape of a rectangle approximately 5 cm in width and a length sufficient to cover the entire linear wound. The knee was held in 151 of flexion, and the foam was secured over the incision by the application of a specialized adhesive drape, provided in the VAC Therapy system. An evacuation tube with side ports was embedded within the reticulated foam, allowing negative pressure to be applied equally over the entire wound bed. The foam-evacuation tube complex attached to a programmable vacuum pump applied a - 125 mmHg continuous vacuum pressure to the wound. The VAC Therapy dressing remained in place for a 48-hour period, after which time clean, dry gauze dressings were applied and changed on daily basis until the wound was dry"</p> <p><b>Group 2 (SPD) intervention:</b> "Patients in the control arm had their surgical wound covered in the operating room with a sterile, dry gauze dressing that was held in place with a perforated, stretchable cloth tape. This initial dressing remained in place for 48 hours after which time clean, dry gauze dressings were applied and changed on a daily basis until the wound was dry."</p> <p><b>Study date/s:</b> not stated</p>	
Outcomes	<ul style="list-style-type: none"> <li>• Days to dry wound</li> <li>• Deep wound infection</li> <li>• Blister formation</li> </ul> <p><b>Time points:</b> patients followed up for 12 months post surgery</p>	
Notes		
<b>Risk of bias</b>		
<b>Bias</b>	<b>Authors' judgement</b>	<b>Support for judgement</b>
Random sequence generation (selection bias)	Unclear risk	<b>Comment:</b> not described
Allocation concealment (selection bias)	Low risk	<b>Evidence:</b> <i>Quote</i> "randomized with blinded envelopes to either the treatment with negative pressure wound therapy group or a control group using sterile gauze"
Blinding of participants and personnel (performance bias) All outcomes	High risk	<b>Evidence:</b> not described <b>Comment:</b> difference in appearance of dressings made blinding impossible
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	<b>Evidence:</b> not described

Howell 2011 (Continued)

Incomplete outcome data (attrition bias) All outcomes	Low risk	<b>Evidence:</b> 51 patients were randomised and 51 completed the study
Selective reporting (reporting bias)	Low risk	<b>Comment:</b> the pre-specified clinical outcomes were presented in Table 1 in the trial report and a post hoc analysis of blister occurrence was shown in Table 2. Infection rates were reported in the results section of the trial report. We could not find a published protocol
Other bias	High risk	No baseline data were presented. In addition, groups contained unequal numbers, which may indicate undisclosed losses in one group The study was supported by KCI, the manufacturer of the negative pressure device

Llanos 2006

Methods	<p><b>Study design:</b> randomised, double-blind controlled trial</p> <p><b>Ethics and informed consent:</b> ethics approved and consent obtained</p> <p><b>Sample size calculation:</b> yes</p> <p><b>ITT analysis:</b> yes</p>
Participants	<p><b>Location:</b> Burn &amp; Plastic Surgery Unit, Santiago, Chile</p> <p><b>Intervention group:</b> n = 30; <b>Control group:</b> n = 30</p> <p><b>Mean age: Intervention group</b> = 34 years (range 20-52); <b>Control group</b> = 34.5 years (range 19-58)</p> <p><b>Inclusion criteria:</b> <i>Quote</i> “all patients who were admitted at the hospital with acute traumatic injuries and skin loss, which hindered primary closure, underwent a surgical cleaning of their wound, and had a quantitative biopsy culture performed on their wound. Those patients whose biopsy culture had a bacterial count lower than 100,000 colony forming units per gram of tissue and who had given informed consent to enter the study were recruited”</p> <p><b>Exclusion criteria:</b> those who, <i>Quote</i> “had burns that covered 20%, or more, of their total body surface; were polytraumatized; had surgical contraindications because of medical, anesthetic (serious associated pathology), or surgical cause (hypoalbuminemia or systemic infection); or were enlisted in other clinical trials”</p>
Interventions	<p><b>Aim/s</b></p> <p><b>Primary :</b> to determine if the negative pressure closure diminishes the area loss of the skin grafts</p> <p><b>Secondary :</b> to determine if:</p> <ul style="list-style-type: none"> <li>● the negative pressure closure shortens hospital stay, or whether secondary wound coverage procedures are needed; and</li> <li>● to determine whether there is a relation between the area loss of the skin graft and the total grafted surface</li> </ul>

	<p><b>Intervention/s in both groups:</b> <i>Quote</i> “The graft was covered with a single layer of parafin gauze dressing (Jelonet, Smith &amp; Nephew, England); then, 3 sheets of polyurethane (high-density foam, Nuris Luisa, Santiago, Chile) with a fenestrated silicone drainage tube between the layers was placed over the gauze and covered with a transparent adhesive dressing (Op site, Smith &amp; Nephew) providing the vacuum seal. We used a double layer under the tube to prevent pressure ulcers at the bed of the suction tube.”</p> <p><b>Group 1 (NPC) intervention:</b> <i>Quote</i> “The suction tube was connected to the central aspiration system at a pressure of -80 mm Hg, and the integrity of the vacuum seal was tested and reinforced with cotton dressing and an elastic gauze bandage if necessary”</p> <p><b>Group 2 (Control) intervention:</b> the control group <i>Quote</i> “only differed from the active group in that it lacked a connection to the central aspiration system (i.e., negative pressure vacuum)”</p> <p><b>Study date/s:</b> May 2003-October 2004</p>	
<p>Outcomes</p>	<ul style="list-style-type: none"> <li>• Area loss of skin graft in cm<sup>2</sup></li> <li>• Need for re-grafting</li> <li>• Length of hospital stay</li> <li>• Complications</li> </ul> <p><b>Validity of measure/s:</b> <i>Quote</i> “Digital photographs, without flash, were taken from a distance of 40 cm from the wound to evaluate the areas of loss at the moment of uncovering the graft. Afterward, these images were analyzed with the Autocad (Autodesk, Inc, 2001, Fremont, CA) software, measuring the loss in cm<sup>2</sup>”</p> <p><b>Time points:</b> fourth postoperative day</p>	
<p>Notes</p>	<p>The intervention was a 'home made' device.</p>	
<p><b>Risk of bias</b></p>		
<p><b>Bias</b></p>	<p><b>Authors' judgement</b></p>	<p><b>Support for judgement</b></p>
<p>Random sequence generation (selection bias)</p>	<p>Low risk</p>	<p><b>Evidence:</b> <i>Quote</i> “Treatment assignment was performed using computer-generated random numbers in permuted blocks of 6”</p>
<p>Allocation concealment (selection bias)</p>	<p>High risk</p>	<p><b>Evidence:</b> <i>Quote</i> “The treatment allocation of each patient was performed by the nurse of the operating room who knew the corresponding assignment”</p> <p><b>Comment:</b> follow-up correspondence with the author indicated <i>Quote</i> “the theatre nurse had a list of randomization with computer generated random numbers”, so allocation was not concealed</p>
<p>Blinding of participants and personnel (performance bias) All outcomes</p>	<p>Unclear risk</p>	<p><b>Evidence for participants:</b> not described <b>Comment:</b> dressings were identical. The only difference was that dressing in the NPC group were connected to an 'active' suction device. Potential for participant to</p>

		<p>notice this</p> <p><b>Evidence for personnel:</b> <i>Quote</i> “The corresponding treatment was notified to the surgeon only once the skin graft had been performed so that the surgeon did not modify his technique according to the assignation of treatment”</p> <p><b>Comment:</b> once surgery was completed, other personnel would have been aware of group assignment (active suction or not) . Whether this would have affected outcomes is unclear</p>
<p>Blinding of outcome assessment (detection bias)</p> <p>All outcomes</p>	<p>Low risk</p>	<p><b>Evidence:</b> <i>Quote</i> “The person in charge of measuring the areas in the photographic register was masked to which intervention the patient had received. That way, at the moment of evaluating the photograph, this person did not know whether or not the patient had undergone NPC. In addition, the data analyst was masked to the groups of intervention at the moment of analyzing the results”</p>
<p>Incomplete outcome data (attrition bias)</p> <p>All outcomes</p>	<p>Low risk</p>	<p><b>Evidence:</b> <i>Quote</i> “All the patients were analyzed in the group to which they were assigned, adhering to the intention-to-treat principle” and “In our study, there were no drop-outs, drop-ins, or noncompliant patients. Furthermore, no patients refused to take part in the study”</p>
<p>Selective reporting (reporting bias)</p>	<p>Low risk</p>	<p><b>Comment:</b> all the pre-specified clinical outcomes were presented in Table 2 and in Figures 4 and 5 in the trial report. Adverse events were reported in the results section. Outcome measures reflected the aims of the intervention and the pre-defined outcomes. A published protocol was not available</p>
<p>Other bias</p>	<p>Low risk</p>	<p><b>Evidence:</b> <i>Quote</i> “The authors have no conflicts of interest with any of the manufacturing companies of the products used in the present study”</p> <p><b>Comment:</b> no other potential biases were identified</p>

Methods	<p><b>Study design:</b> randomised controlled trial</p> <p><b>Ethics and informed consent:</b> the study was approved by the Georgetown University Institutional Review Board. Consent was not specifically stated, but those patients not capable of undergoing informed consent were excluded</p> <p><b>Sample size calculation:</b> yes</p> <p><b>ITT analysis:</b> Available case analysis</p>
Participants	<p><b>Location:</b> Columbus, Ohio, USA</p> <p><b>Intervention group:</b> n = 50; <b>Control group:</b> n = 43</p> <p><b>Mean age: Intervention group</b> = 61.3 years (range 40 - 101); <b>Control group</b> = 61.3 years (range 38 - 86)</p> <p><b>Inclusion criteria:</b> patients scheduled to undergo radial forearm free flap</p> <p><b>Exclusion criteria:</b> <i>Quote</i> "patients not capable of undergoing informed consent and those patients with tape allergies or who otherwise could not tolerate NPWT . . . patients with lower extremity amputations distal to the forefoot were excluded."</p>
Interventions	<p><b>Aim/s</b></p> <p><b>Primary :</b> <i>Quote</i> "to evaluate the effectiveness of NPWT in patients with multiple comorbidities"</p> <p><b>Secondary :</b> <i>Quote</i> "to evaluate factors that contribute to wound complication</p> <p><b>Intervention/s in both groups:</b> <i>Quote</i> "The graft was covered with a single layer of paraffin gauze dressing (Jelonet, Smith &amp; Nephew, England); then, 3 sheets of polyurethane (high-density foam, Nuris Luisa, Santiago, Chile) with a fenestrated silicone drainage tube between the layers was placed over the gauze and covered with a transparent adhesive dressing (Op site, Smith &amp; Nephew) providing the vacuum seal. We used a double layer under the tube to prevent pressure ulcers at the bed of the suction tube."</p> <p><b>Group 1 (NPWT) intervention:</b> <i>Quote</i> "NPWT group, which underwent placement of a V.A.C. system (KCI, San Antonio, TX) along the line of closure set at -125mmHg continuous pressure at the time of closure</p> <p><b>Group 2 (Control) intervention:</b> <i>Quote</i> "the control group, which received a standard dry sterile dressing consisting of a non adhesive silicone layer (Mepitel; Mölnlycke Health Care AB, Göteborg, Sweden) and a bacteriostatic single silver layer (Acticoat, Smith &amp; Nephew, Hull, United Kingdom).</p> <p><b>Study date/s:</b> October 2008 - August 2010.</p>
Outcomes	<ul style="list-style-type: none"> <li>● Wound infection</li> <li>● Dehiscence</li> <li>● Re-operation</li> <li>● LOS</li> </ul> <p><b>Validity of measure/s:</b> not stated</p> <p><b>Time points:</b> <i>Quote</i> "all incisions assessed on the third postoperative day . . . and re-assessed at the first outpatient postoperative visit, as well as any subsequent visit (the last recorded infection was at 66 days post surgery)." However, the abstract stated that "Average follow-up was 113 days"</p>
Notes	
<i>Risk of bias</i>	

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	<b>Evidence:</b> <i>Quote (from correspondence with the author)</i> "Used a randomization generator through Excel in groups of 8 (4 controls, 4 experimental)" <b>Comment:</b> adequate method
Allocation concealment (selection bias)	Low risk	<b>Evidence:</b> <i>Quote (from correspondence with the author)</i> "When the patient was recruited . . . they contacted one of the investigators and the patient was assigned to whichever group was next on the list" <b>Comment:</b> adequate method
Blinding of participants and personnel (performance bias) All outcomes	Low risk	<b>Evidence for participants:</b> not possible <b>Comment:</b> unlikely to affect outcomes <b>Evidence for personnel:</b> not possible <b>Comment:</b> unlikely to affect outcomes
Blinding of outcome assessment (detection bias) All outcomes	Low risk	<b>Evidence:</b> <i>Quote</i> "The evaluations were performed by a member of the research team not involved in the enrolment or the operative treatment and, thus, were blinded as to randomization group" <b>Comment:</b> adequate method
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	<b>Evidence:</b> <i>Quote</i> "Twelve subjects were lost to follow up in the immediate postoperative period and were excluded from the final analysis" <b>Comment:</b> equal number of losses in both groups
Selective reporting (reporting bias)	Low risk	<b>Comment:</b> protocol unavailable, but expected outcomes reported
Other bias	High risk	<b>Evidence:</b> <i>Quote</i> "Drs Attinger and Steinberg are consultants for Kinetic Concepts Incorporated" <b>Comment:</b> study funded by manufacturer. Also, the control group received co-intervention - a bacteriostatic single silver layer (Acticoat, Smith & Nephew, Hull, United Kingdom) with their dressing

Methods	<p><b>Study design:</b> randomised controlled trial</p> <p><b>Ethics and informed consent:</b> ethics approved and consent obtained</p> <p><b>Sample size calculation:</b> no</p> <p><b>ITT analysis:</b> yes</p>	
Participants	<p><b>Location:</b> University hospital in Erlangen, Germany</p> <p><b>Intervention group:</b> n = 9; <b>Control group:</b> n = 10</p> <p><b>Mean age: Intervention group</b> = 66.2 years (SD 17.83); <b>Control group</b> = 70.0 years (SD 11.01)</p> <p><b>Inclusion criteria:</b> <i>Quote</i> "consecutive patients who were scheduled for a total hip arthroplasty (THA) for osteoarthritis of the hip were randomised"</p> <p><b>Exclusion criteria:</b> not stated</p>	
Interventions	<p><b>Aim/s</b></p> <p><b>Primary:</b> <i>Quote</i>: "to evaluate the effect of NPWT on postoperative seroma"</p> <p><b>Secondary:</b> <i>Quote</i> "to evaluate any potential influence wound healing and laboratory inflammatory values."</p> <p><b>Intervention/s in both groups:</b> <i>Quote</i> "The surgical intervention was identical for both groups. All patients received two Redon drains, one in the deep area of the wound close to the prostheses and one above the closed fascia. The postoperative physiotherapy and mobilisation was also identical for both groups. Both groups received perioperative prophylaxis with antibiotics either Augmentin (amoxicillin trihydrate with potassium clavulanate) or ciprofloxacin"</p> <p><b>Group 1 (NPWT) intervention:</b> <i>Quote</i> "The NPWT group was treated with a PREVENA™ system (KCI, San Antonio, USA). The PREVENA system was left on the wound for five days including the day of surgery."</p> <p><b>Group 2 (Control) intervention:</b> the control group received <i>Quote</i> "the standard wound dressing of our department, consisting of a dry wound coverage"</p> <p><b>Study date/s:</b> not stated</p>	
Outcomes	<ul style="list-style-type: none"> <li>● Incidence of seroma (by ultrasound)</li> <li>● Amount of wound drainage in the Redondrain canisters</li> <li>● Duration of prophylactic antibiotics</li> <li>● Secretion from the wound</li> </ul> <p><b>Validity of measure/s:</b> <i>Quote</i> "All patients underwent an ultrasound (Zonare, Z.one Ultra SP 4.2, Erlangen, ZONARE Medical Systems, Inc., Mountain View, USA) of the wound"</p> <p><b>Time points:</b> fifth and tenth post-operative days</p>	
Notes		
<b>Risk of bias</b>		
<b>Bias</b>	<b>Authors' judgement</b>	<b>Support for judgement</b>
Random sequence generation (selection bias)	Unclear risk	Not stated
Allocation concealment (selection bias)	Unclear risk	Not stated

Pachowsky 2011 (Continued)

Blinding of participants and personnel (performance bias) All outcomes	High risk	<b>Evidence for participants:</b> not possible <b>Comment:</b> unlikely to affect outcomes <b>Evidence for personnel:</b> not possible <b>Comment:</b> unlikely to affect outcomes
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Dressings were left in place for 5 days. The ultrasound was performed on day 5. It was unclear if the person performing the ultrasound was aware of the allocated group
Incomplete outcome data (attrition bias) All outcomes	Low risk	All enrolled patients were accounted for in the analyses
Selective reporting (reporting bias)	Unclear risk	Results for outcomes identified in the methods section were reported. We did not see the original protocol
Other bias	Unclear risk	<b>Evidence:</b> <i>Quote</i> "Matthias H. Brem gave scientific presentations for KCI. The PRE-VENA <sup>TM</sup> wound treatment system was provided by KCI free of charge." One patient in the NPWT group removed the Redon drain by himself on the first postoperative day

Petkar 2012

Methods	<b>Study design:</b> randomised controlled trial <b>Ethics and informed consent:</b> yes <b>Sample size calculation:</b> no <b>ITT analysis:</b> all enrolled patients included in analysis
Participants	<b>Location:</b> plastic and reconstructive surgery department of a tertiary referral centre Vellore, Tamil Nadu, India <b>Intervention group:</b> n = 35; <b>Control group:</b> n = 36 <b>Mean age: Intervention group 1 = 35.1 years;Control group 2 = 34.1 years</b> <b>Inclusion criteria:</b> patients undergoing split-skin grafting <b>Exclusion criteria:</b> a known bleeding tendency, repeat grafting for a failed graft and regions which were technically not amenable for application of vacuum closure, e.g. oral commissure, eyelids and hairy scalp in patients unwilling for head tonsuring
Interventions	<b>Aim/s</b> <b>Primary:</b> to assess the effectiveness of NPWT over standard dressings in this population <b>Secondary:</b> None stated <b>Intervention/s in both groups:</b> <i>Quote</i> "The patients were operated by plastic surgery consultants and registrars of a single unit. Soon after the placement of the graft and securing it with staplers or catgut sutures as necessary" <b>Group 1 (NPC) intervention:</b> <i>Quote</i> "only Vaseline gauze was laid on the graft, on

	<p>which a low-density polyurethane foam of 1.5-in.-thickness cut to the size of the graft was placed. A soft, flexible transparent plastic or silicone tube of 5-mm inner diameter and 1 meter length was fenestrated at sides near one of the ends and the same was inserted into the foam by making a shallow slit in the latter. The assembly was covered with a transparent adhesive film (Opsite) whose edges were fastened to the normal skin surrounding the dressing to create an airtight seal. Outer end of the tube was then connected to a continuous wall suction of - 80 mm Hg when the patient was shifted from the operation theatre“</p> <p><b>Group 2 (Control) intervention:</b> <i>Quote</i> ”In the control group, a Vaseline gauze was placed over the graft, cotton bandages were placed and were secured with roller gauze bandage, elastic adhesive bandage or tie-over dressing as deemed necessary in a conventional dressing.“</p> <p><b>Study date/s:</b> May 2003-October 2004</p>	
Outcomes	<ul style="list-style-type: none"> <li>● Graft failure</li> <li>● Percentage of area of skin graft failure</li> <li>● Adverse events</li> </ul> <p><b>Validity of measure/s:</b> quantitative measurements of the donor site were accomplished with the aid of a 1 x 1 cm grid transparency, which was laid over the donor site. The exact borders of the skin graft were then traced onto the overlying grid with a permanent marker</p> <p><b>Time points:</b> follow-up at 2 weeks post surgery (NB graft failure was also measured at 1 month post surgery but it was unclear whether those from the 2-week follow-up had been included in this measure)</p>	
Notes	The intervention was a 'home made' device.	
<b>Risk of bias</b>		
<b>Bias</b>	<b>Authors' judgement</b>	<b>Support for judgement</b>
Random sequence generation (selection bias)	Low risk	<p><b>Evidence:</b> <i>Quote</i> ”Each wound was randomized into study or control group using an open list of computer-generated random numbers.“</p> <p><b>Comment:</b> adequate method</p>
Allocation concealment (selection bias)	High risk	<p><b>Evidence:</b> <i>Quote</i> ”Each wound was randomized into study or control group using an open list of computer-generated random numbers“</p> <p><b>Comment:</b> as some patients had more than one graft wound, it would have been possible, using an open randomisation allocation, to select the intervention for a specific wound</p>
Blinding of participants and personnel (performance bias)	Low risk	<p><b>Evidence for participants:</b> not possible</p> <p><b>Comment:</b> unlikely to affect outcomes</p>

**Petkar 2012** (Continued)

All outcomes		<b>Evidence for personnel:</b> not possible <b>Comment:</b> unlikely to affect outcomes
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	<b>Evidence:</b> <i>Quote</i> "Percentage of graft take was assessed by gross examination on day 9 and then day 14 by the consultants in treating plastic surgery unit of the grade of professor." <b>Comment:</b> unclear whether assessors were aware of group allocation
Incomplete outcome data (attrition bias) All outcomes	Low risk	<b>Comment:</b> all randomised wounds were reported in results
Selective reporting (reporting bias)	Unclear risk	<b>Evidence:</b> <i>Quote</i> "the patient was asked to discontinue the dressing or was decided to undergo re-surgery at the site" <b>Comment:</b> protocol not viewed. Infection not reported. Patients may have undergone further surgery at the location of grafting, but this was not reported in the paper
Other bias	Unclear risk	<b>Comment:</b> wounds, not people were randomised (unit of analysis error)

**Stannard 2012**

Methods	<b>Study design:</b> multi-centre, randomised controlled trial (4 Level one trauma centres) <b>Ethics and informed consent:</b> ethics approved and consent obtained <b>Sample size calculation:</b> no <b>ITT analysis:</b> wounds, not people were assessed
Participants	<b>Location:</b> Columbus, Ohio, USA <b>Intervention group:</b> n = 130 participants; 141 fractures; <b>Control group:</b> n = 119 participants; 122 fractures <b>Mean age: Intervention group</b> not stated; <b>Control group 2</b> not stated <b>Inclusion criteria:</b> people > 18 years of age, who sustained a high-energy tibial plateau, pilon or calcaneus fracture were able to comply with research protocol and willing to give informed consent <b>Exclusion criteria:</b> nonoperative calcaneus, tibia plateau, or pilon fractures; patients with open calcaneus fractures; tibial plateau or calcaneus fractures receiving definitive surgery more than 16 days after injury; pilon fractures receiving definitive surgery more than 21 days after injury; prisoners; pregnant women; patients with one of these fractures as a result of a low-energy mechanism of injury; patients or family members unable or unwilling to sign study informed consent; and patients unable to comply with the protocol

Interventions	<p><b>Aim/s</b>  <b>Primary :</b> <i>Quote</i> “to investigate the use of NPWT to prevent wound dehiscence and infection after high-risk lower extremity trauma  <b>Secondary :</b> None stated  <b>Intervention/s in both groups:</b> dressings or NPWT were applied in the operating room and then changed on postoperative day 2 and every 1 to 2 days thereafter  <b>Group 1 (NPC) intervention:</b> NPWT over the surgical incision after open reduction and internal fixation of the fracture  <b>Group 2 (Control) intervention:</b> standard post operative dressing (dressing not described)  <b>Study date/s:</b> not stated</p>	
Outcomes	<ul style="list-style-type: none"> <li>• Wound infection and dehiscence</li> <li>• Time to discharge from hospital</li> </ul> <p><b>Validity of measure/s:</b> <i>Quote</i> ”All infections were confirmed with cultures“  <b>Time points:</b> Not stated - unclear for how long patients were followed-up</p>	
Notes		
<b>Risk of bias</b>		
<b>Bias</b>	<b>Authors’ judgement</b>	<b>Support for judgement</b>
Random sequence generation (selection bias)	Low risk	<p><b>Evidence:</b> <i>Quote</i> ”Patients were enrolled and then randomized to receive either standard postoperative dressings (control) or NPWT (study)“  <b>Comment:</b> additional author information “the randomization was done via a computer generated randomization program”</p>
Allocation concealment (selection bias)	Unclear risk	<b>Comment:</b> method not clarified
Blinding of participants and personnel (performance bias) All outcomes	Low risk	<p><b>Evidence for participants:</b> not possible  <b>Comment:</b> unlikely to affect outcomes  <b>Evidence for personnel:</b> not possible  <b>Comment:</b> unlikely to affect outcomes</p>
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	<p><b>Evidence:</b> <i>Quote</i> “A patient was diagnosed as having an infection when a combination of clinical signs and symptoms (purulent drainage, erythema, fever, chills, etc) and laboratory data documented the infection. All infections were confirmed with cultures. Wound dehiscence was defined as any separation of the surgical incision that required either local wound care or surgical treatment”</p>

		<b>Comment:</b> not clear whether those assessing outcomes were aware of group assignment
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	<b>Comment:</b> a total of 249 patients were recruited. The same number of patients were reported for both acute and long term follow-up (follow-up period not defined). Given that 4 hospitals were involved in the study, it seems unusual that complete follow-up would have occurred; suggesting an available case analysis may have been performed
Selective reporting (reporting bias)	Low risk	<b>Evidence:</b> <i>Quote</i> "NCT00582998" <b>Comment:</b> registered 9 months after final data collection date, so unclear whether reported outcomes match original protocol. However, infection and dehiscence were the expected outcomes
Other bias	High risk	<b>Evidence:</b> <i>Quote</i> "Funds from corporate/industry were received from Kinetic Concepts, Inc to support this work. Each institution received benefits directed solely to a research fund, foundation, educational institution, or other nonprofit organization which the author(s) has/have been associated. One or more of the author(s) has/have received or will receive benefits for personal or professional use from a commercial party related directly or indirectly to the subject of this manuscript: honoraria and consultancy" <b>Comment:</b> <ul style="list-style-type: none"> <li>• Unequal number of participants in each group</li> <li>• Appears from the protocol that data collection was over many years, but no dates or explanation in manuscript</li> <li>• Results reported per fracture so there is a potential unit of analysis issue</li> </ul>

**Abbreviations**

BMI: body mass index

DVT: deep venous thrombosis

GSUC: (no definition, apart from stating it was similar to another hospital developed device (a subatmospheric pressure wound therapy system; SAWT)

ITT: intention-to-treat  
 KCI: Kinetic Concepts Incorporated  
 LOS: length of stay  
 NPC: negative pressure closure  
 NPD: negative pressure device  
 NPWT: negative pressure wound therapy  
 OR: operating room (theatre)  
 PCA: patient controlled analgesia  
 SAWT: subatmospheric pressure wound therapy system  
 SPD: static pressure dressing  
 SPID: sum of pain intensity differences  
 TKR: total knee replacement  
 TKA: total knee arthroplasty  
 VAC: vacuum assisted closure

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

Study	Reason for exclusion
Albert 2012	No acute wounds were included
Banasiewicz 2013	Included infected wounds
Bondoki 2011	Prospective cohort study
Braakenburg 2006	Chronic and acute wounds were reported together and further information was not available
Eisenhardt 2012	None of our outcomes of interest were included
Grauhan 2013	Alternate allocation at time of surgery was used for group allocation
Hu 2009	Acute, sub-acute and chronic wounds were included. Acute wounds were defined as those that had been 'open' for less than 1 week
Johannesson 2008	The intervention dressing was not a continuous negative pressure device
Kim 2007	The study was not a randomised controlled trial
Moisidis 2004	None of our pre-defined outcomes were reported. No objective measure of graft failure used. Half of the wounds were chronic
Moues 2004	No acute wounds were included
Moues 2007	No acute wounds were included

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

### Mullins 2012

Methods	A health economic model
Participants	Patients enrolled in a randomised controlled trial of patients receiving negative pressure wound therapy over clean, closed surgical incisions ( <a href="#">Stannard 2012</a> )
Interventions	Hypothetical economic model applied national cost dollars to clinical outcomes of the <a href="#">Stannard 2012</a> trial
Outcomes	Potential per patient cost savings of \$5338 for infection and \$1586 for dehiscence
Notes	Conference paper. Waiting for publication with further details about methods

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

### Chan 2011

Trial name or title	A prospective randomised controlled trial of negative pressure suction dressing and early mobilisation in the management of lower leg skin grafts
Methods	Randomised controlled trial
Participants	Patients with lower leg wounds requiring split skin grafting for primary closure, e.g. post planned skin lesion removal or trauma
Interventions	Negative pressure dressing versus static pressure dressing
Outcomes	Primary: graft success at day 5 to 7 when dressing is removed. Secondary: graft success at 6-week follow-up
Starting date	Early 2011
Contact information	<a href="mailto:Mark.Wade@waitematadhb.govt.nz">Mark.Wade@waitematadhb.govt.nz</a> ; <a href="mailto:richard.martin@waitematadhb.govt.nz">richard.martin@waitematadhb.govt.nz</a>
Notes	

## DATA AND ANALYSES

### Comparison 1. Negative pressure wound therapy versus standard dressing

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Surgical site infection	3		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
1.1 Incisional wound	3	232	Risk Ratio (M-H, Fixed, 95% CI)	1.02 [0.41, 2.54]
2 Surgical site infection using wound, not individual, as denominator	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
3 Dehiscence	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
4 Dehiscence using wounds, not individual, as denominator	1		Odds Ratio (M-H, Fixed, 95% CI)	Totals not selected
5 Re-operation	3	212	Risk Ratio (M-H, Fixed, 95% CI)	0.60 [0.34, 1.05]
5.1 Incisional wounds	1	81	Risk Ratio (M-H, Fixed, 95% CI)	0.95 [0.41, 2.20]
5.2 Skin grafts	2	131	Risk Ratio (M-H, Fixed, 95% CI)	0.42 [0.19, 0.92]
6 Seroma/haematoma	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
6.1 Wounds	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
7 Graft failure at 2 weeks	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
8 Skin blisters	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected

### Comparison 2. Non-commercial NPWT versus commercial NPWT device

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Seroma/haematoma	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
1.1 Wounds	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]

### Comparison 3. Non-commercial NPWT versus standard care

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Re-operation	2	131	Risk Ratio (M-H, Fixed, 95% CI)	0.42 [0.19, 0.92]

#### Comparison 4. Funded versus non-funded or unknown funding

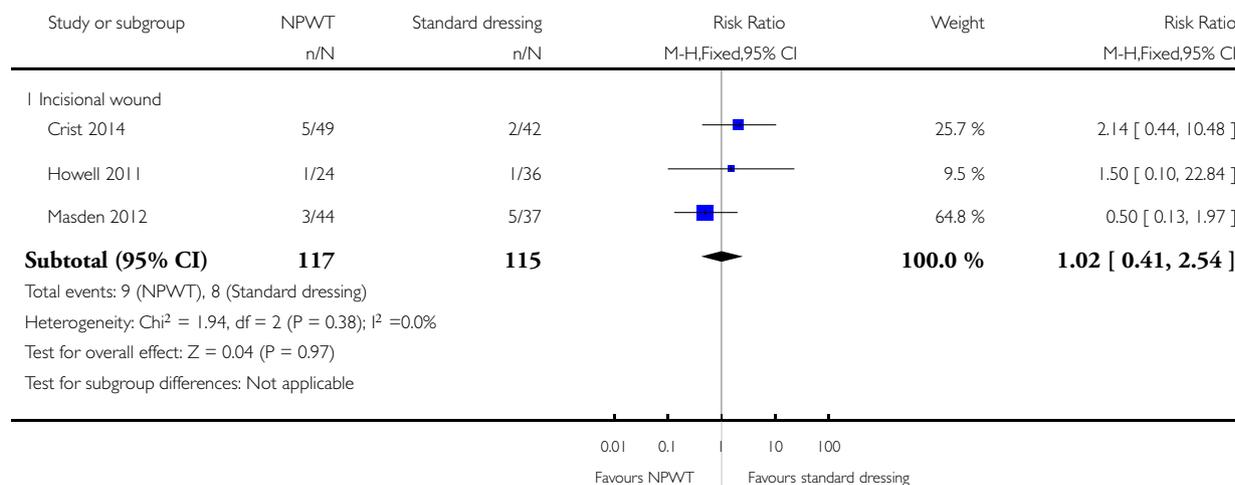
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Any outcome	9	785	Risk Ratio (M-H, Fixed, 95% CI)	0.68 [0.52, 0.87]
1.1 Manufacturer funded	4	426	Risk Ratio (M-H, Fixed, 95% CI)	0.73 [0.54, 0.97]
1.2 Not manufacturer funded	2	141	Risk Ratio (M-H, Fixed, 95% CI)	0.92 [0.47, 1.80]
1.3 Home made device	3	218	Risk Ratio (M-H, Fixed, 95% CI)	0.37 [0.17, 0.78]

#### Analysis 1.1. Comparison 1 Negative pressure wound therapy versus standard dressing, Outcome 1 Surgical site infection.

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

Comparison: 1 Negative pressure wound therapy versus standard dressing

Outcome: 1 Surgical site infection

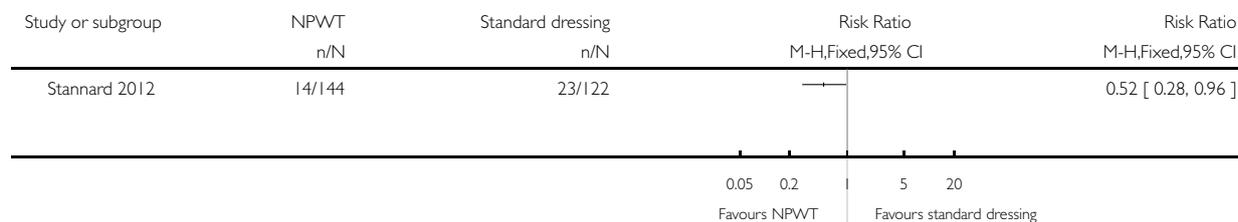


**Analysis 1.2. Comparison 1 Negative pressure wound therapy versus standard dressing, Outcome 2 Surgical site infection using wound, not individual, as denominator.**

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

Comparison: 1 Negative pressure wound therapy versus standard dressing

Outcome: 2 Surgical site infection using wound, not individual, as denominator

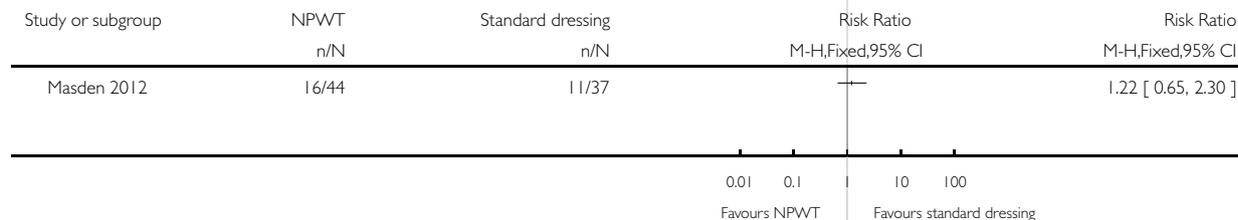


**Analysis 1.3. Comparison 1 Negative pressure wound therapy versus standard dressing, Outcome 3 Dehiscence.**

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

Comparison: 1 Negative pressure wound therapy versus standard dressing

Outcome: 3 Dehiscence

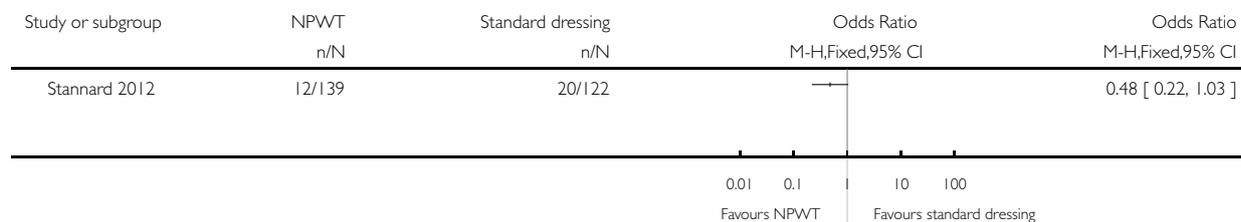


### Analysis 1.4. Comparison 1 Negative pressure wound therapy versus standard dressing, Outcome 4 Dehiscence using wounds, not individual, as denominator.

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

Comparison: 1 Negative pressure wound therapy versus standard dressing

Outcome: 4 Dehiscence using wounds, not individual, as denominator

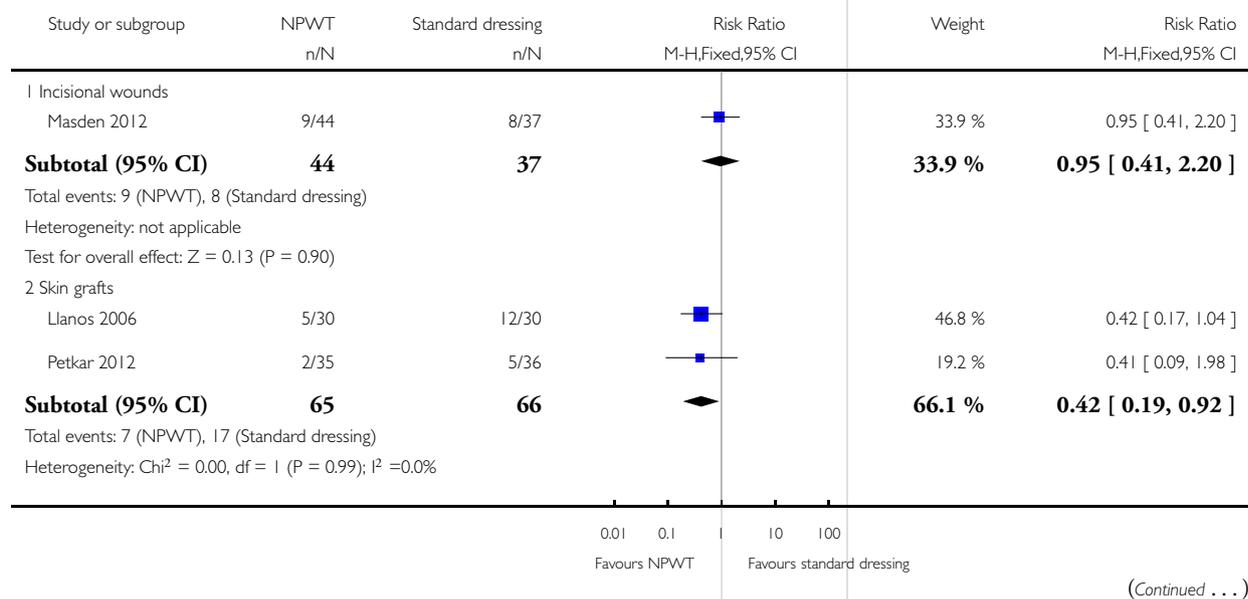


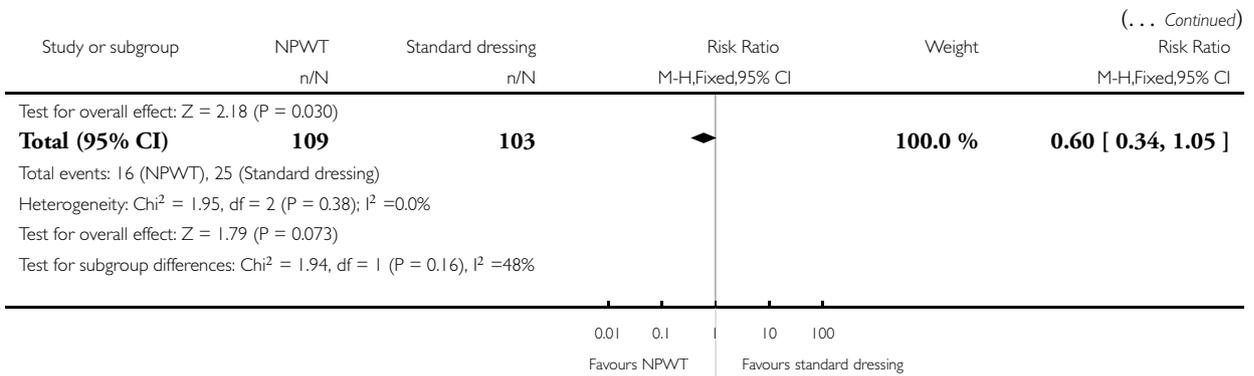
### Analysis 1.5. Comparison 1 Negative pressure wound therapy versus standard dressing, Outcome 5 Re-operation.

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

Comparison: 1 Negative pressure wound therapy versus standard dressing

Outcome: 5 Re-operation



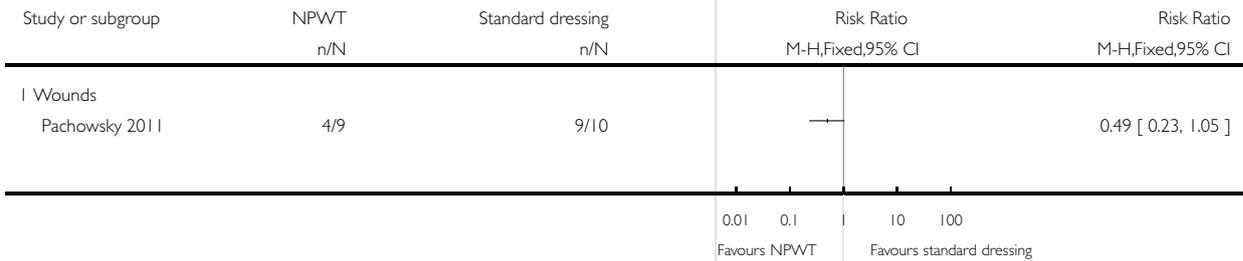


### Analysis 1.6. Comparison 1 Negative pressure wound therapy versus standard dressing, Outcome 6 Seroma/haematoma.

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

Comparison: 1 Negative pressure wound therapy versus standard dressing

Outcome: 6 Seroma/haematoma

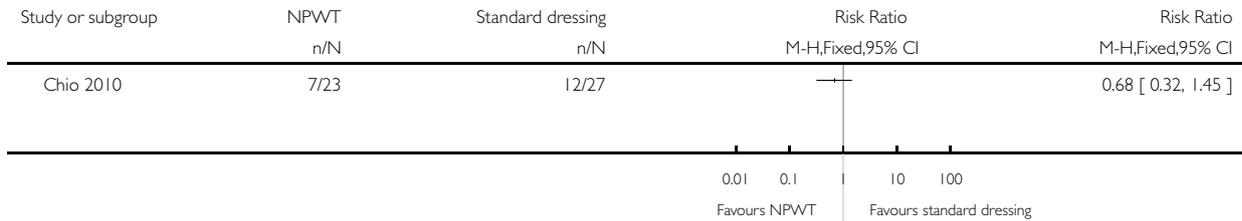


**Analysis 1.7. Comparison 1 Negative pressure wound therapy versus standard dressing, Outcome 7 Graft failure at 2 weeks.**

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

Comparison: 1 Negative pressure wound therapy versus standard dressing

Outcome: 7 Graft failure at 2 weeks

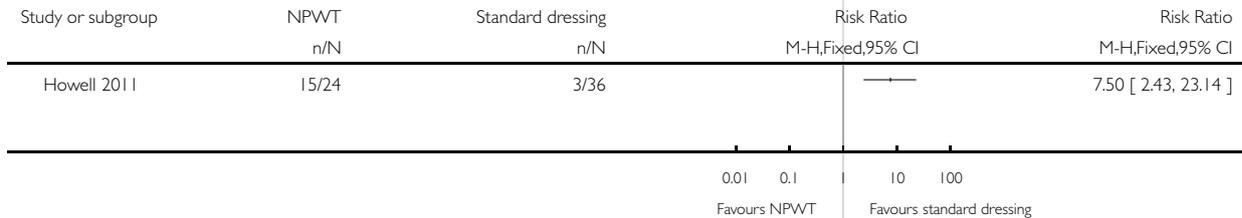


**Analysis 1.8. Comparison 1 Negative pressure wound therapy versus standard dressing, Outcome 8 Skin blisters.**

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

Comparison: 1 Negative pressure wound therapy versus standard dressing

Outcome: 8 Skin blisters

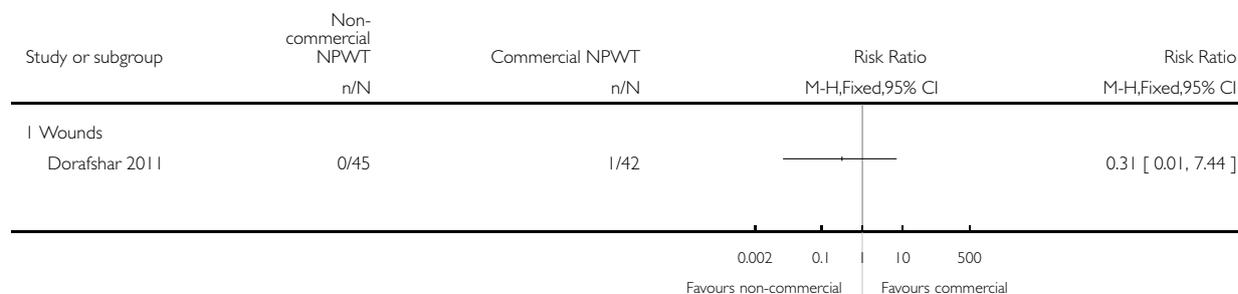


### Analysis 2.1. Comparison 2 Non-commercial NPWT versus commercial NPWT device, Outcome 1 Seroma/haematoma.

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

Comparison: 2 Non-commercial NPWT versus commercial NPWT device

Outcome: 1 Seroma/haematoma

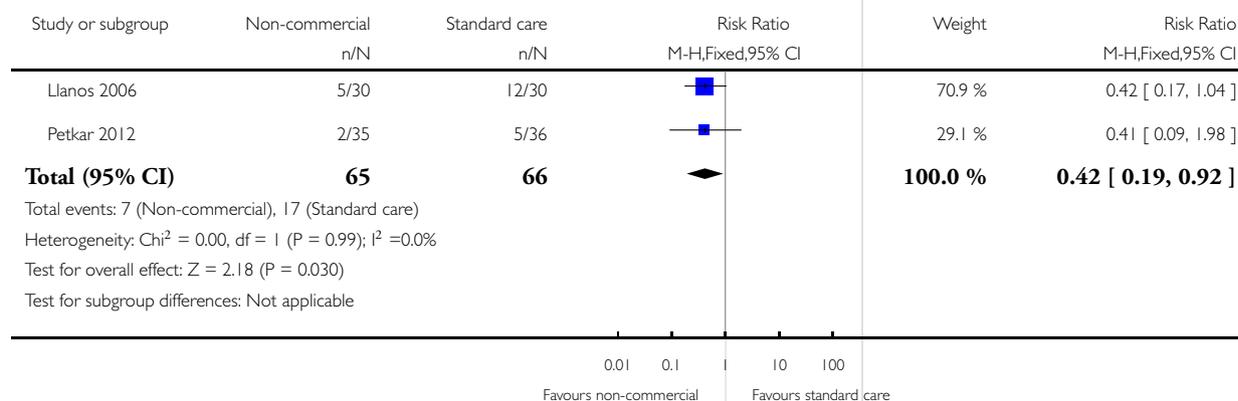


### Analysis 3.1. Comparison 3 Non-commercial NPWT versus standard care, Outcome 1 Re-operation.

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

Comparison: 3 Non-commercial NPWT versus standard care

Outcome: 1 Re-operation

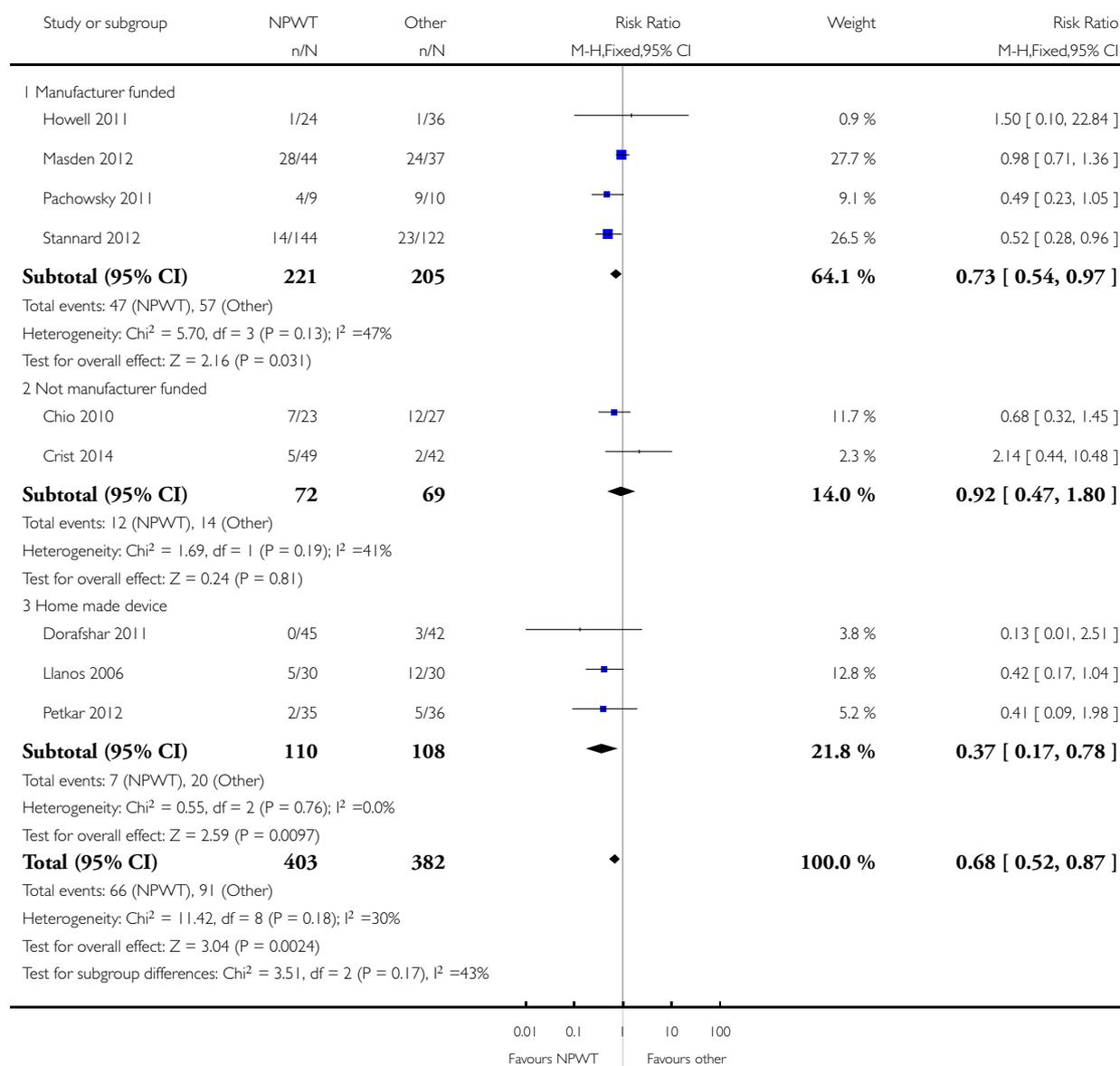


### Analysis 4.1. Comparison 4 Funded versus non-funded or unknown funding, Outcome 1 Any outcome.

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

Comparison: 4 Funded versus non-funded or unknown funding

Outcome: 1 Any outcome



## APPENDICES

### Appendix I. Search methods section from the original review

We searched the following electronic databases for the original version of this review

- the Cochrane Wounds Group Specialised Register (searched 11 November 2011);
- the Cochrane Central Register of Controlled Trials (CENTRAL) (*The Cochrane Library* 2011, Issue 4);
- Database of Abstracts of Reviews of Effects (*The Cochrane Library* 2011, Issue 4);
- Ovid MEDLINE (2005 to October Week 4 2011);
- Ovid MEDLINE (In-Process & Other Non-Indexed Citations 8 November 2011);
- Ovid EMBASE (2009 to 2011 Week 44);
- EBSCO CINAHL (1982 to 4 November 2011).

We used 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)

The search strategies for Ovid MEDLINE, Ovid EMBASE and EBSCO CINAHL can be found in [Appendix 2](#) ; [Appendix 3](#) and [Appendix 4](#) respectively. We combined the Ovid MEDLINE search with the Cochrane Highly Sensitive Search Strategy for identifying randomised trials in MEDLINE: sensitivity- and precision-maximising version (2008 revision) ([Lefebvre 2011](#)). We combined the EMBASE and CINAHL searches with the trial filters developed by the Scottish Intercollegiate Guidelines Network ([SIGN 2011](#)).

We conducted separate searches to identify economic evaluations in the following electronic databases:

- NHS Economic Evaluation Database (*The Cochrane Library* 2011, Issue 3);
- Ovid MEDLINE (1948 to July Week 3 2011);
- Ovid MEDLINE (In-Process & Other Non-Indexed Citations 28 July 2011);
- Ovid EMBASE (1980 to 2011 Week 29);
- EBSCO CINAHL (1982 to 20 July 2011)

We used economics filters developed by Centre for Reviews and Dissemination ([CRD 2010](#)) in combination with terms to describe the condition and intervention in Ovid MEDLINE, Ovid EMBASE and EBSCO CINAHL searches (see [Appendix 5](#); [Appendix 6](#) and [Appendix 7](#) respectively). We did not restrict any of the above searches with respect to language, date of publication or study setting.

We searched the following clinical trials registries for details of relevant protocols and contacted 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.

## Appendix 2. Ovid MEDLINE effectiveness search strategy

1 exp Negative-Pressure Wound Therapy/  
 2 exp Suction/  
 3 exp Vacuum/  
 4 (negative pressure or negative-pressure or TNP).tw.  
 5 (sub-atmospheric or subatmospheric).tw.  
 6 ((seal\* adj surface\*) or (seal\* adj aspirat\*)).tw.  
 7 (wound adj2 suction\*).tw.  
 8 (wound adj5 drainage).tw.  
 9 ((foam adj suction) or (suction adj dressing\*)).tw.  
 10 (vacuum assisted closure technique or VAC).tw.  
 11 ((vacuum adj therapy) or (vacuum adj dressing\*) or (vacuum adj seal\*) or (vacuum adj closure) or (vacuum adj compression) or (vacuum adj pack\*) or (vacuum adj drainage) or (suction\* adj drainage)).tw.  
 12 or/1-11  
 13 exp Surgical Wound Infection/  
 14 exp Surgical Wound Dehiscence/  
 15 (surg\* adj5 infect\*).tw.  
 16 (surg\* adj5 wound\*).tw.  
 17 (surg\* adj5 site\*).tw.  
 18 (surg\* adj5 incision\*).tw.  
 19 (surg\* adj5 dehisc\*).tw.  
 20 (wound\* adj5 dehisc\*).tw.  
 21 (wound\* adj5 dehisc\*).tw.  
 22 or/13-21  
 23 12 and 22  
 24 randomized controlled trial.pt.  
 25 controlled clinical trial.pt.  
 26 randomized.ab.  
 27 placebo.ab.  
 28 clinical trials as topic.sh.  
 29 randomly.ab.  
 30 trial.ti.  
 31 or/24-30  
 32 (animals not (humans and animals)).sh.  
 33 31 not 32  
 34 23 and 33  
 35 (2005\* or 2006\* or 2007\* or 2008\* or 2009\* or 2010\*).ed.  
 36 34 and 35

### Appendix 3. Ovid EMBASE effectiveness search strategy

- 1 exp suction drainage/
- 2 exp vacuum assisted closure/
- 3 (negative pressure or negative-pressure or TNP).tw.
- 4 (sub-atmospheric or subatmospheric).tw.
- 5 ((seal\* adj surface\*) or (seal\* adj aspirat\*)).tw.
- 6 (wound adj2 suction\*).tw.
- 7 (wound adj5 drainage).tw.
- 8 ((foam adj suction) or (suction adj dressing\*)).tw.
- 9 (vacuum assisted closure technique or VAC).tw.
- 10 ((vacuum adj therapy) or (vacuum adj dressing\*) or (vacuum adj seal\*) or (vacuum adj closure) or (vacuum adj compression) or (vacuum adj pack\*) or (vacuum adj drainage) or (suction\* adj drainage)).tw.
- 11 or/1-10
- 12 exp Surgical Wound Infection/
- 13 exp Surgical Wound Dehiscence/
- 14 (surg\* adj5 infection\*).tw.
- 15 (surg\* adj5 wound\*).tw.
- 16 (surg\* adj5 site\*).tw.
- 17 (surg\* adj5 incision\*).tw.
- 18 (surg\* adj5 dehisc\*).tw.
- 19 (wound\* adj5 dehisc\*).tw.
- 20 or/12-19
- 21 11 and 20
- 22 Clinical trial/
- 23 Randomized controlled trials/
- 24 Random Allocation/
- 25 Single-Blind Method/
- 26 Double-Blind Method/
- 27 Cross-Over Studies/
- 28 Placebos/
- 29 Randomized controlled trial\$.tw.
- 30 RCT.tw.
- 31 Random allocation.tw.
- 32 Randomly allocated.tw.
- 33 Allocated randomly.tw.
- 34 (allocated adj2 random).tw.
- 35 Single blind\$.tw.
- 36 Double blind\$.tw.
- 37 ((treble or triple) adj blind\$).tw.
- 38 Placebo\$.tw.
- 39 Prospective Studies/
- 40 or/22-39
- 41 Case study/
- 42 Case report.tw.
- 43 Abstract report/ or letter/
- 44 or/41-43
- 45 40 not 44
- 46 animal/
- 47 human/
- 48 46 not 47
- 49 45 not 48
- 50 21 and 49

51 (2009\* or 2010\* or 2011\*).em.

52 50 and 51

#### **Appendix 4. EBSCO CINAHL effectiveness search strategy**

S22 S12 and S21

S21 S13 or S14 or S15 or S16 or S17 or S18 or S19 or S20

S20 TI wound\* N5 dehis\* or AB wound\* N5 dehis\*

S19 TI surg\* N5 dehis\* or AB surg\* N5 dehis\*

S18 TI surg\* N5 incision\* or AB surg\* N5 incision\*

S17 TI surg\* N5 site\* or AB surg\* N5 site\*

S16 TI surg\* N5 wound\* or AB surg\* N5 wound\*

S15 TI surg\* N5 infection\* or AB surg\* N5 infection\*

S14 (MH "Surgical Wound Dehiscence")

S13 (MH "Surgical Wound Infection")

S12 S1 or S2 or S3 or S4 or S5 or S6 or S7 or S8 or S9 or S10 or S11

S11 TI ( foam suction or suction dressing\* or suction drainage ) or AB ( foam suction or suction dressing\* or suction drainage )

S10 AB vacuum therapy or vacuum dressing\* or vacuum seal\* or vacuum closure or vacuum compression or vacuum pack or vacuum drainage

S9 TI vacuum therapy or vacuum dressing\* or vacuum seal\* or vacuum closure or vacuum compression or vacuum pack or vacuum drainage

S8 TI wound N5 drainage or AB wound N5 drainage

S7 TI wound N5 suction\* or AB wound N5 suction\*

S6 TI ( seal\* N1 surface\* or seal\* N1 aspirat\* ) or AB ( seal\* N1 surface\* or seal\* N1 aspirat\* )

S5 TI ( sub-atmospheric or subatmospheric ) or AB ( sub-atmospheric or subatmospheric )

S4 TI ( negative pressure or negative-pressure or TNP ) or AB ( negative pressure or negative-pressure or TNP )

S3 (MH "Negative Pressure Wound Therapy")

S2 (MH "Vacuum")

S1 (MH "Suction+")

#### **Appendix 5. Ovid MEDLINE economics search strategy**

1 exp Negative-Pressure Wound Therapy/

2 exp Suction/

3 exp Vacuum/

4 (negative pressure or negative-pressure or TNP).tw.

5 (sub-atmospheric or subatmospheric).tw.

6 ((seal\* adj surface\*) or (seal\* adj aspirat\*)).tw.

7 (wound adj2 suction\*).tw.

8 (wound adj5 drainage).tw.

9 ((foam adj suction) or (suction adj dressing\*)).tw.

10 (vacuum assisted closure technique or VAC).tw.

11 ((vacuum adj therapy) or (vacuum adj dressing\*) or (vacuum adj seal\*) or (vacuum adj closure) or (vacuum adj compression) or (vacuum adj pack\*) or (vacuum adj drainage) or (suction\* adj drainage)).tw.

12 or/1-11

13 exp Surgical Wound Infection/

14 exp Surgical Wound Dehiscence/

15 (surg\* adj5 infect\*).tw.

16 (surg\* adj5 wound\*).tw.

17 (surg\* adj5 site\*).tw.

18 (surg\* adj5 incision\*).tw.

19 (surg\* adj5 dehis\*).tw.

20 (wound\* adj5 dehisc\*).tw.  
 21 (wound\* adj5 dehisc\*).tw.  
 22 or/13-21  
 23 12 and 22  
 24 economics/  
 25 exp "costs and cost analysis"/  
 26 economics, dental/  
 27 exp "economics, hospital"/  
 28 economics, medical/  
 29 economics, nursing/  
 30 economics, pharmaceutical/  
 31 (economic\* or cost or costs or costly or costing or price or prices or pricing or pharmaco-economic\*).ti,ab.  
 32 (expenditure\* not energy).ti,ab.  
 33 value for money.ti,ab.  
 34 budget\*.ti,ab.  
 35 or/24-34  
 36 ((energy or oxygen) adj cost).ti,ab.  
 37 (metabolic adj cost).ti,ab.  
 38 ((energy or oxygen) adj expenditure).ti,ab.  
 39 or/36-38  
 40 35 not 39  
 41 letter.pt.  
 42 editorial.pt.  
 43 historical article.pt.  
 44 or/41-43  
 45 40 not 44  
 46 Animals/  
 47 Humans/  
 48 46 not (46 and 47)  
 49 45 not 48  
 50 23 and 49

## Appendix 6. Ovid EMBASE economics search strategy

1 exp suction drainage/  
 2 exp vacuum assisted closure/  
 3 (negative pressure or negative-pressure or TNP).tw.  
 4 (sub-atmospheric or subatmospheric).tw.  
 5 ((seal\* adj surface\*) or (seal\* adj aspirat\*)).tw.  
 6 (wound adj2 suction\*).tw.  
 7 (wound adj5 drainage).tw.  
 8 ((foam adj suction) or (suction adj dressing\*)).tw.  
 9 (vacuum assisted closure technique or VAC).tw.  
 10 ((vacuum adj therapy) or (vacuum adj dressing\*) or (vacuum adj seal\*) or (vacuum adj closure) or (vacuum adj compression) or (vacuum adj pack\*) or (vacuum adj drainage) or (suction\* adj drainage)).tw.  
 11 or/1-10  
 12 exp Surgical Wound Infection/  
 13 exp Surgical Wound Dehiscence/  
 14 (surg\* adj5 infection\*).tw.  
 15 (surg\* adj5 wound\*).tw.  
 16 (surg\* adj5 site\*).tw.  
 17 (surg\* adj5 incision\*).tw.

18 (surg\* adj5 dehis\*).tw.  
 19 (wound\* adj5 dehis\*).tw.  
 20 or/12-19  
 21 11 and 20  
 22 health-economics/  
 23 exp economic-evaluation/  
 24 exp health-care-cost/  
 25 exp pharmacoeconomics/  
 26 or/22-25  
 27 (econom\* or cost or costs or costly or costing or price or prices or pricing or pharmacoeconomic\*).ti,ab.  
 28 (expenditure\* not energy).ti,ab.  
 29 (value adj2 money).ti,ab.  
 30 budget\*.ti,ab.  
 31 or/27-30  
 32 26 or 31  
 33 letter.pt.  
 34 editorial.pt.  
 35 note.pt.  
 36 or/33-35  
 37 32 not 36  
 38 (metabolic adj cost).ti,ab.  
 39 ((energy or oxygen) adj cost).ti,ab.  
 40 ((energy or oxygen) adj expenditure).ti,ab.  
 41 or/38-40  
 42 37 not 41  
 43 exp animal/  
 44 exp animal-experiment/  
 45 nonhuman/  
 46 (rat or rats or mouse or mice or hamster or hamsters or animal or animals or dog or dogs or cat or cats or bovine or sheep).ti,ab,sh.  
 47 or/43-46  
 48 exp human/  
 49 exp human-experiment/  
 50 or/48-49  
 51 47 not (47 and 50)  
 52 42 not 51  
 53 21 and 52

## Appendix 7. EBSCO CINAHL economics search strategy

S45 S22 and S44  
 S44 S40 NOT S43  
 S43 S19 NOT (S19 AND S42)  
 S42 MH "Human"  
 S41 MH "Animal Studies"  
 S40 S35 NOT S39  
 S39 S36 or S37 or S38  
 S38 PT commentary  
 S37 PT letter  
 S36 PT editorial  
 S35 S33 OR S34  
 S34 TI (cost or costs or economic\* or pharmacoeconomic\* or price\* or pricing\*) OR AB (cost or costs or economic\* or pharmacoeconomic\* or price\* or pricing\*)

S33 S29 OR S32  
 S32 S30 OR S31  
 S31 MH “Health Resource Utilization”  
 S30 MH “Health Resource Allocation”  
 S29 S23 NOT S28  
 S28 S24 or S25 or S26 or S27  
 S27 MH “Business+”  
 S26 MH “Financing, Organized+”  
 S25 MH “Financial Support+”  
 S24 MH “Financial Management+”  
 S23 MH “Economics+”  
 S22 S12 and S21  
 S21 S13 or S14 or S15 or S16 or S17 or S18 or S19 or S20  
 S20 TI wound\* N5 dehis\* or AB wound\* N5 dehis\*  
 S19 TI surg\* N5 dehis\* or AB surg\* N5 dehis\*  
 S18 TI surg\* N5 incision\* or AB surg\* N5 incision\*  
 S17 TI surg\* N5 site\* or AB surg\* N5 site\*  
 S16 TI surg\* N5 wound\* or AB surg\* N5 wound\*  
 S15 TI surg\* N5 infection\* or AB surg\* N5 infection\*  
 S14 (MH “Surgical Wound Dehiscence”)  
 S13 (MH “Surgical Wound Infection”)  
 S12 S1 or S2 or S3 or S4 or S5 or S6 or S7 or S8 or S9 or S10 or S11  
 S11 TI foam suction or suction dressing\* or suction drainage or AB foam suction or suction dressing\* or suction drainage  
 S10 AB vacuum therapy or vacuum dressing\* or vacuum seal\* or vacuum closure or vacuum compression or vacuum pack or vacuum drainage  
 S9 TI vacuum therapy or vacuum dressing\* or vacuum seal\* or vacuum closure or vacuum compression or vacuum pack or vacuum drainage  
 S8 TI wound N5 drainage or AB wound N5 drainage  
 S7 TI wound N5 suction\* or AB wound N5 suction\*  
 S6 TI seal\* N1 surface\* or seal\* N1 aspirat\* or AB seal\* N1 surface\* or seal\* N1 aspirat\*  
 S5 TI sub-atmospheric or subatmospheric or AB sub-atmospheric or subatmospheric  
 S4 TI negative pressure or negative-pressure or TNP or AB negative pressure or negative-pressure or TNP  
 S3 (MH “Negative Pressure Wound Therapy”)  
 S2 (MH “Vacuum”)  
 S1 (MH “Suction+”)

## Appendix 8. Risk of bias criteria

### I. 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 provided 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 nonopaque 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 was 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 was likely to introduce bias.

### **Unclear**

Either of the following.

- Insufficient information provided 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 is 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 was 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 is enough to induce clinically relevant bias in intervention effect estimate.
  - For continuous outcome data, plausible effect size (difference in means or standardised difference in means) among missing outcomes is 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 randomised not stated, no reasons for missing data provided).
- The study did not address this outcome.

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

##### Low risk of bias

Either of the following.

- The study protocol is available and all of the study's 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 provided 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.

## Appendix 9. Glossary of terms

Term	Description
Dehiscence	Wound dehiscence is a complication of surgery in which a wound breaks open along the line of the surgical incision
GSUC	GSUC is a system of negative pressure wound therapy. It is based on a gauze dressing moistened with 0.9% normal saline into which a red rubber catheter is inserted. The dressing is then sealed with an occlusive cover and continuous wall suction at -75 mmHg to -80 mmHg applied
Negative pressure wound therapy (NPWT)	NPWT 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 mmHg and -125

(Continued)

	mm Hg ( <a href="#">Ubbink 2008</a> ; <a href="#">Vikatmaa 2008</a> )
Risk ratio (RR)	The risk ratio or relative risk (RR) is the probability that a member of a group who is exposed to an intervention will develop an event relative to the probability that a member of an unexposed group will develop that same event

## WHAT'S NEW

Last assessed as up-to-date: 28 January 2014.

Date	Event	Description
27 August 2014	New search has been performed	First update, new search.
27 August 2014	New citation required but conclusions have not changed	Four trials added ( <a href="#">Crist 2014</a> ; <a href="#">Masden 2012</a> ; <a href="#">Petkar 2012</a> ; <a href="#">Stannard 2012</a> ), no change to conclusions

## HISTORY

Protocol first published: Issue 8, 2011

Review first published: Issue 4, 2012

Date	Event	Description
13 November 2013	Amended	Acknowledgement added to the funders
16 May 2012	Amended	adjustments to text

## CONTRIBUTIONS OF AUTHORS

**Joan Webster:** conceived the review question. Designed and coordinated the review. Extracted data, undertook quality assessment, and analysed and interpreted data. Performed statistical analysis. Wrote and edited the review. Approved the final review prior to submission. Wrote to study authors, experts or companies, and performed previous work that was the foundation of the current review. Updated the review.

**Monica Stankiewicz:** extracted data and checked the quality of data extraction. Checked quality assessment and performed part of data analysis and interpretation. Checked the quality of statistical analysis. Advised on the review and performed part of writing and editing the review. Approved the final review prior to submission. Wrote to study authors, experts or companies, and performed previous work that was the foundation of the current review. Approved the updated review.

**Wendy Chaboyer:** Advised on the review and performed part of writing and editing the review. Approved the final review prior to submission. Performed previous work that was the foundation of the current review. Approved the updated review.

**Paul Scuffham:** advised on part of the review, performed part of writing and editing the review, and approved the final review prior to submission. Performed previous work that was the foundation of the current review. Performed economic analysis. Approved the updated review.

#### **Contributions of editorial base:**

Jo Dumville, Editor: approved the review update prior to submission.

Nicky Cullum: edited the protocol; advised on methodology, interpretation and protocol content. Approved the final review prior to submission.

Sally Bell-Syer: co-ordinated the editorial process. Advised on methodology, interpretation and content. Edited the review and the updated review.

Ruth Foxlee: designed the search strategy and edited the search methods section.

## **DECLARATIONS OF INTEREST**

Prof Scuffham is the director of a unit contracted to the Australian Department of Health and Ageing to undertake external evaluations of industry submissions to the PBAC.

Joan Webster: nothing to declare

Monica Stankiewicz: nothing to declare

Wendy Chaboyer: nothing to declare

## **SOURCES OF SUPPORT**

### **Internal sources**

- Royal Brisbane and Women's Hospital, Australia.

Time to conduct review

- Griffith University, Australia.

Time to conduct review

### **External sources**

- The National Institute for Health research (NIHR) is the sole funder of the Cochrane Wounds Group, UK.

## **DIFFERENCES BETWEEN PROTOCOL AND REVIEW**

We added one intervention: comparisons between different negative pressure devices.

The list of abstracted data was expanded to include:

- study dates;
- number of participants per group;
- information about ethics approval, consent and conflict of interest.

In trials of skin grafts, graft failure is an important outcome. We failed to include this as either a primary or secondary outcome in the original review but believe, for this and for future updates that failure of skin grafts should be included. We also failed to include length of hospital stay, which is important for any economic analysis. Consequently, graft failure and length of hospital stay have been included as additional outcomes post hoc.

- In this update, we removed one primary outcome “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)”. The decision was based on our experience conducting the first version of this review where we noted that “. . . it has become clear to us that this outcome is not appropriate for surgery that is expected to heal by primary intention; most clean surgical wounds will completely heal in a relatively short time. Moreover, determining when a surgical incision is ‘completely healed’ is difficult. Consequently, wound healing should not be included as a primary outcome for future updates”.

- In the first version of the review, any wound complications were considered under the heading ‘Adverse events’. As many of these ‘events’ are qualitatively different and of varying levels of importance, we have now included only ‘Surgical site infection’ and ‘Dehiscence’ under the heading ‘Adverse events’. Other wound-related outcomes that were previously included under the ‘Adverse events’ primary outcome (such as fracture blisters, seromas etc) have been moved to ‘Secondary outcomes’. We have also added two new secondary outcomes; re-operation and graft loss. The first was added as important outcome that indicates the severity of any wound dehiscence or graft loss. Graft loss has been added because it is an important outcome for skin graft studies and previously we did not include any outcomes that were specific to skin grafts.

- We have changed wording in the section ‘Unit of analysis issues’ (we had not anticipated that multiple wounds might be an issue in the original version of the review) and ‘Dealing with missing data’ (to clarify what we intend to do).

## **INDEX TERMS**

### **Medical Subject Headings (MeSH)**

\*Skin Transplantation; \*Wound Healing; Bandages; Negative-Pressure Wound Therapy [instrumentation; \*methods]; Randomized Controlled Trials as Topic; Surgical Procedures, Operative

### **MeSH check words**

Humans