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Negative pressure wound therapy for surgical wounds healing by primary closure (Review)

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[Intervention Review]

Negative pressure wound therapy for surgical wounds healing by primary closure

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ABSTRACT

Background

Indications for the use of negative pressure wound therapy (NPWT) are broad and include prophylaxis for surgical site infections (SSIs). Existing evidence for the effectiveness of NPWT on postoperative wounds healing by primary closure remains uncertain.

Objectives

To assess the effects of NPWT for preventing SSI in wounds healing through primary closure, and to assess the cost-effectiveness of NPWT in wounds healing through primary closure.

Search methods

In June 2019, we searched the Cochrane Wounds Specialised Register; the Cochrane Central Register of Controlled Trials (CENTRAL); Ovid MEDLINE (including In-Process & Other Non-Indexed Citations); Ovid Embase and EBSCO CINAHL Plus. We also searched clinical trials registries and references of included studies, systematic reviews and health technology reports. There were no restrictions on language, publication date or study setting.

Selection criteria

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

Data collection and analysis

At least two review authors independently assessed trials using predetermined inclusion criteria. We carried out data extraction, assessment using the Cochrane 'Risk of bias' tool, and quality assessment according to Grading of Recommendations, Assessment, Development and Evaluations methodology.

Main results

In this third update, we added 15 new randomised controlled trials (RCTs) and three new economic studies, resulting in a total of 44 RCTs (7447 included participants) and five economic studies. Studies evaluated NPWT in the context of a wide range of surgeries including orthopaedic, obstetric, vascular and general procedures. Economic studies assessed NPWT in orthopaedic, obstetric and general surgical settings. All studies compared NPWT with standard dressings. Most studies had unclear or high risk of bias for at least one key domain.

Primary outcomes

Four studies (2107 participants) reported mortality. There is low-certainty evidence (downgraded twice for imprecision) showing no clear difference in the risk of death after surgery for people treated with NPWT (2.3%) compared with standard dressings (2.7%) (risk ratio (RR) 0.86; 95% confidence interval (CI) 0.50 to 1.47; I^2 = 0%). Thirty-nine studies reported SSI; 31 of these (6204 participants), were included in meta-analysis. There is moderate-certainty evidence (downgraded once for risk of bias) that NPWT probably results in fewer SSI (8.8% of participants) than treatment with standard dressings (13.0% of participants) after surgery; RR 0.66 (95% CI 0.55 to 0.80 ; I^2 = 23%). Eighteen studies reported dehiscence; 14 of these (3809 participants) were included in meta-analysis. There is low-certainty evidence (downgraded once for risk of bias and once for imprecision) showing no clear difference in the risk of dehiscence after surgery for NPWT (5.3% of participants) compared with standard dressings (6.2% of participants) (RR 0.88, 95% CI 0.69 to 1.13; I^2 = 0%).

Secondary outcomes

There is low-certainty evidence showing no clear difference between NPWT and standard treatment for the outcomes of reoperation and incidence of seroma. For reoperation, the RR was 1.04 (95% CI 0.78 to 1.41; I^2 = 13%; 12 trials; 3523 participants); for seroma, the RR was 0.72 (95% CI 0.50 to 1.05; I^2 = 0%; seven trials; 729 participants). The effect of NPWT on occurrence of haematoma or skin blisters is uncertain (very low-certainty evidence); for haematoma, the RR was 0.67 (95% CI 0.28 to 1.59; I^2 = 0%; nine trials; 1202 participants) and for blisters the RR was 2.64 (95% CI 0.65 to 10.68; I^2 = 69%; seven trials; 796 participants). The overall effect of NPWT on pain is uncertain (very low-certainty evidence from seven trials (2218 participants) which reported disparate measures of pain); but moderate-certainty evidence suggests there is probably little difference between the groups in pain after three or six months following surgery for lower limb fracture (one trial, 1549 participants). There is also moderate-certainty evidence for women undergoing caesarean sections (one trial, 876 participants) and people having surgery for lower limb fractures (one trial, 1549 participants) that there is probably little difference in quality of life scores at 30 days or 3 or 6 months, respectively.

Cost-effectiveness

Five economic studies, based wholly or partially on trials included in our review, assessed the cost-effectiveness of NPWT compared with standard care. They considered NPWT in four indications: caesarean sections in obese women; surgery for lower limb fracture; knee/hip arthroplasty and coronary artery bypass graft surgery. They calculated quality-adjusted life-years for treatment groups and produced estimates of the treatments' relative cost-effectiveness. The reporting quality was good but the grade of the evidence varied from moderate to very low. There is moderate-certainty evidence that NPWT in surgery for lower limb fracture was not cost-effective at any threshold of willingness-to-pay and that NPWT is probably cost-effective in obese women undergoing caesarean section. Other studies found low or very low-certainty evidence indicating that NPWT may be cost-effective for the indications assessed.

Authors' conclusions

People experiencing primary wound closure of their surgical wound and treated prophylactically with NPWT following surgery probably experience fewer SSI than people treated with standard dressings (moderate-certainty evidence). There is no clear difference in number of deaths or wound dehiscence between people treated with NPWT and standard dressings (low-certainty evidence). There are also no clear differences in secondary outcomes where all evidence was low or very low-certainty. In caesarean section in obese women and surgery for lower limb fracture, there is probably little difference in quality of life scores (moderate-certainty evidence). Most evidence on pain is very low-certainty, but there is probably no difference in pain between NPWT and standard dressings after surgery for lower limb fracture (moderate-certainty evidence). Assessments of cost-effectiveness of NPWT produced differing results in different indications. There is a large number of ongoing studies, the results of which may change the findings of this review. Decisions about use of NPWT should take into account surgical indication and setting and consider evidence for all outcomes.

PLAIN LANGUAGE SUMMARY

Negative pressure wound therapy for surgical wounds healing by primary closure

What is the aim of this review?

The aim of this Cochrane Review was to find out if negative pressure wound therapy (NPWT) has an effect on complications including infections in surgical wounds which are healing by primary closure (where the edges have been brought together, usually by using stitches or staples) and to assess its cost-effectiveness. We collected and analysed all relevant studies to answer this question and found 44 studies analysing NPWT and surgical site complications, and five studies analysing cost-effectiveness. This is a new update of a Cochrane review which was last updated in March 2019.

Key messages

NPWT probably reduces the incidence of surgical site infection (SSI) in surgical wounds healing by primary closure – this is moderate-certainty evidence and new studies could change this finding. It is not clear what effect NPWT has on reopening of the wound ("dehiscence") and risk of death - this is low-certainty evidence. Results for other complications also show no clear difference with NPWT treatment. NPWT is probably cost-effective for caesarean section wounds in obese women and probably not cost-effective for fracture surgery wounds. Evidence for the cost-effectiveness of NPWT in other surgical wounds is less certain.

What was studied in the review?

A potential complication of surgery is the development of SSI which can occur at the site of a surgical incision. The incidence of SSI can be as high as 40%, with an increased infection risk linked with age, diet, weight, diabetes, heart disease and cancer. An SSI can cause pain and discomfort, as well as increasing a person's length of hospital stay and cost of treatment. Dehiscing (separation of wound edges) may occur if a wound fails to heal. Wound infection and weight can increase the risk of dehiscence.

NPWT is a sealed wound dressing attached to a vacuum pump which sucks fluid away from the wound. This may assist with wound healing and reduce risk of infection.

There has been a large number of new studies over the last decade as NPWT is increasingly being assessed for different surgical wound types. We assessed the effect of NPWT on risk of death, SSI and dehiscence.

What are the main results of the review?

We found 44 studies analysing NPWT and surgical site complications and five studies analysing cost-effectiveness of NPWT. A total of 7447 participants have been included in the review. A wide variety of surgeries are included such as knee and hip operations, caesarean sections, operations for broken bones and abdominal surgeries. Most participants were enrolled in North America, Europe or Australasia.

NPWT was compared with a standard dressing (e.g. gauze) in all 44 studies. A variety of NPWT systems was used. Only four studies reported risk of death; little difference was shown between NPWT and standard dressing and the evidence is low certainty. We pooled the SSI results of 31 studies; NPWT probably reduces the risk of SSI compared with standard dressings (moderate-certainty evidence). Fourteen studies which reported on dehiscence were combined; the low-certainty evidence suggests no clear difference between NPWT and standard care.

In the cost-effectiveness analysis, two studies looked at women with caesarean sections, one looked at people with lower limb fractures, one at knee and hip surgeries, and one at heart surgery. All these studies used clinical information from studies included in this review. There is moderate-certainty evidence that NPWT is probably cost-effective for caesarean section wounds in obese women and probably not cost-effective for fracture surgery wounds. Evidence for the cost-effectiveness of NPWT in other surgical wounds is low or very low-certainty.

How up to date is this review?

We searched for studies that had been published up to June 2019.

SUMMARY OF FINDINGS

Summary of findings 1. Negative pressure wound therapy compared with standard dressing for surgical wounds healing by primary closure

Negative pressure wound therapy compared with standard dressing for surgical wounds healing by primary closure

Patient or population: adult patients with surgical wounds healing by primary closure
Setting: general surgical, orthopaedic or obstetric wards in acute care hospitals
Intervention: negative pressure wound therapy (NPWT)
Comparison: standard dressing

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with standard dressing	Risk with NPWT				
Mortality (proportion of participants dying in each group at follow-up of between 30 days and six months)	Study population		RR 0.86 (0.50 to 1.47)	2107 (4 studies)	⊕⊕⊝⊝ Low[1]	There is no clear difference in mortality between people treated with NPWT and standard dressings after surgery. Only 4 of 44 trials reported this and incidence was low; resulting in wide confidence intervals.
	23 per 1000	5 fewer deaths per 1000 people (13 fewer to 9 more)				
Surgical site infection (proportion of participants in each group with SSI; follow-up of 30 days except where other time points specified as primary outcome measure in study)	Study population		RR 0.66 (0.55 to 0.80)	6204 (31 studies)	⊕⊕⊕⊝ Moderate[2]	NPWT probably decreases the incidence of surgical site infection compared with a standard dressing. Risk of bias in various domains affecting half the participants reduces the certainty of the evidence to moderate.
	130 per 1000	43 fewer SSI per 1000 people (58 fewer to 26 fewer)				
Dehiscence (proportion of participants in each group with wound dehiscence; follow-up of 30 days except where other time points specified as primary outcome measure in study)	Study population		RR 0.88 (0.69 to 1.13)	3809 (14 studies)	⊕⊕⊝⊝ Low[3]	There is no clear difference in dehiscence between people treated with NPWT and standard dressings.
	62 per 1000	9 fewer dehiscence per 1000 people (19 fewer to 8 more)				
	Study population		RR 1.04 (0.78 to 1.41)	3523 (12 studies)		

Reoperation (proportion of participants in each group requiring reoperation for reasons related to wound; follow-up of 30 days except where other time points specified as primary outcome measure in study)	72 per 1000	3 more reoperations per 1000 people (16 fewer to 29 more)			⊕⊕⊖⊖ Low[3]	There is no clear difference in reoperation between people treated with NPWT and standard dressings.
Seroma (proportion of participants in each group with seroma; follow-up of 30 days except where other time points specified as primary outcome measure in study)	Study population		RR 0.72 (0.50 to 1.05)	1591 (7 studies)	⊕⊕⊖⊖ Low[4]	There is no clear difference in the incidence of seroma between people treated with NPWT and standard dressings.
	104 per 1000	29 fewer seroma per 1000 people (52 fewer to 5 more)				
Haematoma (proportion of participants in each group with haematoma; follow-up of 30 days except where other time points specified as primary outcome measure in study)	Study population		RR 0.67 (0.28 to 1.59)	1202 (9 studies)	⊕⊖⊖⊖ Very low[5]	It is uncertain if the incidence of haematoma is increased or decreased when NPWT is compared with a standard dressing.
	23 per 1000	7 fewer haematoma (16 fewer to 14 more)				
Skin blisters (proportion of participants in each group with at least one skin blister; follow-up of 30 days except where other time points specified as primary outcome measure in study)	Study population		RR 2.64 (0.65 to 10.68)	796 (7 studies)	⊕⊖⊖⊖ Very low[6]	It is uncertain if there is a higher risk of developing skin blisters when NPWT is compared with a standard dressing.
	48 per 1000	78 more blistering cases per 1000 people (17 fewer to 461 more)				

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the __relative effect__ of the intervention (and its 95% CI).

CI: confidence interval; **NPWT:** negative pressure wound therapy; **RR:** risk ratio

GRADE Working Group grades of evidence
High certainty: We are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: We are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: Our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.

Very low certainty: We have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

[1]Downgraded twice for very serious imprecision resulting from very low event rates which produced wide confidence intervals.
[2]Downgraded once for high risk of bias in various domains, affecting approximately 50% of participants.
[3]Downgraded once for high risk of bias in various domains and once for imprecision.
[4]Downgraded twice for very serious imprecision.
[5]Downgraded once for high risk of bias in various domains and twice for very serious imprecision.
[6]Downgraded once for high risk of bias in various domains, once for imprecision and once for inconsistency.

BACKGROUND

Description of the condition

An estimated 4511 operations per 100,000 population are carried out annually worldwide, equating to one operation each year for every 22 people (Lancet Commission on Global Surgery 2015). This figure is higher in high-income countries. For example, in Australia in 2013/14, there were approximately 2.4 million surgical procedures in a population of 23.4 million, or around one operation each year for every 10 people (ABS 2014). One of the complications of surgery is surgical site infection (SSI), which is an infection that occurs at the site of a surgical incision or in an organ space within 30 days of the surgery. The overall incidence of SSI is 1.9% (Berrios-Torres 2017), but it may be as high as 40% in some populations (Maehara 2017). As well as causing pain and discomfort for the patient, SSI increases the length of hospital stay and the cost of treatment (De Lissovoy 2009).

Surgical wounds generally heal by primary closure during which the wound edges are brought together so that they are adjacent to each other. 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). Some types of surgical wounds, such as sternal wounds, are more difficult to heal due to their anatomical position or an increased likelihood of infection (Toeg 2017); so too are surgical wounds in patients with certain types of underlying characteristics such as advanced age or medical conditions including malnutrition, uncontrolled diabetes, cardiovascular disease, compromised immunity, and morbid obesity (Baronski 2008; Waisbren 2010; Winfield 2016).

Failure of a wound to heal may also be the result of dehiscence (separation of the wound edges). Reasons for dehiscence are either technical, such as sutures breaking, cutting through tissue or knots slipping, or inadequate splinting (Baronski 2008), or patient-related factors such as wound infection and obesity (Sandy-Hodgetts 2015). 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. Where evisceration occurs, the mortality rate in the postoperative period may be as high as 45% (Kenig 2012).

Description of the intervention

Negative pressure wound therapy (NPWT) has been used to treat wounds since the late 1990s (Fleischmann 1997; Morykwas 1997). Negative pressure wound therapy has been recommended for a diverse range of lesions including open abdominal wounds (Stevens 2009), open fractures (Stannard 2009), burn wounds (Kantak 2016), 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 after clean surgery in obese patients (Dragu 2011). Negative pressure wound therapy is increasingly being used prophylactically on closed incisional wounds to prevent surgical site complications (De Vries 2016; Webster 2014), as well as being used on wounds healing by secondary intention (left open to heal from the bottom up) such as chronic or infected wounds (Dumville 2015).

Negative pressure wound therapy 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) system (KCI, San Antonio, Texas) (Morykwas 1997). However, alternatives have been developed and are being used (Visser 2017). Portable versions of the device have been introduced for use in community settings (Hurd 2014; Ousey 2014). An emerging advance has been the addition of 'instillations' of sterile water, saline, antiseptics, or antibiotics to VAC therapy, as in new negative pressure wound therapy with instillation (NPWTi) systems such as V.A.C. VeraFlo Therapy (KCI, San Antonio, Texas) (Gabriel 2014; Gupta 2016).

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 in this process is unclear. Experimental evidence suggests that NPWT may assist wound healing by increasing local blood flow and the production of granulation tissue (Xia 2014), and may encourage other changes to the microenvironment of the wound by reducing bacterial contamination, oedema, and exudate (Banwell 2003). Other mechanisms for healing have been investigated using animal models. For example, an increase in fibrocytes (stem cells involved in wound healing) was demonstrated in an NPWT-treated group of diabetic rats compared with a control group (Chen 2017). Expressions of vascular endothelial growth factor receptors, which are involved in healing, were also seen to increase when NPWT was compared with a control group of rabbits (Tanaka 2016). One of the basic theoretical principles underpinning the development of NPWT is that it increases perfusion or blood flow. However, this was challenged in an experimental study using healthy volunteers that showed that local blood flow decreased as suction pressure increased (Kairinos 2009), while a study in closed incisional wounds in a porcine model (Malmsjö 2014) found little impact on wound perfusion with any tested system, and some slight decreases in blood flow in superficial tissue. In closed incisions healing by primary intention, NPWT also delivers a sealed environment, preventing or reducing bacterial entry to the wound, while removing blood and exudate from the wound. A systematic review of laboratory studies in both acute and chronic wound models (Glass 2014) suggests that NPWT shifts the cytokine profile to being less inflammatory, but that, although there may be differences in mechanisms between acute and chronic wounds, in both cases wound healing is promoted through changes in the expression of multiple enzymes such as the matrix metallo-proteinases. There are multiple probable mediators of a possible effect of NPWT on wound healing in closed surgical incisions and these are not yet fully understood.

Why it is important to do this review

Surgical wounds that become infected and/or 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. Negative pressure wound therapy was approved by the US Food and Drug Administration

(FDA) for the treatment of non-healing wounds in 1995 (Kloth 2002). More recently, a multinational 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 2016), 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 the use of the treatment in certain circumstances (FDA 2009a; FDA 2009b).

Since the introduction of NPWT, there has been an explosion of publications (over 2600 in the last 10 years), which have been influential in changing practice. Along with an increase in primary studies and other non-research publications, there has been a concomitant increase in the number of systematic reviews (Hyldig 2016; Ingargiola 2013; Karlakki 2013; Ubbink 2008; Vikatmaa 2008; Willy 2017). Many of these reviews have included non-randomised controlled trials; have considered both acute and chronic wounds; and, as with the primary studies, many have received industry sponsorship (Kairinos 2014). In addition, concerns have been raised about the premature termination of studies (Gregor 2008). It is therefore unsurprising that some recent reviews have concluded that the evidence for the effectiveness of NPWT remains uncertain (Hyldig 2016; Webster 2014; WHO 2016). None of the reviews published to date have included formal cost-effectiveness studies. NPWT is a rapidly expanding therapy with widening indications for its use, so new trials continue to emerge. Consequently, an updated systematic review was required to summarise the current evidence for the effect of NPWT on the healing of surgical wounds by primary closure.

A glossary of main terms is given in Appendix 1.

OBJECTIVES

To assess the effects of NPWT for preventing surgical site infection in wounds healing through primary closure, and to assess the cost-effectiveness of NPWT in wounds healing through primary closure.

METHODS

Criteria for considering studies for this review

Types of studies

For changes to this section since the protocol (Webster 2011) and previous versions of the review (Webster 2014; Webster 2019), please see Differences between protocol and review.

We included published or unpublished randomised controlled trials (RCTs) or cluster RCTs that evaluated the effects of NPWT on surgical wounds healing by primary closure. We excluded cross-over trials and quasi-randomised studies where, for example, treatment allocation was made through alternation or by date of birth.

We also included 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).

Types of participants

We included trials involving people of any age and in any care setting that assessed the use of NPWT for uninfected surgical wounds healing by primary closure in all intervention groups. We excluded trials where NPWT was used as a dressing following a skin graft (including split-skin grafts and full-skin grafts); flap closure surgery; skin graft donor sites; or surgery involving harvesting veins following flap elevation. We also excluded wounds that could not be closed immediately due to damaged tissue (e.g. in severe trauma), infection, or chronicity (wounds healing by delayed primary intention or secondary intention).

Types of interventions

The primary intervention was NPWT for closed surgical incisions delivered by any mode, or simple closed-system suction drainage; continuously or intermittently over any time period and at any pressure. The comparison interventions were any standard dressing (e.g. gauze) or any advanced dressing (e.g. hydrogels, alginates, hydrocolloids); or comparisons between different negative pressure devices. The use of a particular negative pressure system, device or protocol (e.g. different pressures) had to be the only systematic difference between the intervention groups.

Types of outcome measures

Primary outcomes

- Mortality (all cause)
- Surgical site infection (superficial, deep or organ space)
- Dehiscence

Secondary outcomes

- Reoperation
- Readmission to hospital within 30 days for a wound-related complication
- Seroma, expressed as the proportion of participants in each group with seroma
- Haematoma, expressed as the proportion of participants in each group with haematoma
- Skin blisters, expressed as the proportion of participants in each group with blisters
- Pain (measured by any valid pain assessment instrument)
- Quality of life (measured by any valid assessment instrument and including utility scores representing health-related quality of life)
- Incremental cost-effectiveness ratio (ICER) or other measure of relative cost-effectiveness

We accepted study authors' definitions of SSI, dehiscence and wound-related complications requiring reoperation. We anticipated that outcomes would be reported at 30 days but accepted any duration of follow-up unless otherwise specified. Where data were reported at multiple durations of follow-up we used data at 30 days or equivalent time point unless another duration was specified as the primary measure in the study.

Search methods for identification of studies

In June 2019, we searched the Cochrane Wounds Specialised Register; the Cochrane Central Register of Controlled Trials (CENTRAL); Ovid MEDLINE (including In-Process & Other Non-Indexed Citations); Ovid Embase and EBSCO CINAHL Plus. We also searched clinical trials registries for ongoing and unpublished studies, and scanned reference lists of relevant included studies as well as reviews, meta-analyses and health technology reports to identify additional studies. There were no restrictions with respect to language, date of publication or study setting.

Electronic searches

We searched the following electronic databases to identify reports of relevant clinical trials and cost effectiveness studies:

- the Cochrane Wounds Specialised Register (searched 20 June 2019);
- the Cochrane Central Register of Controlled Trials (CENTRAL; 2019, Issue 5) in the Cochrane Library (searched 20 June 2019);
- Ovid MEDLINE including In-Process & Other Non-Indexed Citations (1946 to 20 June 2019);
- Ovid Embase (1974 to 20 June 2019);
- EBSCO CINAHL Plus (Cumulative Index to Nursing and Allied Health Literature; 1937 to 20 June 2019).

We searched the NHS (National Health Service) Economic Evaluation Database (NHS EED; 2015, Issue 2) for the previous version of this review (Webster 2019). As NHS EED has not been updated since 2015 we did not search it for this update.

The search strategies for the Cochrane Wounds Specialised Register, CENTRAL, Ovid MEDLINE, Ovid Embase and EBSCO CINAHL Plus can be found in Appendix 2. 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 2019). We combined the Embase search with the Ovid Embase filter developed by the UK Cochrane Centre (Lefebvre 2019). We combined the CINAHL Plus searches with the trial filters developed by the Scottish Intercollegiate Guidelines Network (SIGN 2019). There were no restrictions with respect to language, date of publication or study setting. We combined Ovid MEDLINE, Ovid Embase and EBSCO CINAHL Plus searches with filters developed by the Centre for Reviews and Dissemination for the identification of economic studies (CRD 2013).

We also searched the following clinical trials registries:

- ClinicalTrials.gov (www.clinicaltrials.gov) (searched 26 June 2019);
- World Health Organization (WHO) International Clinical Trials Registry Platform (http://apps.who.int/trialsearch/Default.aspx) (searched 26 June 2019).

Search strategies for clinical trial registries can be found in Appendix 2. Details of the search strategies used for the previous version of the review are given in Webster 2019.

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 where key information was missing or unclear. In the first version of this review, we contacted the manufacturers and distributors of devices used to deliver NPWT, such as vacuum-assisted (VAC) closure (KCI, San Antonio, Texas); SNaP Wound Care System Dressing (Spiracur Inc, Sunnyvale, California); Venturi Avanti and Venturi Compact (Talley Group, Romsey, UK); and RENASYS EZ (Smith & Nephew, Hull, UK). We did not contact manufacturers or distributors for this update.

Data collection and analysis

We carried out data collection and analysis according to the methods stated in the published protocol (Webster 2011), which were based on the *Cochrane Handbook for Systematic Reviews of Interventions* (Li 2019). Changes from the protocol or previous published versions of the review are documented in Differences between protocol and review.

Two authors on the previous version of this review were authors of some of the papers included in the review. To prevent any form of bias, neither of them were involved in extracting data or assessing quality for any of the studies in which they were investigators.

Selection of studies

Two review authors independently reviewed titles and abstracts identified by the search. We retrieved full reports of all potentially relevant trials for further assessment of eligibility based on the inclusion criteria. We settled differences of opinion by consensus. There was no blinding of study authorship.

Data extraction and management

Two review authors independently extracted the following data using a predesigned 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;
- prospective registration on a clinical trials registry;
- information about ethics approval, consent, and conflict of interest;
- source of funding;
- economic data (healthcare costs);
- outcomes.

For cost-effectiveness studies, we additionally extracted data relating to study design, analytical approach, sources of effectiveness and cost data, perspective, utility valuation, measures of benefit, and analysis of uncertainty.

Any discrepancies were resolved through discussion. One review author entered data into the Review Manager 5 software (Review Manager 2014); and a second author checked the data for accuracy. Where necessary, we attempted to contact study authors of the original reports for clarification. When more than one publication

arose from a study, we extracted data from all relevant publications but did not duplicate data.

Assessment of risk of bias in included studies

Two review authors independently assessed the eligible trials for risk of bias using the Cochrane tool for assessing risk of bias (Li 2019). This tool addresses six specific domains, namely sequence generation, allocation concealment, blinding, incomplete outcome data, selective outcome reporting, and other potential sources of bias (see Appendix 3 for details of the criteria on which our judgements were based). We assessed blinding and completeness of outcome data for each outcome separately. We completed a 'Risk of bias' table for each eligible study. Any disagreements between review authors were resolved by consensus. We contacted investigators of included trials to resolve any ambiguities. Assessment of risk of bias is presented as a 'Risk of bias' summary figure, which shows all the judgements in a cross-tabulation of study by entry.

We reported bias, and more generally study limitations within economic evaluations, using the checklist from the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) (Husereau 2013), and used the scoring system reported by Hope 2017 to assess the overall quality of each study, expressed as a percentage. Specifically, we allocated 1 point for each item that was fully met, 1/2 point if the item was partially met, and 0 for each item that was not met. We summed the total score and calculated a percentage (total score/total number of items less any non-applicable (N/A) item). We classified the quality of a report as follows: 85% or higher as excellent; 70% to 84% as very good quality; 55% to 70% as good quality; and below 55% as poor quality.

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 and lack of evidence of effect for most outcomes, 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. For economic studies, we focused on measures of relative cost-effectiveness such as the incremental cost-effectiveness ratio (ICER) as reported in the primary study.

Unit of analysis issues

If included studies had randomised at the participant level and measured outcomes at the wound level, we planned to treat the participant as the unit of analysis when the number of wounds assessed appeared equal to the number of participants (e.g. one wound per person). Where studies randomised wounds or body parts as opposed to individuals and there were multiple wounds per participant, and we were unable to obtain further information from trialists, we did not include them in the meta-analysis but instead presented narrative summaries of the results in Appendix 4.

We also included studies with split-body designs, where patients undergoing bilateral procedures were enrolled and one wound was randomised to one treatment and the other to the alternative treatment. These approaches are similar to the 'split-mouth' approach (Lesaffre 2009). These studies should be analysed using paired data which reflects the reduced variation in evaluating different treatments on the same person. However, it was unclear whether such an analysis had been undertaken. We have noted this lack of clarity in the 'Risk of bias' assessment and in the notes in the Characteristics of included studies table. These studies were analysed separately from the parallel group trials and the results are presented in Appendix 4.

In some cases, trials enrolled a mixture of participants undergoing unilateral and bilateral procedures and it was not possible to separate the paired and unpaired data. We noted the results of these trials but did not analyse them further; results are presented in Appendix 4.

Dealing with missing data

Where it appeared that data had been excluded from the analyses, we attempted to contact authors for these missing data. If data remained missing despite our best efforts to obtain them, we conducted an available-case analysis, based on the numbers of participants for whom outcome data were known. No imputations were made. We did not conduct planned best-case and worst-case analyses, nor did we calculate SDs from standard errors (SE) (Li 2019).

Assessment of heterogeneity

Assessment of heterogeneity can be a complex, multifaceted process. Firstly, we considered clinical and methodological heterogeneity, that is, the degree to which the included studies varied in terms of participant, intervention, outcome, and characteristics such as length of follow-up. This assessment of clinical and methodological heterogeneity was supplemented by information regarding statistical heterogeneity, assessed using the Chi^2 test (we considered a significance level of $P < 0.10$ to indicate statistically significant heterogeneity) in conjunction with the I^2 statistic (Higgins 2003). The I^2 examines the percentage of total variation across RCTs that is due to heterogeneity rather than chance (Higgins 2003). In general, I^2 values of 40% or less may not be important (Higgins 2003), while values of more than 75% or more indicate considerable heterogeneity (Deeks 2011). However, these figures are only a guide, and it has been recognised that statistical tests and metrics may miss important heterogeneity. Thus, while these were assessed, the overall assessment of heterogeneity assessed these measures in combination with the methodological and clinical assessment of heterogeneity. Where there was evidence of high heterogeneity we attempted to explore this further; see Data synthesis for details on how we handled potential heterogeneity in the data analyses.

Assessment of reporting biases

We assessed selective outcome reporting for each trial as part of our appraisal of risk of bias. In addition, as a large number of trials were included in the meta-analysis for one of our primary outcomes (surgical site infection), we also assessed publication bias using a funnel plot (Li 2019). We note the particular risk of outcome reporting bias for a post hoc exploration which we undertook of

superficial and deep SSI and its implications for the certainty of the data.

Data synthesis

Where studies were clinically similar and outcome measurements comparable, we pooled results using a random-effects model and reported the pooled estimate together with its 95% CI. Where statistical synthesis of data from more than one study was not possible or considered inappropriate, we conducted a narrative review of eligible studies.

We were unable to pre specify the amount of clinical, methodological, and statistical heterogeneity in the included studies, thus we used a random-effects approach for meta-analysis. Conducting meta-analysis with a fixed-effect model in the presence of even minor heterogeneity may provide overly narrow CIs. We would only have used a fixed-effect approach when clinical and methodological heterogeneity was assessed as minimal, and the assumption that a single underlying treatment effect was being estimated held. Chi^2 and I^2 were used to quantify heterogeneity but were not used to guide the choice of a model for meta-analysis. We would have exercised caution when meta-analysed data were at risk of small-study effects because, in such a case, use of a random-effects model may be unsuitable. In this case, or where there were other reasons to question the selection of a fixed-effect or random-effects model, we planned to assess the impact of the approach using sensitivity analyses to compare results from alternate models, but this was not implemented (Thompson 1999).

We presented data using forest plots where possible. For dichotomous outcomes, we presented the summary estimate as an RR with 95% CI. Where continuous outcomes were measured, we presented an MD with 95% CI; we planned to pool SMD estimates where studies measured the same outcome using different methods.

Economic analyses

We have presented a tabulated analysis of the identified economic data in accordance with current guidance on the use of economics methods in the preparation of Cochrane Reviews (Shemilt 2019). We classified the economic evaluation according to the framework described by Husereau and colleagues (Husereau 2013). We tabulated the main characteristics and results of the identified economic evaluation studies and augmented these with a narrative description. The methods used are discussed, and the key results of the studies compared. We assessed the quality of the studies using the CHEERS checklist (Husereau 2013).

We expected the results of cost-effectiveness studies 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 placed the results of the economic studies in context and entailed a discussion of scenarios that were likely to lead to the most cost-effective use of the therapy, as well as the least cost-effective use.

We intended to capture and report all substantial costs that were observed to differ between participants administered NPWT and participants administered standard care as part of the economic analysis. However, we did not treat cost or resource use as an outcome in itself but as a component of cost-effectiveness. We therefore used the currency and price year together with the principal sources of resource costings in each original study. The primary trial outcome (adverse events) is relevant to the economic analysis as it may indicate a difference in the number of hospital bed days and specialist time required and a possible improvement in quality of life of the participant.

We examined information on the change in health-related quality of life via utilities measured by a multi-attribute utility instrument (MAUI) or other approaches (such as the time trade-off, standard gamble) where possible. These data are ideally reported in trials for both the group treated with NPWT and a control group receiving the comparator wound care. We assessed the utility data 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 planned to discuss the potential impact on health-related quality of life attributable to the intervention as part of the analysis. As with cost and resource use data, we treated utility data as a component of cost-effectiveness. If differences were observed in the rates of adverse events, wound infections, and complications resulting from the treatment of the wound, we planned to discuss the economic implications as part of the economic analysis.

Subgroup analysis and investigation of heterogeneity

Investigations of heterogeneity were not required as inconsistency was low for all outcomes, nor did we consider any population, intervention, or comparator subanalyses to be appropriate. We had originally planned a range of subgroup analyses in the protocol for this review, including type of setting, type of device, type of surgery, and type of comparison dressing. Based on the current interest in NPWT as a treatment for wounds healing by primary intention, and given the available data, we have conducted one of these suggested analyses: a subgroup analysis for different types of surgery defined in line with broad clinical grouping. We have also presented the data subgrouped by types of surgery based on contamination class. The decision to define surgery in two ways was a post hoc decision resulting in an exploratory analysis and, as with all subgroup analysis, the results should be interpreted with caution.

Subgroup analyses by type of surgery have been conducted for SSI - the primary outcome for which sufficient studies were available. For the outcome of dehiscence, we have grouped the studies in the analysis by their broad clinical grouping but have not implemented the subgroup analysis as there were too few studies in some groups.

For the outcome of SSI, we also performed an exploratory post hoc analysis in which we looked at studies which reported separate data for superficial SSIs and for deeper infections (classed as "deep" or "deep and organ space" SSIs), or which only reported either superficial or deep infection. Where infections were reported using the Szilagyi classification, we considered Szilagyi class I or II to be superficial and class III to be deep infections.

Sensitivity analysis

We performed a sensitivity analysis on the primary outcomes of SSI and dehiscence to assess the influence of removing studies classified as being at high risk of bias from the meta-analysis. We excluded studies that were assessed as having high or unclear risk of bias in the key domains of adequate generation of the

randomisation sequence, adequate allocation concealment, and blinding of outcome assessor.

'Summary of findings' tables and GRADE assessment of the certainty of the evidence

We have presented the main outcomes of the review in a 'Summary of findings' (SoF) table. This table presents key information concerning the quality of the evidence, the magnitude of the effects of the interventions examined, and the sum of available data for the main outcomes (Schünemann 2019a). 'Summary of findings' tables also include an overall grading of the evidence related to each of the primary outcomes, using the GRADE approach. The GRADE approach defines the certainty of a body of evidence as the extent to which one can be confident that an estimate of effect or association is close to the true quantity of specific interest. The quality of a body of evidence involves consideration of within-trial risk of bias, directness of evidence, heterogeneity, precision of effect estimates, and risk of publication bias (Schünemann 2019b). We planned to create a separate SoF table for each comparison evaluated. We have presented the following outcomes in the SoF table for the comparison of NPWT with standard care:

- incidence of mortality;
- incidence of surgical site infection;
- incidence of dehiscence;
- Incidence of reoperation;
- incidence of seroma;
- incidence of haematoma;
- incidence of skin blisters.

For other outcomes, we conducted a GRADE assessment and presented these assessments in a narrative format within the Results section but did not present them in separate 'Summary of findings' tables. We based the GRADE assessment of cost-effectiveness evidence on the RCT evidence on which the evaluation was based.

RESULTS

Description of studies

See Characteristics of included studies; Characteristics of excluded studies; Characteristics of studies awaiting classification; Characteristics of ongoing studies. Outcome data for intervention studies are given in Table 1 and Table 2; economic data are summarised in Table 3.

Results of the search

We searched for both intervention studies and economic evaluations: The results of these searches are reported separately below, and summarised in Figure 1. Over the lifetime of the review, we have now assessed a total of 1872 records from electronic searches as abstracts for intervention studies with 659 screened at full-text stage, although many of these were clinical trial registry records. For economic evaluation studies, we have assessed 387 records as abstracts and ten as full texts.

Figure 1. Study flow diagram.

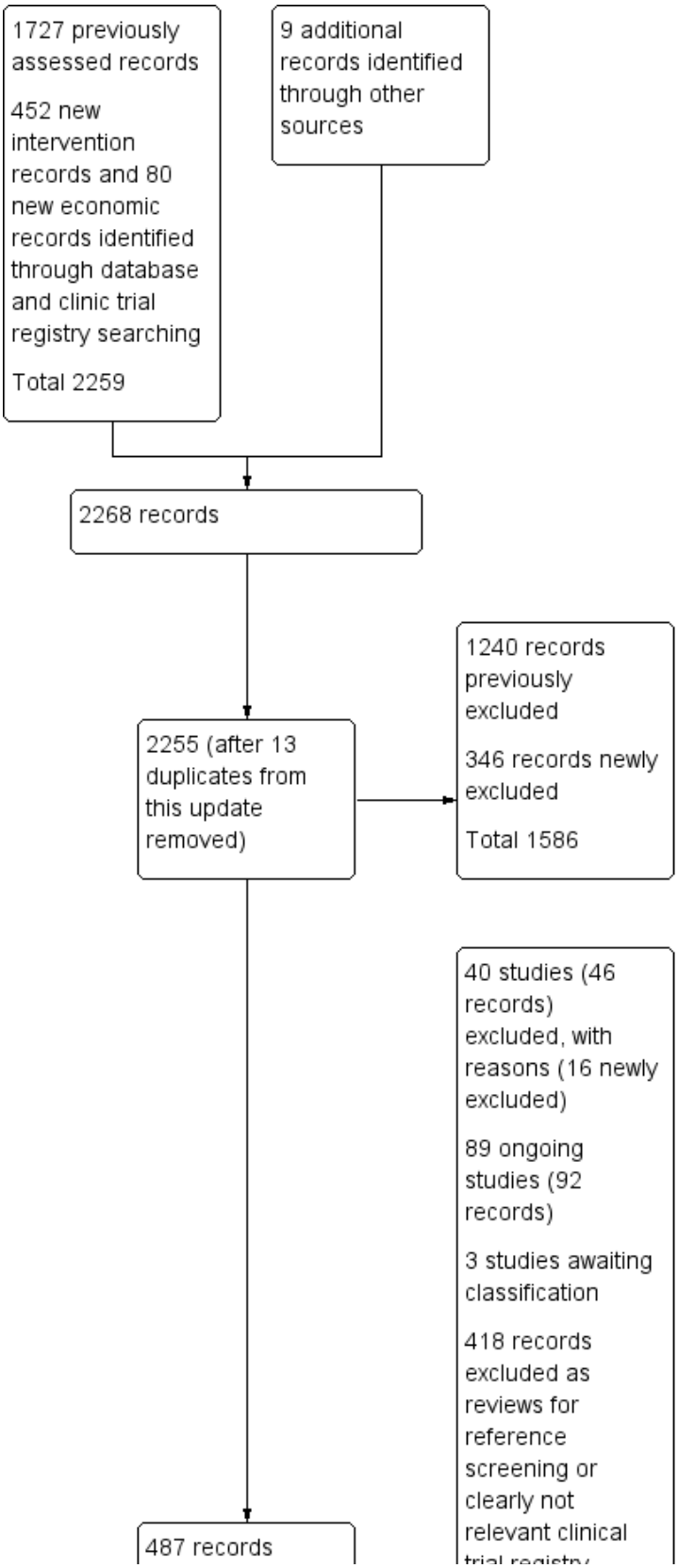
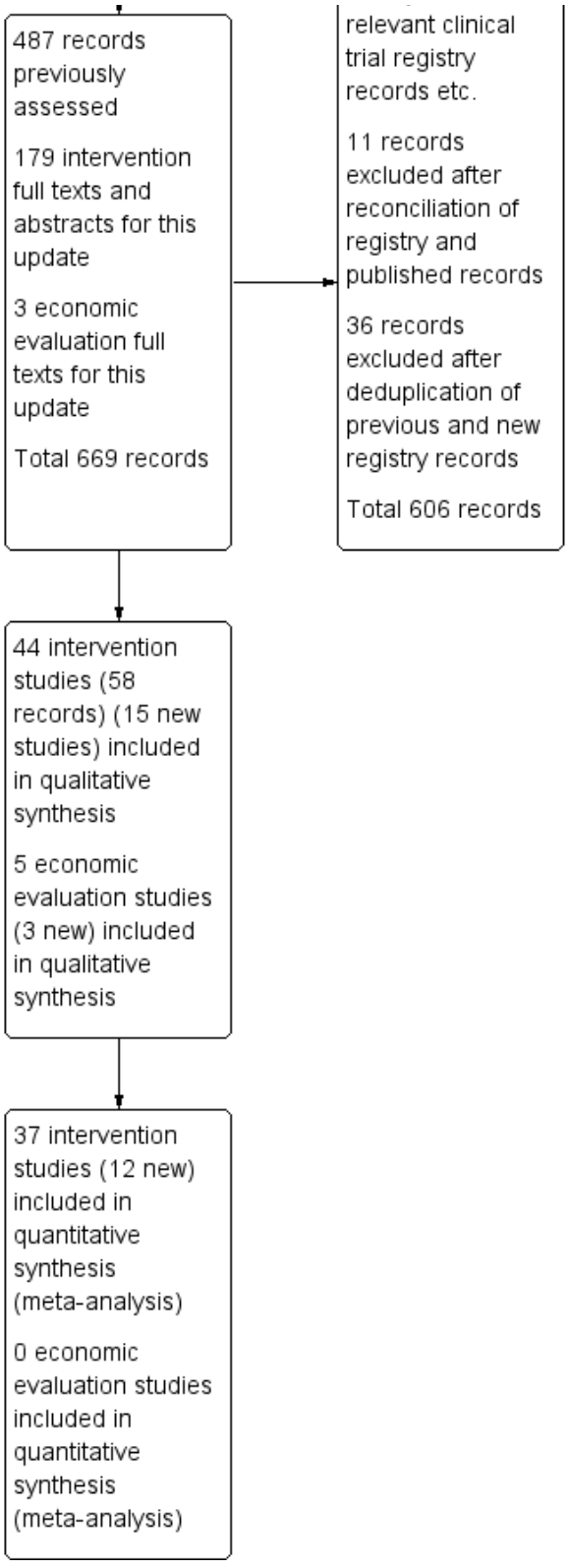


Figure 1. (Continued)



Interventions search

For this third update, we identified 452 unique new interventions records through our electronic search including the search of trial registry platforms. We retrieved 179 publications for inspection including full texts, abstracts, trial registry records and references identified from citation checking. From these, 14 new intervention studies reported in 16 records were eligible for inclusion in

the review; three were reported in abstract form only. We also identified one other new included study (Galiano 2018) and two new excluded studies (Krishnamoorthy 2012; Stannard 2006) plus additional records for previously identified trials (total of nine records) through reference checking and cross-referencing of trial database records. The previous update included 30 intervention studies, one of which we have now excluded (Frazee 2018) because it did not assess an eligible comparison.

This update therefore includes 44 intervention studies reported in 58 records, of which 15 studies are newly identified (Bobkiewicz 2018; Galiano 2018; Giannini 2018; Gombert 2018; Hyldig 2019a; Javed 2018; Keeney 2019; Kwon 2018; Martin 2019; Murphy 2019; Newman 2019; Schmid 2018; Shim 2018; WHIST 2019a; Wihbey 2018) and 29 were previously included (Chaboyer 2014; Crist 2014; Crist 2017; DiMuzio 2017; Engelhardt 2016; Gillespie 2015; Gunatilake 2017; Howell 2011; Hussamy 2017; Karlakki 2016; Kuncewitch 2017; Lee 2017a; Lee 2017b; Leon 2016; Lozano-Balderas 2017; Manoharan 2016; Masden 2012; Nordmeyer 2016; O'Leary 2017; Pauser 2016; Pachowsky 2012; Pleger 2018; Ruhstaller 2017; Sabat 2016; Shen 2017; Stannard 2012; Tanaydin 2018; Tuuli 2017; Witt-Majchrzac 2015). Ten of these studies were reported in abstract form only. We are grateful to the authors of the WHIST 2019a study for extensive personal communication which enabled the study to be included in this version of the review.

Economic analysis search

Electronic searches for previous versions of the review yielded 307 references and yielded two included studies (Heard 2017; Nherera 2017). For this update, we identified a further 80 publications; two of which were retrieved for full-text examination; both of these were included (Hyldig 2019b; Nherera 2018). We also included the WHIST study (WHIST 2019b) which was identified through the intervention searches and personal communication with the authors, bringing the number of included economic evaluations to five. All of these studies were based on RCTs included in the intervention review (Chaboyer 2014; Hyldig 2019b; Karlakki 2016; WHIST 2019a; Witt-Majchrzac 2015).

Included studies

Types of participants

In this update, we included 15 additional intervention studies enrolling 4470 participants (Bobkiewicz 2018; Galiano 2018; Giannini 2018; Gombert 2018; Hyldig 2019a Javed 2018; Keeney 2019; Kwon 2018; Martin 2019; Murphy 2019; Newman 2019; Schmid 2018; Shim 2018; WHIST 2019a; Wihbey 2018). The review now includes 7447 participants. The newly identified studies were larger than those in previous versions of the review, including in particular, the WHIST 2019a trial in fractures (1548 participants) and the Hyldig 2019a study in women having caesarean sections (876 participants). Sample sizes now range from 19 to 1548 participants and half of trials (22/44) included at least 100 participants.

Participants had a wide range of surgical procedures, including obstetric, orthopaedic, vascular and general surgeries:

- Eight studies enrolled people undergoing knee or hip arthroplasties (Giannini 2018; Gillespie 2015; Howell 2011; Karlakki 2016; Keeney 2019; Manoharan 2016; Newman 2019 Pachowsky 2012).
- Seven studies enrolled women undergoing caesarean section (Chaboyer 2014; Gunatilake 2017; Hussamy 2017; Hyldig 2019a; Ruhstaller 2017; Tuuli 2017; Wihbey 2018).
- Seven studies enrolled people having peripheral vascular procedures (DiMuzio 2017; Engelhardt 2016; Gombert 2018; Kwon 2018; Lee 2017b; Pleger 2018; Sabat 2016).
- Seven studies enrolled people undergoing abdominal procedures (Bobkiewicz 2018; Kuncewitch 2017; Leon 2016; Lozano-Balderas 2017; Murphy 2019; O'Leary 2017; Shen 2017).
- Six studies enrolled people undergoing surgery for limb fracture (Crist 2014; Crist 2017; Nordmeyer 2016; Pauser 2016; Stannard 2012); WHIST 2019a.
- Two studies enrolled people undergoing cardiac surgery (Lee 2017a; Witt-Majchrzac 2015).
- Two studies enrolled people undergoing hepatopancreatiobiliary procedures (Javed 2018; Martin 2019).
- In two studies participants were undergoing breast surgery Galiano 2018; Tanaydin 2018).
- One study (Masden 2012) included mixed wound types.
- One study (Shim 2018) enrolled people requiring surgery for hand injuries.
- One study (Schmid 2018) enrolled people having inguinal lymph node dissection.

Most studies were conducted in North America (21 studies), Europe (16 studies) or Australasia (three studies); Israel and South Korea were also represented and two studies did not report where they were conducted.

Types of interventions

Most studies used one of a small number of commercially available NPWT systems:

- Seven studies used the vacuum-assisted closure (VAC) negative pressure device (KCI, San Antonio, Texas), set to −125 mmHg (Crist 2014; Crist 2017; Howell 2011; Lozano-Balderas 2017; Masden 2012; Stannard 2012; Wihbey 2018).
- Thirteen studies used the PICO system (Smith & Nephew, Hull, UK) (Chaboyer 2014; Galiano 2018; Giannini 2018; Gillespie 2015; Hyldig 2019a; Keeney 2019; Karlakki 2016; Martin 2019; Nordmeyer 2016; O'Leary 2017; Tanaydin 2018; Tuuli 2017; Witt-Majchrzac 2015).
- Sixteen studies used the PREVENA system (KCI, San Antonio, Texas) (DiMuzio 2017; Engelhardt 2016; Gombert 2018; Gunatilake 2017; Javed 2018; Kwon 2018; Lee 2017a; Lee 2017b; Manoharan 2016; Murphy 2019; Newman 2019; Pachowsky 2012; Pauser 2016; Pleger 2018; Ruhstaller 2017; Sabat 2016).
- A minority of studies did not specify the device but described it in varying degrees of detail (Bobkiewicz 2018; Hussamy 2017; Kuncewitch 2017; Leon 2016; Schmid 2018; Shen 2017; WHIST 2019a),
- One study (Shim 2018) used CuraVac (CGBio, Seongnam-si, Gyeonggido, Korea).

Comparators were mostly described as standard care, standard dressings, usual care or conventional dressings, care or therapy. Where specified, dressings were most commonly described as gauze or nonadherent or containing these components. A small number of studies reported using dressings with specific properties

such as silver or iodine-impregnated dressings and some reported the use of steri-strips in some or all wounds.

Types of economic assessments

All of the five included economic studies used clinical effectiveness data, in particular data on SSIs, from RCTs included in this review to assess measures of cost-effectiveness; several also derived resource use and cost data from the trial data but other sources were also used to inform estimates of cost-effectiveness.

Two obstetric surgery studies looked at use of NPWT in women undergoing caesarean section (Heard 2017; Hyldig 2019b); these were based on the RCTs of Chaboyer 2014 and Hyldig 2019a, respectively. Heard 2017 used the perspective of the Australian public healthcare provider with resources priced in AUD (Australian dollars) at 2014 values; while Hyldig 2019b used a Danish healthcare perspective; resource costs in Euro were reported after transformation from Danish Krona at 2015 values.

Two orthopaedic surgery studies were also identified. The WHIST 2019b study was undertaken alongside the WHIST 2019a RCT in people having surgery for lower limb fractures. Nherera 2017 looked at NPWT in people having knee and hip arthroplasties and was based on Karlakki 2016. Both studies were undertaken in a UK context with an NHS perspective and resources priced in pounds sterling (GBP) at 2017/18 and 2015/16 values, respectively. WHIST 2019b also used an NHS and personal social services (PSS) (including indirect costs) perspective.

Finally, an assessment in general surgery, Nherera 2018, looked at people having coronary artery bypass graft (CABG) surgery and was based on Witt-Majchrzac 2015. A German Statutory Health Insurance payer perspective was employed and resource costs were priced in Euro.

All studies used resource costs and clinical outcome data to assess the quality-adjusted life year gained (QALY). A QALY is a generic measure of disease burden including both the quality and the quantity of life lived (NICE 2013; NICE 2018), and can be used in combination with cost data to assess the value for money of medical interventions (NICE 2013). One QALY equates to one year in perfect health and a year of less than perfect health is worth less than one, while death is considered to be worth zero (Heard 2017). The estimated incremental cost-effectiveness ratio (ICER) considers the mean cost per QALY. Some studies used the ICER(s), together with their 95% credible intervals (CrI) to calculate the probability of NPWT being cost-effective at particular "willingness-to-pay" thresholds.

Excluded studies

The previous update of this review excluded a total of 24 studies (for reasons see Characteristics of excluded studies). For this update, we excluded one previously included study (Frazee 2018) which we determined did not assess an eligible comparison. We identified and excluded 15 new studies for the following reasons: ineligible population (Costa 2018; Joos 2015; Muller-Sloof 2018; Sinha 2016; Stannard 2006; Zotes 2015); ineligible intervention (Bi 2017; Erne 2018; Walker 2018); ineligible study design Athanasiou 2018; Chang 2018; Fleming 2018; Svensson-Bjork 2018; ineligible comparison (e.g. NPWT was not the only difference between groups) (Krishnamoorthy 2012; Trofa 2019). This brought the total number of excluded studies to 40. Two of these were identified through reference checking and cross-referencing of trial records (Stannard 2006; Krishnamoorthy 2012). We also identified additional references for a number of already excluded studies.

Ongoing studies

Screening by two review authors identified a total of 89 ongoing studies, primarily from the trial registry search; this number incorporates 28 newly identified studies and several published protocols identified from the main database search. Some studies listed as ongoing in the previous version of the review have now been identified as published studies and moved to included or excluded studies, as appropriate. For this new update, we identified five published protocols (Gillespie 2016; Jorgensen 2018; Masters 2018; Mihaljevic 2015; Sandy-Hodgetts 2017) in addition to the two we had previously included (Nguyen 2017; SUNRRISE 2017). We also identified a number of trial registry records which we have judged to represent ongoing potentially relevant studies. We were able to link some previously listed trial records to included or excluded studies or to published protocols so the total number of ongoing studies is now 89 (the previous version of the review contained 77). Two trials were recorded as terminated without sufficient data for analysis; we did not include these records.

Studies awaiting classification

There are three studies awaiting classification pending author contact, one of which was newly identified for this update (Nagata 2018) and two of which were included in the previous review (NCT00654641; NCT00724750). Some studies listed as pending classification in the previous version of the review have now been identified as published studies and moved to included, excluded or ongoing studies, as appropriate.

Risk of bias in included studies

Given that we anticipated unclear or high risks of performance bias in all studies due to the nature of the intervention (Appendix 3), we regarded the domains of sequence generation, allocation concealment and detection bias as having key importance: eight studies (Chaboyer 2014; Giannini 2018; Gillespie 2015; Gombert 2018; Masden 2012; Murphy 2019; Tanaydin 2018; WHIST 2019a) were at low risk of bias for all three of these domains. Conversely, twelve studies were at high risk for one or more of these (Galiano 2018; Gunatilake 2017; Karlakki 2016; Kwon 2018; Lozano-Balderas 2017; Manoharan 2016; O'Leary 2017; Schmid 2018; Shen 2017; Shim 2018; Wihbey 2018; Witt-Majchrzac 2015). The remaining 24 studies were at unclear risk of bias for one or more of these domains.

We included a number of studies reported only in abstract form; these had multiple domains at unclear risk of bias because of the constraints of the form in which they were published. Three studies were planned interim analyses (Martin 2019; Sabat 2016; Schmid 2018). A number of studies used designs which either mixed paired and unpaired data (for example, by recruiting participants with a mixture of unilateral and bilateral wounds and randomising them differently) or simply used different units of randomisation and analysis (Howell 2011; Kwon 2018; Pleger 2018; Sabat 2016; Stannard 2012). Four studies employed split-person designs and it was not clear whether the paired data had been taken into account in the analysis (Galiano 2018; Manoharan 2016; Schmid 2018; Tanaydin 2018). These studies were all considered to have

a high or unclear risk of bias for the domain of other sources of bias, depending on the reporting of the study and whether other considerations were present.

See Figure 2 and Figure 3 for the 'Risk of bias' summary; details of the risk of bias judgements for each domain and their rationales for each study are given in Characteristics of included studies. Risk of bias, or more specifically study quality, for the economic studies is shown in Table 4.

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

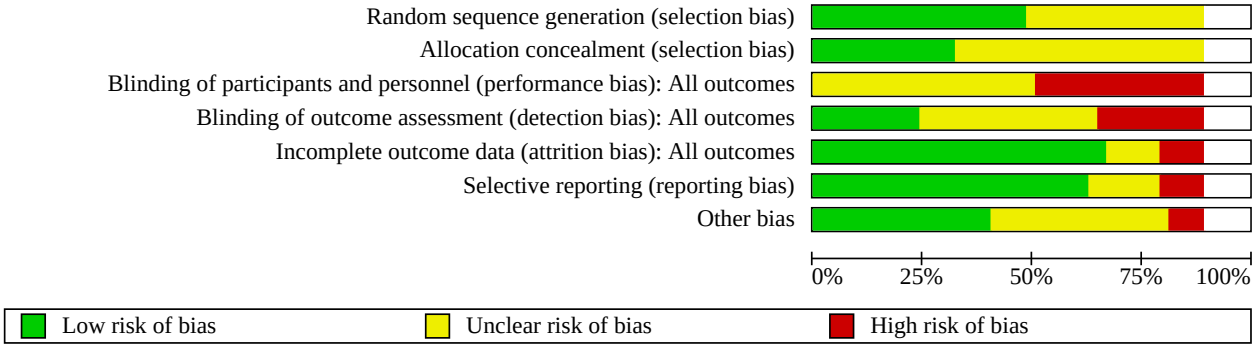


Figure 3. Risk of bias summary: review authors' judgements about each risk of bias item for each included study.

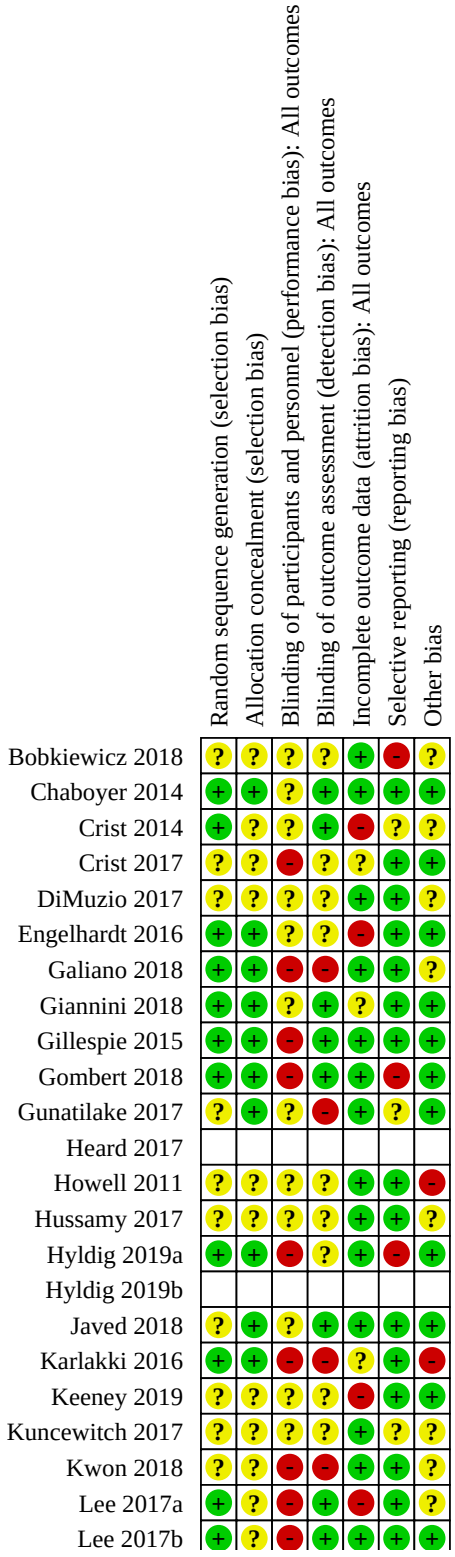
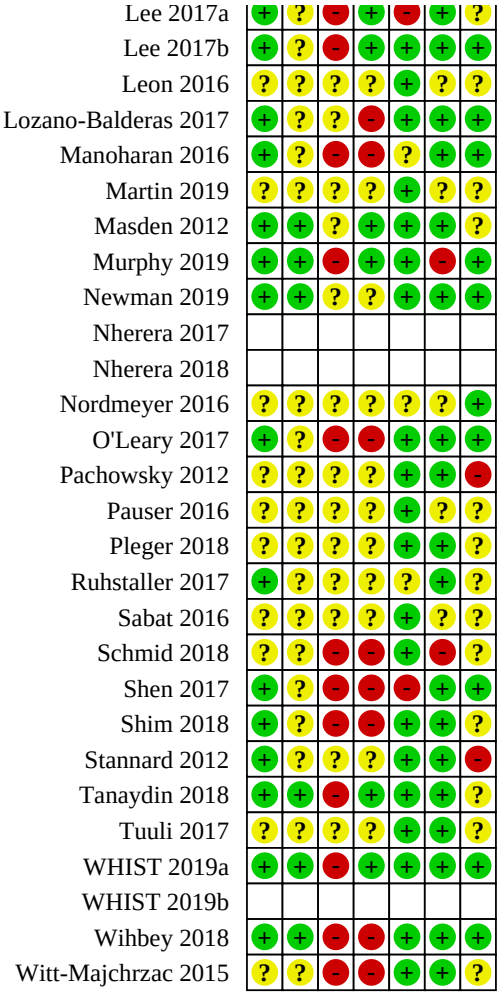


Figure 3. (Continued)



Risk of bias in economic studies

We used the CHEERS checklist, Husereau 2013, to assess the quality of the reports of the five included economic studies (Heard 2017; Hyldig 2019b; Nherera 2017; Nherera 2018; WHIST 2019b). All studies scored > 80% on the checklist, indicating very good reporting quality. Additionally, data for the Nherera 2017 study and the Nherera 2018 were drawn from the Karlakki 2016 and Witt-Majchrzac 2015 trials, which were at high risk for detection bias. The two items that were least well addressed were 'Measurement and valuation of preference based outcomes' and 'Choice of model'. The full assessments for each study are shown in Table 4.

The lead author in the Nherera 2017 and Nherera 2018 studies was an employee of Smith & Nephew, which manufactures the intervention product used in the studies.

Effects of interventions

See: **Summary of findings 1** Negative pressure wound therapy compared with standard dressing for surgical wounds healing by primary closure

See Summary of findings 1 for the main comparison: NPWT compared with standard dressing for surgical wounds healing by primary closure. Studies which reported a relevant outcome but which could not be included in the pooled analysis because of methodological or reporting issues are noted and reported fully in Appendix 4. As random-effects analyses were used throughout, each pooled result presented is an average effect, rather than a common effect and should be interpreted as such.

Comparison 1: NPWT compared with standard dressing (44 trials, 7447 participants)

All of the studies for this comparison compared a negative pressure device with a standard dressing. The included surgery types were diverse: study devices varied by manufacturer, and standard dressings differed based on individual hospital preference.

Primary outcomes

Primary outcome data are summarised in Table 1.

Mortality (follow-up period 30 days to 90 days or unspecified)

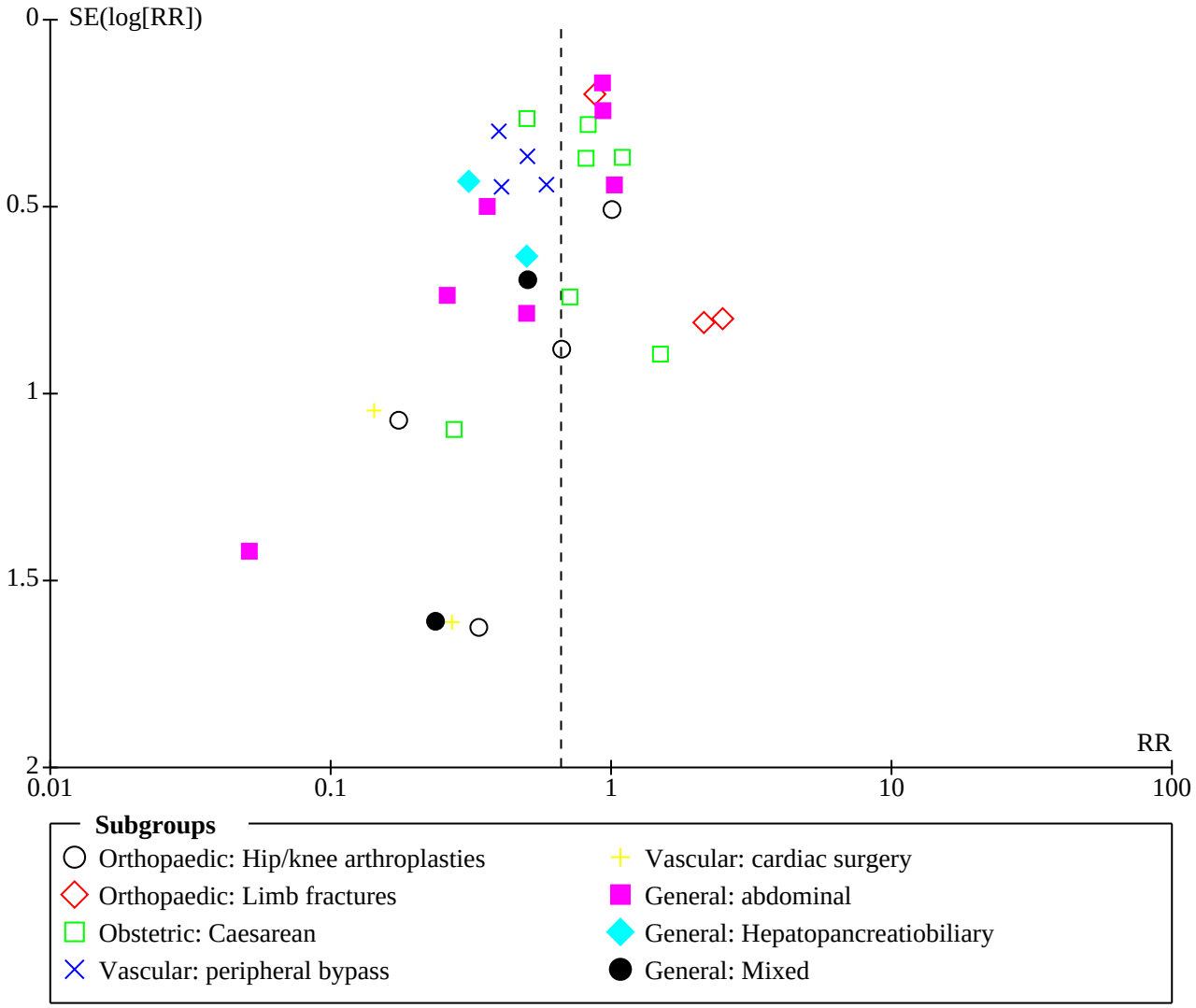
Four studies (2107 participants) reported mortality, these data were pooled. There may be little difference in mortality between

people treated with NPWT (25/1074 (2.3%)) and those treated with standard dressings (28/1033 (2.7%)). The RR was 0.86 (95% CI 0.50 to 1.47; I^2 = 0%) (Analysis 1.1). This was low-certainty evidence downgraded twice for very serious imprecision due to small numbers of events which produced wide confidence intervals which include the possibility of both harm and benefit as well as no effect. Using mortality data recorded at 3 months instead of 6 months in the largest trial (WHIST 2019a, with data for 1456 participants) made little difference to the pooled effect estimate (RR 0.76, 95% CI 0.42 to 1.39; I^2 = 0%).

Surgical site infection (follow-up period 30 days to 12 months or unspecified)

Thirty-nine studies (6917 participants) reported this outcome. We pooled incident SSI data from 31 studies (6204 participants). The evidence showed that NPWT probably reduces the incidence of SSI in participants treated with NPWT: 273/3115 (8.8%) compared with standard dressing 402/3089 (13.0%); RR 0.66 (95% CI 0.55 to 0.80; I^2 = 23%) (Analysis 1.2). This is moderate-certainty evidence downgraded once for high risk of bias in domains other than performance bias; half the studies with approximately 50% of the analysis weight were at high risk of bias in one or more domains (excluding performance bias). We assessed this analysis for evidence of publication bias but there was no clear evidence of this despite some asymmetry in the funnel plot (Figure 4); we judged that the effect estimate was unlikely to have been substantively influenced by this.

Figure 4. Funnel plot of comparison: 1 Negative pressure wound therapy versus standard dressing, outcome: 1.2 Surgical site infection.



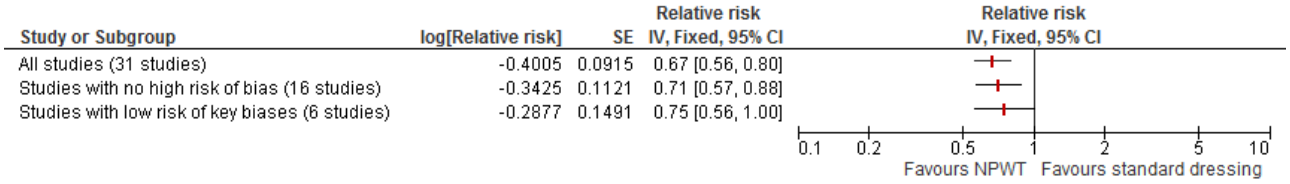
Sensitivity analyses

We applied a prespecified sensitivity analysis which included only the six studies (2229 participants) which reported SSI and were judged to be at low risk of bias in the key domains of randomisation, allocation concealment and blinding of outcome assessment. This produced a less clear estimate of the effect of NPWT (RR 0.75, 95% CI 0.56 to 1.00; I^2 = 29%) based on 119/1135 (10.4%) SSI in NPWT groups compared with 148/1094 (13.5%) in standard dressing groups. However, the evidence remains moderate certainty, downgraded once for imprecision.

A post hoc analysis which included studies with no domain at high risk of bias (except performance bias) found a result very similar to the main analysis even though there were many fewer participants (16 studies; 3282 participants; RR 0.71; 95% CI 0.57 to 0,88; I^2 = 0%) based on 128/1664 (7.7%) SSI in NPWT groups compared with 177/1618 (10.9%) in standard dressing groups. We ran this analysis to explore the impact of removing all studies with any domain at high risk of bias but retaining those where risk of bias in key domains was unclear; this is a common approach to sensitivity analysis in Cochrane reviews. A formal GRADE assessment for a post hoc analysis is not appropriate but this result, together with the prespecified analysis suggests that the result of the main analysis is likely to be robust to known high risk of bias in the studies contributing data.

The results of the primary analysis and the two sensitivity analyses (exploratory and a priori) are shown in Figure 5: as can be seen, the lower bound of the 95% CI appears unaltered by reductions in both numbers of participants and events and risks of bias. The estimate of effect shows limited sensitivity but the upper bound of the 95% CI moves towards the line of no effect as numbers of participants decrease and uncertainties around key risks of bias also decrease. This suggests that the widening of the confidence intervals is not simply a consequence of increasing imprecision but reflects a tendency for studies which are not known to be free from key biases to produce larger estimates of effect. It may also reflect the greater influence in the analysis of the low risk of bias WHIST trial which only assessed deep SSI.

Figure 5. Effect estimates for SSI: primary analysis and sensitivity analyses



Subgroup analyses

Of the prespecified subgroup analyses, we were only able to conduct the comparison based on different types of surgery: conducted in two different ways type of surgery (e.g. treatment of limb fractures; caesarean sections etc.) and contamination class. The results of these analyses are shown in Analysis 1.2 and Analysis 1.3. There was no clear evidence of a difference between the subgroups based on type of surgery (I^2 for subgroup differences = 44.3% and P associated with X^2 for subgroup differences = 0.08)) or between subgroups based on contamination classes (I^2 for subgroup differences = 38.3% and P associated with X^2 for subgroup differences = 0.18). The type of SSI assessed is not independent of the surgical indication (e.g. some fracture surgery studies focus on deep SSI) and we consider this below.

Types of SSI

In this update, we also looked at studies which reported separate data for superficial SSIs and for deeper infections (classed as deep or deep and organ space SSIs), or which only reported either superficial or deep infections. This is an exploratory analysis as we did not pre specify that we would assess the classes of infection identified separately. This analysis includes studies which reported more detailed information about the outcome of SSI or which specified that they would only include SSIs which were superficial or deep. For these analyses to be considered reliable, we would need to obtain this level of detail from all the included studies: this is very low-certainty evidence but these results suggest that we might usefully explore uncertainty as to whether NPWT acts equally for all types of SSI.

Superficial SSI: eighteen studies reported SSIs which were identified as being superficial. Where studies reported Szilagyi classification, we considered Szilagyi class I or II SSIs to be superficial. Fifteen of these (2783 participants) contributed data to a pooled estimate of effect. The RR was 0.58 (0.42 to 0.79); I^2 = 41% (Analysis 1.4).

Deep SSI: twenty studies reported SSIs which were identified as being deep. Where studies reported deep and organ/space SSIs separately, we combined these for this analysis. Where studies reported Szilagyi classification, we considered Szilagyi class III SSIs to be deep. Seventeen studies (4279 participants) contributed data to a pooled estimate of effect. The RR was 0.94 (0.71 to 1.25; I^2 = 0%) (Analysis 1.5).

Summary of findings for SSI

There is moderate-certainty evidence from a large number of participants across a range of surgical indications that NPWT following surgery probably results in a lower risk of SSI compared with standard dressings. This evidence was downgraded once due to risks of bias in various domains. In a sensitivity analysis which only included the six trials with low risk of bias in key domains (approximately one-third of the total participants), the evidence remains moderate certainty but shows a less clear difference between NPWT and standard dressings; this evidence was downgraded once due to imprecision.

Dehiscence (follow-up period 30 days to an average of 113 days or unspecified)

Eighteen studies reported dehiscence. We combined results from 14 studies (3809 participants) that compared NPWT with standard dressings. Low-certainty evidence suggests that there is no clear

difference in dehiscence between NPWT (102/1920 (5.3%)) and standard dressings (117/1889 (6.2%)) (RR 0.88; 95% CI 0.69 to 1.13; I^2 = 0%) (Analysis 1.6). The evidence was downgraded once for risk of bias and once for imprecision as the number of events was relatively low (219) despite the large number of participants; and the 95% CI included both benefit and harm as well as no effect.

Sensitivity and subgroup analyses

We applied a prespecified sensitivity analysis which included only the three studies (1552 participants) which reported dehiscence and were judged to be at low risk of bias in the key domains of randomisation, allocation concealment and blinding of outcome assessment. This did not substantially change the estimate of the effect of NPWT (RR 0.79, 95% CI 0.29 to 2.18; I^2 = 37%) based on 19/793 (2.4%) dehiscences in NPWT groups compared with 19/759 (2.5%) in standard dressing groups. The evidence remains low certainty as it is downgraded twice for very serious imprecision.

We have presented the analysis with studies arranged according to the type of surgery undertaken for information only; the number of studies in the analysis meant that some subgroups are represented by a single study and we have not undertaken any analysis of the effect of subgroups.

Summary of findings for dehiscence

Low-certainty evidence suggests no clear difference in dehiscence between participants treated with NPWT and those treated with standard dressings following surgery.

Secondary outcomes

Secondary outcome data are summarised in Table 2.

Reoperation (follow-up period 30 days to an average of 113 days or unspecified)

Fourteen trials assessed reoperation. We were able to combine data from 12 of these (3523 analysed participants). The pooled RR was 1.04 (95% CI 0.78 to 1.41; I^2 = 13%). This was low-certainty evidence which suggests that there is no clear difference in the incidence of reoperation between NPWT compared with standard dressings. Evidence was downgraded once for high risk of bias (various domains) and once for imprecision due to low numbers of events (136 reoperations in total) producing wide confidence intervals which include the possibility of both benefit and harm as well as no effect of the intervention. The WHIST 2019a study also reported much smaller numbers of subsequent surgeries as being due to wound complications; these data are shown in Table 2.

Wound-related readmission to hospital within 30 days (follow-up period 10 days to 90 days)

Eleven trials assessed wound-related readmissions. We were able to combine data from nine of these (1591 participants). The pooled RR was 0.88 (95% CI 0.57 to 1.35; I^2 = 0%). This is low-certainty evidence of no clear difference, downgraded twice for imprecision; low numbers of events resulted in wide confidence intervals which include the possibility of both benefit and harm as well as no difference between the groups. (Analysis 1.8).

Seroma (follow-up period 10 days to 6 weeks)

Nine trials reported the incidence of seroma. We were able to combine data from seven of these (729 participants). The pooled RR was 0.72 (95% CI 0.50 to 1.05; I^2 = 0%). This is low-certainty evidence of no clear difference, downgraded twice for imprecision due to low numbers of events resulting in wide confidence intervals which include both benefit and harm as well as no effect. (Analysis 1.9).

Haematoma (follow-up period 30 days to 6 weeks)

Thirteen studies reported on haematoma. We were able to pool data from nine trials (1202 participants). The effect of NPWT on haematoma is uncertain. The pooled RR was 0.67 (95% CI 0.28 to 1.59; I^2 = 0%). This evidence is very low certainty, downgraded once for risk of bias and twice for very serious imprecision; the number of events was very low (25) and this resulted in wide, fragile confidence intervals which included both the possibility of benefit and harm as well as no effect. (Analysis 1.10).

Skin blisters (follow-up period 6 weeks to 12 months)

Eight studies reported on skin blistering and we were able to pool seven of these with 796 participants. It is uncertain whether there is a higher risk of developing skin blisters with NPWT compared with standard dressings (RR 2.64; 95% CI 0.65 to 10.68; I^2 = 69%). An eighth study (Howell 2011) had unit of analysis issues and is reported in Appendix 4; this study was stopped early due to the high rate of blistering in the NPWT group. This evidence is very low certainty, downgraded once for inconsistency, once for risk of bias and twice for imprecision (Analysis 1.11).

Pain

Seven studies (2218 participants) assessed pain, but the data could not be pooled. One (Gombert 2018) stated that pain was assessed but did not report results of the assessment. Results from two of the studies reported "no difference" in pain (O'Leary 2017; Ruhstaller 2017). Another study (Gunatilake 2017) reported that there were more participants in the NPWT group with reductions in incisional pain both at rest (39/46 (84.8%) versus 20/46 (43.5%); P < 0.001) and with incisional pressure (42/46 (91.3%) versus 25/46 (54.3%); P < 0.001), compared with standard care. One study (Tuuli 2017) reported a lower pain level in the NPWT group (NPWT median = 0, interquartile range (IQR) = 0 to 1; standard dressing median = 1, IQR = 0 to 3; P = 0.02). The large (1549 participants) WHIST 2019a trial also reported median and interquartile ranges for each group assessed on a visual analogue scale (VAS) at three and six months postsurgery. The figures at three months were 3.0 (IQR 1.0 to 6.0) for the NPWT group compared with 4.0 (IQR 2.0 to 5.0) in the standard dressing group. At six months, the figures for the two groups were identical. The proportions of participants with neuropathic pain were also reported. Giannini 2018 reported pain at dressing change giving the mean, median and range for each group as NPWT 2.6, 2 (1 to 6) compared with 4.8, 5 (2 to 7).

Overall, the evidence is very low certainty, downgraded twice for imprecision and once for risk of bias. However, the evidence from the WHIST 2019a trial suggests that there is probably little difference between the groups after fracture surgery when assessed at three or six months (moderate certainty).

Quality of life

Quality of life was measured using a recognised scale by five studies (Chaboyer 2014; Hyldig 2019a; Karlakki 2016; Lee 2017a; WHIST 2019a). In four cases, these estimates were then used to inform calculations of QALY in subsequent or integrated cost-effectiveness analyses. The data from Chaboyer 2014 and Karlakki 2016 were not

reported although they were then used in the cost-effectiveness analyses. Another study Manoharan 2016 reported some data but did not use a validated scale; we have not analysed this further.

Lee 2017a reported EuroQol-5D (EQ-5D) scores for the NPWT group of 78 (26 participants) and 63 for the standard dressing group (17 participants). No measures of variance were reported and we could not analyse the data further.

Hyldig 2019a used the EQ-5D-5L and reported EQ-Index and EQ-VAS at 30 days together with 95% CI for each group of obese women having caesarean sections. The scoring algorithm was not reported but the Danish-specific context was considered. The mean difference in the EQ-Index was 0.00 (95% CI -0.01 to 0.01). For the EQ-VAS the mean difference was 1.00 (95% CI -1.23 to 3.23).

WHIST 2019a reported EQ-5D-3L; EQ-VAS and Disability Rating Index (DRI), each at both three and six months scored using the UK algorithm. We report the three-month data here (this is based on more participants); six-month data is detailed in Table 3. The mean and SD EQ-5D for the NPWT group was 0.5 (0.29) compared with 0.6 (0.30) in the standard dressing group giving a mean difference of -0.10 (95% CI -0.14 to -0.06). For the EQ-VAS, the results were 64.1 (22.24) compared with 64.7 (21.15) giving a mean difference of -0.60 (95% CI -3.28 to 2.08) but this difference was not sustained at six months. The results of the DRI were 51.6 (23.46) in the NPWT group compared with 51.1 (23.92) in the standard dressing group giving a mean difference of 0.50 (95% CI -2.50 to 3.50). Approximately 60% of the 1548 participants in the trial contributed to each estimate.

We have chosen not to pool the data from Hyldig 2019a and WHIST 2019a because of the very different surgical indications and time points of the assessments. This evidence is impacted on by the fact that it is not based on all the participants in WHIST but nevertheless is moderate-certainty evidence that, at relevant time points for each surgical indication, there is probably little clinically important difference in the quality of life of participants assessed by aspects of the EQ-5D.

Economic outcomes

We focus here on the relative cost-effectiveness of NPWT and standard dressings; the costs and QALY estimates which contribute to these are detailed in Table 3 and Appendix 5.

Using the CHEERS checklist (for a summary of ratings, see Table 4), we rated the overall quality of all the reports as very good, but the studies used different modelling assumptions. Results therefore depend on which resources are incorporated into the model, and on the cost-effectiveness threshold used. We note that large numbers of participants were included in the trials informing two of the analyses, providing evidence for key areas of obstetric and orthopaedic surgery. GRADE assessments were based on the RCTs which provided the clinical inputs to the assessments in all cases, and the utility data in all except one instance (costs were derived from a range of sources).

Incremental cost-effectiveness ratio (ICER)

All of the studies used QALY along with costs data to inform an estimate of relative cost-effectiveness.

In caesarean sections in obese women, Hyldig 2019b concluded that NPWT was dominant to standard dressings but did not report the base case ICERs (ICERs were reported for subgroups). Heard 2017 concluded that NPWT is probably cost-effective relative to standard care, estimating an ICER value of GBP 20.65 per QALY gained. This is moderate-certainty evidence downgraded once for imprecision.

In orthopedic surgery, the WHIST 2019b study reported a base case ICER of GBP 396,531 using an NHS/PSS perspective, other perspectives and sensitivity analyses produced higher estimates. Based on these estimated ICERs, NPWT was calculated to have a very low probability of cost-effectiveness at any willingness-to-pay threshold considered. This is high-certainty evidence assessed in terms of deep SSI; it is moderate-certainty evidence for SSI overall, downgraded once for indirectness.

Based on deterministic results, Nherera 2017 estimated that NPWT was dominant over standard dressings in hip or knee replacement surgery, as NPWT was cost-saving and improved QALYs.This was based on clinical data from the Karlakki 2016 trial from which utility estimates were also derived. This is low-certainty evidence downgraded once for imprecision and once for risk of bias.

In general surgery, in people undergoing CABG surgery, Nherera 2018 concluded that NPWT was dominant to standard dressings for both SSIs avoided and QALY gained but did not report the ICER. This was based on clinical data from the Witt-Majchrzac 2015 trial; but utility estimates were derived from the published literature. This is very low-certainty evidence downgraded twice for imprecision and once for risk of bias.

DISCUSSION

Summary of main results

Wound complications

This systematic review synthesises RCT evidence on the effects of NPWT on death, SSI and dehiscence following acute surgery in which wounds are primarily closed. We added 15 additional RCTs (4470 participants) to this third update, bringing the total number of RCTs to 44 (7447 participants). This is more than double the number of participants in the previous version of the review. We have also added three cost-effectiveness studies, bringing the total to five, and the number of participants included in source trials to 2811.

With the addition of a substantial number of RCTs - and a very substantial number of participants - there is moderate-certainty evidence that NPWT probably reduces the incidence of SSI in surgical wounds healing by primary closure. Sensitivity analyses suggested that the upper bound of the confidence interval may not be robust to the effects of risk of bias in the included studies. Evidence was downgraded once for high risks of bias across various domains in trials which contributed approximately half the participants in the analysis and when only studies with low risk of bias in key domains were considered the difference between the groups was not clear. Pre-planned subgroup analyses did not show clear evidence of differential effects across different types of surgery. Exploratory analysis of reported SSI data suggested that there is scope for investigating the types of SSI for which NPWT may be most effective; exploratory analysis of available data raises the possibility that superficial SSI is reduced with little difference in deep SSI. The results of the large high quality publicly funded WHIST trial in fracture surgery which only assessed deep SSI would tend to support this.

Whilst we found moderate-certainty evidence suggesting that, compared with standard dressings, NPWT probably results in fewer SSI, the evidence for our other primary outcomes - mortality and dehiscence - was low certainty and showed no clear differences between the groups. In the case of mortality, the evidence was downgraded twice for imprecision, as low numbers of events made for very wide confidence intervals which included the possibility of both benefit and harm as well as no effect. For dehiscence, we downgraded once for imprecision and once for risks of bias across various domains; certainty remained low in a sensitivity analysis including only trials with low risks of bias in key domains as it was then downgraded twice for imprecision.

For our secondary outcomes, we generally found no clear difference. There is low-certainty evidence that there may be little or no difference between NPWT and standard dressings for the outcomes of reoperation, readmission, and seroma. For haematoma and skin blisters, we are uncertain what the effect of NPWT is compared with standard dressings because the evidence was very low certainty. Evidence was downgraded because of imprecision due to small numbers of events and in some cases also because of risks of bias across various domains. Inconsistency was also present in the analysis of blistering. For pain, the evidence was disparate, being reported for different time points and using different measures; in many cases, it was very poorly reported. Where data were available, most studies, including the large and well-conducted WHIST trial, found little difference between the groups. This is very low-certainty evidence overall, downgraded for imprecision and risk of bias across most studies, but the evidence from WHIST is of moderate certainty. For quality of life, there is moderate-certainty evidence that there is probably little difference in EQ-5D scores between participants treated with NPWT and standard dressings at time points relevant to the surgery involved.

Economic outcomes

Five economic studies, Heard 2017; Hyldig 2019b; Nherera 2017; Nherera 2018; WHIST 2019b, based on results from five RCTs, Chaboyer 2014; Hyldig 2019a; Karlakki 2016; WHIST 2019a; Witt-Majchrzac 2015, compared the cost-effectiveness of NPWT with standard dressings. The economic evaluations used different methods and different perspectives and relied on source data from very different trials. The economic studies were well reported but our further assessment of the certainty of the evidence rests on our assessments of the trials which contributed clinical data to the models. The trials on which the economic analyses were based varied considerably. While the sample sizes of three of the studies were relatively small (80 to 220 participants) (Chaboyer 2014; Karlakki 2016; Witt-Majchrzac 2015), in two cases the trials were large; Hyldig 2019b was based on a trial in 876 women whilst WHIST 2019b used data from a trial which enrolled 1548 participants with lower limb fractures. Two studies were at low risk of bias other than performance bias (Chaboyer 2014; WHIST 2019a). In Hyldig 2019a, one domain was at unclear risk of bias and one at high risk while Karlakki 2016; and Witt-Majchrzac 2015 had multiple domains with high or unclear risks of bias. The type of SSI considered in the clinical and cost-effectiveness analyses also differed between the trials; the WHIST 2019a trial considered only deep SSI whilst all the other studies considered all types of SSI and superficial SSI predominated.

Results of the analyses based on these trials also differed. Three studies across three different surgical indications (caesarean section in obese women; joint arthroplasty and CABG) found that NPWT was a dominant strategy (Hyldig 2019b; Nherera 2017; Nherera 2018). However, Heard 2017 reported that total costs for the episode of care in caesarean section were higher with NPWT than with standard dressings and found that value for money from NPWT was relatively low. In the WHIST 2019b study, NPWT was not cost-effective in fracture surgery at any threshold of willingness-to-pay.

The measurement of costs was reasonable in all studies although different healthcare system perspectives were employed. The measurement of health states, using the SF-12 version 2 in Heard 2017, the SF-36 in Nherera 2017, and versions of the EQ-5D in Hyldig 2019b and WHIST 2019b was also reasonable. However, the approach to scoring the SF-36 in Nherera 2017, which used a non-preferenced based algorithm developed in the 1990s, is questionable, especially since the SF-6D, a preference-based scoring algorithm for the SF-36 with country-specific weights for the UK (Kharroubi 2007), the USA (Craig 2013), and other countries, is available. Without using a preference-based scoring system, the gains in QALYs estimated by Nherera 2017 may have been over- or understated. In Nherera 2018, the valuations of health states were derived from published literature rather than from the trial participants.

All cost-effectiveness estimates should be interpreted in the context of the certainty of the clinical evidence base. In the case of NPWT in primary closure of surgical wounds, this is judged to be moderate or low for most outcomes with very low-certainty evidence for some outcomes which are likely to be important to patients, such as blistering of the skin and pain. The largest trial with a low overall risk of bias supported an analysis which did not find NPWT to be cost-effective while a small trial with low risks of bias supported an analysis which showed low value for NPWT. The less certain evidence from other trials supports analyses which found NPWT was cost-effective. Consequently, there is moderate-certainty evidence that NPWT is probably not cost-effective for fracture surgery, high-certainty evidence that it is not cost-effective if only deep SSI are considered, and moderate-certainty evidence that it probably is cost-effective for caesarean sections in obese women. Evidence for cost-effectiveness in arthroplasty or CABG surgery is low and very low certainty, respectively.

Overall completeness and applicability of evidence

Indications for the use of NPWT following surgery are broadening (Acosta 2017; DeCarbo 2010; Pellino 2015; Webb 2017), with a range of new systems on the market, including those designed for use on closed, clean wounds (Allen 2011; Gabriel 2014; Gupta 2016).

Studies included in this review used NPWT across a wide range of surgical indications. However, the majority of the participants were undergoing a small number of procedures - orthopaedic surgery for either limb fracture or knee/hip arthroplasty and obstetric surgery (caesarean section) each represent approximately 25% of participants in the review, and peripheral vascular surgery represents almost 10% of participants. Although other procedures were represented, there is proportionally much less evidence for these.

While many trials were small (half had fewer than 100 participants), there were a number of large studies. Eight trials had more than 200 participants; three had more than 400 and one randomised over

1500 people. The three largest trials together accounted for almost 40% of the participants and were undertaken in the two areas most represented in the review: caesarean section and fracture surgery.

Because of the number of trials and the number of participants in caesarean section surgery, there are several substantial trials enrolling only women in the review and a majority of the women in these studies were obese. Since obese patients have higher rates of SSI (Althumairi 2016), these studies represent a population of particular interest. There were no studies involving children.

The magnitude of the negative pressure applied varied between trials and it is unclear whether different pressures produce different outcomes. Animal studies indicate that performance is similar across the range of pressures used in the included trials (Morykwas 2001).

Another limitation in the studies was the variation in durations of follow-up, which ranged from the 10th postoperative day to 12 months after surgery. This is partly the result of the different level of follow-up appropriate to different surgical indications - for instance, the two largest trials were in lower limb fracture surgery and caesarean; longer follow-up is required for the former indication compared with the latter. However, in many cases short duration of follow-up is likely to have missed instances of SSI and other events occurring after discharge from hospital and may contribute to an under-estimation of SSI incidence in both the NPWT and standard dressing groups. Description of the criteria used for SSI diagnosis and other events also varied and was sometimes absent, meaning that the true comparability of events between trials is uncertain.

In some cases, we know that trials only assessed deep SSI. In particular, the largest study, the WHIST trial, only assessed deep SSI. Evidence from our exploratory analysis of trials reporting events which we know to be superficial or deep from the trial reports suggests that there may be a differential effect, with NPWT having a greater impact on superficial than deep infections. This would be important to explore given the proportionally greater clinical impact of deep infections.

Cost-effectiveness evidence was limited to trial-based evaluations using evidence from RCTs included in the effectiveness review. Inclusion of other relevant, high quality studies using model-based evaluations (drawing on different types of evidence) might change the cost-effectiveness evidence base. We did not, however, identify any such studies in the searches conducted for this review.

Finally, the included studies were limited, as although there was a wide geographical spread, almost all the studies were from higher income countries.

Quality of the evidence

The certainty of the evidence is moderate for the primary outcome of SSI but low for the primary outcomes of mortality and dehiscence. Evidence for most secondary outcomes is low or very low, due to risks of bias, small sample sizes, and wide confidence intervals that included both an effect and no effect or even a harm of the intervention. There is moderate-certainty evidence for quality of life in two indications and for pain in one indication. The evidence for cost-effectiveness is moderate certainty that NPWT is probably not cost-effective in fracture surgery and low or very low-certainty evidence that it may be cost effective in other indications.

Limitations in study design, implementation and reporting

We assessed risk of bias 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 found that all but three of the included studies, Chaboyer 2014; Gillespie 2015; WHIST 2019a, showed limitations in study design and implementation or reporting of these, which have been reported elsewhere in the review (Figure 3). We had particular concern, where blinding of the intervention is difficult or impossible, that there was subsequent uncertainty about allocation concealment and blinding of outcome assessment. We assumed the risk of performance bias to be unclear unless there was information to the contrary and we did not downgrade for high risk of performance bias alone. We did downgrade for high risk of bias in all other domains including detection bias where a substantial number of studies had a high risk. A number of studies used non-standard designs and it was not clear that these were adequately accounted for in the authors' analyses. Where this was the case, we did not include the studies in the meta-analyses we conducted but reported them separately; this included several studies which adopted an intra-individual (split-body) approach analogous to the 'split-mouth' design (Lesaffre 2009).

Another consideration was the involvement of industry in at least 23 (where reported) of the 44 included trials. Authors from the Karlakki 2013 trial disclosed conflicts of interest, with all benefiting from funding from the manufacturer of the NPWT device. There continues to be a concern with the issue of manufacturer sponsorship in studies of healthcare products. For example, a review of the effect of manufacturer involvement on studies of NPWT examined 24 studies where 19 had manufacturer involvement. Importantly, 18 of the 19 manufacturer-funded studies showed a positive effect for the manufacturer's product, while one was "impartial" (Kairinos 2014).

Indirectness of evidence

There was no indirectness, as the participants, interventions, and outcomes in the included studies were within the scope of the published review protocol. However, the evidence may not be directly relevant to children undergoing surgery. The high proportion of the participants in particular surgical indications may also be considered in assessing the relevance of the review to a particular population, although we did not find evidence of statistical differences in the effect estimates between different types of surgery.

Unexplained heterogeneity or inconsistency of results

Statistical heterogeneity was low for almost all of the outcomes we assessed and, although there was substantial clinical heterogeneity, subgroup analysis for the primary outcome suggests that this did not substantially impact on our results. There was also variation in aspects of clinical methods, with negative pressure devices, control dressings, length of follow-up and definition of SSI varying between studies but the low levels of statistical heterogeneity in our analyses - and visual inspection of forest plots - suggest that, with the exception of the outcome of skin blistering, these factors did not substantially impact on effect estimates. We consider that differences in study characteristics may be responsible for some of the variability which was observed, as larger trials with less risk of bias were not evenly distributed across

surgical indications. We also consider that the type (severity) of SSI considered may be a potential source of heterogeneity, based on exploratory analyses, and that further research is required in this area. The type of SSI assessed and reported was not independent of the surgical indication evaluated and this needs to be taken into account when considering these results. Standardised methods for assessing and reporting pain in studies of NPWT are needed to improve the evidence base in this important outcome.

Imprecision of results

This update of our review included a large number of participants from newly identified trials. The confidence intervals for the primary outcome of SSI were not large but they are relatively wide in view of the number of participants now included in our analysis. Confidence intervals were wide in all of the other pooled outcomes, with most crossing 1, indicating uncertainty about whether NPWT was associated with an increase or reduction in outcomes. The imprecision was due to studies being underpowered to assess what in many cases were uncommon events. The low certainty of the evidence for most outcomes stems wholly or partly from this imprecision. However it may be that case that NPWT does have little or no effect on some of the outcomes assessed and that this is accurately reflected in confidence intervals which cross the line of no effect.

Publication bias

We feel confident that our comprehensive electronic searches, coupled with reference checking and cross-checking of trial registry searches, identified all existing, published RCTs addressing the review question, helping to limit bias in the review process. The funnel plot (Figure 4) includes all published studies that reported on SSI, but a failure to include results from any unpublished studies may have affected the plot's relative symmetry. However, there are a large number of studies (88 ongoing trials) identified primarily through a search of the clinical trial registries. Whilst many of these are ongoing, or were scheduled to conclude only recently, there are a number which have concluded some time previously but have not yet been published or had results uploaded to the registry.

Potential biases in the review process

Clearly described procedures were followed to prevent potential bias in the review process. We conducted a careful literature search, and the methods we used were transparent and reproducible. It is possible that studies published in journals that were outside our search strategy may have been missed. We attempted to contact ten authors, but only two responded. Consequently, we may have underestimated the quality of some studies, simply because their publications did not include the information we required to assess study quality. We have already mentioned our concern about commercial funding, which may have influenced the results of our review. Three of the authors of previous versions of this review (Webster, Chaboyer, and Scuffham) were also investigators of studies included in the review (Chaboyer 2014; Gillespie 2015; Heard 2017). We were careful to ensure that the trials in which they were involved were critically appraised and that the data were extracted by others. None of the authors of this review has any conflicts of interest or associations with manufacturers of products included in the review. Differences between the published protocol, previous versions of this review (Webster 2011), and the methods used for this update have been described, and a rationale provided in the Differences between protocol and review section.

Agreements and disagreements with other studies or reviews

One early systematic review of NPWT included chronic and acute wounds and was published before seven of our included trials were undertaken (Ubbink 2008); it also included an earlier trial that we excluded from our review (Moisidis 2004), so results are not comparable. Our findings also differ from those of two other systematic reviews that evaluated the effectiveness of NPWT for incisional wounds. Important differences in the inclusion criteria account for the differences: the first review included 10 RCTs and five observational studies (Ingargiola 2013), and the second review included 33 publications, seven of which were RCTs, with the remainder consisting of a combination of non-comparative case series, comparative cohort studies, and comparative laboratory studies (Karlakki 2013). The most recent systematic review of NPWT for closed surgical wounds included 10 trials and found a reduction in the rate of SSI and seroma in the NPWT group (Hyldig 2016). The review included one trial (Grauhan 2013), which we excluded because it was a quasi-RCT. It also included data that the author obtained from personal correspondence with the investigator of an unpublished trial, to which we had no access. More recent systematic reviews have focused on specific surgical indications (caesarean section, laparotomy) and have included non-randomised studies as well as RCTs (Sahebally 2018; Yu 2018). Although we have included many more RCTs, our conclusions are consistent with previous general reviews including RCTs; that is, that the quality of the studies may limit any firm conclusions regarding the relative effectiveness of NPWT and standard dressings while the results of further RCTs are likely to affect findings. This conclusion is consistent with evidence-based recommendations for the use of NPWT, which cover a range of applications, including NPWT for acute wounds (Krug 2011), but differs from the latest World Health Organization (WHO) guideline for the prevention of surgical site infection (WHO 2016). The WHO guideline states: "The panel suggests the use of prophylactic negative pressure wound therapy (pNPWT) in adult patients on primarily closed surgical incisions in high-risk wounds". However, the recommendation was labelled "conditional" based on a number of issues, including low-quality evidence and the inclusion of non-RCT evidence. Finally, Willy 2017 published international multidisciplinary consensus recommendations suggesting the use of NPWT for a number of patient categories, including those at high risk of SSI. The review contained 100 studies (including RCTs, case series, editorials, cohort studies, technical reports, systematic reviews, and expert opinion), so the conclusions are highly uncertain. In addition, two employees of Acelity, NPWT device manufacturers, were involved in preparing the manuscript, and all of the authors of the review are consultants to an Acelity company (Willy 2017).

AUTHORS' CONCLUSIONS

Implications for practice

NPWT for surgical wounds healing by primary closure probably reduces the rate of SSI compared with standard wound dressings. This conclusion is based on moderate-certainty evidence which was affected by high risk of bias in approximately half the included trials. Although there were some large, generally well-conducted studies included in the review, these were concentrated in a few surgical indications (caesarean section, fracture surgery, hip and knee arthroplasty and abdominal surgery). A concomitantly high

proportion of the participants were undergoing these procedures. Although we did not find evidence for substantial differences between the different types of surgery, this weighting should be borne in mind. There may be no or little difference in the occurrence of many important complications associated with surgical incisions, including mortality, dehiscence, reoperation, readmission to hospital and seroma (low-certainty evidence of no clear effect). The effects of NPWT on the incidence of haematoma, skin blisters and pain are uncertain. NPWT probably does not substantively alter quality of life scores following fracture surgery or caesarean section. Estimates of cost-effectiveness should be interpreted in the context of the healthcare system, the surgical indication and the uncertainty underlying the studies on which the modelling is based.

Implications for research

Use of NPWT for closed surgical incisions remains a topic of interest, with a very large number of records of ongoing studies identified in our review of clinical trials registries. In particular, a very large study of NPWT in caesarean section is underway (NCT03009110). Review updates will be required to include the data from trials as they become available. A living systematic review may be an appropriate undertaking given the rapidly increasing volume of literature and the number of currently ongoing studies, while sharing of individual participant data from studies would contribute to understanding of circumstances in which NPWT may be beneficial. If further new trials are undertaken - perhaps in surgical indications with relatively sparse data and a high incidence of SSI - the type (severity) of SSI should be recorded using recognised classifications. There is scope for research to use the data from the extant and ongoing studies to identify the types of SSI which may be most likely to be avoided if NPWT is used. Such research may also support the investigation of mechanisms which may underlie the potentially differential effects of NPWT on different types of SSI. The risk of SSI occurring varies across surgical indications and the impact of superficial and deep SSI differ both clinically and from a cost-effectiveness perspective; these factors should be considerations in further exploration of existing data and in any new primary research.

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

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

Bobkiewicz 2018

Study characteristics	
Methods	**Study design:** randomised controlled trial **Study grouping:** parallel **Ethics and informed consent:** Not reported **Follow-up period:** Not reported **Sample size estimate:** Not reported **ITT analysis:** yes,**number randomised:** 30, **number analysed:** 30 **Funding:** Not reported **Preregistration:** Not reported
Participants	**Location:** Poland **Intervention group:** 15**control group:** 15 **Mean age:** not reported **Inclusion criteria:** People undergoing surgery for stoma reversal **Exclusion criteria:** Not reported
Interventions	**Aim/s:** to investigate the efficiency of closed incision negative pressure wound therapy (ciNPWT) portable system on the incidence rate of SSI after stoma reversal surgery **Group 1 (NPWT) intervention:** closed incision negative pressure wound therapy portable system changed every 3 days or earlier in case of unsealed system or absorbed entirely with wound exudate **Group 2 (control) intervention:** standard dressing changed every day **Study date/s:** Not reported
Outcomes	• SSI • Wound dehiscence • Haematoma **Validity of measure/s:** Superficial SSI was defined according to definition of Centers for Disease Control and Prevention. **Time points:** Not reported
Notes	Abstract only

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	No information provided
Allocation concealment (selection bias)	Unclear risk	No information provided

Bobkiewicz 2018 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	No information provided but, for both participants and personnel, frequency of dressing changes differed systematically meaning blinding was unlikely to be successful
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No information provided
Incomplete outcome data (attrition bias) All outcomes	Low risk	All randomised participants included in analysis for SSI
Selective reporting (reporting bias)	High risk	Partial reporting of some outcomes
Other bias	Unclear risk	Insufficient information to determine if there was additional risk of bias

Chaboyer 2014

Study characteristics	
Methods	**Study design:** randomised controlled trial **Study grouping:** parallel **Ethics and informed consent:** yes **Follow-up period:** 6 weeks **Sample size estimate:** pilot study **ITT analysis:** yes, **number randomised:** 92, **number analysed:** 87 **Funding:** non-industry **Preregistration:** yes
Participants	**Location:** Queensland, Australia **Intervention group:** n = 35,**control group:** n = 35 **Mean age: intervention group** = 30.6 years (IQR 5.5),**control group** = 30.7 years (IQR 5.0) **Inclusion criteria:** booked for elective caesarean section; pre-pregnancy BMI ≥ 30; able to provide consent **Exclusion criteria:** women whose condition changed to require urgent caesarean section; previous participation in the trial; existing infection
Interventions	**Aim/s:** to assess the feasibility of a definitive RCT to test the effectiveness and safety of prophylactic NPWT in obese women after caesarean section **Group 1 (NPWT) intervention:** PICO dressing applied over the primarily closed incision by the surgeon in the operating room. Dressing was left on for 4 days or longer if drainage continued, unless soiled or dislodged. **Group 2 (control) intervention:** Comfeel dressing applied over the primarily closed incision by the surgeon in the operating room. Dressing was left on for 4 days or longer if drainage continued, unless soiled or dislodged. **Study date/s:** July 2012 to April 2014
Outcomes	• surgical site infection

Chaboyer 2014 *(Continued)*

- type of SSI
- hospital readmission
- dehiscence; blisters
- haematoma

Validity of measure/s: CDC definitions and criteria for superficial, deep, and organ/space SSI were used for the primary outcome and SF-12 for quality of life.

Time points: 1, 2, 3, and 4 weeks postsurgery

Notes

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote "computer generated 1:1 ratio with blocks of randomly varying sizes"
Allocation concealment (selection bias)	Low risk	A centralised web-based randomised service was accessed.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	There was no information on this.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote "a separate person ... assessed the outcome and was blinded to the allocation".
Incomplete outcome data (attrition bias) All outcomes	Low risk	2 women in the intervention group and 3 in the control group were lost to follow-up, but an ITT analysis was used.
Selective reporting (reporting bias)	Low risk	Planned outcomes reported. Protocol registered on ANZCTR
Other bias	Low risk	No other biases detected

Crist 2014

Study characteristics

Methods

Study design: randomised controlled trial
Study grouping: parallel

Ethics and informed consent: ethics approved and consent obtained

Follow-up period: 12 months

Sample size calculation: not stated

ITT analysis: available-case analysis

Funding: non-industry

Crist 2014 *(Continued)*

	Preregistration: yes
Participants	**Location:** USA **Intervention group:** n = 55,**control group:** n = 60 **Mean age: intervention group** = 47.2 years (SD 19.6),**control group** = 48.3 years (SD 20.1). Data extracted from results section of ClinicalTrials.gov (NCT00635479) **Inclusion criteria:** patients that had undergone an open surgical exposure for hip, pelvis, or acetabular fracture **Exclusion criteria:** none stated
Interventions	**Aim/s:** 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 **Group 1 (NPWT) intervention:** quote "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". **Group 2 (control) intervention:** quote "standard gauze dressing"; description not provided **Study date/s:** not provided
Outcomes	• infection • LOS • total serious adverse events **Validity of measure/s:** not provided **Time points:** followed for 12 months
Notes	Conference abstract. Additional information provided by the investigator and from a search of ClinicalTrials.gov (NCT00635479).

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	**Evidence:** quote "computer randomization" **Comment:** correspondence with author
Allocation concealment (selection bias)	Unclear risk	**Evidence:** quote "opaque sealed envelope opened in the OR" **Comment:** correspondence with author; but unclear whether envelopes were sequentially numbered?
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Insufficient information
Blinding of outcome assessment (detection bias) All outcomes	Low risk	**Evidence:** quote "yes" **Comment:** correspondence with author
Incomplete outcome data (attrition bias) All outcomes	High risk	**Evidence:** quote "55 patients randomised to the NPWT group and 60 patients randomised 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". **Comment:** 10.9% participants in NPWT group and 30.0% of those in control group were lost to follow-up.

Crist 2014 *(Continued)*

Selective reporting (reporting bias)	Unclear risk	**Comment:** protocol registered on ClinicalTrials.gov with identifier (NCT00635479). Expected outcomes were reported in the abstract, but other outcomes specified 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	**Comment:** no other biases detected

Crist 2017

Study characteristics	
Methods	**Study design:** randomised controlled trial **Study grouping:** parallel **Ethics and informed consent:** ethics approved and consent obtained **Follow-up period:** not stated **Sample size calculation:** not stated **ITT analysis: number randomised:** 71, **number analysed:** 66 **Funding:** no external funding **Preregistration:** not stated
Participants	**Location:** USA **Intervention group:** n = 33, **control group:** n = 33 **Mean age (range): intervention group** = 44 (19 to 87), **control group** = 43 (18 to 92) **Inclusion criteria:** patients at least 18 years of age with an acetabular fracture that required ORIF **Exclusion criteria:** less than 18 years old; pregnant; unable to provide informed consent; or if their injury could be treated nonoperatively or percutaneously
Interventions	**Aim/s:** to determine if iNPWT decreased the risk of deep infection when used over primarily closed surgical incisions for acetabular fracture ORIF **Group 1 (NPWT) intervention:** iNPWT (VAC; KCI, San Antonio, TX) over their surgically closed incision **Group 2 (control) intervention:** a standard postoperative (dry gauze) dressing **Study date/s:** March 2008 to September 2012
Outcomes	• infection **Validity of measure/s:** the clinical diagnosis of infection was determined from the drainage at the operative site in addition to 1 or more of the classic signs and symptoms of inflammation (redness, heat, swelling, pain). Deep infections were those that required operative debridement. Bacteriological cultures obtained at the time of operative debridement. **Time points:** 10 to 21 days, 6 weeks, 12 weeks, and every 6 to 8 weeks thereafter until bony union occurred
Notes	

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**

Crist 2017 *(Continued)*

Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "we did not blind the patients and staff to treatment group." Comment: No blinding of personnel or participants
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Approximately 7% of participants were lost to follow-up; reasons for losses were not reported. No more information provided
Selective reporting (reporting bias)	Low risk	Expected outcomes reported
Other bias	Low risk	None detected

DiMuzio 2017

Study characteristics	
Methods	**Study design:** randomised controlled trial **Study grouping:** parallel **Ethics and informed consent:** not provided **Follow-up period:** 30 days **Sample size calculation:** not stated **ITT analysis: number randomised:** 120, **number analysed:** 120 **Funding:** not stated **Preregistration:** not stated
Participants	**Location:** Philadelphia, USA **Intervention group (high risk):** n = 59,**control group (high risk):** n = 60, **(3 arms: low risk:** n = 21**)** **Mean age:** not provided **Inclusion criteria:** femoral incisions closed primarily following elective vascular surgery **Exclusion criteria:** none stated
Interventions	**Aim/s:** to prospectively evaluate negative pressure therapy as a means to decrease wound complications and associated healthcare costs **Group 1 (NPWT) intervention:** NPWT **Group 2 (control) intervention:** standard gauze dressing **Study date/s:** not provided

DiMuzio 2017 *(Continued)*

Outcomes	• infection • LOS • reoperation • readmission **Validity of measure/s:** not provided **Time points:** over 30 days
Notes	Conference abstract

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	No information reported
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	140 (3 arms) were enrolled and analysed.
Selective reporting (reporting bias)	Low risk	Planned outcomes reported
Other bias	Unclear risk	No other biases detected.

Engelhardt 2016

Study characteristics

Methods	**Study design:** randomised controlled trial **Study grouping:** parallel **Ethics and informed consent:** ethics approved and consent obtained **Follow-up period:** primary endpoint of the study was the occurrence of SSIs **Sample size calculation:** not stated **ITT analysis:** no **number randomised:** 141, **number analysed:** 132 **Funding:** not stated **Preregistration:** not stated

Engelhardt 2016 *(Continued)*

Participants	**Location:** Germany **Intervention group (high risk):** n = 64,**control group (high risk):** n = 68 **Mean age (range): intervention group** = 72 (64 to 75),**control group** = 70 (60 to 78) **Inclusion criteria:** all consecutive patients scheduled for vascular surgery with a femoral cutdown; age > 18 years and the need for an open, nonemergency surgical procedure for peripheral arterial disease or aneurysm involving the femoral artery using a longitudinal femoral cutdown in the groin **Exclusion criteria:** dementia (not capable of informed consent) and declining to participate
Interventions	**Aim/s:** to determine whether closed-incision negative pressure therapy is able to reduce SSI rate in the groin after vascular surgery **Group 1 (NPWT) intervention:** NPWT was applied on the closed skin intraoperatively. The system is comprised of a therapy unit containing a pump with a 45-millilitre canister delivering a continuous negative pressure of 125 mmHg and a self adhesive dressing with a foam bolster that manifolds the negative pressure to the incision area. A special polyester interface layer protects the skin from direct contact with the foam bolster, while at the same time allowing delivery of negative pressure and fluid removal. **Group 2 (control) intervention:** absorbent adhesive dressing **Study date/s:** January 2012 and October 2014
Outcomes	• infection **Validity of measure/s:** all wounds were documented with photos and classified according to the Szilagyi classification. Grade I infections only involved the skin (dermal infection); grade II extended to the subcutaneous tissue without reaching the vessels; and grade III finally involved the artery or bypass. **Time points:** 5th postoperative day and 6 weeks after surgery
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Random assignment of the participants to the 2 treatment groups was performed according to an external randomisation sequence.
Allocation concealment (selection bias)	Low risk	Sealed randomisation envelopes were provided by an external institution. On eligibility confirmation, the sequential randomisation envelope was opened, and the assignment was allocated.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Insufficient information
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "all wounds were documented by photography and classified according to the Szilagyi classification". **Comment:** unclear whether outcome assessment was blinded
Incomplete outcome data (attrition bias) All outcomes	High risk	ITT not used; 141 participants were randomised, and 132 completed the study; 9 participants (6%) did not complete follow-up due to urgent reoperation or death during follow-up.
Selective reporting (reporting bias)	Low risk	Planned outcomes reported

Engelhardt 2016 *(Continued)*

Other bias	Low risk	None detected

Galiano 2018

Study characteristics	
Methods	**Study design:** randomised controlled trial **Study grouping:** Intra-individual (split person) **Ethics and informed consent:** ethics approval was first obtained at the institution of the principal investigator (R.D.G.), institutional review board at Northwestern University, Chicago, (STU00062369 - 5/22/2012), and at each of the other sites. Before entry into the study, all patients signed informed consent forms. **Follow-up period:** 21 days (90 days) **Sample size estimate:** 197 patients would be required to detect an absolute difference of 10% in the complication rate between bilateral breasts treated either with NPWT or SC dressings, assuming 20% of wounds treated with SC dressings and 10% of wounds treated with NPWT develop a healing complication (a 50% reduction) and that there were 26% discordant pairs. This is on the basis of a 2-sided McNemar's test at the α = 5% level of significance and 80% power. The sample size was rounded up to 200. **ITT analysis:** yes, **number randomised:** 200, **number analysed:** 199 **Funding:** Smith & Nephew Wound Management, Inc. **Preregistration:** registered under the name "A prospective, randomised, intra-patient, comparative, open, multi-centre study to evaluate the efficacy of a single-use negative pressure wound therapy (NPWT) System on the prevention of postsurgical incision healing complications in patients undergoing reduction mammaplasty," ClinicalTrials.gov identification number NCT01640366 (http://clinicaltrials.gov/show/NCT1640366)
Participants	**Location:** Multi-centre across 6 sites – United States (n = 3), France (n = 1), South Africa (n = 1), Netherlands (n = 1) **Intervention group:** n = 199, **control group:** n = 199 **Mean age:** 35.7 (18–65), **intervention group:** 35.7 (18–65), **control group:** 35.7 (18–65) **Inclusion criteria:** women aged > 18 years who had undergone elective surgery for bilateral reduction mammaplasty and having postsurgical incisions of similar length on each breast were included in the study. **Exclusion criteria:** presurgical – pregnancy or lactation, using steroids or other immune modulators known to affect healing, history of radiation of the breast, tattoos in the area of the incision, skin conditions such as cutis laxa that would result in poor healing or widened scars, patients with a known significant history of scar problems (i.e. hypertrophic scarring or keloids), and known allergies to product components. Postsurgical – incisions still actively bleeding and incisions > 12 inches (30 cm) maximum linear dimension
Interventions	**Aim/s:** To assess the efficacy and cost-effectiveness of the Single-Use Negative Pressure Wound Therapy (NPWT) system (PICO) with regard to the reduction of postsurgical incision healing complications during the immediate postoperative treatment phase, and to assess the medium-term aesthetic appearance and quality of the resultant scar, in patients undergoing reduction mammoplasty, compared with standard care **Group 1 (NPWT) intervention:** The NPWT device was PICO (Smith & Nephew Medical Limited, Hull, United Kingdom), a portable, single- use (disposable after 7 days) NPWT system delivering -80mm Hg (nominal) negative pressure to the wound surface. Treatment commenced on day 0 and lasted up to 14 days. The pump has a 7-day lifespan, and the associated PICO NPWT dressing is left in place up to 7 days. Each PICO kit comes with 2 NPWT dressings, so, according to the needs of the individual patient and the level of exudate, dressing changes were permitted before 7 days at the investigator's clinical judgement. Participating physicians were advised to discontinue treatment on day 14 and return patients to SC (see below) if the incision was still not closed at this time point. **Group 2 (control) intervention:** 3M STERI-Strip (3M Health Care, St. Paul, Minn.). STERI-Strips were placed along the entire axis of the incision and covered with a dry gauze dressing or nonadherent dressing. Alternatively, investigators could use a nonadherent dry dressing if STERI-Strips were not deemed appropriate by the principal investigator at that site.

Galiano 2018 *(Continued)*

	Study date/s: 1 June 2012 to 9 April 2014
Outcomes	• SSI • Dehiscence • Haematoma • Seroma **Validity of measure/s:** N/R **Time points:** 21 days after surgery
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote “Treatment randomization was within-patient (i.e., right or left breast) via a central Web site, www.SealedEnvelope.com”. Comment: Computerised generation of randomisation sequence
Allocation concealment (selection bias)	Low risk	Quote “Treatment randomization was within-patient (i.e., right or left breast) via a central Web site, www.SealedEnvelope.com”. Comment: Centralised service used for allocation
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote "Treatment could not be blinded". Comment: Participants and personnel could not be blinded.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Quote "Treatment could not be blinded". Comment: This was stated as a limitation for personnel and there was no information that another individual performed the outcome assessment.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: Low attrition rate; only one participant was not included in the analysis
Selective reporting (reporting bias)	Low risk	Comment: All prespecified outcomes reported
Other bias	Unclear risk	Comment: Unclear if the analysis took account of the paired data resulting from the split-person design

Giannini 2018

Study characteristics

Methods	**Study design:** randomised controlled trial **Study grouping:** parallel **Ethics and informed consent:** ethics approved and consent obtained **Follow-up period:** 7 days

Giannini 2018 *(Continued)*

	Sample size estimate: power analysis based on 80% chance of detecting decrease in ASEPSIS score from 10 to 5 **ITT analysis:** per protocol analysis, **number randomised:** 110, **number analysed:** 100 **Funding:** Smith & Nephew **Preregistration:** not reported
Participants	**Location:** Italy (single site) **Intervention group:** 58,**control group:** 52 **Mean age: intervention group** 66.0 (8.9),**control group** 66.8 (11.5) **Inclusion criteria:** patients aged 40–80 years old, indicated for hip or knee revision performed through the same surgical approach of primary surgery (hip: direct lateral approach, knee: medial parapatellar approach) **Exclusion criteria:** patients undergoing revision surgery due to periprosthetic fracture or prosthetic joint infection, antibiotic therapy within the last month; declined to take part in the study
Interventions	**Aim/s:** To compare the effectiveness in wound healing of negative pressure wound therapy versus a standard dressing in patients who underwent hip or knee revision surgery **Group 1 (NPWT) intervention:** single use, 80mmHg sub-atmospheric NPWT dressing (PICO, Smith & Nephew, UK) changed only if the dressing was completely saturated with fluids **Group 2 (control) intervention:** a traditional povidone-iodine gauze and patch wound dressing (a sterile folded non-woven gauze swabs, Rays Spa, Italy, and Hypafix dressing retention tape, Essity Aktiebolag, Sweden) changed depending on the wound leakage **Study date/s:** February 2013 to June 2015
Outcomes	• SSI: The severity of wound infection measured by the ASEPSIS score - a quantitative scoring method using objective criteria based on wound appearance to evaluate wound infection (higher score = worse wound healing; a score > 10 = the increasing probability and severity of infection) • Pain (VAS) at dressing change • Blisters **Validity of measure/s:** The reference for the ASEPSIS score was given in the study report, suggesting the ASEPSIS score is valid. **Time points:** 7 days
Notes	The leading author received honoraria from Smith & Nephew and the study was financially supported by Smith & Nephew.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote "Randomisation was performed by a web based, independent randomisation service (Sealed Envelope, UK) to ensure allocation concealment. The allocation was created using permuted blocks." Computer-generated randomisation sequence
Allocation concealment (selection bias)	Low risk	Quote "Randomisation was performed by a web based, independent randomisation service (Sealed Envelope, UK) to ensure allocation concealment. The allocation was created using permuted blocks." Independent randomisation service used to conceal allocation

Giannini 2018 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Blinding was not reported but different criteria for dressing changes would have revealed allocation to both participants and personnel.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote "the clinician was blinded regarding to the treatment group". The clinician undertaking the wound evaluation was blinded to treatment group.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Quote "A number of patients (n = 10) were excluded from the data analysis due to septic loosening of the prosthesis once the results of microbiological and histological examinations were obtained". Comment: 8 participants in the treatment group and 2 in the control group were excluded from the analysis on this basis of the reason of septic loosening which could only be detected postoperatively. The power calculation allowed for a 20% dropout but it's not clear how this differential removal from the analysis may have affected the results.
Selective reporting (reporting bias)	Low risk	No evidence of selective reporting
Other bias	Low risk	No evidence of any other source of bias

Gillespie 2015

Study characteristics	
Methods	**Study design:** randomised controlled trial **Study grouping:** parallel **Ethics and informed consent:** yes **Follow-up period:** 6 weeks **Sample size estimate:** pilot study **ITT analysis:** yes, **number randomised:** 70, **number analysed:** 70 **Funding:** non-industry **Preregistration:** yes
Participants	**Location:** Queensland, Australia **Intervention group:** n = 35,**control group:** n = 35 (primary hip arthroplasty) **Mean age: intervention group** = 62.5 years (SD 12.4),**control group** = 63.8 years (SD 14.0) **Inclusion criteria:** undergoing elective primary total hip arthroplasty, aged >/= 18 years, able to provide informed consent and attended hospital preadmission clinic **Exclusion criteria:** people with an existing infection, had previously participated in the trial or were unable to speak and understand English
Interventions	**Aim/s:** to assess the use of NPWT on surgical sites to prevent infections and other wound complications after elective primary arthroplasty and to determine the feasibility of conducting a larger trial **Group 1 (NPWT) intervention:** PICO dressing applied over the primarily closed incision by the surgeon in the operating room. On day 5 the dressing was changed to OPSITE Post-Op Visible.

Gillespie 2015 *(Continued)*

	Group 2 (control) intervention: Comfeel dressing reinforced with 2 absorbent dressings, and then with a self adhesive, non-woven tape, which was applied over the primarily closed incision by the surgeon in the operating room. Participants were discharged with their dressing intact. **Study date/s:** March 2013 to May 2014
Outcomes	• SSI • dehiscence • haematoma • seroma • hospital readmission • cost of dressings **Validity of measure/s:** CDC definitions and criteria for superficial, deep, and organ/space SSI were used for the primary outcome. **Time points:** 30 days and 6 weeks postsurgery
Notes	Investigator contacted for additional details.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "computer generated randomised schedule 1:1 ratio in randomly varying blocks was prepared by the statistician on the research team (not involved in recruitment)".
Allocation concealment (selection bias)	Low risk	Quote: "on skin closure, the RNA opened the next sealed, opaque, numbered envelope".
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote:"Masking was not possible for those administering the intervention, and nor was it possible to mask the patients receiving it". Comment: personnel and participants were not blinded.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "the independent outcome assessors as well as the data analyst were blinded to group allocation".
Incomplete outcome data (attrition bias) All outcomes	Low risk	An ITT analysis was used.
Selective reporting (reporting bias)	Low risk	Planned outcomes reported. Protocol pre-registered on ANZCTR
Other bias	Low risk	None detected

Gombert 2018

Study characteristics

Methods	**Study design:** randomised controlled trial **Study grouping:** parallel **Ethics and informed consent:** ethics approved and consent obtained

Gombert 2018 *(Continued)*

	Follow-up period: 30 days **Sample size estimate:** yes, based on SSI rate expected in treatment group (3%) and difference of 0.14 between groups with 10% dropout **ITT analysis:** no, **number randomised:** 204, **number analysed:** 188 **Funding:** Acelity, San Antonio, TX, USA. **Preregistration:** Yes
Participants	**Location:** Germany (two sites) **Intervention group:** 98,**control group:** 90 **Mean age: intervention group** 67.9 (10.1), **control group** 65.2 (8.4) **Inclusion criteria:** Vascular surgery for peripheral arterial disease involving longitudinal groin incision for vascular surgical procedures involving the arterial system of the lower extremity or the iliac arteries; a comorbidity profile including smoking (active or past history), cardiac risk factors (e.g. hypertension, coronary heart disease, or history of myocardial infarction), and metabolic disorders (e.g. diabetes, dyslipidaemia, hyperhomocysteinaemia, or chronic renal failure). Dyslipidaemia was defined as hypertriglyceridaemia (> 150 mg/dL) or hypercholesterolaemia (total cholesterol > 200 mg/dL). Chronic kidney disease was defined as glomerular filtration rate (GFR) < 60 mL/min/1.73m^2 **Exclusion criteria:** Age below 18 years, pregnancy, local skin infection, simultaneous participation in another clinical trial, and immunosuppressive medication; emergency procedures. When a groin incision was performed on both sides, only one side was randomised and assessed for this study.
Interventions	**Aim/s:** to assess the potential benefits of ciNPT application after groin incisions for vascular surgery **Group 1 (NPWT) intervention:** closed incision negative pressure therapy (ciNPT); Prevena (continuous pressure of 125 mmHg); removed 5-7 days postoperatively, after which no further wound dressings were used unless SSIs occurred **Group 2 (control) intervention:** Cosmopore E (Hartmann, Heidenheim, Germany) was applied as the wound dressing, changed daily **Study date/s:** July 2015-May 2017
Outcomes	• SSI (7 days after the surgery) • Pain • Readmission • Surgical revision (reoperation) **Validity of measure/s:** SSI were clinically assessed and classified using the Szilagyi classification (grades I-III) **Time points:** 7, 15, 30 days
Notes	Register: Clinicaltrials.gov NCT02395159

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote "The randomisation sequence was computer generated using the random allocation rule, and allocation was implemented using a centralised web based system to ensure allocation concealment." Computer-generated randomisation sequence
Allocation concealment (selection bias)	Low risk	Quote "The randomisation sequence was computer generated using the random allocation rule, and allocation was implemented using a centralised web based system to ensure allocation concealment."

Gombert 2018 *(Continued)*

		Centralised allocation system
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote "The nature of the therapy meant that double blinded treatment was not possible. Furthermore, blinding of the vascular surgeons was not achievable". Personnel could not be blinded.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote "Until the seventh day after surgery, each wound was assessed by two physicians. From this point, the wound was assessed by at least three professionals (triple assessment). The involved wound care nurses were blinded. Furthermore, each wound was documented by photography."
Incomplete outcome data (attrition bias) All outcomes	Low risk	16 randomised participants were neither treated nor analysed; their group assignment was unclear. 6 of these did not undergo groin surgery (screening failures), 10 needed reoperation within 48 hours for occlusion of the treated vessel and were treated as dropouts. Fully documented.
Selective reporting (reporting bias)	High risk	Pain data and other device-related complications did not appear to be reported despite being assessed. Trial protocol obtained
Other bias	Low risk	No evidence of other sources of bias. We note that antibiotics were used in more people in the control group than in the NPWT group.

Gunatilake 2017

Study characteristics	
Methods	**Study design:** randomised controlled trial **Study grouping:** parallel **Ethics and informed consent:** yes **Follow-up period:** 42 ± 10 days **Sample size estimate:** not stated **ITT analysis:** yes, **number randomised:** 92, **number analysed:** 92 **Funding:** non-industry **Preregistration:** yes
Participants	**Location:** Texas, USA **Intervention group:** n = 46,**control group:** n = 46 **Mean age (SD): intervention group** = 30.4 (5.7),**control group** = 29.7 (5) **Inclusion criteria:** 18 years of age with BMI 35 kg/m^2 at the time of delivery **Exclusion criteria:** women with skin or systemic infections, chorioamnionitis (defined by maternal fever + 1 clinical criterion), critical illness, or high-risk for anaesthesia (ASA class P4, P5, or P6)
Interventions	**Aim/s:** to compare short-term clinical outcomes among obese pregnant women undergoing caesarean delivery who received ciNPT or a standard-of-care dressing **Primary outcome/s:** SSO: unanticipated local inflammation, wound infection, seroma, haematoma, dehiscence, and need for surgical or antibiotic intervention **Secondary outcome/s:** not stated

Gunatilake 2017 *(Continued)*

	Group 1 (NPWT) intervention: a sterile, "peel-and-place" multilayer dressing (wicking fabric, reticulated foam, and adhesive) was placed over participant's closed incision. The dressing's tubing was then attached to a compact, portable negative pressure therapy unit that delivered 125 mmHg of continuous pressure to the dressing and removed exudates into a disposable canister. Duration of ciNPT was 5 to 7 days, immediately following surgery. **Group 2 (control) intervention:** Steri-Strips (3M Health Care, ½ inch, St Paul, MN), sterile gauze, and Tegaderm (3M Health Care, transparent film dressings (nonpenetrable barrier)) were applied to the closed surgical incision for at least 1 day and no longer than 2 days. **Study date/s:** between 2012 and 2014
Outcomes	• postoperative SSOs: included unanticipated local inflammatory response, prolonged drainage, fluid collection, dehiscence, and surgical site intervention • surgical interventions: included antimicrobials for SSI, surgical drainage of the incision, surgical incision packing, adjunctive negative-pressure therapy, debridement, or reoperation **Validity of measure/s:** wound scoring system; surgical site assessments included the supplementary outcomes of incisional pain scores at rest and with pressure on the closed incision, as measured by the Wong–Baker Faces Scale **Time points:** all participants were followed up postoperatively for 42 ± 10 days via periodic incisional assessments (postoperative days 1, 2, 6, 14, and 42).
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Study personnel obtained the next sequentially numbered, opaque randomisation envelope, which contained the randomly assigned treatment group for the participant.
Allocation concealment (selection bias)	Low risk	Study personnel obtained the next sequentially numbered, opaque randomisation envelope, which contained the randomly assigned treatment group for the participant.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Insufficient information
Blinding of outcome assessment (detection bias) All outcomes	High risk	Although a standardised wound scoring system was utilised to minimise bias, the postoperative examiner was privy to the treatment group.
Incomplete outcome data (attrition bias) All outcomes	Low risk	An ITT analysis was used.
Selective reporting (reporting bias)	Unclear risk	Planned outcomes reported. Protocol preregistered on ClinicalTrials.gov (identifier NCT01450631).
Other bias	Low risk	None detected.

Heard 2017

Study characteristics	
Methods	**Study design:** Cost-effectiveness analysis. Data drawn from the Chaboyer 2014 RCT **Analytical approach:** Trial-based evaluation **Effectiveness data:** Data from pilot RCT (N = 87) (Chaboyer 2014). Key effectiveness inputs were SSI and quality of life (SF-12) at up to 4 weeks post-discharge in trial. **Perspective:** Australian public health care provider **Utility valuations:** QALYs were calculated from SF-12 data. QoL indices (utility weights) were calculated using the method of Brazier and Roberts. QALYs were estimated from the utility weights using the standard area under the curve method. **Adjustment:** QALYs were adjusted for differences in baseline SF-12 indices using the regression-based adjustment of Manca, Hawkins and Sculpher. **Measure of benefit:** surgical site infection avoided; QALY **Cost data:** measured in AUSD; in hospital resource use data were collected by direct observation or chart audit during the trial. Included cost of intervention, nursing time for dressing changes, hospital (inpatient) care. No discount rate was applied due to the short time horizon. **Analysis of uncertainty:** A nonparametric bootstrap with 1000 replications was used to construct 95% percentile method confidence intervals (CIs) for the estimates. A sensitivity analysis used only post-discharge QALYs, ignoring the period of hospitalisation (the base case analysis calculating QALYs from utility weights assumed that the change in QoL over the hospital stay was linear). **Funding:** Office of Health and Medical Research, Queensland Health, the National Health and Medical Research Council Centre of Research Excellence in Nursing and a Gold Coast University Hospital Private Practice grant
Participants	**Location:** Obstetric unit, Australia **Intervention group:** n = 46,**control group:** n = 46 (obese women (> 30 BMI) undergoing elective CS) **Mean age: intervention group** = 30.6 years (SD 5.5),**control group** = 30.7 years SD 5.0) **Inclusion criteria:** booked for elective CS; pre-pregnancy BMI > 30; able to provide consent **Exclusion criteria:** women whose condition changed to require urgent CS; previous participation in the trial; existing infection
Interventions	**Aim/s:** To evaluate whether NPWT is cost-effective compared with standard care in preventing surgical site infection among obese women undergoing caesarean section **Group 1 (NPWT) intervention:** NPWT: PICO (Smith and Nephew) dressing applied over the primarily closed incision by the surgeon in the operating room. Dressing was left on for 4 days, or longer if drainage continued, unless soiled or dislodged (n = 44) in Heard 2017 trial) **Group 2 (Comparator)** intervention: Comfeel dressing applied over the primarily closed incision by the surgeon in the operating room. Dressing was left on for 4 days, or longer if drainage continued, unless soiled or dislodged (n = 43 in a trial). **Study date/s:** July 2012 to April 2014
Outcomes	For data see Heard 2017 and for clinical data see Chaboyer 2014 in additional table 1 • Surgical site infection • Costs (AUSD) • QALY (measure of benefit). • ICER with 95% CI (AUSD per unit outcome) to inform probability of intervention being cost-effective

Heard 2017 *(Continued)*

Notes	Authors' conclusions: NPWT may be cost-effective in the prophylactic treatment of surgical wounds following elective caesarean section in obese women. Larger trials could clarify the cost-effectiveness of NPWT as a prophylactic treatment for SSI. Sensitive capture of QALYs and cost offsets will be important given the high level of uncertainty around the point estimate cost-effectiveness ratio which was close to conventional thresholds. Quality rating according to the CHEERS checklist was 83.3%.

Howell 2011

Study characteristics	
Methods	**Study design:** randomised controlled trial **Ethics and informed consent:** not reported **Sample size calculation:** yes **Follow-up period:** 12 months **ITT analysis:** all participants completed the study. **Funding:** the study was supported by KCI, the manufacturer of the negative pressure device.
Participants	**Location:** New York University Hospital for Joint Disorders, New York, NY, USA **Intervention group:** n = 24,**control group:** n = 36 **Mean age:** not reported **Inclusion criteria:** 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 **Exclusion criteria:** patient refusal to participate in the study, revision total knee replacement, prior knee surgery (except arthroscopy), and patients with documented diabetes mellitus
Interventions	**Aim/s:** to compare the number of days to dry wound in a negative pressure dressings group compared with a static pressure dressings group**Intervention/s in both groups:** "all patients received three doses of peri-operative intravenous antibiotics and were maintained on subcutaneous DVT prophylaxis for 30 days after surgery". **Group 1 (NPWT) intervention:** "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 NPWT 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 NPWT 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". **Group 2 (SPD) intervention:** "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". **Study date/s:** not stated
Outcomes	• days to dry wound • deep wound infection

Howell 2011 *(Continued)*

- blister formation

Time points: participants followed up for 12 months postsurgery

Notes		
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	**Comment:** not described
Allocation concealment (selection bias)	Unclear risk	Quote: "randomised with blinded envelopes to either the treatment with negative pressure wound therapy group or a control group using sterile gauze" Comment: unclear if envelopes were sequentially numbered or opaque
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	**Comment:** insufficient information
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	**Evidence:** not described
Incomplete outcome data (attrition bias) All outcomes	Low risk	**Evidence:** 51 participants were randomised, and 51 completed the study.
Selective reporting (reporting bias)	Low risk	**Comment:** the prespecified 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 could indicate undisclosed losses in 1 group.

Hussamy 2017

Study characteristics	
Methods	**Study design:** randomised controlled trial **Ethics and informed consent:** not reported **Sample size calculation:** yes **Follow-up period:** not stated **ITT analysis:** yes **Funding:** not stated
Participants	**Location:** Texas, USA **Intervention group:** n = 222,**control group:** n = 219 **Mean age:** not reported

Hussamy 2017 *(Continued)*

	Inclusion criteria: women with class III obesity (BMI > 40 kg/m^2) undergoing caesarean delivery **Exclusion criteria:** women on anticoagulation, with HIV infection, sensitive skin disorders, or silver or acrylic allergies
Interventions	**Aim/s:** to compare the efficacy of closed incision negative pressure therapy (ciNPT) with a standard surgical dressing in the prevention of postoperative wound morbidity in women with class III obesity undergoing caesarean delivery **Group 1 (NPWT) intervention:** a ciNPT dressing at time of caesarean **Group 2 (control) intervention:** a standard surgical dressing **Study date/s:** January 2015 to July 2016 (18 months)
Outcomes	• wound morbidity including wound disruption requiring the use of antimicrobials, prolonged postoperative hospitalisation, hospital readmission, or reoperation within 30 days of delivery **Validity of measure/s:** not stated **Time points:** not stated
Notes	Only the abstract was available.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not stated
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not stated
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not stated
Incomplete outcome data (attrition bias) All outcomes	Low risk	441 participants were enrolled and analysed.
Selective reporting (reporting bias)	Low risk	Expected outcomes were reported in the abstract.
Other bias	Unclear risk	Not stated

Hyldig 2019a

Study characteristics

Methods	**Study design:** pragmatic randomised controlled trial **Study grouping:** parallel

Hyldig 2019a *(Continued)*

	Ethics and informed consent: yes **Follow-up period:** 30 days **Sample size estimate:** yes; a sample size of 870 for a reduction in surgical site infection of 50% in the intervention group compared with an expected baseline event rate of 10% in the control group, with a two-sided 5% significance level and a power of 80% **ITT analysis:** yes (for surgical site infection only),**number randomised:** 876, **number analysed:** 876 for surgical site infection and 827 for other outcomes **Funding:** grants from the University of Southern Denmark, Odense University Hospital, the Region of Southern Denmark, Lundbeckfonden, and an unrestricted grant from the iNPWT device manufacturer Smith & Nephew (devices and operating funding) **Preregistration:** yes; ClinicalTrials.gov (NCT 01890720)
Participants	**Location:** Denmark (two tertiary referral centres and three Danish teaching hospitals) **Intervention group:** n = 432, **control group:** n = 444 (6 received iNWPT dressing) **Mean age:** a range from 18 to 46 years across groups; **intervention group:** 32 (SD 5), **control group** 32 (SD 5) **Inclusion criteria:** pregnant women undergoing elective or emergency caesarean section, aged >= 18 years; who had a prepregnancy body mass index >= 30 kg/m2, and could read and understand Danish **Exclusion criteria:** women who had given informed consent but subsequently delivered vaginally
Interventions	**Aim/s:** to investigate the effectiveness of prophylactic iNPWT after caesarean section in obese women; hypothesis: iNPWT would be associated with fewer surgical site infection and other wound complications (i.e., wound exudate and dehiscence) compared with standard postoperative dressing. **Group 1 (NPWT) intervention:** incisional negative pressure wound therapy (iNPWT; PICO, SIZE 10 * 30 cm or 10 * 40 cm, Smith & Nephew, Hull, UK) in which dressing was left in situ for approximately 5 days **Group 2 (control) intervention:** standard postoperative dressing in which dressing was left in situ for at least 24 hours **Study date/s:** September 2013 to October 2016
Outcomes	• Surgical site infection, those infections requiring antibiotic treatment within the first 30 days after caesarean section • Deep surgical site infection, those infections requiring surgery • Minor dehiscence, defined as a gap between the sides of the wound • Health-related quality of life (EQ-5D-5L) • Readmissions to hospital/contact to the general practitioner on suspicion of infection following caesarean section (listed in ClinicalTrials.gov) **Validity of measure/s:** **Time points:** within the first 30 days after surgery
Notes	Results were submitted to ClinicalTrials.gov in September 2018 but were not posted online. Could contact authors to request such data

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Participants were randomised in the operating theatre during surgery using a web-based randomisation programme with a 1:1 allocation ratio and random block sizes of 4–6, stratified by centre and type of caesarean section (emergency versus elective)." Comment: low risk of bias due to valid random sequence generation

Hyldig 2019a *(Continued)*

Allocation concealment (selection bias)	Low risk	Quote: "The random allocation sequence was generated by an external data manager with no clinical involvement in the study". Comment: low risk of bias due to likely appropriate approach taken to conceal randomisation process
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "Blinding was not possible due to the nature of the intervention". Comment: high risk of bias because it was clearly stated no blinding of participants and personnel
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	ITT analysis was conducted for surgical site infection and for other outcomes; only 22 of 432 in Group 1 and 27 of 444 in Group 2 were excluded from analyses. Low risk of attrition bias
Selective reporting (reporting bias)	High risk	Readmission to hospital/contact to the GP was listed on ClinicalTrials.gov but not presented in the full text. High risk of reporting bias
Other bias	Low risk	None detected

Hyldig 2019b

Study characteristics	
Methods	**Study design:** cost-effectiveness analysis (economic evaluation based on the Hyldig 2019a RCT) **Analytical approach:** Decision-analytic model **Effectiveness data**: Data from a multicentre RCT (n = 876) (Hyldig 2019a): SSI. Both risk and severity of infection were incorporated. The Danish crosswalk value sets were used to derive preference-based index values. **Perspective:** Danish healthcare **Utility valuations:** QALYs informed by EuroQol EQ-5D-5L (scoring algorithm not specified but Danish-specific context taken into account) were calculated based on SSI costs for superficial and deep SSIs avoided including antibiotic prescription costs and need for further surgery. **Measure of benefit**: surgical site infection avoided; QALY **Cost data:** Costs were estimated using data from four Danish National Databases and analysed from a Danish healthcare perspective with a time horizon of 3 months after birth. Conversion from DK to Euro using the year 2015 value. No discount rate was applied. Total costs consisted of four cost components: hospital costs; costs of using GPs; costs of antibiotics; and postoperative dressing cost. These were all from the Cost Database. Costs of iNPWT dressing was Euro 151.40, including device itself and time costs for its application. **Analysis of uncertainty:** probabilistic sensitivity analysis including an expanded time horizon and an extrapolation of QALY gain to 5 years (3% annual discount). Deterministic sensitivity analyses conducted to permit determination of possible uncertainty in the ICER that would result from a change in a single parameter in the analysis. Scenario analyses to evaluate the impact of missing cost and QALY data, and the influence of one outlier on the ICER.

Hyldig 2019b *(Continued)*

	A subgroup analysis stratifying by BMI explored the impact of the intervention in women with a pre-pregnancy BMI >/= 35.
Participants	**Location:** Denmark (two tertiary referral centres and three Danish teaching hospitals) **Intervention group:** n = 432, **control group:** n = 444 **Mean age:** a range from 18 to 46 years across groups; **intervention group:** 32 (SD 5), **control group** 32 (SD 5) **Inclusion criteria:** pregnant women undergoing elective or emergency caesarean section, aged >= 18 years; who had a pre-pregnancy body mass index >= 30 kg/m2, and could read and understand Danish **Exclusion criteria:** women who had given informed consent but subsequently delivered vaginally
Interventions	**Aim/s:** To evaluate the cost-effectiveness of incisional negative pressure wound therapy (iNPWT) in preventing surgical site infection in obese women after caesarean section **Group 1 (NPWT) intervention:** Incisional negative pressure wound therapy (iNPWT; PICO, SIZE 10 x 30 cm or 10 x 40 cm, Smith & Nephew, Hull, UK) in which dressing was left in situ for approximately 5 days (n = 432 in a trial) **Group 2 (control) intervention:** Standard postoperative dressing in which dressing was left in situ for at least 24 hours (n = 444 in a trial) **Study date/s:** September 2013 to October 2016
Outcomes	For data see Hyldig 2019b and for clinical data see Hyldig 2019a in additional table 1 SSI Costs (Euro) QALY (measure of benefit). ICER with 95% CrI to inform probability of strategy being cost-effective/dominant using the willingness-to-pay threshold of 30,000 Euro/QALY
Notes	**Authors' conclusions**: Incisional NPWT appears to be cost saving compared with standard dressings but this finding is not statistically significant. The cost savings were primarily found in women with a pre-pregnancy BMI ≥ 35 kg/m^2. **Funding:** University of Southern Denmark, Odense University Hospital, the Region of Southern Denmark, Lundbeckfonden, and an unrestricted grant from the iNPWT device manufacturer Smith & Nephew (devices and operating funding) **Quality assessment:** CHEERS score 91.7%

Javed 2018

Study characteristics	
Methods	**Study design:** randomised controlled trial **Study grouping:** parallel **Ethics and informed consent:** yes **Follow-up period:** 30 days after operations **Sample size estimate:** yes; a sample size of 124 patients was assumed to provide a power of 80% to detect a 20% relative reduction in surgical site infection incidence (decreasing from 30% to 10%) at a 2-sided alpha level of 0.05 **ITT analysis:** yes; **number randomised:** 124, **number analysed:** 123

Javed 2018 *(Continued)*

	Funding: KCI/Acelity (Grant number #125164) **Preregistration:** Not reported
Participants	**Location:** America (single site) **Intervention group:** n = 62, **control group:** n = 62 **Mean age: intervention group** mean 66.4 (SD 9.3) years, **control group** 66.1 (9.0) **Inclusion criteria:** adults (18 yrs of age) who had a SSI risk score of 1 as defined by the risk score proposed by Poruk et al. This included patients who had received neoadjuvant chemotherapy, preoperative biliary stenting, or both. **Exclusion criteria:** pancreaticoduodenectomies (PD) performed minimally invasively or known allergies or sensitivity to silver or acrylic adhesives
Interventions	**Aim/s:** to evaluate the efficacy of negative pressure wound therapy for surgical-site infection (SSI) after open pancreaticoduodenectomy **Group 1 (NPWT) intervention:** negative pressure wound therapy (NPWT) device is shown in Figure S1. The PREVENA™ CUSTOMIZABLE™ device is comprised of a PREVENA™ CUSTOMIZABLE™ dressing, sealing strips, KCI drapes, and Interface Pad. **Group 2 (control) intervention:** standard closure technique **Study date/s:** January 2017 through February 2018
Outcomes	• Surgical site infection defined by the National Health Safety Network definition of the Centers for Disease Control and Prevention (CDC) • Need for reoperation • 30-day readmission related to SSI • Cost of hospitalisation **Validity of measure/s:** **Time points:** 30 days after operation
Notes	Haematoma, seroma, or skin separation were considered under the outcome of surgical site infection (SSI) according to the judgement criteria used for SSI. Data of these outcomes were not extracted or used for this review.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Using the simple randomization method, a random allocation sequence was generated." "Once the surgeon committed to performing a PD by ruling out metastatic disease or inoperable local vascular involvement, the circulating nurse contacted the research staff for randomization. The presealed envelope was opened to randomize the patient." Comment: unclear risk of bias because the method of generating random sequence was not specified
Allocation concealment (selection bias)	Low risk	Quote: "Allocation concealment was achieved by printing allocation onto a gray-shaded card that was folded and sealed in a secured envelope before initiation of the study". Comment: low risk of bias given an appropriate strategy was used to conceal allocation
Blinding of participants and personnel (performance bias)	Unclear risk	Quote: "All patients also received standard infection-prevention measures..." Comment: insufficient information on blinding of participants and personnel

Javed 2018 *(Continued)*
All outcomes

Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "patients' EMR were reviewed independently by the principal investigator (MJW) blinded to study-group assignments to determine if SSI was documented at any time during the 30-day postoperative period. " Comment: low risk of bias for SSI because the outcome assessors were blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: Low risk of bias because 123 of 124 participants randomised were analysed. One of the 62 participants that were randomised to Group 2 (Control) was excluded from the analysis because the surgeon decided to use NPWT for that person rather than the control intervention.
Selective reporting (reporting bias)	Low risk	All outcomes listed in the Methods were reported in the Results.
Other bias	Low risk	None detected

Karlakki 2016

Study characteristics	
Methods	**Study design:** randomised controlled trial **Study grouping:** parallel **Ethics and informed consent:** yes **Follow-up period:** 6 weeks **Sample size estimate:** pilot study **ITT analysis:** yes, **number randomised:** 220, **number analysed:** 209 **Funding:** study funded through a grant from Smith & Nephew UK to cover the cost of NPWT dressings and data collection costs. 2 investigators declared they had funding and consultancy fees from Smith & Nephew. **Preregistration:** no
Participants	**Location:** Oswestry, UK **Intervention group:** n = 110,**control group:** n = 110 **Mean age (SD): intervention group** = 69 (9.0),**control group** = 69.2 (9.0) **Inclusion criteria:** patients undergoing total hip or knee arthroplasties (for any indication) with any of 3 consultant surgeons **Exclusion criteria:** patients who had known allergies to dressing, were undergoing revision joint surgery, were unwilling to attend additional clinics, and those on warfarin were excluded.
Interventions	**Aim/s:** to evaluate the effectiveness of incisional negative pressure wound therapy dressing (iNPWTd) **Group 1 (NPWT) intervention:** PICO dressing applied over the primarily closed incision by the surgeon in the operating room. Dressing was left on for 4 days, or longer if drainage continued, unless soiled or dislodged. **Group 2 (control) intervention:** Comfeel dressing applied over the primarily closed incision by the surgeon in the operating room. Dressing was left on for 4 days, or longer if drainage continued, unless soiled or dislodged. **Study date/s:** July 2012 to April 2014

Karlakki 2016 *(Continued)*

Outcomes	• SSI • blisters • haematoma • hospital readmission **Validity of measure/s:** not described **Time points:** 1, 2, and 6 weeks postsurgery
Notes	Investigator contacted for additional details

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "the randomisation was performed using sealed opaque envelopes with a block size of 20 shuffled envelopes". **Comment:** no sequence generation was required.
Allocation concealment (selection bias)	Low risk	Quote: "the randomisation was performed using sealed opaque envelopes with a block size of 20 shuffled envelopes". **Comment:** allocation was unknown until envelope opened.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "This was a non-blinded single-centre randomised controlled parallel group study". Comment: non-blinded study
Blinding of outcome assessment (detection bias) All outcomes	High risk	Outcome assessors were aware of group allocation.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	7.3% in intervention group and 2.7% in control group PP analysis **Comment**: more participants were excluded from the analysis in the intervention group (8 intervention vs 3 control).
Selective reporting (reporting bias)	Low risk	Expected outcomes reported
Other bias	High risk	Intervention participants were seen in a wound clinic at 1 week, and control participants were not.

Keeney 2019

Study characteristics

Methods	**Study design:** randomised controlled trial **Study grouping:** parallel **Ethics and informed consent:** yes **Follow-up period:** 35 days

Keeney 2019 *(Continued)*

	Sample size estimate: not reported **ITT analysis:** no; **number randomised:** 526; **number analysed:** 398 **Funding:** Institution of authors received research funding from Smith & Nephew Orthopaedics that was related to this study. **Preregistration:** not reported
Participants	**Location:** America (one site) **Intervention group:** 185 analysed; **control group:** 213 analysed **Mean age: intervention group** 60.6 years, **control group** 60.5 **Inclusion criteria:** consenting age, surgical treatment with primary or revision THA, surgical treatment with primary or revision TKA; and having an advanced technology device capable of digital photography **Exclusion criteria:** pregnancy, history of poor compliance with medical treatment, allergy to silicone adhesives or polyurethane films, and unwillingness to participate in an RCT
Interventions	**Aim/s:** to assess whether a portable iNPWT device affects wound appearance, postoperative wound drainage, dressing-related complications, wound healing complications, infection rates, and reoperation rates when compared with a standard of care (SOC) postoperative dressing **Group 1 (NPWT) intervention:** incisional negative pressure wound therapy (iNPWT), a battery-operated, portable NPWT device with an exchangeable cartridge (PICO, Smith & Nephew Orthopaedics, Memphis, TN) with negative pressure applied at 80 mmHg (± 20 mmHg) for an initial period of 7 days **Group 2 (control) intervention:** a standard of care (SOC) postoperative dressing, including nonadherent incisional cover (Adaptic or Xeroform gauze), 4 4 inch gauze, and an abdominal dressing. Dressings were changed on postoperative day 2 with subsequent dressing changes performed at 3- to 5-day intervals until the incision was dry. **Study date/s:** enrolment between April 1, 2014, and January 31, 2017
Outcomes	• Superficial and late wound infection rates 7/185 vs. 8/213 • Return to the operating room to manage a wound-related concern within the first 3 months **Validity of measure/s:**. **Time points:**
Notes	The number of patients randomised in either group was not reported. The authors also reported wound appearance; all-cause complications, wound drainage, and dressing concerns outcomes. These outcomes were not extracted for this review. Regarding outcomes of interest to this review, the authors also stated that "*Two patients in each group underwent surgical treatment for a superficial wound infection during the first 90 days after surgery... Four TKA patients in the standard dressing control group were returned to the operating room within the first 35 days for management of a wound-related complication but deep infection was not diagnosed*". These data were not extracted for this review because it was unclear whether they were systematically collected.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "A total of 526 patients (22.5%) consented to participate in the study and were randomised into either the iNPWT device or SOC dressing treatment groups". Comment: unclear risk of bias because no method of generating random sequence was specified

Keeney 2019 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Understandably difficult to blind participants and personnel in this trial
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "Wound appearance was assessed from patient-provided incision photographs by a single trained research team member, blinded to time point and group, using a previously published and validated 100-mm visual analog scale." Comment: it appears that only wound appearance outcome was assessed in a blinding way. However, this outcome was not of interest to this review. It is unclear whether blinding of outcome assessment was undertaken for other outcomes.
Incomplete outcome data (attrition bias) All outcomes	High risk	Quote: "A total of 526 patients (22.5%) consented to participate in the study and were randomised ... After the initial randomization, 94 patients were excluded ... After excluding 34 unicompartmental knee arthroplasty patients, 398 patients remained for assessment..." Comment: high risk of bias because a high proportion of randomised participants (24%, 128 of 526) were excluded from data analysis.
Selective reporting (reporting bias)	Low risk	All outcomes mentioned in the Methods were reported in the Results though the reporting appeared to be implicit.
Other bias	Low risk	None detected

Kuncewitch 2017

Study characteristics	
Methods	**Study design:** randomised controlled trial **Study grouping:** parallel **Ethics and informed consent:** not reported **Follow-up period:** not reported **Sample size estimate:** not reported **ITT analysis:** yes, **number randomised:** 73, **number analysed:** 73 **Funding:** not reported **Preregistration:** not reported
Participants	**Location:** not reported **Intervention group:** n = 36,**control group:** n = 37 **Mean age (SD):** not reported **Inclusion criteria:** high-risk surgical oncology patients undergoing laparotomy **Exclusion criteria:** not stated
Interventions	**Aim/s:** to investigate the effects of NPWT on short- and long-term wound outcomes in people undergoing pancreatectomy

Kuncewitch 2017 *(Continued)*

	Group 1 (NPWT) intervention: NPWT **Group 2 (control) intervention:** standard surgical dressing **Study date/s:** 2012 to 2016
Outcomes	• postoperative wound complications in the first 30 days • incisional hernia rates • rates of pancreatic fistula • delayed gastric emptying **Validity of measure/s:** not described **Time points:** not stated
Notes	Only the abstract was available.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not stated
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not stated
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not stated
Incomplete outcome data (attrition bias) All outcomes	Low risk	73 participants were enrolled and analysed.
Selective reporting (reporting bias)	Unclear risk	Expected outcomes were reported in the abstract.
Other bias	Unclear risk	Abstract only

Kwon 2018

Study characteristics

Methods	**Study design:** randomised controlled trial **Study grouping:** parallel **Ethics and informed consent:** yes **Follow-up period:** 30 days **Sample size estimate:** pilot study informed the calculation which was based on power 0.80 to demonstrate reduction from 30% to 15% in SSI. This was based on incisions not patients.

Kwon 2018 *(Continued)*

	ITT analysis: no,**number randomised:** 123,**number analysed:** 119 incisions was the unit of analysis; 24 participants had 48 incisions **Funding:** performed without any support, financial or otherwise, from the makers of the Prevena dressing **Preregistration:** not stated
Participants	**Location:** USA single hospital **Intervention group:** 59,**control group:** 60 incisions; 24 people contributed 48 incisions (24 to each group) **Mean age: intervention group** 64.6 (44-83), **control group** 67.4 (41-84) **Inclusion criteria:** patients aged 18 years and older undergoing elective vascular surgery under the supervision of the Division of Vascular and Endovascular Surgery at Thomas Jefferson University Hospital involving unilateral or bilateral groin incisions; presence of any of the following criteria: body mass index (BMI) > 30 kg/m^2; significant pannus overlying groin skin or abnormal skin as evidenced by fungal infection; reoperative groin surgery; placement of prosthetic vascular graft; poor nutrition (BMI < 18 kg/m2, cachectic in appearance); immunosuppression (use of any immunosuppressive medications); and poorly controlled diabetes (hemoglobin A1c >8%) **Exclusion criteria:** emergency operation and those unwilling or unable to provide informed consent
Interventions	**Aim/s:** to determine whether application of a negative pressure dressing (Prevena Incision Management System) is superior to a standard surgical dressing in preventing vascular groin wound complications and their associated hospital costs. **Group 1 (NPWT) intervention:** negative pressure dressing (Prevena) applied according to the manufacturer's instructions. It involved application of an antibiotic sponge (0.019% ionic silver), cut to cover the closed groin wound, covered by a clear occlusive dressing attached to a suction device that applied -125 mmHg pressure. This device was inspected daily and left in place for 5 days, after which a dry gauze dressing was placed, inspected and replaced daily until discharge. **Group 2 (control) intervention:** standard surgical dressing consisting of gauze covered by Tegaderm (3M, St. Paul, Minn). This dressing was removed on postoperative day 2 and replaced with a dry gauze dressing that was inspected and replaced daily until discharge. **Study date/s:** January 1st, 2015 to December 31st, 2016
Outcomes	• SSI • (skin) dehiscence • lymph leakage (seroma or fistula) but no separate data on seroma • haematoma • reoperation • hospital readmission • costs **Validity of measure/s:** The Szilagyi classification of vascular wound infection was also used to classify the infection. **Time points:** daily until hospital discharge; within 10 to 14 days, whereupon staples were removed; and within 25 to 30 days to complete the study
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement

Kwon 2018 *(Continued)*

Random sequence generation (selection bias)	Unclear risk	Quote "They used a coin toss to determine whether the patient was to receive standard dressing or negative pressure therapy. To maintain 1:1 randomization as well as to provide future analysis using internal controls, any high-risk patient undergoing bilateral groin incisions would receive both a standard dressing and negative pressure therapy". Comment: adequate method for the unilateral surgery; unclear for the bilateral
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "Other than the fact that the 30-day examination occurred without the overt knowledge of the patient's initial treatment, no blinding was instituted". Comment: The surgical team, clinical staff, and patient were not blinded to the intervention status.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Quote: " Wound assessment was made by both the primary surgeon and nurse practitioners.....Furthermore, a major limitation to the study was that it was not a blinded study and therefore subject to observer bias. Assessment of complications is qualitative, and ultimate management of infections, such as opening an infected wound, was left to the discretion of the attending surgeon." Comment: Outcome assessment was performed by an unblinded assessor.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "Because a contralateral complication would penalize the uncomplicated groin incision in terms of LOS and hospital variable costs, in this circumstance the uncomplicated groin incision data were dropped from consideration in terms of LOS and variable costs". "As such, for the high-risk, standard dressing group (n = 60), five were dropped because of a contralateral complication (n = 55); for the high-risk, Prevena group (n = 59), eight were dropped because of a contralateral complication (n = 51)"; In the intervention group, two incisions discontinued intervention because of graft failure postoperative Day 1; In the control group, two incisions discontinued intervention because of reopening of incision for graft failure postoperative Day 1 and fatal myocardial infarction post-operative Day 3. Comment: Clear from the study how many participants withdrew and the reasons
Selective reporting (reporting bias)	Low risk	Comment: protocol not found, but according to the method, all results were reported.
Other bias	Unclear risk	This was a planned? interim analysis after 80% recruitment with a stopping guideline if 50% reduction in SSI. The unit of analysis was the incision and the unit of randomisation appeared to be the incision where there was bilateral incision. Unclear how this paired data dealt with in analysis

Lee 2017a

Study characteristics	
Methods	**Study design:** randomised controlled trial **Study grouping:** parallel

Lee 2017a *(Continued)*

	Ethics and informed consent: yes **Follow-up period:** 6 weeks **Sample size estimate:** not reported **ITT analysis:** no, **number randomised:** 60, **number analysed:** 44 **Funding:** KCI USA Incorporated, an Acelity company **Preregistration:** yes
Participants	**Location:** Canada **Intervention group:** n = 33,**control group:** n = 27 **Mean age (± SD): intervention group** = 67.1 (± 7.2),**control group** = 68.3 (± 9.7) **Inclusion criteria:** receiving an isolated elective or semi-elective CABG and above 18 years of age living within 1 hour of the institution **Exclusion criteria:** emergent surgery, previous CABG or lower leg surgical intervention, severe peripheral vascular disease, dialysis-dependent renal failure, and chronic steroid administration
Interventions	**Aim/s:** to establish the safety and feasibility of using NPWT on the GSV harvest site postcardiac surgery and to examine the effects on infection, complications, and overall patient function **Group 1 (NPWT) intervention:** NPWT device was placed at the time of GSV harvest in the operating room and then maintained in situ until the day prior to hospital discharge or to a maximum of 7 days. The device was removed if poorly tolerated by the participant or for any safety concerns. **Group 2 (control) intervention:** conventional dry gauze dressings **Study date/s:** not stated
Outcomes	• rates of device complication and malfunction • rates of SSI, lower leg complications, discharge date, and quality of life at discharge and 6 weeks **Validity of measure/s:** complications were classified as major if they required a medical or surgical intervention. All complications and device malfunctions were recorded. The total length of therapy with the NPWT device was recorded, and also if therapy was prematurely interrupted for any reason. SSIs was determined through assessment of the ASEPSIS score. The incidence of leg complications was also examined including pain, heaviness, weakness, stiffness, itching, paraesthesia, numbness, burning, discolouration, rash, and oedema. These complications were graded as 'not present', 'mild', 'moderate', and 'severe'. Only the moderate and severe complaints were included for incidence analysis. Discharge dates were also recorded for all participants. Self reported assessments of mobility, overall pain or discomfort, feelings of anxiety or depression, ability for self care, and ability to perform usual activities were performed. These measures were graded as no issues, some issues, and severe issues or inability. Quality of life was also measured using the EQ-5D-3L Measure of Health Status. **Time points:** initial and 6 weeks
Notes	33 vs 27 participants randomised; high loss to follow-up recorded

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Consented patients were randomised by use of sealed ballot envelopes in a 1-to-1 fashion.
Allocation concealment (selection bias)	Unclear risk	Not stated

Lee 2017a *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "We performed a prospective, randomised, single-blind, single centre, clinical feasibility study". Comment: Single-blinded - and the person who was blinded was the outcome assessor.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	A research assistant blinded to the grouping assessed the incision and participant prior to discharge and at 6 weeks postoperatively. A second, unblinded research assistant recorded and managed any device-related complications. Participants were discharged based on standardised institutional discharge criteria.
Incomplete outcome data (attrition bias) All outcomes	High risk	12 participants were lost to follow-up at 6 weeks, 4 in the NPWT group and 8 in the control group. These participants were not included in the data analysis.
Selective reporting (reporting bias)	Low risk	Planned outcomes reported. Protocol registered on ClinicalTtrials.gov (NCT01698372)
Other bias	Unclear risk	High loss to follow-up without reasons for loss being provided; unclear whether additional risks of bias

Lee 2017b

Study characteristics	
Methods	**Study design:** randomised controlled trial **Study grouping:** parallel **Ethics and informed consent:** yes **Follow-up period:** 90 days **Sample size estimate:** yes **ITT analysis:** no, **number randomised:** 102, **number analysed:** 102 **Funding:** not company funded **Preregistration:** yes
Participants	**Location:** Canada **Intervention group:** n = 53,**control group:** n = 49 **Mean age: intervention group** = 69 ± 10,**control group** = 68 ± 10 **Inclusion criteria:** patients with 1 of the following 3 risk factors for SSIs were enrolled in the trial: obesity defined as a BMI of > 30 kg/m^2, previous femoral artery exposure, or presence of minor or major ischaemic tissue loss. **Exclusion criteria:** patients with pre-existing groin infection, a known allergy to dressing material, or those who could not be followed postoperatively were excluded from the study.
Interventions	**Aim/s:** to perform an RCT to study the role of NPWT on SSI in primarily closed groin incisions after lower extremity revascularisation in vascular surgery patients **Group 1 (NPWT) intervention:** NPWT remained on until either hospital discharge or postoperative day 8, whichever occurred earlier. **Group 2 (control) intervention:** standard gauze dressing (the dressing removed on postoperative day 2, and then had daily dressing changes with inspection of the wound)

Lee 2017b *(Continued)*

	Study date/s: August 2014 to December 2015
Outcomes	• the incidence of SSI within 30 days of revascularisation • duration of hospital stay • SSI within 90 days • reoperation and readmission rate owing to SSI within 90 days • mortality within 90 days **Validity of measure/s:** SSI was diagnosed using the CDC guideline as a superficial or deep infection. The Szilagyi classification of vascular wound infection was also used to classify the infection. **Time points:** once discharged, both groups were followed up in the clinic at 30 and 90 postoperative days.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Eligible patients were randomised to NPWT or a standard sterile gauze dressing using an internet-based software, sealedenvelope.com (London, UK), using block randomisation.
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "patients and surgeons were not blinded to the treatment they had received". Comment: no blinding of participants or personnel
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Wounds were inspected at each clinic visit by a wound specialist nurse who was blinded to the treatment groups. If she was uncertain, the staff physician determined the presence or absence of an SSI. An SSI could also be diagnosed by the patient care team if there were clinical signs and symptoms of infection.
Incomplete outcome data (attrition bias) All outcomes	Low risk	102 participants were enrolled and analysed.
Selective reporting (reporting bias)	Low risk	Planned outcomes reported. Protocol registered on ClinicalTrials.gov (NCT02084017)
Other bias	Low risk	No other biases detected

Leon 2016

Study characteristics

Methods	**Study design:** prospective, randomised, multicentre study **Study grouping:** parallel **Ethics and informed consent:** not reported **Follow-up period:** not reported

Leon 2016 *(Continued)*

	Sample size estimate: not reported **ITT analysis:** yes, **number randomised:** 81, **number analysed:** 81 **Funding:** not reported **Preregistration:** not reported
Participants	**Location:** Spain **Intervention group:** n = 47,**control group:** n = 34 **Mean age (SD):** not reported **Inclusion criteria:** patients undergoing open and programmed colorectal surgery **Exclusion criteria:** not stated
Interventions	**Aim/s:** to evaluate the benefits of negative pressure therapy to reduce surgical site infection rate in open colorectal surgery **Group 1 (NPWT) intervention:** NPWT **Group 2 (control) intervention:** usual dressing group **Study date/s:** not reported
Outcomes	• SSI rate **Validity of measure/s:** not described **Time points:** a daily evaluation through hospitalisation and a 15- and 30-day evaluation
Notes	Only the abstract was available.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not stated
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not stated
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not stated
Incomplete outcome data (attrition bias) All outcomes	Low risk	All enrolled participants were accounted for in the analyses.
Selective reporting (reporting bias)	Unclear risk	Not stated
Other bias	Unclear risk	Abstract only

Lozano-Balderas 2017

Study characteristics	
Methods	**Study design:** randomised controlled trial **Ethics and informed consent:** ethics approved **Sample size calculation:** no **ITT analysis:** yes, **number randomised:** 81, **number analysed:** 81 **Follow-up period:** healed (when in hospital) or in a 30-day period after surgery (if discharged) **Funding:** non-industry **Preregistration:** yes
Participants	**Location:** Mexico **Intervention group:** n = 25,**control group:** n = 27, **(3 arms: delayed primary closure group:** n = 29**)** **Median age (IQR): intervention group** = 32 (22 to 46);**control group** = 30 (20 to 43) **Inclusion criteria:** minimum age of 18; a laparotomised wound with class III or IV (contaminated/dirty-infected) surgical wounds **Exclusion criteria:** not specified
Interventions	**Aim/s:** to compare infection rates between primary, delayed primary, and vacuum-assisted closures in contaminated/dirty-infected surgical wounds **Group 1 (NPWT) intervention:** the VAC was used with routine changes of dressings every 48 hours until healthy granulation tissue was found and a surgeon decided to close it. **Group 2 (control) intervention:** subcutaneous tissue was approximated with polyglycolic acid, and polypropylene was used for the skin. **Study date/s:** January to July 2014
Outcomes	• SSI **Validity of measure/s:** according to the CDC Surgical Wound Classification **Time points:** daily when in hospital or in a 30-day period after surgery
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "patients were allocated to each group with the software Research Randomizer® (Urbaniak, G. C., & Plous, S., Version 4.0)".
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	No information
Blinding of outcome assessment (detection bias) All outcomes	High risk	Outcome assessors were aware of group allocation.

Lozano-Balderas 2017 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Low risk	81 participants were enrolled and analysed.
Selective reporting (reporting bias)	Low risk	Expected outcomes reported. Protocol retrospectively registered on ClinicalTrials.gov (NCT02649543).
Other bias	Low risk	No other biases detected

Manoharan 2016

Study characteristics	
Methods	**Study design:** randomised controlled trial **Study grouping:** bilateral knees were randomised to intervention or control knees **Ethics and informed consent:** yes **Sample size estimate:** yes, but sample did not reach target, stopped due to financial constraints **Follow-up period:** 10 days **ITT analysis:** yes, **number randomised:** 21, **number analysed:** 21 **Funding:** KCI, Acelity Inc provided the negative pressure wound therapy dressings for the study. **Preregistration:** retrospectively registered as ANZCTR 12615001350516
Participants	**Location:** Queensland, Australia **Intervention group:** n = 21 knees,**control group:** n = 21 knees **Mean age (range):** 66 (45 to 80) **Inclusion criteria:** patients undergoing a bilateral knee arthroplasty **Exclusion criteria:** aged < 18 years or pregnant
Interventions	**Aim/s:** to assess the effect of NPWT on outcomes after primary arthroplasty **Group 1 (NPWT) intervention:** the intervention group received PREVENA Incision Management System, Acelity, KCI, which was placed over the closed surgical incision under sterile conditions at the end of the procedure. The NPWT device provided a continuous negative pressure of 125 mmHg for a duration of 8 days. **Group 2 (control) intervention:** the conventional dry dressing was placed over the closed surgical incision under sterile conditions at the end of the procedure. Neither the type of control dressing nor when the dressing was removed was reported. **Study date/s:** February to December 2014
Outcomes	• SSI • blisters • cost • QoL **Validity of measure/s:** no **Time points:** 10 to 12 days postsurgery
Notes	Investigator contacted for additional details

Manoharan 2016 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Simple randomisation was performed by the research assistants via online computer software that indicated the side to which the intervention, NPWT, would be applied.
Allocation concealment (selection bias)	Unclear risk	The surgeons were notified on the day of surgery, before the commencement of the procedure. It was also unclear if consecutive patients for each of the 3 surgeons were recruited.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "A final evaluation form at the outpatient review assessed the patients rated experience and preference for type of dressing. The final incision assessment was performed by the surgeon and clinic nurse and was witnessed by one of the research assistants. There were no independent observers attached to this assessment." Comment: Patients were aware of assignment, appeared that surgeons were not blinded.
Blinding of outcome assessment (detection bias) All outcomes	High risk	The final incision assessment was performed by the surgeon and clinic nurse and witnessed by 1 of the research assistants. There were no independent observers attached to this assessment.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	It was unclear if all participants were accounted for in the results as the numbers analysed for each outcome were not stated.
Selective reporting (reporting bias)	Low risk	Expected outcomes reported. Protocol retrospectively registered as ANZCTR 12615001350516.
Other bias	Low risk	No other biases detected

Martin 2019

Study characteristics

Methods	**Study design:** RCT **Study grouping:** parallel **Ethics and informed consent:** not reported **Follow-up period:** one year **Sample size estimate:** not reported **ITT analysis:** yes, number randomised: 40, number analysed: 40 (not clearly reported) **Funding:** Not stated **Preregistration:** Not stated
Participants	**Location:** not reported **Intervention group:** 20,**control group:** 20 **Mean age:** 60.82 years,**intervention group** NR **control group** NR **Inclusion criteria:** patients undergoing hepatectomy or pancreatectomy

Martin 2019 *(Continued)*

	Exclusion criteria: not reported
Interventions	**Aim/s:** to evaluate the effect of NPWT on SSI in this population (patients who have had hepatectomy or pancreatectomy) **Group 1 (NPWT) intervention:** incisional NPWT (PICO TM, Smith & Nephew, Hull, UK) **Group 2 (control) intervention:** sterile island dressing **Study date/s:** not reported
Outcomes	• SSI • dehiscence **Validity of measure/s:** Not reported **Time points:** Not reported
Notes	Abstract only

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote "Patients were randomised". Comment: method of generating randomisation sequence was not clear.
Allocation concealment (selection bias)	Unclear risk	Quote "Patients were randomised". Comment: unclear if appropriate methods were used to conceal allocation
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Comment: appeared likely that it would be impossible to blind participants or personnel to treatment allocation but insufficient information
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: unclear who assessed the outcomes or whether they were blinded to treatment allocation
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: All participants appeared to be included in the analysis.
Selective reporting (reporting bias)	Unclear risk	Comment: insufficient information
Other bias	Unclear risk	Comment: No evidence of other bias but insufficient information to be sure

Masden 2012

Study characteristics

Methods	**Study design:** randomised controlled trial **Ethics and informed consent:** 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.

Masden 2012 *(Continued)*

	Sample size calculation: yes **Follow-up period:** mean 113 days **ITT analysis:** available-case analysis **Funding:** 2 of the investigators are consultants for KCI, and the study was funded by the manufacturer of the intervention product..
Participants	**Location:** Columbus, Ohio, USA **Intervention group:** n = 50,**control group:** n = 43 **Mean age: intervention group** = 61.3 years (range 40 to 101),**control group** = 61.3 years (range 38 to 86) **Inclusion criteria:** patients scheduled to undergo radial forearm free flap **Exclusion criteria:** "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".
Interventions	**Aim/s:** to evaluate the effect of NPWT on closed surgical incisions. Prospective randomised controlled clinical trial comparing NPWT to standard dry dressings on surgical incisions **Primary:** "to evaluate the effectiveness of NPWT in patients with multiple comorbidities" **Secondary:** "to evaluate factors that contribute to wound complication" **Intervention/s in both groups:** "the graft was covered with a single layer of paraffin gauze dressing (Jelonet, Smith & Nephew, UK); 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 (Opsite, Smith & Nephew, UK) providing the vacuum seal. We used a double layer under the tube to prevent pressure ulcers at the bed of the suction tube". **Group 1 (NPWT) intervention:** "NPWT group ... underwent placement of a V.A.C. system (KCI, San Antonio, Texas) along the line of closure set at −125 mmHg continuous pressure at the time of closure". **Group 2 (control) intervention:** "the control group ... 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 & Nephew, Hull, UK)". **Study date/s:** October 2008 to August 2010
Outcomes	• wound infection • dehiscence • reoperation • LOS **Validity of measure/s:** not stated **Time points:** "all incisions assessed on the third postoperative day ... and reassessed 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".
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	**Evidence:** quote (from correspondence with the author): "used a randomization generator through Excel in groups of 8 (4 controls, 4 experimental)" **Comment:** adequate method

Masden 2012 *(Continued)*

Allocation concealment (selection bias)	Low risk	**Evidence:** quote (from correspondence with the author): "when the patient was recruited ... they contacted one of the investigators and the patient was assigned to whichever group was next on the list". **Comment:** adequate method
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Insufficient information
Blinding of outcome assessment (detection bias) All outcomes	Low risk	**Evidence:** quote: "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". **Comment:** adequate method
Incomplete outcome data (attrition bias) All outcomes	Low risk	**Evidence:** quote: "twelve subjects were lost to follow-up in the immediate postoperative period and were excluded from the final analysis". **Comment:** equal number of losses in both groups
Selective reporting (reporting bias)	Low risk	**Comment:** protocol unavailable, but expected outcomes reported
Other bias	Unclear risk	**Comment:** the standard dressing contained a silver layer, which may have influenced the outcome.

Murphy 2019

Study characteristics	
Methods	**Study design:** randomised controlled trial **Study grouping:** 2 parallel groups **Ethics and informed consent:** ethics approved and consent obtained **Follow-up period:** 30 days **Sample size estimate:** yes **ITT analysis:** no, **number randomised:** 300, **number analysed:** 284; 16 participants "randomised in error") were not included in analysis **Funding:** yes **Preregistration:** yes
Participants	**Location:** two separate sites within a single hospital system (London Health Sciences Centre, London, Ontario, Canada) **Intervention group:** 144 analysed,**control group:** 140 analysed **Mean age: intervention group** 64 years, **control group** 64 years **Inclusion criteria:** patients who were 18 years or older and scheduled for planned (elective) colorectal resection via laparotomy with midline incision (or booked for laparoscopy if converted to an open procedure with midline incision). Eligible surgical procedures included: segmental, subtotal or total colectomies, as well as low and ultra-low anterior resection.

Murphy 2019 *(Continued)*

	Exclusion criteria: patients who undergoing abdominoperineal resection (APR), pelvic exenteration, emergent colectomy or patients with bowel perforation at the time of operation, who were pregnant, palliative (life expectancy under 3 months) or had a known sensitivity to the NPWT device
Interventions	**Aim/s:** to determine if negative pressure wound therapy (NPWT) reduces surgical site infection (SSI) in primarily closed incision after open and laparoscopic-converted colorectal surgery **Group 1 (NPWT) intervention:** NPWT via a continuous vacuum set to -125 mm Hg which remained on until postoperative day (POD) 5 or the date of hospital discharge, whichever came first **Group 2 (control) intervention:** gauze adhesive dressing which was removed on POD 2 and changed daily thereafter **Study date/s:** January 2015 to February 2017
Outcomes	• SSI • mortality • reoperation **Validity of measure/s:** not reported **Time points:** 30 days postsurgery
Notes	Funding: industry grant from Kinetic Concepts Inc (San Antonio TX). The devices were also supplied free of charge.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: “Randomization will take place centrally using random permutated blocks of 4, 6 or 8 and will be stratified based on site (University Hospital or Victoria Hospital) of the operation.” Comment: adequate method
Allocation concealment (selection bias)	Low risk	Quote: “After the fascia is closed a member of the surgical team will use a centralized web-server to randomize the patient.” Comment: adequate method
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "we performed a single-institution, prospective, randomised, open label, blind endpoint trial". Comment: This was an open-label trial; participants and personnel were not blinded.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: “The primary outcome was assessed by a blinded member of our Stoma Wound and Ostomy (SWOT) team or a physician uninvolved in the patient’s care at POD five if the patient was in hospital or on the date of discharge if prior to POD five, as well as at the postoperative clinic visit occurring within the first 30 postoperative days.” Comment: adequate method
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: “Sixteen patients were excluded from the main analysis. Of the 284 patients remaining, we analyzed patients according to assigned group (144 NPWT and 140 Standard Dressing). There was no difference in demographics, type, or surgery performed or indication for surgery between groups.”

Murphy 2019 *(Continued)*

		Comment: clear from the study how many participants were excluded; these 16 participants were excluded because they were randomised in error, with reasons given.
Selective reporting (reporting bias)	High risk	Quote: "Secondary outcomes assessed will include the need for, and duration of, at-home nursing care (home care) related to SSI. Additional secondary outcomes assessed will include the length of hospital stay, the number of return visits related to a potential or actual SSI, and cost." Comment: According to the protocol, some secondary outcomes were not reported in the results.
Other bias	Low risk	No evidence of other risk of bias

Newman 2019

Study characteristics	
Methods	**Study design:** Randomised controlled trial **Study grouping:** Parallel **Ethics and informed consent:** **Follow-up period:** 12 weeks **Sample size estimate:** determined using an estimated wound complication rate (associated with current standard of care protocols) of 20% and a desired wound complication rate of 5%. Using a significance level of 0.05 with a power of 80%, the sample was estimated at 160 total subjects, with 80 subjects assigned to each group. **ITT analysis:** yes,**number randomised:** 160, **number analysed:** 179 **Funding:** KCI/Acelity Inc. (San Antonio TX) **Preregistration:** Yes
Participants	**Location:** US Hospital **Intervention group:** 80,**control group:** 80 **Mean age: intervention group** 65 (SD 11), **control group** 65 (SD 11) **Inclusion criteria:** patients who were scheduled to undergo revision THA or TKA by one of the 6 fellowship-trained orthopaedic surgeons met at least one of the following criteria: body mass index greater than 35 kg/m^2, use of anticoagulants other than aspirin, peripheral vascular disease, depression, diabetes mellitus, current smoker, history of a periprosthetic joint infection in the limb undergoing revision surgery, on immunomodulators or corticosteroids, current history of cancer or haematological malignancy, inflammatory arthritis, renal failure or dialysis, malnutrition, liver disease, history of organ transplant, or human immunodeficiency virus infection **Exclusion criteria:** lived more than 100 miles from the hospital, less than 18 years of age, had a silver allergy, had a history of wound coverage with soft tissue flaps on the index joint, or had a recent acute wound complication (i.e. defined as less than 4 weeks since previous surgery in the affected joint). Additionally, patients were excluded if they were enrolled in another interventional study, had no risk factors, undergoing a conversion arthroplasty, were not having implants revised, surgery was cancelled, altered mental status, and were screened but already met enrolment capacity.
Interventions	**Aim/s:** to compare the use of ciNPWT with our standard of care dressing in revision arthroplasty patients who were at high risk to develop wound complications

Newman 2019 *(Continued)*

	Group 1 (NPWT) intervention: ciNPWT device (PREVENA; KCI/Acelity, San Antonio, TX) for at least 2 days unless a wound complication was reported **Group 2 (control) intervention:** standard of care silver-impregnated wound dressing (AQUACEL; ConvaTec, Greensboro, NC) for at least 7 days unless a wound complication was reported **Study date/s:** eligibility assessed from August 2014 to January 2017
Outcomes	• SSI • Dehiscence • Haematoma • Blisters • Readmission • Reoperation **Validity of measure/s:** Clear definitions given but not using validated measures **Time points:** 2, 4 and 12 weeks
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote "Patients who consented and enrolled to be included in the study were block randomised by categorizing as hip or knee surgery groups and then were assigned a sealed, opaque envelope that was randomly generated by an independent researcher who allocated them." Comment: computer-generated randomisation sequence
Allocation concealment (selection bias)	Low risk	Quote "an independent researcher [ ] who allocated them groups and then were assigned a sealed, opaque envelope that was randomly generated by an independent researcher who allocated them to receive either a ciNPWT device (PREVENA; KCI/Acelity, San Antonio, TX) or the standard of care silver-impregnated wound dressing (AQUACEL; ConvaTec, Greensboro, NC). The envelopes were opened on the day of surgery and the surgeon was informed as to which group the patient was randomly assigned at the time of dressing placement. After a patient consented to be involved in the study, the next sequential envelope was selected." Comment: central allocation generated opaque sealed sequential envelopes.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	The nature of the intervention makes blinding of participants and some personnel very difficult but no clear information
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote "Wounds were examined at 2, 4, and 12 weeks after the procedure. Any complication reported was visualized at the time of the evaluation." Comment: did not state who performed the outcome assessment or whether they were blinded to intervention group
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote "One patient in the treatment arm was lost to follow-up and was not included in the analyses." Comment: All except one participant were included in the analysis.

Newman 2019 *(Continued)*

Selective reporting (reporting bias)	Low risk	All of the planned outcomes were fully reported.
Other bias	Low risk	No evidence of additional bias and reasonable reporting to suggest none.

Nherera 2017

Study characteristics	
Methods	**Study design:** cost-effectiveness analysis (based on the Karlakki 2016 RCT) **Analytical approach:** Trial-based decision analytic model (Based on Karlakki 2016, N = 220) **Effectiveness data:** Data from the UK trial (Karlakki 2016) **Perspective:** UK National Health Service **Utility valuations:** Time horizon of 6 weeks for surgical site complications (SSI) avoided and length of stay. Expected complications in standard care taken from the RCT. No discount rate was applied due to the short time horizon. Complications were assumed to have standard costs, readmission was excluded from the base case. Utility values were obtained from converting quality of life that was measured using SF-36. **Measure of benefit:** surgical site complication avoided; QALY (obtained from the NICE guideline on surgical site infections 2008) **Cost data**: Costs derived from standard cost references with resource utilisation valued in GBP (2015/16). Costs were also converted to USD by factor 1.42. (1) NHS reference costs of relevant medical diagnosis groups used for inpatient care (with confidence intervals). Model assumes all standard care dressing costs and nursing costs included in these. (2) Cost of a GP visit taken from Unit Costs and Social Care 2015–2016; (3) costs of oral antibiotics taken from the national Drug Tariff; length of stay (not considered in costs) (4) Cost of NPWT was taken from the national Drug Tariff. **Analysis of uncertainty:** Sensitivity analysis used to model discounted price for intervention through NHS bulk purchasing; additional length of stay following complications and readmission. Baseline data were varied across the 95% CI from the trial. Probabilistic sensitivity analysis for cost-effectiveness at willingness-to-pay threshold
Participants	**Location:** UK hospital **Intervention group:** n = 110,**control group:** n = 110 **Mean age (SD): intervention group** = 69 (9.0),**control group** = 69.2 (9.0) **Inclusion criteria:** patients undergoing THAs or TKAs (for any indication) with 3 consultant surgeons (SLK, NMG, and RDB – authors of this study) **Exclusion criteria:** patients who had known allergies to dressing, were undergoing revision joint surgery, were unwilling to attend additional clinics, and those on warfarin were excluded.
Interventions	**Aim/s:** To evaluate the cost-effectiveness of single-use negative pressure wound therapy in patients undergoing primary hip and knee replacements **Group 1 (NPWT) intervention:** Incisional negative pressure wound therapy dressing (iNPWTd) PICO dressing applied over the primarily closed incision by the surgeon in the operating room. Dressing was left on for one week (n = 110). **Group 2 (Control) intervention:** conventional dressing (either Mepore (Mölnlycke Health Care AB) or Tegaderm (3M Health Care Ltd)) applied over the primarily closed incision by the surgeon in the operating room. Dressing was left on for an unspecified period, and changed to OPSITE Post-Op Visible dressing on the second post-operative day (n = 110).

Nherera 2017 *(Continued)*

	All patients received enoxaparin postsurgery. **Study date/s:** July 2012 to April 2014
Outcomes	For data see Nherera 2017 and for clinical data see Karlakki 2016 in additional table 1 Costs (GBP) SSI complications avoided QALY (measure of benefit) Probability of being cost-effective using NICE threshold of £20,000/QALY
Notes	Funding: two authors are employees of Smith & Nephew. The Karlakki 2016 RCT was funded by Smith & Nephew. Authors' conclusions: Single-use negative pressure wound therapy can be considered a cost-saving intervention to reduce surgical site complications following primary hip and knee replacements compared with standard care. Providers should consider targeting therapy to those patients at elevated risk of surgical site complications to maximise efficiency. Quality rating using the CHEERS checklist was 85.4%.

Nherera 2018

Study characteristics	
Methods	**Study design:** cost-effectiveness analysis (based partly on the Witt-Majchrzac 2015 RCT) **Analytical approach:** Decision analytic model **Effectiveness data:** baseline data on revision operations, length of stay, readmissions to hospital, and mortality were derived from single-centre prospective observational study over 36 months in Germany. Effectiveness data for NPWT were taken from the trial (n = 80) of Witt-Majchrzak 2015 (SSI and wound dehiscence). A length of stay reduction was applied from a meta-analysis (Strugala & Martin). All-cause mortality was obtained from German Federal Statistical Office and assumptions about relationship between mortality and revision surgery applied from literature. **Perspective:** Germany Statutory Health Insurance payer **Utility valuations:** Health state utilities were sourced from published literature including discharge with and without complications from study by Tuffaha 2015. **Measure of benefit:** Wound healing without complications (complications avoided); QALY **Cost data:** Costs derived from standard cost references, resource utilisation valued in Euro. Inpatient care taken data from Cristofolini. Patient stay costs from hospital management site; reimbursement cost for procedure from Germany Diagnosis Relater group Report Browser 2017. Standard care dressing's costs and nursing costs covered in the diagnosis-related group costs. Rehabilitation costs obtained from a study by Zeidler. One community doctor and cardiologist visit cost, and the cost of community nurse visit once a week estimated. No discounting done due to a short time horizon (12 weeks). **Analysis of uncertainty:** One-way sensitivity analyses; probabilistic sensitivity analyses using Monte Carlo simulation; subgroup analysis for people with high BMI.
Participants	**Location:** Hospital, Poland **Intervention group:** n = 40,**control group:** n = 40 **Mean age: intervention group** = 66.2 (± 8), 53 to 80,**control group** = 62.1 (± 9.1), 41 to 78 **Inclusion criteria:** patients who underwent an off-pump coronary artery bypass grafting procedure, using the internal mammary artery

Nherera 2018 *(Continued)*

	Exclusion criteria: not stated
Interventions	**Aim/s:** To estimate the cost-effectiveness of single use negative pressure wound therapy (sNPWT) compared with standard of care in patients following coronary artery bypass grafting surgery (CABG) procedure to reduce surgical site complications (SSC) defined as dehiscence and sternotomy infections **Group 1 (NPWT) intervention:** Primary closure with NPWT (PICO, Smith & Nephew) using continuous negative pressure of −80 mmHg. Dressing changed on day 2 or 3 and on day 5 or 6 after surgery. **Group 2 (control)** Conventional dressings applied after primary closure. Dressings changed daily **Study date/s:** not stated
Outcomes	**Outcomes** (for data see additional table 1; for clinical data see Witt-Majchrzac 2015) Costs Wound healing without complication (complications avoided); QALY (measure of benefit) ICER Probability of being cost-effective
Notes	Authors' conclusions: The sNPWT can be considered a cost-saving intervention that reduces surgical site complications following CABG surgery compared with standard care. We however recommend that additional economic studies should be conducted as new evidence on the use of sNPWT in CABG patients becomes available to validate the results of this economic analysis. Funding: NR for economic evaluation; see Witt-Majchrzac 2015 for RCT funding Quality rating using the CHEERS checklist was 87.0%.

Nordmeyer 2016

Study characteristics	
Methods	**Study design:** randomised controlled trial **Study grouping:** parallel **Ethics and informed consent:** yes **Sample size estimate:** no **Follow-up period:** unknown **ITT analysis:** yes, **number randomised:** 20, **number analysed:** unclear **Funding:** unclear. MHB gave scientific presentations for KCI. **Preregistration:** no
Participants	**Location:** Nuremberg, Germany **Intervention group:** n = 10,**control group:** n = 10 **Mean age: intervention group** = 52.3 (16.3),**control group** = 57.8 (15.2) **Inclusion criteria:** patients with spinal fractures who were scheduled for internal fixation **Exclusion criteria:** not reported
Interventions	**Aim/s:** to evaluate the different aspects of wound healing in spinal fractures treated with internal fixation

Nordmeyer 2016 *(Continued)*

	Group 1 (NPWT) intervention: the iNPWT group was treated with a PICO system (Smith & Nephew, UK). The PICO system was left on the wound for 5 days including the day of surgery. In addition to daily clinical examination, all wounds/seroma were analysed by ultrasonography on day 5 and day 10 after surgery. **Group 2 (control) intervention:** standard department wound dressing consisting of dry wound coverage (compresses attached to the skin) was used. **Study date/s:** not reported
Outcomes	• seroma **Validity of measure/s:** ultrasound was used as a standardised imaging modality to detect seromas in the wound area. **Time points:** day 5 and day 10 after surgery
Notes	Investigator contacted for additional details

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Numbers analysed were not reported.
Selective reporting (reporting bias)	Unclear risk	Only seroma reported, not wound infection; unclear if all planned outcomes addressed.
Other bias	Low risk	None identified

O'Leary 2017

Study characteristics

Methods	**Study design:** randomised controlled trial **Study grouping:** parallel **Ethics and informed consent:** yes **Sample size estimate:** yes, but it was based on a reduction in SSI from 35% to 10%

O'Leary 2017 *(Continued)*

	ITT analysis: yes, **number randomised:** 50, **number analysed:** 49 **Follow-up period:** 30 days **Funding:** support was received from Smith & Nephew. The authors were responsible for trial design, data analysis, and manuscript writing. The decision to publish trial results was made between study authors and study sponsors. **Preregistration:** ClinicalTrials.gov registration NCT02780453 (registered after study completed – May 2016)
Participants	**Location:** Limerick, Ireland **Intervention group:** n = 25,**control group:** n = 25 **Mean age: intervention group** = 58 (range 31 to 73),**control group** = 63 (range 33 to 76) **Inclusion criteria:** patients undergoing elective or emergency open abdominal surgery with a clean, clean-contaminated, or contaminated wound **Exclusion criteria:** dirty wound; BMI ≥ 40; ASA grade > 3
Interventions	**Aim/s:** to assess the effect of NPWT on SSI **Group 1 (NPWT) intervention:** PICO dressing (Smith & Nephew) was applied to the wound by the operating surgeon, and the edges of the dressing were reinforced with self adherent tape. **Group 2 (control) intervention:** transparent waterproof dressing (Smith & Nephew) **Study date/s:** February 2013 to April 2016
Outcomes	• SSI • reoperation • pain **Validity of measure/s:** CDC definitions and criteria for superficial, deep, and organ/space SSI were used for the primary outcome. A visual analogue scale was used to assess pain. **Time points:** day 4 and day 30 postsurgery
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomisation codes were generated on www.randomization.com.
Allocation concealment (selection bias)	Unclear risk	Allocation was performed using a "closed envelope method".
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote "A randomised, controlled, open-label trial" Comment: no blinding
Blinding of outcome assessment (detection bias) All outcomes	High risk	Quote: "the ... study assessor was a senior member of the operating surgical team. The study assessor was not blinded to the treatment group".
Incomplete outcome data (attrition bias) All outcomes	Low risk	1 participant was removed from the intervention arm for a protocol violation, but ITT analysis was provided.

O'Leary 2017 *(Continued)*

Selective reporting (reporting bias)	Low risk	Expected outcomes reported, but the study protocol was published after the completion of the trial.
Other bias	Low risk	No other bias identified

Pachowsky 2012

Study characteristics	
Methods	**Study design:** randomised controlled trial **Ethics and informed consent:** ethics approved and consent obtained. **Sample size calculation:** no **ITT analysis:** yes, **number randomised:** 19, **number analysed:** 19 **Follow-up period:** 10 days **Funding:** support received from Smith & Nephew. The authors were responsible for trial design, data analysis, and manuscript writing. The decision to publish trial results was made between study authors and study sponsors. **Preregistration:** no
Participants	**Location:** University Hospital, Erlangen, Germany **Intervention group:** n = 9,**control group:** n = 10 **Mean age: intervention group** = 66.2 years (SD 17.83),**control group** = 70.0 years (SD 11.01) **Inclusion criteria:** "consecutive patients who were scheduled for a total hip arthroplasty (THA) for osteoarthritis of the hip were randomised". **Exclusion criteria:** not stated
Interventions	**Aim/s:** to evaluate the use of NPWT to improve wound healing after total hip arthroplasty **Intervention/s in both groups:** "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". **Group 1 (NPWT) intervention:** "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". **Group 2 control:** the control group received "the standard wound dressing of our department, consisting of a dry wound coverage". **Study date/s:** not stated
Outcomes	• incidence of seroma (by ultrasound) • amount of wound drainage in the Redon drain canisters • duration of prophylactic antibiotics • secretion from the wound **Validity of measure/s:** "all patients underwent an ultrasound (Zonare, Z.one Ultra SP 4.2, Erlangen, ZONARE Medical Systems, Inc., Mountain View, USA) of the wound". **Time points:** day 5 and day 10 of postoperative period
Notes	

Pachowsky 2012 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not stated
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not stated
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 group to which the participant had been allocated.
Incomplete outcome data (attrition bias) All outcomes	Low risk	All enrolled participants were accounted for in the analyses.
Selective reporting (reporting bias)	Low risk	Results for outcomes identified in the methods section were reported. We did not see the original protocol.
Other bias	High risk	**Evidence:** quote: "Matthias H. Brem gave scientific presentations for KCI. The PREVENA wound treatment system was provided by KCI free of charge". Support was received from Smith & Nephew. The authors were responsible for trial design, data analysis, and manuscript writing. The decision to publish trial results was made between study authors and study sponsors. 1 participant in the NPWT group removed the Redon drain by himself on the first postoperative day.

Pauser 2016

Study characteristics	
Methods	**Study design:** randomised controlled trial **Study grouping:** parallel **Ethics and informed consent:** yes **Sample size estimate:** no **Follow-up period:** 10 days **ITT analysis:** yes, **number randomised:** 21, **number analysed:** 21 **Funding:** "Prevena wound treatment system was provided by KCI free of charge". **Preregistration:** no
Participants	**Location:** Nuremberg, Germany **Intervention group:** n = 11,**control group:** n = 10

Pauser 2016 *(Continued)*

	Mean age: intervention group = 81.6 ± 5.2 years,**control group** = 82.6 ± 8.6 years **Inclusion criteria:** patients with femoral neck fracture who were scheduled for hip hemiarthroplasty **Exclusion criteria:** not stated
Interventions	**Aim/s:** "to evaluate different aspects of wound healing after fractures of the femoral neck treated by hemiarthroplasty" **Group 1 (NPWT) intervention:** the iNPWT group was treated with a PREVENA system (KCI, San Antonio, Texas). The PREVENA system was left on the wound for 5 days including the day of surgery. **Group 2 control:** control group received the standard wound dressing of our department, consisting of a dry wound coverage (compresses attached to the skin). **Study date/s:** not reported
Outcomes	• seroma **Validity of measure/s:** ultrasound was used as a standardised imaging modality to detect seromas in the wound area. **Time points:** day 5 and day 10 after surgery
Notes	Investigator contacted for additional details

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information given
Allocation concealment (selection bias)	Unclear risk	Insufficient information given
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Insufficient information given
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information given
Incomplete outcome data (attrition bias) All outcomes	Low risk	All those recruited appear to have been included in the analysis.
Selective reporting (reporting bias)	Unclear risk	Unclear if all the planned outcomes were reported fully
Other bias	Unclear risk	Data for the NPWT group reported at day 5 and day 10, but data for the control group only reported overall

Pleger 2018

Study characteristics

Methods	**Study design:** randomised controlled trial

Pleger 2018 *(Continued)*

	Study grouping: parallel **Ethics and informed consent:** yes **Sample size estimate:** no **Follow-up period:** 30 days postoperatively **ITT analysis:** yes, **number randomised:** 129 groin incisions (100 participants), **number analysed:** 129 incisions **Funding:** "funded by our own department, without any financial or scientific involvement or support from KCI, ACELITY Company" **Preregistration:** no
Participants	**Location:** Germany **Intervention group:** n = 58 incisions,**control group:** n = 71 incisions **Mean age: intervention group** = 71 (range 54 to 89),**control group** = 66.5 (range 41 to 86) **Inclusion criteria:** vascular procedures with access to the common femoral artery with at least 1 of the known main risk factors of wound healing: age > 50 years, diabetes mellitus, renal insufficiency, malnutrition, obesity, and chronic obstructive pulmonary disease **Exclusion criteria:** not stated
Interventions	**Aim/s:** to investigate the effectiveness of ciNPT compared with conventional therapy with regard to the incidence of groin WHC on postoperative days 5 to 7 and 30 and the incidence of surgery revisions 30 days postoperatively after various vascular surgeries **Group 1 (NPWT) intervention:** ciNPT applied for postoperative days 5 to 7 **Group 2 (control) intervention:** a conventional adhesive plaster that was changed daily **Study date/s:** 1 February to 30 October 2015
Outcomes	• wound complications including SSI **Validity of measure/s:** Szilagyi classification **Time points:** the first evaluation took place on postoperative days 5 to 7 during the hospital stay, while the second evaluation was conducted on postoperative day 30 in the outpatient clinic.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information given
Allocation concealment (selection bias)	Unclear risk	Insufficient information given
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Insufficient information given
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not stated

Pleger 2018 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Low risk	All those recruited appear to have been included in the analysis.
Selective reporting (reporting bias)	Low risk	Results for outcomes identified in the methods section were reported. We did not see the original protocol.
Other bias	Unclear risk	Unequal number of participants in each group; results reported per fracture, so there is a potential unit of analysis issue.

Ruhstaller 2017

Study characteristics	
Methods	**Study design:** randomised controlled trial **Study grouping:** parallel **Ethics and informed consent:** not reported **Follow-up period:** not reported **Sample size estimate:** not reported **ITT analysis:** yes, **number randomised:** 136, **number analysed**: not stated **Funding:** KCI collaborated in the trial. **Preregistration:** yes
Participants	**Location:** Philadelphia, USA **Intervention group:** n = 67,**control group:** n = 69 **Mean age:** not reported **Inclusion criteria:** BMI greater than or equal to 30 kg/m^2 at less than or equal to 22 weeks of gestation; woman is labouring; woman is having an unplanned caesarean section; woman will have Pfannenstiel skin incision; has the ability to take a picture and email it to a secure account; receives prenatal care in the University of Pennsylvania health system and plans to follow up postpartum in the system; is 18 years of age or older **Exclusion criteria:** woman cannot read or speak English; is not 18 years of age or older; does not have ability to send a picture by email; has pre-existing diabetes mellitus (type 1 or type 2), is using chronic steroids or immunosuppressants, OR is being actively treated for a malignancy; woman is undergoing a scheduled caesarean section; woman is allergic to silver
Interventions	**Aim/s:** to determine whether NPWT lowers the rate of wound complications in obese pregnant women undergoing an unscheduled intrapartum caesarean section **Group 1 (NPWT) intervention:** NPWT device (PREVENA Incision Management System; Acelity) **Group 2 control:** standard postcaesarean wound care (not defined) **Study date/s:** not stated

Outcomes	Planned outcomes:
	
	• primary outcome variable is wound complications defined as:
	  * any readmission for a wound issue within 4 weeks of discharge;
	  * infection;
	  * wound breakdown.
	• quality of life

Ruhstaller 2017 *(Continued)*

	Reported outcomes: • SSI • blisters • reoperation **Validity of measure/s:** not reported **Time points:** 4 weeks postsurgery
Notes	Only the abstract and CTR report were available at the time of preparation of this review. Investigator contacted for additional details

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Once decision for caesarean delivery was established, randomisation was performed using a computer-generated randomisation scheme (Research Electronic Data Capture (REDCap)).
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	**Intervention group:** n = 61/67 (91%);**control group:** n = 58/69 (84%). It was unclear from the abstract if reasons for loss to follow-up were similar across groups.
Selective reporting (reporting bias)	Low risk	Results for outcomes identified in the methods section were reported.
Other bias	Unclear risk	No other bias identified but insufficient reporting

Sabat 2016

Study characteristics

Methods	**Study design:** 1:1 parallel-group randomised controlled trial **Study grouping:** parallel **Ethics and informed consent:** yes **Sample size estimate:** no **Follow-up period:** 4 months **ITT analysis:** no

Sabat 2016 *(Continued)*

	Funding: not stated **Preregistration:** not stated
Participants	**Location:** Philadelphia, USA **Intervention group:** n = 33 wounds,**control group:** n = 30 wounds (total 49 participants) **Mean age:** not reported **Inclusion criteria:** people undergoing open vascular surgery involving a groin incision **Exclusion criteria:** not stated
Interventions	**Aim/s:** to compare the effect of postoperative negative pressure therapy to conventional dressings on wound occurrences **Group 1 (NPWT) intervention:** NPWT device **Group 2 control:** conventional dressing (gauze and Tegaderm) **Study date/s:** not stated
Outcomes	• SSI • wound dehiscence
Notes	Abstract only; unit analysis

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not stated
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not stated
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not stated
Incomplete outcome data (attrition bias) All outcomes	Low risk	All those recruited appear to have been included in the analysis.
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	Unit of analysis issue - unclear if accounted for

Schmid 2018

Study characteristics

Methods	**Study design:** Randomised controlled trial

Schmid 2018 *(Continued)*

	Study grouping: Parallel group **Ethics and informed consent:** Not reported **Follow-up period:** 14 days **Sample size estimate:** Not reported **ITT analysis: number randomised:** 25, **number analysed:** 25 **Funding:** Not reported **Preregistration:** Yes
Participants	**Location:** Germany **Intervention group:** n = 25,**control group:** n = 25 **Mean age: intervention group:** Not reported, **control group:** Not reported **Inclusion criteria:** Patients with penile cancer and indication for bilateral inguinal lymph node dissection (tumour stage ≥ pT1 G2 or palpable inguinal enlarged lymph nodes) **Exclusion criteria:** Status post inguinal surgery
Interventions	**Aim/s:** To prospectively analyse the effect of an epidermal vacuum wound dressing on lymphorroe, complications and reintervention in patients with inguinal lymphadenectomy for penile cancer **Group 1 (NPWT) intervention:** Epidermal negative-pressure wound dressings (Prevena) for 7-8 days **Group 2 (control) intervention:** Conventional compression bandages for 24 hours **Study date/s:** May 2013 –
Outcomes	• Reintervention (reoperation?) • SSI may be included in wound complications but not reported **Validity of measure/s:** No definition of SSI reported **Time points:** 14 days
Notes	Planned interim analysis. Abstract only

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote “Patients were randomised to receive conventional wound care and suction drainage on one side (conventional) vs. epidermal vacuum wound dressing (VAC) and suction drainage on the other side”. Comment: No indication how the randomisation sequence was generated
Allocation concealment (selection bias)	Unclear risk	No statement
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study (no masking) (obtained from protocol)
Blinding of outcome assessment (detection bias) All outcomes	High risk	Open study (no masking) (obtained from protocol)

Schmid 2018 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote "We present the results of the first planned interim analysis after 25 patients".
Selective reporting (reporting bias)	High risk	Not all prespecified secondary outcomes reported (obtained from protocol)
Other bias	Unclear risk	Abstract so limited reporting - no obvious source of bias but insufficient information to be certain

Shen 2017

Study characteristics	
Methods	**Study design:** randomised controlled trial **Study grouping:** parallel **Ethics and informed consent:** yes **Sample size estimate:** yes (based on a real SSI reduction of 6% from 17% to 11%) **Follow-up period:** 30 days **ITT analysis:** yes, **number randomised:** 375, **number analysed**: 265 **Funding:** non-industry **Preregistration:** yes
Participants	**Location:** Wake Forest University Health Sciences, North Carolina, USA **Intervention group:** n = 187,**control group:** n = 188 **Median age (range): intervention group** = 59.5 (25 to 85),**control group** = 62 (30 to 81) **Inclusion criteria:** patients who underwent open resection of intra-abdominal neoplasms, where the scheduled procedure was to be performed via midline laparotomy and was a clean-contaminated (class II) case (includes gastric, small bowel, and colorectal resections, as well as bile or pancreatic duct transections); the patient had the ability to understand and the willingness to sign a written informed consent document (either directly or via a legally authorised representative) **Exclusion criteria:** emergent cases; pregnant patients; clean (class I), contaminated (class III), and dirty (class IV) procedures; patients on chronic immunosuppressive medications, including steroids, within the past 3 months; patients with a history of skin allergy to iodine or adhesive drapes were not included in the study
Interventions	**Aim/s:** to decrease the incidence of superficial and deep SSIs **Group 1 (NPWT) intervention:** PICO dressing applied over the primarily closed incision by the surgeon in the operating room. Dressing was left on for 4 days, or longer if drainage continued, unless soiled or dislodged. **Group 2 control:** Comfeel dressing applied over the primarily closed incision by the surgeon in the operating room. Dressing was left on for 4 days, or longer if drainage continued, unless soiled or dislodged. **Study date/s:** July 2012 to April 2014
Outcomes	• SSI • seroma • haematoma

Shen 2017 *(Continued)*

- incisional cellulitis
- dehiscence
- wound opening for any reason

Validity of measure/s: CDC definitions for SSI were used.

Time points: 30 days after surgery

Notes	Investigator contacted for additional details

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "the program nQuery was used to create the randomization schema". The study used permuted-block randomisation with varying block sizes.
Allocation concealment (selection bias)	Unclear risk	Quote: "an email was sent the day before surgery to the attending surgeon about to which treatment arm the patient had been assigned". **Comment:** scope for surgeons to anticipate the randomisation sequence
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "There was no blinding of the patients or care providers to the study intervention. An email was sent the day before surgery to the attending surgeon about to which treatment arm the patient had been assigned". Comment: patients and participants were not blinded.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Investigator team assessed outcomes.
Incomplete outcome data (attrition bias) All outcomes	High risk	Approximately 30% of participants were lost to follow-up or excluded from each arm of the trial. However, reasons for losses were similar between groups. NPWT group: 2 died and 19 were reoperated; standard care group: 5 died and 16 were reoperated
Selective reporting (reporting bias)	Low risk	Prospectively reported. Outcomes were consistent with proposal (National Cancer Institute CCSG P30CA012197).
Other bias	Low risk	No other bias identified

Shim 2018

Study characteristics

Methods	**Study design:** randomised controlled trial **Study grouping:** parallel **Ethics and informed consent:** yes **Follow-up period:** 1 year **Sample size estimate:** no **ITT analysis:** yes, **number randomised:** 51, **number analysed:** 51

Shim 2018 *(Continued)*

	Funding: Not reported **Preregistration:** Not reported
Participants	**Location: Korea;** single-centre (hospital) **Intervention group:** 30, **control group:** 21 **Mean age: intervention group** 38.77 ± 1.68, **control group** 41.38 ± 10.92 **Inclusion criteria:** > 20 years, acute multi-tissue hand injury of moderate severity (assessed by HISS score 21-50), underwent reconstruction within 3 days after injury by two surgeons **Exclusion criteria:** history of impaired motor function, injury to the peripheral nerves and/or vessels distal to the wrist, or a bone fracture requiring transarticular fixation with a Kirchner (K) wire, a congenital hand deformity, an operation history on the same hand, and underlying diseases including autoimmune diseases such as rheumatoid arthritis or systemic lupus erythematosus or those taking medications that could influence wound healing
Interventions	**Aim/s:** To compare outcomes in patients with acute hand injury who were managed with or without NPWT after reconstructive surgery **Group 1 (NPWT) intervention:** NPWT (CuraVAC, CGBio, Seongnam-si, Gyeonggi-do, Korea) applied at a pressure of 75 mmHg in continuous mode and secondary dressing including Vaseline gauze **Group 2 (control) intervention:** Conventional dressing, including vaseline gauze was applied over the closed skin using polyurethane foam with a compressible elastic bandage, and a short arm splint was applied in a functional position; dressing and NPWT were changed every 3 days. **Study date/s:** January 2013 - December 2016
Outcomes	• SSI/infection • haematoma • wound disruption (dehiscence) **Validity of measure/s:** unclear what definition was used for infection **Time points:** 1 month and 1 year
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Patients were randomly assigned to the control or experimental group following a simple randomization procedure (computerized random numbers) achieved using opaque envelopes". Comment: randomisation with computer
Allocation concealment (selection bias)	Unclear risk	Quote: "Patients were randomly assigned to the control or experimental group following a simple randomization procedure (computerized random numbers) achieved using opaque envelopes. Allocation information to each group was not provided to reduce bias". Comment: allocation concealed with opaque envelopes but these were not noted as sequentially numbered
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote "This was a prospective open trial". Comment: No blinding of participants or personnel

Shim 2018 *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	High risk	Quote "This was a prospective open trial". Comment: No blinding of outcome assessment
Incomplete outcome data (attrition bias) All outcomes	Low risk	No patients lost to follow-up
Selective reporting (reporting bias)	Low risk	All prespecified outcomes fully reported
Other bias	Unclear risk	No evidence of other bias but reporting insufficient to be certain

Stannard 2012

Study characteristics	
Methods	**Study design:** multicentre randomised controlled trial (four centres, each a level 1 trauma centre) **Ethics and informed consent:** ethics approved and consent obtained **Sample size calculation:** no **Follow-up period:** not reported **ITT analysis:** wounds, not people were assessed **Funding:** "funds from corporate/industry were received from Kinetic Concepts, Inc to support this work".
Participants	**Location:** Columbus, Ohio, USA **Intervention group:** n = 130, participants; 141 fractures,**control group:** n = 119 participants; 122 fractures **Mean age:** not stated **Inclusion criteria:** people > 18 years of age who had sustained a high-energy tibial plateau, pilon, or calcaneus fracture and were able to comply with research protocol and willing to give informed consent **Exclusion criteria:** non-operative 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	**Aim/s:** "to investigate the use of NPWT to prevent wound dehiscence and infection after high-risk lower extremity trauma" **Intervention/s in both groups:** dressings or NPWT were applied in the operating room and then changed on postoperative day 2 and every 1 to 2 days thereafter. **Group 1 (NPWT) intervention:** NPWT over the surgical incision after open reduction and internal fixation of the fracture **Group 2 (control) intervention:** standard postoperative dressing (dressing not described) **Study date/s:** not stated
Outcomes	• wound infection and dehiscence • time to discharge from hospital

Stannard 2012 *(Continued)*

Validity of measure/s: "all infections were confirmed with cultures".

Time points: not stated - unclear for how long participants were followed up

Notes

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	**Evidence:** quote: "patients were enrolled and then randomised to receive either standard postoperative dressings (control) or NPWT (study)". **Comment:** additional author information: "the randomization was done via a computer generated randomization program".
Allocation concealment (selection bias)	Unclear risk	**Comment:** method not clarified
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	**Evidence for participants:** not possible **Comment:** unlikely to affect outcomes **Evidence for personnel:** not possible **Comment:** unlikely to affect outcomes
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	**Evidence:** quote: "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". **Comment:** not clear whether those assessing outcomes were aware of group assignment
Incomplete outcome data (attrition bias) All outcomes	Low risk	**Comment:** a total of 249 participants were recruited. The same number of participants 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 that an available-case analysis may have been performed.
Selective reporting (reporting bias)	Low risk	**Comment:** registered in CTR (NCT00582998) 9 months after final data collection date, so it is unclear whether reported outcomes matched the original protocol. However, infection and dehiscence were the expected outcomes.
Other bias	High risk	**Comment:** • unequal number of participants in each group • appeared from the protocol that data collection was over many years, but no dates or explanation in manuscript • results reported per fracture, so there is a potential unit of analysis issue

Tanaydin 2018

Study characteristics

Tanaydin 2018 *(Continued)*

Methods	**Study design:** randomised controlled trial **Study grouping:** parallel **Ethics and informed consent:** ethics approved and consent obtained **Sample size calculation:** no **Follow-up period:** 365 days postsurgery **ITT analysis:** wounds (breasts), not people were assessed **Funding:** funded by Smith & Nephew Ltd, who provided the PICO dressings and the Cutometer and financed a research assistant for carrying out the assessments and measurements
Participants	**Location:** the Netherlands **Intervention group:** n = 32,**control group:** n = 32 (participants served as their own control) **Mean age (range):** 40.9 (18 to 61) **Inclusion criteria:** patients > 18 years of age who underwent bilateral superomedial pedicle Wise-pattern breast reduction mammoplasty and had postsurgical incisions of similar length on each breast **Exclusion criteria:** pregnancy or lactation, using steroids, or other immune modulators known to affect wound healing; history of radiation of the breast; tattoos in the area of the incision; skin conditions such as cutis laxa that would result in poor healing or widen scars, history of radiation of the breast, patients with a known significant history of hypertrophic scarring or keloids, and postsurgical incisions still actively bleeding, exposure of blood vessels, organs, bone, or tendon at the base of the reference wound; and incisions > 12 inches (30 cm) maximum linear dimension
Interventions	**Aim/s:** to evaluate the effectiveness of postsurgery incision treatment comparing a portable disposable NPWT system with standard care using fixation strips **Group 1 (NPWT) intervention:** a single-use NPWT system without an exudate canister **Group 2 (control) intervention:** fixation strips (Steri-Strip; 3M, St Paul, Minnesota, USA) **Study date/s:** 1 June 2012 to 9 April 2014
Outcomes	• the number of wound-healing complications within 21 days • aesthetic appearance and quality of scarring (additional measurements at 42, 90, 180, and 365 days) **Validity of measure/s:** wound-healing complications were defined as delayed healing (surgical incision not 100% closed at day 7 postsurgery), or occurrence of dehiscence or infection within 21 days postsurgery **Time points:** all included participants (N = 32) had follow-up visits and assessments at screening (presurgery), day 0 (baseline, postsurgery), day 7, 21, 42, 90, 180, and 365 postsurgery.
Notes	The breasts were randomised and served as own control.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote "Randomization was used for allocation of NPWT and fixation strip to the right or left breast incision site per patient, using sealed envelopes. Treatment site information was accessed digitally (www.sealedenvelope.com) upon the start of the treatment postsurgically." Comment: appears to be a computerised method of sequence generation
Allocation concealment (selection bias)	Low risk	Quote "Randomization was used for allocation of NPWT and fixation strip to the right or left breast incision site per patient, using sealed envelopes. Treat-

Tanaydin 2018 *(Continued)*

		ment site information was accessed digitally (www.sealedenvelope.com) upon the start of the treatment postsurgically." Comment: appears to be a web-based allocation centre
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "As NPWT and fixation strips are optically different, blinding of the physician and patients was not feasible". Comment: Participants and personnel were not blinded.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "as NPWT and fixation strips are optically different, blinding of the physician and patients was not feasible; however, data analysis was performed blinded".
Incomplete outcome data (attrition bias) All outcomes	Low risk	32 enrolled participants were accounted for in the analyses.
Selective reporting (reporting bias)	Low risk	Expected outcomes reported. Protocol retrospectively registered as NL40698.068.12/METC12-3-026
Other bias	Unclear risk	This was a 'split-body' or 'intra-individual' design where a person with 2 wounds had 1 wound randomised to each treatment. It was not clear whether the analysis took this into account.

Tuuli 2017

Study characteristics	
Methods	**Study design:** randomised controlled trial (abstract only available) **Study grouping:** parallel **Ethics and informed consent:** not recorded **Sample size estimate:** not recorded **Follow-up period:** 30 days **ITT analysis:** yes, **number randomised:** 120, **number analysed:** 120 **Funding:** non-industry **Preregistration:** yes (NCT02578745). Registered 11 June 2012
Participants	**Location:** St Louis, Missouri, USA **Intervention group:** n = 60,**control group:** n = 60 **Mean age:** not recorded **Inclusion criteria:** • gestational age ≥ 23 weeks • BMI ≥ 30 at the time of delivery • planned or unplanned caesarean delivery (procedure in which NPWT is being tested) **Exclusion criteria:** • not available for postoperative follow-up

Tuuli 2017 *(Continued)*

	• contraindication to NPWT applicable to women undergoing caesarean: pre-existing infection around incision site, bleeding disorder, therapeutic anticoagulation, allergy to any component of the dressing (e.g. silicone, adhesive tape)
Interventions	**Aim/s:** to assess the feasibility of a definitive RCT to test the effectiveness and safety of prophylactic NPWT in obese women after caesarean section **Group 1 (NPWT) intervention:** prophylactic NPWT with the PICO device (Smith & Nephew). Removed at discharge (usually on day 4) **Group 2 (control) intervention:** standard wound dressing (routine postoperative wound dressing consisting of layers of gauze and adhesive tape). The dressing was removed 24 to 48 hours. **Study date/s:** October 2016 to March 2016
Outcomes	• **Primary outcome/s:** composite of superficial or deep surgical site infection; wound separation ≥ 2 cm; SSI; haematoma; seroma • **Secondary outcome/s:** pain score on postoperative day 2 and skin reactions **Validity of measure/s:** wound infection defined by CDC criteria (information extracted from CTR) **Time points:** 30 days
Notes	Investigator contacted for additional details

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information in abstract to permit judgement
Allocation concealment (selection bias)	Unclear risk	Insufficient information in abstract to permit judgement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Insufficient information in abstract to permit judgement
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information in abstract to permit judgement
Incomplete outcome data (attrition bias) All outcomes	Low risk	Abstract indicated that 120 participants were randomised and 120 analysed. This was consistent with the number proposed in NCT02578745.
Selective reporting (reporting bias)	Low risk	Reporting was consistent with outcomes proposed in NCT02578745..
Other bias	Unclear risk	None detected. Independently funded trial, however no baseline data presented

Hussamy 2017

Study characteristics

Hussamy 2017 *(Continued)*

Methods	**Study design:** randomised controlled trial **Ethics and informed consent:** not reported **Sample size calculation:** yes **Follow-up period:** not stated **ITT analysis:** yes **Funding:** not stated
Participants	**Location:** Texas, USA **Intervention group:** n = 222,**control group:** n = 219 **Mean age:** not reported **Inclusion criteria:** women with class III obesity (BMI > 40 kg/m^2) undergoing caesarean delivery **Exclusion criteria:** women on anticoagulation, with HIV infection, sensitive skin disorders, or silver or acrylic allergies
Interventions	**Aim/s:** to compare the efficacy of closed incision negative pressure therapy (ciNPT) with a standard surgical dressing in the prevention of postoperative wound morbidity in women with class III obesity undergoing caesarean delivery **Group 1 (NPWT) intervention:** a ciNPT dressing at time of caesarean **Group 2 (control) intervention:** a standard surgical dressing **Study date/s:** January 2015 to July 2016 (18 months)
Outcomes	• wound morbidity including wound disruption requiring the use of antimicrobials, prolonged postoperative hospitalisation, hospital readmission, or reoperation within 30 days of delivery **Validity of measure/s:** not stated **Time points:** not stated
Notes	Only the abstract was available.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not stated
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not stated
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not stated
Incomplete outcome data (attrition bias) All outcomes	Low risk	441 participants were enrolled and analysed.

Hussamy 2017 *(Continued)*

Selective reporting (reporting bias)	Low risk	Expected outcomes were reported in the abstract.
Other bias	Unclear risk	Not stated

Hyldig 2019a

Study characteristics	
Methods	**Study design:** pragmatic randomised controlled trial **Study grouping:** parallel **Ethics and informed consent:** yes **Follow-up period:** 30 days **Sample size estimate:** yes; a sample size of 870 for a reduction in surgical site infection of 50% in the intervention group compared with an expected baseline event rate of 10% in the control group, with a two-sided 5% significance level and a power of 80% **ITT analysis:** yes (for surgical site infection only),**number randomised:** 876, **number analysed:** 876 for surgical site infection and 827 for other outcomes **Funding:** grants from the University of Southern Denmark, Odense University Hospital, the Region of Southern Denmark, Lundbeckfonden, and an unrestricted grant from the iNPWT device manufacturer Smith & Nephew (devices and operating funding) **Preregistration:** yes; ClinicalTrials.gov (NCT 01890720)
Participants	**Location:** Denmark (two tertiary referral centres and three Danish teaching hospitals) **Intervention group:** n = 432, **control group:** n = 444 (6 received iNWPT dressing) **Mean age:** a range from 18 to 46 years across groups; **intervention group:** 32 (SD 5), **control group** 32 (SD 5) **Inclusion criteria:** pregnant women undergoing elective or emergency caesarean section, aged >= 18 years; who had a prepregnancy body mass index >= 30 kg/m2, and could read and understand Danish **Exclusion criteria:** women who had given informed consent but subsequently delivered vaginally
Interventions	**Aim/s:** to investigate the effectiveness of prophylactic iNPWT after caesarean section in obese women; hypothesis: iNPWT would be associated with fewer surgical site infection and other wound complications (i.e., wound exudate and dehiscence) compared with standard postoperative dressing. **Group 1 (NPWT) intervention:** incisional negative pressure wound therapy (iNPWT; PICO, SIZE 10 * 30 cm or 10 * 40 cm, Smith & Nephew, Hull, UK) in which dressing was left in situ for approximately 5 days **Group 2 (control) intervention:** standard postoperative dressing in which dressing was left in situ for at least 24 hours **Study date/s:** September 2013 to October 2016
Outcomes	• Surgical site infection, those infections requiring antibiotic treatment within the first 30 days after caesarean section • Deep surgical site infection, those infections requiring surgery • Minor dehiscence, defined as a gap between the sides of the wound • Health-related quality of life (EQ-5D-5L) • Readmissions to hospital/contact to the general practitioner on suspicion of infection following caesarean section (listed in ClinicalTrials.gov) **Validity of measure/s:**

Hyldig 2019a *(Continued)*

	Time points: within the first 30 days after surgery
Notes	Results were submitted to ClinicalTrials.gov in September 2018 but were not posted online. Could contact authors to request such data

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Participants were randomised in the operating theatre during surgery using a web-based randomisation programme with a 1:1 allocation ratio and random block sizes of 4–6, stratified by centre and type of caesarean section (emergency versus elective)." Comment: low risk of bias due to valid random sequence generation
Allocation concealment (selection bias)	Low risk	Quote: "The random allocation sequence was generated by an external data manager with no clinical involvement in the study". Comment: low risk of bias due to likely appropriate approach taken to conceal randomisation process
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "Blinding was not possible due to the nature of the intervention". Comment: high risk of bias because it was clearly stated no blinding of participants and personnel
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	ITT analysis was conducted for surgical site infection and for other outcomes; only 22 of 432 in Group 1 and 27 of 444 in Group 2 were excluded from analyses. Low risk of attrition bias
Selective reporting (reporting bias)	High risk	Readmission to hospital/contact to the GP was listed on ClinicalTrials.gov but not presented in the full text. High risk of reporting bias
Other bias	Low risk	None detected

Hyldig 2019b

Study characteristics

Methods	**Study design:** cost-effectiveness analysis (economic evaluation based on the Hyldig 2019a RCT) **Analytical approach:** Decision-analytic model **Effectiveness data**: Data from a multicentre RCT (n = 876) (Hyldig 2019a): SSI. Both risk and severity of infection were incorporated. The Danish crosswalk value sets were used to derive preference-based index values. **Perspective:** Danish healthcare **Utility valuations:** QALYs informed by EuroQol EQ-5D-5L (scoring algorithm not specified but Danish-specific context taken into account) were calculated based on SSI costs for superficial and deep SSIs avoided including antibiotic prescription costs and need for further surgery.

Hyldig 2019b *(Continued)*

	Measure of benefit: surgical site infection avoided; QALY **Cost data:** Costs were estimated using data from four Danish National Databases and analysed from a Danish healthcare perspective with a time horizon of 3 months after birth. Conversion from DK to Euro using the year 2015 value. No discount rate was applied. Total costs consisted of four cost components: hospital costs; costs of using GPs; costs of antibiotics; and postoperative dressing cost. These were all from the Cost Database. Costs of iNPWT dressing was Euro 151.40, including device itself and time costs for its application. **Analysis of uncertainty:** probabilistic sensitivity analysis including an expanded time horizon and an extrapolation of QALY gain to 5 years (3% annual discount). Deterministic sensitivity analyses conducted to permit determination of possible uncertainty in the ICER that would result from a change in a single parameter in the analysis. Scenario analyses to evaluate the impact of missing cost and QALY data, and the influence of one outlier on the ICER. A subgroup analysis stratifying by BMI explored the impact of the intervention in women with a pre-pregnancy BMI >/= 35.
Participants	**Location:** Denmark (two tertiary referral centres and three Danish teaching hospitals) **Intervention group:** n = 432, **control group:** n = 444 **Mean age:** a range from 18 to 46 years across groups; **intervention group:** 32 (SD 5), **control group** 32 (SD 5) **Inclusion criteria:** pregnant women undergoing elective or emergency caesarean section, aged >= 18 years; who had a pre-pregnancy body mass index >= 30 kg/m2, and could read and understand Danish **Exclusion criteria:** women who had given informed consent but subsequently delivered vaginally
Interventions	**Aim/s:** To evaluate the cost-effectiveness of incisional negative pressure wound therapy (iNPWT) in preventing surgical site infection in obese women after caesarean section **Group 1 (NPWT) intervention:** Incisional negative pressure wound therapy (iNPWT; PICO, SIZE 10 x 30 cm or 10 x 40 cm, Smith & Nephew, Hull, UK) in which dressing was left in situ for approximately 5 days (n = 432 in a trial) **Group 2 (control) intervention:** Standard postoperative dressing in which dressing was left in situ for at least 24 hours (n = 444 in a trial) **Study date/s:** September 2013 to October 2016
Outcomes	For data see Hyldig 2019b and for clinical data see Hyldig 2019a in additional table 1 SSI Costs (Euro) QALY (measure of benefit). ICER with 95% CrI to inform probability of strategy being cost-effective/dominant using the willingness-to-pay threshold of 30,000 Euro/QALY
Notes	**Authors' conclusions**: Incisional NPWT appears to be cost saving compared with standard dressings but this finding is not statistically significant. The cost savings were primarily found in women with a pre-pregnancy BMI ≥ 35 kg/m^2. **Funding:** University of Southern Denmark, Odense University Hospital, the Region of Southern Denmark, Lundbeckfonden, and an unrestricted grant from the iNPWT device manufacturer Smith & Nephew (devices and operating funding) **Quality assessment:** CHEERS score 91.7%

Javed 2018

Study characteristics	
Methods	**Study design:** randomised controlled trial **Study grouping:** parallel **Ethics and informed consent:** yes **Follow-up period:** 30 days after operations **Sample size estimate:** yes; a sample size of 124 patients was assumed to provide a power of 80% to detect a 20% relative reduction in surgical site infection incidence (decreasing from 30% to 10%) at a 2-sided alpha level of 0.05 **ITT analysis:** yes; **number randomised:** 124, **number analysed:** 123 **Funding:** KCI/Acelity (Grant number #125164) **Preregistration:** Not reported
Participants	**Location:** America (single site) **Intervention group:** n = 62, **control group:** n = 62 **Mean age: intervention group** mean 66.4 (SD 9.3) years, **control group** 66.1 (9.0) **Inclusion criteria:** adults (18 yrs of age) who had a SSI risk score of 1 as defined by the risk score proposed by Poruk et al. This included patients who had received neoadjuvant chemotherapy, preoperative biliary stenting, or both. **Exclusion criteria:** pancreaticoduodenectomies (PD) performed minimally invasively or known allergies or sensitivity to silver or acrylic adhesives
Interventions	**Aim/s:** to evaluate the efficacy of negative pressure wound therapy for surgical-site infection (SSI) after open pancreaticoduodenectomy **Group 1 (NPWT) intervention:** negative pressure wound therapy (NPWT) device is shown in Figure S1. The PREVENA™ CUSTOMIZABLE™ device is comprised of a PREVENA™ CUSTOMIZABLE™ dressing, sealing strips, KCI drapes, and Interface Pad. **Group 2 (control) intervention:** standard closure technique **Study date/s:** January 2017 through February 2018
Outcomes	• Surgical site infection defined by the National Health Safety Network definition of the Centers for Disease Control and Prevention (CDC) • Need for reoperation • 30-day readmission related to SSI • Cost of hospitalisation **Validity of measure/s:** **Time points:** 30 days after operation
Notes	Haematoma, seroma, or skin separation were considered under the outcome of surgical site infection (SSI) according to the judgement criteria used for SSI. Data of these outcomes were not extracted or used for this review.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Using the simple randomization method, a random allocation sequence was generated." "Once the surgeon committed to performing a PD by ruling out metastatic disease or inoperable local vascular involvement, the cir-

Javed 2018 *(Continued)*

		culating nurse contacted the research staff for randomization. The presealed envelope was opened to randomize the patient." Comment: unclear risk of bias because the method of generating random sequence was not specified
Allocation concealment (selection bias)	Low risk	Quote: "Allocation concealment was achieved by printing allocation onto a gray-shaded card that was folded and sealed in a secured envelope before initiation of the study". Comment: low risk of bias given an appropriate strategy was used to conceal allocation
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "All patients also received standard infection-prevention measures..." Comment: insufficient information on blinding of participants and personnel
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "patients' EMR were reviewed independently by the principal investigator (MJW) blinded to study-group assignments to determine if SSI was documented at any time during the 30-day postoperative period. " Comment: low risk of bias for SSI because the outcome assessors were blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: Low risk of bias because 123 of 124 participants randomised were analysed. One of the 62 participants that were randomised to Group 2 (Control) was excluded from the analysis because the surgeon decided to use NPWT for that person rather than the control intervention.
Selective reporting (reporting bias)	Low risk	All outcomes listed in the Methods were reported in the Results.
Other bias	Low risk	None detected

Karlakki 2016

Study characteristics	
Methods	**Study design:** randomised controlled trial **Study grouping:** parallel **Ethics and informed consent:** yes **Follow-up period:** 6 weeks **Sample size estimate:** pilot study **ITT analysis:** yes, **number randomised:** 220, **number analysed:** 209 **Funding:** study funded through a grant from Smith & Nephew UK to cover the cost of NPWT dressings and data collection costs. 2 investigators declared they had funding and consultancy fees from Smith & Nephew. **Preregistration:** no
Participants	**Location:** Oswestry, UK **Intervention group:** n = 110,**control group:** n = 110 **Mean age (SD): intervention group** = 69 (9.0),**control group** = 69.2 (9.0)

Karlakki 2016 *(Continued)*

	Inclusion criteria: patients undergoing total hip or knee arthroplasties (for any indication) with any of 3 consultant surgeons **Exclusion criteria:** patients who had known allergies to dressing, were undergoing revision joint surgery, were unwilling to attend additional clinics, and those on warfarin were excluded.
Interventions	**Aim/s:** to evaluate the effectiveness of incisional negative pressure wound therapy dressing (iNPWTd) **Group 1 (NPWT) intervention:** PICO dressing applied over the primarily closed incision by the surgeon in the operating room. Dressing was left on for 4 days, or longer if drainage continued, unless soiled or dislodged. **Group 2 (control) intervention:** Comfeel dressing applied over the primarily closed incision by the surgeon in the operating room. Dressing was left on for 4 days, or longer if drainage continued, unless soiled or dislodged. **Study date/s:** July 2012 to April 2014
Outcomes	• SSI • blisters • haematoma • hospital readmission **Validity of measure/s:** not described **Time points:** 1, 2, and 6 weeks postsurgery
Notes	Investigator contacted for additional details

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "the randomisation was performed using sealed opaque envelopes with a block size of 20 shuffled envelopes". **Comment:** no sequence generation was required.
Allocation concealment (selection bias)	Low risk	Quote: "the randomisation was performed using sealed opaque envelopes with a block size of 20 shuffled envelopes". **Comment:** allocation was unknown until envelope opened.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "This was a non-blinded single-centre randomised controlled parallel group study". Comment: non-blinded study
Blinding of outcome assessment (detection bias) All outcomes	High risk	Outcome assessors were aware of group allocation.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	7.3% in intervention group and 2.7% in control group PP analysis **Comment**: more participants were excluded from the analysis in the intervention group (8 intervention vs 3 control).
Selective reporting (reporting bias)	Low risk	Expected outcomes reported

Karlakki 2016 *(Continued)*

Other bias	High risk	Intervention participants were seen in a wound clinic at 1 week, and control participants were not.

Keeney 2019

Study characteristics	
Methods	**Study design:** randomised controlled trial **Study grouping:** parallel **Ethics and informed consent:** yes **Follow-up period:** 35 days **Sample size estimate:** not reported **ITT analysis:** no; **number randomised:** 526; **number analysed:** 398 **Funding:** Institution of authors received research funding from Smith & Nephew Orthopaedics that was related to this study. **Preregistration:** not reported
Participants	**Location:** America (one site) **Intervention group:** 185 analysed; **control group:** 213 analysed **Mean age: intervention group** 60.6 years, **control group** 60.5 **Inclusion criteria:** consenting age, surgical treatment with primary or revision THA, surgical treatment with primary or revision TKA; and having an advanced technology device capable of digital photography **Exclusion criteria:** pregnancy, history of poor compliance with medical treatment, allergy to silicone adhesives or polyurethane films, and unwillingness to participate in an RCT
Interventions	**Aim/s:** to assess whether a portable iNPWT device affects wound appearance, postoperative wound drainage, dressing-related complications, wound healing complications, infection rates, and reoperation rates when compared with a standard of care (SOC) postoperative dressing **Group 1 (NPWT) intervention:** incisional negative pressure wound therapy (iNPWT), a battery-operated, portable NPWT device with an exchangeable cartridge (PICO, Smith & Nephew Orthopaedics, Memphis, TN) with negative pressure applied at 80 mmHg (± 20 mmHg) for an initial period of 7 days **Group 2 (control) intervention:** a standard of care (SOC) postoperative dressing, including nonadherent incisional cover (Adaptic or Xeroform gauze), 4 4 inch gauze, and an abdominal dressing. Dressings were changed on postoperative day 2 with subsequent dressing changes performed at 3- to 5-day intervals until the incision was dry. **Study date/s:** enrolment between April 1, 2014, and January 31, 2017
Outcomes	• Superficial and late wound infection rates 7/185 vs. 8/213 • Return to the operating room to manage a wound-related concern within the first 3 months **Validity of measure/s:**. **Time points:**
Notes	The number of patients randomised in either group was not reported. The authors also reported wound appearance; all-cause complications, wound drainage, and dressing concerns outcomes. These outcomes were not extracted for this review. Regarding outcomes of interest to this review, the authors also stated that "*Two patients in each group underwent surgical treatment for a superficial wound infec-*

Keeney 2019 *(Continued)*

tion during the first 90 days after surgery... Four TKA patients in the standard dressing control group were returned to the operating room within the first 35 days for management of a wound-related complication but deep infection was not diagnosed". These data were not extracted for this review because it was unclear whether they were systematically collected.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "A total of 526 patients (22.5%) consented to participate in the study and were randomised into either the iNPWT device or SOC dressing treatment groups". Comment: unclear risk of bias because no method of generating random sequence was specified
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Understandably difficult to blind participants and personnel in this trial
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "Wound appearance was assessed from patient-provided incision photographs by a single trained research team member, blinded to time point and group, using a previously published and validated 100-mm visual analog scale." Comment: it appears that only wound appearance outcome was assessed in a blinding way. However, this outcome was not of interest to this review. It is unclear whether blinding of outcome assessment was undertaken for other outcomes.
Incomplete outcome data (attrition bias) All outcomes	High risk	Quote: "A total of 526 patients (22.5%) consented to participate in the study and were randomised ... After the initial randomization, 94 patients were excluded ... After excluding 34 unicompartmental knee arthroplasty patients, 398 patients remained for assessment..." Comment: high risk of bias because a high proportion of randomised participants (24%, 128 of 526) were excluded from data analysis.
Selective reporting (reporting bias)	Low risk	All outcomes mentioned in the Methods were reported in the Results though the reporting appeared to be implicit.
Other bias	Low risk	None detected

Kuncewitch 2017

Study characteristics

Methods	**Study design:** randomised controlled trial **Study grouping:** parallel **Ethics and informed consent:** not reported **Follow-up period:** not reported

Kuncewitch 2017 *(Continued)*

	Sample size estimate: not reported **ITT analysis:** yes, **number randomised:** 73, **number analysed:** 73 **Funding:** not reported **Preregistration:** not reported
Participants	**Location:** not reported **Intervention group:** n = 36,**control group:** n = 37 **Mean age (SD):** not reported **Inclusion criteria:** high-risk surgical oncology patients undergoing laparotomy **Exclusion criteria:** not stated
Interventions	**Aim/s:** to investigate the effects of NPWT on short- and long-term wound outcomes in people undergoing pancreatectomy **Group 1 (NPWT) intervention:** NPWT **Group 2 (control) intervention:** standard surgical dressing **Study date/s:** 2012 to 2016
Outcomes	• postoperative wound complications in the first 30 days • incisional hernia rates • rates of pancreatic fistula • delayed gastric emptying **Validity of measure/s:** not described **Time points:** not stated
Notes	Only the abstract was available.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not stated
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not stated
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not stated
Incomplete outcome data (attrition bias) All outcomes	Low risk	73 participants were enrolled and analysed.
Selective reporting (reporting bias)	Unclear risk	Expected outcomes were reported in the abstract.

Kuncewitch 2017 *(Continued)*

Other bias	Unclear risk	Abstract only

Kwon 2018

Study characteristics	
Methods	**Study design:** randomised controlled trial **Study grouping:** parallel **Ethics and informed consent:** yes **Follow-up period:** 30 days **Sample size estimate:** pilot study informed the calculation which was based on power 0.80 to demonstrate reduction from 30% to 15% in SSI. This was based on incisions not patients. **ITT analysis:** no,**number randomised:** 123,**number analysed:** 119 incisions was the unit of analysis; 24 participants had 48 incisions **Funding:** performed without any support, financial or otherwise, from the makers of the Prevena dressing **Preregistration:** not stated
Participants	**Location:** USA single hospital **Intervention group:** 59,**control group:** 60 incisions; 24 people contributed 48 incisions (24 to each group) **Mean age: intervention group** 64.6 (44-83), **control group** 67.4 (41-84) **Inclusion criteria:** patients aged 18 years and older undergoing elective vascular surgery under the supervision of the Division of Vascular and Endovascular Surgery at Thomas Jefferson University Hospital involving unilateral or bilateral groin incisions; presence of any of the following criteria: body mass index (BMI) > 30 kg/m^2; significant pannus overlying groin skin or abnormal skin as evidenced by fungal infection; reoperative groin surgery; placement of prosthetic vascular graft; poor nutrition (BMI < 18 kg/m2, cachectic in appearance); immunosuppression (use of any immunosuppressive medications); and poorly controlled diabetes (hemoglobin A1c >8%) **Exclusion criteria:** emergency operation and those unwilling or unable to provide informed consent
Interventions	**Aim/s:** to determine whether application of a negative pressure dressing (Prevena Incision Management System) is superior to a standard surgical dressing in preventing vascular groin wound complications and their associated hospital costs. **Group 1 (NPWT) intervention:** negative pressure dressing (Prevena) applied according to the manufacturer's instructions. It involved application of an antibiotic sponge (0.019% ionic silver), cut to cover the closed groin wound, covered by a clear occlusive dressing attached to a suction device that applied -125 mmHg pressure. This device was inspected daily and left in place for 5 days, after which a dry gauze dressing was placed, inspected and replaced daily until discharge. **Group 2 (control) intervention:** standard surgical dressing consisting of gauze covered by Tegaderm (3M, St. Paul, Minn). This dressing was removed on postoperative day 2 and replaced with a dry gauze dressing that was inspected and replaced daily until discharge. **Study date/s:** January 1st, 2015 to December 31st, 2016
Outcomes	• SSI • (skin) dehiscence • lymph leakage (seroma or fistula) but no separate data on seroma • haematoma

Kwon 2018 *(Continued)*

- reoperation
- hospital readmission
- costs

Validity of measure/s: The Szilagyi classification of vascular wound infection was also used to classify the infection.

Time points: daily until hospital discharge; within 10 to 14 days, whereupon staples were removed; and within 25 to 30 days to complete the study

Notes

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote "They used a coin toss to determine whether the patient was to receive standard dressing or negative pressure therapy. To maintain 1:1 randomization as well as to provide future analysis using internal controls, any high-risk patient undergoing bilateral groin incisions would receive both a standard dressing and negative pressure therapy". Comment: adequate method for the unilateral surgery; unclear for the bilateral
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "Other than the fact that the 30-day examination occurred without the overt knowledge of the patient's initial treatment, no blinding was instituted". Comment: The surgical team, clinical staff, and patient were not blinded to the intervention status.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Quote: " Wound assessment was made by both the primary surgeon and nurse practitioners.....Furthermore, a major limitation to the study was that it was not a blinded study and therefore subject to observer bias. Assessment of complications is qualitative, and ultimate management of infections, such as opening an infected wound, was left to the discretion of the attending surgeon." Comment: Outcome assessment was performed by an unblinded assessor.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "Because a contralateral complication would penalize the uncomplicated groin incision in terms of LOS and hospital variable costs, in this circumstance the uncomplicated groin incision data were dropped from consideration in terms of LOS and variable costs". "As such, for the high-risk, standard dressing group (n = 60), five were dropped because of a contralateral complication (n = 55); for the high-risk, Prevena group (n = 59), eight were dropped because of a contralateral complication (n = 51)"; In the intervention group, two incisions discontinued intervention because of graft failure postoperative Day 1; In the control group, two incisions discontinued intervention because of reopening of incision for graft failure postoperative Day 1 and fatal myocardial infarction post-operative Day 3. Comment: Clear from the study how many participants withdrew and the reasons
Selective reporting (reporting bias)	Low risk	Comment: protocol not found, but according to the method, all results were reported.

Kwon 2018 *(Continued)*

Other bias	Unclear risk	This was a planned? interim analysis after 80% recruitment with a stopping guideline if 50% reduction in SSI. The unit of analysis was the incision and the unit of randomisation appeared to be the incision where there was bilateral incision. Unclear how this paired data dealt with in analysis

Lee 2017a

Study characteristics	
Methods	**Study design:** randomised controlled trial **Study grouping:** parallel **Ethics and informed consent:** yes **Follow-up period:** 6 weeks **Sample size estimate:** not reported **ITT analysis:** no, **number randomised:** 60, **number analysed:** 44 **Funding:** KCI USA Incorporated, an Acelity company **Preregistration:** yes
Participants	**Location:** Canada **Intervention group:** n = 33,**control group:** n = 27 **Mean age (± SD): intervention group** = 67.1 (± 7.2),**control group** = 68.3 (± 9.7) **Inclusion criteria:** receiving an isolated elective or semi-elective CABG and above 18 years of age living within 1 hour of the institution **Exclusion criteria:** emergent surgery, previous CABG or lower leg surgical intervention, severe peripheral vascular disease, dialysis-dependent renal failure, and chronic steroid administration
Interventions	**Aim/s:** to establish the safety and feasibility of using NPWT on the GSV harvest site postcardiac surgery and to examine the effects on infection, complications, and overall patient function **Group 1 (NPWT) intervention:** NPWT device was placed at the time of GSV harvest in the operating room and then maintained in situ until the day prior to hospital discharge or to a maximum of 7 days. The device was removed if poorly tolerated by the participant or for any safety concerns. **Group 2 (control) intervention:** conventional dry gauze dressings **Study date/s:** not stated
Outcomes	• rates of device complication and malfunction • rates of SSI, lower leg complications, discharge date, and quality of life at discharge and 6 weeks **Validity of measure/s:** complications were classified as major if they required a medical or surgical intervention. All complications and device malfunctions were recorded. The total length of therapy with the NPWT device was recorded, and also if therapy was prematurely interrupted for any reason. SSIs was determined through assessment of the ASEPSIS score. The incidence of leg complications was also examined including pain, heaviness, weakness, stiffness, itching, paraesthesia, numbness, burning, discolouration, rash, and oedema. These complications were graded as 'not present', 'mild', 'moderate', and 'severe'. Only the moderate and severe complaints were included for incidence analysis. Discharge dates were also recorded for all participants. Self reported assessments of mobility, overall pain or discomfort, feelings of anxiety or depression, ability for self care, and ability to perform usual activities were performed. These measures were graded as no issues, some issues, and severe issues or inability. Quality of life was also measured using the EQ-5D-3L Measure of Health Status.

Lee 2017a *(Continued)*

	Time points: initial and 6 weeks
Notes	33 vs 27 participants randomised; high loss to follow-up recorded

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Consented patients were randomised by use of sealed ballot envelopes in a 1-to-1 fashion.
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "We performed a prospective, randomised, single-blind, single centre, clinical feasibility study". Comment: Single-blinded - and the person who was blinded was the outcome assessor.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	A research assistant blinded to the grouping assessed the incision and participant prior to discharge and at 6 weeks postoperatively. A second, unblinded research assistant recorded and managed any device-related complications. Participants were discharged based on standardised institutional discharge criteria.
Incomplete outcome data (attrition bias) All outcomes	High risk	12 participants were lost to follow-up at 6 weeks, 4 in the NPWT group and 8 in the control group. These participants were not included in the data analysis.
Selective reporting (reporting bias)	Low risk	Planned outcomes reported. Protocol registered on ClinicalTtrials.gov (NCT01698372)
Other bias	Unclear risk	High loss to follow-up without reasons for loss being provided; unclear whether additional risks of bias

Lee 2017b

Study characteristics

Methods	**Study design:** randomised controlled trial **Study grouping:** parallel **Ethics and informed consent:** yes **Follow-up period:** 90 days **Sample size estimate:** yes **ITT analysis:** no, **number randomised:** 102, **number analysed:** 102 **Funding:** not company funded **Preregistration:** yes
Participants	**Location:** Canada **Intervention group:** n = 53,**control group:** n = 49 **Mean age: intervention group** = 69 ± 10,**control group** = 68 ± 10

Lee 2017b *(Continued)*

	Inclusion criteria: patients with 1 of the following 3 risk factors for SSIs were enrolled in the trial: obesity defined as a BMI of > 30 kg/m^2, previous femoral artery exposure, or presence of minor or major ischaemic tissue loss. **Exclusion criteria:** patients with pre-existing groin infection, a known allergy to dressing material, or those who could not be followed postoperatively were excluded from the study.
Interventions	**Aim/s:** to perform an RCT to study the role of NPWT on SSI in primarily closed groin incisions after lower extremity revascularisation in vascular surgery patients **Group 1 (NPWT) intervention:** NPWT remained on until either hospital discharge or postoperative day 8, whichever occurred earlier. **Group 2 (control) intervention:** standard gauze dressing (the dressing removed on postoperative day 2, and then had daily dressing changes with inspection of the wound) **Study date/s:** August 2014 to December 2015
Outcomes	• the incidence of SSI within 30 days of revascularisation • duration of hospital stay • SSI within 90 days • reoperation and readmission rate owing to SSI within 90 days • mortality within 90 days **Validity of measure/s:** SSI was diagnosed using the CDC guideline as a superficial or deep infection. The Szilagyi classification of vascular wound infection was also used to classify the infection. **Time points:** once discharged, both groups were followed up in the clinic at 30 and 90 postoperative days.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Eligible patients were randomised to NPWT or a standard sterile gauze dressing using an internet-based software, sealedenvelope.com (London, UK), using block randomisation.
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "patients and surgeons were not blinded to the treatment they had received". Comment: no blinding of participants or personnel
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Wounds were inspected at each clinic visit by a wound specialist nurse who was blinded to the treatment groups. If she was uncertain, the staff physician determined the presence or absence of an SSI. An SSI could also be diagnosed by the patient care team if there were clinical signs and symptoms of infection.
Incomplete outcome data (attrition bias) All outcomes	Low risk	102 participants were enrolled and analysed.
Selective reporting (reporting bias)	Low risk	Planned outcomes reported. Protocol registered on ClinicalTrials.gov (NCT02084017)
Other bias	Low risk	No other biases detected

Leon 2016

Study characteristics	
Methods	**Study design:** prospective, randomised, multicentre study **Study grouping:** parallel **Ethics and informed consent:** not reported **Follow-up period:** not reported **Sample size estimate:** not reported **ITT analysis:** yes, **number randomised:** 81, **number analysed:** 81 **Funding:** not reported **Preregistration:** not reported
Participants	**Location:** Spain **Intervention group:** n = 47,**control group:** n = 34 **Mean age (SD):** not reported **Inclusion criteria:** patients undergoing open and programmed colorectal surgery **Exclusion criteria:** not stated
Interventions	**Aim/s:** to evaluate the benefits of negative pressure therapy to reduce surgical site infection rate in open colorectal surgery **Group 1 (NPWT) intervention:** NPWT **Group 2 (control) intervention:** usual dressing group **Study date/s:** not reported
Outcomes	• SSI rate **Validity of measure/s:** not described **Time points:** a daily evaluation through hospitalisation and a 15- and 30-day evaluation
Notes	Only the abstract was available.

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Not stated
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not stated
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not stated

Leon 2016 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Low risk	All enrolled participants were accounted for in the analyses.
Selective reporting (reporting bias)	Unclear risk	Not stated
Other bias	Unclear risk	Abstract only

Lozano-Balderas 2017

Study characteristics	
Methods	**Study design:** randomised controlled trial **Ethics and informed consent:** ethics approved **Sample size calculation:** no **ITT analysis:** yes, **number randomised:** 81, **number analysed:** 81 **Follow-up period:** healed (when in hospital) or in a 30-day period after surgery (if discharged) **Funding:** non-industry **Preregistration:** yes
Participants	**Location:** Mexico **Intervention group:** n = 25,**control group:** n = 27, **(3 arms: delayed primary closure group:** n = 29**)** **Median age (IQR): intervention group** = 32 (22 to 46);**control group** = 30 (20 to 43) **Inclusion criteria:** minimum age of 18; a laparotomised wound with class III or IV (contaminated/dirty-infected) surgical wounds **Exclusion criteria:** not specified
Interventions	**Aim/s:** to compare infection rates between primary, delayed primary, and vacuum-assisted closures in contaminated/dirty-infected surgical wounds **Group 1 (NPWT) intervention:** the VAC was used with routine changes of dressings every 48 hours until healthy granulation tissue was found and a surgeon decided to close it. **Group 2 (control) intervention:** subcutaneous tissue was approximated with polyglycolic acid, and polypropylene was used for the skin. **Study date/s:** January to July 2014
Outcomes	• SSI **Validity of measure/s:** according to the CDC Surgical Wound Classification **Time points:** daily when in hospital or in a 30-day period after surgery
Notes	

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Quote: "patients were allocated to each group with the software Research Randomizer® (Urbaniak, G. C., & Plous, S., Version 4.0)".

Lozano-Balderas 2017 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	No information
Blinding of outcome assessment (detection bias) All outcomes	High risk	Outcome assessors were aware of group allocation.
Incomplete outcome data (attrition bias) All outcomes	Low risk	81 participants were enrolled and analysed.
Selective reporting (reporting bias)	Low risk	Expected outcomes reported. Protocol retrospectively registered on ClinicalTrials.gov (NCT02649543).
Other bias	Low risk	No other biases detected

Manoharan 2016

Study characteristics	
Methods	**Study design:** randomised controlled trial **Study grouping:** bilateral knees were randomised to intervention or control knees **Ethics and informed consent:** yes **Sample size estimate:** yes, but sample did not reach target, stopped due to financial constraints **Follow-up period:** 10 days **ITT analysis:** yes, **number randomised:** 21, **number analysed:** 21 **Funding:** KCI, Acelity Inc provided the negative pressure wound therapy dressings for the study. **Preregistration:** retrospectively registered as ANZCTR 12615001350516
Participants	**Location:** Queensland, Australia **Intervention group:** n = 21 knees,**control group:** n = 21 knees **Mean age (range):** 66 (45 to 80) **Inclusion criteria:** patients undergoing a bilateral knee arthroplasty **Exclusion criteria:** aged < 18 years or pregnant
Interventions	**Aim/s:** to assess the effect of NPWT on outcomes after primary arthroplasty **Group 1 (NPWT) intervention:** the intervention group received PREVENA Incision Management System, Acelity, KCI, which was placed over the closed surgical incision under sterile conditions at the end of the procedure. The NPWT device provided a continuous negative pressure of 125 mmHg for a duration of 8 days. **Group 2 (control) intervention:** the conventional dry dressing was placed over the closed surgical incision under sterile conditions at the end of the procedure. Neither the type of control dressing nor when the dressing was removed was reported.

Manoharan 2016 *(Continued)*

	Study date/s: February to December 2014
Outcomes	• SSI • blisters • cost • QoL **Validity of measure/s:** no **Time points:** 10 to 12 days postsurgery
Notes	Investigator contacted for additional details

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Simple randomisation was performed by the research assistants via online computer software that indicated the side to which the intervention, NPWT, would be applied.
Allocation concealment (selection bias)	Unclear risk	The surgeons were notified on the day of surgery, before the commencement of the procedure. It was also unclear if consecutive patients for each of the 3 surgeons were recruited.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "A final evaluation form at the outpatient review assessed the patients rated experience and preference for type of dressing. The final incision assessment was performed by the surgeon and clinic nurse and was witnessed by one of the research assistants. There were no independent observers attached to this assessment." Comment: Patients were aware of assignment, appeared that surgeons were not blinded.
Blinding of outcome assessment (detection bias) All outcomes	High risk	The final incision assessment was performed by the surgeon and clinic nurse and witnessed by 1 of the research assistants. There were no independent observers attached to this assessment.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	It was unclear if all participants were accounted for in the results as the numbers analysed for each outcome were not stated.
Selective reporting (reporting bias)	Low risk	Expected outcomes reported. Protocol retrospectively registered as ANZCTR 12615001350516.
Other bias	Low risk	No other biases detected

Martin 2019

Study characteristics

Methods	**Study design:** RCT **Study grouping:** parallel **Ethics and informed consent:** not reported **Follow-up period:** one year

Martin 2019 *(Continued)*

	Sample size estimate: not reported **ITT analysis:** yes, number randomised: 40, number analysed: 40 (not clearly reported) **Funding:** Not stated **Preregistration:** Not stated
Participants	**Location:** not reported **Intervention group:** 20,**control group:** 20 **Mean age:** 60.82 years,**intervention group** NR **control group** NR **Inclusion criteria:** patients undergoing hepatectomy or pancreatectomy **Exclusion criteria:** not reported
Interventions	**Aim/s:** to evaluate the effect of NPWT on SSI in this population (patients who have had hepatectomy or pancreatectomy) **Group 1 (NPWT) intervention:** incisional NPWT (PICO TM, Smith & Nephew, Hull, UK) **Group 2 (control) intervention:** sterile island dressing **Study date/s:** not reported
Outcomes	• SSI • dehiscence **Validity of measure/s:** Not reported **Time points:** Not reported
Notes	Abstract only

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote "Patients were randomised". Comment: method of generating randomisation sequence was not clear.
Allocation concealment (selection bias)	Unclear risk	Quote "Patients were randomised". Comment: unclear if appropriate methods were used to conceal allocation
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Comment: appeared likely that it would be impossible to blind participants or personnel to treatment allocation but insufficient information
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: unclear who assessed the outcomes or whether they were blinded to treatment allocation
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: All participants appeared to be included in the analysis.
Selective reporting (reporting bias)	Unclear risk	Comment: insufficient information

Martin 2019 *(Continued)*

Other bias	Unclear risk	Comment: No evidence of other bias but insufficient information to be sure

Masden 2012

Study characteristics	
Methods	**Study design:** randomised controlled trial **Ethics and informed consent:** 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. **Sample size calculation:** yes **Follow-up period:** mean 113 days **ITT analysis:** available-case analysis **Funding:** 2 of the investigators are consultants for KCI, and the study was funded by the manufacturer of the intervention product..
Participants	**Location:** Columbus, Ohio, USA **Intervention group:** n = 50,**control group:** n = 43 **Mean age: intervention group** = 61.3 years (range 40 to 101),**control group** = 61.3 years (range 38 to 86) **Inclusion criteria:** patients scheduled to undergo radial forearm free flap **Exclusion criteria:** "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".
Interventions	**Aim/s:** to evaluate the effect of NPWT on closed surgical incisions. Prospective randomised controlled clinical trial comparing NPWT to standard dry dressings on surgical incisions **Primary:** "to evaluate the effectiveness of NPWT in patients with multiple comorbidities" **Secondary:** "to evaluate factors that contribute to wound complication" **Intervention/s in both groups:** "the graft was covered with a single layer of paraffin gauze dressing (Jelonet, Smith & Nephew, UK); 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 (Opsite, Smith & Nephew, UK) providing the vacuum seal. We used a double layer under the tube to prevent pressure ulcers at the bed of the suction tube". **Group 1 (NPWT) intervention:** "NPWT group ... underwent placement of a V.A.C. system (KCI, San Antonio, Texas) along the line of closure set at −125 mmHg continuous pressure at the time of closure". **Group 2 (control) intervention:** "the control group ... 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 & Nephew, Hull, UK)". **Study date/s:** October 2008 to August 2010
Outcomes	• wound infection • dehiscence • reoperation • LOS **Validity of measure/s:** not stated

Masden 2012 *(Continued)*

	Time points: "all incisions assessed on the third postoperative day ... and reassessed 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".
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	**Evidence:** quote (from correspondence with the author): "used a randomization generator through Excel in groups of 8 (4 controls, 4 experimental)" **Comment:** adequate method
Allocation concealment (selection bias)	Low risk	**Evidence:** quote (from correspondence with the author): "when the patient was recruited ... they contacted one of the investigators and the patient was assigned to whichever group was next on the list". **Comment:** adequate method
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Insufficient information
Blinding of outcome assessment (detection bias) All outcomes	Low risk	**Evidence:** quote: "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". **Comment:** adequate method
Incomplete outcome data (attrition bias) All outcomes	Low risk	**Evidence:** quote: "twelve subjects were lost to follow-up in the immediate postoperative period and were excluded from the final analysis". **Comment:** equal number of losses in both groups
Selective reporting (reporting bias)	Low risk	**Comment:** protocol unavailable, but expected outcomes reported
Other bias	Unclear risk	**Comment:** the standard dressing contained a silver layer, which may have influenced the outcome.

Murphy 2019

Study characteristics

Methods	**Study design:** randomised controlled trial **Study grouping:** 2 parallel groups **Ethics and informed consent:** ethics approved and consent obtained **Follow-up period:** 30 days **Sample size estimate:** yes **ITT analysis:** no, **number randomised:** 300, **number analysed:** 284; 16 participants "randomised in error") were not included in analysis

Murphy 2019 *(Continued)*

	Funding: yes **Preregistration:** yes
Participants	**Location:** two separate sites within a single hospital system (London Health Sciences Centre, London, Ontario, Canada) **Intervention group:** 144 analysed,**control group:** 140 analysed **Mean age: intervention group** 64 years, **control group** 64 years **Inclusion criteria:** patients who were 18 years or older and scheduled for planned (elective) colorectal resection via laparotomy with midline incision (or booked for laparoscopy if converted to an open procedure with midline incision). Eligible surgical procedures included: segmental, subtotal or total colectomies, as well as low and ultra-low anterior resection. **Exclusion criteria:** patients who undergoing abdominoperineal resection (APR), pelvic exenteration, emergent colectomy or patients with bowel perforation at the time of operation, who were pregnant, palliative (life expectancy under 3 months) or had a known sensitivity to the NPWT device
Interventions	**Aim/s:** to determine if negative pressure wound therapy (NPWT) reduces surgical site infection (SSI) in primarily closed incision after open and laparoscopic-converted colorectal surgery **Group 1 (NPWT) intervention:** NPWT via a continuous vacuum set to -125 mm Hg which remained on until postoperative day (POD) 5 or the date of hospital discharge, whichever came first **Group 2 (control) intervention:** gauze adhesive dressing which was removed on POD 2 and changed daily thereafter **Study date/s:** January 2015 to February 2017
Outcomes	• SSI • mortality • reoperation **Validity of measure/s:** not reported **Time points:** 30 days postsurgery
Notes	Funding: industry grant from Kinetic Concepts Inc (San Antonio TX). The devices were also supplied free of charge.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: “Randomization will take place centrally using random permutated blocks of 4, 6 or 8 and will be stratified based on site (University Hospital or Victoria Hospital) of the operation.” Comment: adequate method
Allocation concealment (selection bias)	Low risk	Quote: “After the fascia is closed a member of the surgical team will use a centralized web-server to randomize the patient.” Comment: adequate method
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "we performed a single-institution, prospective, randomised, open label, blind endpoint trial". Comment: This was an open-label trial; participants and personnel were not blinded.
Blinding of outcome assessment (detection bias)	Low risk	Quote: “The primary outcome was assessed by a blinded member of our Stoma Wound and Ostomy (SWOT) team or a physician uninvolved in the pa-

Murphy 2019 *(Continued)*

All outcomes		tient's care at POD five if the patient was in hospital or on the date of discharge if prior to POD five, as well as at the postoperative clinic visit occurring within the first 30 postoperative days." Comment: adequate method
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "Sixteen patients were excluded from the main analysis. Of the 284 patients remaining, we analyzed patients according to assigned group (144 NPWT and 140 Standard Dressing). There was no difference in demographics, type, or surgery performed or indication for surgery between groups." Comment: clear from the study how many participants were excluded; these 16 participants were excluded because they were randomised in error, with reasons given.
Selective reporting (reporting bias)	High risk	Quote: "Secondary outcomes assessed will include the need for, and duration of, at-home nursing care (home care) related to SSI. Additional secondary outcomes assessed will include the length of hospital stay, the number of return visits related to a potential or actual SSI, and cost." Comment: According to the protocol, some secondary outcomes were not reported in the results.
Other bias	Low risk	No evidence of other risk of bias

Newman 2019

Study characteristics	
Methods	**Study design:** Randomised controlled trial **Study grouping:** Parallel **Ethics and informed consent:** **Follow-up period:** 12 weeks **Sample size estimate:** determined using an estimated wound complication rate (associated with current standard of care protocols) of 20% and a desired wound complication rate of 5%. Using a significance level of 0.05 with a power of 80%, the sample was estimated at 160 total subjects, with 80 subjects assigned to each group. **ITT analysis:** yes,**number randomised:** 160, **number analysed:** 179 **Funding:** KCI/Acelity Inc. (San Antonio TX) **Preregistration:** Yes
Participants	**Location:** US Hospital **Intervention group:** 80,**control group:** 80 **Mean age: intervention group** 65 (SD 11), **control group** 65 (SD 11) **Inclusion criteria:** patients who were scheduled to undergo revision THA or TKA by one of the 6 fellowship-trained orthopaedic surgeons met at least one of the following criteria: body mass index greater than 35 kg/m^2, use of anticoagulants other than aspirin, peripheral vascular disease, depression, diabetes mellitus, current smoker, history of a periprosthetic joint infection in the limb undergoing revision surgery, on immunomodulators or corticosteroids, current history of cancer or haematological malignancy, inflammatory arthritis, renal failure or dialysis, malnutrition, liver disease, history of organ transplant, or human immunodeficiency virus infection

Newman 2019 *(Continued)*

	Exclusion criteria: lived more than 100 miles from the hospital, less than 18 years of age, had a silver allergy, had a history of wound coverage with soft tissue flaps on the index joint, or had a recent acute wound complication (i.e. defined as less than 4 weeks since previous surgery in the affected joint). Additionally, patients were excluded if they were enrolled in another interventional study, had no risk factors, undergoing a conversion arthroplasty, were not having implants revised, surgery was cancelled, altered mental status, and were screened but already met enrolment capacity.
Interventions	**Aim/s:** to compare the use of ciNPWT with our standard of care dressing in revision arthroplasty patients who were at high risk to develop wound complications **Group 1 (NPWT) intervention:** ciNPWT device (PREVENA; KCI/Acelity, San Antonio, TX) for at least 2 days unless a wound complication was reported **Group 2 (control) intervention:** standard of care silver-impregnated wound dressing (AQUACEL; ConvaTec, Greensboro, NC) for at least 7 days unless a wound complication was reported **Study date/s:** eligibility assessed from August 2014 to January 2017
Outcomes	• SSI • Dehiscence • Haematoma • Blisters • Readmission • Reoperation **Validity of measure/s:** Clear definitions given but not using validated measures **Time points:** 2, 4 and 12 weeks
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote "Patients who consented and enrolled to be included in the study were block randomised by categorizing as hip or knee surgery groups and then were assigned a sealed, opaque envelope that was randomly generated by an independent researcher who allocated them." Comment: computer-generated randomisation sequence
Allocation concealment (selection bias)	Low risk	Quote "an independent researcher [ ] who allocated them groups and then were assigned a sealed, opaque envelope that was randomly generated by an independent researcher who allocated them to receive either a ciNPWT device (PREVENA; KCI/Acelity, San Antonio, TX) or the standard of care silver-impregnated wound dressing (AQUACEL; ConvaTec, Greensboro, NC). The envelopes were opened on the day of surgery and the surgeon was informed as to which group the patient was randomly assigned at the time of dressing placement. After a patient consented to be involved in the study, the next sequential envelope was selected." Comment: central allocation generated opaque sealed sequential envelopes.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	The nature of the intervention makes blinding of participants and some personnel very difficult but no clear information

Newman 2019 *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote "Wounds were examined at 2, 4, and 12 weeks after the procedure. Any complication reported was visualized at the time of the evaluation." Comment: did not state who performed the outcome assessment or whether they were blinded to intervention group
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote "One patient in the treatment arm was lost to follow-up and was not included in the analyses." Comment: All except one participant were included in the analysis.
Selective reporting (reporting bias)	Low risk	All of the planned outcomes were fully reported.
Other bias	Low risk	No evidence of additional bias and reasonable reporting to suggest none.

Nherera 2017

Study characteristics	
Methods	**Study design:** cost-effectiveness analysis (based on the Karlakki 2016 RCT) **Analytical approach:** Trial-based decision analytic model (Based on Karlakki 2016, N = 220) **Effectiveness data:** Data from the UK trial (Karlakki 2016) **Perspective:** UK National Health Service **Utility valuations:** Time horizon of 6 weeks for surgical site complications (SSI) avoided and length of stay. Expected complications in standard care taken from the RCT. No discount rate was applied due to the short time horizon. Complications were assumed to have standard costs, readmission was excluded from the base case. Utility values were obtained from converting quality of life that was measured using SF-36. **Measure of benefit:** surgical site complication avoided; QALY (obtained from the NICE guideline on surgical site infections 2008) **Cost data**: Costs derived from standard cost references with resource utilisation valued in GBP (2015/16). Costs were also converted to USD by factor 1.42. (1) NHS reference costs of relevant medical diagnosis groups used for inpatient care (with confidence intervals). Model assumes all standard care dressing costs and nursing costs included in these. (2) Cost of a GP visit taken from Unit Costs and Social Care 2015–2016; (3) costs of oral antibiotics taken from the national Drug Tariff; length of stay (not considered in costs) (4) Cost of NPWT was taken from the national Drug Tariff. **Analysis of uncertainty:** Sensitivity analysis used to model discounted price for intervention through NHS bulk purchasing; additional length of stay following complications and readmission. Baseline data were varied across the 95% CI from the trial. Probabilistic sensitivity analysis for cost-effectiveness at willingness-to-pay threshold
Participants	**Location:** UK hospital **Intervention group:** n = 110,**control group:** n = 110 **Mean age (SD): intervention group** = 69 (9.0),**control group** = 69.2 (9.0) **Inclusion criteria:** patients undergoing THAs or TKAs (for any indication) with 3 consultant surgeons (SLK, NMG, and RDB – authors of this study) **Exclusion criteria:** patients who had known allergies to dressing, were undergoing revision joint surgery, were unwilling to attend additional clinics, and those on warfarin were excluded.

Nherera 2017 *(Continued)*

Interventions	**Aim/s:** To evaluate the cost-effectiveness of single-use negative pressure wound therapy in patients undergoing primary hip and knee replacements **Group 1 (NPWT) intervention:** Incisional negative pressure wound therapy dressing (iNPWTd) PICO dressing applied over the primarily closed incision by the surgeon in the operating room. Dressing was left on for one week (n = 110). **Group 2 (Control) intervention:** conventional dressing (either Mepore (Mölnlycke Health Care AB) or Tegaderm (3M Health Care Ltd)) applied over the primarily closed incision by the surgeon in the operating room. Dressing was left on for an unspecified period, and changed to OPSITE Post-Op Visible dressing on the second post-operative day (n = 110). All patients received enoxaparin postsurgery. **Study date/s:** July 2012 to April 2014
Outcomes	For data see Nherera 2017 and for clinical data see Karlakki 2016 in additional table 1 Costs (GBP) SSI complications avoided QALY (measure of benefit) Probability of being cost-effective using NICE threshold of £20,000/QALY
Notes	Funding: two authors are employees of Smith & Nephew. The Karlakki 2016 RCT was funded by Smith & Nephew. Authors' conclusions: Single-use negative pressure wound therapy can be considered a cost-saving intervention to reduce surgical site complications following primary hip and knee replacements compared with standard care. Providers should consider targeting therapy to those patients at elevated risk of surgical site complications to maximise efficiency. Quality rating using the CHEERS checklist was 85.4%.

Nherera 2018

Study characteristics	
Methods	**Study design:** cost-effectiveness analysis (based partly on the Witt-Majchrzac 2015 RCT) **Analytical approach:** Decision analytic model **Effectiveness data:** baseline data on revision operations, length of stay, readmissions to hospital, and mortality were derived from single-centre prospective observational study over 36 months in Germany. Effectiveness data for NPWT were taken from the trial (n = 80) of Witt-Majchrzak 2015 (SSI and wound dehiscence). A length of stay reduction was applied from a meta-analysis (Strugala & Martin). All-cause mortality was obtained from German Federal Statistical Office and assumptions about relationship between mortality and revision surgery applied from literature. **Perspective:** Germany Statutory Health Insurance payer **Utility valuations:** Health state utilities were sourced from published literature including discharge with and without complications from study by Tuffaha 2015. **Measure of benefit:** Wound healing without complications (complications avoided); QALY **Cost data:** Costs derived from standard cost references, resource utilisation valued in Euro. Inpatient care taken data from Cristofolini. Patient stay costs from hospital management site; reimbursement cost for procedure from Germany Diagnosis Relater group Report Browser 2017. Standard care dress-

Nherera 2018 *(Continued)*

	ing's costs and nursing costs covered in the diagnosis-related group costs. Rehabilitation costs obtained from a study by Zeidler. One community doctor and cardiologist visit cost, and the cost of community nurse visit once a week estimated. No discounting done due to a short time horizon (12 weeks). **Analysis of uncertainty:** One-way sensitivity analyses; probabilistic sensitivity analyses using Monte Carlo simulation; subgroup analysis for people with high BMI.
Participants	**Location:** Hospital, Poland **Intervention group:** n = 40,**control group:** n = 40 **Mean age: intervention group** = 66.2 (± 8), 53 to 80,**control group** = 62.1 (± 9.1), 41 to 78 **Inclusion criteria:** patients who underwent an off-pump coronary artery bypass grafting procedure, using the internal mammary artery **Exclusion criteria:** not stated
Interventions	**Aim/s:** To estimate the cost-effectiveness of single use negative pressure wound therapy (sNPWT) compared with standard of care in patients following coronary artery bypass grafting surgery (CABG) procedure to reduce surgical site complications (SSC) defined as dehiscence and sternotomy infections **Group 1 (NPWT) intervention:** Primary closure with NPWT (PICO, Smith & Nephew) using continuous negative pressure of −80 mmHg. Dressing changed on day 2 or 3 and on day 5 or 6 after surgery. **Group 2 (control)** Conventional dressings applied after primary closure. Dressings changed daily **Study date/s:** not stated
Outcomes	**Outcomes** (for data see additional table 1; for clinical data see Witt-Majchrzac 2015) Costs Wound healing without complication (complications avoided); QALY (measure of benefit) ICER Probability of being cost-effective
Notes	Authors' conclusions: The sNPWT can be considered a cost-saving intervention that reduces surgical site complications following CABG surgery compared with standard care. We however recommend that additional economic studies should be conducted as new evidence on the use of sNPWT in CABG patients becomes available to validate the results of this economic analysis. Funding: NR for economic evaluation; see Witt-Majchrzac 2015 for RCT funding Quality rating using the CHEERS checklist was 87.0%.

Nordmeyer 2016

Study characteristics	
Methods	**Study design:** randomised controlled trial **Study grouping:** parallel **Ethics and informed consent:** yes **Sample size estimate:** no **Follow-up period:** unknown **ITT analysis:** yes, **number randomised:** 20, **number analysed:** unclear

Nordmeyer 2016 *(Continued)*

	Funding: unclear. MHB gave scientific presentations for KCI. **Preregistration:** no
Participants	**Location:** Nuremberg, Germany **Intervention group:** n = 10,**control group:** n = 10 **Mean age: intervention group** = 52.3 (16.3),**control group** = 57.8 (15.2) **Inclusion criteria:** patients with spinal fractures who were scheduled for internal fixation **Exclusion criteria:** not reported
Interventions	**Aim/s:** to evaluate the different aspects of wound healing in spinal fractures treated with internal fixation **Group 1 (NPWT) intervention:** the iNPWT group was treated with a PICO system (Smith & Nephew, UK). The PICO system was left on the wound for 5 days including the day of surgery. In addition to daily clinical examination, all wounds/seroma were analysed by ultrasonography on day 5 and day 10 after surgery. **Group 2 (control) intervention:** standard department wound dressing consisting of dry wound coverage (compresses attached to the skin) was used. **Study date/s:** not reported
Outcomes	• seroma **Validity of measure/s:** ultrasound was used as a standardised imaging modality to detect seromas in the wound area. **Time points:** day 5 and day 10 after surgery
Notes	Investigator contacted for additional details

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Numbers analysed were not reported.
Selective reporting (reporting bias)	Unclear risk	Only seroma reported, not wound infection; unclear if all planned outcomes addressed.
Other bias	Low risk	None identified

O'Leary 2017

Study characteristics	
Methods	**Study design:** randomised controlled trial **Study grouping:** parallel **Ethics and informed consent:** yes **Sample size estimate:** yes, but it was based on a reduction in SSI from 35% to 10% **ITT analysis:** yes, **number randomised:** 50, **number analysed:** 49 **Follow-up period:** 30 days **Funding:** support was received from Smith & Nephew. The authors were responsible for trial design, data analysis, and manuscript writing. The decision to publish trial results was made between study authors and study sponsors. **Preregistration:** ClinicalTrials.gov registration NCT02780453 (registered after study completed – May 2016)
Participants	**Location:** Limerick, Ireland **Intervention group:** n = 25,**control group:** n = 25 **Mean age: intervention group** = 58 (range 31 to 73),**control group** = 63 (range 33 to 76) **Inclusion criteria:** patients undergoing elective or emergency open abdominal surgery with a clean, clean-contaminated, or contaminated wound **Exclusion criteria:** dirty wound; BMI ≥ 40; ASA grade > 3
Interventions	**Aim/s:** to assess the effect of NPWT on SSI **Group 1 (NPWT) intervention:** PICO dressing (Smith & Nephew) was applied to the wound by the operating surgeon, and the edges of the dressing were reinforced with self adherent tape. **Group 2 (control) intervention:** transparent waterproof dressing (Smith & Nephew) **Study date/s:** February 2013 to April 2016
Outcomes	• SSI • reoperation • pain **Validity of measure/s:** CDC definitions and criteria for superficial, deep, and organ/space SSI were used for the primary outcome. A visual analogue scale was used to assess pain. **Time points:** day 4 and day 30 postsurgery
Notes	

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Randomisation codes were generated on www.randomization.com.
Allocation concealment (selection bias)	Unclear risk	Allocation was performed using a "closed envelope method".

O'Leary 2017 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote "A randomised, controlled, open-label trial" Comment: no blinding
Blinding of outcome assessment (detection bias) All outcomes	High risk	Quote: "the ... study assessor was a senior member of the operating surgical team. The study assessor was not blinded to the treatment group".
Incomplete outcome data (attrition bias) All outcomes	Low risk	1 participant was removed from the intervention arm for a protocol violation, but ITT analysis was provided.
Selective reporting (reporting bias)	Low risk	Expected outcomes reported, but the study protocol was published after the completion of the trial.
Other bias	Low risk	No other bias identified

Pachowsky 2012

Study characteristics	
Methods	**Study design:** randomised controlled trial **Ethics and informed consent:** ethics approved and consent obtained. **Sample size calculation:** no **ITT analysis:** yes, **number randomised:** 19, **number analysed:** 19 **Follow-up period:** 10 days **Funding:** support received from Smith & Nephew. The authors were responsible for trial design, data analysis, and manuscript writing. The decision to publish trial results was made between study authors and study sponsors. **Preregistration:** no
Participants	**Location:** University Hospital, Erlangen, Germany **Intervention group:** n = 9,**control group:** n = 10 **Mean age: intervention group** = 66.2 years (SD 17.83),**control group** = 70.0 years (SD 11.01) **Inclusion criteria:** "consecutive patients who were scheduled for a total hip arthroplasty (THA) for osteoarthritis of the hip were randomised". **Exclusion criteria:** not stated
Interventions	**Aim/s:** to evaluate the use of NPWT to improve wound healing after total hip arthroplasty **Intervention/s in both groups:** "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". **Group 1 (NPWT) intervention:** "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". **Group 2 control:** the control group received "the standard wound dressing of our department, consisting of a dry wound coverage". **Study date/s:** not stated

Pachowsky 2012 *(Continued)*

Outcomes	• incidence of seroma (by ultrasound) • amount of wound drainage in the Redon drain canisters • duration of prophylactic antibiotics • secretion from the wound **Validity of measure/s:** "all patients underwent an ultrasound (Zonare, Z.one Ultra SP 4.2, Erlangen, ZONARE Medical Systems, Inc., Mountain View, USA) of the wound". **Time points:** day 5 and day 10 of postoperative period
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not stated
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not stated
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 group to which the participant had been allocated.
Incomplete outcome data (attrition bias) All outcomes	Low risk	All enrolled participants were accounted for in the analyses.
Selective reporting (reporting bias)	Low risk	Results for outcomes identified in the methods section were reported. We did not see the original protocol.
Other bias	High risk	**Evidence:** quote: "Matthias H. Brem gave scientific presentations for KCI. The PREVENA wound treatment system was provided by KCI free of charge". Support was received from Smith & Nephew. The authors were responsible for trial design, data analysis, and manuscript writing. The decision to publish trial results was made between study authors and study sponsors. 1 participant in the NPWT group removed the Redon drain by himself on the first postoperative day.

Pauser 2016

Study characteristics

Methods	**Study design:** randomised controlled trial **Study grouping:** parallel **Ethics and informed consent:** yes

Pauser 2016 *(Continued)*

	Sample size estimate: no **Follow-up period:** 10 days **ITT analysis:** yes, **number randomised:** 21, **number analysed:** 21 **Funding:** "Prevena wound treatment system was provided by KCI free of charge". **Preregistration:** no
Participants	**Location:** Nuremberg, Germany **Intervention group:** n = 11,**control group:** n = 10 **Mean age: intervention group** = 81.6 ± 5.2 years,**control group** = 82.6 ± 8.6 years **Inclusion criteria:** patients with femoral neck fracture who were scheduled for hip hemiarthroplasty **Exclusion criteria:** not stated
Interventions	**Aim/s:** "to evaluate different aspects of wound healing after fractures of the femoral neck treated by hemiarthroplasty" **Group 1 (NPWT) intervention:** the iNPWT group was treated with a PREVENA system (KCI, San Antonio, Texas). The PREVENA system was left on the wound for 5 days including the day of surgery. **Group 2 control:** control group received the standard wound dressing of our department, consisting of a dry wound coverage (compresses attached to the skin). **Study date/s:** not reported
Outcomes	• seroma **Validity of measure/s:** ultrasound was used as a standardised imaging modality to detect seromas in the wound area. **Time points:** day 5 and day 10 after surgery
Notes	Investigator contacted for additional details

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information given
Allocation concealment (selection bias)	Unclear risk	Insufficient information given
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Insufficient information given
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information given
Incomplete outcome data (attrition bias) All outcomes	Low risk	All those recruited appear to have been included in the analysis.

Pauser 2016 *(Continued)*

Selective reporting (reporting bias)	Unclear risk	Unclear if all the planned outcomes were reported fully
Other bias	Unclear risk	Data for the NPWT group reported at day 5 and day 10, but data for the control group only reported overall

Pleger 2018

Study characteristics	
Methods	**Study design:** randomised controlled trial **Study grouping:** parallel **Ethics and informed consent:** yes **Sample size estimate:** no **Follow-up period:** 30 days postoperatively **ITT analysis:** yes, **number randomised:** 129 groin incisions (100 participants), **number analysed:** 129 incisions **Funding:** "funded by our own department, without any financial or scientific involvement or support from KCI, ACELITY Company" **Preregistration:** no
Participants	**Location:** Germany **Intervention group:** n = 58 incisions,**control group:** n = 71 incisions **Mean age: intervention group** = 71 (range 54 to 89),**control group** = 66.5 (range 41 to 86) **Inclusion criteria:** vascular procedures with access to the common femoral artery with at least 1 of the known main risk factors of wound healing: age > 50 years, diabetes mellitus, renal insufficiency, malnutrition, obesity, and chronic obstructive pulmonary disease **Exclusion criteria:** not stated
Interventions	**Aim/s:** to investigate the effectiveness of ciNPT compared with conventional therapy with regard to the incidence of groin WHC on postoperative days 5 to 7 and 30 and the incidence of surgery revisions 30 days postoperatively after various vascular surgeries **Group 1 (NPWT) intervention:** ciNPT applied for postoperative days 5 to 7 **Group 2 (control) intervention:** a conventional adhesive plaster that was changed daily **Study date/s:** 1 February to 30 October 2015
Outcomes	• wound complications including SSI **Validity of measure/s:** Szilagyi classification **Time points:** the first evaluation took place on postoperative days 5 to 7 during the hospital stay, while the second evaluation was conducted on postoperative day 30 in the outpatient clinic.
Notes	

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**

Pleger 2018 *(Continued)*

Random sequence generation (selection bias)	Unclear risk	Insufficient information given
Allocation concealment (selection bias)	Unclear risk	Insufficient information given
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Insufficient information given
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not stated
Incomplete outcome data (attrition bias) All outcomes	Low risk	All those recruited appear to have been included in the analysis.
Selective reporting (reporting bias)	Low risk	Results for outcomes identified in the methods section were reported. We did not see the original protocol.
Other bias	Unclear risk	Unequal number of participants in each group; results reported per fracture, so there is a potential unit of analysis issue.

Ruhstaller 2017

Study characteristics	
Methods	**Study design:** randomised controlled trial **Study grouping:** parallel **Ethics and informed consent:** not reported **Follow-up period:** not reported **Sample size estimate:** not reported **ITT analysis:** yes, **number randomised:** 136, **number analysed**: not stated **Funding:** KCI collaborated in the trial. **Preregistration:** yes
Participants	**Location:** Philadelphia, USA **Intervention group:** n = 67,**control group:** n = 69 **Mean age:** not reported **Inclusion criteria:** BMI greater than or equal to 30 kg/m^2 at less than or equal to 22 weeks of gestation; woman is labouring; woman is having an unplanned caesarean section; woman will have Pfannenstiel skin incision; has the ability to take a picture and email it to a secure account; receives prenatal care in the University of Pennsylvania health system and plans to follow up postpartum in the system; is 18 years of age or older **Exclusion criteria:** woman cannot read or speak English; is not 18 years of age or older; does not have ability to send a picture by email; has pre-existing diabetes mellitus (type 1 or type 2), is using chronic steroids or immunosuppressants, OR is being actively treated for a malignancy; woman is undergoing a scheduled caesarean section; woman is allergic to silver

Ruhstaller 2017 *(Continued)*

Interventions	**Aim/s:** to determine whether NPWT lowers the rate of wound complications in obese pregnant women undergoing an unscheduled intrapartum caesarean section **Group 1 (NPWT) intervention:** NPWT device (PREVENA Incision Management System; Acelity) **Group 2 control:** standard postcaesarean wound care (not defined) **Study date/s:** not stated

Outcomes	Planned outcomes:
	
	• primary outcome variable is wound complications defined as:
	  * any readmission for a wound issue within 4 weeks of discharge;
	  * infection;
	  * wound breakdown.
	• quality of life
	
	Reported outcomes:
	
	• SSI
	• blisters
	• reoperation
	
	Validity of measure/s: not reported
	
	Time points: 4 weeks postsurgery

Notes	Only the abstract and CTR report were available at the time of preparation of this review. Investigator contacted for additional details

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Once decision for caesarean delivery was established, randomisation was performed using a computer-generated randomisation scheme (Research Electronic Data Capture (REDCap)).
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	**Intervention group:** n = 61/67 (91%);**control group:** n = 58/69 (84%). It was unclear from the abstract if reasons for loss to follow-up were similar across groups.
Selective reporting (reporting bias)	Low risk	Results for outcomes identified in the methods section were reported.
Other bias	Unclear risk	No other bias identified but insufficient reporting

Sabat 2016

Study characteristics	
Methods	**Study design:** 1:1 parallel-group randomised controlled trial **Study grouping:** parallel **Ethics and informed consent:** yes **Sample size estimate:** no **Follow-up period:** 4 months **ITT analysis:** no **Funding:** not stated **Preregistration:** not stated
Participants	**Location:** Philadelphia, USA **Intervention group:** n = 33 wounds,**control group:** n = 30 wounds (total 49 participants) **Mean age:** not reported **Inclusion criteria:** people undergoing open vascular surgery involving a groin incision **Exclusion criteria:** not stated
Interventions	**Aim/s:** to compare the effect of postoperative negative pressure therapy to conventional dressings on wound occurrences **Group 1 (NPWT) intervention:** NPWT device **Group 2 control:** conventional dressing (gauze and Tegaderm) **Study date/s:** not stated
Outcomes	• SSI • wound dehiscence
Notes	Abstract only; unit analysis

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Not stated
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not stated
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not stated
Incomplete outcome data (attrition bias)	Low risk	All those recruited appear to have been included in the analysis.

Sabat 2016 *(Continued)*
All outcomes

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	Unit of analysis issue - unclear if accounted for

Schmid 2018

Study characteristics	
Methods	**Study design:** Randomised controlled trial **Study grouping**: Parallel group **Ethics and informed consent:** Not reported **Follow-up period:** 14 days **Sample size estimate:** Not reported **ITT analysis: number randomised:** 25, **number analysed:** 25 **Funding:** Not reported **Preregistration:** Yes
Participants	**Location:** Germany **Intervention group:** n = 25,**control group:** n = 25 **Mean age: intervention group:** Not reported, **control group:** Not reported **Inclusion criteria:** Patients with penile cancer and indication for bilateral inguinal lymph node dissection (tumour stage ≥ pT1 G2 or palpable inguinal enlarged lymph nodes) **Exclusion criteria:** Status post inguinal surgery
Interventions	**Aim/s:** To prospectively analyse the effect of an epidermal vacuum wound dressing on lymphorroe, complications and reintervention in patients with inguinal lymphadenectomy for penile cancer **Group 1 (NPWT) intervention:** Epidermal negative-pressure wound dressings (Prevena) for 7-8 days **Group 2 (control) intervention:** Conventional compression bandages for 24 hours **Study date/s:** May 2013 –
Outcomes	• Reintervention (reoperation?) • SSI may be included in wound complications but not reported **Validity of measure/s:** No definition of SSI reported **Time points:** 14 days
Notes	Planned interim analysis. Abstract only

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote “Patients were randomised to receive conventional wound care and suction drainage on one side (conventional) vs. epidermal vacuum wound dressing (VAC) and suction drainage on the other side”.

Schmid 2018 *(Continued)*

		Comment: No indication how the randomisation sequence was generated
Allocation concealment (selection bias)	Unclear risk	No statement
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study (no masking) (obtained from protocol)
Blinding of outcome assessment (detection bias) All outcomes	High risk	Open study (no masking) (obtained from protocol)
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote "We present the results of the first planned interim analysis after 25 patients".
Selective reporting (reporting bias)	High risk	Not all prespecified secondary outcomes reported (obtained from protocol)
Other bias	Unclear risk	Abstract so limited reporting - no obvious source of bias but insufficient information to be certain

Shen 2017

Study characteristics	
Methods	**Study design:** randomised controlled trial **Study grouping:** parallel **Ethics and informed consent:** yes **Sample size estimate:** yes (based on a real SSI reduction of 6% from 17% to 11%) **Follow-up period:** 30 days **ITT analysis:** yes, **number randomised:** 375, **number analysed**: 265 **Funding:** non-industry **Preregistration:** yes
Participants	**Location:** Wake Forest University Health Sciences, North Carolina, USA **Intervention group:** n = 187,**control group:** n = 188 **Median age (range): intervention group** = 59.5 (25 to 85),**control group** = 62 (30 to 81) **Inclusion criteria:** patients who underwent open resection of intra-abdominal neoplasms, where the scheduled procedure was to be performed via midline laparotomy and was a clean-contaminated (class II) case (includes gastric, small bowel, and colorectal resections, as well as bile or pancreatic duct transections); the patient had the ability to understand and the willingness to sign a written informed consent document (either directly or via a legally authorised representative) **Exclusion criteria:** emergent cases; pregnant patients; clean (class I), contaminated (class III), and dirty (class IV) procedures; patients on chronic immunosuppressive medications, including steroids, within the past 3 months; patients with a history of skin allergy to iodine or adhesive drapes were not included in the study

Shen 2017 *(Continued)*

Interventions	**Aim/s:** to decrease the incidence of superficial and deep SSIs **Group 1 (NPWT) intervention:** PICO dressing applied over the primarily closed incision by the surgeon in the operating room. Dressing was left on for 4 days, or longer if drainage continued, unless soiled or dislodged. **Group 2 control:** Comfeel dressing applied over the primarily closed incision by the surgeon in the operating room. Dressing was left on for 4 days, or longer if drainage continued, unless soiled or dislodged. **Study date/s:** July 2012 to April 2014
Outcomes	• SSI • seroma • haematoma • incisional cellulitis • dehiscence • wound opening for any reason **Validity of measure/s:** CDC definitions for SSI were used. **Time points:** 30 days after surgery
Notes	Investigator contacted for additional details

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "the program nQuery was used to create the randomization schema". The study used permuted-block randomisation with varying block sizes.
Allocation concealment (selection bias)	Unclear risk	Quote: "an email was sent the day before surgery to the attending surgeon about to which treatment arm the patient had been assigned". **Comment:** scope for surgeons to anticipate the randomisation sequence
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "There was no blinding of the patients or care providers to the study intervention. An email was sent the day before surgery to the attending surgeon about to which treatment arm the patient had been assigned". Comment: patients and participants were not blinded.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Investigator team assessed outcomes.
Incomplete outcome data (attrition bias) All outcomes	High risk	Approximately 30% of participants were lost to follow-up or excluded from each arm of the trial. However, reasons for losses were similar between groups. NPWT group: 2 died and 19 were reoperated; standard care group: 5 died and 16 were reoperated
Selective reporting (reporting bias)	Low risk	Prospectively reported. Outcomes were consistent with proposal (National Cancer Institute CCSG P30CA012197).
Other bias	Low risk	No other bias identified

Shim 2018

Study characteristics	
Methods	**Study design:** randomised controlled trial **Study grouping:** parallel **Ethics and informed consent:** yes **Follow-up period:** 1 year **Sample size estimate:** no **ITT analysis:** yes, **number randomised:** 51, **number analysed:** 51 **Funding:** Not reported **Preregistration:** Not reported
Participants	**Location: Korea;** single-centre (hospital) **Intervention group:** 30, **control group:** 21 **Mean age: intervention group** 38.77 ± 1.68, **control group** 41.38 ± 10.92 **Inclusion criteria:** > 20 years, acute multi-tissue hand injury of moderate severity (assessed by HISS score 21-50), underwent reconstruction within 3 days after injury by two surgeons **Exclusion criteria:** history of impaired motor function, injury to the peripheral nerves and/or vessels distal to the wrist, or a bone fracture requiring transarticular fixation with a Kirchner (K) wire, a congenital hand deformity, an operation history on the same hand, and underlying diseases including autoimmune diseases such as rheumatoid arthritis or systemic lupus erythematosus or those taking medications that could influence wound healing
Interventions	**Aim/s:** To compare outcomes in patients with acute hand injury who were managed with or without NPWT after reconstructive surgery **Group 1 (NPWT) intervention:** NPWT (CuraVAC, CGBio, Seongnam-si, Gyeonggi-do, Korea) applied at a pressure of 75 mmHg in continuous mode and secondary dressing including Vaseline gauze **Group 2 (control) intervention:** Conventional dressing, including vaseline gauze was applied over the closed skin using polyurethane foam with a compressible elastic bandage, and a short arm splint was applied in a functional position; dressing and NPWT were changed every 3 days. **Study date/s:** January 2013 - December 2016
Outcomes	• SSI/infection • haematoma • wound disruption (dehiscence) **Validity of measure/s:** unclear what definition was used for infection **Time points:** 1 month and 1 year
Notes	

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Quote: "Patients were randomly assigned to the control or experimental group following a simple randomization procedure (computerized random numbers) achieved using opaque envelopes". Comment: randomisation with computer

Shim 2018 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	Quote: "Patients were randomly assigned to the control or experimental group following a simple randomization procedure (computerized random numbers) achieved using opaque envelopes. Allocation information to each group was not provided to reduce bias". Comment: allocation concealed with opaque envelopes but these were not noted as sequentially numbered
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote "This was a prospective open trial". Comment: No blinding of participants or personnel
Blinding of outcome assessment (detection bias) All outcomes	High risk	Quote "This was a prospective open trial". Comment: No blinding of outcome assessment
Incomplete outcome data (attrition bias) All outcomes	Low risk	No patients lost to follow-up
Selective reporting (reporting bias)	Low risk	All prespecified outcomes fully reported
Other bias	Unclear risk	No evidence of other bias but reporting insufficient to be certain

Stannard 2012

Study characteristics	
Methods	**Study design:** multicentre randomised controlled trial (four centres, each a level 1 trauma centre) **Ethics and informed consent:** ethics approved and consent obtained **Sample size calculation:** no **Follow-up period:** not reported **ITT analysis:** wounds, not people were assessed **Funding:** "funds from corporate/industry were received from Kinetic Concepts, Inc to support this work".
Participants	**Location:** Columbus, Ohio, USA **Intervention group:** n = 130, participants; 141 fractures,**control group:** n = 119 participants; 122 fractures **Mean age:** not stated **Inclusion criteria:** people > 18 years of age who had sustained a high-energy tibial plateau, pilon, or calcaneus fracture and were able to comply with research protocol and willing to give informed consent **Exclusion criteria:** non-operative 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

Stannard 2012 *(Continued)*

Interventions	**Aim/s:** "to investigate the use of NPWT to prevent wound dehiscence and infection after high-risk lower extremity trauma" **Intervention/s in both groups:** dressings or NPWT were applied in the operating room and then changed on postoperative day 2 and every 1 to 2 days thereafter. **Group 1 (NPWT) intervention:** NPWT over the surgical incision after open reduction and internal fixation of the fracture **Group 2 (control) intervention:** standard postoperative dressing (dressing not described) **Study date/s:** not stated
Outcomes	• wound infection and dehiscence • time to discharge from hospital **Validity of measure/s:** "all infections were confirmed with cultures". **Time points:** not stated - unclear for how long participants were followed up
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	**Evidence:** quote: "patients were enrolled and then randomised to receive either standard postoperative dressings (control) or NPWT (study)". **Comment:** additional author information: "the randomization was done via a computer generated randomization program".
Allocation concealment (selection bias)	Unclear risk	**Comment:** method not clarified
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	**Evidence for participants:** not possible **Comment:** unlikely to affect outcomes **Evidence for personnel:** not possible **Comment:** unlikely to affect outcomes
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	**Evidence:** quote: "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". **Comment:** not clear whether those assessing outcomes were aware of group assignment
Incomplete outcome data (attrition bias) All outcomes	Low risk	**Comment:** a total of 249 participants were recruited. The same number of participants 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 that an available-case analysis may have been performed.
Selective reporting (reporting bias)	Low risk	**Comment:** registered in CTR (NCT00582998) 9 months after final data collection date, so it is unclear whether reported outcomes matched the original protocol. However, infection and dehiscence were the expected outcomes.

Stannard 2012 *(Continued)*

Other bias	High risk	**Comment:** • unequal number of participants in each group • appeared from the protocol that data collection was over many years, but no dates or explanation in manuscript • results reported per fracture, so there is a potential unit of analysis issue

Tanaydin 2018

Study characteristics	
Methods	**Study design:** randomised controlled trial **Study grouping:** parallel **Ethics and informed consent:** ethics approved and consent obtained **Sample size calculation:** no **Follow-up period:** 365 days postsurgery **ITT analysis:** wounds (breasts), not people were assessed **Funding:** funded by Smith & Nephew Ltd, who provided the PICO dressings and the Cutometer and financed a research assistant for carrying out the assessments and measurements
Participants	**Location:** the Netherlands **Intervention group:** n = 32,**control group:** n = 32 (participants served as their own control) **Mean age (range):** 40.9 (18 to 61) **Inclusion criteria:** patients > 18 years of age who underwent bilateral superomedial pedicle Wise-pattern breast reduction mammoplasty and had postsurgical incisions of similar length on each breast **Exclusion criteria:** pregnancy or lactation, using steroids, or other immune modulators known to affect wound healing; history of radiation of the breast; tattoos in the area of the incision; skin conditions such as cutis laxa that would result in poor healing or widen scars, history of radiation of the breast, patients with a known significant history of hypertrophic scarring or keloids, and postsurgical incisions still actively bleeding, exposure of blood vessels, organs, bone, or tendon at the base of the reference wound; and incisions > 12 inches (30 cm) maximum linear dimension
Interventions	**Aim/s:** to evaluate the effectiveness of postsurgery incision treatment comparing a portable disposable NPWT system with standard care using fixation strips **Group 1 (NPWT) intervention:** a single-use NPWT system without an exudate canister **Group 2 (control) intervention:** fixation strips (Steri-Strip; 3M, St Paul, Minnesota, USA) **Study date/s:** 1 June 2012 to 9 April 2014
Outcomes	• the number of wound-healing complications within 21 days • aesthetic appearance and quality of scarring (additional measurements at 42, 90, 180, and 365 days) **Validity of measure/s:** wound-healing complications were defined as delayed healing (surgical incision not 100% closed at day 7 postsurgery), or occurrence of dehiscence or infection within 21 days postsurgery **Time points:** all included participants (N = 32) had follow-up visits and assessments at screening (presurgery), day 0 (baseline, postsurgery), day 7, 21, 42, 90, 180, and 365 postsurgery.
Notes	The breasts were randomised and served as own control.

Tanaydin 2018 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote "Randomization was used for allocation of NPWT and fixation strip to the right or left breast incision site per patient, using sealed envelopes. Treatment site information was accessed digitally (www.sealedenvelope.com) upon the start of the treatment postsurgically." Comment: appears to be a computerised method of sequence generation
Allocation concealment (selection bias)	Low risk	Quote "Randomization was used for allocation of NPWT and fixation strip to the right or left breast incision site per patient, using sealed envelopes. Treatment site information was accessed digitally (www.sealedenvelope.com) upon the start of the treatment postsurgically." Comment: appears to be a web-based allocation centre
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "As NPWT and fixation strips are optically different, blinding of the physician and patients was not feasible". Comment: Participants and personnel were not blinded.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "as NPWT and fixation strips are optically different, blinding of the physician and patients was not feasible; however, data analysis was performed blinded".
Incomplete outcome data (attrition bias) All outcomes	Low risk	32 enrolled participants were accounted for in the analyses.
Selective reporting (reporting bias)	Low risk	Expected outcomes reported. Protocol retrospectively registered as NL40698.068.12/METC12-3-026
Other bias	Unclear risk	This was a 'split-body' or 'intra-individual' design where a person with 2 wounds had 1 wound randomised to each treatment. It was not clear whether the analysis took this into account.

Tuuli 2017

Study characteristics

Methods	**Study design:** randomised controlled trial (abstract only available) **Study grouping:** parallel **Ethics and informed consent:** not recorded **Sample size estimate:** not recorded **Follow-up period:** 30 days **ITT analysis:** yes, **number randomised:** 120, **number analysed:** 120 **Funding:** non-industry **Preregistration:** yes (NCT02578745). Registered 11 June 2012

Tuuli 2017 *(Continued)*

Participants	**Location:** St Louis, Missouri, USA **Intervention group:** n = 60,**control group:** n = 60 **Mean age:** not recorded **Inclusion criteria:** • gestational age ≥ 23 weeks • BMI ≥ 30 at the time of delivery • planned or unplanned caesarean delivery (procedure in which NPWT is being tested) **Exclusion criteria:** • not available for postoperative follow-up • contraindication to NPWT applicable to women undergoing caesarean: pre-existing infection around incision site, bleeding disorder, therapeutic anticoagulation, allergy to any component of the dressing (e.g. silicone, adhesive tape)
Interventions	**Aim/s:** to assess the feasibility of a definitive RCT to test the effectiveness and safety of prophylactic NPWT in obese women after caesarean section **Group 1 (NPWT) intervention:** prophylactic NPWT with the PICO device (Smith & Nephew). Removed at discharge (usually on day 4) **Group 2 (control) intervention:** standard wound dressing (routine postoperative wound dressing consisting of layers of gauze and adhesive tape). The dressing was removed 24 to 48 hours. **Study date/s:** October 2016 to March 2016
Outcomes	• **Primary outcome/s:** composite of superficial or deep surgical site infection; wound separation ≥ 2 cm; SSI; haematoma; seroma • **Secondary outcome/s:** pain score on postoperative day 2 and skin reactions **Validity of measure/s:** wound infection defined by CDC criteria (information extracted from CTR) **Time points:** 30 days
Notes	Investigator contacted for additional details

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information in abstract to permit judgement
Allocation concealment (selection bias)	Unclear risk	Insufficient information in abstract to permit judgement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Insufficient information in abstract to permit judgement
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information in abstract to permit judgement
Incomplete outcome data (attrition bias) All outcomes	Low risk	Abstract indicated that 120 participants were randomised and 120 analysed. This was consistent with the number proposed in NCT02578745.

Tuuli 2017 *(Continued)*

Selective reporting (reporting bias)	Low risk	Reporting was consistent with outcomes proposed in NCT02578745..
Other bias	Unclear risk	None detected. Independently funded trial, however no baseline data presented

WHIST 2019a

Study characteristics	
Methods	**Study design:** randomised controlled trial **Study grouping:** parallel **Ethics and informed consent:** ethical approval and consent obtained (appropriate procedures for retrospective consent where necessary) **Follow-up period:** 6 months **Sample size estimate:** yes, full published statistical analysis plan; 1540 required to provide 90% power to detect reduction in deep infection from 15% to 9% with 20" loss to follow-up **ITT analysis:** yes,**number randomised:** 1548 (1629 randomised but 81 did not consent or were ineligible), **number analysed:** 1547 **Funding:** National Institute for Health Research (NIHR) Health Technology Assessment programme **Preregistration:** yes
Participants	**Location:** UK (24 sites) **Intervention group:** n = 785; **control group:** n = 763 **Mean age: intervention group** </= 40: 283 (36.1%); > 40: 501 (63.9%), **control group** </= 40: 278 (36.4%); > 40: 485 (63.6%) **Inclusion criteria:** adult patients (16 years minimum) presenting to hospital within 72 hours of sustaining major trauma and who required a surgical incision to treat a fractured lower limb **Exclusion criteria:** open fracture of the lower limb that could not be closed primarily; evidence that the patient would be unable to adhere to trial procedures or complete questionnaires
Interventions	**Aim/s:** To assess the deep surgical site infection (SSI) rate, disability, quality of life, patient assessment of the surgical scar and resource use in patients with surgical incisions associated with fractures following major trauma to the lower limbs, treated with incisional negative-pressure wound therapy (NPWT) versus standard dressings (cost-effectiveness was also assessed) **Group 1 (NPWT) intervention:** NPWT uses a non-adherent absorbent dressing covered with a semi-permeable dressing. A sealed tube connects the dressing to a built-in mini-pump that creates a partial vacuum over the wound. NPWT applied as per treating surgeon's normal practice and according to manufacturer's instructions **Group 2 (control) intervention:** standard dressing (non-adhesive layer covered by sealed dressing or bandage) **Study date/s:** September 2016 to April 2018
Outcomes	• SSI (deep), i.e. wound infection involving the tissues deep to the skin • dehiscence (forms part of deep SSI criteria) • health-related quality of life (EQ-5D) and Disability rating index (DRI) • pain (and neuropathic pain) • resource use • cost-effectiveness

WHIST 2019a *(Continued)*

- death (reported in Table 10 as a reason of dropout)
- reoperation (further surgery)

Validity of measure/s: CDC definitions and criteria were used for deep infection (30 days and 90 days as per original and revised criteria)

Time points: pre-injury, post-injury, 30 days, 3 months, 6 months

Notes	Current Controlled Trials ISRCTN 12702354 and UKCRN Portfolio ID20416 Funding (cost-effectiveness assessment) National Institute for Health Research (NIHR) Health Technology Assessment programme

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote "Randomisation was on a 1:1 basis, using a validated computer randomisation program managed centrally by the Oxford Clinical Trials Research Unit... all participants were being randomised to treatment groups by simple randomisation without reference to their minimisation factors". Comment: adequate method of sequence generation
Allocation concealment (selection bias)	Low risk	Quote "Randomisation was on a 1:1 basis, using a validated computer randomisation program managed centrally by the Oxford Clinical Trials Research Unit". Comment: Central allocation using a secure remote system; allocated treatment administered immediately after receipt of allocation
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote "As the wound dressings and topical devices were clearly visible, the treating surgeon and trial participants could not be blinded to treatment allocation". Patients and personnel could not be blinded.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote "the treating surgeons were not involved in study follow-up assessments or data collection for the trial. Data from clinical reporting forms was entered onto a central database administered by a data clerk in the trial central office. Wound photographs taken at outpatient clinic at approximately 30 days postsurgery were reviewed independently by two experienced assessors (tissue viability specialist) blinded to the treatment allocation." Blinded outcome assessment
Incomplete outcome data (attrition bias) All outcomes	Low risk	Primary outcome all accounted for; other outcomes had available case analysis.
Selective reporting (reporting bias)	Low risk	Comment: Fully reported. A planned mortality analysis was not undertaken because < 5% participants died before 30 days. planned analyses undertaken or deviations accounted for in plan.
Other bias	Low risk	Comprehensively reported and no evidence of other sources of bias

WHIST 2019b

Study characteristics	
Methods	**Study design:** cost-effectiveness analysis based on the WHIST 2019a RCT) **Analytical approach:** Trial-based decision model **Effectiveness data:** SSI (deep) and QoL (EQ-5D) both derived from WHIST 2019 (UK multicentre RCT, N = 1548) **Perspective:** NHS and personal social services (PSS) perspectives **Utility valuations:** EQ-5D and NHS/PSS resource use values derived from 623 trial participants with complete profiles. **Measure of benefit:** QALY calculated using EQ-5D-3L utility scores using UK scoring algorithm **Cost data:** Unit direct medical costs associated with the intervention obtained from the NHS Supply Chain Catalogue 2018/2019. These include cost of standard dressing, the costs of orthotic cast, the cost associated with dressing change, the cost per working hour of the nurse (obtained from the Personal Social Service Research Unit (PSSRU) 2018). The cost of inpatient care derived using the NHS HRG4+ 2017/18 Reference Cost Grouper and the NHS Reference Costs 2017/18. Unit costs of medical items other than those directly attributable to the intervention sourced from the NHS Reference Costs. Medication costs sourced from the BNF. Unit costs for direct non-medical cost items obtained from PSSRU. The costs of aids and adaptations obtained from the NHS Supply Chain Catalogue. The total cost per patient for additional (private) cost items incurred by patients and their next-of-kin obtained from the patients directly. The daily median wage obtained from the Office for National Statistics. Cost data were derived from the key resource inputs of the WHIST 2019 trial and expressed in 2017/2018 UK pounds sterling (£) (completed case analyses); a societal perspective was considered in a sensitivity analysis. Unit costs adjusted to 2017/2018 prices using the NHS Hospital & Community Health Services (HCHS) index for health service resources. No discounting of costs applied due to a short-time horizon. **Analysis of uncertainty:** results of ICERs and cost-effectiveness acceptability curves (CEACs) generated via nonparametric bootstrapping with 1,000 replicas for accommodating sampling (or stochastic) uncertainty and varying levels of willingness-to-pay. sensitivity analysis incorporated societal perspective; 3 different willingness-to-pay thresholds considered
Participants	**Location:** UK hospitals **Intervention group:** n =785, **control group:** n = 763 **Mean age:** </= 40: 283 (36.1%); > 40: 501 (63.9%), **control group** </= 40: 278 (36.4%); > 40: 485 (63.6%) **Inclusion criteria:** adult patients (16 years minimum) presenting to hospital within 72 hours of sustaining major trauma and who required a surgical incision to treat a fractured lower limb **Exclusion criteria:** open fracture of the lower limb that could not be closed primarily; evidence that the patient would be unable to adhere to trial procedures or complete questionnaires
Interventions	**Aim/s:** To investigate, using appropriate statistical and economic analysis methods, the resource use, and thereby the cost effectiveness, of NPWT versus standard dressing for wounds associated with major trauma to the lower limbs **Group 1 (NPWT) intervention:** NPWT using a non-adherent absorbent dressing covered with a semi-permeable dressing. A sealed tube connects the dressing to a built-in mini-pump that creates a partial vacuum over the wound. NPWT applied as per treating surgeon's normal practice and according to manufacturer's instructions (n = 785 in the trial) **Group 2 (control)** Standard dressing (non-adhesive layer covered by sealed dressing or bandage) (n = 763 in the trial) **Study date/s:** October 2016 to March 2016
Outcomes	**Outcomes** (for data see additional table 1 for WHIST 2019b, and for clinical data WHIST 2019a;) Costs (GBP)

WHIST 2019b *(Continued)*

	QALY (measure of benefit) ICER Probability of being cost-effective at three different thresholds
Notes	**Funding:** NIHR **Authors' conclusions:** Contrary to the existing literature, incisional NPWT do not provide a clinical or economic benefit for patients having surgical incisions associated with major trauma to the lower limb. Notes: Not currently a separate publication for cost-effectiveness, data taken from monograph which focuses on RCT Quality rating using the CHEERS checklist was 89.1%

Wihbey 2018

Study characteristics	
Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel **Ethics and informed consent:** Institutional review board approval was obtained from the Dartmouth Committee for the Protection of Human Subjects on April 21, 2015 (#00005211) and from the Southern New Hampshire Medical Center Clinical Trials Office (#2015-01). Women were recruited and consented to participate in this study before the onset of active labor during any routine prenatal visit or inpatient admission. **Follow-up period:** 30 days **Sample size estimate:** Yes. 400 women (200 prophylactic negative pressure wound therapy, 200 standard dressing) would need to be recruited to have an 80% power to detect a 50% decrease in superficial surgical site infection (assuming P < .05). **ITT analysis:** Yes, **number randomised:** 166, **number analysed:** 166 **Funding:** The devices used in this study were provided by an unrestricted research grant from KCI Medical (San Antonio, Texas). **Preregistration:** Yes. This trial was registered with clinical-trials.gov (Clinical Trial Registration: NCT02390401).
Participants	**Location:** Two centres (USA) **Intervention group:** n = 80, **control group:** n = 86 **Mean age: intervention group** 31 ± 6, **control group** 30.2 ± 5 **Inclusion criteria:** Women undergoing caesarean delivery for a viable neonate and their BMI on admission to the labor and delivery floor was 35 or higher **Exclusion criteria:** Women who were younger than 18 years old, did not speak English, had an allergy to silver or adhesives products, or who had a skin incision that would not fit the device or standard dressing (e.g. “T” skin incision)
Interventions	**Aim/s:** To compare the occurrence of superficial surgical site infections in women with class II or III obesity as defined by the Centers for Disease Control and Prevention using prophylactic negative pressure wound therapy compared with standard dressings after caesarean delivery **Group 1 (NPWT) intervention:** Prophylactic NPWT supplied by KCI Medical (San Antonio, Texas) was applied at the time of primary skin closure at caesarean delivery and was placed over the closed surgi-

Wihbey 2018 *(Continued)*

	cal incision under sterile conditions and removed between postoperative day 5 and 7 at the time of incision check **Group 2 (control) intervention:** Standard dressing after caesarean delivery was applied using a sterile technique. If subcuticular closure was used, sterile slim adhesive strips (also known as Steri-Strips) were applied. For both sub-cuticular and staple closure, the dressing consisted of a sterile nonadherent wound dressing (also known as Telfa), a sterile gauze, and a waterproof transparent adhesive dressing (also known as Tegaderm). The standard dressing was removed on postoperative day 2. **Study date/s:** January 2015-January 2017
Outcomes	• Primary outcome: occurrence of surgical site infection defined according to Centers for Disease Control and Prevention criteria (superficial SSI) • Composite wound complication, including superficial, deep, or organ-space surgical site infection; • Wound dehiscence • Seroma within 30 days of surgery • Haematoma within 30 days of surgery • 30-day readmission, 30-day reoperation **Validity of measure/s:** Centers for Disease Control and prevention criteria were used. **Time points:** 1 week and 30 days postoperatively
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "A randomization program (www.randomization. com, Alberta, Canada) was used to generate sealed opaque envelopes with study assignment. Women were randomised at the conclusion of the cesarean delivery, during skin closure, when the envelopes were opened by a circulating operating room nurse. Two randomization strata were created using permuted blocks with varying block sizes for women with BMIs from 35 to less than 40 and women with BMIs of 40 or higher and for each site to ensure equal distribution of study allocation across these two separate BMI categories and sites." Comment: Appropriate method of sequence generation
Allocation concealment (selection bias)	Low risk	Quote: "A randomization program (www.randomization. com, Alberta, Canada) was used to generate sealed opaque envelopes with study assignment. Women were randomised at the conclusion of the cesarean delivery, during skin closure, when the envelopes were opened by a circulating operating room nurse. Two randomization strata were created using permuted blocks with varying block sizes for women with BMIs from 35 to less than 40 and women with BMIs of 40 or higher and for each site to ensure equal distribution of study allocation across these two separate BMI categories and sites." Comment: centrally generated sequence of sealed opaque envelopes. Sequential numbering of envelopes may be inferred
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "We conducted a randomised controlled, nonblinded, multicenter study". Comment: not blinded
Blinding of outcome assessment (detection bias) All outcomes	High risk	Quote: "We conducted a randomised controlled, nonblinded, multicenter study".

Wihbey 2018 *(Continued)*

		Comment: not blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	Small attrition rate. Worst case scenario analysis performed for patients lost to follow-up
Selective reporting (reporting bias)	Low risk	All prespecified outcomes fully reported
Other bias	Low risk	No evidence of other sources of bias; adequate reporting

Witt-Majchrzac 2015

Study characteristics	
Methods	**Study design:** randomised controlled trial **Study grouping:** parallel **Ethics** yes **and informed consent:** not stated **Follow-up period:** 6 weeks **Sample size estimate:** no **ITT analysis:** yes, **number randomised:** 80, **number analysed:** 80 **Funding:** not stated **Preregistration:** no
Participants	**Location:** Olsztyn, Poland **Intervention group:** n = 40,**control group:** n = 40 **Mean age: intervention group** = 66.2 (± 8), 53 to 80,**control group** = 62.1 (± 9.1), 41 to 78 **Inclusion criteria:** patients who underwent an off-pump coronary artery bypass grafting procedure, using the internal mammary artery **Exclusion criteria:** not stated
Interventions	**Aim/s:** not stated **Group 1 (NPWT) intervention:** primary closure with NPWT (PICO, Smith & Nephew) using continuous negative pressure of −80 mmHg. Dressing changed on day 2 or 3 and on day 5 or 6 after surgery **Group 2 control:** conventional dressings were applied after closure. Dressings changed daily **Study date/s:** not stated
Outcomes	**Primary outcome/s:** surgical site infection **Secondary outcome/s:** dehiscence, blisters, reoperation
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Authors stated only that participants were randomised, without describing method of randomisation.

Witt-Majchrzac 2015 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote "An open label prospective study" Comment: open label study with no blinding
Blinding of outcome assessment (detection bias) All outcomes	High risk	Quote "An open label prospective study" Comment: open label study with no blinding
Incomplete outcome data (attrition bias) All outcomes	Low risk	There was no attrition in either arm of the trial.
Selective reporting (reporting bias)	Low risk	While no study protocol was available, outcomes identified in the aims were reported (although it is unclear if the authors may have a priori identified other outcomes that were not reported on).
Other bias	Unclear risk	Baseline imbalance in age; NPWT group was older

Abbreviations

APR: abdominoperineal resection
ASA: American Society of Anesthesiologists
ASEPSIS: ASEPSIS score - a quantitative scoring method using objective criteria based on wound appearance to evaluate wound infection
AUSD: Australian dollars
BMI: body mass index
BNF: British National Formulary
CABG: coronary artery bypass graft
CDC: US Centers for Disease Control and Prevention
CEACs: cost-effectiveness acceptability curves
CHEERS: Checklist for Economic Evaluation for Health Interventions
CI: confidence interval
ciNPT: closed incision negative pressure therapy
Crl:credible interval
CS: caesarean section
CTR: clinical trials registry
DK: Danish Krona
DRI: Disability Rating Index
DVT: deep venous thrombosis
EMR: electronic medical record
EQ-5D-3L/5L: EuroQoL 5D questionnaire, version 3L
GP: general practitioner
GSV: great saphenous vein
HCHS: hospital and community health services
HISS: Hand Injury Severity Score
ICER: Incremental cost effectiveness ratio
iNPWT: incisional negative pressure wound therapy
IQR: interquartile range
ITT: intention-to-treat
LOS: length of stay
NHS:National Health Service (United Kingdom)
NPC: negative pressure closure
NPD: negative pressure device
NPWT: negative pressure wound therapy

OR: operating room (theatre)
ORIF: open reduction and internal fixation surgery
PCA: patient-controlled analgesia
PD: pancreaticoduodenectomies
POD: postoperative day
PP analysis: per-protocol
PSSRU: Personal Social Service Research Unit
QALY: quality-adjusted life year
QoL: quality of life
RCT: randomised controlled trial
SAWT: subatmospheric pressure wound therapy system
SD: standard deviation
SF-12: 12-item Short Form Health Survey
SF-36: 36-item Short Form Health Survey
SNPWT: single-use negative pressure wound therapy
SOC: standard of care
SPD: static pressure dressing
SPID: sum of pain intensity differences
SSC: surgical site complications
SSI: surgical site infection
SSO: surgical site occurrence
THA: total hip arthroplasty
TKR: total knee replacement
TKA: total knee arthroplasty
USD: United States dollars
VAC: vacuum-assisted closure
VAS: visual analogue scale
WHC: wound-healing complication

WHIST 2019b

Study characteristics

Methods	**Study design:** cost-effectiveness analysis based on the WHIST 2019a RCT) **Analytical approach:** Trial-based decision model **Effectiveness data:** SSI (deep) and QoL (EQ-5D) both derived from WHIST 2019 (UK multicentre RCT, N = 1548) **Perspective:** NHS and personal social services (PSS) perspectives **Utility valuations:** EQ-5D and NHS/PSS resource use values derived from 623 trial participants with complete profiles. **Measure of benefit:** QALY calculated using EQ-5D-3L utility scores using UK scoring algorithm **Cost data:** Unit direct medical costs associated with the intervention obtained from the NHS Supply Chain Catalogue 2018/2019. These include cost of standard dressing, the costs of orthotic cast, the cost associated with dressing change, the cost per working hour of the nurse (obtained from the Personal Social Service Research Unit (PSSRU) 2018). The cost of inpatient care derived using the NHS HRG4+ 2017/18 Reference Cost Grouper and the NHS Reference Costs 2017/18. Unit costs of medical items other than those directly attributable to the intervention sourced from the NHS Reference Costs. Medication costs sourced from the BNF. Unit costs for direct non-medical cost items obtained from PSSRU. The costs of aids and adaptations obtained from the NHS Supply Chain Catalogue. The total cost per patient for additional (private) cost items incurred by patients and their next-of-kin obtained from the patients directly. The daily median wage obtained from the Office for National Statistics. Cost data were derived from the key resource inputs of the WHIST 2019 trial and expressed in 2017/2018 UK pounds sterling (£) (completed case analyses); a societal perspective was considered in a sensitivity analysis.

WHIST 2019b *(Continued)*

	Unit costs adjusted to 2017/2018 prices using the NHS Hospital & Community Health Services (HCHS) index for health service resources. No discounting of costs applied due to a short-time horizon. **Analysis of uncertainty:** results of ICERs and cost-effectiveness acceptability curves (CEACs) generated via nonparametric bootstrapping with 1,000 replicas for accommodating sampling (or stochastic) uncertainty and varying levels of willingness-to-pay. sensitivity analysis incorporated societal perspective; 3 different willingness-to-pay thresholds considered
Participants	**Location:** UK hospitals **Intervention group:** n =785, **control group:** n = 763 **Mean age:** </= 40: 283 (36.1%); > 40: 501 (63.9%), **control group** </= 40: 278 (36.4%); > 40: 485 (63.6%) **Inclusion criteria:** adult patients (16 years minimum) presenting to hospital within 72 hours of sustaining major trauma and who required a surgical incision to treat a fractured lower limb **Exclusion criteria:** open fracture of the lower limb that could not be closed primarily; evidence that the patient would be unable to adhere to trial procedures or complete questionnaires
Interventions	**Aim/s:** To investigate, using appropriate statistical and economic analysis methods, the resource use, and thereby the cost effectiveness, of NPWT versus standard dressing for wounds associated with major trauma to the lower limbs **Group 1 (NPWT) intervention:** NPWT using a non-adherent absorbent dressing covered with a semi-permeable dressing. A sealed tube connects the dressing to a built-in mini-pump that creates a partial vacuum over the wound. NPWT applied as per treating surgeon's normal practice and according to manufacturer's instructions (n = 785 in the trial) **Group 2 (control)** Standard dressing (non-adhesive layer covered by sealed dressing or bandage) (n = 763 in the trial) **Study date/s:** October 2016 to March 2016
Outcomes	**Outcomes** (for data see additional table 1 for WHIST 2019b, and for clinical data WHIST 2019a;) Costs (GBP) QALY (measure of benefit) ICER Probability of being cost-effective at three different thresholds
Notes	**Funding:** NIHR **Authors' conclusions:** Contrary to the existing literature, incisional NPWT do not provide a clinical or economic benefit for patients having surgical incisions associated with major trauma to the lower limb. Notes: Not currently a separate publication for cost-effectiveness, data taken from monograph which focuses on RCT Quality rating using the CHEERS checklist was 89.1%

Wihbey 2018

Study characteristics	
Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel **Ethics and informed consent:** Institutional review board approval was obtained from the Dartmouth Committee for the Protection of Human Subjects on April 21, 2015 (#00005211) and from the Southern

Wihbey 2018 *(Continued)*

	New Hampshire Medical Center Clinical Trials Office (#2015-01). Women were recruited and consented to participate in this study before the onset of active labor during any routine prenatal visit or inpatient admission. **Follow-up period:** 30 days **Sample size estimate:** Yes. 400 women (200 prophylactic negative pressure wound therapy, 200 standard dressing) would need to be recruited to have an 80% power to detect a 50% decrease in superficial surgical site infection (assuming P < .05). **ITT analysis:** Yes, **number randomised:** 166, **number analysed:** 166 **Funding:** The devices used in this study were provided by an unrestricted research grant from KCI Medical (San Antonio, Texas). **Preregistration:** Yes. This trial was registered with clinical-trials.gov (Clinical Trial Registration: NCT02390401).
Participants	**Location:** Two centres (USA) **Intervention group:** n = 80, **control group:** n = 86 **Mean age: intervention group** 31 ± 6, **control group** 30.2 ± 5 **Inclusion criteria:** Women undergoing caesarean delivery for a viable neonate and their BMI on admission to the labor and delivery floor was 35 or higher **Exclusion criteria:** Women who were younger than 18 years old, did not speak English, had an allergy to silver or adhesives products, or who had a skin incision that would not fit the device or standard dressing (e.g. "T" skin incision)
Interventions	**Aim/s:** To compare the occurrence of superficial surgical site infections in women with class II or III obesity as defined by the Centers for Disease Control and Prevention using prophylactic negative pressure wound therapy compared with standard dressings after caesarean delivery **Group 1 (NPWT) intervention:** Prophylactic NPWT supplied by KCI Medical (San Antonio, Texas) was applied at the time of primary skin closure at caesarean delivery and was placed over the closed surgical incision under sterile conditions and removed between postoperative day 5 and 7 at the time of incision check **Group 2 (control) intervention:** Standard dressing after caesarean delivery was applied using a sterile technique. If subcuticular closure was used, sterile slim adhesive strips (also known as Steri-Strips) were applied. For both sub-cuticular and staple closure, the dressing consisted of a sterile nonadherent wound dressing (also known as Telfa), a sterile gauze, and a waterproof transparent adhesive dressing (also known as Tegaderm). The standard dressing was removed on postoperative day 2. **Study date/s:** January 2015-January 2017
Outcomes	• Primary outcome: occurrence of surgical site infection defined according to Centers for Disease Control and Prevention criteria (superficial SSI) • Composite wound complication, including superficial, deep, or organ-space surgical site infection; • Wound dehiscence • Seroma within 30 days of surgery • Haematoma within 30 days of surgery • 30-day readmission, 30-day reoperation **Validity of measure/s:** Centers for Disease Control and prevention criteria were used. **Time points:** 1 week and 30 days postoperatively
Notes	
Risk of bias	

Wihbey 2018 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "A randomization program (www.randomization. com, Alberta, Canada) was used to generate sealed opaque envelopes with study assignment. Women were randomised at the conclusion of the cesarean delivery, during skin closure, when the envelopes were opened by a circulating operating room nurse. Two randomization strata were created using permuted blocks with varying block sizes for women with BMIs from 35 to less than 40 and women with BMIs of 40 or higher and for each site to ensure equal distribution of study allocation across these two separate BMI categories and sites." Comment: Appropriate method of sequence generation
Allocation concealment (selection bias)	Low risk	Quote: "A randomization program (www.randomization. com, Alberta, Canada) was used to generate sealed opaque envelopes with study assignment. Women were randomised at the conclusion of the cesarean delivery, during skin closure, when the envelopes were opened by a circulating operating room nurse. Two randomization strata were created using permuted blocks with varying block sizes for women with BMIs from 35 to less than 40 and women with BMIs of 40 or higher and for each site to ensure equal distribution of study allocation across these two separate BMI categories and sites." Comment: centrally generated sequence of sealed opaque envelopes. Sequential numbering of envelopes may be inferred
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "We conducted a randomised controlled, nonblinded, multicenter study". Comment: not blinded
Blinding of outcome assessment (detection bias) All outcomes	High risk	Quote: "We conducted a randomised controlled, nonblinded, multicenter study". Comment: not blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	Small attrition rate. Worst case scenario analysis performed for patients lost to follow-up
Selective reporting (reporting bias)	Low risk	All prespecified outcomes fully reported
Other bias	Low risk	No evidence of other sources of bias; adequate reporting

Witt-Majchrzac 2015

Study characteristics	
Methods	**Study design:** randomised controlled trial **Study grouping:** parallel **Ethics** yes **and informed consent:** not stated **Follow-up period:** 6 weeks **Sample size estimate:** no **ITT analysis:** yes, **number randomised:** 80, **number analysed:** 80

Witt-Majchrzac 2015 *(Continued)*

	Funding: not stated **Preregistration:** no
Participants	**Location:** Olsztyn, Poland **Intervention group:** n = 40,**control group:** n = 40 **Mean age: intervention group** = 66.2 (± 8), 53 to 80,**control group** = 62.1 (± 9.1), 41 to 78 **Inclusion criteria:** patients who underwent an off-pump coronary artery bypass grafting procedure, using the internal mammary artery **Exclusion criteria:** not stated
Interventions	**Aim/s:** not stated **Group 1 (NPWT) intervention:** primary closure with NPWT (PICO, Smith & Nephew) using continuous negative pressure of −80 mmHg. Dressing changed on day 2 or 3 and on day 5 or 6 after surgery **Group 2 control:** conventional dressings were applied after closure. Dressings changed daily **Study date/s:** not stated
Outcomes	**Primary outcome/s:** surgical site infection **Secondary outcome/s:** dehiscence, blisters, reoperation
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Authors stated only that participants were randomised, without describing method of randomisation.
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote "An open label prospective study" Comment: open label study with no blinding
Blinding of outcome assessment (detection bias) All outcomes	High risk	Quote "An open label prospective study" Comment: open label study with no blinding
Incomplete outcome data (attrition bias) All outcomes	Low risk	There was no attrition in either arm of the trial.
Selective reporting (reporting bias)	Low risk	While no study protocol was available, outcomes identified in the aims were reported (although it is unclear if the authors may have a priori identified other outcomes that were not reported on).
Other bias	Unclear risk	Baseline imbalance in age; NPWT group was older

Abbreviations

APR: abdominoperineal resection

ASA: American Society of Anesthesiologists

ASEPSIS: ASEPSIS score - a quantitative scoring method using objective criteria based on wound appearance to evaluate wound infection

AUSD: Australian dollars
BMI: body mass index
BNF: British National Formulary
CABG: coronary artery bypass graft
CDC: US Centers for Disease Control and Prevention
CEACs: cost-effectiveness acceptability curves
CHEERS: Checklist for Economic Evaluation for Health Interventions
CI: confidence interval
ciNPT: closed incision negative pressure therapy
Crl:credible interval
CS: caesarean section
CTR: clinical trials registry
DK: Danish Krona
DRI: Disability Rating Index
DVT: deep venous thrombosis
EMR: electronic medical record
EQ-5D-3L/5L: EuroQoL 5D questionnaire, version 3L
GP: general practitioner
GSV: great saphenous vein
HCHS: hospital and community health services
HISS: Hand Injury Severity Score
ICER: Incremental cost effectiveness ratio
iNPWT: incisional negative pressure wound therapy
IQR: interquartile range
ITT: intention-to-treat
LOS: length of stay
NHS:National Health Service (United Kingdom)
NPC: negative pressure closure
NPD: negative pressure device
NPWT: negative pressure wound therapy
OR: operating room (theatre)
ORIF: open reduction and internal fixation surgery
PCA: patient-controlled analgesia
PD: pancreaticoduodenectomies
POD: postoperative day
PP analysis: per-protocol
PSSRU: Personal Social Service Research Unit
QALY: quality-adjusted life year
QoL: quality of life
RCT: randomised controlled trial
SAWT: subatmospheric pressure wound therapy system
SD: standard deviation
SF-12: 12-item Short Form Health Survey
SF-36: 36-item Short Form Health Survey
SNPWT: single-use negative pressure wound therapy
SOC: standard of care
SPD: static pressure dressing
SPID: sum of pain intensity differences
SSC: surgical site complications
SSI: surgical site infection
SSO: surgical site occurrence
THA: total hip arthroplasty
TKR: total knee replacement
TKA: total knee arthroplasty
USD: United States dollars
VAC: vacuum-assisted closure

VAS: visual analogue scale
WHC: wound-healing complication

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

Study	Reason for exclusion
Al-Inany 2002	Ineligible intervention
Albert 2012	No acute wounds were included.
Anderson 2014	Feasibility study. Predefined criteria used to assess feasibility included: recruitment (> 75% participation); loss to follow-up (< 10%); intervention fidelity (= 95%); and interrater reliability (kappa = 0.8). Assessment of clinical outcomes was not planned or conducted.
Athanasiou 2018	Commentary on an RCT; not original research
Banasiewicz 2013	Included infected wounds
Bi 2017	Ineligible intervention
Bondokji 2011	Prospective cohort study
Braakenburg 2006	Chronic and acute wounds were reported together, and further information was not available.
Chang 2018	Discussion article
Chiang 2017	Open wounds
Chio 2010	Skin graft study
Costa 2018	Ineligible population - wounds healing by secondary intention
Dorafshar 2012	The study used NPWT to treat existing non-healing skin graft wounds.
Eisenhardt 2012	Skin graft study; no inclusion of wounds healing by primary closure
Erne 2018	Ineligible intervention
Fleming 2018	Ineligible study design - not an RCT
Frazee 2018	Ineligible comparison
Grauhan 2013	Quasi-randomised study: "A total of 156 patients were enrolled and allocated to 2 study groups, alternating according to the time of operation".
Hu 2009	Acute, subacute, 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.
Joos 2015	Commentary on an RCT in wounds healing by secondary intention
Kim 2007	The study was not a randomised controlled trial.
Krishnamoorthy 2012	Use of NPWT was not the only difference between the groups.

Study	Reason for exclusion
Li 2016	Quasi-randomisation (by odd and even numbers)
Llanos 2006	Skin graft study
Moisidis 2004	Skin graft study; no inclusion of wounds healing by primary closure
Mouës 2004	No inclusion of acute wounds
Mouës 2007	No inclusion of acute wounds
Muller-Sloof 2018	Ineligible population
Pellino 2014	Non-randomised study in people with Crohn's disease
Petkar 2012	Skin graft study
Rahmanian-Schwarz 2012	Included chronic and acute wounds, and these were not separately reported
Sinha 2016	Ineligible population; infected wounds
Stannard 2006	Ineligible population; not closed incision wounds
Svensson-Bjork 2018	Non-randomised subgroup of RCT participants
Trofa 2019	Ineligible comparison
Visser 2017	The vacuum therapy device was a syringe inserted subcutaneously into the dressing, which was used to create a vacuum. Consequently, it was not a standard, continuous pressure device.
Walker 2018	Ineligible intervention
Yu 2017	A drain was left inside the wound, so not strictly a primarily closed wound.
Zotes 2015	Ineligible population; infected wounds

NPWT: negative pressure wound therapy

Characteristics of studies awaiting classification *[ordered by study ID]*

Nagata 2018

Methods	**Study design:** Randomised controlled trial **Study grouping:** Intra-individual **Ethics and informed consent:** N/A **Follow-up period:** 6 months **Sample size estimate:** Target sample size of 20 (sample size estimate calculation not reported) **ITT analysis:** yes, **number randomised:** 13, **number analysed:** 13 **Funding:** None **Preregistration:** This trial was registered under the name “Tissue Expander (TE) Insertion Comparison of Negative Pressure Fixation (NPF) and Film Dressing (FD) Effects on Suture Wound

Nagata 2018 *(Continued)*

	Open Label Randomized Single Facility Comparison Test," UMIN Clinical Trial Registry number UMIN000014424.
Participants	**Location:** Single-centre – Japan **Intervention group:** n = 13, **control group:** n = 13 **Mean age:** 46.2, **intervention group** 46.2, **control group** 46.2 **Inclusion criteria:** Women aged 18 to 65 years undergoing tissue expander insertion for two-stage breast reconstruction after mastectomy were included. **Exclusion criteria:** Excluded patients were those who (1) did not provide consent, (2) received radiotherapy after surgery, (3) had an adverse reaction to the adhesive film, (4) had a local infection or wound dehiscence at study initiation, or (5) underwent tissue expander replacement with a silicone breast implant within 6 months after the first operation.
Interventions	**Aim/s:** To evaluate the effects of negative-pressure fixation on scar appearance and histochemical properties in comparison to those for film dressing without negative pressure **Group 1 (NPWT) intervention:** Application of negative pressure inside polyurethane foam (Hydrosite Plus; Smith & Nephew, London, United Kingdom) sealed by a film dressing (Airwall; Kyowa, Osaka, Japan) **Group 2 (control) intervention:** Film dressing **Study date/s:** 3 July 2014 to 31 August 2016
Outcomes	• Visual analogue scale • Scar width • Immunohistochemistry **Validity of measure/s:** N/A **Time points:** 6 months postoperative
Notes	

NCT00654641

Methods	Randomised controlled trial
Participants	Obese women undergoing caesarean delivery
Interventions	Negative pressure wound therapy versus standard wound closure
Outcomes	Total number of women experiencing a wound complication
Notes	

NCT00724750

Methods	Randomised controlled trial
Participants	Hospitalised patients with acute wounds resulting from either trauma, dehiscence, or surgical complications

NCT00724750 *(Continued)*

Interventions	Gauze suction (G-SUC) negative pressure wound therapy versus vacuum-assisted closure device (VAC) negative pressure wound therapy
Outcomes	Per cent change per day in wound surface area; per cent change per day in wound volume
Notes	

G-SUC: gauze suction
HOOS: hip disability and osteoarthritis outcome score
KOOS: knee disability and osteoarthritis outcome score
VAC: vacuum-assisted closure
VAS: visual analogue scale
VR-12: Veterans RAND 12-Item Health Survey

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

ACTRN12615000175572

Study name	Do suction assisted negative pressure dressings reduce the incidence of surgical site infections after abdominal surgery: a randomized controlled trial
Methods	Randomised controlled trial
Participants	Patients undergoing laparotomy (where abdominal incision breaches peritoneum, and wound is large enough to at least fit the surgeon's hand)
Interventions	Negative pressure wound therapy versus standard dressing used with a clear film with an absorbent layer
Outcomes	Wound infection; patient satisfaction
Starting date	2015
Contact information	peeyau.tan@monashhealth.org
Notes	

ACTRN12618000026224p

Study name	Effect of negative pressure dressing versus standard wound dressing on the rate of wound dehiscence in patients undergoing pilonidal surgery
Methods	Randomised controlled trial
Participants	Patients undergoing pilonidal surgery
Interventions	Negative pressure wound therapy versus standard wound dressings
Outcomes	Rate of wound dehiscence; time taken for the wound to fully heal; rate of disease recurrence; analgesia requirements for the wound; ratio of wound size; patient satisfaction 2 months postoperatively; QoL
Starting date	2017

ACTRN12618000026224p *(Continued)*

Contact information	Ram.Nataraja@monashhealth.org
Notes	

ACTRN12618001611213

Study name	The effect of PICO dressings on surgical site infection following bowel resection: a randomised controlled trial
Methods	Randomised controlled trial
Participants	All adults (aged 18 and over) undergoing elective or emergency small or large bowel resection
Interventions	Negative pressure wound therapy (PICO dressing) versus standard dressing
Outcomes	SSI; Patient and Observer Scar Assessment Scale (POSAS); patient satisfaction
Starting date	2018
Contact information	Alexandra.Gordon@midcentraldhb.govt.nz
Notes	

ACTRN12618002006224

Study name	EffiCacY of neGative pressure wound therapy in the preventioN of surgical woUnd complicationS in the cesarean section at risk population: a randomised multi-centre trial, the CYGNUS trial
Methods	Randomised controlled trial
Participants	Pregnant women between 18-50 years undergoing caesarean section
Interventions	Negative pressure wound therapy versus standard dressing
Outcomes	SSI; wound dehiscence
Starting date	2018
Contact information	kylie.sandy-hodgetts@uwa.edu.au
Notes	

ChiCTR -IOR-15006439

Study name	Prevention surgical site infection with using negative pressure wound therapy in abdominal incision
Methods	Parallel randomised controlled trial

ChiCTR -IOR-15006439 *(Continued)*

Participants	High-risk patients: including abdominal surgery for malignancy, colorectal, abdominal wall reconstruction
Interventions	Negative pressure wound therapy versus routine approach
Outcomes	Rate of surgical site infection
Starting date	2015
Contact information	hpzhangly@163.com
Notes	

DRKS00006199

Study name	Postoperative negative pressure incision therapy following open colorectal surgery: a randomized-controlled trial
Methods	Randomised controlled trial
Participants	Patients undergoing planned elective open colorectal surgery via median or transverse laparotomy
Interventions	Negative pressure wound therapy versus standard wound dressings
Outcomes	Rate of SSI; length of hospital stay; rate of reoperations; rate of antibiotic therapy; duration of postoperative negative pressure incision therapy (intervention arm only); wound pain assessed with VAS; rate of wound complications other than wound infections; rate of serious adverse events
Starting date	1 October 2015
Contact information	Unclear
Notes	

DRKS00011033

Study name	Evaluation of negative pressure incisional therapy in urgent gastro-intestinal surgery for reduction of superficial surgical site infections compared to non-occlusive conventional plaster - a prospective, randomized, controlled, multicenter clinical trial
Methods	Randomised controlled trial
Participants	Patients undergoing urgent laparotomy due to an acute gastrointestinal disorder
Interventions	Negative pressure wound therapy versus non-occlusive conventional plaster
Outcomes	SSI; prolongation of hospitalisation due to SSI; cosmetic result; safety endpoints: AEs, SAEs
Starting date	21 September 2016
Contact information	Unclear

DRKS00011033 *(Continued)*

Notes	

DRKS00015136

Study name	Negative pressure wound therapy (NPWT) on closed incisions to prevent surgical site infection in HPB-surgery
Methods	Randomised controlled trial
Participants	Patients > 49 years of age undergoing hepato-pancreato-biliary surgery with midline, transverse or L-formed laparotomy
Interventions	Negative wound pressure therapy (Prevena) versus standard dressing (plaster bandage)
Outcomes	Superficial and deep incisional SSI; haematoma, seroma, dehiscence, necrosis; fascial dehiscence; EQ-5D-5L; usage of antibiotics; secondary intervention and reoperation
Starting date	2019
Contact information	frank.brennfleck at ukr.de
Notes	

Gillespie 2016

Study name	Negative pressure wound therapy versus standard care dressing to prevent surgical site infections in obese women undergoing caesarean section
Methods	Randomised controlled trial
Participants	Obese women following caesarean section
Interventions	Negative pressure wound therapy versus standard wound dressings
Outcomes	Presence of SSI; wound complications; hospital readmissions; hospital length of stay; QoL
Starting date	2015
Contact information	b.gillespie@griffith.edu.au
Notes	

ISRCTN12702354

Study name	Wound healing in surgical trauma
Methods	Randomised controlled trial
Participants	Major trauma patients aged 16 years or over requiring surgery to treat a broken leg

ISRCTN12702354 *(Continued)*

Interventions	Negative pressure wound therapy versus standard-of-care wound dressing
Outcomes	Deep infection rate; QoL; wound healing; number and nature of further surgical interventions; cost-effectiveness; long-term disability; chronic neuropathic pain
Starting date	January 2016
Contact information	WHIST@ndorms.ox.ac.uk
Notes	

ISRCTN31224450

Study name	Negative pressure therapy in large incisional hernia surgery
Methods	Randomised controlled trial (case-control)
Participants	Patients undergoing elective surgery for incisional hernia with diameters exceeding 10 cm
Interventions	Negative pressure wound therapy versus traditional dressing
Outcomes	Primary: volume accumulated in the drains every 24 hours in millilitres; number of days needed to reduce this volume under 50 mL per 24 hours Secondary: postoperative complications; cost
Starting date	1 February 2013
Contact information	drcarlesolona@gmail.com
Notes	

ISRCTN55305726

Study name	WHITE 7 - WHISH – wound healing in surgery for hip fractures
Methods	Randomised controlled trial
Participants	Adults aged 65 years or older with a hip fracture that requires surgery
Interventions	Negative pressure wound therapy versus standard wound dressing
Outcomes	Deep infection; mortality rate; QoL; complications and surgical interventions; cost consequences and resource use; mobility; residential status; recruitment rate; retention rate
Starting date	1 March 2017
Contact information	lucy.sansom@ndorms.ox.ac.uk
Notes	

Jorgensen 2018

Study name	Prevention of seroma following inguinal lymph node dissection with prophylactic, incisional, negative-pressure wound therapy (SEROMA trial)
Methods	Randomised controlled trial
Participants	Patients ≥18 years undergoing inguinal lymph node dissection for metastatic melanoma
Interventions	Negative pressure wound therapy (Smith & Nephew) versus standard dressing (Micropore)
Outcomes	Seroma; cumulative volume of aspirated seromas; cumulative number of seroma aspirations; SSI; days until the last suction drain(s) removed; cumulative volume of collected lymph fluid; EQ-5D-5L; wound dehiscence; necrosis; haematoma; length of hospitalisation; readmission times; reoperation; lymphoedema; lymphoedema-related quality of life; regional recurrence of melanoma
Starting date	2018
Contact information	jens.sorensen@rsyd.dk
Notes	Duplicate with NCT03433937

JPRN000030936

Study name	A randomized phase II study to evaluate efficacy of negative pressure wound therapy on prophylaxis of the incisional hernia after reversal of temporaly [sic] diverting stoma
Methods	Randomised controlled trial
Participants	Patients 20-85 years with temporary stoma and planned closure following initial surgery
Interventions	Negative pressure wound therapy versus standard therapy
Outcomes	Incidence of radiological incisional hernia after one year of surgery
Starting date	2018
Contact information	skomat2718@gmail.com
Notes	

KCT0004063

Study name	The effectiveness of negative pressure wound dressing for the wound healing after stoma closure: an prospective, open-label, randomized control study
Methods	Randomised controlled study
Participants	Patients 20-85 years with ileostomy or colostomy undergoing reversal
Interventions	Negative pressure wound therapy versus standard dressing

KCT0004063 *(Continued)*

Outcomes	Complete wound healing period; SSI; number of wound dressings; number of wound visits; length of hospital stay; patient and observer scar assessment scale (POSAS)
Starting date	2019
Contact information	+82-53-620-3580
Notes	

Masters 2018

Study name	Randomised controlled feasibility trial of standard wound management versus negative-pressure wound therapy in the treatment of adult patients having surgical incisions for hip fractures
Methods	Randomised controlled trial
Participants	Patients > 65 years undergoing surgery for hip fracture
Interventions	Negative pressure wound therapy versus standard care
Outcomes	SSI (deep infection); EQ-5D-5L; mobility; mortality; late complications
Starting date	2017
Contact information	james.masters@ndorms.ox. ac.uk
Notes	

Mihaljevic 2015

Study name	Postoperative negative-pressure incision therapy following open colorectal surgery (Poniy): a randomized-controlled trial
Methods	Randomised controlled trial
Participants	All adult (≥ 18 years of age) surgical patients scheduled for elective open colorectal surgery
Interventions	Negative-pressure incision therapy device versus standard dressing
Outcomes	SSI; length of hospital stay; reoperation; duration of postoperative antibiotic treatment; duration of negative-pressure incision therapy; wound pain; wound complications; serious adverse events
Starting date	2014
Contact information	kleeff@tum.de
Notes	

NCT01450631

Study name	The use of the Prevena incision management system on post-surgical cesarean section incisions
Methods	Randomised controlled trial
Participants	Patients undergoing caesarean section procedures using a subcuticular skin closure technique within the next 42 days
Interventions	PREVENA Incision Management System versus standard-of-care dressing
Outcomes	Incidence of postoperative surgical site occurrences post-caesarean section surgery
Starting date	2011
Contact information	Robert Heine, Duke University
Notes	

NCT01770067

Study name	Prophylactic treatment of high-risk patients with cardiovascular implantable electronic devices (CIED) with continuous in-situ ultra high-dose antibiotics (CITA) under regulated negative pressure-assisted wound therapy (RNPT)
Methods	Randomised controlled trial
Participants	Patients undergoing cardiovascular implantable electronic devices surgery
Interventions	High-dose antibiotics (CITA) under regulated negative pressure-assisted wound therapy (RNPT) versus CITA
Outcomes	Lack of CIED infection
Starting date	February 2013
Contact information	Unknown
Notes	

NCT01891006

Study name	Intervention for postpartum infections following caesarean section (APIPICS)
Methods	Randomised controlled trial
Participants	Patients 18 years of age or older with postpartum infections following caesarean section
Interventions	Negative pressure wound therapy versus standard wound dressing
Outcomes	Frequency of re-rupture in each study group; length of hospitalisation; readmission to hospital; decreased health-related quality of life score; cosmetic outcome
Starting date	2013

NCT01891006 *(Continued)*

Contact information	Nana Hyldig
Notes	

NCT01905397

Study name	Negative pressure wound therapy to reduce surgical site infection
Methods	Randomised controlled trial
Participants	Scheduled for an elective surgery in either open CRS or open HPBS
Interventions	Negative pressure wound therapy versus conventional wound therapy
Outcomes	Incidence of surgical site infection; characterisation of surgical site infection; length of hospital stay
Starting date	2013
Contact information	Trey Blazer, Duke University
Notes	

NCT01913132

Study name	PICO above incisions after vascular surgery
Methods	Randomised controlled trial
Participants	Patients 18 years of age and above undergoing elective vascular surgery
Interventions	Negative pressure wound therapy with PICO versus standard dressing
Outcomes	Wound infection; cost
Starting date	2013
Contact information	Stefan Acosta, Skåne University Hospital
Notes	

NCT02020018

Study name	Negative pressure wound therapy for prevention of poststernotomy infection
Methods	Randomised controlled trial
Participants	Patients undergoing open heart surgery
Interventions	Negative pressure wound therapy versus standard wound dressings

NCT02020018 *(Continued)*

Outcomes	Wound infection after open-heart surgery; reoperation for wound infection; length of stay
Starting date	December 2013
Contact information	Unknown
Notes	

NCT02064270

Study name	PICO: A prospective, randomized, controlled clinical study to assess the prevention of postsurgical incision healing complications in patients undergoing primary or revision Knee Arthroplasty (KA) or Total Hip Arthroplasty (THA), treated with either Single-Use Negative Pressure Wound Therapy (NPWT) or standard postsurgical dressings
Methods	Randomised controlled trial
Participants	Patient is scheduled to have a surgical procedure for total knee arthroplasty or total hip arthroplasty (primary or revision procedure).
Interventions	Negative pressure wound therapy versus standard postsurgical dressings
Outcomes	Incision appearance based on VAS; drainage amount; user-friendliness for patient; number of participants with complications; return to the operating room; need for antibiotics
Starting date	Protocol dated March 2016
Contact information	JP Stannard
Notes	stannardj@health.missouri.edu

NCT02118558

Study name	Negative pressure wound therapy – PREVENA – in prevention of infections after total knee arthroplasty (TKA)
Methods	Randomised controlled trial
Participants	Patients undergoing knee arthroplasty
Interventions	Negative pressure wound therapy versus standard prophylactic therapy
Outcomes	Proportion of infections; number of participants recommended to undergo further procedural intervention due to infection
Starting date	June 2014
Contact information	Unknown
Notes	

NCT02127281	
Study name	
Methods	Randomised controlled trial
Participants	Patients with a scheduled revision total hip or knee arthroplasty procedure
Interventions	PREVENA versus control
Outcomes	Number of participants with wound complications; reoperation rates; readmission rates; knee flexion; HOOS and KOOS scores at 90 days postoperatively; timed-up-and-go test; hip range of motion (flexion); VR-12 questionnaire; hip range of motion; knee extension
Starting date	
Contact information	
Notes	

NCT02302222	
Study name	The management of closed surgical incisions resulting from incisional hernia repair and/or functional panniculectomy using the Prevena Customizable dressing
Methods	Randomised controlled trial
Participants	Adults undergoing panniculectomy or hernia repair; BMI ≥ 30; preoperatively assessed to undergo a procedure resulting in a clean/clean-contaminated wound
Interventions	PREVENA Customizable Dressing with ACTIV.A.C. therapy unit versus standard dressing
Outcomes	Incidence of SSI or dehiscence within 30 days of surgery; incidence of clinically relevant intervention (antimicrobial treatment, drainage, debridement, reoperation, application of NPWT) within 30 days of surgery
Starting date	2015
Contact information	Not stated
Notes	

NCT02309944	
Study name	Negative pressure wound therapy in obese gynecologic oncology patients
Methods	Randomised controlled trial
Participants	Patients undergoing laparotomy for suspected gynecologic malignancy
Interventions	Negative pressure wound therapy versus standard wound management

NCT02309944 *(Continued)*

Outcomes	Rate of wound complications; time from surgery to starting adjuvant therapy among those with confirmed malignancies
Starting date	May 2015
Contact information	mhgerber@umn.edu
Notes	

NCT02331485

Study name	Randomised control study to assess the role of negative pressure wound therapy (NPWT) in the management of wound in surgical patient
Methods	Randomised controlled trial
Participants	Patients undergoing laparotomy with 1 of: high BMI; malignancy; malnutrition; type 2 diabetes; emergency surgery; postradiochemotherapy; steroids; open colorectal resection; and at least 2 of: smoking; age > 75 years; diffuse atherosclerotic disease involving arteries
Interventions	Negative pressure wound therapy (PICO + Acticoat group) versus standard wound management
Outcomes	Reduction in wound infection by 50%; reduction in length of hospital stay; decrease in antibiotic use for wound infection management; decreased cost of patient treatment
Starting date	August 2014
Contact information	mikazanowski@gmail.com; sebastian.smolarek79@gmail.com
Notes	

NCT02348034

Study name	A randomized controlled trial exploring the ability of negative pressure wound therapy (NPWT) to reduce colorectal surgical site infections (SSI)
Methods	Randomised controlled trial
Participants	Patients undergoing elective colorectal surgery
Interventions	PREVENA dressing versus usual care
Outcomes	Presence/absence of superficial surgical site infection; presence/absence of intervention-related side effects
Starting date	November 2015
Contact information	gag511@mail.usask.ca
Notes	

NCT02389023

Study name	Comparison of Prevena negative pressure incision management system vs. standard dressing after vascular surgery
Methods	Randomised controlled trial
Participants	Not stated
Interventions	PREVENA incision management system versus standard gauze dressing
Outcomes	Surgical site infection, major wound non-infectious complications, or graft infection; surgical site infection alone; patient satisfaction; total costs; length of index hospital stay and any readmission; major adverse limb event (MALE) or postoperative death
Starting date	2015
Contact information	daniel.bertges@uvmhealth.edu; lisa.smith@med.uvm.edu
Notes	

NCT02408835

Study name	Negative pressure wound therapy in groin dissection
Methods	Randomised controlled trial
Participants	Patients undergoing inguinal lymphadenectomy for metastatic carcinoma of cutaneous origin
Interventions	Negative pressure wound therapy versus conventional wound care
Outcomes	Time to wound healing; wound infection; lymphoedema; need for further surgical interventions to achieve wound healing; scar appearance; patient-reported outcomes
Starting date	July 2015
Contact information	s.mcallister@qub.ac.uk
Notes	

NCT02492854

Study name	Standard versus PICO dressings in lower-extremity bypass patients (PICO-LEB)
Methods	Randomised controlled trial
Participants	Patients undergoing lower extremity bypass using ipsilateral great saphenous vein harvest
Interventions	PICO single-use negative pressure dressings versus sterile gauze dressings
Outcomes	Infection of surgical site incision; function and quality of life; resource utilisation in dollars
Starting date	2015

NCT02492854 *(Continued)*

Contact information	Jeffrey.Siracuse@bmc.org; twtcheng@bu.edu
Notes	

NCT02509260

Study name	Prevena incisional negative pressure wound therapy in re-operative colorectal surgery
Methods	Randomised controlled trial
Participants	Patients undergoing open reoperative colorectal surgery
Interventions	Negative pressure wound therapy versus standard wound dressings
Outcomes	Occurrence of superficial surgical site infection; length of hospital stay; cost-effectiveness; clinical efficacy of the device in relation to the degree of contamination
Starting date	July 2015
Contact information	ASHBURJ@ccf.org
Notes	

NCT02558764

Study name	Effects of preventive negative pressure wound therapy with PICO on surgical wounds of kidney transplant patients
Methods	Randomised controlled trial
Participants	Patients admitted for cadaveric kidney transplant surgery
Interventions	Negative pressure wound therapy versus basic wound contact absorbent dressings
Outcomes	Post-kidney transplant wound complication rates
Starting date	November 2015
Contact information	Unknown
Notes	

NCT02578745

Study name	Prophylactic incisional care in obese women at cesarean (PICO-C)
Methods	Randomised controlled trial
Participants	Patients with planned or unplanned caesarean delivery with a BMI ≥ 30 at the time of delivery

NCT02578745 *(Continued)*

Interventions	Prophylactic NPWT versus standard dressing
Outcomes	Surgical site infection or other wound complications; individual components of composite wound complications; pain score on 0-to-10 scale; positive wound cultures and specific organisms such as MRSA; prophylactic negative pressure-related adverse events including blisters
Starting date	2015
Contact information	Methodius G Tuuli, Washington University School of Medicine
Notes	

NCT02664168

Study name	A comparative study to assess the prevention of surgical site infection (SSIs) in revision total joint arthroplasty patients treated with single-use negative pressure wound therapy (PICO) or standard care dressings (AQUACEL Ag surgical dressing)
Methods	Randomised controlled trial
Participants	Patients undergoing revision total knee arthroplasty or revision total hip arthroplasty
Interventions	Single-use negative pressure wound therapy versus AQUACEL Ag surgical dressing
Outcomes	Incidence of surgical site infection
Starting date	January 2016
Contact information	tiffany.morrison@rothmaninstitute.com
Notes	

NCT02682316

Study name	Negative pressure wound therapy in post-operative incision management
Methods	Randomised controlled trial
Participants	Women of any BMI undergoing a laparotomy procedure for a presumed gynaecologic malignancy, or morbidly obese
Interventions	Negative pressure wound therapy versus usual standard dry gauze
Outcomes	Number of postoperative wound complications
Starting date	February 2016
Contact information	Mario Leitao
Notes	

NCT02790385

Study name	Negative pressure wound therapy - a multi-centered randomized control trial (NPWT)
Methods	Randomised controlled trial
Participants	Patients undergoing posterior spinal surgery categorised as high risk for infection
Interventions	Negative pressure wound therapy versus standard gauze treatment
Outcomes	Wound infection; time for wound closure; cosmetic results; caregiver/parental satisfaction; wound dehiscence; foreign body reaction
Starting date	July 2014
Contact information	Unknown
Notes	

NCT02799667

Study name	Do single use negative pressure dressings reduce wound complications in obese women after caesarean delivery?
Methods	Randomised controlled trial
Participants	Obese women (BMI > 40 kg/m^2) undergoing caesarean delivery
Interventions	Negative pressure wound therapy versus conventional dressing
Outcomes	Presence of wound complications
Starting date	May 2016
Contact information	sbakaysa@tuftsmedicalcenter.org
Notes	

NCT02892435

Study name	Prevena incision management system vs conventional management for wound healing
Methods	Randomised controlled trial
Participants	Patients submitted to contaminated or dirty abdominal surgery
Interventions	Negative pressure wound therapy versus conventional dressing
Outcomes	SSI; reduction in wound complications in participants with associated risk factors (e.g. diabetes, obesity, and cancer)
Starting date	November 2014

NCT02892435 *(Continued)*

Contact information	alessia.garzi@gmail.com
Notes	

NCT02901405

Study name	NPWT in soft tissue sarcoma surgery
Methods	Randomised controlled trial
Participants	Adults undergoing primary soft tissue sarcoma excision that is primarily closed
Interventions	Negative pressure wound therapy versus standard dressings
Outcomes	Surgical site infection; time to wound dryness; delay to discharge from hospital; adverse events; cost analysis
Starting date	2016
Contact information	ashish.mahendra@ggc.scot.nhs.uk
Notes	

NCT02901613

Study name	Prophylactic post-cesarean incisional negative-pressure wound therapy in morbidly obese patients
Methods	Randomised controlled trial
Participants	Morbidly obese patients who have undergone caesarean section
Interventions	Negative pressure wound therapy versus standard dry sterile dressing
Outcomes	Wound complications
Starting date	August 2016
Contact information	denefrc@mail.amc.edu
Notes	

NCT02926924

Study name	Prophylactic application of an incisional wound vac to prevent wound complications in obese spine surgery patients
Methods	Randomised controlled trial
Participants	Patients scheduled to have posterior spine surgery; BMI ≥ 35

NCT02926924 *(Continued)*

Interventions	Wound VAC versus standard dressing
Outcomes	Postoperative infection requiring return to operating room
Starting date	2016
Contact information	jaimeeg@med.umich.edu
Notes	

NCT02954835

Study name	Negative pressure therapy for groin wounds
Methods	Randomised controlled trial
Participants	Patients undergoing vascular surgery with a groin incision
Interventions	PREVENA versus traditional dressing
Outcomes	Infection rate
Starting date	2016
Contact information	thomas.bernik@ehmchealth.org; courtney.woodhull@ehmchealth.org
Notes	

NCT02967627

Study name	VAC dressings for colorectal resections (VACCRR)
Methods	Randomised controlled trial
Participants	Patients undergoing elective colorectal resection for benign or malignant disease
Interventions	Negative pressure wound therapy versus sterile gauze dressing
Outcomes	SSI; wound complication; length of stay; wound-related visits postsurgery; need for and duration of home care; blistering/reaction to wound dressings; postoperative complications
Starting date	November 2016
Contact information	mitchell.webb@alumni.ubc.ca
Notes	

NCT03000010

Study name	Wound Vac bandage comparison after spinal fusion (WV)

NCT03000010 *(Continued)*

Methods	Randomised controlled trial
Participants	Patients with neuromuscular scoliosis undergoing posterior spinal fusion
Interventions	Incisional wound VAC versus normal gauze bandage group
Outcomes	Prevention of wound dehiscence or infection
Starting date	2016
Contact information	mcburke@med.umich.edu
Notes	

NCT03009110

Study name	Preventing adverse incisional outcomes at cesarean multicenter trial (Prevena-C)
Methods	Randomised controlled trial
Participants	Women undergoing planned or unplanned caesarean delivery
Interventions	Negative pressure wound therapy versus standard wound dressings
Outcomes	Frequency of superficial or deep surgical site infections
Starting date	February 2017
Contact information	martins@wudosis.wustl.edu
Notes	

NCT03010137

Study name	Incisional negative pressure wound therapy in high risk patients undergoing panniculectomy: a prospective randomized controlled trial
Methods	Randomised controlled trial
Participants	Patients undergoing panniculectomy in preparation for renal transplantation
Interventions	Negative pressure wound therapy versus standard closure
Outcomes	Wound-healing complications; time to drain removal; scarring; pain; QoL
Starting date	December 2015
Contact information	cbailey@ucdavis.edu
Notes	

NCT03021668

Study name	Comparison between wound vacuum dressing and standard closure to reduce rates of surgical site infections
Methods	Randomised controlled trial
Participants	Patient to undergo pancreaticoduodenectomy for pancreatic tumours at the Johns Hopkins Hospital
Interventions	PREVENA Peel & Place dressing versus standard closure of surgical incision
Outcomes	Rate of surgical site infection; prolonged length of stay; rate of readmission; time to adjuvant therapy
Starting date	2017
Contact information	Matthew J Weiss, Johns Hopkins University
Notes	

NCT03061903

Study name	Closed incision negative pressure therapy vs standard care (Prevena)
Methods	Randomised controlled trial
Participants	Patients undergoing primary total hip arthroplasty through a direct anterior approach with: diabetes; obesity (BMI > 30); active smoking; previous hip surgery
Interventions	PREVENA versus AQUACEL
Outcomes	Prevalence of wound complications; duration of wound-healing delay; length of hospital stay; number of days on antibiotic therapy; average cost of wound treatment
Starting date	2017
Contact information	mh3818@cumc.columbia.edu; rs3464@cumc.columbia.edu
Notes	

NCT03069885

Study name	iNPWT in immediate breast reconstruction
Methods	Randomised controlled trial
Participants	Patients ≥ 18 admitted for immediate breast reconstruction
Interventions	Negative pressure wound therapy versus standard wound dressings
Outcomes	Time to removal of surgical drains; SSI; skin necrosis; hospitalisation time; participant and observer assessment of the scars; patient satisfaction and quality of life

NCT03069885 *(Continued)*

Starting date	November 2017
Contact information	Aarhus University Hospital
Notes	

NCT03082664

Study name	Negative pressure wound therapy to prevent wound complications following cesarean section in high risk patients
Methods	Randomised controlled trial
Participants	Caesarean section in high-risk obstetric patients
Interventions	Negative pressure wound therapy versus standard wound dressings
Outcomes	Wound complications: wound breakdown, infection, separation, dehiscence
Starting date	June 2015
Contact information	meghanhill@obgyn.arizona.edu
Notes	

NCT03144726

Study name	RCT on NPWT for incisions following major lower-limb amputation to reduce surgical site infection
Methods	Randomised controlled trial
Participants	Any patient 18 years or older undergoing amputation of the lower limb, either an above-knee amputation or below-knee amputation
Interventions	Negative pressure wound therapy versus standard dressing
Outcomes	Surgical site infection; length of stay; antibiotic use; reoperation; death
Starting date	2017
Contact information	oonagh.scallan@lhsc.on.ca
Notes	

NCT03175718

Study name	INPWT on wound complications & clinical outcomes after lower extremity sarcoma surgery preop radiation therapy patients (VAC)
Methods	Randomised controlled trial

NCT03175718 *(Continued)*

Participants	Patients with lower extremity soft tissue sarcoma confirmed by tissue pathology
Interventions	VAC wound dressing versus wound dressing
Outcomes	Wound complications including reoperation for superficial or deep site infection; quality of life; functional outcome; overall cost
Starting date	2017
Contact information	yalmosuli@ohri.ca; jdobransky@ohri.ca
Notes	

NCT03180346

Study name	A prospective, randomized, comparative study to assess the prevention of surgical site infection (SSIs) in revision total joint arthroplasty patients treated with single-use negative pressure wound therapy (PICO) or standard care dressings (AQUACEL Ag surgical dressing)
Methods	Randomised controlled trial
Participants	Patients undergoing revision total knee arthroplasty or revision total hip arthroplasty
Interventions	Negative pressure wound therapy versus standard care
Outcomes	SSI
Starting date	March 2017
Contact information	Unknown
Notes	

NCT03250442

Study name	Evaluating the outcomes for incisional application of negative pressure for nontraumatic amputations
Methods	Randomised controlled trial
Participants	Patient requires closure of a non-traumatic transmetatarsal amputation, below-knee amputation, knee disarticulation, or above-knee amputation.
Interventions	PREVENA device versus standard dry dressing
Outcomes	Proportion of postoperative incision complications between the 2 arms; length of hospital stay; number of surgically related wound readmissions; Medical Outcomes Study 12-item Short Form Health Survey (SF-12); percentage of closed incisions remaining closed at 1, 2, and 3 months post-hospital discharge
Starting date	2017

NCT03250442 *(Continued)*

Contact information	paul.j.kim@gunet.georgetown.edu
Notes	

NCT03269968

Study name	Use of negative pressure wound therapy in morbidly obese women after cesarean delivery
Methods	Randomised controlled trial
Participants	Obese women undergoing elective caesarean delivery
Interventions	Negative pressure wound therapy versus standard wound dressings
Outcomes	Composite wound complication; patient survey
Starting date	October 2017
Contact information	Tetsuya Kawakita (tetsuya.x.kawakita@medstar.net)
Notes	

NCT03274466

Study name	Closed incision negative pressure therapy versus standard of care surgical dressing in revision total knee arthroplasty (PROMISES)
Methods	Randomised controlled trial
Participants	Patient requires a TKA revision defined as: a 1-stage aseptic revision procedure; a 1-stage septic exchange procedure for acute postoperative infection; removal of cement spacer and re-implantation procedure; open reduction and internal fixation of periprosthetic fractures.
Interventions	Closed incision negative pressure therapy (ciNPT) versus standard-of-care dressing
Outcomes	Surgical site complications; surgical site infection; deep surgical site infection
Starting date	2017
Contact information	eric.synatschk@acelity.com; jane.hart@kci1.com
Notes	

NCT03321799

Study name	Comparison of negative pressure wound therapy versus conventional dressings for the prevention of wound complications after revision THA
Methods	Randomised controlled trial

NCT03321799 *(Continued)*

Participants	Patients > 18 years of age undergoing a revision total hip arthroplasty procedure
Interventions	Negative pressure wound therapy versus sterile antimicrobial dressings
Outcomes	Wound complications; reoperation; cost comparison
Starting date	2017
Contact information	chris.culvern@rushortho.com
Notes	

NCT03345771

Study name	Antimicrobial barrier dressing versus closed-incision negative pressure therapy in the obese primary total joint arthroplasty
Methods	Randomised controlled trial
Participants	Patients identified at preoperative testing to have an elevated BMI (> 35)
Interventions	Negative pressure wound therapy versus antimicrobial barrier dressing
Outcomes	Visual analogue scale pain score; wound evaluation scale
Starting date	2017
Contact information	Afshin.Anoushiravani@nyumc.org
Notes	

NCT03346694

Study name	Reducing surgical site infection rates using an alternative sternal dressing
Methods	Randomised controlled trial
Participants	Patients who will undergo cardiac surgery via a sternotomy incision
Interventions	Standard island dressing versus PREVENA negative pressure versus Mepilex Border Post-Op Ag
Outcomes	Rates of surgical site infection pertaining to each dressing studied; impact of alternative dressings on rates of sternal wound incision infection
Starting date	2017
Contact information	jackboyd@stanford.edu; jniesen@stanfordhealthcare.org
Notes	

NCT03395613

Study name	Negative pressure incision management system in infrainguinal vascular surgery
Methods	Randomised controlled trial
Participants	Not stated
Interventions	Negative pressure wound therapy versus standard sterile gauze dressing
Outcomes	Postoperative SSI; postoperative SSI within 90 days; antibiotic prescriptions for skin and soft tissue infections; postoperative SSI within 90 days requiring surgical revision; adverse events directly related the NPWT dressing; major lower limb amputation and/or mortality; changes in reported quality of life; assessment of healthcare-related costs; assessment of quality of life during the first 7-day period
Starting date	2018
Contact information	alireza.daryapeyma@sll.se; rebecka.hultgren@sll.se
Notes	

NCT03402945

Study name	Prevention of infections in cardiac surgery (PICS) Prevena study (PICS-Prevena)
Methods	Randomised controlled trial - 4-arm factorial design
Participants	Patients ≥ 18 years of age undergoing open-heart surgery
Interventions	PREVENA and cefazolin versus PREVENA and cefazolin and vancomycin versus standard wound dressing and cefazolin versus standard wound dressing and cefazolin and vancomycin
Outcomes	Adherence to the wound management system; adherence to the antibiotic regimen; loss of follow-up; deep incisional and organ/space sternal surgical site infection; wound dehiscence; Clostridium difficile infection; mortality in participants with an active infection; intensive care unit and hospital stay; pain on day 7; acute kidney injury
Starting date	2018
Contact information	prevena@phri.ca
Notes	

NCT03414762

Study name	PICO negative pressure wound therapy in obese women undergoing elective cesarean delivery
Methods	Randomised controlled trial
Participants	Obese women undergoing elective caesarean delivery
Interventions	Negative pressure wound therapy versus standard wound dressings

NCT03414762 *(Continued)*

Outcomes	Surgical site occurrence; surgical incision intervention
Starting date	November 2018
Contact information	Sarah Pachtman (spachtman@northwell.edu)
Notes	

NCT03458663

Study name	Randomized trial comparing Prevena and ActiV.A.C. system to conventional care after Bascom's cleft lift surgery
Methods	Randomised controlled trial
Participants	Patients with recurrence after previous surgery for pilonidal disease, cases of poor postoperative healing, or primary extensive/fistulating disease referred to Randers Regional Hospital for assessment for reconstructive Bascom's cleft lift surgery
Interventions	PREVENA versus conventional postoperative care
Outcomes	Primary healing; health perception; long-term healing; early recurrence; postoperative pain
Starting date	2018
Contact information	susahaas@rm.dk; marlesoe@rm.dk
Notes	

NCT03460262

Study name	Negative pressure wound therapy for prevention of groin infection following vascular surgery (PICO)
Methods	Randomised controlled trial
Participants	High-risk patients undergoing vascular surgery with groin incision (without ongoing infection)
Interventions	PICO versus standard cutiplast
Outcomes	Rate of wound complications
Starting date	2018
Contact information	parla.astarci@uclouvain.be; julien.possoz@uclouvain.be
Notes	

NCT03512470

Study name	Clinical study on the prevention of surgical wound complications for aneurysmal thoracic-abdominal aortic pathology using the "PREVENA" system (TVAC)
Methods	Randomised controlled trial
Participants	Patients with surgical wounds to treat thoracic-abdominal aortic pathology
Interventions	PREVENA versus standard medication
Outcomes	Reduction of surgical site infections; reduction of adverse events
Starting date	2018
Contact information	domenico.baccellieri@hsr.it; elisa.simonini@hsr.it
Notes	

NCT03576222

Study name	Prospective, randomized, comparative study about effects of preventive negative pressure therapy With PICO or standard care dressing (MEPORE) on surgical wounds after large incisional hernia repair
Methods	Randomised controlled trial
Participants	Patients 18 -90 years undergoing surgical repair of large incisional hernia (type W2 or W3)
Interventions	Negative pressure wound therapy (PICO dressing) versus standard therapy (MEPORE dressing)
Outcomes	SSI
Starting date	1 May 2017
Contact information	Hospital Universitari La Fe
Notes	

NCT03632005

Study name	A prospective randomized clinical trial comparing incisional negative pressure wound therapy to conventional sterile dressing in patients undergoing thoracolumbar posterior spine surgery
Methods	Randomised controlled trial
Participants	Patients ≥ 17 years who require spine surgery with a posterior midline incision that involves the thoracic, lumbar and/or sacral spine
Interventions	Negative pressure wound therapy (Prevena) versus standard dressing
Outcomes	SSI; revision; acute spinal cord injury
Starting date	18 March 2017

NCT03632005 *(Continued)*

Contact information	allan.aludino@vch.ca; leilani.reichl@vch.ca
Notes	

NCT03688438

Study name	Post Operative Wound Complications in Patients With BMI ≥35kg/m2 After Posterior Lumbar Spine Surgery: a Randomized Clinical Trial of Closed-Incision Negative-Pressure Therapy
Methods	Randomised controlled trial
Participants	Patients ≥18 years with BMI ≥35 kg/m^2 undergoing posterior lumbar fusion with or without inter-body fusion
Interventions	Closed-Incision Negative-Pressure Therapy (WoundVac) versus standard dressing
Outcomes	Wound complication; days to dry wound
Starting date	15 October 2018
Contact information	spineresearch@nortonhealthcare.org; kelly.bratcher2@nortonhealthcare.org
Notes	

NCT03700086

Study name	Efficacy of a disposable negative wound pressure device in reducing the incidence of wound infection after HPB surgery: a pilot randomized controlled trial
Methods	Randomised controlled trial
Participants	Patients ≥ 18 years undergoing HPB clean-contaminated procedures, median laparotomy
Interventions	Negative pressure wound therapy (PICO dressing) versus standard dressing
Outcomes	SSI; rate of discontinuation of negative wound pressure therapy; seromas; haematomas; major morbidities; Stony Brook Scar Evaluation Scale Score; costs
Starting date	30 September 2018
Contact information	luca.landoni@aovr.veneto.it; claudio.bassi@univr.it
Notes	

NCT03716687

Study name	Prophylactic negative pressure wound therapy for high risk laparotomy wounds. Randomized prospective clinical trial
Methods	Randomised controlled trial

NCT03716687 *(Continued)*

Participants	Patients 18-80 years undergoing high risk laparotomy
Interventions	Negative pressure wound therapy (Hartmann) versus standard dressing
Outcomes	SSI; full thickness abdominal wall dehiscence requiring reoperation
Starting date	1 November 2018
Contact information	bankybalazs@gmail.com; fulop.andras2@gmail.com
Notes	

NCT03773575

Study name	Evaluation of closed incision negative pressure dressing (PREVENA) to prevent lower extremity amputation wound complications
Methods	Randomised controlled trial
Participants	Patients ≥ 18 years undergoing lower extremity amputation
Interventions	Negative pressure wound therapy (Prevena) versus standard dressing
Outcomes	Wound complications; length of stay; 30-day return to operating room; 30-day hospital readmissions; dehiscence; seroma; lymph leak; infection; haematoma; ischaemia; necrosis; hospital costs
Starting date	15 January 2019
Contact information	laura.anatale.tardiff@jefferson.edu
Notes	

NCT03781206

Study name	Efficacy of negative pressure wound therapy (NPWT) for prevention of wound infection and improvement of wound healing after stoma reversal
Methods	Randomised controlled trial
Participants	Patients ≥ 18 years who underwent elective open or laparoscopic rectal resection ostomy construction (loop/end ileostomy; loop/end colostomy) for either oncological and inflammatory bowel disease indications
Interventions	Negative pressure wound therapy (PICO) versus standard care
Outcomes	SSI; wound healing timing; EQ-5D-5L; McGill pain questionnaire
Starting date	1 April 2019
Contact information	annalisa.maroli@humanitas.it
Notes	

NCT03816293

Study name	SUpPress SSI - single use negative pressure wound therapy (NPWT) to reduce surgical site infections (SUpPressSSI)
Methods	Randomised controlled trial
Participants	Patients ≥ 18 years undergoing caesarean section, abdominal hysterectomy or colon procedures and either obese (BMI > 30 kg/m^2) or diabetic
Interventions	Negative pressure wound therapy (Prevena) versus standard dressing
Outcomes	SSI; length of stay; readmission; seroma; haematoma; dehiscence
Starting date	1 May 2019
Contact information	Susan Bleasdale, University of Illinois at Chicago
Notes	

NCT03820219

Study name	A pilot study comparing incisional negative pressure wound therapy (Prevena) to conventional sterile dressing in patients undergoing thoracolumbar posterior spine surgery
Methods	Randomised controlled trial
Participants	All patients ≥ 17 years who require spine surgery with a posterior midline incision that involves the thoracic, lumbar and/or sacral spine
Interventions	Negative pressure wound therapy (Prevena) versus standard dressing
Outcomes	SSI; seroma or dehiscence; resource time commitment; return visits
Starting date	15 March 2019
Contact information	Unknown
Notes	

NCT03871023

Study name	The use of prophylactic negative wound therapy in emergency and elective laparotomy wounds
Methods	Randomised controlled trial (3 treatment arms)
Participants	All patients > 18 years of age undergoing a laparotomy
Interventions	Negative pressure wound therapy (Prevena) versus negative pressure wound therapy (PICO) versus standard therapy

NCT03871023 *(Continued)*

Outcomes	Superficial site infection (Southampton scoring system); wound dehiscence; wound healing/cosmesis; length of stay; home care therapy
Starting date	6 November 2019
Contact information	donlonn@tcd.ie
Notes	

NCT03886818

Study name	Evaluation of the efficacy of negative pressure wound therapy on incisional wound healing after a total ankle arthroplasty: a randomized study
Methods	Randomised controlled trial
Participants	Patients ≥ 18 years undergoing total ankle arthroplasty
Interventions	Negative pressure wound therapy (PICO) versus standard dressing
Outcomes	Number of days from suture removal to achieve complete wound healing; rate of technical failures of the PICO device, and type of failure; number and type of adverse effects related to the PICO device; rate of wound healing complications: presence of exudate; blister; necrosis; wound dehiscence; SSI; surgical revision; incremental cost-effectiveness ratio
Starting date	1 April 2019
Contact information	jean-luc.besse@chu-lyon.fr; stephanie.vincente01@chu-lyon.fr
Notes	

NCT03900078

Study name	Inzisionelle negative drucktherapie nach resektion von weichteiltumoren - eine prospektive, randomisierte, kontrollierte klinische studie
Methods	Randomised controlled trial
Participants	Patients ≥ 18 years with soft tissue tumour of extremities or trunk with expected resection of > 10cm tissue in any dimension
Interventions	Negative pressure wound therapy versus standard dressing
Outcomes	Amount of drainage fluid; wound complications; wound margin perfusion
Starting date	1 December 2018
Contact information	mehran.dadras@bergmannsheil.de; bjorn.behr@rub.de
Notes	

NCT03905213

Study name	Impact of the use of three dressings in the prevention of surgical wound infection in patients undergoing major cardiac surgery: a clinical prospective and randomized study
Methods	Randomised controlled trial (3 treatment arms)
Participants	Patients ≥ 18 years undergoing cardiac surgery
Interventions	Negative pressure wound therapy (PICCO) versus absorbent dressing (MEPILEX) versus standard dressing (MEPORE)
Outcomes	Surgical wound infection; hospital stay; antimicrobial consumption; dressing consumption cost
Starting date	1 September 2019
Contact information	massus@hotmail.es; javier.hortal@gamil.com
Notes	

NCT03935659

Study name	Negative pressure wound therapy for surgical site infection prevention in vascular surgery patients undergoing common femoral artery exposure
Methods	Randomised controlled trial
Participants	Adults ≥ 18 years with one or more of: body mass index >30 kg/m^2; critical limb ischaemia; procedure time > 240 min; end stage renal disease on dialysis; glycated hemoglobin ≥ 8.5%; transfusion ≥ 3 units packed red blood cells; previous femoral artery cut-down
Interventions	Negative pressure wound therapy versus standard dressing
Outcomes	Superficial SSI; mortality; limb loss; emergency department visit for wound complication; local reaction to negative wound dressing
Starting date	26 March 2018
Contact information	LKABBAN1@hfhs.org; arteil1@hfhs.org
Notes	

NCT03948412

Study name	Negative pressure wound therapy (PREVENA) versus standard dressings for incision management after renal transplant (IMPART)
Methods	Randomised controlled trial
Participants	Patients ≥ 18 years undergoing renal transplant
Interventions	Negative pressure wound therapy (Prevena) versus standard dressing

NCT03948412 *(Continued)*

Outcomes	Wound complications; length of hospital stay; graft function; delayed graft function; pain score; scar quality; EQ-5D-5L; graft function; ASEPSIS wound score
Starting date	10 May 2019
Contact information	Linda.Pallot@health.nsw.gov.au
Notes	

Nguyen 2017

Study name	Incisional negative pressure wound therapy following colorectal resection: preliminary report from a single site, prospective, randomized control trial
Methods	Single-institution, prospective, randomised, open-label, superiority trial
Participants	Patients scheduled for elective colorectal resection with or without creation of an ostomy (open or laparoscopic)
Interventions	Patients will be randomised to receive NPWT or conventional dressings.
Outcomes	Primary outcomes will be wound complications within the first 30 postoperative days. SSI rate will also be reported as a subgroup analysis. Secondary outcomes will include length of stay, number of postoperative visits in the 30-day period, complications, wound VAC-specific complications, and patient satisfaction.
Starting date	Unclear
Contact information	University of British Columbia (no contact details available)
Notes	Very limited information available.

NL6488

Study name	PREventing Surgical Site occurrences using negative pressURE wound therapy?
Methods	Randomised controlled trial
Participants	Patients scheduled for elective, open abdominal wall reconstruction
Interventions	Negative pressure wound therapy versus conventional wound care
Outcomes	Surgical site occurrence; QoL; recurrence 1 year after surgery; individual components of primary outcome SSO; peri-incisional SSO; percentage of participants with signs of SSO on photographs by blinded outcome assessment; frequency and type of procedures related to SSO; hospital stay after surgery in days; earlier removal of iNPWT because of SSO; emergency department visits after discharge; readmission; non-primary outcome complications; cost-effectiveness
Starting date	2017
Contact information	p.r.zwanenburg@amc.nl

NL6488 *(Continued)*

Notes	Previously registered as NTR6675; starting date may not reflect previous registration

NTR6481

Study name	Randomized controlled clinical trial incisional NPWT versus sterile surgical dressing for surgical wounds after arterial vascular surgery
Methods	Randomised controlled trial
Participants	Patients undergoing bypass: aortic-iliacal, iliacal-femoral, femoral-femoral, femoral-popliteal, femoral-crural, femoral-tibial; endarterectomy: iliacal, femoral; reconstruction aneurysm: femoral; embolectomy: iliacal, femoral
Interventions	Incisional negative pressure wound therapy versus sterile surgical dressing
Outcomes	Incidence of wound complications; complete wound-healing percentages; hospital stay in days; additional surgery; readmissions; extra visits to the outpatient clinic
Starting date	2017
Contact information	prevenastudie@haaglandenmc.nl
Notes	

Sandy-Hodgetts 2017

Study name	Effectiveness of negative pressure wound therapy (NPWT) in the prevention of postoperative surgical wound dehiscence in at risk patients following abdominal surgery; a multicentre randomised control trial
Methods	Randomised controlled trial
Participants	Patients undergoing an abdominal surgical procedure that uses a midline laparotomy as the surgical entry
Interventions	Negative pressure wound therapy versus standard wound dressings
Outcomes	Occurrence of surgical wound dehiscence; occurrence of surgical site infection, economic analysis
Starting date	2012
Contact information	kylie.sandy-hodgetts@curtin.edu.au
Notes	

SUNRRISE 2017

Study name	SUNRRISE: Single Use Negative pRessure dressing for Reduction In Surgical site infection following Emergency laparotomy

SUNRRISE 2017 *(Continued)*

Methods	Randomised controlled trial
Participants	Patients undergoing emergency laparotomy
Interventions	Portable single-use NPWT dressings Standard dressings
Outcomes	SSI at 30 days; length of stay; readmission; reintervention; adverse events; pain; HRQoL; cost-effectiveness
Starting date	November 2017
Contact information	Dr Laura Magill, University of Birmingham, UK
Notes	ISRCTN17599457

TCTR20170331001

Study name	Antiseptic dressing versus negative pressure dressing techniques for uncomplicated pediatric appendicitis, randomized controlled trial
Methods	Randomised controlled trial (3 treatment arms)
Participants	Patients < 15 years undergoing surgery for uncomplicated appendicitis
Interventions	Negative pressure dressing versus antiseptic dressing versus conventional dressing
Outcomes	Wound infection; time to heal; wound seroma; wound dehiscence
Starting date	29 March 2017
Contact information	goofywasun@gmail.com
Notes	

AE: adverse event
ASEPSIS: ASEPSIS score - a quantitative scoring method using objective criteria based on wound appearance to evaluate wound infection
BMI: body mass index
CABG: coronary artery bypass graft
CIED: cardiovascular implantable electronic devices
cINPT: closed incision negative pressure wound therapy
CITA: continuous in-situ ultra high dose antibiotics
CRS: cryoreduction surgery
CS: caesarean section
EQ-5D-5L: EuroQoL 5D questionnaire 5L version
HOOS: hip disability and osteoarthritis outcome score
HPB(S): hepatopancreatobiliary (surgery)
HRQoL: health-related quality of life
iNPWT: incisional negative pressure wound therapy
KA: knee arthroplasty
KOOS: knee disability and osteoarthritis outcome score
LDex: lymphedema index
LYMQOL: Lymphoedema Quality-of-Life Questionnaire

MALE: major adverse limb event
MRSA: methicillin-resistant Staphylococcus aureus
NPWT: negative pressure wound therapy
POSAS: Patient and Observer Scar Assessment Scale
QoL: quality of life
RCT: randomised controlled trial
RNPT: regulated negative pressure-assisted wound therapy
SAE: serious adverse event
SF-12: 12-item Short Form Health Survey
SSI: surgical site infection
SSO: surgical site occurrence
THA: total hip arthroplasty
TKA: total knee arthroplasty
VAC: vacuum-assisted closure
VAS: visual analogue scale
VR-12: Veterans RAND 12-Item Health Survey

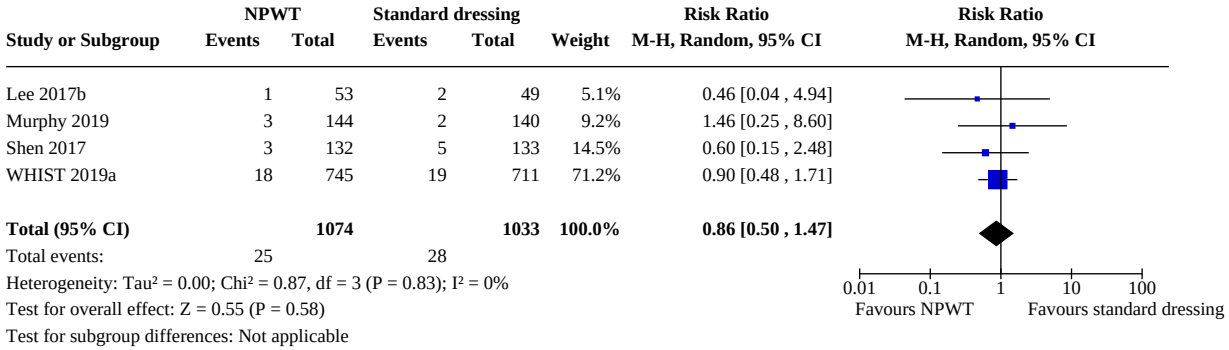
DATA AND ANALYSES

Comparison 1. Negative pressure wound therapy versus standard dressing

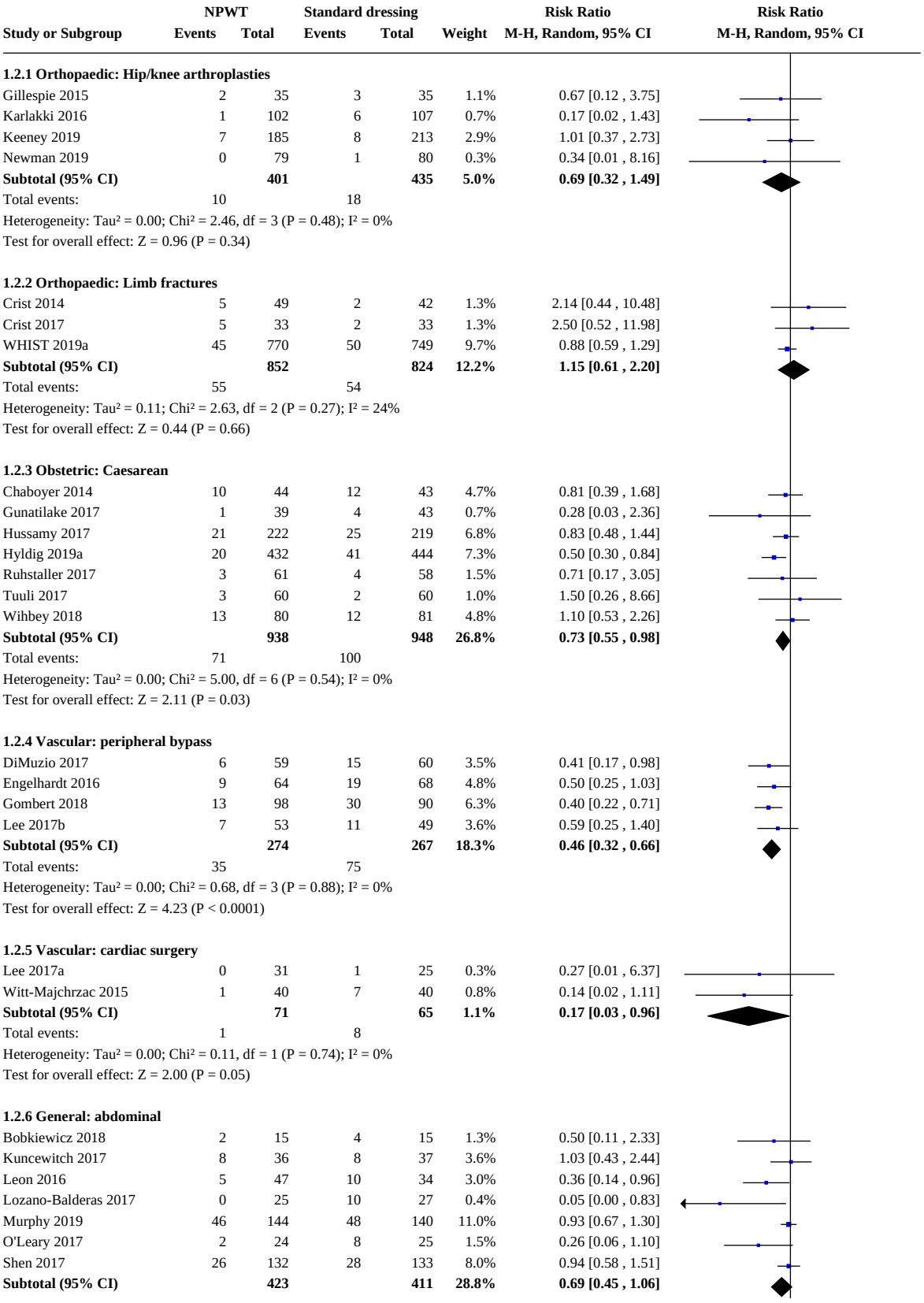
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.1 Mortality	4	2107	Risk Ratio (M-H, Random, 95% CI)	0.86 [0.50, 1.47]
1.2 Surgical site infection	31	6204	Risk Ratio (M-H, Random, 95% CI)	0.66 [0.55, 0.80]
1.2.1 Orthopaedic: Hip/knee arthroplasties	4	836	Risk Ratio (M-H, Random, 95% CI)	0.69 [0.32, 1.49]
1.2.2 Orthopaedic: Limb fractures	3	1676	Risk Ratio (M-H, Random, 95% CI)	1.15 [0.61, 2.20]
1.2.3 Obstetric: Caesarean	7	1886	Risk Ratio (M-H, Random, 95% CI)	0.73 [0.55, 0.98]
1.2.4 Vascular: peripheral bypass	4	541	Risk Ratio (M-H, Random, 95% CI)	0.46 [0.32, 0.66]
1.2.5 Vascular: cardiac surgery	2	136	Risk Ratio (M-H, Random, 95% CI)	0.17 [0.03, 0.96]
1.2.6 General: abdominal	7	834	Risk Ratio (M-H, Random, 95% CI)	0.69 [0.45, 1.06]
1.2.7 General: Hepatopancreatiobiliary	2	163	Risk Ratio (M-H, Random, 95% CI)	0.36 [0.18, 0.73]
1.2.8 General: Mixed	2	132	Risk Ratio (M-H, Random, 95% CI)	0.45 [0.13, 1.56]
1.3 SSI grouped by contamination class	31	6204	Risk Ratio (M-H, Random, 95% CI)	0.66 [0.55, 0.80]
1.3.1 Clean	12	1670	Risk Ratio (M-H, Random, 95% CI)	0.55 [0.39, 0.78]
1.3.2 Clean-contaminated	15	2831	Risk Ratio (M-H, Random, 95% CI)	0.72 [0.58, 0.90]
1.3.3 Contaminated	1	1519	Risk Ratio (M-H, Random, 95% CI)	0.88 [0.59, 1.29]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.3.4 Dirty	3	184	Risk Ratio (M-H, Random, 95% CI)	0.27 [0.06, 1.12]
1.4 SSI (superficial)	15	2783	Risk Ratio (M-H, Random, 95% CI)	0.58 [0.42, 0.79]
1.5 SSI (deep)	17	4429	Risk Ratio (M-H, Random, 95% CI)	0.94 [0.71, 1.25]
1.6 Dehiscence	14	3809	Risk Ratio (M-H, Random, 95% CI)	0.88 [0.69, 1.13]
1.6.1 Orthopaedic: hip/knee arthroplasty	2	229	Risk Ratio (M-H, Random, 95% CI)	0.43 [0.08, 2.35]
1.6.2 Orthopaedic: limb fracture	1	1401	Risk Ratio (M-H, Random, 95% CI)	0.27 [0.06, 1.32]
1.6.3 Obstetric: caesarean	4	1470	Risk Ratio (M-H, Random, 95% CI)	1.06 [0.39, 2.89]
1.6.4 Vascular: peripheral	1	119	Risk Ratio (M-H, Random, 95% CI)	0.46 [0.17, 1.25]
1.6.5 Vascular: cardiac	1	80	Risk Ratio (M-H, Random, 95% CI)	1.00 [0.06, 15.44]
1.6.6 General: abdominal	2	338	Risk Ratio (M-H, Random, 95% CI)	0.82 [0.22, 3.04]
1.6.7 General: hepatopancreatiobiliary	1	40	Risk Ratio (M-H, Random, 95% CI)	0.50 [0.05, 5.08]
1.6.8 General: mixed	2	132	Risk Ratio (M-H, Random, 95% CI)	1.28 [0.69, 2.37]
1.7 Reoperation	12	3523	Risk Ratio (IV, Random, 95% CI)	1.04 [0.78, 1.41]
1.8 Readmission	9	1591	Risk Ratio (M-H, Random, 95% CI)	0.88 [0.57, 1.35]
1.9 Seroma	7	729	Risk Ratio (M-H, Random, 95% CI)	0.72 [0.50, 1.05]
1.10 Haematoma	9	1202	Risk Ratio (M-H, Random, 95% CI)	0.67 [0.28, 1.59]
1.11 Skin blisters	7	796	Risk Ratio (M-H, Random, 95% CI)	2.64 [0.65, 10.68]

Analysis 1.1. Comparison 1: Negative pressure wound therapy versus standard dressing, Outcome 1: Mortality

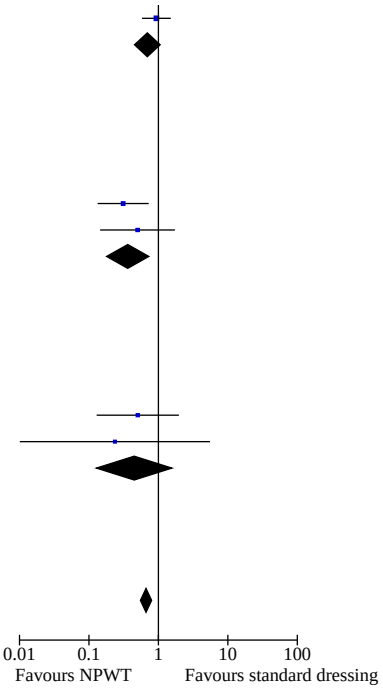


Analysis 1.2. Comparison 1: Negative pressure wound therapy versus standard dressing, Outcome 2: Surgical site infection

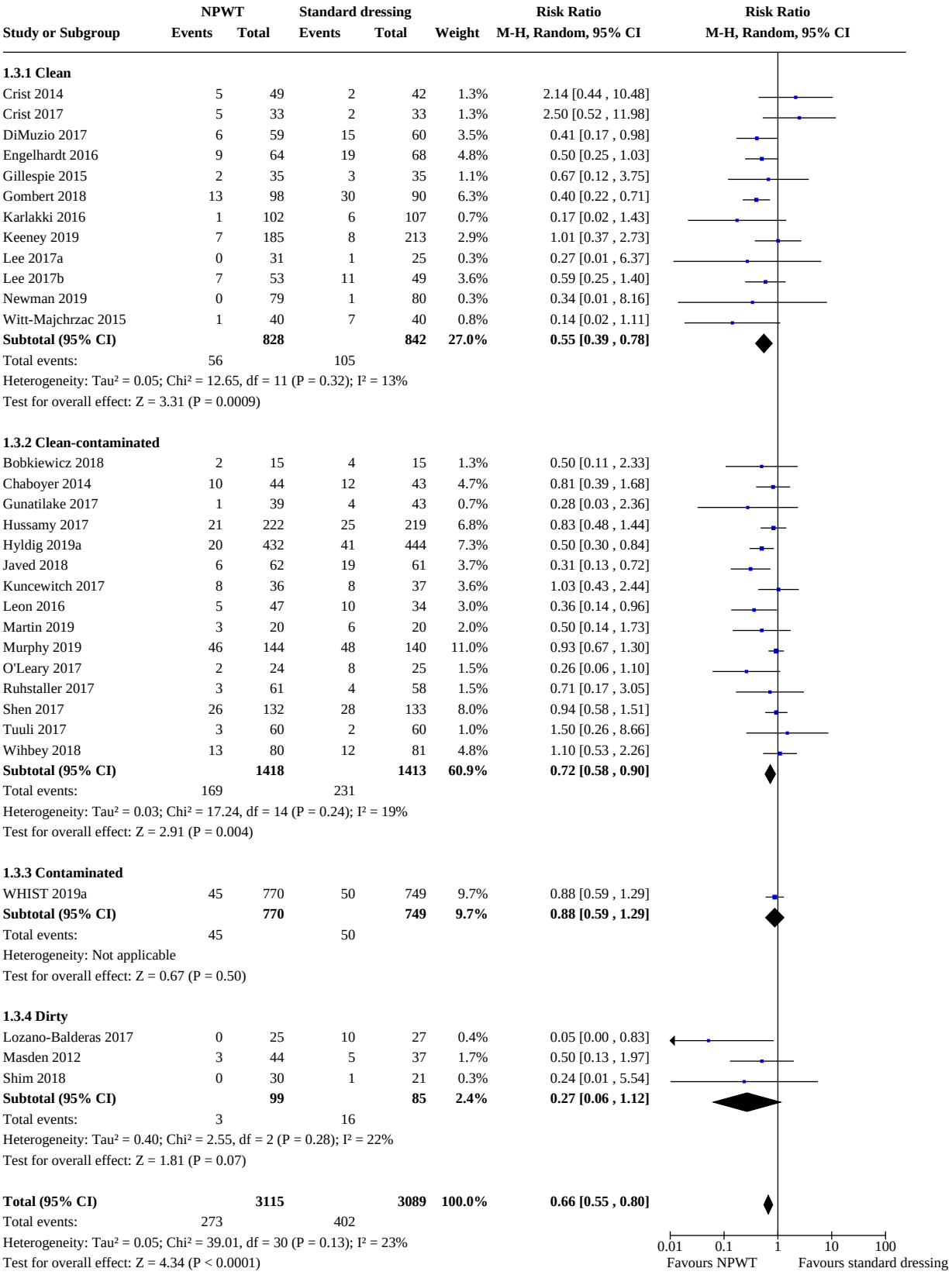


Analysis 1.2. (Continued)

Shen 2017	26	132	28	133	8.0%	0.94 [0.58 , 1.51]
Subtotal (95% CI)		**423**		**411**	**28.8%**	**0.69 [0.45 , 1.06]**
Total events:	89		116			
Heterogeneity: Tau² = 0.12; Chi² = 11.04, df = 6 (P = 0.09); I² = 46%						
Test for overall effect: Z = 1.70 (P = 0.09)						
1.2.7 General: Hepatopancreatiobiliary						
Javed 2018	6	62	19	61	3.7%	0.31 [0.13 , 0.72]
Martin 2019	3	20	6	20	2.0%	0.50 [0.14 , 1.73]
Subtotal (95% CI)		**82**		**81**	**5.7%**	**0.36 [0.18 , 0.73]**
Total events:	9		25			
Heterogeneity: Tau² = 0.00; Chi² = 0.39, df = 1 (P = 0.53); I² = 0%						
Test for overall effect: Z = 2.85 (P = 0.004)						
1.2.8 General: Mixed						
Masden 2012	3	44	5	37	1.7%	0.50 [0.13 , 1.97]
Shim 2018	0	30	1	21	0.3%	0.24 [0.01 , 5.54]
Subtotal (95% CI)		**74**		**58**	**2.0%**	**0.45 [0.13 , 1.56]**
Total events:	3		6			
Heterogeneity: Tau² = 0.00; Chi² = 0.19, df = 1 (P = 0.66); I² = 0%						
Test for overall effect: Z = 1.26 (P = 0.21)						
Total (95% CI)		**3115**		**3089**	**100.0%**	**0.66 [0.55 , 0.80]**
Total events:	273		402			
Heterogeneity: Tau² = 0.05; Chi² = 39.01, df = 30 (P = 0.13); I² = 23%						
Test for overall effect: Z = 4.34 (P < 0.0001)						
Test for subgroup differences: Chi² = 12.58, df = 7 (P = 0.08), I² = 44.3%						

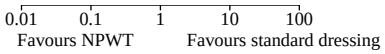


Analysis 1.3. Comparison 1: Negative pressure wound therapy versus standard dressing, Outcome 3: SSI grouped by contamination class



Analysis 1.3. (Continued)

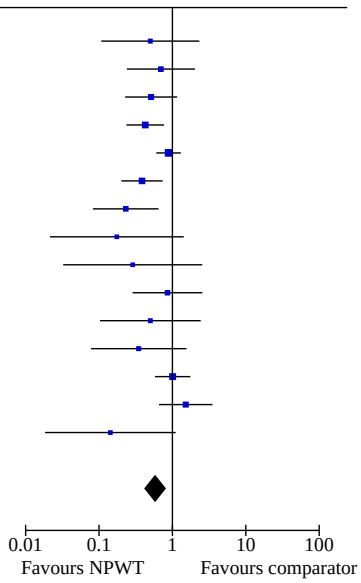
Heterogeneity: Tau² = 0.05; Chi² = 39.01, df = 30 (P = 0.13); I² = 23%
Test for overall effect: Z = 4.34 (P < 0.0001)
Test for subgroup differences: Chi² = 4.87, df = 3 (P = 0.18), I² = 38.3%



Analysis 1.4. Comparison 1: Negative pressure wound therapy versus standard dressing, Outcome 4: SSI (superficial)

Study or Subgroup	NPWT Events	NPWT Total	Standard dressing Events	Standard dressing Total	Weight	Risk Ratio M-H, Random, 95% CI
Bobkiewicz 2018	2	15	4	15	3.4%	0.50 [0.11 , 2.33]
Chaboyer 2014	5	44	7	43	6.0%	0.70 [0.24 , 2.03]
Engelhardt 2016	7	58	16	68	8.4%	0.51 [0.23 , 1.16]
Gombert 2018	13	98	28	90	11.5%	0.43 [0.24 , 0.77]
Hussamy 2017	20	37	25	41	15.0%	0.89 [0.60 , 1.30]
Hyldig 2019a	12	432	32	444	10.6%	0.39 [0.20 , 0.74]
Javed 2018	4	62	17	61	6.3%	0.23 [0.08 , 0.65]
Karlakki 2016	1	102	6	107	2.0%	0.17 [0.02 , 1.43]
Keeney 2019	1	185	4	213	1.9%	0.29 [0.03 , 2.55]
Kuncewitch 2017	5	36	6	37	5.8%	0.86 [0.29 , 2.56]
Martin 2019	2	20	4	20	3.3%	0.50 [0.10 , 2.43]
O'Leary 2017	2	24	6	25	3.6%	0.35 [0.08 , 1.55]
Shen 2017	21	132	21	133	12.1%	1.01 [0.58 , 1.75]
Wihbey 2018	12	80	8	81	8.1%	1.52 [0.66 , 3.52]
Witt-Majchrzac 2015	1	40	7	40	2.1%	0.14 [0.02 , 1.11]
Total (95% CI)		**1365**		**1418**	**100.0%**	**0.58 [0.42 , 0.79]**
Total events:	108		191			

Heterogeneity: Tau² = 0.13; Chi² = 23.78, df = 14 (P = 0.05); I² = 41%
Test for overall effect: Z = 3.40 (P = 0.0007)
Test for subgroup differences: Not applicable



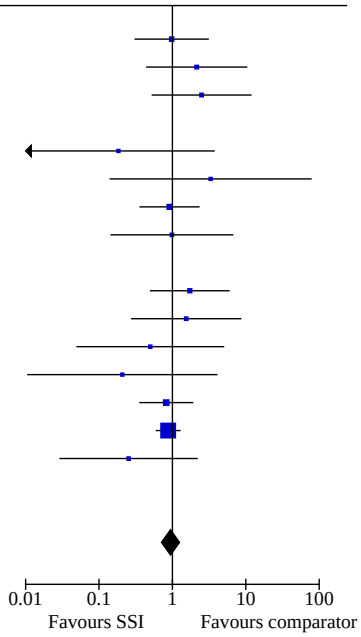
Analysis 1.5. Comparison 1: Negative pressure wound therapy versus standard dressing, Outcome 5: SSI (deep)

Study or Subgroup	NPWT Events	NPWT Total	Standard dressing Events	Standard dressing Total	Weight	Risk Ratio M-H, Random, 95% CI
Chaboyer 2014	5	44	5	43	5.8%	0.98 [0.30 , 3.14]
Crist 2014	5	49	2	42	3.2%	2.14 [0.44 , 10.48]
Crist 2017	5	33	2	33	3.2%	2.50 [0.52 , 11.98]
Engelhardt 2016	0	58	0	68		Not estimable
Gombert 2018	0	98	2	90	0.9%	0.18 [0.01 , 3.78]
Hussamy 2017	1	37	0	41	0.8%	3.32 [0.14 , 78.97]
Hyldig 2019a	8	432	9	444	8.9%	0.91 [0.36 , 2.35]
Javed 2018	2	62	2	61	2.1%	0.98 [0.14 , 6.76]
Karlakki 2016	0	102	0	107		Not estimable
Keeney 2019	6	185	4	213	5.1%	1.73 [0.49 , 6.03]
Kuncewitch 2017	3	36	2	37	2.7%	1.54 [0.27 , 8.69]
Martin 2019	1	20	2	20	1.5%	0.50 [0.05 , 5.08]
O'Leary 2017	0	24	2	25	0.9%	0.21 [0.01 , 4.12]
Shen 2017	9	132	11	133	11.1%	0.82 [0.35 , 1.92]
WHIST 2019a	45	770	50	749	52.2%	0.88 [0.59 , 1.29]
Wihbey 2018	1	80	4	81	1.7%	0.25 [0.03 , 2.22]
Witt-Majchrzac 2015	0	40	0	40		Not estimable
Total (95% CI)	**2202**		**2227**		**100.0%**	**0.94 [0.71 , 1.25]**
Total events:	91		97			

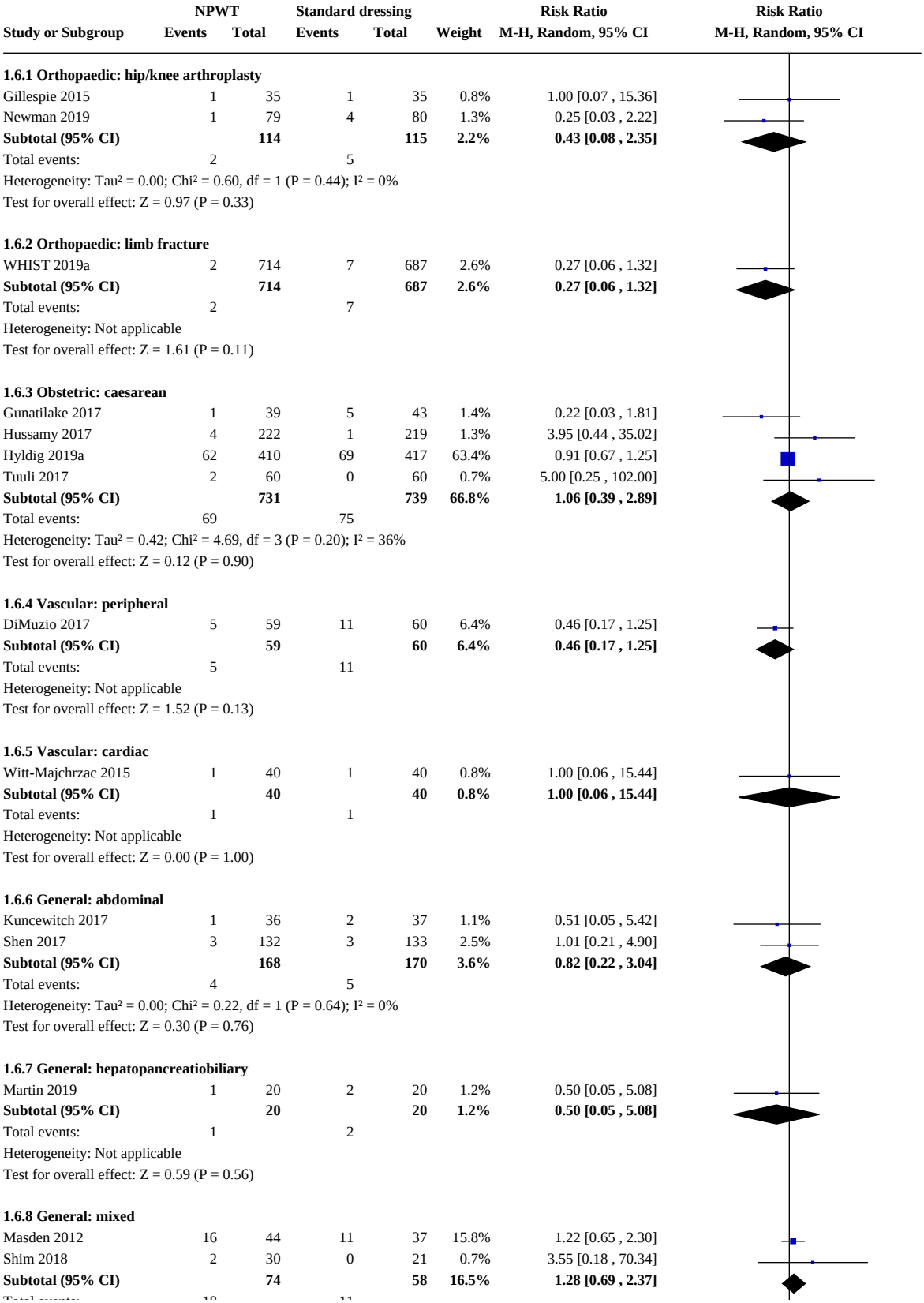
Heterogeneity: Tau² = 0.00; Chi² = 8.39, df = 13 (P = 0.82); I² = 0%

Test for overall effect: Z = 0.42 (P = 0.67)

Test for subgroup differences: Not applicable

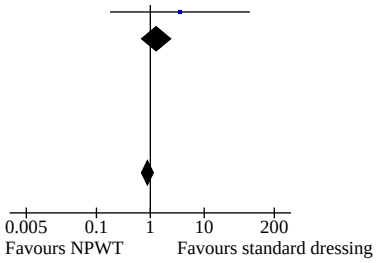


Analysis 1.6. Comparison 1: Negative pressure wound therapy versus standard dressing, Outcome 6: Dehiscence



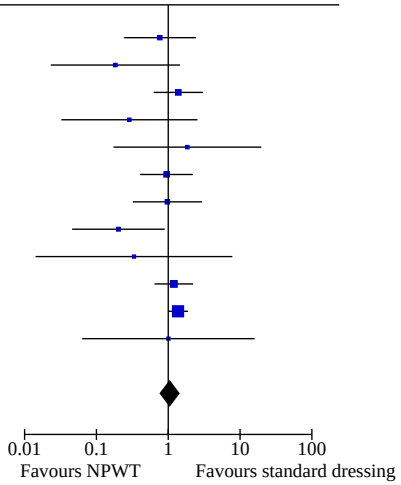
Analysis 1.6. (Continued)

Shim 2018	2	30	0	21	0.7%	3.55 [0.18 , 70.34]
Subtotal (95% CI)		**74**		**58**	**16.5%**	**1.28 [0.69 , 2.37]**
Total events:	18		11			
Heterogeneity: Tau² = 0.00; Chi² = 0.48, df = 1 (P = 0.49); I² = 0%						
Test for overall effect: Z = 0.78 (P = 0.43)						
Total (95% CI)		**1920**		**1889**	**100.0%**	**0.88 [0.69 , 1.13]**
Total events:	102		117			
Heterogeneity: Tau² = 0.00; Chi² = 12.20, df = 13 (P = 0.51); I² = 0%						
Test for overall effect: Z = 0.97 (P = 0.33)						
Test for subgroup differences: Chi² = 6.14, df = 7 (P = 0.52), I² = 0%						



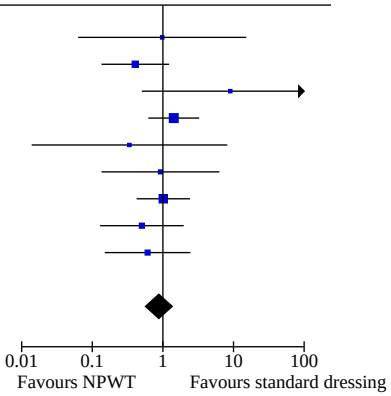
Analysis 1.7. Comparison 1: Negative pressure wound therapy versus standard dressing, Outcome 7: Reoperation

Study or Subgroup	NPWT Events	NPWT Total	Standard dressing Events	Standard dressing Total	Weight	Risk Ratio IV, Random, 95% CI
Gombert 2018	5	98	6	90	6.1%	0.77 [0.24 , 2.42]
Gunatilake 2017	1	39	6	43	2.0%	0.18 [0.02 , 1.46]
Hussamy 2017	14	222	10	219	11.7%	1.38 [0.63 , 3.04]
Keeney 2019	1	185	4	213	1.8%	0.29 [0.03 , 2.55]
Lee 2017b	2	53	1	49	1.5%	1.85 [0.17 , 19.76]
Masden 2012	9	44	8	37	10.4%	0.95 [0.41 , 2.20]
Murphy 2019	6	144	6	140	6.5%	0.97 [0.32 , 2.94]
Newman 2019	2	79	10	80	3.8%	0.20 [0.05 , 0.90]
O'Leary 2017	0	25	1	25	0.9%	0.33 [0.01 , 7.81]
Shen 2017	19	132	16	133	17.0%	1.20 [0.64 , 2.22]
WHIST 2019a	83	578	56	534	37.1%	1.37 [1.00 , 1.88]
Wihbey 2018	1	180	1	181	1.1%	1.01 [0.06 , 15.95]
Total (95% CI)		**1779**		**1744**	**100.0%**	**1.04 [0.78 , 1.41]**
Total events:	143		125			
Heterogeneity: Tau² = 0.04; Chi² = 12.71, df = 11 (P = 0.31); I² = 13%						
Test for overall effect: Z = 0.29 (P = 0.77)						
Test for subgroup differences: Not applicable						



Analysis 1.8. Comparison 1: Negative pressure wound therapy versus standard dressing, Outcome 8: Readmission

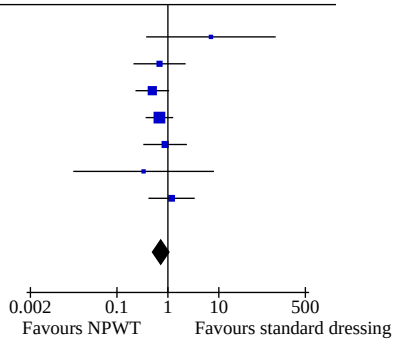
Study or Subgroup	NPWT Events	NPWT Total	Standard dressing Events	Standard dressing Total	Weight	Risk Ratio M-H, Random, 95% CI
Chaboyer 2014	1	44	1	43	2.5%	0.98 [0.06 , 15.13]
DiMuzio 2017	4	59	10	60	15.6%	0.41 [0.14 , 1.23]
Gillespie 2015	4	35	0	35	2.3%	9.00 [0.50 , 161.13]
Hussamy 2017	13	222	9	219	27.6%	1.42 [0.62 , 3.27]
Karlakki 2016	0	107	1	108	1.9%	0.34 [0.01 , 8.17]
Lee 2017b	2	53	2	49	5.1%	0.92 [0.14 , 6.31]
Newman 2019	9	79	9	80	25.1%	1.01 [0.42 , 2.42]
Shen 2017	3	118	6	119	10.2%	0.50 [0.13 , 1.97]
Wihbey 2018	3	80	5	81	9.7%	0.61 [0.15 , 2.46]
Total (95% CI)		**797**		**794**	**100.0%**	**0.88 [0.57 , 1.35]**
Total events:	39		43			
Heterogeneity: Tau² = 0.00; Chi² = 7.07, df = 8 (P = 0.53); I² = 0%						
Test for overall effect: Z = 0.60 (P = 0.55)						
Test for subgroup differences: Not applicable						



Analysis 1.9. Comparison 1: Negative pressure wound therapy versus standard dressing, Outcome 9: Seroma

Study or Subgroup	NPWT Events	NPWT Total	Standard dressing Events	Standard dressing Total	Weight	Risk Ratio M-H, Random, 95% CI
Gillespie 2015	3	35	0	35	1.6%	7.00 [0.37 , 130.69]
Kuncewitch 2017	4	36	6	37	10.0%	0.69 [0.21 , 2.23]
Pachowsky 2012	4	9	9	10	24.1%	0.49 [0.23 , 1.05]
Pauser 2016	6	11	8	10	35.9%	0.68 [0.37 , 1.27]
Shen 2017	7	132	8	133	14.3%	0.88 [0.33 , 2.36]
Tuuli 2017	0	60	1	60	1.4%	0.33 [0.01 , 8.02]
Wihbey 2018	7	80	6	81	12.7%	1.18 [0.42 , 3.36]
Total (95% CI)		**363**		**366**	**100.0%**	**0.72 [0.50 , 1.05]**
Total events:	31		38			

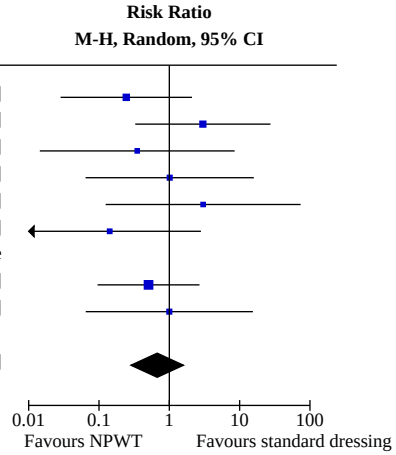
Heterogeneity: Tau² = 0.00; Chi² = 5.06, df = 6 (P = 0.54); I² = 0%
Test for overall effect: Z = 1.71 (P = 0.09)
Test for subgroup differences: Not applicable



Analysis 1.10. Comparison 1: Negative pressure wound therapy versus standard dressing, Outcome 10: Haematoma

Study or Subgroup	NPWT Events	NPWT Total	Standard dressing Events	Standard dressing Total	Weight	Risk Ratio M-H, Random, 95% CI
Chaboyer 2014	1	44	4	43	16.0%	0.24 [0.03 , 2.10]
Gillespie 2015	3	35	1	35	15.1%	3.00 [0.33 , 27.46]
Karlakki 2016	0	102	1	107	7.3%	0.35 [0.01 , 8.48]
Newman 2019	1	79	1	80	9.7%	1.01 [0.06 , 15.91]
Shen 2017	1	132	0	133	7.3%	3.02 [0.12 , 73.53]
Shim 2018	0	30	2	21	8.3%	0.14 [0.01 , 2.81]
Tuuli 2017	0	60	0	60		Not estimable
Wihbey 2018	2	80	4	81	26.5%	0.51 [0.10 , 2.69]
Witt-Majchrzac 2015	1	40	1	40	9.9%	1.00 [0.06 , 15.44]
Total (95% CI)		**602**		**600**	**100.0%**	**0.67 [0.28 , 1.59]**
Total events:	9		14			

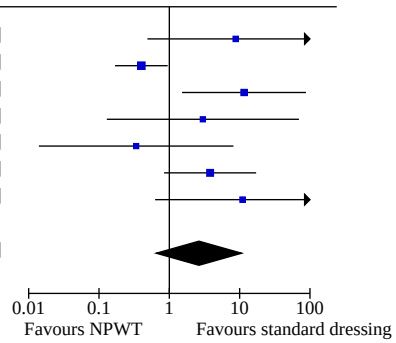
Heterogeneity: Tau² = 0.00; Chi² = 4.94, df = 7 (P = 0.67); I² = 0%
Test for overall effect: Z = 0.90 (P = 0.37)
Test for subgroup differences: Not applicable



Analysis 1.11. Comparison 1: Negative pressure wound therapy versus standard dressing, Outcome 11: Skin blisters

Study or Subgroup	NPWT Events	NPWT Total	Standard dressing Events	Standard dressing Total	Weight	Risk Ratio M-H, Random, 95% CI
Chaboyer 2014	4	44	0	43	11.7%	8.80 [0.49 , 158.66]
Giannini 2018	6	50	15	50	21.4%	0.40 [0.17 , 0.95]
Karlakki 2016	11	102	1	107	15.6%	11.54 [1.52 , 87.78]
Manoharan 2016	1	21	0	21	10.7%	3.00 [0.13 , 69.70]
Newman 2019	0	79	1	80	10.5%	0.34 [0.01 , 8.16]
Ruhstaller 2017	8	61	2	58	18.3%	3.80 [0.84 , 17.17]
Witt-Majchrzac 2015	5	40	0	40	11.8%	11.00 [0.63 , 192.56]
Total (95% CI)		**397**		**399**	**100.0%**	**2.64 [0.65 , 10.68]**
Total events:	35		19			

Heterogeneity: Tau² = 2.19; Chi² = 19.57, df = 6 (P = 0.003); I² = 69%
Test for overall effect: Z = 1.36 (P = 0.17)
Test for subgroup differences: Not applicable



ADDITIONAL TABLES

Table 1. Primary outcome data

Study	Wounds characteristics	Comparison	Time points	Mortality	SSI	Dehiscence	Note
Bobkiewicz 2018 abstract	Stoma reversal surgery	Group A: ciNPWT Group B: standard dressing	Not reported	-	Group A: 2/15 Group B: 4/15	"In the standard dressing group the incidence of wound dehiscence was higher"	Superficial SSI defined according to CDC
Chaboyer 2014	Caesarean section in obese women	Group A: PICO dressing Group B: Comfeel dressing	1, 2, 3, and 4 weeks post-surgery	-	Group A: 10/44 Group B: 12/43	-	-
Crist 2014	Open reduction and internal fixation of hip, pelvis, and acetabular fracture surgery	Group A: NPWT Group B: standard gauze dressing	12 months	-	Group A: 5/49 Group B: 2/42	-	-
Crist 2017	Open reduction internal fixation (ORIF) for acetabular fractures	Group A: NPWT Group B: standard gauze dressing	10 to 21 days, 6 weeks, 12 weeks, and every 6 to 8 weeks thereafter until bony union occurred	-	Group A: 5/33 Group B: 2/33 *completed-case analysis - 5 lost after randomisation but group allocation not known*	-	Infection defined as "deep infection"
DiMuzio 2017 Abstract	Groin wounds	Group A (59, high risk): NPWT dressing Group B (60, high risk): standard gauze dressing Group C (21, low risk): standard gauze dressing	30 days	-	Group A: 6/59 Group B: 15/60 Group C: 1/21	Group A: 8.5% Group B: 18.3% Group C: 4.8%	Contacted authors for full text Group C not included in data analysis due to baseline heterogeneity
Engelhardt 2016	Groin wound	Group A: NPWT	5 and 42 days	-	Group A: 9/64	-	-

Table 1. Primary outcome data *(Continued)*

		Group B: conventional dressing			Group B: 19/68		
Galiano 2018	Breast surgery	Group A: NPWT, 199 wounds Group B: standard dressings, 199 wounds	21 days	-	Group A 4/199 Group B 6/199	Group A 32/199 Group B 52/199	
Giannini 2018	Hip and knee prosthetic revision	Group A single use NPWT (PICO) Group B povidone-iodine gauze and patch wound dressing	7 days	-	The severity of wound infection measured by the ASEPSIS score (higher score = worse wound healing; a score > 10 = the increasing probability and severity of infection) mean (SD) of the score: 3.0 (1.89) in Group A; 5.1 (3.89) in Group B	-	-
Gillespie 2015	Primary hip arthroplasty	Group A: PICO dressing Group B: Comfeel dressing	30 days and 6 weeks postsurgery	-	Group A: 2/35 Group B: 3/35	Group A: 1/35 Group B: 1/35	QoL reported in Heard 2017.
Gombert 2018	Vascular surgery (groin) for PAD	Group A NPWT (Prevena) Group B Cosmopore dressing	30 days	-	Group A 13/98 Group B 30/90	-	-
Gunatilake 2017	Caesarean	Group A: NPWT Group B: standard care dressing	42 ± 10 days postoperatively (days 1, 2, 6, 14, and 42)	-	Group A: 1/39 Group B: 4/43	Group A: 1/39 Group B: 5/43	ITT: n = 92; 82 completed the study
Howell 2011	Knee arthroplasty	Group A: NPWT Group B: gauze dressing	Followed up for 12 months postsurgery	-	Group A: 1/24 Group B: 1/36	-	-
Hussamy 2017 Abstract	Caesarean	Group A (222): NPWT Group B (219): standard dressing	30 days postdelivery	-	*Superficial SSI* Group A: 20/222 Group B: 25/219	Group A: 4/222 Group B: 1/219	Unable to contact authors

Table 1. Primary outcome data *(Continued)*

					Organ SSI Group A: 1/222 Group B: 0/219		
Hyldig 2019a	Caesarean	Group A (432): NPWT Group B (444): standard dressing	30 days after operation	-	SSI Group A: 20/432 Group B: 41/444 Deep SSI Group A: 8/410 Group B: 9/417	Group A: 62/410 Group B: 69/417	
Javed 2018	Open pancreaticoduodenectomy	Group A: NPWT Group B: standard closure	30 days after operation	-	SSI Group A: 6/62 Group B: 19/61 Superficial SSI Group A: 4/62 Group B: 17/61 Deep SSI Group A: 2/62 Group B: 2/61	-	
Karlakki 2016	Total hip or knee arthroplasties	Group A: PICO dressing Group B: Comfeel dressing	1, 2, and 6 weeks post-surgery	-	Group A: 2/102 Group B: 6/107	-	-
Keeney 2019	Hip and knee total joint arthroplasty	Group A: iNPWT Group B: conventional wound dressing	7, 14 and 35 days after operations; 2 years	-	Superficial and late wound infection rates Group A: 7/185 Group B: 8/213	-	Additional data on return to operating rooms; and infection outcome were

Table 1. Primary outcome data *(Continued)*

							presented in Characteristics of included studies..
Kuncewitch 2017 Abstract	Pancreatectomy	Group A: NPWT Group B: standard surgical dressing	30 days post-surgery follow-up	-	*Superficial SSI* Group A: 5/36 Group B: 6/37 *Deep SSI* Group A: 3/36 Group B: 2/37	Group A: 1/36 Group B: 2/37	Unable to contact authors
Kwon 2018	Vascular groin incisions (high risk)	Group A: NPWT Group B: standard gauze	30 days	-	Any Group A 6/59 Group B 12/60 Major Group A 5/59 Group B 12/60	Any Group A 1/59 Group B 1/60 Major Group A 0/59 Group B 0/60	
Lee 2017a	Great saphenous vein harvest	Group A: NPWT Group B: standard surgical dressing	Initial assessment: not specified; endpoint assessment: 6 weeks	-	Group A: 0/31 Group B: 1/25	-	2 participants died (sepsis; stroke). 2 participants were delirious and unable to complete QoL, all other objective evaluations were done (all 4 in NPWT).
Lee 2017b	High-risk groin wounds	Group A: NPWT Group B: standard care	30 days and 90 days	Mortality within 90 days:	*In-hospital SSI* Group A: 1/53 Group B: 1/49	-	Latest time point of SSI data used for analysis

Table 1. Primary outcome data *(Continued)*

				Group A: 1/53 Group B: 2/49	*30-day SSI* Group A: 6/53 Group B: 9/49 *90-day SSI* Group A: 7/53 Group B: 11/49		
Leon 2016 Abstract	Open colorectal surgery	Group A: NPWT Group B: usual dressing	15-day and 30-day evaluation	-	Group A: 5/47 Group B: 10/34	-	Unable to contact authors
Lozano-Balderas 2017	Laparotomised patients with class III or IV (contaminated/dirty-infected) surgical wounds	Group A: vacuum-assisted closure Group B: primary closure Group C: delayed primary closure	Daily when in hospital or in a 30-day period after surgery	-	Group A: 0/25 Group B: 10/27 Group C: 5/29	-	Group C (delayed primary closure) not included in data analysis due to irrelevant wounds.
Manoharan 2016	Primary arthroplasty	Group A: NPWT Group B: conventional dry dressing	10 to 12 days postsurgery	-	-	-	-
Martin 2019	Hepatectomy or pancreatectomy	Group A: NPWT (PICO) Group B: sterile island dressing	Not reported	-	Deep space Group A: 2/20 Group B: 4/20 Superficial Group A: 1/20 Group B: 2/20	Group A: 1/20 Group B: 2/20 all mild to moderate - all associated with SSI	Abstract only
Masden 2012	Radial forearm free flap	Group A: NPWT Group B: dry dressing	Not clear	-	Group A: 3/44 Group B: 5/37	Group A: 16/44 Group B: 11/37	-
Murphy 2019	Colorectal resections	Group A: NPWT	30 days	Group A 3/144	Group A 46/144		

Table 1. Primary outcome data *(Continued)*

		Group B: standard gauze dressing		Group B 2/140	Group B 48/140		
Newman 2019	Total hip or knee replacements	Group A: ciNPWT Group B: standard silver dressing	12 weeks	-	Group A: 0/79 Group B: 1/80	Dehiscence Group A 1/79 Group B 4/80	
Nordmeyer 2016	Spinal fractures treated with internal fixation	Group A: PICO dressing Group B: standard dressing	Day 5 and day 10 after surgery	-	-	-	-
O'Leary 2017	Open abdominal surgery	Group A: PICO dressing Group B: transparent waterproof dressing	Day 4 and day 30 postsurgery	-	Group A: 2/24 Group B: 8/25	-	-
Pachowsky 2012	Hip arthroplasty	Group A: NPWT Group B: standard dressing	Day 5 and day 10 in postoperative period	-	-	-	Very small sample size
Pauser 2016	Fractures of the femoral neck treated by hemiarthroplasty	Group A: NPWT Group B: standard dressing	Day 5 and day 10 after surgery	-	-	-	Very small sample size
Pleger 2018	Groin wound	Group A: NPWT (n = 58 incisions) Group B: control dressing (n = 71 incisions)	Days 5 to 7 and 30 after surgery	-	Group A: 1/58 Group B: 10/71	*Superficial wound dehiscence* Group A: 3/58 Group B: 4/71 *Deep wound dehiscence with fat necrosis* Group A: 1/58 Group B: 4/71	Unit of analysis error: 100 participants with 129 groin incisions

Table 1. Primary outcome data *(Continued)*

Ruhstaller 2017	Unplanned caesarean section	Group A: NPWT Group B: standard care	4 weeks post-surgery	-	Group A: 3/61 Group B: 4/58	-	-
Sabat 2016 Abstract	Groin wounds in vascular surgery	Group A: NPWT Group B: conventional dressing (gauze and Tegaderm)	4 months post-surgery	-	Group A: 2/30 Group B: 7/33	Group A: 3/30 Group B: 8/33	-
Schmid 2018 Abstract	Inguinal lymph node dissection	Group A: NPWT (Prevena) Group B: conventional compression bandages	14 days after surgery	–	–	–	-
Shen 2017	Open resection of intra-abdominal neoplasms	Group A: PICO dressing Group B: Comfeel dressing	30 days after surgery	Group A: 3/132 Group B: 5/133	Group A: 26/132 Group B: 28/133	Group A: 3/132 Group B: 3/133	-
Shim 2018	Reconstructive surgery for acute hand injuries	Group A: NPWT Group B: conventional dressing	1 month and 1 year	-	Group A: 0/30 Group B: 1/21	Wound disruption Group A: 2/30 Group B: 0/21	-
Stannard 2012	Tibial plateau, pilon, or calcaneus fracture	Group A: NPWT Group B: standard dressing	Not stated	-	Group A: 14/144 Group B: 23/122	Group A: 12/139 Group B: 20/122	Unit of analysis error
Tanaydin 2018	Bilateral breast reduction mammoplasty	Group A: NPWT Group B: standard care (fixation strips)	21 days	-	-	Group A: 5/32 Group B: 10/32	32 participants served as their own control.
Tuuli 2017	Caesarean delivery	Group A: NPWT Group B: standard dressing	30 days	-	Group A: 3/60 Group B: 2/60	Group A: 2/60 Group B: 0/60	-

Table 1. Primary outcome data *(Continued)*

WHIST 2019a	Lower limb fracture	Group A: NPWT Group B: standard dressing	30 days 90 days	Planned analysis could not be conducted 3-month Group A 12/745 Group B 15/711 6-month Group A 18/745 Group B 19/711	Deep infection 30 days Group A 45/770 Group B 50/749 90 days (available case data) Group A 72/629 Group B 78/590	Dehisced but not deep SSI 30 days Group A 2/714 Group B 7/687 90 days Group A 2/563 Group B 2/525 14 of those with deep infection dehisced or deliberately opened	
Wihbey 2018	Caesarean delivery	Group A: NPWT Group B: standard dressing	1 week and 30 days follow-up	–	Superficial Group A: 12/80 Group B: 8/81 Deep Group A: 0/80 Group B 0/81 Organ Group A: 1/80 Group B 4/81	Group A: 14/80 Group B: 13/81	-
Witt-Majchrzac 2015	Coronary artery bypass surgery	Group A: NPWT Group B: conventional dressing	6 weeks follow-up	-	Group A: 1/40 Group B: 7/40	Group A: 1/40 Group B: 1/40	-

ASEPSIS: ASEPSIS score - a quantitative scoring method using objective criteria based on wound appearance to evaluate wound infection
cINPWT: closed incisional negative pressure wound therapy
CDC: Center for Disease Control
ICER: incremental cost-effectiveness ratio
IQR: interquartile range
ITT: intention-to-treat
NPWT: negative pressure wound therapy
ORIF: Open reduction internal fixation
PAD: peripheral arterial disease
QALY: quality-adjusted life year

QoL: quality of life
SD: standard deviation
SSI: surgical site infection

Table 2. Secondary outcome data

Study	Wound characteristics	Comparison	Time-points	Reoperation	Readmission	Seroma	Haematoma	Skin blisters	Pain	Quality of Life	Notes
Bobkiewicz 2018	Stoma reversal surgery	Group A: ciNPWT Group B: standard dressing	Not reported	-	-	-	"In the standard dressing group the incidence of haematoma was higher"	-	-	-	Superficial SSI defined according to CDC
Chaboyer 2014	Caesarean section in obese women	Group A: PICO dressing Group B: Comfeel dressing	1, 2, 3, and 4 weeks post-surgery	Group A: 1/44 Group B: 1/43	-	-	Group A: 1/44 Group B: 4/43	Group A: 4/44 Group B: 0/43		-	
Crist 2014	Open reduction and internal fixation of hip, pelvis, and acetabular fracture surgery	Group A: NPWT Group B: standard gauze dressing	12 months	-	-	-	-	-	-	-	
Crist 2017	Open reduction internal fixation (ORIF) for acetabular fractures	Group A: NPWT Group B: standard gauze dressing	10 to 21 days, 6 weeks, 12 weeks,	-	-	-	-	-	-	-	Infection defined as "deep infection"

Table 2. Secondary outcome data *(Continued)*

			every 6 to 8 weeks thereafter until bony union occurred								
DiMuzio 2017	Groin wounds	Group A (59, high risk): NPWT dressing Group B (60, high risk): standard gauze dressing Group C (21, low risk): standard gauze dressing	30 days	-	Group A: 6.8% Group B: 16.7% Group C: 4.8%	-	-	-	-	-	Contacted authors for full text Group C not included in data analysis due to baseline heterogeneity
Engelhardt 2016	Groin wound	Group A: NPWT Group B: conventional dressing	5 and 42 days	-	-	-	-	-	-	-	
Galiano 2018	Breast surgery	Group A: NPWT 199 wounds Group B: standard dressings 199 wounds	21 days	-	-	Group A 0/199 Group B 1/199	Group A 2/199 Group B 3/199	-	-	-	
Giannini 2018	Hip and knee prosthetic revision	Group A single use NPWT (PICO) Group B povidone-iodine gauze and patch wound dressing	7 days	-	-	-	-	Group A 6/50 Group B 15/50	Pain at dressing change Group A mean 2.6 (median 2, range 1-6) Group B mean 4.8 (median	-	

Table 2. Secondary outcome data *(Continued)*

									5, range 2-7)		
Gillespie 2015	Primary hip arthroplasty	Group A: PICO dressing Group B: Comfeel dressing	30 days and 6 weeks postsurgery	-	Group A: 4/35 Group B: 0/35	Group A: 3/35 Group B: 0/35	Group A: 3/35 Group B: 1/35	-	-	-	QoL reported in Heard 2017.
Gombert 2018	Vascular surgery (groin) for PAD	Group A NPWT (prevena) Group B Cosmopore dressing	30 days	Group A 5/98 Group B 6/90	-	-	-	-	Assessed but not reported	-	
Gunatilake 2017	Caesarean	Group A: NPWT Group B: standard care dressing	42 ± 10 days postoperatively (days 1, 2, 6, 14, and 42)	Group A: 1/39 Group B: 6/43	-	-	-	-	Pain reductions at rest Group A: 39/46 Group B: 20/46 Pain reductions with incisional pressure Group A: 42/46 Group B: 25/46	-	ITT: n = 92; 82 completed the study
Howell 2011	Knee arthroplasty	Group A: NPWT Group B: gauze dressing	12 months postsurgery	-	-	-	-	Group A: 15/24 Group B: 3/36		-	

Table 2. Secondary outcome data *(Continued)*

Hussamy 2017	Caesarean section	Group A: NPWT Group B: standard dressing	30 days post-delivery	Group A: 14/222 Group B: 10/219	Group A: 13/222 Group B: 9/219	-	-	-	-	-	Unable to contact authors
Hyldig 2019a	Caesarean section	Group A: NPWT Group B: standard dressing	30 days after operation	-	Mentioned in ClinicalTrials.gov but outcome data not reported	-	-	-	-	EQ index value Group A: mean = 0.86, 95% CI 0.85–0.87 Group B: mean = 0.86, 95% CI 0.84–0.87 Overall self-rated health status (EQ VAS) Group A: mean = 83, 95% CI 82–85; Group B: mean = 82, 95% CI 80–83	
Javed 2018	Open pancreaticoduodenectomy	Group A: NPWT Group B: standard closure	30 days after operation	Need for reoperation (RR, 0.25; 95%	Rate of 30-day readmis-	-	-	-	-	-	

Table 2. Secondary outcome data *(Continued)*

				CI, 0.03–2.32; P = 0.21)	sion for SSI (RR, 0.49; 95% CI, 0.13–1.88; P = 0.32) Rate of 30-day read-mis-sion (RR, 0.41; 95% CI, 0.15–1.09; P = 0.07)						
Kar-lakki 2016	Total hip or knee arthroplasties	Group A: PICO dressing Group B: Comfeel dressing	1, 2, 6 weeks postsurgery	-	Group A: 0/107 Group B: 1/108	-	Group A: 0/102 Group B: 1/107	Group A: 11/102 Group B: 1/107	-	-	
Keeney 2019	Hip and knee total joint arthroplasty	Group A: iNPWT Group B: conventional wound dress-ing	7, 14, 35 days after opera-tions; 2 years	Return to the op-erating room to manage a wound-re-lated con-cern with-in the first 3 months Group A: 1/185 Group B: 4/213	-	-	-	-	-	-	Addition-al data on return to operating rooms; and infection outcome were pre-sented in Character-istics of in-cluded stud-ies.

Table 2. Secondary outcome data *(Continued)*

Kuncewitch 2017	Pancreatectomy	Group A: NPWT Group B: standard surgical dressing	30 days post-surgery follow-up	-	-	Group A: 4/36 Group B: 6/37	-	-	-		Unable to contact authors
Kwon 2018	Vascular groin incisions (high risk)	Group A: NPWT Group B: standard gauze	30 days	Group A 5/59 Group B 11/60	Group A 4/59 Group B 10/60	Reported composite outcome including seroma only	Any Group A 0/59 Group B 1/60 Major Group A 0/59 Group B 1/60	-	-	-	
Lee 2017a	Great saphenous vein harvest	Group A: NPWT Group B: standard surgical dressing	Initial assessment: not specified; endpoint assessment: 6 weeks	-	-	-	-	-	-	EQ-5D-3L: Group A (n = 26): 78 Group B (n = 17): 63 P = 0.172	2 participants died (sepsis; stroke). 2 participants were delirious and unable to complete QoL, all other objective evaluations were done (all 4 in NPWT).
Lee 2017b	High-risk groin wounds	Group A: NPWT	30 days and 90 days	Group A: 2/53	Group A: 2/53	-	-	-	-	-	Latest time point of SSI

Table 2. Secondary outcome data *(Continued)*

		Group B: standard care		Group B: 1/49 *for SSI*	Group B: 2/49 *for SSI*						data used for analysis.
Leon 2016	Open colorectal surgery	Group A: NPWT Group B: usual dressing	15-day and 30-day evaluation	-	-	-	-	-	-	-	Unable to contact authors
Lozano-Balderas 2017	Laparotomised patients with class III or IV (contaminated/dirty-infected) surgical wounds	Group A: vacuum-assisted closure Group B: primary closure Group C: delayed primary closure	Daily when in hospital or in a 30-day period after surgery	-	-	-	-	-	-	-	Group C (delayed primary closure) not included in data analysis due to irrelevant wounds
Manoharan 2016	Primary arthroplasty	Group A: NPWT Group B: conventional dry dressing	10 to 12 days postsurgery	-	-	-	-	Group A: 1/21 Group B: 0/21		-	
Martin 2019	Hepatectomy or pancreatectomy	Group A: NPWT (PICO) Group B: sterile island dressing	Not reported	-	-	-	-	-	-	-	Abstract only
Masden 2012	Radial forearm free flap	Group A: NPWT Group B: dry dressing	Not clear	Group A: 9/44 Group B: 8/37	-	-	-	-	-	-	
Murphy 2019	Colorectal resections	Group A NPWT Group B standard gauze dressing	30 days	Group A 6/144 Group B 6/140	-	-	-	-	-	-	
Newman 2019	Total hip or knee replacements	Group A: ciNPWT Group B: standard silver dressing	12 weeks	Reoperation	Readmission	-	Haematoma	Skin blisters	-	-	

Table 2. Secondary outcome data *(Continued)*

				2 weeks Group A 0/79 Group B 1/80 4 weeks Group A 1/79 Group B 3/80 12 weeks Group A 2/79 Group B 10/80	2 weeks Group A 5/79 Group B 6/80 4 weeks Group A 9/79 Group B 9/80 12 weeks Group A 16/79 Group B 19/80		Group A 1/79 Group B 1/80	Group A 0/79 Group B 1/80			
Nordmeyer 2016	Spinal fractures treated with internal fixation	Group A: PICO dressing Group B: standard dressing	Day 5 and day 10 after surgery	-	-	-	-	-	-	-	
O'Leary 2017	Open abdominal surgery	Group A: PICO dressing Group B: transparent waterproof dressing	Day 4 and day 30 post-surgery	Group A: 0/25 Group B: 1/25	-	-	-	-	Reported "no difference"	-	
Pachowsky 2012	Hip arthroplasty	Group A: NPWT Group B: standard dressing	Day 5 and day 10 in postoperative period	-	-	Group A: 4/9 Group B: 9/10	-	-	-	-	Very small sample size

Table 2. Secondary outcome data *(Continued)*

Pauser 2016	Fractures of the femoral neck treated by hemi-arthroplasty	Group A: NPWT Group B: standard dressing	Day 5 and day 10 after surgery	-	-	Group A: 6/11 Group B: 8/10	-	-	-	-	Very small sample size
Pleger 2018	Groin wound	Group A: NPWT (n = 58 incisions) Group B: control dressing (n = 71 incisions)	Days 5 to 7 and 30 after surgery	-	-	Group A: 0/58 Group B: 1/71	Group A: 0/58 Group B: 8/71	-	-	-	Unit of analysis error: 100 participants with 129 groin incisions
Ruhstaller 2017	Unplanned caesarean section	Group A: NPWT Group B: standard care	4 weeks postsurgery	-	-	-	-	Group A: 8/61 Group B: 2/58	Reported "no difference"	-	
Sabat 2016	Groin wounds in vascular surgery	Group A: NPWT Group B: conventional dressing (gauze and Tegaderm)	4 months postsurgery	-	-	-	-	-	-	-	
Schmid 2018	Inguinal lymph node dissection	Group A: NPWT (Prevena) Group B: conventional compression bandages	14 days after surgery	Group A: 11/25 Group B: 12/25	-	-	-	-	-	-	
Shen 2017	Open resection of intra-abdominal neoplasms	Group A: PICO dressing Group B: Comfeel dressing	30 days after surgery	Group A: 19/132 Group B: 16/133	Group A: 3/118 Group B: 6/119	Group A: 7/132 Group B: 8/133	Group A: 1/132 Group B: 0/133	-	-	-	

Table 2. Secondary outcome data *(Continued)*

Shim 2018	Reconstructive surgery for acute hand injuries	Group A: NPWT Group B: conventional dressing	1 month and 1 year	-	-	-	Group A: 0/30 Group B: 2/21	-	-	-		
Stannard 2012	Tibial plateau, pilon, or calcaneus fracture	Group A: NPWT Group B: standard dressing	Not stated	-	-	-	-	-	-	-	Unit of analysis error	
Tanaydin 2018	Bilateral breast reduction mammoplasty	Group A: NPWT Group B: standard care (fixation strips)	21 days	-	-	-	-	-	-	-	32 participants served as their own control.	
Tuuli 2017	Caesarean delivery	Group A: NPWT Group B: standard dressing	30 days	-	-	Group A: 0/60 Group B: 1/60	Group A: 0/60 Group B: 0/60	-	Pain score (on 0-to-10 scale) was significantly lower with prophylactic NPWT (median (IQR): 0 (0, 1) vs 1 (0, 3), P = 0.02)	-		
WHIST 2019a	Lower limb fracture	Group A NPWT Group B standard dressing	30 days 90 days	Deliberate surgical reopening or surgical treatment of wound complications Group A	-	-	-	-	VAS (median IQR) 3 months Group A 3.0 (1.0, 6.0) 365	DRI 3 months Group A 51.6 (23.46) (507) Group B		

Table 2. Secondary outcome data *(Continued)*

					2/715
					1/573
					Group B
					2/688
					2/575
					Further surgery
					Group A
					83/578
					Group B 56/534
				Group B 4.0 (2.0, 5.0) 339	51.1 (23.92) (456)
				6 months	6 months
				Group A 3.0 (1.0, 5.0) 419	Group A 40.6 (24.98) (469)
				Group B 3.0 (1.0, 5.0) 368	Group B 40.2 (26.73) 432
				Proportion with neuropathic pain (DN4 >/= 3) also reported	EQ-5D (utility) 3 months
					Group A 0.5 (0.29) 528
					Group B 0.5 (0.30) 470
					6 months
					Group A 0.6 (0.28) 486
					Group B 0.6 (0.29) 446
					EQ-5D (VAS) 3 months
					Group A 64.1 (22.24) 531

Table 2. Secondary outcome data *(Continued)*

										Group B 64.7 (22.78) 478 6 months Group A 69.7 (21.15) 489 Group B 69.4 (21.76) 449
Wihbey 2018	Caesarean delivery	Group A: NPWT Group B: standard dressing	1 week and 30 days follow-up	Group A: 1/80 Group B: 1/81	Group A: 3/80 Group B: 5/81	Group A: 7/80 Group B: 6/81	Group A: 2/80 Group B: 4/81	-	-	-
Wittmajchrzac 2015	Coronary artery bypass surgery	Group A: NPWT Group B: conventional dressing	6 weeks follow-up	-	-	-	Group A: 1/40 Group B: 1/40	Group A: 5/40 Group B: 0/40		-

CDC: Center for Disease Control
cINPWT: closed incisional negative pressure wound therapy
CI: confidence interval
DN4: DN4 (Douleur Neuropathique 4) questionnaire
DRI: Disability Rating Index
EQ(VAS): EuroQoL Visual Analogue Scale
EQ-5D-3L: EuroQoL 5D questionnaire, version 3L
INPWT: incisional negative pressure wound therapy
IQR: inter-quartile range
ITT: intention-to-treat
NPWT: negative pressure wound therapy
PAD: peripheral arterial disease

QoL: quality of life
RR: relative risk/risk ratio
SSI: surgical site infection
VAS: visual analogue scale

Table 3. Economic outcome data

Economic Study	RCT base	Population and perspective	Comparison	Time points	Dressing-related costs	Resource use	QALY	Relative cost effectiveness (e.g. ICER)	Notes
Heard 2017	Chaboyer 2014	Population: Obese women undergoing Caesarean section Perspective: Australian public health care provider	Group A: PICO dressing Group B: Comfeel dressing	4 weeks	NPWT AUD 180 Standard AUD 5 Dressing change cost (nurse time) AUD 35 for each group	Group A (44): 2871.5 ± 182.1 AUD Group B (43): 2806.6 ± 260.4 AUD	Group A (44): 0.067 ± 0.01 Group B (43): 0.066 ± 0.01	Per SSI prevented: ICER AUD 1347 (95% CI dominant to 41,873) Per QALY gained iCER AUD 42,340 (95% CI dominant to 884,019)	Data drawn from Chaboyer 2014
Hyldig 2019b	Hyldig 2019a	Population: Obese women undergoing Caesarean section Perspective: Danish healthcare	NPWT Standard dressing	30 days	NPWT €151.40 Standard €0.67 (assumed included in cost of treatment)	Total healthcare costs NPWT €5793.60 Standard €5840.89 Cost difference €47.29	NPWT 0.863 Control 0.856	ICER not reported for all participants; NPWT reported as dominant; subgroups reported	Data drawn from Hyldig 2019a
Nherera 2017	Karlakki 2016	Population: People undergoing total hip/knee arthroplasty Perspective: UK NHS	NPWT Standard dressing	6 weeks	Cost of NPWT £144 (120 to 150). Standard dressings assumed zero	Group A (102): 5602 ± 7954 GBP Group B (107): 6713 ± 9559 GPB	Group A (102): 0.116 ± 0.01 Group B (107): 0.115 ± 0.01	ICER not reported but NPWT described as technically dominant	Data drawn from Karlakki 2016
Nherera 2018	Witt-Majchrzac 2015	Population: People undergoing coronary artery bypass surgery Perspective: German Statutory Health Insurance payer	NPWT Standard dressing	6 weeks	NPWT €153.00 (114.75 - 191.25) above standard cost	NPWT €19,986 Standard €20,572	NPWT 0.8904 Standard 0.8593	NPWT reported as dominant for both SSI avoided and QALY gained in base case analysis	Data drawn from Witt-Majchrzac 2015

Table 3. Economic outcome data *(Continued)*

							+0.0311 for NPWT		
WHIST 2019b	WHIST 2019a	Population: People undergoing surgery for lower limb fracture Perspective: UK NHS and PSS	NPWT Standard dressing	3 months 6 months	Cost of intervention including dressing (plus cast, initial inpatient care, antibiotics, dressing changes) Group A £5420.66 (5559.95) Group B £4774.15 (4633.18)	Total cost after initial intervention - baseline to 6 months NHS and PSS Group A £3100.83 (11251.93) Group B £2330.83 (7863.51) Societal (inc NHS & PSS) Group A £6248.64 (13074.32) Group B £6027.23 (17737.28)	Group A 0.40 (0.22) Group B 0.41 (0.24)	£396,531/QALY gained (NHS & PSS perspective) £679,482 per QALY gained (societal perspective) £454,903 per QALY (complete case analysis)	Data drawn from WHIST 2019a
-	DiMuzio 2017 [1]	Groin wounds	NPWT Standard dressing	30 days	-	Group A: USD 30,492 Group B: USD 36,537 NPWT reduced cost per patient of USD 6045 (USD 30,492 + USD 500 (device) in NWPT group vs USD 36,537 in dressing group)	-	-	Data not linked to cost-effectiveness
-	Gillespie 2015 [1]	Total hip/knee arthroplasty	NPWT	30 days	Group A: AUS 38.4 ± AUS 13.6	-	-	-	Data not linked to

Table 3. Economic outcome data *(Continued)*

			Standard dressing	6 weeks	Group B: AUS 3.01 ± AUS 1.2				cost-effectiveness
-	Javed 2018 [1]	Open pancreaticoduodenectomy	NPWT Standard dressing	30 days	-	Median cost of hospitalisation $43,823 (IQR, $36,820–$59,352) No between group data	-	-	Data not linked to cost-effectiveness
-	Kwon 2018 [1]	Vascular groin incisions (high risk)	NPWT Standard dressing	30 days	-	Costs (hospital) Group A $29,292 +/- 6 $29,320 (n 51; range, $8816-$192,658) Group B $30,678 6 $23,338 (n ¼ 55; range, $9071-$131,464) Costs (post index procedure) Group A 30,492 +/- $30,678 ($8816-$192,658) Group B $36,537 +/- $28,889 (range, $9071-$131,4640	-	-	Data not linked to cost-effectiveness
	Manoharan 2016	Primary arthroplasty	NPWT	10-12 days	Group A: AUS 285.94 ± AUS 28.54	-			Data not linked to cost-effectiveness

Table 3. Economic outcome data *(Continued)*

	Standard dressing		Group B: AUS 43.51 ± AUS 64.23

[1] RCTs reporting cost data which were not subsequently used in an economic analysis
AUD: Australian dollars
CI: confidence intervals
GBP: pounds sterling (UK pounds)
ICER: incremental cost-effectiveness ratio
NHS: National Health Service (UK)
NPWT: negative pressure wound therapy
PSS: personal social services
QALY: quality adjusted life year
SSI: surgical site infection
UK: United Kingdom
USD: United States dollar

Table 4. Quality assessment of economic studies using the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) checklist

Sections	Items	Item number	Heard 2017	Hyldig 2019b	Nherera 2017	Nherera 2018	WHIST 2019a
Title and abstract	Title	1	✓	✓	✓	✓	X
	Abstract	2	✓	✓	✓	✓	≠*
Introduction	Background and objectives	3	✓	✓	✓	✓	✓
Methods	Target population and subgroups	4	✓	✓	✓	✓	✓
	Setting and locations	5	✓	✓	✓	✓	✓
	Study perspectives	6	✓	✓	✓	✓	✓
	Comparators	7	✓	✓	✓	✓	✓
	Time horizon	8	X	✓	✓	✓	✓
	Discount rate	9	✓	✓	✓	✓	✓
	Choice of health outcomes	10	✓	✓	≠	✓	✓

Table 4. Quality assessment of economic studies using the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) checklist *(Continued)*

	Measurement of effectiveness	11a	≠	≠	N/A	≠	≠
		11b	N/A	N/A	✓	≠	N/A
	Measurement and valuation of preference-based outcomes	12	≠	✓	≠	X	✓
	Estimating resources and costs	13a	✓	✓	N/A	N/A	✓
		13b	N/A	N/A	✓	✓	N/A
	Currency, price date and conversion	14	✓	✓	≠	✓	✓
	Choice of model	15	≠	≠	≠	✓	≠
	Assumptions	16	✓	✓	✓	✓	✓
	Analytical methods	17	✓	✓	✓	✓	✓
Results	Study parameters	18	✓	✓	✓	✓	✓
	Incremental costs and outcomes	19	✓	✓	✓	≠	✓
	Characterising uncertainty	20a	≠	≠	N/A	N/A	✓
		20b	N/A	N/A	≠	≠	N/A
	Characterising heterogeneity	21	X	✓	✓	N/A	N/A
Discussion	Study findings, limitations, generalisability and current knowledge	22	✓	✓	✓	✓	✓
Others	Source of funding	23	✓	✓	X	X	✓
	Conflicts of interest	24	✓	✓	✓	✓	✓
Total			20/24 (83.3%)	22.5/24 (91.7%)	20.5/24 (85.4%)	20/23* (87.0%)	20.5/23* (89.1%)

✓ Item met in full; ≠ Item partially met; X Item not met; N/A = Not applicable
*Scored out of 23 because item 21 is not applicable to these studies

APPENDICES

Appendix 1. 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.
Negative pressure wound therapy (NPWT)	Negative pressure wound therapy 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 mmHg (Ubbink 2008; Vikatmaa 2008).
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.

Appendix 2. Search strategies

Cochrane Wounds Specialised Register

1 MESH DESCRIPTOR Negative-Pressure Wound Therapy EXPLODE ALL AND INREGISTER

2 MESH DESCRIPTOR Suction EXPLODE ALL AND INREGISTER

3 MESH DESCRIPTOR Vacuum EXPLODE ALL AND INREGISTER

4 "negative pressure" or negative-pressure or TNP or NWPT or NPWT AND INREGISTER

5 (sub-atmospheric or subatmospheric) AND INREGISTER

6 ((seal* next surface*) or (seal* next aspirat*)) AND INREGISTER

7 (wound near3 suction*) AND INREGISTER

8 (wound near3 drainage) AND INREGISTER

9 ((foam next suction) or (suction next dressing*)) AND INREGISTER

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) AND INREGISTER

11 ("vacuum-assisted") AND INREGISTER

12 #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 AND INREGISTER

13 MESH DESCRIPTOR Surgical Wound Infection EXPLODE ALL AND INREGISTER

14 MESH DESCRIPTOR Surgical Wound Dehiscence EXPLODE ALL AND INREGISTER

15 surg* near5 infect* AND INREGISTER

16 surg* near5 wound* AND INREGISTER

17 surg* near5 site* AND INREGISTER

18 surg* near5 incision* AND INREGISTER

19 surg* near5 dehisc* AND INREGISTER

20 wound* near5 dehisc* AND INREGISTER

21 #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 AND INREGISTER

22 #12 AND #21 AND INREGISTER

The Cochrane Central Register of Controlled Clinical Trials (CENTRAL) and NHS Economic Evaluation Database (NHS EED)

#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 or NWPT or NPWT):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"):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

Ovid MEDLINE - RCT

1 exp Negative-Pressure Wound Therapy/

2 exp Suction/

3 exp Vacuum/

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

11 ((vacuum adj therapy) or (vacuum adj dressing*) or (vacuum adj seal*) or (vacuum adj closure) or (vacuum adj assist*) or (vacuum adj compression) or (vacuum adj pack*) or (vacuum adj drainage) or (suction* adj drainage) or VAC).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 randomi?ed.ab.

27 placebo.ab.

28 clinical trials as topic.sh.

29 randomly.ab.

30 trial.ti.

31 or/24-30

32 exp animals/ not humans.sh.

33 31 not 32

34 23 and 33

Ovid MEDLINE – Economic

1 exp Negative-Pressure Wound Therapy/

2 exp Suction/

3 exp Vacuum/

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

11 ((vacuum adj therapy) or (vacuum adj dressing*) or (vacuum adj assist*) or (vacuum adj seal*) or (vacuum adj closure) or (vacuum adj compression) or (vacuum adj pack*) or (vacuum adj drainage) or (suction* adj drainage) or VAC).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 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 pharmacoeconomic*).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

Ovid Embase – RCT

1 exp suction drainage/

2 exp vacuum assisted closure/

3 (negative pressure or negative-pressure or TNP or NPWT or NWPT).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.tw.

10 ((vacuum adj therapy) or (vacuum adj dressing*) or (vacuum adj seal*) or (vacuum adj assist*) or (vacuum adj closure) or (vacuum adj compression) or (vacuum adj pack*) or (vacuum adj drainage) or (suction* adj drainage) or VAC).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 Randomized controlled trials/

23 Single-Blind Method/

24 Double-Blind Method/

25 Crossover Procedure/

26 (random* or factorial* or crossover* or cross over* or cross-over* or placebo* or assign* or allocat* or volunteer*).ti,ab.

27 (doubl* adj blind*).ti,ab.

28 (singl* adj blind*).ti,ab.

29 or/22-28

30 exp animals/ or exp invertebrate/ or animal experiment/ or animal model/ or animal tissue/ or animal cell/ or nonhuman/

31 human/ or human cell/

32 and/30-31

33 30 not 32

34 29 not 33

35 21 and 34

Ovid Embase - Economic

1 exp suction drainage/

2 exp vacuum assisted closure/

3 (negative pressure or negative-pressure or TNP or NPWT or NWPT).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.tw.

10 ((vacuum adj therapy) or (vacuum adj dressing*) or (vacuum adj seal*) or (vacuum adj assist*) or (vacuum adj closure) or (vacuum adj compression) or (vacuum adj pack*) or (vacuum adj drainage) or (suction* adj drainage) or VAC).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 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

EBSCO CINAHL Plus - RCT

S37 S23 AND S36

S36 S24 OR S25 OR S26 OR S27 OR S28 OR S29 OR S30 OR S31 OR S32 OR S33 OR S34 OR S35

S35 TI allocat* random* or AB allocat* random*

S34 MH "Quantitative Studies"

S33 TI placebo* or AB placebo*

S32 MH "Placebos"

S31 TI random* allocat* or AB random* allocat*

S30 MH "Random Assignment"

S29 TI randomi?ed control* trial* or AB randomi?ed control* trial*

S28 AB (singl* or doubl* or trebl* or tripl*) and AB (blind* or mask*)

S27 TI (singl* or doubl* or trebl* or tripl*) and TI (blind* or mask*)

S26 TI clinic* N1 trial* or AB clinic* N1 trial*

S25 PT Clinical trial

S24 MH "Clinical Trials+"

S23 S12 AND S22

S22 S13 OR S14 OR S15 OR S16 OR S17 OR S18 OR S19 OR S20 OR S21

S21 TI (wound* N5 dehisc*) OR AB (wound* N5 dehisc*)

S20 TI (surg* N5 dehisc*) OR AB (surg* N5 dehisc*)

S19 TI (surg* N5 incision*) OR AB (surg* N5 incision*)

S18 TI (surg* N5 site*) OR AB (surg* N5 site*)

S17 TI (surg* N5 wound*) OR AB (surg* N5 wound*)

S16 TI (surg* N5 infection*) OR AB (surg* N5 infection*)

S15 (MH "Surgical Wound Dehiscence")

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 TI vacuum-assisted OR AB vacuum-assisted

S9 TI (vacuum therapy or vacuum dressing* or vacuum seal* or vacuum closure or vacuum compression or vacuum pack or vacuum drainage or vacuum assisted or VAC) OR AB (vacuum therapy or vacuum dressing* or vacuum seal* or vacuum closure or vacuum compression or vacuum pack or vacuum drainage or vacuum assisted or VAC)

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 NPWT or NWPT) OR AB (negative pressure or negative-pressure or TNP or NPWT or NWPT)

S3 (MH "Negative Pressure Wound Therapy")

S2 (MH "Vacuum")

S1 (MH "Suction+")

EBSCO CINAHL Plus – Economic

S46 S23 AND S45

S45 S41 NOT S44

S44 S19 NOT (S19 AND S43)

S43 MH "Human"

S42 MH "Animal Studies"

S41 S36 NOT S40

S40 S37 or S38 or S39

S39 PT commentary

S38 PT letter

S37 PT editorial

S36 S34 OR S35

S35 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*)

S34 S30 OR S33

S33 S31 OR S32

S32 MH "Health Resource Utilization"

S31 MH "Health Resource Allocation"

S30 S24 NOT S29

S29 S25 OR S26 or S27 OR S28

S28 MH "Business+"

S27 MH "Financing, Organized+"

S26 MH "Financial Support+"

S25 MH "Financial Management+"

S24 MH "Economics+"

S23 S12 AND S22

S22 S13 OR S14 OR S15 OR S16 OR S17 OR S18 OR S19 OR S20 OR S21

S21 TI (wound* N5 dehisc*) OR AB (wound* N5 dehisc*)

S20 TI (surg* N5 dehisc*) OR AB (surg* N5 dehisc*)

S19 TI (surg* N5 incision*) OR AB (surg* N5 incision*)

S18 TI (surg* N5 site*) OR AB (surg* N5 site*)

S17 TI (surg* N5 wound*) OR AB (surg* N5 wound*)

S16 TI (surg* N5 infection*) OR AB (surg* N5 infection*)

S15 (MH "Surgical Wound Dehiscence")

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 TI vacuum-assisted OR AB vacuum-assisted

S9 TI (vacuum therapy or vacuum dressing* or vacuum seal* or vacuum closure or vacuum compression or vacuum pack or vacuum drainage or vacuum assisted or VAC) OR AB (vacuum therapy or vacuum dressing* or vacuum seal* or vacuum closure or vacuum compression or vacuum pack or vacuum drainage or vacuum assisted or VAC)

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 NPWT or NWPT) OR AB (negative pressure or negative-pressure or TNP or NPWT or NWPT)

S3 (MH "Negative Pressure Wound Therapy")

S2 (MH "Vacuum")

S1 (MH "Suction+")

US National Institutes of Health Ongoing Trials Register (ClinicalTrials.gov)

(surgery OR surgical OR postoperative OR operative OR incision OR incisional OR incisions) AND (negative pressure OR vacuum assisted OR NPWT OR TNP) | incision dehiscence

(surgery OR surgical OR postoperative OR operative OR incision OR incisional OR incisions) AND (negative pressure OR vacuum assisted OR NPWT OR TNP) | incision infection

(surgery OR surgical OR postoperative OR operative OR incision OR incisional OR incisions) AND (negative pressure OR vacuum assisted OR NPWT OR TNP) | operative wound

(surgery OR surgical OR postoperative OR operative OR incision OR incisional OR incisions) AND (negative pressure OR vacuum assisted OR NPWT OR TNP) | postoperative complications

(surgery OR surgical OR postoperative OR operative OR incision OR incisional OR incisions) AND (negative pressure OR vacuum assisted OR NPWT OR TNP) | postoperative infection

(surgery OR surgical OR postoperative OR operative OR incision OR incisional OR incisions) AND (negative pressure OR vacuum assisted OR NPWT OR TNP) | surgery

(surgery OR surgical OR postoperative OR operative OR incision OR incisional OR incisions) AND (negative pressure OR vacuum assisted OR NPWT OR TNP) | surgical incision

(surgery OR surgical OR postoperative OR operative OR incision OR incisional OR incisions) AND (negative pressure OR vacuum assisted OR NPWT OR TNP) | surgical site infection

(surgery OR surgical OR postoperative OR operative OR incision OR incisional OR incisions) AND (negative pressure OR vacuum assisted OR NPWT OR TNP) | surgical wound

(surgery OR surgical OR postoperative OR operative OR incision OR incisional OR incisions) AND (negative pressure OR vacuum assisted OR NPWT OR TNP) | surgical wound dehiscence

(surgery OR surgical OR postoperative OR operative OR incision OR incisional OR incisions) AND (negative pressure OR vacuum assisted OR NPWT OR TNP) | seroma

World Health Organization International Clinical Trials Registry Platform

"negative pressure" or "vacuum assisted" or NPWT or TNP
AND
surgery or surgical or postoperative or operative or incision or incisional or incisions

Appendix 3. 'Risk of bias' criteria

1. Was the allocation sequence randomly generated?

Low risk of bias

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

High risk of bias

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

Unclear

Insufficient information about the sequence generation process is 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 permit a definitive 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 it is 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 is 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 are unlikely to be related to true outcome (for survival data, censoring is unlikely to be introducing bias).
- Missing outcome data are 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 is 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 is likely to be related to true outcome, with either an 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

Either 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 the suggestion of selective outcome reporting?

Low risk of bias

Either of the following.

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

High risk of bias

Any one of the following.

- Not all of the study's prespecified primary outcomes have been reported.
- One or more primary outcomes are reported using measurements, analysis methods, or subsets of the data (e.g. subscales) that were not prespecified.
- One or more reported primary outcomes were not prespecified (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 is 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;
- had extreme baseline imbalance;
- 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 4. Results of studies not included in pooled analyses

This appendix contains the results of studies which reported specified outcomes but could not be included in the pooled analyses we conducted; together with brief explanations of the methodological or reporting issues for this.

Primary outcomes

Mortality

There were no studies which reported mortality and could not be included in the pooled analysis

SSI

Seven studies (Galiano 2018; Giannini 2018; Howell 2011; Kwon 2018; Pleger 2018; Sabat 2016; Schmid 2018; Stannard 2012) reported SSI data but could not be included in the pooled analysis.

One study in 100 people undergoing revision surgery on hip or knee prostheses (Giannini 2018) reported the ASEPSIS score (Wilson 1986). The authors reported that the mean score was 3.0 (SD 1.89) in the NPWT group compared with 5.1 (SD 3.89) in the standard dressing group; higher scores are indicative of a worse outcome. We could not analyse this data further, as the component elements of the score were not reported.

Several studies randomised or analysed wounds rather than individuals. Stannard 2012 reported results for this outcome including 249 participants who had sustained open fractures, requiring surgery for closure. Randomisation was by individual participant, but some participants had multiple wounds. Outcome data were collected and analysed by wound, not participant, so we have not carried out further analysis as clustering was not taken into account in this study. The investigators reported that there were 14/144 (9.7%) SSIs in the NPWT group compared with 23/122 (18.9%) SSIs in the standard dressing group. Pleger 2018 randomised 100 participants with 129 groin wounds, and outcome data were collected and analysed by groin wound. The investigators reported that there were 1/58 (1.7%) SSIs in the NPWT group compared with 10/71 (14.1%) SSIs in the standard dressing group. Sabat 2016 enrolled 49 people undergoing peripheral vascular surgery and randomised 63 wounds. The investigators reported 2/30 (6.7%) SSI in the NPWT compared with 7/33 in the standard dressing group (21.2%). Kwon 2018 used a design which combined a parallel group approach for most participants undergoing peripheral vascular surgery (75/99), with a split person design for 24 participants with bilateral surgeries, and then analysed all data at the level of the surgical incision. It is not clear how the combined design and different types of data (paired and unpaired) were accounted for in the analysis and the two were not reported separately, so we have not carried out further analysis. The investigators reported 6/59 (10.2%) SSIs in the NPWT group compared with 12/60 (20.0%) in the standard dressing group. Howell 2011 also included some participants with more than one wound (51 participants with 60 wounds) in knee arthroplasty; numbers of SSI were reported as 1/24 in the NPWT group compared with 1/36 in the standard dressing group.

Galiano 2018 used a split person design in women undergoing bilateral breast surgery. The reported results were 4/199 (2%) SSI in the NPWT and 6/199 (3%) in the standard dressing group. Schmid 2018 also used a split person design in inguinal lymph node removal. The reported results were 11/25 SSI in the NPWT group and 12/25 in the standard dressing group. In both studies, it was unclear whether the analysis accounted for paired data.

Superficial SSI

Kwon 2018, Howell 2011 and Pleger 2018 were not included in the analysis because of the use of wounds as the unit of analysis and/or randomisation (see above). We note the results reported for these studies as follows: Kwon 2018 3/59 compared with 5/60; Howell 2011 0/24 compared with 0/36 and Pleger 2018 5/58 compared with 28/71 superficial SSIs (incisions were the unit of analysis in each case).

Deep SSI

Kwon 2018, Howell 2011 and Pleger 2018 were not included in the analysis because of the use of wounds as the unit of analysis and/or randomisation (see above). We note the results reported for these studies as follows: Kwon 2018 3/59 versus 7/60; Howell 2011 1/24 compared with 1/36 and Pleger 2018 0/58 versus 2/71 deep SSIs (incisions were the unit of analysis in each case).

Dehiscence

Four studies (Galiano 2018; Pleger 2018; Stannard 2012; Tanaydin 2018) reported dehiscence data but could not be included in the pooled analysis.

Two studies reported dehiscence, but randomised wounds as opposed to individuals. Stannard 2012 assessed dehiscence in participants with an open fracture requiring surgical closure. Participants were randomised individually, but more than one wound per participant were included in the results. We did not have individual patient data, and the trial investigators did not account for clustering in their analysis, so further analysis was not undertaken (NPWT 12/139 (8.6%) versus standard dressing 20/122 (16.4%)). Pleger 2018 randomised 100 participants with 129 groin wounds, and outcome data were collected and analysed by groin wound. There were 3/58 (5.2%) superficial dehiscences in the NPWT group compared with 4/71 (5.6%) in the standard dressing group, and 1/58 (1.7%) deep wound dehiscences with fat necrosis in the NPWT group compared with 4/71 (5.6%) in the standard dressing group. Sabat randomised 63 wounds from 49 participants undergoing peripheral vascular surgery and reported 3/30 instances of dehiscence in the NPWT group compared with 8/33 in the standard dressing group.

Two studies in breast surgery reported dehiscence, but in each case they employed a split person design in women undergoing bilateral surgery (Galiano 2018; Tanaydin 2018); in neither study was it clear whether the analysis took the paired data into account. Although these studies were not included in the main pooled analysis, we were able to combine them separately. The two studies reported 37/231 dehiscences in the NPWT group compared with 62/231 in the standard dressing group. The pooled RR was 0.60 (95% CI 0.41 to 0.86; $I^2 = 0\%$).

Secondary outcomes

Reoperation

Two studies (Javed 2018; Kwon 2018) reported on reoperation but could not be included in the pooled analysis.

One trial reported data which allowed us to use only a generic inverse variance approach to calculate an RR. Javed 2018 enrolled 123 participants undergoing open pancreaticoduodenectomy and had a RR of 0.25 (95% CI 0.03 to 2.08) for reoperation.

One trial (Kwon 2018) used a mixed design involving both paired and unpaired data which we report but have not analysed further. The authors reported that there were 5/59 reoperations in the NPWT group compared with 11/60 with standard dressings.

Readmission

Two studies (Javed 2018; Kwon 2018) reported on readmission but could not be included in the pooled analysis.

One trial reported an RR but not the data used to calculate it. Javed 2018 enrolled 123 participants undergoing open pancreaticoduodenectomy and had a RR of 0.41 (95% CI 0.15 to 1.09) for all readmissions at 30 days. An RR for SSI-related readmission was also reported.

One trial (Kwon 2018) used a mixed design involving both paired and unpaired data which we report but have not analysed further. The authors reported that there were 4/59 (6.8%) readmissions in the NPWT group compared with 10/60 (16.7%) with standard dressings.

Seroma

Two studies (Galiano 2018; Pleger 2018) reported on seroma but could not be included in the pooled analysis.

Pleger 2018, randomising 100 participants with 129 groin wounds, reported 0/58 seromas in the NPWT group compared with 1/71 in the standard dressing group. Galiano 2018 used a split person design in breast surgery and reported zero events in the NPWT arm (0/199) and one (1/199) in the standard dressing arm.

Haematoma

Four studies (Bobkiewicz 2018; Galiano 2018; Kwon 2018; Pleger 2018) reported on haematoma but could not be included in the pooled analysis.

Pleger 2018, randomising 100 participants with 129 groin wounds, reported that there were 0/58 haematoma in the NPWT group compared with 8/71 in the standard dressing group. Kwon 2018 used a mixed design involving both paired and unpaired data which we report but have not analysed further. The authors reported that there were zero events (0/59) in the NPWT group compared with 1/60 with standard dressings. Galiano 2018 used a split person design in breast surgery and reported 2/199 events in the NPWT arm and 3/199 in the standard dressing arm. One trial Bobkiewicz 2018 enrolled 30 participants and reported narratively that "In the standard dressing group the incidence of hematoma was higher" but gave no further information.

Blisters

One study (Howell 2011) reported blisters and could not be included in the pooled analysis.

Howell 2011 included some participants with more than one wound (51 participants with 60 wounds) in knee arthroplasty; numbers of people with skin blistering were 15/24 versus 3/36.

Pain

There was no pooled analysis for pain so all studies are discussed in the main text.

QoL

There was no pooled analysis for pain; all studies are discussed in the main text.

Economic outcomes

We did not conduct pooled analyses of economic data; all studies are discussed in the main text and in Appendix 5.

Appendix 5. Cost effectiveness results used to inform relative cost effectiveness

There were five studies which used data from RCTs included in this review to assess measures of cost-effectiveness. Two of these looked at use of NPWT in obstetric surgery - obese women undergoing caesarean section (Heard 2017; Hyldig 2019b); these were based on the RCTs of Chaboyer 2014 and Hyldig 2019a, respectively. Two evaluations considered people having orthopaedic surgery. The WHIST 2019b study was undertaken alongside the WHIST 2019a RCT in people having surgery for lower limb fractures. Nherera 2017 looked at NPWT in people having knee and hip arthroplasties and was based on Karlakki 2016. Finally, Nherera 2018 looked at people having CABG surgery and was based on Witt-Majchrzac 2015. Four studies included a formal cost-effectiveness analysis as part of their intervention (Chaboyer 2014; Hyldig 2019a; Karlakki 2016; WHIST 2019a) while another contributed data to a cost-effectiveness study (Witt-Majchrzac 2015; Nherera 2018). Three studies were pilot studies with small sample sizes but Hyldig 2019a and WHIST 2019a were large publicly funded trials with strong methodology and reporting.

In addition five studies which did not assess cost-effectiveness reported information on dressing costs or resource use (DiMuzio 2017; Gillespie 2015; Javed 2018; Kwon 2018; Manoharan 2016).

Dressing Costs

All five of the cost-effectiveness studies (Heard 2017; Hyldig 2019b; Nherera 2017; Nherera 2018; WHIST 2019b) and two additional RCTs (Gillespie 2015; Manoharan 2016) reported on dressing costs. In each case, NPWT was substantially more costly than the comparator treatment (Table 3). The studies reported dressing costs in different ways, with some summarising for the whole treatment period and others reporting costs per day or per dressing change; the largest trial WHIST 2019b reported a total treatment cost which incorporated the dressing cost but also the fracture cast, initial inpatient care, antibiotics and dressing changes. Cost data for dressings are reported in Table 3. All studies reported that NPWT represented a higher dressing cost than standard dressings.

Resource use

Resource use was costed for all the economic studies based on RCTs and costs related to resource use were also reported by three RCTs which did not undertake a cost-effectiveness analysis (DiMuzio 2017; Javed 2018; Kwon 2018). Data on costs are reported in Table 3. We focus on the information used, together with QALYs, to inform the analyses of cost-effectiveness.

Obstetric surgery: Caesarean sections in obese women

Chaboyer 2014 included obese women undergoing caesarean section (n = 70); Heard 2017, was based on Chaboyer 2014, and assessed resources in AUD at 2014 values. Data on costs were based on dressing costs, nursing time, length of hospital stay, and post-discharge costs (readmission, visits to healthcare professionals, and medications). Heard 2017 reported additional costs of AUD 133 for NPWT over standard dressings. Hyldig 2019a was a much larger trial which also enrolled obese women undergoing caesarean section (n = 876); Hyldig

2019b was based on this study and assessed resources in DK transformed into Euro; they found an additional cost difference of 47.29 Euro for NPWT over standard dressings.

Orthopaedic surgery: lower limb fracture surgery

Participants in WHIST 2019a were undergoing surgery for lower limb fracture; the cost-effectiveness analysis WHIST 2019b was based on this. Unit direct medical costs associated with the intervention were obtained from the NHS Supply Chain Catalogue 2018/2019. These included cost of standard dressing, the costs of orthotic cast, the cost associated with dressing change, the cost per working hour of the nurse (obtained from the Personal Social Service Research Unit (PSSRU) 2018). The cost of inpatient care was derived using NHS reference Costs 2017/18. Unit costs of additional medical items were also sourced from the NHS reference costs and medication costs were sourced from the British National Formulary (BNF). Unit costs for direct non-medical cost items were obtained from Personal Social Services Research Unit. Other costs were obtained from the NHS Supply Chain Catalogue, the patients and their next of kin and the Office for National Statistics. Cost data were derived from the key resource inputs of the WHIST 2019 trial and expressed in 2017/2018 GBP; a societal perspective was considered in a sensitivity analysis. Unit costs were adjusted to 2017/2018 prices using the NHS Hospital & Community Health Services (HCHS) index for health service resources. There was no discounting of costs applied due to a short-time horizon. The total costs up to six months taking an NHS and PSS perspective showed a mean difference of 770.00 GBP (95% CI 206.51 to 1333.49) more for NPWT compared with standard dressing. A societal perspective also showed a greater cost to NPWT but with much wider confidence intervals (MD 221.41 GBP, 95% CI -1334.37 to 1777.19).

Orthopaedic surgery: hip or knee arthroplasty

Participants in the Karlakki 2016 study were those scheduled for routine knee or hip arthroplasties (n = 220). Nherera 2017, was based on Karlakki 2016, and derived costs from standard cost references for the NPWT device from the UK National Drug Tariff and an assumption that each patient used two NPWT dressings. Inpatient care was based on the average of National Health Service reference costs for knee and hip arthroplasties, which, it was assumed, included the cost of the standard care dressing and nursing time. Costs associated with routine postdischarge care were not included because these costs would be similar across groups. Finally, for those who experienced a complication, an assumption was made that they had two general practitioner visits and received one prescription of antibiotics. Resource use was valued in GBP at 2015/16 values. Nherera 2017 reported cost savings of GBP 1132 for NPWT compared with standard dressings

General surgery: CABG surgery

Participants in the Witt-Majchrzac 2015 trial (n = 80) underwent CABG surgery. They contributed clinical data to Nherera 2018 which drew both its utility and cost data from other sources. Nherera 2018 found a cost saving of 586 Euro with NPWT compared with standard dressings.

Quality-adjusted life year (QALY)

Each study took a different approach to the resource use and costs used to inform the model; details are provided in Characteristics of included studies. Three studies did not report SD for the QALY estimates for each group, one study reported 95% CIs for the mean difference in QALY. Given this, we have opted not to impute SD for the majority of studies which do not report them and instead to provide an overall narrative summary.

Across all studies, despite different methods of calculating QALY and the four different surgical indications represented, the differences in QALY between NPWT and standard dressings were uniformly extremely small.

Obstetric surgery: Caesarean sections in obese women

Heard 2017 calculated QALYs using the 12-item Short Form Health Survey (SF-12) version 2, scored with the UK preference-based algorithm (Brazier 2004), Hyldig 2019b calculated QALYs using the EQ-5D-3L utility scores. Hyldig 2019b reported QALY values of 0.863 in the NPWT group compared with 0.856 in the standard dressing group: mean difference 0.007 (95% CI -0.008 to 0.022). Heard 2017 reported QALY values of 0.067 (SD 0.01) in the NPWT group compared with 0.066 (SD 0.01) in the standard dressing group:mean difference 0.00 (-0.00 to 0.01).

Orthopaedic surgery: lower limb fracture surgery

WHIST 2019b calculated QALYs using the EQ-5D-3L utility scores. WHIST 2019b reported QALY values of 0.40 (0.22) for the NPWT group compared with 0.41 (SD 0.24) in the standard dressing group: mean difference -0.01 (95% CI -0.03 to 0.01).

Orthopaedic surgery: hip or knee arthroplasty

Nherera 2017 calculated QALYs using the 36-item Short Form Health Survey (SF-36) with a regression-based scoring algorithm developed from a sample of Jewish Israelis sampled between 1993 and 1994 (Shmueli 1999). Nherera 2017 reported QALY values of 0.116 for the NPWT group compared with 0.115 in the standard dressing group; no SDs were reported.

General surgery: CABG surgery

Nherera 2018 calculated health state utilities to generate QALYs using published literature including a study looking at discharge from hospital with and without complications (Tuffaha 2015). QALY values were reported as 0.8904 in the NPWT group compared with 0.8593 in the standard dressing group.

Across all studies, despite different methods of calculating QALY and the four different surgical indications represented, the differences in QALYs between NPWT and standard dressings were uniformly extremely small.

WHAT'S NEW

Date	Event	Description
9 June 2020	Amended	Republished as Open Access.
2 May 2020	New citation required and conclusions have changed	Updated. Conclusions changed.
2 May 2020	New search has been performed	Third update. New search. 15 new intervention studies and three new economic studies included. Three new co-authors added, En Lin Goh, Chunhu Shi and Adam Reid.

HISTORY

Protocol first published: Issue 8, 2011
Review first published: Issue 4, 2012

Date	Event	Description
1 March 2019	New search has been performed	Second update: new citation: conclusions not changed. New search, 25 new studies included. 'Summary of findings' table added. Four new co-authors added, Gill Norman, Zhenmi Liu, Jo Dumville and Laura Chiverton.
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 (Crist 2014; Masden 2012; Petkar 2012; Stannard 2012), no change to conclusions.
13 November 2013	Amended	Acknowledgement added to the funders.
16 May 2012	Amended	Adjustments to text

CONTRIBUTIONS OF AUTHORS

Gill Norman : designed the review update; coordinated the review update; extracted data; checked quality of data extraction; analysed or interpreted data; undertook quality assessment; checked quality assessment; performed statistical analysis; produced the first draft of the review update; contributed to writing or editing the review update; wrote to study authors/experts/companies; performed economic analysis; approved final review update prior to submission; is guarantor of the review update.

En Lin Goh: extracted data; checked quality of data extraction; analysed or interpreted data; undertook quality assessment; checked quality assessment; checked quality of statistical analysis; contributed to writing or editing the review update; advised on the review update; approved final review update prior to submission.

Jo Dumville: conceived the review; analysed or interpreted data; checked quality of statistical analysis; contributed to writing or editing the review update; advised on the review update; secured funding; approved final review update prior to submission.

Chunhu Shi: extracted data; checked quality of data extraction; analysed or interpreted data; undertook quality assessment; checked quality assessment; contributed to writing or editing the review update; performed economic analysis; approved final review update prior to submission.

Zhenmi Liu: extracted data; undertook quality assessment; contributed to writing or editing the review update; approved final review update prior to submission.

Laura Chiverton: extracted data; checked quality of data extraction; contributed to writing or editing the review update; approved final review update prior to submission.

Monica Stankiewicz: extracted data; undertook quality assessment; contributed to writing or editing the review update; approved final review update prior to submission.

Adam Reid: checked quality of data extraction; analysed or interpreted data; contributed to writing or editing the review update; advised on the review update; approved final review update prior to submission.

Contributions of editorial base

Nicky Cullum (Coordinating Editor): advised on methodology, interpretation, and content; edited and approved the review update prior to publication.

Gill Rizzello (Managing Editor): coordinated the editorial process; advised on interpretation, and content; edited the updated review.

Sophie Bishop (Information Specialist): edited the search methods section and search strategy and ran the search for this update.

Tom Patterson (Editorial Assistant): edited the plain language summary and reference sections for this update.

DECLARATIONS OF INTEREST

Gill Norman: my employment at the University of Manchester was funded by the National Institute for Health Research and focused on high-priority Cochrane Reviews in the prevention and treatment of wounds. My work on this review was supported by the NIHR Manchester Biomedical Research Centre.

En Lin Goh: none known.

Jo Dumville: I received research funding from the NIHR for the production of systematic reviews focusing on high-priority Cochrane reviews in the prevention and treatment of wounds. This research was co-funded by the NIHR Manchester Biomedical Research Centre and partly funded by the National Institute for Health Research Collaboration for Leadership in Applied Health Research and Care (NIHR CLAHRC) Greater Manchester.

Chunhu Shi: none known.

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

Laura Chiverton: my work on this review was supported by the NIHR Manchester Biomedical Research Centre.

Monica Stankiewicz: none known.

Adam Reid: none known.

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Internal sources

- Royal Brisbane and Women's Hospital, Australia

  Time to conduct review
- Griffith University, Australia

  Time to conduct review
- Division of Nursing, Midwifery and Social Work, School of Health Sciences, Faculty of Biology, Medicine and Health, University of Manchester, UK

External sources

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

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- National Institute for Health Research (NIHR) Systematic Review Fellowships (NIHR-RMFI-2015-06-52 Zhenmi Liu), UK
- National Institute for Health Research Collaboration for Leadership in Applied Health Research and Care (NIHR CLAHRC) Greater Manchester Centre, UK

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- NIHR Manchester Biomedical Research Centre, UK

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DIFFERENCES BETWEEN PROTOCOL AND REVIEW

Changes in the 2020 update

- We have excluded one study which was previously included in error; it did not report an eligible comparison.
- We have made some changes to the inclusion criteria; primarily to clarify that trials in wounds with pre-existing infections were excluded from the review. We have also removed the outcomes of dressing cost, resource use and QALY measures as independent outcomes. We have continued to record information on these and have presented it in additional tables and an appendix to the review but we have shifted the focus of the cost-effectiveness review to assessments of relative cost-effectiveness reported as ICERs.
- We have clarified that we extracted and reported data on adverse events such as seroma and haematoma only as the number of participants in each group with an event.
- We have altered the way in which we dealt with the likelihood of performance bias in included studies in order to better recognise the role this may play even in trials in which it is hard to avoid.
- We have undertaken some exploratory analyses of the primary outcome of SSI to see if there is the potential for additional research into the impact of NPWT on SSI classed as superficial or deep and we have also undertaken an additional sensitivity analysis to further explore the impact of risk of bias on the effect estimate and its confidence intervals for this outcome.
- We have somewhat revised our approach to GRADE assessments in terms of risk of bias and have only downgraded where high risk of bias was present and the potential impact of this was considered substantive. Previously we had downgraded where key domains had an unclear risk of bias. This new approach reflects the advice from GRADE working group.
- We have removed readmission to hospital from the 'Summary of findings' table in order to conform with MECIR guidance that this should include no more than seven outcomes.

Changes in the 2019 update

- We changed the title and the focus of the review. In previous versions, we included studies that investigated skin grafts and also those investigating surgical wounds expected to heal by primary intention. In the 2019 version of the review, we did not include studies of skin grafts. This decision was made after consultation with the Editorial base and was based on the following considerations: the healing mechanisms and outcome measures are different for graft sites and incisional wounds, so there was a clear, clinical reason for focusing on one type of wound; we also clarified that trials using NPWT following surgery that involved harvesting veins following flap elevation would also be excluded. Outcomes measures from these trials (such as flap necrosis, lymphorrhagia, and lymphoedema) also differed from primary closure surgery. In addition, the number of trials reporting outcomes following the application of NPWT has been growing exponentially, with the majority of these trials focusing on previously uninvestigated types of surgery using primary closure. Because of this, it seemed timely to focus this review only on 'primary closure' surgery.
- We modified the wording of the title from 'primary intention' to 'primary closure'. The wording change was needed because closure by primary intention would mean the inclusion of grafts and flap surgery trials, whereas primary closure means the surgical edges are approximated and held together with sutures, glue, etc. Primary closure is the simplest closure technique and more accurately reflects the intention of the review.
- We removed the outcome 'graft failure' in line with the new focus of the review.
- We removed the outcome 'time to complete healing', as this outcome was deemed not to be appropriate for surgical wounds expected to heal by primary intention (it is difficult or impossible to determine or define the point of healing for a wound healing in this way).

For this reason, 'proportion of surgical wounds healing by primary intention that completely heal' was removed for the first update and 'reoperation' added (see also 'Changes in previous versions' below).

- We added one additional outcome: 'readmission within 30 days for a wound-related complication'. We believe this outcome is important because, while readmission for repeat surgery is one of our current outcomes, the reason for readmission is not always stated in study reports.
- We split 'adverse events' into 'surgical site infection' and 'dehiscence'.
- We removed the words 'and including utility scores representing health-related quality of life' from the outcome 'healthcare costs' and included it under the outcome 'quality of life'.
- We split one of our secondary outcomes, 'seroma/haematoma', into two separate outcomes. This decision was based on differing definitions and aetiologies of the two conditions. A seroma is a collection of clear, serous fluid, which sometimes collects under a surgical wound, whereas a haematoma is a collection of blood outside a blood vessel.
- We changed the outcome 'fracture blisters' to 'skin blisters', as some blisters are associated with dressings that cover wounds from surgery that is not fracture surgery.
- We have split 'cost' into four separate outcomes: 'dressing-related costs', 'resource use', 'incremental cost per quality-adjusted life year', and 'estimated incremental cost-effectiveness ratio'.
- We broke up costs into two categories. The first ('dressing-related costs') is a simple cost comparison from the intervention study reports, and the second ('cost') is a full economic analysis from the two cost-effectiveness studies. This analysis contains three outcomes: resource use, incremental cost per quality-adjusted life year, and estimated incremental cost-effectiveness ratio.
- We added three additional items of data extraction: 'source of funding', 'prospective registration on a clinical trials registry', and 'economic data (healthcare costs)'. We made these additions to reflect the importance of prospective registration in the assessment of risk of bias in several domains, and in response to the insistence in many quality journals on prospectively registering clinical trials as a quality measure.
- We updated our search strategies, adding new terms for negative pressure wound therapy, and changed the term 'surgical' to 'surgical site infection' in the trial registries' search.
- We included an additional (standard) sensitivity analysis with the following wording: "We performed a sensitivity analysis on the primary outcomes (surgical site infection) to assess the influence of removing studies classified as being at high risk of bias from the meta-analysis. We excluded studies that were assessed as having high or unclear risk of bias in the key domains of adequate generation of the randomisation sequence, adequate allocation concealment, and blinding of outcome assessor. We planned but were unable to undertake a similar analysis for the outcome of dehiscence."
- We removed allocation concealment and type of randomisation from the sensitivity analyses; they are included in the new sensitivity analyses described above. We removed duration of follow-up from the sensitivity analyses.
- We changed one subgroup analysis from 'type of surgery (traumatic wounds, reconstructive procedures, other post-surgical wounds; skin grafts)' to 'type of surgery' without qualification.
- We removed one comparison (industry funded versus non-industry funded) following advice from the Editorial base. We removed one comparison (one negative pressure closure method compared with another), as the study providing data for this comparison, Dorafshar 2012, has now been excluded in line with the new focus of the review on surgical wounds healing by primary closure only.
- We updated the methods used to assess heterogeneity and taken this into account in our analyses; we changed methods of analysis as appropriate to the evidence that is now included in this updated version.
- We used the method for classifying economic evaluation described by Husereau and colleagues (Husereau 2013), rather than the evaluation described by Drummond 2005. This decision was based on the knowledge that the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) checklist has become the standard for economic evaluations. The checklist was developed in collaboration with a range of organisations, and includes Drummond as a co-author.
- We added a 'Summary of findings' table to the review and used a GRADE assessment of the certainty of the evidence throughout.

Changes to previous versions

We added a comparison (one negative pressure closure method compared with another) to the previous version of this review, but this has now been removed (see comment above).

We expanded the list of extracted data from the protocol 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 protocol for the original review. We also failed to include length of hospital stay, which is important for any economic analysis. Consequently, we included graft failure and length of hospital stay as additional outcomes post hoc.

- In a previous update, we removed the 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)". This 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, we considered any wound complications under the heading 'adverse events'. As many of these 'events' are qualitatively different and of varying levels of importance, we subsequently included only 'surgical site infection' and 'dehiscence' under the heading 'adverse events'. We moved other wound-related outcomes that were previously included under the primary outcome 'adverse events' (such as fracture blisters, seromas, etc.) to the secondary outcomes. We changed 'graft loss' to 'graft failure' and added it as a separate outcome because it is an important outcome for skin graft studies, and in our protocol we did not include any outcomes that were specific to skin grafts. We also added a new secondary outcome, 'reoperation', as this is an important outcome that indicates the severity of any wound dehiscence or graft loss.
- We changed the wording in the sections 'Unit of analysis issues' (we had not anticipated in the original version of the review that multiple wounds might be an issue) and 'Dealing with missing data' (to clarify what we intended to do).

INDEX TERMS

Medical Subject Headings (MeSH)

Bandages; Blister [epidemiology]; Hematoma [epidemiology]; Negative-Pressure Wound Therapy [economics] [instrumentation] [*methods] [mortality]; Orthopedic Procedures; Quality-Adjusted Life Years; Randomized Controlled Trials as Topic; Reoperation [statistics & numerical data]; Seroma [epidemiology]; *Skin Transplantation; Surgical Procedures, Operative [mortality]; Surgical Wound Dehiscence [epidemiology] [*prevention & control]; Surgical Wound Infection [epidemiology] [*prevention & control]; *Wound Healing; Wounds and Injuries [surgery]

MeSH check words

Humans