TECHNOLOGY REVIEW (MINI-HTA)

NEGATIVE PRESSURE WOUND THERAPY

Malaysian Health Technology Assessment Section (MaHTAS)
Medical Development Division
Ministry of Health Malaysia
004 /2023

Malaysian Health Technology Assessment Section (MaHTAS)
Medical Development Division
Ministry of Health Malaysia
Level 4, Block E1, Precinct 1
Government Office Complex
62590, Putrajaya
Tel: 603 8883 1229

Available online via the official Ministry of Health Malaysia website: http://www.moh.gov.my

CITATION:
Erni ZR, KNK Abd Rahim and Izzuna MMG. Negative Pressure Wound Therapy. Ministry of Health Malaysia: Malaysian Health Technology Assessment Section (MaHTAS); 2023. 60 p. Report No.: 004/2023.

DISCLOSURE: The author of this report has no competing interest in this subject and the preparation of this report is entirely funded by the Ministry of Health Malaysia.

AUTHORS

Dr. Erni Zurina Romli
Senior Principal Assistant Director
Malaysian Health Technology Assessment Section (MaHTAS)
Medical Development Division
Ministry of Health Malaysia

Madam Ku Nurhasni Ku Abd. Rahim (Pharmacist)
Senior Principal Assistant Director
Malaysian Health Technology Assessment Section (MaHTAS)
Medical Development Division
Ministry of Health Malaysia

Dr. Izzuna Mudla Mohamed Ghazali
Public Health Physician
Deputy Director
Malaysian Health Technology Assessment Section (MaHTAS)
Medical Development Division
Ministry of Health Malaysia

EXTERNAL REVIEWER

Dato' Dr. Harikrishna K.R. Nair
Head of Wound Care Unit
Hospital Kuala Lumpur

EXECUTIVE SUMMARY

Background

Wound care is particularly challenging in the face of demographic shift towards ageing population and the rising trend of obesity as well as non-communicable diseases, such as diabetes mellitus, hypertension and chronic kidney disease. In Malaysia, the management of chronic wound such as diabetic foot ulcer bring about a total cost per patient per annum of MYR 5,981 in public and MYR 8,581 in private setting, with more than 260,000 people with diabetes estimated to have foot ulcers at any given time. The surgical site infections represent significant burden in the management of surgical wounds. They are associated with prolonged hospitalisation, time spent in an intensive care unit (ICU), readmission to hospital, long-term disability, the spread of antibiotic resistance, substantial financial burden and high costs for patients and families. There is a wide range of treatment modalities used for acute and chronic wounds. With the advancement in the therapeutic and clinical management for wound healing and tissue regeneration, an instrumental-based therapy called negative pressure wound therapy (NPWT) is slowly gaining popularity as adjunct wound treatment to facilitate fast healing of acute and chronic wounds.

Objective

The objective of this systematic review and economic evaluation was to assess the effectiveness, safety and cost-effectiveness of NPWT as a treatment modality for acute and chronic wounds.

Methods

Part A: Systematic review

A comprehensive search was conducted on the following databases without any restriction on publication language and publication status. The Ovid interface: Ovid MEDLINE(R) ALL <1946 to May 22, 2023>; EBM Reviews - Cochrane Database of Systematic Reviews <2005 to May 16, 2023>; EBM Reviews - NHS Economic Evaluation Database <1st Quarter 2016>. Searches were also run in PubMed. Google was used to search for additional web-based materials and information. Additional articles were identified from reviewing the references of retrieved articles. Last search was conducted on 22 May 2023.

Part B: Economic evaluation

A decision tree was developed in Microsoft Excel to estimate the expected costs and health outcomes associated with the use of NPWT and standard of care in reducing surgical site infection. The base case analysis provides the expected cost and outcome when the intervention was given to adult patients who undergone surgeries. The analysis was conducted using the healthcare provider perspective and considers a short-term time horizon on the basis that surgical complications may occur relatively soon after surgery.

Results and Conclusions

Part A: Systematic review

A total of 9,059 titles was identified through the Ovid interface and PubMed. After removing the duplicates, appraising and applying the inclusion and exclusion criteria, only 27 full text articles were eligible to be included for qualitative synthesis. The selected full text articles comprised of 11 systematic reviews and meta-analyses, and 16 economic evaluation studies.

Effectiveness

Ten systematic reviews and meta-analyses reported on the effectiveness of NPWT as treatment modality for acute and chronic wounds.

Five studies reported on the outcome of surgical site infection for closed surgical wounds. The findings showed that across a range of surgical indications, NPWT following surgery resulted in a lower risk of surgical site infection and wound dehiscence compared with standard dressings. (**Table 1**)

Another six included studies reported on the outcome of the effect of NPWT on wound healing. The NPWT had better effect on wound healing compared to standard care across various type of acute and chronic wounds heal by secondary intention except for lower limb open fracture wounds. There was uncertainty of evidence on the benefit of NPWT on open abdominal wound in view of heterogenous pooling results. (**Table 2**)

Table 1: Comparison of NPWT with standard wound dressings for outcome of surgical site infection and wound dehiscence in closed surgical incisions

STUDY	Surgical Site Infection	Wound dehiscence
Overall Population		
Cochrane review (2022) (62 RCTS)	**Pooled RR** 0.73, 95%CI 0.63 to 0.85	**Pooled RR** 0.97, 95%CI 0.82 to 1.16
Subpopulation: Caesarean section in women with obesity		
Angarita AM et al (2021) SR & Meta-analysis (11 RCTs)	**Pooled RR** 0.79, 95%CI 0.65 to 0.96	**Pooled RR** 0.99, 95%CI 0.79 to 1.24
Subpopulation: Closed incisions in breast surgery		
Song J et al. (2023) SR & Meta-analysis (12 RCTs)	**Pooled OR** 0.59, 95%CI 0.36 to 0.96	**Pooled OR** 0.54, 95%CI 0.39 to 0.75
Subpopulation: Sternal wound post cardiac surgery		
Biancari F et al. (2022) SR & Meta-analysis (2 RCTS and 8 cohort studies)	**Pooled RR** 0.54, 95%CI 0.34 to 0.84	-

Subpopulation: Closed surgical wound after orthopaedics trauma surgery		
Xie W et al. (2021) SR & Meta-analysis (4 RCTs and 8 cohort studies)	Superficial SSI: **Pooled OR** 0.23, 95%CI 0.11 to 0.49 Deep SSI: **Pooled OR** 0.65, 95%CI 0.48 to 0.88	**Pooled OR** 0.41, 95%CI 0.21 to 0.80

Table 2: Comparison of NPWT with standard wound dressings for outcome of wound healing in wounds heals by secondary intention

STUDY	**Outcome of wound healing**
Overall Population	
Zens Y et al. (2020) SR & Meta-analysis (48 RCTs)	**Pooled OR** 1.56, 95%CI 1.15 to 2.13
Subpopulation: Open surgical abdominal wounds	
Cirocchi R et al. (2016) SR & Meta-analysis (2 RCT and 4 cohort studies)	**Fascial closure:** Pooled OR 0.74, 95%CI 0.27 to 2.06, p=0.57, I^2 83% **Postoperative enteroatmospheric fistulae rate**: Pooled OR 0.63, 95%CI 0.12 to 3.15; p = 0.57, I^2 69% **Postoperative abdominal abscess rate**: Pooled OR 0.42, 95%CI 0.13 to 1.34, p = 0.14, I^2 54% **Postoperative mortality rate**: Pooled OR 0.46 95%CI 0.23 to 0.91, p = 0.03, I^2 72%
Subpopulation: Open fracture wounds	
Cochrane review (2018) (4 RCTs)	At 6 weeks: Pooled RR 1.01, 95%CI 0.81 to 1.27
Subpopulation: Burn wounds	
Lin DZ et al. (2021) SR & Meta-analysis (6 RCTs)	**Graft take rate at the first week:** SMD 2.62, 95%CI 1.01 to 4.22, p = 0.001 **Infection rate at the first week:** Pooled OR 0.12, 95%CI 0.02 to 0.87, p = 0.04
Subpopulation: Chronic wound – Diabetic foot ulcers	
Chen L et al. (2021) SR & Meta-analysis (9 RCTs)	**Healing rate :** Pooled OR 3.6, 95%CI 2.38 to 5.45, p < 0.001 **Granulation tissue formation time:** MD (in days) -8.95, 95%CI -10.26 to -7.64, p<0.001
Subpopulation: Chronic wound - Grade III/IV pressure ulcers	
Song YP et al. (2021) SR & Meta-analysis (16 RCTs)	**Healing rate** : Pooled RR 1.32, 95%CI 1.32 to 1.70 **Wound healing time**: WMD (in days) -16.47, 95%CI -22.36 to -10.59, p< 0.001

Safety

NPWT is considered a safe treatment. Treatment related adverse events includes allergic skin reaction and skin blister, which are comparable to standard wound care. Serious adverse events like bleeding, infection, injuries and death are rare. They are mostly associated with unsafe use of NPWT.

Cost-effectiveness

Sixteen economic evaluation studies reported on the cost-effectiveness of NPWT as treatment modality for acute and chronic wounds. The included studies comprised of 12 cost-effectiveness analyses, one budget impact analysis and three cost analyses, comparing NPWT with standard care. Most studies were conducted from the perspective of healthcare provider in hospital setting. They were mostly from United Kingdom, USA and European countries.

Evidence from economic evaluation studies tend to suggest that NPWT is likely to be cost saving treatment in the management of wound, particularly in high risk patients with BMI ≥ 35 and severe systemic disease.

Part B: Economic evaluation

The use of NPWT was found to be effective with an estimated additional cost incurred compared with standard of care. In order to improve the access to this treatment in a resource limited setting, a careful selection of patient would ensure the optimal benefit of NPWT as an alternative option for wound management.

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ABBREVIATION

AE	adverse event
CI	confidence interval
DFUs	diabetic foot ulcers
ICER	incremental cost-effectiveness ratio
LOS	length of hospital stay
MD	mean difference
MOH	ministry of health
NHS	National Health Service
NPWT	negative pressure wound therapy
OR	odd ratio
PAD	peripheral vascular disease
ROBIS	risk of bias in systematic reviews
RR	relative risk
SSI	surgical site infection
U.S.FDA	U.S. Food and Drug Administration
VAC	vacuum-assisted closure

1.0 BACKGROUND

Burden of Wound Care

Wound care is particularly challenging in the face of demographic shift towards ageing population and the rising trend of obesity as well as non-communicable diseases, such as diabetes mellitus, hypertension and chronic kidney disease.[1] The elderly population is more prone to acute and chronic wounds as well as diabetic foot ulcer. Patients suffer from diabetes mellitus have 15% to 25% chances of developing diabetic foot ulcer during their lifetime.[2] It is estimated that a global prevalence rate of 12.8% for pressure ulcer in hospitalised patients, many of which are acquired during hospitalisation for an acute episode of illness or injury.[3] Around the world, wounds may pose a significant clinical and economic burden to healthcare systems, and social burden to society at large. Based on a retrospective analysis of 5% of the Medicare dataset, including both acute and chronic wounds, it was estimated that 8.2 million Medicare beneficiaries had at least one type of wound, with financial burden to Medicare ranging from USD $28.1 billion to USD $96.8 billion in the United States (US) in 2014.[4] In 2012, the cost associated with wound management in United Kingdom (UK) was estimated at £4.5 to £5.1 billion.[5] The annual prevalence of wounds increased by 71% between 2012/2013 and 2017/2018. There was a substantial increase in resource use over this period and patient management cost increased by 48% to £8.3 billion in real terms, of which £5.6 billion was associated with managing unhealed wounds.[5, 6] Eighty-one per cent of the total annual UK's National Health Service (NHS) cost was incurred in the community.[6] Similarly, in Singapore's second largest hospital, between 2013 and 2017, there were a total of 56,583 wound-related inpatient admissions for 41,461 patients, with a 95.1% increase in wound episodes (142 and 277 wound episodes per 1000 inpatient admissions in 2013 and 2017, respectively).[7] Based on 2017 dataset, the gross healthcare costs for all inpatient wound episodes stand at USD $216 million (SGD $293 million) within hospital care and USD $596,000 (SGD $807,000) within primary care settings. The average gross charge per wound episode was USD $12,967 (SGD $17,558).[7] The average length of stay for each wound episode was 17.7 days, which was 2.4 times that of an average acute admission. Among the 12,218 patients with 16,674 wound episodes in 2017, 71.5% were more than 65 years of age with an average Charlson Comorbidity Index of 7.2.[7] In Malaysia, the management of chronic wound such as diabetic foot ulcer bring about a total cost per patient per annum of MYR 5,981 in public and MYR 8,581 in private setting, with more than 260,000 people with diabetes estimated to have foot ulcers at any given time.[8] Outpatient visits cost represents 50% of the overall cost. Meanwhile, based on three local studies, the incidence of surgical site infections (SSIs) in Malaysia ranged between 11.7% to 17.2%.[9-11] The SSIs represent significant burden in the management of surgical wounds. They are associated with prolonged hospitalisation, time spent in an intensive care unit (ICU), readmission to hospital, long-term disability, the spread of antibiotic resistance, substantial financial burden and high costs for patients and families.[12]

Treatment Modalities in Wound Care

There is a wide range of treatment modalities used for acute and chronic wounds, which includes swabbing for infection, cleaning the wound bed from the tissue debris, tissue transplantation, platelet therapy, cell therapy, applying wound dressing and instrumental methods.[3] The choice of treatments depends on the type of wound, treatment setting (varies from home care to highly specialized hospital care) and healthcare resources. Wound dressing still remains a preferred choice of wound treatment due to ease of application and economically cheaper.[3] With the advancement in the therapeutic and clinical management for wound healing and tissue regeneration, an instrumental-based therapy called negative pressure wound therapy (NPWT) is slowly gaining popularity as adjunct wound treatment to facilitate fast healing of acute and chronic wounds.[13] Its popularity is attributed to wide marketing, assumed safety and recent improvement made to device, such as increased accuracy and efficiency in smart pressure portable device.[14] Despite having higher material cost compared to traditional wound dressing, it is claimed that the cost may be offset by the benefits of reduced healing time, reduced nursing staff time and expense, decreased length of hospital stay and facilitation of patient transfer to lower-cost care settings.[13]

2.0 OBJECTIVE

The objective of this systematic review and economic evaluation was to assess the effectiveness, safety and cost-effectiveness of NPWT as a treatment modality for acute and chronic wounds.

3.0 TECHNICAL FEATURE

Negative pressure wound therapy is a therapeutic dressing system, intended for use to facilitate wound healing and prophylactically prevent surgical site complications especially surgical site infection (SSI). The NPWT includes a sealed dressing over a wound, a suction pump that creates the negative pressure to the wound surface and a drainage tube going from inside the dressing or its surface to a canister within the pump unit (Figure 1). [15] The wound is covered or packed with an open-cell foam (Figure 2A) or gauze dressing (Figure 2B) and sealed with an occlusive drape.[16] Dressings are usually changed two to three times per week. The therapy is delivered by a stationary or portable vacuum pump, and pressure can be applied either continuously or intermittently. Negative pressure settings range from -50 mmHg to -125 mmHg.[17] Hence, the prescription of NPWT should specify the type of wound filling material (foam or gauze dressing and any wound adjunct, such as a protective nonadherent, petrolatum or silver dressing), negative pressure setting, therapy setting (continuous, intermittent or variable) and frequency of dressing changes.

There are a broad range of NPWT devices in the market, produced by different manufacturers for different applications with varying features, wear times (ranging from seven to 30 days), fluid handling properties and cost.[18] The NPWT has been used as treatment modality for wound since the late 1990s.[17] The longest-established device is the vacuum-assisted closure (VAC) system (V.A.C.®, a registered trademark

of KCl).[19] In 2010s, the portable version of NPWT device made its way into the market for the use in the community setting.[20, 21] Today, NPWT is based on newer technologies such as computer-assistance, small hand-held and mechanically powered devices as well as additional feature of instilling sterile water, saline, topical antiseptics or topical antibiotics, making NPWT to have more diversified portfolio of wound care.[14]

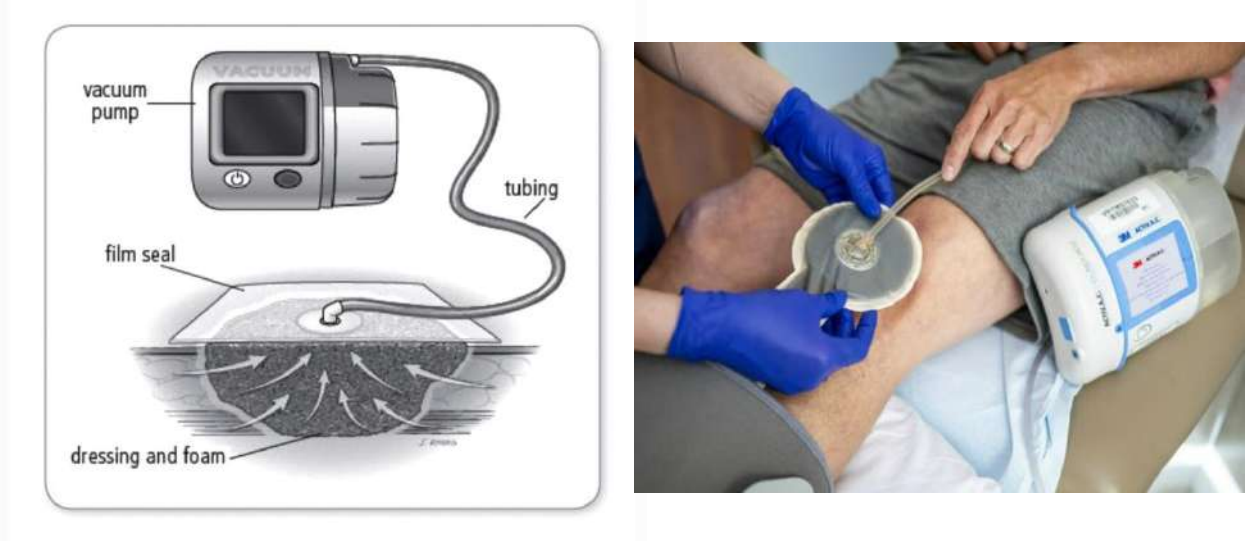
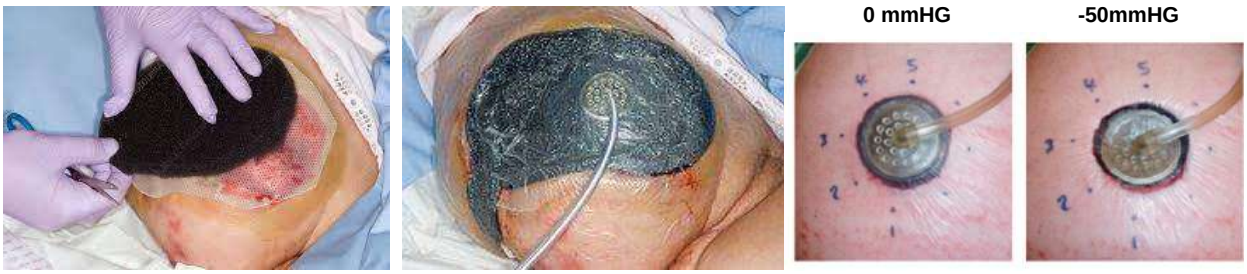
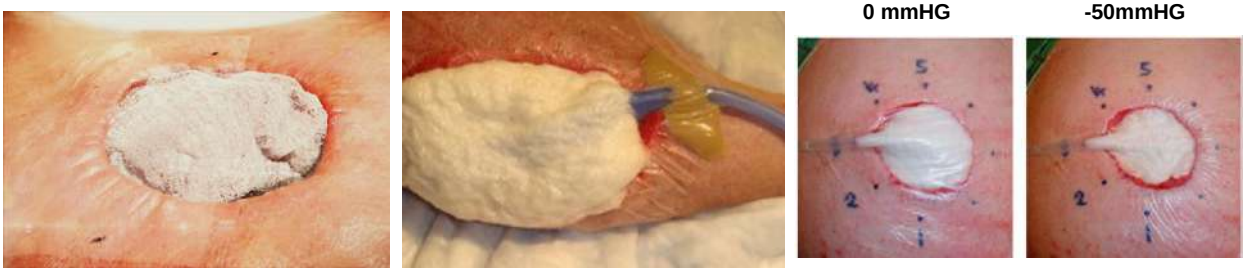


Figure 1: Negative Pressure Wound Therapy [15]



(A) Open-cell foam dressing



(B) Gauze dressing

Figure 2: Application of negative pressure wound therapy, showing open cell foam (A) or gauze (B) as contact layer through which sub atmospheric pressure is applied, once the area has been sealed with an impermeable, adhesive drape. As the negative pressure is applied, the dressing takes on a hard and wrinkled appearance. [16]

4.0 METHODS

4.1 PART A: SYSTEMATIC REVIEW OF LITERATURE

4.1.1 Searching

A comprehensive search was conducted on the following databases without any restriction on publication language and publication status. The Ovid interface: Ovid MEDLINE(R) ALL 1946 to May 22, 2023; EBM Reviews - Cochrane Database of Systematic Reviews 2005 to May 16, 2023; EBM Reviews - NHS Economic Evaluation Database 1st Quarter 2016. Searches were also run in PubMed. Google was used to search for additional web-based materials and information. Additional articles were identified from reviewing the references of retrieved articles. Last search was conducted on 22 May 2023.

Appendix 1 showed the detailed search strategies.

4.1.2 Selection

A reviewer screened the titles and abstracts against the inclusion and exclusion criteria and then evaluated the selected full text articles for final article selection. The selection of articles was done by one reviewer and reviewed by another reviewer.

The inclusion and exclusion criteria were:

Inclusion criteria

Population/ Problem	Adult patients with acute or chronic wound healing either by primary or secondary intention
Interventions	Negative pressure wound therapy
Comparators	Standard wound care
Outcomes	**i.** Efficacy: surgical site infection, wound healing **ii.** Safety: adverse events or procedure-related complications **iii.** Economic implication (cost, cost-effectiveness)
Study design	Health Technology Assessment (HTA), Systematic Review, Meta-analysis Randomised Controlled Trial (RCT), Non-randomised trial, cohort, case-control, cross-sectional and economic evaluation studies.
	English full text articles

Exclusion criteria

Study design	Studies conducted in animals, case series or case reports
	Non English full text articles

Relevant articles were critically appraised using The Cochrane Collaboration's tools. Data were extracted and summarised in evidence table as in Appendix 2.

4.2 PART B: ECONOMIC EVALUATION

A simplified decision tree model was constructed using TreeAge Pro® and Microsoft Excel to estimate the expected costs and health outcomes associated with the use of NPWT and standard of care in reducing SSI (Figure 3).

The base case analysis provides the expected cost and outcome when the intervention was given to adult patients who undergone surgery. The analysis was conducted using the healthcare provider perspective and considers a short-term time horizon on the basis that surgical complications may occur relatively soon after surgery.

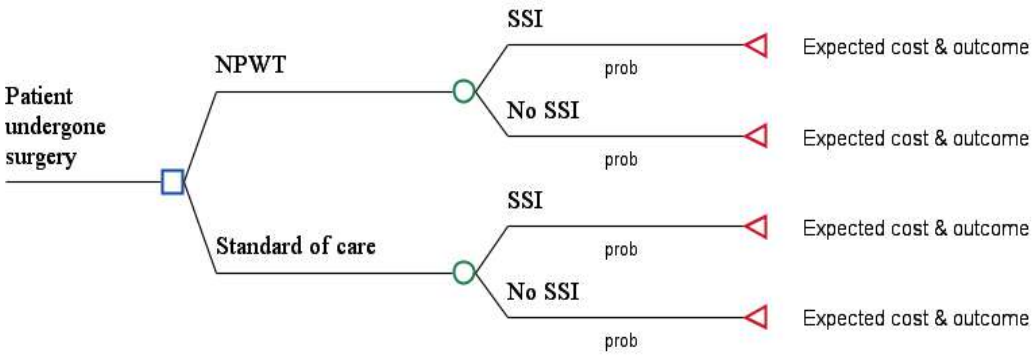


Figure 3: Decision tree model

The parameter used in this analysis is illustrated as Table 1. The estimated SSI risk reduction was based on closed surgical wounds. The cost parameters included in this analysis was based on direct medical costs from Ministry of Health (MOH) perspective. The cost of NPWT devices and consumables range from MYR550.00 to MYR32,500.00. For the equivalent annual cost for reusable equipment calculation, a 5% interest rate was applied with an estimated lifespan of five years to determine the annuity factor. The equivalent annual cost per patient were calculated by dividing the economic cost of capital with the number of patients over the use of equipment per year. Maintenance cost was also included in the equivalent annual cost calculation using the equation as described in the published literature.[22, 23]

Table 1: Model parameter

Parameter	Estimate	Source
Incidence of SSI	11.7% - 17.2%	[9, 10]
SSI risk (pooled RR)	0.73	[17]
Standard of care	MYR 525	[8]
Average cost of hospitalisation (SSI) (Year 2017-2020)	MYR5,981.63 - MYR 11,911.81	[24]
Proportion of single use	50%	*estimate

Several assumptions were applied during the model construct and analysis. The assumptions were derived based on the available literature and local data. For the calculation of equivalent annual cost, the estimated average number or patient using one unit of NPWT device is approximately four patients per month with average of one unit consumable used by each patient. One time visit for follow up is required for NPWT patients and double the frequency of follow up for standard of care. All patients were hospitalised to receive treatment of SSI, but no difference was assumed for surgical related hospitalisation cost. In view of the variation of NPWT sets, single use NPWT was used for patient with no SSI.

5.0 RESULTS

5.1 PART A: SYSTEMATIC REVIEW OF LITERATURE

A total of 9,059 titles was identified through the Ovid interface and PubMed, and 11 titles were identified from references of retrieved articles. After removal of duplicate articles, 4,389 titles were screened using the inclusion and exclusion criteria. Of these, 219 relevant abstracts were retrieved in full text. After reading, appraising and applying the inclusion and exclusion criteria, only 25 full text articles were eligible to be included for qualitative synthesis. The 26 selected full text articles comprised of 11 systematic reviews and meta-analyses, and 15 economic evaluation studies. The selection of studies is as shown on Figure 4.

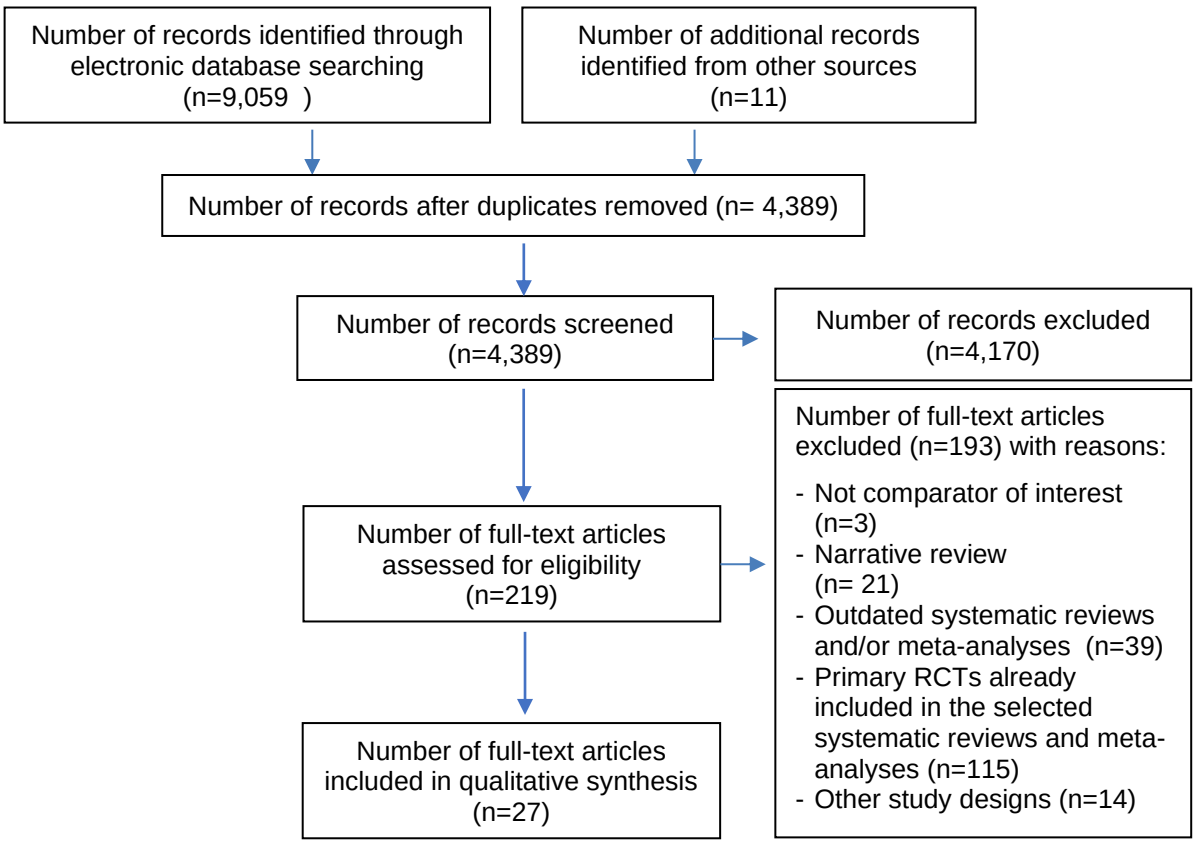


Figure 4: Flow chart of study selection

Assessment of risk of bias in included studies

Risk of bias was assessed using Risk of Bias in Systematic reviews (ROBIS) for systematic review and meta-analysis. These assessments involved answering a pre-specified question of those criteria assessed and assigning a judgement relating to the risk of bias.

Risk of bias assessment for included systematic review and meta-analysis

Eleven included systematic review and meta-analysis were rated to have an overall low risk of bias. All the studies had pre-specified their clinical questions and inclusion criteria for study eligibility. No language restriction was applied in any of the study. The method used to identify and select the studies was clearly described. All studies provided the search terms and the full search strategy used. The inclusion assessment, appraisal and data collection process were reported to have been conducted independently by at least two reviewers. The quantitative synthesis (meta-analysis) undertaken was considered appropriate. Statistical heterogeneity was addressed accordingly, and sensitivity analyses were used to assess the robustness the findings. (Table 2)

Table 2: Summary of risk of bias assessment for systematic review and meta-analysis using ROBIS

REVIEW	D1	D2	D3	D4	OVERALL
Norman et al.[17]	+	+	+	+	+
Angarita AM et al.[26]	+	+	+	+	+
Song J et al.[27]	+	+	+	+	+
Biancari F et al.[28]	+	+	+	+	+
Xie W et al.[29]	+	+	+	+	+
Zens Y et al.[30]	+	+	+	+	+
Cirocchi R et al.[31]	+	+	+	+	+
Iheozor-Ejiofor et al.[32]	+	+	+	+	+
Lin DZ et al.[33]	+	+	+	+	+
Chen L et al.[34]	+	+	+	+	+
Song YP et al.[35]	+	+	+	+	+

Domains
D1: Study eligibility
D2: Identification and selection of studies
D3: Data collection and study appraisal
D4: Synthesis and findings

Judgement
High risk
Unclear
Low risk

5.1.1 EFFECTIVENESS

Closed surgical incisions

An updated Cochrane review (2022), assessed the effects of NPWT for preventing surgical site infection (SSI) in wounds healing through primary closure.[17] A total of 62 RCTs with 13,340 patients was included in the review. The studies evaluated a wide range of surgeries, including orthopaedics, obstetric, vascular and general procedures. All studies compared NPWT (delivered by any mode, or simple closed-system suction drainage; continuously or intermittently over any time period and at any pressure) with standard dressings (gauze, silver or iodine-impregnated dressings, steri-strips). Most studies was judged by Cochrane authors to have unclear or high risk of bias for at least one key domain. The results showed a moderate-certainty evidence across a range of surgical indications that NPWT following surgery probably resulted in a lower risk of SSI compared with standard dressings [pooled relative risk (RR) was 0.73 [95% Confidence Interval (CI) 0.63 to 0.85], p<0.0001; I^2 29%]. There was no significant difference in dehiscence between participants treated with NPWT and those treated with standard dressings following surgery [pooled RR 0.97 (95%CI 0.82 to 1.16, p=0.76; I^2 4%). There was no clear difference in reoperation rate and wound-related readmission to hospital where most evidence was low or very low certainty.[17]

A systematic review and meta-analysis by Shiroky J et al. (2020) reported a significant reduction in length of stay (LOS) among NPWT patients compared to standard dressing in four studies involving vascular and lower limb surgeries [pooled mean difference (MD) -1.17 days, 95%CI -2.19 to -0.16, p=0.02; I^2 43%] and in another two studies [median and interquartile range days: 6.0 (6.0 - 9.0) versus 10.0 (7.0 -13.0), n = 60; and mean 6.1 versus 14.7 days, n= 49, respectively]. However, there was no difference in LOS across treatment arms in the other 12 included studies of various surgical procedures in the review. [25]

Subpopulations

a. <u>Caesarean section in women with obesity</u>

Angarita AM et al (2021) performed a systematic review and meta-analysis of 11 RCTs evaluating prophylactic use of NPWT in reducing wound complications among women with obesity after caesarean delivery compared with standard postoperative dressings.[26] There was a significantly decreased risk of wound infection favouring NPWT compared with standard dressing (pooled RR 0.79, 95%CI 0.65 to 0.96, I^2 0%; nine studies). However, there was no difference in the risk of wound dehiscence (pooled RR 0.99, 95%CI 0.79 to 1.24, I^2 11%; eight studies), seroma (pooled RR 1.03, 95%CI 0.67 to 1.58, I^2 0%; five studies), haematoma (pooled RR 0.83, 95%CI 0.38 to 1.81, I^2 22%; six studies), readmission for wound complications (pooled RR 1.41, 95%CI 0.88 to 2.27, I^2 0%; six studies), antibiotic use (pooled RR 0.87, 95%CI 0.75 to 1.01, I^2 0%; five studies) and reoperation for wound complication (pooled RR 1.12, 95%CI 0.66 to 1.90, I^2 0%; six studies).[26]

b. Closed incisions in breast surgery

Song J et al. (2023) performed a meta-analysis to assess the effect of prophylactic application of NPWT compared to standard dressing for closed incisions in breast cancer surgery.[27] The pooled results showed significantly lower SSI (OR 0.59, 95%CI 0.36 to 0.96, p= 0.03, I^2 0%; seven studies), wound dehiscence (OR 0.54, 95%CI 0.39 to 0.75, p < 0.001, I^2 26%; eight studies) and wound necrosis (OR 0.44, 95%CI 0.27 to 0.71, p< 0.001, I2 20%; five studies) in women with closed incisions in breast cancer surgery compared with standard dressings. The NPWT did not show any significant difference in wound seroma (OR 0.73, 95%CI 0.32 to 1.65, p=0.45, I^2 86%; eight studies) and haematoma (OR 0.73, 95%CI 0.33 to 1.59, p=0.001; I^2 86%; five studies) compared with standard dressings.[27]

c. Sternal wound post cardiac surgery

Biancari F et al. (2022) performed a systematic review and meta-analysis of ten studies (two RCTS and eight cohort studies) involving patients with sternal wound post cardiac surgery comparing NPWT with standard dressing.[28] The pooled analysis revealed NPWT was associated with a lower risk of any SSI (pooled rates 4.5% versus 9.0%, RR 0.54, 95%CI 0.34 to 0.84, I^2 48%; nine studies), superficial SSI (pooled rates 3.8% versus 4.4%, RR 0.63, 95%CI 0.29 to 1.36, I^2 65%; eight studies), and deep SSI (pooled rates 1.8% vs. 4.7%, RR 0.46, 95%CI 0.26 to 0.74, I^2 0%; nine studies), but such a difference was not statistically significant for superficial SSI.[28]

c. Closed surgical wound after orthopaedics trauma surgery

Xie W et al. (2021) performed a meta-analysis assessing the effect of negative pressure wound therapy compared with conventional wound dressings on closed incisions in orthopaedic trauma surgery.[29] The authors included 12 studies (four RCTs and eight cohort studies) in the analysis. Negative pressure wound therapy had significantly lower deep SSI (pooled OR 0.65, 95%CI 0.48 to 0.88, p = 0.005, I^2 38%; 10 studies), superficial SSI (pooled OR 0.23, 95%CI 0.11 to 0.49, p=0.0002, I^2 0%; seven studies) and wound dehiscence (pooled OR 0.41, 95%CI 0.21 to 0.80, p=0.009, I^2 0%; three studies) compared with conventional wound dressings. However, NPWT had no significant effect on the length of hospital stay (MD 0.29, 95%CI -2.00 to 2.58, p=0.80, I^2 93%; three studies) compared with conventional wound dressings in patients with closed incisions in orthopaedic trauma surgery.[29]

Wounds heal by secondary intention

A systematic review and meta-analysis by Zens Y et al. (2020) assessed the effects of NPWT in comparison to standard wound care on wounds healing by secondary intention in any care setting, across various types of surgical, traumatic and chronic wounds.[30] The authors included 48 RCTs comprising of 4,315 patients. The meta-analysis showed a statistically significant effect of wound healing in favour of NPWT (pooled OR 1.56, 95%CI 1.15 to 2.13, p = 0.008, I^2 0%;14 studies). A meta-analysis of hospital stay (in days) showed a significant difference in favour of NPWT (MD − 4.78, 95%CI − 7.79 to − 1.76, p = 0.005, I^2 21.9%; 11 studies). The author concluded that their review of NPWT versus standard wound care in patients with wounds healing

by secondary intention showed some advantages of NPWT with regard to wound closure and hospital stay.[30]

Subpopulations

a. Open surgical abdominal wound

Cirocchi R et al. (2016) performed a systematic review and meta-analysis to compare effect of NPWT and other temporary abdominal closure techniques (Bogota bag technique, mesh-foil laparostomy, laparostomy-adhesive impermeable with midline zip) in patients treated with open abdomen technique.[31] The review included eight studies (two RCTs and six cohorts), comprising of 1,225 patients. The authors stated that the risk of bias in the RCTs was high, and all but one of the cohort studies were rated as 'fair' quality. Clinical heterogeneity between the studies was also noted, for example with respect to the variability in NPWT systems and in the comparator groups. The pooled analysis showed that there was no statistically significant difference in fascial closure (63.5% versus 69.5%; pooled OR 0.74, 95%CI 0.27 to 2.06, p = 0.57, I^2 83%), postoperative enteroatmospheric fistulae rate [2.1% versus 5.8%; pooled OR 0.63, 95%CI 0.12 to 3.15; p = 0.57, I^2 69%), postoperative bleeding rate (5.7% versus 14.9%; pooled OR 0.58, 95%CI 0.05 to 6.84, p = 0.87, I^2 61%) or postoperative abdominal abscess rate (2.4% versus 5.6%; pooled OR 0.42, 95%CI 0.13 to 1.34, p = 0.14, I^2 54%). However, there was a statistically significant difference between the groups for postoperative mortality rate and (28.5% versus 41.4%; pooled OR 0.46 95%CI 0.23 to 0.91, p = 0.03, I^2 72%) and length of stay in the intensive care unit (in days) (MD −4.53, 95% CI −5.46 to 3.60, p < 0.00001, I^2 6%), favouring NPWT. The authors noted that for several outcomes, the confidence intervals were wide, and inconsistency was high. Based on the results they concluded that from the current available data NPWT seems to be associated with a trend toward better outcomes compared to the use of no NPWT. However, they emphasized the need for caution given the weaknesses in the studies and the clinical and statistical heterogeneity.[31]

b. Open fracture wounds

In a Cochrane systematic review, Iheozor-Ejiofor et al. (2018) evaluated the effectiveness of NPWT for treating open fracture wounds. Four studies compared NPWT with standard care for open fracture wounds.[32] All studies used NPWT following surgical debridement until wounds were ready for coverage or closure surgery. The authors concluded that there is moderate-certainty evidence for no clear difference between NPWT and standard care on the proportion of wounds healed at six weeks (RR 1.01, 95%CI 0.81 to 1.27) and in risk of wound infection at 30 days (RR 0.48, 95% CI 0.20 to 1.13).[32]

c. Burn wounds

Lin DZ et al. (2021) systematically reviewed and meta-analysed the evidence for the effectiveness of NPWT in improving burn wound healing.[33] Six RCTs comprising of 701 patients were included. The NPWT alone or in combination with split-thickness skin graft (STSG) and/ or dermal substitute (DS) was compared with STSG, DS and conventional dressing. The pooled analysis indicated an overall significantly improved graft take rate at the first week in the NPWT groups compared with comparator groups

[standardised mean difference (SMD) 2.62, 95%CI 1.01 to 4.22, p = 0.001] and a significantly lower infection rate (OR: 0.12, 95%CI 0.02 to 0.87, p = 0.04). An improved graft take rate at first week was noted in the following three subgroups: (a) NPWT and DS compared with DS (SMD: 5.93, 95%CI 4.27 to 7.60, p < 0.0001), (b) NPWT compared with DS (SMD: 8.52, 95%CI 6.05 to 11.00, p < 0.00001), and (c) NPWT to conventional dressing therapy alone (SMD: 1.91, 95%CI 1.03 to 2.79, p < 0.00001). No significant difference in graft take rate at first week was observed between the treatment combination of NPWT + DS + STSG groups and treatment combination DS + STSG groups (SMD: 0.2, 95% CI −0.40 to 0.79, p = 0.65). No significant difference was found when comparing the NPWT + STSG groups and the STSG alone group (SMD: 0.63, 95%CI −0.86 to 2.13, p = 0.41). The authors concluded that NPWT promotes better graft take rate than conventional dressing therapy. The evidence on combination with DS or STSG showed that NPWT provides a better condition for DS to adhere, but little improvement with STSG.[33]

d. Chronic wounds

Diabetic foot ulcers

Chen L et al. (2021) performed a systematic review and meta-analysis to investigate the effect of NPWT on wound healing, in comparison to standard wound care (standard moist wound care, normal saline dressing, regular topical dressing) in population of patients with diabetic foot ulcers.[34] A total of nine RCTs comprising of 943 patients were included. The pooled analysis using the fixed effects model showed that the healing rate of the NPWT group was significantly higher than the standard group (OR 3.6, 95%CI 2.38 to 5.45, p < 0.001; six studies). The granulation tissue formation time of the NPWT group was significantly less than the standard group (MD -8.95, 95%CI -10.26 to -7.64, p<0.001; three studies). However, the difference in amputation rate between both groups was no statistically significant (OR 0.33, 95%CI 0.09 to 1.26, p=0.10; six studies). The authors concluded that NPWT can effectively accelerate wound healing, [34]

Grade III/IV pressure ulcers

Song YP et al. (2021) performed a meta-analysis to identify the potential benefits of NPWT for grade III/IV pressure ulcers compared with standard wound care.[35] Traditional standard wound care refers to the treatment of chronic wounds with frequent (three to four times daily) saline moist dressings. The authors included 16 RCTs comprising of 629 patients in the analysis. The use of NPWT was associated with a higher complete ulcer healing rate compared with standard wound care (61.54% versus 36.90%; pooled RR 1.32, 95%CI 1.32 to 1.70; eight RCTs). The pooled analysis also showed a significant difference in wound healing time between NPWT and standard wound care [weighted mean difference (WMD) -16.47 days, 95%CI -22.36 to - 10.59, p≤ 0.001; 10 studies]. The authors concluded that their analysis indicated that NPWT was associated with greater improvements and shorter healing time for grade III/IV pressure ulcers.[35]

5.1.2 SAFETY

The NPWT device for reduction of wound complications are classified as U.S. Food and Drug Administration (FDA) Class II device (special controls). The final order was issued on October, 12 2021.[36] The classification provides a reasonable assurance of safety and effectiveness, as well as, improve patients' access to the device. This classification does not include devices intended for organ space wounds.

FDA has identified the following risks to health associated specifically with this type of device and the measures required to mitigate these risks in Table 3.

Table 3: Negative Pressure Wound Therapy Device for reduction of wound complications risks and mitigation measures [36]

Identified risks	Mitigation measures
1. Adverse tissue reaction	Biocompatibility evaluation
2. Infection	Sterilization validation, Shelf life testing, and Labeling
3. Electrical shock or electromagnetic interference with other devices	Electromagnetic compatibility testing, Electrical safety testing, and Labeling
4. Damage to underlying tissue (e.g., wound maceration, uncontrolled bleeding) due to: - Mechanical failure - Software malfunction - Use error	Clinical data; Non-clinical performance testing; Usability testing; Shelf life testing; Software verification, validation, and hazard analysis; and Labeling
5. Increase in wound complications due to use error	Clinical data, Usability testing, and Labeling

Serious adverse events associated with NPWT is rare. However, it can occur wherever NPWT devices are used, including hospitals, long-term health care facilities and at home. The commonly reported adverse events are bleeding, injuries, infection and death. The U.S. FDA issued a safety warning to healthcare professionals and consumers in 2009 [37] and updated the warning in 2011 [38]. A total of 12 deaths and 174 injuries were reported between 2007-2011. Most deaths occurred when patients were treated **at home** or in **long-term care facilities.**

Bleeding was the most serious injury and occurred in all 12 reported deaths and in 86 of the reported injuries.[37, 38] Bleeding occurred in patients who had blood vessel grafts, wound infection, those receiving anticoagulant, and during removal of dressings attached to the tissues. Patients with bleeding required emergency room visits and/or hospitalisation and were treated with surgery to stop the bleeding and blood transfusions.

Seventy-six reports indicated that the patient developed an infection from the original open wound or from retention of dressing pieces in the wound. Foam dressing pieces, either adhering to tissues or embedded in the wound, were observed in 32 of the injury reports; the majority of these patients required surgical procedures to remove the retained pieces, wound debridement and drainage, and treatment of wound dehiscence, as well as additional hospitalisation and antibiotics. [37, 38]

Similarly, between 2008 and 2009, the Pennsylvania Patient Safety Authority received 419 reports related to the application or management of NPWT.[13] Complications associated to NPWT were described in 112 (27%) reports and included bleeding, evisceration of bowel, retained sponges, infection, maceration, and compromise of tissue surrounding the wound. Other reports comprised of events associated with physical orders and patient assessment before initiation of treatment (5%), events citing monitoring and ongoing assessment issues (47%) and a combination of some or all of the above categories of events (21%).[13]

Following the reports, FDA Safety Communications and Public Health Notifications issued the recommendations to healthcare providers for safe use of NPWT in 2011. These included the contraindications of use in specific type of wounds and special considerations in patients with specific risk factors or characteristics as listed below.[38]

Type of wounds or conditions which are contraindicated in NPWT [38]

a. Necrotic tissue with eschar present
b. Untreated osteomyelitis
c. Non-enteric and unexplored fistula
d. Malignancy in the wound
e. Exposed vasculature
f. Exposed nerves
g. Exposed anastomotic site
h. Exposed organs

Patient risk factors/characteristics to consider before NPWT use [38]

a. Patients at high risk for bleeding and haemorrhage
b. Patients on anticoagulants or platelet aggregation inhibitors patients with:
    - friable vessels and infected blood vessels
    - vascular anastomosis
    - infected wounds
    - osteomyelitis
    - exposed organs, vessels, nerves, tendons, and ligaments
    - sharp edges in the wound (i.e. bone fragments)
    - spinal cord injury (stimulation of sympathetic nervous system)
    - enteric fistulas
c. Patients requiring: MRI, Hyperbaric chamber, Defibrillation
d. Patient size and weight
e. Use near vagus nerve (bradycardia)
f. Circumferential dressing application
g. Mode of therapy - intermittent versus continuous negative pressure

Treatment related adverse events

In systematic review by Shiroky J et al. (2020), one RCT reported on adverse allergic skin reaction (n=294) and six RCTs recorded incidence of skin blisters (n=617). However, there was no significant difference identified with respect to the skin blister between NPWT and standard dressing (pooled RR 3.45, 95%CI 0.82 to14.48, I^2 79%, low certainty). [25]

An RCT conducted Gillespie BM et al. (2021) reported dressing related adverse events, which included skin blistering, itchiness, and rash.[39] The authors observed a two percentage point increase in the absolute risk of skin blistering among women in the closed incision NPWT group, which was statistically significant [4.0%(40) versus 2.3% (23); RR 1.72 (95%CI 1.04 to 2.85); p = 0.03].[39]

5.1.3 COST/COST-EFFECTIVENESS

Sixteen economic evaluation studies reported on the cost-effectiveness of NPWT as treatment modality for acute and chronic wounds. The included studies comprised of 12 cost-effectiveness analyses, one budget impact analysis and three cost analyses, comparing NPWT with standard care. Most studies were conducted from the perspective of healthcare provider in hospital setting. They were mostly from United Kingdom, USA and European countries.

Closed surgical wound

Nherera LM et al. (2021) conducted cost-effectiveness analysis for the use of single NPWT compared with standard care in patients following vascular, colorectal, cardiothoracic, orthopaedic, C-section and breast surgery from the UK National Health Service (NHS) and US payer perspective over a 12-week time horizon.[40] The prophylactic use of NPWT following closed surgical incisions was found to be a cost-saving intervention for both the UK and the US analysis when compared to standard of care. Overall NPWT was less costly and resulted in improved clinical outcomes (fewer complications and increased QALYs) compared with standard care. The model estimates the cost savings per patient to be £105 from the UK NHS perspective, while from the US payer perspective, NPWT saves $637 per patient. There were more savings when higher-risk patients with diabetes, or a BMI ≥30kg/m2 or an ASA≥3 were considered. Hence, patients at higher risk should be targeted first as they benefit more from NPWT.[40]

Caesarean sections in obese women

Hyldig N et al. (2019) performed a cost-effectiveness analysis of incisional NPWT (PICO™; Smith & Nephew, Hull, UK) in preventing surgical site infection in obese women after caesarean section from Danish healthcare perspective with a time horizon of 3 months after birth.[41] The total healthcare costs per woman were €5793.60 for NPWT and €5840.89 for standard postoperative dressings. Incisional NPWT was the dominant strategy because it was both less expensive and more effective. However, no statistically significant difference was found for costs or QALYs. At a

willingness-to-pay threshold of €30,000, the probability of the intervention being cost-effective was 92.8%. A subgroup analysis stratifying by BMI showed that the cost saving of the intervention was mainly driven by the benefit to women with a pre-pregnancy BMI ≥35 kg/m^2.[41]

An economic evaluation was conducted by Heard C et al. (2017) to evaluate the cost-effectiveness of NPWT (PICO^{TM} Smith and Nephew, Hull, UK) compared to standard care (Comfeel Plus® dressing, Coloplast, Denmark), for the prevention of SSI in obese women undergoing elective caesarean section. The evaluation was assumed from Australian public health care provider perspective and time horizon to four weeks post-discharge.[42] The willingness-to-pay threshold was set at AU$50,000 per QALY. Patients receiving NPWT each received health care costing AU$5887 (±1038) and reported 0.069 (±0.010) QALYs compared to AU$5754 (±1484) and 0.066 (±0.010) QALYs for patients receiving standard care. NPWT may be slightly more costly and more effective than standard care, The ICERs were estimated to be AU$1347 (95% CI dominant to $41,873) per SSI prevented and AU$42,340 (95%CI dominant to AU$884,019) per QALY gained. However, the ICERs exhibit substantial uncertainty, as indicated by the very wide 95%CIs. The authors concluded that NPWT may be cost-effective in the prophylactic treatment of surgical wounds following elective caesarean section in obese women.[42]

A cost-effectiveness study by Whitty JA et al. (2023) reported contradicting findings.[43] The analysis was also considered from Australian health service perspective and time horizon of four weeks post-discharge. The NPWT (PICO, Smith & Nephew, Hull, UK) was associated with AU$162 (95%CI −AU$170 to AU$494) higher cost per person and an additional $12,849 (95%CI −$62,138 to $133,378) per SSI avoided. There was no detectable difference in QALYs between NPWT and standard dressing groups. However, there werw high levels of uncertainty around both cost and QALY estimates. There was a 20% likelihood that NPWT would be considered cost-effective at a willingness- to-pay threshold of AU$50 000 per QALY. The authors concluded NPWT for the prevention of SSI in obese women undergoing CS is unlikely to be cost-effective in terms of health service resources and is currently unjustified for routine use for this purpose.[43]

Orthopaedic surgery

Nherera LM et al. (2017) sought to evaluate the cost-effectiveness of NPWT (single-use NPWT) in patients undergoing primary hip and knee replacement from UK National Health Service perspective over 6-week time horizon.[44] The NPWT was dominant over standard dressings (film dressings) in hip or knee replacement surgery, as NPWT was cost-saving and improved QALYs. The cost/patient was £5,602 and £6,713 for single-use negative pressure wound therapy and standard care respectively resulting in cost-saving of £1,132 in favour of single-use negative pressure wound therapy. Greater savings were observed in subgroups of higher risk patients with BMI ≥ 35 and ASA ≥ 3, £7,955 and £7,248, respectively.[44]

Costa ML et al. (2020) performed a cost-effectiveness analysis of NPWT in comparison to standard dressing (a non-adhesive layer applied directly to the wound, covered by a sealed dressing or bandage) for the management of surgical wound among patients with lower limb fracture requiring surgical intervention, from the

perspective of NHS and Personal Social Service over 6-month time horizon.[45] The ICER in the base-case analysis was £396,531 per QALY gained, which indicated that NPWT had higher costs and marginally better outcomes than standard dressings. The health economic evaluation therefore indicated that incisional negative-pressure wound therapy is very unlikely to be cost-effective at the willingness-to-pay threshold of £20,000 and £30,000 per QALY.[45]

Vascular surgery

Svensson-Björk R et al. (2021) evaluated the cost-effectiveness of NPWT (PICO™, Smith & Nephew, Hull, UK) compared to standard dressings [ViTri Pad (ViTri medical, Stockholm, Sweden) or OPSITE Post-op visible (Smith & Nephew, Hull, UK)] for the prevention of SSIs after open inguinal vascular surgery from Swedish healthcare perspective.[46] The NPWT is considered cost-effective over standard dressings in patients undergoing open inguinal vascular surgery with the ICER €1,853 per SSI avoided (due to reduced SSI incidence at no higher costs).[46]

Budget impact analysis was conducted by Nicolazzo D (2023) for NPWT in the management of surgical wound post vascular surgery among patients suffering from peripheral arterial disease (PAD) and at risk of postoperative complications, compared to treatment with traditional dressings.[47] The analysis assumed the Italian hospital perspective and considered a 12-month time horizon. The cost that mainly affects the overall hospital resources absorption is related to the hospitalisation phase (€5250 for NPWT versus €7280 for traditional dressings). With the use of NPWT, there is a reduction of 2.5 days of post-surgery hospitalisation equal to a cost reduction of €2030. The routine use of NPWT would lead to an economic saving per patient equal to 15% (€1722).[47]

Cardiac surgery

Nherera LM et al. (2018) performed cost-effectiveness analysis of NPWT (single use NPWT) compared to standard care (standard wwound dressing) in patients following coronary artery bypass grafting surgery (CABG) procedure to reduce surgical site complications defined as dehiscence and sternotomy infections.[48] A decision analytic model was constructed from the Germany Statutory Health Insurance payer's perspective over a 12-week time horizon. The model estimated sNPWT resulted in 0.989 complications avoided compared to 0.952 and the estimated QALYs were 0.8904 and 0.8593 per patient compared to standard care. The estimated mean cost per patient was €19,986 for sNPWT compared to €20,572 for standard care resulting in cost-saving of €586. Bigger saving (€1586) was observed when patients with BMI ≥ 30 are prophylactically treated with sNPWT than with standard care dressings.[48]

Wounds heal by secondary intention

Adult patients with severe open fractures of the lower limb (post wound debridement)

An economic evaluation was conducted by Petrou et al. (2019) from the perspective of the United Kingdom NHS and Personal Social Services.[49] Cost- effectiveness was determined over a 12-month period. The NPWT is unlikely to be a cost-effective

strategy for improving outcomes in adult patients with severe open fractures of the lower limb. The base case analysis produced an ICER of £267,910 per QALY gained, reflecting higher costs on average (£678, 95%CI -£1082 to £2438) and only marginally higher QALYS (0.002; 95% CI -0.054 to 0.059) in the NPWT group. The probability that NPWT is cost-effective in this patient population did not exceed 27% across a range of cost-effectiveness thresholds (24.4% at the widely used £20,000 cost-effectiveness threshold), while mean net monetary benefits were negative across a range of cost-effectiveness thresholds. This result remained robust to several sensitivity and subgroup analyses.[40]

Acute traumatic wounds

Älgå A et al. (2022) performed a cost analysis of NPWT in comparison with standard treatment (wound dressings with non-adhesive sterile gauze covered with a bandage) for acute traumatic wound over extremities in public hospital setting.[50] The analysis was done from the perspective of healthcare provider in Iran. The overall cost for treatment was higher in the NPWT group compared to the standard treatment group (healthcare cost per patient: USD 3117.8 versus USD 2975.90). The author concluded that the use of NPWT as routine treatment of traumatic injuries in resource-limited setting cannot be recommended.[50]

Diabetic Foot Ulcers

Alipour V et al. (2021) conducted cost-effectiveness analysis of NPWT in comparison to traditional wound care for the treatment of patients with diabetic foot ulcers (DFUs) in Iran from the perspective of health care providers.[51] A 7-state Markov model with 1-year time horizon and monthly cycle was constructed. With its greater QALYs and lower costs, NPWT is considered the more effective wound treatment strategy. The expected costs per patient per year using a NPWT treatment strategy (US$5165 ± 3258) were US$4668 lower than those of a traditional wound care treatment strategy (US$9833 ± 5861).[51]

A post hoc retrospective analysis by Driver VR (2014) indicated that for patients with DFUs who achieved complete wound closure, the median cost per 1 cm2 of closure was US$1,227 with NPWT and US$1,695 with advanced moist wound therapy, which showed greater cost-effectiveness in the NPWT group for treating recalcitrant wounds.[52]

Another cost analysis study by Vaidhya N et al. (2015) demonstrated similar findings. The mean number of dressing and total cost of dressings needed to achieve satisfactory healing in the NPWT group, were less than for the conventional dressing (moist gauze dressing) group.[2] The mean number of dressing applied were 7.46(SD ± 2.25) in NPWT group versus 69.8(SD ± 11.93) in conventional dressing group ($p < 0.001$). Wound was ready for either skin grafting or secondary suturing in 17.2(SD ± 3.55) days in NPWT groups, compared to 34.9 (SD ± 5.96) days in the control group ($p < 0.001$). Average cost of NPWT and conventional dressing was Indian Rupee (Rs.) 3,750 and 7,000, respectively.[2]

Two analyses (Flack S, 2008 and Whitehead SJ, 2011) based on economic models also concluded that, compared to patients treated with advanced wound care, patients

treated with NPWT had increased QALYs and a higher healing rate at a lower cost from the US and French payers' perspectives.[53, 54] The model results by Flack S et al. demonstrated improved healing rates (61% versus 59%), more QALYs (0.54 versus 0.53) and an overall lower cost of care ($52,830 versus $61,757 per person) for patients treated with NPWT (VAC KCI Medical) compared with advanced dressings in US.[53] The results of a cohort study by Whitehead et al suggested that the patients treated with NPWT (V.A.C. Therapy) experienced more QALYs (0·787 versus 0·784) and improved healing rates (50·2% versus 48·5%) at a lower total cost of care (€24,881 versus €28,855 per patient per year) when compared with advanced wound care (Adaptic® and Algosteril®). Therefore, it is considered the more effective wound treatment alternative from the perspective of the French payers. The model has shown that, on average, annual savings of approximately €4000 can be realised for a DFU patient treated with NPWT in France.[54]

5.2 PART B: ECONOMIC EVALUATION

From the base case analysis, the use of NPWT was found to be effective with an additional cost of MYR 385 per patient to the healthcare system with a reduced SSI probability of 0.03. Therefore, the estimated incremental cost effectiveness ratio (ICER) was approximately MYR 12,600 per SSI averted.

One way sensitivity analysis was conducted to determine the parameter uncertainty and the result is shown as Table 4. The use of NPWT in surgical patients will incur additional cost to the healthcare system yielded an estimated ICER between cost-saving and MYR 30,000 per SSI averted.

Table 4: One way sensitivity analysis

Parameter	**Estimated ICER**
Price Per Case (Severity of Illness 3)	MYR 6,681
Higher incidence of SSI	MYR 6,923
Reduction of NPWT (consumable) cost by (50%)	Cost-saving – MYR 8,502
Higher NPWT (consumable) cost	MYR 30,381

Access to the treatment in a resource limited setting can be improved by a careful selection of patient and effective consumables price negotiation would ensure the optimal benefit of NPWT as an alternative option for wound management is achieved.

6.0 LIMITATIONS

PART A: SYSTEMATIC REVIEW OF LITERATURE

This technology review has several limitations. Only English full text articles were included in this review. Hence, there is a possibility that potentially relevant studies published in languages other than English could have been missed. The findings and interpretations are limited by the quality and quantity of available evidence.

PART B: ECONOMIC EVALUATION

Based on the review of cost effectiveness analysis, the use of NPWT showed variation in the ICER as most of the analysis has a specific subgroup population and the result of the cost effectiveness analysis reflected its use for a specific type of surgical patient. However, further analyses as a subgroup analysis according to the type of surgery was not conducted in view of limitation in the availability of the local data for this analysis. There was also a variation in the type and availability of conventional and advanced dressing that were available in the healthcare facilities. Thus, the estimation of costs for all the possible combination of treatment or wound management was not possible in this analysis. This analysis was also limited by the costing perspective. There may be a potential of more costs savings from societal perspective as suggested by the literature which may improve the cost effectiveness of NPWT. The potential cost savings from societal perspective and spill-over costs include indirect costs incurred by the patient through absenteeism from work, out–of-pocket payments to treat SSI infections, cost of avoiding pain and suffering and the negative effect on the quality-of-life and cost needed to prevent antimicrobial resistance associated with SSI.[55] In terms of measuring the uncertainty, probabilistic sensitivity analysis was not conducted due to the limitation of available data.

7.0 CONCLUSIONS

Based on retrievable evidence, the use of NPWT may potentially reduce the risk of surgical site infections and wound dehishence in closed surgical wounds across range of surgical procedures. The NPWT is associated with better wound healing in comparison with standard wound care across different type of wounds except for lower limb open fracture wounds. The NPWT is considered a safe treatment. Treatment related adverse events includes allergic skin reaction and skin blister, which are comparable to standard wound care. Serious adverse events like bleeding, infection, injuries and death are rare. They are mostly associated with unsafe use of NPWT. Evidence from economic evaluation studies tend to suggest that NPWT is likely to be cost saving treatment in the management of wound, particularly in high risk patients with BMI ≥ 35 and severe systemic disease. Based on economic analysis, the use of NPWT in surgical patient will incur additional cost to the healthcare system yielded an ICER between MYR3,300 to MYR 34,000 per SSI averted. However, there may be a potential of more cost savings from societal perspective which may improve the cost effectiveness of NPWT.

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9.0 APPENDICES

Appendix 1: SEARCH STRATEGY

Database: Ovid MEDLINE(R) <1946 to May 22, 2023>

Search strategy

#	Search Details	Results
1	acute wound.tw	529
2	SURGICAL WOUND/	1747
3	((surgical or incisional or burn or trauma) adj1 wound).tw	9212
4	chronic wound.tw	2826
5	((diabetic or pressure) adj1 ulcer$).tw	9719
6	((primary or first) adj1 (intention or closure)).tw	7606
7	(secondary adj1 (intention or closure)).tw	1670
8	((open* or clos*) adj5 wound*).tw	23087
9	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8	52130
10	NEGATIVE PRESSURE WOUND THERAPY/	3936
11	negative pressure wound therapy.tw	2968
12	(vacuum assisted closure technique or VAC).tw	3629
13	((vacuum adj therapy) or (vacuum adj dressing$) or (vacuum adj seal$) or (vacuum adj closure) or (vacuum adj compression) or (vacuum adj pack$) or (vacuum adj drainage) or (suction$ adj drainage)).tw.	4579
14	10 or 11 or 12 or 13	12007
15	9 and 14	2297

Database: EBM Reviews - Cochrane Database of Systematic Reviews <2005 to May 16, 2023>

Search strategy

#	Search Details	Results
1	acute wound.tw	18
2	SURGICAL WOUND/	0
3	((surgical or incisional or burn or trauma) adj1 wound).tw	201
4	chronic wound.tw	28
5	((diabetic or pressure) adj1 ulcer$).tw	148
6	((primary or first) adj1 (intention or closure)).tw	83
7	(secondary adj1 (intention or closure)).tw	47
8	((open* or clos*) adj5 wound*).tw	233
9	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8	503
10	NEGATIVE PRESSURE WOUND THERAPY/	0
11	negative pressure wound therapy.tw	29
12	(vacuum assisted closure technique or VAC).tw	21
13	((vacuum adj therapy) or (vacuum adj dressing$) or (vacuum adj seal$) or (vacuum adj closure) or (vacuum adj compression) or (vacuum adj pack$) or (vacuum adj drainage) or (suction$ adj drainage)).tw.	26
14	10 or 11 or 12 or 13	56
15	9 and 14	38

Database : PUBMED

Search strategy

#	Search Details	Results
1	((((((((((((((((((((((acute wound) OR (acute wound[MeSH Terms])) OR (acute wound[Text Word])) OR (surgical wound)) OR (surgical wound[MeSH Terms])) OR (surgical wound[Text Word])) OR (incisional wound)) OR (incisional wound[MeSH Terms])) OR (incisional wound[Text Word])) OR (burn wound)) OR (burn wound[MeSH Terms])) OR (burn wound[Text Word])) OR (trauma wound)) OR (trauma wound[MeSH Terms])) OR (trauma wound[Text Word])) OR (chronic wound)) OR (chronic wound[MeSH Terms])) OR (chronic wound[Text Word])) OR (diabetic ulcer)) OR (diabetic ulcer[MeSH Terms])) OR (diabetic ulcer[Text Word])) OR (pressure ulcer)) OR (pressure ulcer[MeSH Terms])) OR (pressure ulcer[Text Word])	1,331,960
2	((((((((((negative pressure wound therapy) OR (negative pressure wound therapy[MeSH Terms])) OR (negative pressure wound therapy[Text Word])) OR (npwt)) OR (npwt[MeSH Terms])) OR (npwt[Text Word])) OR (vacuum assisted closure technique)) OR (vacuum assisted closure technique[MeSH Terms])) OR (vacuum assisted closure technique[Text Word]))OR (vacuum therapy)) OR (vacuum therapy[MeSH Terms])) OR (vacuum therapy[Text Word])	14,903
3	**#1 AND #4**	6,724

Appendix 2: EVIDENCE TABLE

Evidence Table : **EFFECTIVENESS AND SAFETY**
Question : How effective and safe is NPWT as therapeutic dressing for acute and chronic wounds?

Bibliographic citation	Study Design/ Methods	LE	Number of Patients & Patient Characteristics	Intervention	Comparison	Length of Follow-up (If Applicable)	Outcome Measures/Effect Size
1. Norman G, Shi C, Goh EL, et al. Negative pressure wound therapy for surgical wounds healing by primary closure. Cochrane Database Syst Rev. 2022;4(4)	Systematic review & meta-analysis **Objective:** To assess the effects of NPWT for preventing SSI in wounds healing through primary closure **Methods:** <u>1. Searching</u> - the Cochrane Wounds Specialised Register (searched 6 January 2021) the Cochrane Central Register of Controlled Trials (CENTRAL; 2020, Issue 12) in the Cochrane Library (searched 6 January 2021); Ovid MEDLINE including In-Process & Other Non-Indexed Citations (1946 to 6 January 2021); OvidEmbase(1974 to 6 January 2021); EBSCO CINAHL Plus (Cumulative Index to Nursing and Allied Health Literature; 1937 to 6 January 2021). - Clinical trials registries and references of included studies, systematic reviews and health technology reports.	**I**	62 RCTs (13,340 included participants) Studies evaluated NPWT in a wide range of surgeries, including orthopaedic, obstetric, vascular and general procedures. All studies compared NPWT with standard dressings.	NPWT	Standard dressing	Up to 12 months	**NPWT versus standard dressing** <u>Primary outcomes</u> **Outcome 1: Mortality (**11 studies: 6384 participants) RR 0.78 [95%CI 0.47-1.30]; I^2 0% There is low-certainty evidence showing there may be a reduced risk of death after surgery for people treated with NPWT (0.84%) compared with standard dressings (1.17%) but there is uncertainty around this as confidence intervals include risk of benefits and harm. **Outcome 2:SSI (**44 studies:11,403 participants) RR 0.73 [95%CI 0.63-0.85]; I^2 29% There is moderate-certainty evidence that NPWT probably results in fewer SSIs (8.7% of participants) than treatment with standard dressings (11.75%) after surgery. **Outcome 3: SSI grouped by contamination class** **3.1 Clean:** RR 0.58 [95%CI 0.41- 0.81]; I^2 26% **3.2 Clean-contaminated:** RR 0.83 [95%CI 0.72-0.96]; I^2 13% **3.3 Contaminated:** RR 0.78 [95%CI 0.28-2.14]; I^2 50% **Outcome 4: Superficial SSI** RR 0.70 [95%CI 0.53-0.92]; I^2 70% Twenty-two studies (5539 participants) contributed data to a pooled estimate of effect. **Outcome 5: Deep SSI** RR 0.95 [95% 0.76-1.18]; I^2 0% Twenty-two studies (8521 participants) contributed data to a pooled estimate of effect.

Bibliographic citation	Study Design/ Methods	LE	Number of Patients & Patient Characteristics	Intervention	Comparison	Length of Follow-up (If Applicable)	Outcome Measures/Effect Size
	There were no restrictions on language, publication date or study setting. 2. Selection **Inclusion criteria** Published or unpublished RCTs or cluster-RCTs that evaluated the effects of NPWT on surgical wounds healing by primary closure. **Exclusion criteria** Cross- over trials and quasi-randomised studies where, for example, treatment allocation was made through alternation or by date of birth.						**Outcome 6: Dehiscence (**23 studies: 8724 participants) RR 0.97 [95%CI 0.82-1.16]; I^2 4% There is moderate-certainty evidence that there is probably little or no difference in dehiscence between people treated with NPWT (6.62%) and those treated with standard dressing (6.97%), although there is imprecision around the estimate that includes risk of benefit and harms. Evidence was downgraded for imprecision, risk of bias, or a combination of these. Secondary outcomes **Outcome 7: Reoperation** (follow-up period 30 days to an average of 113 days or unspecified) (18 studies: 6272 participants) RR 1.13 [95%CI 0.91-1.41]; I^2 2% This is low- certainty evidence which suggests that, while there may be an increase in the incidence of reoperation for people treated NPWT compared with standard dressings, this is uncertain because the confidence intervals included both benefit and harm. Evidence was downgraded once for high risk of bias (various domains) and once for imprecision due to low numbers of events (330 reoperations in total) producing wide confidence intervals which included the possibility of both benefit and harm as well as no effect of the intervention. **Outcome 8: Wound-related readmission to hospital within 30 days (follow-up period 10 days to 90 days)** (15 studies: 5853 participants) RR 0.98 [95%CI 0.70-1.38]; I^2 14% This is low- certainty evidence of no clear difference, downgraded twice for imprecision; low numbers of events resulted in wide confidence intervals which included the possibility of both benefit and harm as well as no difference between the groups. **Outcome 9: Seroma** (15 studies**:** 5436 participants)(low-certainty evidence) RR 0.82 [95%CI 0.65-1.05]; I^2 0% There may be a reduced risk of seroma for people treated with NPWT but this is imprecise.

Bibliographic citation	Study Design/ Methods	LE	Number of Patients & Patient Characteristics	Intervention	Comparison	Length of Follow-up (If Applicable)	Outcome Measures/Effect Size
							Outcome 10: Haematoma (follow-up period 30 days to 6 weeks) (17 trials; 5909 participants)(very low-certainty evidence). RR 0.79 [95%CI 0.48-1.30]; I^2 0% The effect of NPWT on haematoma is uncertain **Outcome 11: Skin blisters (follow-up period 6 weeks to 12 months**)(11 studies: 5015 participants) RR 3.55 (95CI% 1.43-8.77); I^2 74% For skin blisters, there is low-certainty evidence that people treated with NPWT may be more likely to develop skin blisters compared with those treated with standard dressing **Outcome 12: Pain** RR 1.52 (95CI% 0.20-11.31]; I^2 34% There is low-certainty evidence of little to no difference in reported pain between groups. Pain was measured in different ways and most studies could not be pooled; this GRADE assessment is based on all fourteen trials reporting pain; the pooled RR for the proportion of participants who experienced pain was from two studies; 632 participants. **Authors' conclusions** People with primary closure of their surgical wound and treated prophylactically with NPWT following surgery probably experience fewer SSIs than people treated with standard dressings but there is probably no difference in wound dehiscence (moderate-certainty evidence). There may be a reduced risk of death after surgery for people treated with NPWT compared with standard dressings but there is uncertainty around this as confidence intervals include risk of benefit and harm (low-certainty evidence). People treated with NPWT may experience more instances of skin blistering compared with standard dressing treatment (low-certainty evidence). There are no clear differences in other secondary outcomes where most evidence is low or very low-certainty. Decisions about use of NPWT should take into account surgical indication and setting and consider evidence for all outcomes.

Evidence Table : **EFFECTIVENESS AND SAFETY**
Question : How effective and safe is NPWT as therapeutic dressing for acute and chronic wounds?

Bibliographic citation	Study Design/ Methods	LE	Number of Patients & Patient Characteristics	Intervention	Comparison	Length of Follow-up (If Applicable)	Outcome Measures/Effect Size
2. Angarita AM, Jayakumaran J, Di Mascio D, et al. Prophylactic negative pressure wound therapy on wound complications after caesarean delivery in women with obesity: a meta-analysis of randomized controlled trials. Am J Obstet Gynecol MFM. 2022;4(3):100617.	Systematic review and meta-analysis **Objective:** To assess whether negative pressure wound therapy affects the rate of wound complications when applied to women with obesity after caesarean delivery (CD) compared with standard postoperative dressings. **Methods:** Systematic literature search was performed through PubMed, Scopus, ClinicalTrials.gov, and the Cochrane Central Register of Controlled Trials as electronic databases, from the inception of each data- base to January 2021, with randomized controlled trial as the publication type. There was no restriction applied for language or geographic location. <u>Inclusion criteria</u> 1. Only RCTs comparing prophylactic NPWT with any other type of postoperative incision dressing after CD for preventing wound complications. 2. Authors considered published and unpublished trials. <u>Exclusion criteria</u> 1. Quasi-randomized trials (ie, trials in which allocation was done on the basis of a pseudo-random sequence. 2. Studies of surgical procedures other than CD, no prophylactic use of NPWT, no comparison group, and studies without outcome data relevant to wound infection or complications. <u>Risk of bias assessment</u> Cochrane Risk of Bias 2 tool for RCTs <u>Primary outcome</u> The rate of wound complications, defined as a composite of wound infection, separation or	**I**	11 RCTs, which included 5746 participants (2869 in the NPWT group vs 2877 in the standard dressing group) *Stitely et al. (2012)* *Chaboyer et al. (2014)* *Gunatilake et al. (2017)* *Ruhstaller et al. (2017)* *Hyldig et al. (2018)* *Tuuli et al. (2017)* *Wihbey et al. (2018)* *Hussamy et al. (2019)* *Tuuli et al. (2020)* *Peterson et al. (2021)* *Gillespie et al.(2021)* All studies were published between 2012 and 2021. All studies were parallel-group RCTs. **Sample size** 54 to 2035 <u>Study site(s)</u> -Multicenter (5 studies) -Single center (6 studies) All studies were parallel-group RCTs. <u>Country</u> USA (8 studies) Australia (2 studies) Denmark (1 study)	NPWT - Noncommercial NPWT therapy (1 studies) - PICO (suction 80 mmHg)(5 studies) - Prevena (suction 125 mm Hg) (5 studies)	Standard postoperative dressing - Comfeel Plus dressing (1 study) - Steri-Strips (1 study) - Telfa bandage (4 studies) - Sterile gauze and adhesive tape (6 studies) - Tegaderm (3 studies) - Hydrocolloid or transparent dressing (1 study)	Up to 30 days	**1. The effect of prophylactic NPWT on wound complications after caesarean delivery (4 studies)** Prophylactic NPWT was not associated with a significant change in the rate of wound complications compared with standard postoperative dressings. RR 1.00 (95%CI 0.81−1.23); I^2 0% **2. The effect of prophylactic NPWT on wound infection after caesarean delivery** There was a significantly decreased rate of wound infection favouring NPWT compared with standard dressing. RR 0.79 (95%CI 0.66− 0.96); I^2 0% **3. The effect of prophylactic NPWT on rate of wound dehiscence, seroma, hematoma, readmission for wound complications, antibiotic use and reoperation for wound complications** There was no difference in the rate of wound dehiscence, seroma, hematoma, readmission for wound complications, antibiotic use, and reoperation for wound complications. **Wound dehiscence (8 studies)** RR 0.99 (95%CI 0.79−1.24); I^2 11% **Seroma (5 studies)** RR 1.03 (95%CI 0.67−1.58); I^2 0% **Hematoma (6 studies)** RR 0.83 (95%CI 0.38−1.81); I^2 22% **Readmission for wound complications (6 studies)**

Bibliographic citation	Study Design/ Methods	LE	Number of Patients & Patient Characteristics	Intervention	Comparison	Length of Follow-up (If Applicable)	Outcome Measures/Effect Size
	dehiscence, hematoma, seroma, or readmission secondary to a wound concern. <u>Secondary outcome</u> Antibiotic use for wound complication, reoperation for wound complication, and skin changes (including skin maceration or blisters). The quality of evidence was assessed for **primary** and **secondary** outcomes using the Grading of Recommendations, Assessment, Development, and Evaluations (GRADE) approach.						RR 1.41 (95%CI 0.88−2.27); I^2 0% **Antibiotic use** RR 0.87 (95%CI 0.75−1.01); I^2 0% **Reoperation for wound complication** RR 1.12 (95%CI 0.66−1.90); I^2 0% **4. Adverse events** Women in the NPWT group were 4 times more likely to have an adverse skin reaction than the women that had standard dressings RR 4.59 (95%CI 1.29−16.38); I^2 82% **CONCLUSION:** Compared with standard postoperative incision dressings, negative pressure wound therapy did not affect the rate of wound complications but decreased the frequency of wound infections when applied to women with obesity after caesarean delivery. However, results should be interpreted with caution, as wound infection outcome includes different definitions per the individual trials.

Evidence Table : **EFFECTIVENESS AND SAFETY**
Question : How effective and safe is NPWT as therapeutic dressing for acute and chronic wounds?

Bibliographic citation	Study Design/ Methods	LE	Number of Patients & Patient Characteristics	Intervention	Comparison	Length of Follow-up (If Applicable)	Outcome Measures/Effect Size
3. Song J, Liu X, Wu T. Effectiveness of prophylactic application of negative pressure wound therapy in stopping surgical site wound problems for closed incisions in breast cancer surgery: A meta-analysis. Int Wound J. 2023;20(2):241-250.	Systematic review & meta-analysis **Objective:** To evaluate the effectiveness of the prophylactic application of negative pressure wound therapy in stopping surgical site wound problems for closed incisions in breast cancer surgery. **Methods:** Systematic literature search was performed through OVID, Embase, PubMed, and Google Scholar till March 2022. Statistical analysis was performed using the RevMan version 5.3 (The Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen, Denmark). The present meta-analysis was based on the dichotomous method with a random- or fixed-effect model to calculate the odds ratio (OR), and 95% confidence interval (CI). The I2 index was calculated which was between 0 and 100 (%). Values of about 0%, 25%, 50%, and 75% indicated no, low, moderate, and high heterogeneity, respectively. Inclusion criteria 1. The study was a prospective study, observational study, RCT or retrospective study. 2. The target population was women with closed incisions in breast cancer surgery. 3. The intervention program was based on the prophylactic application of negative pressure wound therapy and standard dressings. 4. The study included the prophylactic application of negative pressure wound therapy compared with standard dressings. Exclusion criteria 1. Studies that did not determine the influences of pro- phylactic application of negative pressure wound therapy in stopping surgical site wound problems for closed incisions in breast cancer surgery 2. Studies with women managed with other than the prophylactic application of negative pressure wound therapy and standard dressings 3. Studies did not focus on the effect of comparative results.	**I**	12 included studies with 2223 women with closed incisions in breast cancer surgery at the baseline. Published between 2014 and 2022 **Sample size** 17 to 665 **Countries** UK (3 studies) USA (2 studies) Italy (2 studies) Netherlands (3 studies) Germany (1 study) Korea (1 study)	NPWT	Standard dressing	NR	**NPWT versus standard dressing** Outcome 1**: Total wound problems** OR 0.62 (95%CI 0.43-0.90, p=0.01) with moderate heterogeneity (I^2 = 57%) Outcome 2**: Surgical site wound infection** OR 0.59 (95% CI 0.36-0.96, p=0.03) with no heterogeneity (I^2 = 0%) Outcome 3**: Wound dehiscence** OR 0.54 (95%CI 0.39-0.75, p<0.001) with low heterogeneity (I^2 = 26%) Outcome 4**: Wound necrosis** OR 0.44 (95%CI 0.27-0.71, p<0.001) with no heterogeneity (I^2 = 20%) Outcome 5: **Wound seroma** OR 0.73 (95%CI 0.32-1.65, p=0.45) with high heterogeneity (I^2 = 86%) Outcome 6: **Hematoma** OR 0.73 (95%CI 0.33-1.59, p = 0.001) with high heterogeneity (I^2 = 86%) **Conclusion** With the prophylactic application of negative pressure wound therapy, women had a significantly lower total wound problem, lower surgical site wound infection, lower wound dehiscence, and lower wound necrosis, in women with closed incisions in breast cancer surgery compared with standard dressings. However, prophylactic application of negative pressure wound therapy did not show any significant difference in wound seroma, and hematoma compared with standard dressings.

Evidence Table : **EFFECTIVENESS AND SAFETY**
Question : How effective and safe is NPWT as therapeutic dressing for acute and chronic wounds?

Bibliographic citation	Study Design/ Methods	LE	Number of Patients & Patient Characteristics	Intervention	Comparison	Length of Follow-up (If Applicable)	Outcome Measures/Effect Size
4. Biancari F, Santoro G, Provenzano F, et al. Negative-Pressure Wound Therapy for Prevention of Sternal Wound Infection after Adult Cardiac Surgery: Systematic Review and Meta-Analysis. J Clin Med. 2022;11(15).	Systematic review & meta-analysis **Objective:** To assess the impact of NPWT in preventing sternal wound infection (SWI) in adult patients undergoing cardiac surgery **Methods:** Systematic literature search was performed through PubMed, Scopus and Google Statistical analysis was performed using the RevMan (Review Manager Web, Version 1.22.0. The Cochrane Collaboration, 2020) and Open Meta-Analyst (Brown University, Providence, RI, USA) software. <u>Inclusion criteria</u> 1. Studies that reported the outcomes of patients who underwent any adult cardiac surgery procedure. 2. Provide data on negative-pressure wound therapy for the prevention of sternal wound infection 3. Provide data on standard sternal wound dressing 4. Provide data on postoperative surgical site infection of the sternal wound and the mediastinum 5. Studies that include patients aged 18 years or older 6. Studies that published in English language as a full article and published later than 2000. <u>Exclusion criteria</u> Studies that 1. Data are not clear or inaccurate 2. No information on surgical site infection 3. Data presented only in the abstract 4. Lack of comparative data on standard wound therapyArticle published in a non-English language. **Outcome measures** The primary outcome of this analysis was any SWI. Secondary outcomes were superficial SWI and deep SWI. The definition criteria of these outcomes were those originally reported in each study.	**I**	10 included studies with 6886 participants (2 RCTs and 8 cohort studies)	NPWT	Sternal wound dressing	NR	1. NPWT was associated with a lower risk of any SWI (nine studies: pooled rates 4.5% vs. 9.0%, RR 0.54, 95% CI 0.34–0.84, I^2 48%). 2. NPWT was associated with a lower risk of superficial SWI (eight studies: pooled rates 3.8% vs. 4.4%, RR 0.63, 95% CI 0.29–1.36, I^2 65%). 3. NPWT was associated with a lower risk of deep SWI (nine studies: pooled rates 1.8% vs. 4.7%, RR 0.46, 95% CI 0.26–0.74, I^2 0%) **NNT for any SWI** – 22.2 **NNT for deep SWI** – 34.5 **Conclusion** This pooled analysis showed that NPWT may prevent postoperative SWI after adult cardiac surgery. NPWT is expected to be particularly useful in patients at risk for surgical site infection and may significantly reduce the burden of resources needed to treat such a complication

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5. Xie W, Dai L, Qi Y, et al. Negative pressure wound therapy compared with conventional wound dressings for closed incisions in orthopaedic trauma surgery: A meta-analysis. Int Wound J. 2022;19(6):1319-1328.	Systematic review & meta-analysis **Objective:** To evaluate the effect of negative pressure wound therapy compared with conventional wound dressings on closed incisions in orthopaedic trauma surgery. **Methods:** A systematic search of Embase, PubMed, Cochrane Library, OVID, and Google scholar till October 2021, by a blend of keywords and related words for negative pressure wound therapy, conventional wound dressing, closed incisions, orthopaedic trauma surgery, surgical site infection, wound dehiscence, and length of hospital stay. <u>Inclusion criteria</u> 1. The study was a randomised controlled trial, prospective study, or retrospective study. 2. The target population is subjects with closed incisions in orthopaedic trauma surgery. 3. The intervention programme was negative pressure wound therapy. 4. The study included comparisons between the negative pressure wound therapy and conventional wound dressings <u>Exclusion criteria</u> 1. Studies that did not determine the effect of negative pressure wound therapy compared with conventional wound dressings on closed incisions in orthopaedic trauma surgery 2. Studies with subjects with dressings other than negative pressure wound therapy 3. Studies that did not focus on the effect of comparative results. The 'risk of bias tool' from the RoB 2: A revised Cochrane risk-of-bias tool for randomised trials was used to measure methodological quality.	**I**	12 included RCTs (3555 participants with closed incisions in orthopaedic trauma surgery at the start of the study) Published between 2010 and 2021 All studies evaluated the effect of negative pressure wound therapy compared with conventional wound dressings on closed incisions in orthopaedic trauma surgery. **Sample size:** 65 to 1519 participants **Country** United States (6 studies) China (2 studies) Netherlands (1 study) England (1 study) UK (1 study) Italy (1 study)	NPWT	Conventional wound dressings	NR	**1. Superficial Surgical Site Infection** (7 studies: 438 participants) OR 0.23 (95% CI 0.11–0.49, p = 0.31) with no heterogeneity (I^2 = 0%) **2. Lower Deep Surgical Site Infection** (10 studies: 1699 participants) OR 0.65 (95%CI 0.48– 0.88, p = 0.005) with low heterogeneity (I^2 = 38%) **3. Wound Dehiscence** (3 studies: 392 participants) OR 0.41 (95%CI 0.21–0.80, p= 0.009) with no heterogeneity (I^2 = 0%) Negative pressure wound therapy had significantly lower deep surgical site infection, superficial surgical site infection and wound dehiscence compared with conventional wound dressings in subjects with closed incisions in orthopaedic trauma surgery. **4. Length Of Hospital Stay** (3 studies: 188 participants) MD 0.29 (95%CI -2.00- 2.58, p = 0.80) with high heterogeneity (I^2 = 93%) Negative pressure wound therapy had no significant effect on the length of hospital stay. **CONCLUSIONS** Negative pressure wound therapy had significantly lower deep surgical site infection, superficial surgical site infection, and wound dehiscence; however, negative pressure wound therapy had no significant effect on the length of hospital stay compared with conventional wound dressings in subjects with closed incisions in orthopaedic trauma surgery.

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6. Zens Y, Barth M, Bucher HC, et al. Negative pressure wound therapy in patients with wounds healing by secondary intention: a systematic review and meta- analysis of randomised controlled trials. Syst Rev. 2020;9(1):238.	Systematic review & meta-analysis **Objective:** To compare the patient-relevant benefits and harms of NPWT with standard wound therapy (SWT) in patients with wounds healing by secondary intention. **Methods:** The authors searched for RCTs in MEDLINE, Embase, the Cochrane Central Register of Controlled Trials, and study registries (last search: July 2018) and screened reference lists of relevant systematic reviews and health technology assessments. Manufacturers and investigators were asked to provide unpublished data. Eligible studies investigated at least one patient-relevant outcome (e.g. wound closure). We assessed publication bias and, if feasible, performed meta-analyses, grading the results into different categories (hint, indication or proof of a greater benefit or harm)	**I**	48 included studies with 4315 patients Published between 1998 and 2016. **Sample size**: 12 - 460 patients 2-arm studies (n = 46) 3-arm study (n=1) 4-arm Monocentric (n=35) Multicenter (n=13) Inpatient setting (38 studies) Outpatient setting (10 studies) **Type of wounds** 1. Amputation wounds (1 study) 2. Pressure ulcers (2 studies) 3. Diabetic foot wounds (6 studies) 4. Diabetic ulcer wounds (1 study) 5. Foot wounds (1 study) 6. Fasciotomy wounds due to compartment syndrome (1 study) 7. Necrotizing fasciitis wounds (2 studies) 8. Open fractures (7 studies) 9. Open abdominal wounds (4 studies) 10. Pilonidal sinus wounds (2 studies) 11. Open thorax wounds (1 study) 12. Traumatic wounds of various causes (3 studies) 13. Leg ulcer wounds (4 studies) 14. Burns (2 studies) 15. Groyne wounds caused by infection (1 study) 16. Various other wounds due to diseases and/or traumatic or iatrogenic causes (10 studies)	NPWT	Standard wound care or standard dressings (sterilised gauze or moist gauze; alginate; hydrofiber; silver-dressing; polyurethanes)	Up to 12 months	**1. Wound healing** (14 studies: 1094 participants) There is a statistically significant effect in favour of NPWT (pooled OR 1.56, 95%CI 1.15 to 2.13, p = 0.008) **2. Time to wound healing after intervention and surgical wound closure (< 6 weeks yes/no)(**3 studies:100 participants) There was a statistically significant effect in favour of NPWT after 6 weeks (OR 16.07, 95%CI 3.19 to 80.97, p = 0.018). **3. For hospital stay (in days)(**11 studies: 978 participants) There is a statistically significant difference in favour of NPWT (pooled MD − 4.78, 95% CI − 7.79 to − 1.76, p = 0.005) **4. Hospital stay (> 1 month yes/no)** (4 studies: 200 participants) There was a statistically significant effect in favour of NPWT (pooled OR 0.07, 95% CI 0.02 to 0.17, p = 0.003). **CONCLUSIONS** This systematic review of NPWT versus SWT in patients with wounds healing by secondary intention showed some advantages of NPWT with regard to wound closure and hospital stay.

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7. Cirocchi R, Birindelli A, Biffl WL, et al. What is the effectiveness of the negative pressure wound therapy (NPWT) in patients treated with open abdomen technique? A systematic review and meta-analysis. J Trauma Acute Care Surg. 2016;81(3):575-584.	Systematic review & meta-analysis **Objective:** To compare negative pressure wound therapy (NPWT) with non NPWT techniques as **temporary abdominal closure** (TAC) and define if one technique has better outcomes than the other with regard to primary fascial closure, postoperative 30-day mortality and morbidity, enteroatmospheric fistulae, abdominal abscess, bleeding, and length of stay. **Methods:** According to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement and the Cochrane Hand- book for Systematic Reviews of Interventions, an online literature research (until July 1, 2015) was performed on MEDLINE, PubMed, Cochrane Central Register of Controlled Trials, and Cochrane Library databases. No language restriction was made. **Risk of bias assessment** The evaluation of potential risk of bias for each trial of the included RCTs was performed according to Cochrane ROB tool. The methodological quality of cohort studies was evaluated according to the modified grading system of the Scottish Intercollegiate Grading Network. <u>Inclusion criteria</u> 1. Randomized and nonrandomized comparative studies. 2. All patients undergoing open abdomen 3. Active negative pressure peritoneal therapy versus no active negative pressure peritoneal therapy.	**I**	8 included studies with 1225 participants (2 RCTs and 4 cohort studies) Published between 2008 and 2015 **Country** Turkey (1 study)(**3%** of participants) Italy (1 study) (**5%** of participants) Bulgaria (1 study) (**9%** of participants) USA (1 study) (**42%** of participants) Slovakia (1 study) (**9%** of participants) Poland (1 study) (**3%** of participants) Austria (1 study)(**20%** of participants) UK (1 study) (**47%** of participants) All patients underwent **Temporary Abdominal Closure** **Indications** Intra-abdominal sepsis (73%) Abdominal injuries (21%) Abdominal compartment syndrome (6%)	NPWT (VAC)	1. Bogota bag technique 2. Mesh-foil laparostomy 3. Laparostomy (adhesive impermeable with midline zip)	30 days	**1. Primary Fascial Closure** (8 studies) There was no statistically significant difference in the rate of fascial closure laparostomy between those in the NPWT group (459 of 723 (63.5%) and those in the conventional group without NPWT (69.5%). **OR 0.74 (95%CI 0.27–2.06; p = 0.57)** There was considerable heterogeneity between studies (I^2 = 83%). **2. Postoperative 30-day Mortality Rate (**8 studies) There was a significantly lower postoperative 30-day mortality rate in the NPWT group (28.5%) compared with the non-NPWT group (41.4%). **OR 0.46 (95%CI 0.23–0.91; p = 0.03)** There was considerable heterogeneity between studies (I^2 = 72%). **3. Postoperative Enteroatmospheric Fistulae** (4 studies) The enteroatmospheric fistula (EAF) rate was lower in the NPWT group (2.1%) compared with the non-NPWT group (5.8%), but the difference was not statistically significant **OR 0.63 (95%CI 0.12–3.15; p = 0.57); I^2 69%** **4. Postoperative Abdominal Abscess** (2 studies: 1 RCT and 1 cohort study) The abdominal abscess rate was lower in the NPWT group (2.4%) than in the non-

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							NPWT group (5.6%) but it was not statistically significant. **OR 0.42 (95%CI 0.13–1.34; p = 0.14); I^2 54%)** **5. Postoperative Bleeding Rate** (2 studies: cohort studies) The rate was lower in the NPWT group (5.7%) than in the no-NPWT group (14.9%), but it was not statistically significant. **OR 0.58 (95%CI 0.05–6.84; p = 0.87); I^2 61%** **6. Postoperative Length of Stay in ICU** (3 studies: 1 RCT and 2 cohort studies) The length of stay in ICU was significantly lower in the NPWT group than in the non-NPWT group **Mean difference, −4.53 days (95%CI, −5.46 to 3.60; p < 0.00001); I^2 6%** **CONCLUSIONS** The current systematic review and meta-analysis supports the use of NPWT in the temporary abdominal closure technique used in the care of the open abdomen. Based on the present analysis, we might conclude that NPWT is associated with better outcome than no NPWT. We observed a trend toward improved primary fascial closure, a statistically significantly reduced ICU length of stay and a lower 30-day mortality, and a trend to a reduction in the overall 30-day complication rate, the rate of EAF formation, the rate of postoperative abscess formation, and bleeding complications.

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							However, given the weaknesses in the primary studies, their small sample size and often conflicting direction of effect, particularly with the outcome of primary fascial closure and the rate of EAF formation, these observations must be interpreted cautiously, although they do reflect the current evidence from the data as presented.

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8. Iheozor-Ejiofor Z, Newton K, Dumville JC, et al. Negative pressure wound therapy for open traumatic wounds. Cochrane Database Syst Rev. 2018;7(7):Cd012522.	Systematic review & meta-analysis **Objective:** To assess the effects of NPWT for treating open traumatic wounds in people managed in any care setting. **Methods:** A systematic search of 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. The authors 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. <u>Inclusion criteria</u> 1. Published and unpublished randomised controlled trials (RCTs), including cluster RCTs, irrespective of language of report. We planned to exclude cross-over trials, as they are not an appropriate design in this context. 2. RCTs recruiting people (adults and children) described in the primary report as having open traumatic wounds involving either soft tissue wounds (including for example blunt degloving injuries (where skin is completely torn off underlying tissue) and gunshot wounds), or open fractures, managed in any care setting. 3. RCTs in which the use of a specific NPWT intervention during the treatment period was the only systematic difference between treatment groups. The authors anticipated that likely comparisons would include the use of NPWT during the care pathway compared with no use of NPWT or comparison of different types/brands of NPWT used during the care pathway.	**I**	7 included RCTs with 1377 participants Sample sizes ranged from 40 to 586 participants. Published from 2008-2017 - Two-arm, parallel-group RCTs (6 studies) - Three-arm trial (1 study) **Country** China (1 study) India (1 study) Iran (1 study) Kenya (1 study) Turkey(1 study) UK (1 study) USA (1 study)	NPWT	Conventional dressing (sterilised dressing/saline wet to moist dressings)	10 days to 67 months	**1. Complete wound healing at 6 weeks** (1 study:460 participants) There is no clear difference in number of wounds healed between NPWT 125mmHg and standard care in open fracture wounds over 6 weeks of follow-up **RR 1.01 (95%CI 0.81 to 1.27)** **2. Wound infection at 30 days** (4 studies: 596 participants) **RR 0.48 (95%CI 0.20 to 1.13), I^2 56%** It is uncertain whether there are differences in risk of wound infection between NPWT 125 mmHg and standard care. **3. Adverse events** One study presented data on post-operative complications related to the relevant open fracture 12 months following randomisation. These are presented here as further surgery and other wound-related complications in the trial. There were 111 further wound- related surgical events in the standard care arm and 95 in the NPWT arm. There were 43 other post-operative complications in the standard care arm and 39 in the NPWT arm. No difference was reported as statistically significant in the trial report. **4. Time to closure or coverage surgery** Time to closure or coverage surgery was reported in two studies analysing 151 participants. Mean time to further surgery ranged between 4 to 8.3 days with NPWT and 3.2 to 9.8 days with standard care. **5. Health-related quality of life** This evidence is from two studies (518 participants) that measured health-related quality of life at 3

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	Exclusion criteria 1. RCTs recruiting people with traumatic wounds due to burns (including exclusion of blast-related injuries that are likely to be burns). 2. Cross-over trials, as they are not an appropriate design in this context. 3. Studies using quasi-randomisation. 4. Studies that recruited people with trauma wounds that were not treated as open wounds prior to closure. These were considered solely to be surgical wounds healing by primary intention and would be included in the review focused on these wounds						months, 6 months, 9 months and 12 months. One study used the short form-36 (SF-36), reporting the physical component score (PCS score) in participants who were infected. One study used the SF-12 and EQ-5D utility and also assessed data at 12 months. There is probably no clear difference in the EQ-5D utility score at 12 months between NPWT and standard care (**MD -0.01, 95% CI -0.08 to 0.06; 364 participants**); moderate-certainty evidence downgraded once for imprecision. There is no clear difference in SF-12 PCS score (**MD -0.50, 95% CI -4.08 to 3.08; 329 participants**); low-certainty evidence downgraded twice for imprecision. **CONCLUSIONS** There is moderate-certainty evidence for no clear difference between NPWT and standard care on the proportion of wounds healed at six weeks for open fracture wounds. Moderate-certainty evidence means that the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different. It is uncertain whether there is a difference in risk of wound infection, adverse events, time to closure or coverage surgery or health-related quality of life between NPWT and standard care for any type of open traumatic wound.

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9. Lin DZ, Kao YC, Chen C, et al. Negative pressure wound therapy for burn patients: A meta-analysis and systematic review. Int Wound J. 2021;18(1):112- 123.	Systematic review & meta-analysis **Objective:** To assess the effectiveness of NPWT for improving burn wound healing. **Methods:** A systematic search of the PubMed database to identify relevant studies published from the inception of the database until May 16, 2020, using the following keywords: "NPWT" OR "negative pressure" AND "burn." Only results in English and Chinese were included. Inclusion criteria: (a) The included population was patients with burn wounds, (b) The applied intervention was NPWT, (c) NPWT was compared with other therapies for burn wounds, and (d) at least one quantitative outcome was reported. Exclusion criteria: Studies that were not in English or Chinese, used non-human experimental groups or evaluated unrelated outcomes were excluded. Case reports, case series, and retrospective data analyses were also excluded. **Quality assessment** Cochrane risk of bias tool was used to assess the studies' potential risk of bias after data collection. The GRADE (Grading of Recommendations, Assessment, Development, and Evaluation) approach was used for rating the quality of evidence for each comparison, and GRADEpro GDT was used to summarise the GRADE results in a table.	**I**	6 RCTs that included a total of 701 patients Published between 2011 and 2019 and investigated varying degree and TBSA of burn wounds.	NPWT 1. Intermittent mode (2 studies) 2. Continuous mode (4 studies) **Pressure magnitude** 1. −125 mmHg (3 studies) 2. −80 mmHg (2 studies) 3. −70 mmHg (1 study)	1. Split-thickness Skin Graft (STSG) 2. Dermal Substitute (DS) 3. Porcine Acellular Dermal Matrix (ADM) 4. Conventional dressing	3 months postoperation	**1. Graft take rate in the first week** (5 studies) The pooled analysis indicated an overall significantly improved graft take rate in the first week in the NPWT groups compared with control groups (standardised mean difference [SMD]: **2.62 [95%CI 1.01 to 4.22]; I^2 94%, p = 0.001**). Improved graft take rate at first week was noted in the following three subgroups: (a) NPWT and DS compared with DS **SMD = 5.93 (95%CI 4.27 to 7.60); p < 0.0001** (b) NPWT compared with DS **SMD = 8.52 (95%CI 6.05 to11.00); p < 0.00001** (c) NPWT to conventional dressing therapy alone **SMD = 1.91 (95%CI 1.03 to 2.79); p < 0.00001** No significant difference in graft take rate at first week was observed between the experimental (NPWT + DS + STSG) groups and the control (DS+STSG) groups **SMD = 0.2 [95%CI −0.40 to 0.79]; p = 0.65** No significant difference was found between the NPWT+STSG experimental groups and the control groups using STSG alone **SMD = 0.63 [95%CI −0.86 to 2.13]; I^2 86%, p = 0.41** **2. Complication rates** **(a) Infection rate** The pooled analysis showed significantly lower odds compared with control groups. **OR = 0.12 (95%CI 0.02 to 0.87); I^2 78%, p = 0.04**

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							(b) Overall complication rate (4 studies) No significant reduction of odds in the NPWT groups in the pooled analysis **OR = 0.59 (95%CI 0.16 to 2.17); I^2 78%, p = 0.42** **CONCLUSIONS** The results indicate that NPWT is a safe method for stimulating healing and lowering the infection rate of burn wounds. NPWT can be part of general burn management, and its incorporation into burn treatment guidelines is recommended.

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10. Chen L, Zhang S, Da J, et al. A systematic review and meta-analysis of efficacy and safety of negative pressure wound therapy in the treatment of diabetic foot ulcer. Ann Palliat Med. 2021;10(10):10830-10839.	Systematic review & meta-analysis **Objective:** To investigate the effectiveness and safety of NPWT for the treatment of diabetic foot ulcers **Methods:** The databases of PubMed, Embase, Ovid, and Cochrane library were selected as search platforms. RCTs published after 2010 were searched with the keyword "vacuum-assisted closure therapy" OR "negative pressure wound therapy" OR "diabetic foot". The Cochrane Review Handbook was used to assess the bias of the literatures. The software RevMan 5.4 was used for analysis to obtain a forest plot and funnel plot. Inclusion criteria **(I)** The type of literature was randomized controlled trial (RCT); **(II)** Year of publication was after 2010; **(III)** participants were all patients with DF; **(IV)** The study divided the participants into the intervention group and control group for the study. Exclusion criteria (I) Non-RCT; (II) Study with total sample size less than 10; (III) Non-diabetes-induced foot trauma; (IV) Studies lacking outcome measures or with incomplete data.	**I**	9 included RCTs with 943 participants **Sample size**: ranged from 22 to 345 The age range of participants was 50.3–69.5 years. The intervention time ranged from 7 to 56 days. **Country** India (4 studies) German (1 study) Iran (1 study) Poland (1 study) Pakistan (1 study) New Zealand (1 study)	NPWT (VAC)	Conventional wound treatment 1. Standard moist wound care (1 study) 2. Regular topical dressing (6 studies) 3. Normal saline soaking (1 study) 4. Coventional dressing (1 study)	1-6 months	**1. Wound healing rate** (6 studies) Combined analysis using the fixed effects model showed that the wound healing rate difference of the two groups was statistically significant. **Pooled OR =3.60 (95%CI 2.38 to 5.45); I^2 0%, p<0.001** **2. Granulation tissue formation time** (3 studies) Combined analysis using fixed effects model showed that the difference in granulation tissue formation time between NPWT and Conventional wound care was statistically significant. **MD =−8.95 (95%CI −10.26 to −7.64); I^2 0% p<0.001** **3. Incidence of adverse events** (2 studies) Combined analysis using fixed effects model showed that the adverse events rate difference between the two groups was not statistically significant **Pooled OR =0.49 (95%CI 0.10 to 2.42); I^2 0%, p=0.38** **4. Amputation rate** (6 studies) Combined analysis using the fixed effects model showed that the difference in amputation rate between the two groups was not statistically significant **Pooled OR =0.33 (95%CI 0.09 to 1.26); I^2 0%, p=0.10** **CONCLUSIONS** The results showed that NPWT can effectively accelerate wound healing, which is equally safe with general routine treatment. However, the negative pressure value should be appropriately maintained and adjusted to avoid bleeding tendency of the wound.

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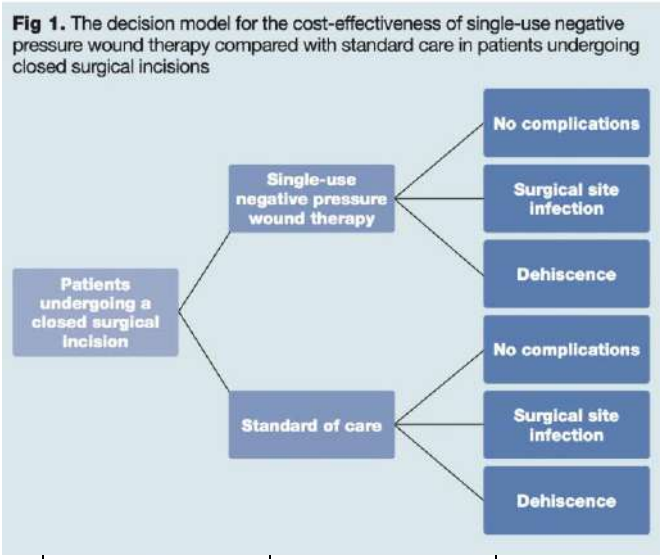
11. Song YP, Wang L, Yuan BF, et al. Negative-pressure wound therapy for III/IV pressure injuries: A meta-analysis. Wound Repair Regen. 2021;29(1):20-33	Systematic review & meta-analysis **Objective:** To investigate whether NPWT increase the rate of pressure injuries (PI) healing, reduced wound healing time and pain in patients, and improved disease, compare to standard wound care (SWC) **Methods:** Seven databases (PubMed, Cochrane Library, Embase, Web of science, CNKI, WanFang and VIP) were searched up to December of 2019. The search included the following MeSH terms: Pressure Ulcer, Decubitus, Negative-Pressure Wound Therapy, Vacuum Assisted Closure, Suction, Vacuum and Randomized Controlled Trial. <u>Inclusion criteria</u> Patients meet the III or IV PIs diagnostic criteria according to NPUAP; I (intervention): NPWT devices used for PIs compared with SWC; C (comparison): Any type of the SWC such as moist gauze and various wound dressings; O (outcome): the primary outcomes were the rate of complete healing and PIs healing time; the secondary outcomes were pain score, the time of dressing change, hospitalization cost and the condition of the exudate and the	**I**	16 inlcuded RCTs with 629 patients. **Sample size:** 12 to 74 **Country** USA (1 study), India (2 studies) UK (1 study) China (12 studies)	NPWT	Standard wound care (SWC)	Up to 10 months	**1. Wound healing time** (10 studies) The comparisons of the difference from pre- to post-intervention between NPWT and SWC revealed a statistically significant moderate effect size **WMD = -16.47 days (95%CI -22.36 to - 10.59) days; I^2 98.2%, p ≤ 0.001** **2. The condition of the exudate** (2 studies) Two studies evaluated the condition of the exudate. Since the evaluation results were not unified, the authors used descriptive analysis. Hong et al. showed that the ratio of exudate in the NPWT group was 29.41% and 75% in the first week and the second week, respectively, and their proportion was smaller than the SWC group. Dwivedi et al.'s study reported exudate levels at the sixth and ninth weeks. The data showed that the mean and standard deviation (1.52±0.68, 0.14±0.35) in the NPWT group were smaller than the mean and standard deviation (2.17±0.49, 1.35±0.75) in the SWC. **3. The condition of the wound improvement** (3 studies) Three studies evaluated the improvement of PIs including ulcer volume reduction rate, wound reduction rate and the length, width and height of PIs. Ford and Ali et al. mentioned that the volume reduction rate of PIs in the NPWT group (57% and 56.7%) was greater than that in the SWC group (25% and 30%). Ali et al. also reported a reduction in 90% of wounds in the NPWT group during the follow-up, compared with only 63.33% of the wounds in the SWC group. Dwivedi et al. showed that the height, width and depth of the wounds in the NPWT group were significantly lower than those in the SWC group (length: week-6: 3.05±1.99, 4.23±1.87; week-9: 1.52±1.66, 3.24±1.65; width: week-6: 2.57±2.12, 3.51±1.64; week-9: 1.19±1.33, 2.55±1.72; depth: week-6: 1.84±1.51, 1.95±0.56; week-9: 1.19±1.33, 1.16± 0.5). **4. Pain of III/IV PIs** (3 studies) The use of NPWT showed to be a significant advantage that relieved the pain in hospital compared to SWC **WMD = -2.39 (95%CI −3.47 to -1.30), I^2 = 93.5% p≤0.0001**

Bibliographic citation	Study Design/ Methods	LE	Number of Patients & Patient Characteristics	Intervention	Comparison	Length of Follow-up (If Applicable)	Outcome Measures/Effect Size
	wound improvement. S (study design): only RCTs that compared NPWT with SWC in patients with PIs were selected. Exclusion criteria **(1)** no RCT was performed; **(2)** no comparison between NPWT and SWC; **(3)** study did not show corresponding one of the needed outcomes such as the mean, the standard deviation or the RR; **(4)** multiple intervention measures.						**4. Dressing change workload** (8 studies) The comparison revealed a statistically significant effect respectively **SMD = -3.61 (95%CI -4.57 to - 2.66); I^2 85.4%, p ≤ 0.001** In China the data for the effect of the time of dressing change during the trails showed that the **SMD =-3.82 (-4.85, -2.78) (I^2=86.7%; p ≤ 0.001**). Sensitivity analysis showed the result is robust. **5. Hospital costs** (3 studies) Hospitalization cost of NPWT was significantly different compared with SWC group [**SMD = -2.55 (95%CI −4.07 to -1.03), p <0.01**]. Sensitivity analysis showed the result was robust. **CONCLUSIONS** Treatment with NPWT was associated with increased the healing rate, shorter the wound healing time, decreased patients' financial burden and suffering and workload of medical staff compared with SWC.

Evidence Table : **COST-EFFECTIVENESS**
Question : How cost-effective is NPWT as therapeutic dressing for acute and chronic wounds?

Bibliographic citation	Study Design/ Methods	LE	Number of Patients & Patient Characteristics	Intervention	Comparison	Length of Follow-up (If Applicable)	Outcome Measures/Effect Size
12. Nherera LM, Saunders C, Verma S, et al. Single-use negative pressure wound therapy reduces costs in closed surgical incisions: UK and US economic evaluation. J Wound Care. 2021;30(Sup5):S23-s31. **Countries** United Kingdom and USA	Cost-effectiveness analysis **Objective:** To evaluate the cost-effectiveness of sNPWT compared with standard care in reducing surgical site complications following closed surgical incisions. **Methods:** A decision analytic model was developed to explore the total costs and health outcomes associated with the use of the interventions in patients following vascular, colorectal, cardiothoracic, orthopaedic, C-section and breast surgery from the UK National Health Service (NHS) and US payer perspective over a 12-week time horizon. The authors modelled complications avoided (surgical site infection (SSI) and dehiscence) using data from a recently published meta- analysis. Cost data were sourced from published literature, NHS reference costs and Centers for Medicare and Medicaid Services. The authors conducted subgroup analysis of patients with diabetes, an American Society of Anesthesiologists (ASA) score ≥3 and body mass index (BMI) ≥30kg/m2. A sensitivity analysis was also conducted.		Adult patients over 18 years old who attend hospital for a closed surgical procedure of any type. (C-section, colorectal surgery, orthopaedic surgery, cardiothoracic surgery, plastics/ breast surgery and vascular surgery)	Single-use	Standard care	12 weeks	sNPWT resulted in better clinical outcomes and overall savings of £105 per patient from the UK perspective and $637 per patient from the US perspective. There were more savings when higher-risk patients with diabetes, or a BMI ≥30kg/m^2 or an ASA≥3 were considered. We conducted both one-way and probabilistic sensitivity analysis, and the results suggested that this conclusion is robust. **CONCLUSIONS** The findings suggest that the use of sNPWT following closed surgical incisions saves cost when compared with standard care because of reduced incidence of SSC. Patients at higher risk should be targeted first as they benefit more from sNPWT. This analysis is underpinned by strong and robust clinical evidence from both randomised and observational studies.

Fig 1. The decision model for the cost-effectiveness of single-use negative pressure wound therapy compared with standard care in patients undergoing closed surgical incisions



Evidence Table : **COST-EFFECTIVENESS**
Question : How cost-effective is NPWT as therapeutic dressing for acute and chronic wounds?

Bibliographic citation	Study Design/ Methods	LE	Number of Patients & Patient Characteristics	Intervention	Comparison	Length of Follow-up (If Applicable)	Outcome Measures/Effect Size
13. Hyldig N, Joergensen JS, Wu C, et al. Cost-effectiveness of incisional negative pressure wound therapy compared with standard care after caesarean section in obese women: a trial-based economic evaluation. Bjog. 2019;126(5):619-627. **Country** Denmark	Cost-effectiveness analysis **Objective:** To evaluate the cost-effectiveness of incisional negative pressure wound therapy (iNPWT) in preventing surgical site infection in obese women after caesarean section. **Methods:** **Design**: A cost-effectiveness analysis conducted alongside a clinical trial. **Setting**: Five obstetric departments in Denmark. **Population** Women with a pregestational body mass index (BMI) ≥30 kg/m2. **Method:** We used data from a randomised controlled trial of 876 obese women who underwent elective or emergency caesarean section and were subsequently treated with iNPWT (n = 432) or a standard dressing (n = 444). Costs were estimated using data from four Danish National Databases and analysed from a healthcare perspective with a time horizon of 3 months after birth. **Main outcome measures** Cost-effectiveness based on incremental cost per surgical site infection avoided and per quality-adjusted life-year (QALY) gained.		876 women with a pre-pregnancy BMI of ≥30 kg/m2 who had an emergency or planned CS were randomised to iNPWT (n = 432) or a standard post- operative dressing (n = 444) and followed for 30 days post-CS.	NPWT	Standard dressing	3 months	The total healthcare costs per woman were €5793.60 for iNPWT and €5840.89 for standard dressings. Incisional NPWT was the dominant strategy because it was both less expensive and more effective; However, no statistically significant difference was found for costs or QALYs. At a willingness-to-pay threshold of €30,000, the probability of the intervention being cost-effective was 92.8%. A subgroup analysis stratifying by BMI shows that the cost saving of the intervention was mainly driven by the benefit to women with a pre-pregnancy BMI ≥35 kg/m2. **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/m2.

Evidence Table : **COST-EFFECTIVENESS**
Question : How cost-effective is NPWT as therapeutic dressing for acute and chronic wounds?

Bibliographic citation	Study Design/ Methods	LE	Number of Patients & Patient Characteristics	Intervention	Comparison	Length of Follow-up (If Applicable)	Outcome Measures/Effect Size
14. Heard C, Chaboyer W, Anderson V, et al. Cost-effectiveness analysis alongside a pilot study of prophylactic negative pressure wound therapy. J Tissue Viability. 2017;26(1):79-84. **Country** Australia	Cost-effectiveness analysis **Objective:** To evaluate whether NPWT is cost-effective compared to standard care, for the prevention of surgical site infection (SSI) in obese women undergoing elective caesarean section, and inform development of a larger trial. **Methods:** An economic evaluation was conducted alongside a pilot randomised controlled trial at one Australian hospital, in which women were randomised to NPWT (n = 44) or standard care (n = 43). A public health care provider perspective and time horizon to four weeks post-discharge was adopted. Cost-effectiveness assessment was based on incremental cost per SSI prevented and per quality-adjusted life year (QALY) gained.		87 obese (BMI>30 kg/m^2) women were recruited during the scheduled pre-operative visit before elective caesarean section booked prior to the commencement of labour.	NPWT	Standard care	4 weeks post-discharge	Patients receiving NPWT each received health care costing AU$5887 (±1038) and reported 0.069 (±0.010) QALYs compared to AU$5754 (±1484) and 0.066 (±0.010) QALYs for patients receiving standard care. NPWT may be slightly more costly and more effective than standard care, with estimated incremental cost-effectiveness ratios (ICERs) of AU$1347 (95%CI dominant- $41,873) per SSI prevented and AU$42,340 (95%CI dominant- $884,019) per QALY gained. However, there was considerable uncertainty around these estimates. **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.

Evidence Table : **COST-EFFECTIVENESS**
Question : How cost-effective is NPWT as therapeutic dressing for acute and chronic wounds?

Bibliographic citation	Study Design/ Methods	LE	Number of Patients & Patient Characteristics	Intervention	Comparison	Length of Follow-up (If Applicable)	Outcome Measures/Effect Size
15. Whitty JA, Wagner AP, Kang E, et al. Cost-effectiveness of closed incision negative pressure wound therapy in preventing surgical site infection among obese women giving birth by caesarean section: An economic evaluation (DRESSING trial). Aust N Z J Obstet Gynaecol. 2023. **Country** Australia	Cost effectiveness and cost utility analyses **Objective:** To assess the cost-effectiveness of closed incision (ci)-NPWT compared to standard dressings for prevention of SSI in obese women giving birth by caesarean section (CS). **Methods:** Cost-effectiveness and cost-utility analyses from a health service perspective were undertaken alongside a multicentre pragmatic randomised controlled trial, which recruited women with a pre-pregnancy body mass index ≥30 kg/m^2 giving birth by elective/semi-urgent CS who received ci-NPWT (n = 1017) or standard dressings (n = 1018). Resource use and health-related quality of life (SF-12v2) collected during admission and for four weeks post-discharge were used to derive costs and quality-adjusted life years (QALYs).		Women with a pre-pregnancy body mass index of ≥30 kg/m2 giving birth by elective or semi-urgent CS, were stratified by hospital and randomised to receive ci-NPWT (n = 1017) or standard dressing (n = 1018).	ci-NPWT	standard dressings	four weeks post-discharge	ci-NPWT was associated with AUD$162 (95%CI −$170 to $494) higher cost per person and an additional $12 849 (95%CI −$62 138 to $133 378) per SSI avoided. There was no detectable difference in QALYs between groups; however, there are high levels of uncertainty around both cost and QALY estimates. There is a 20% likelihood that ci-NPWT would be considered cost-effective at a willingness-to-pay threshold of $50 000 per QALY. Per protocol and complete case analyses gave similar results, suggesting that findings are robust to protocol deviators and adjustments for missing data. **CONCLUSIONS** -ci-NPWT for the prevention of SSI in obese women undergoing CS is unlikely to be cost-effective in terms of health service resources and is currently unjustified for routine use for this purpose.

Evidence Table : **COST-EFFECTIVENESS**
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Bibliographic citation	Study Design/ Methods	LE	Number of Patients & Patient Characteristics	Intervention	Comparison	Length of Follow-up (If Applicable)	Outcome Measures/Effect Size
16. Nherera LM, Trueman P, Karlakki SL. Cost-effectiveness analysis of single-use negative pressure wound therapy dressings (sNPWT) to reduce surgical site complications (SSC) in routine primary hip and knee replacements. Wound Repair Regen. 2017;25(3):474-482. **Country** United Kingdom	Cost-effectiveness analysis **Objective:** To evaluate the cost-effectiveness of single-use negative pressure wound therapy in patients undergoing primary hip and knee replacements using effectiveness data from a recently completed non-blinded randomized controlled trial. **Methods:** A decision analytic model was developed from **UK National Health Service perspective** using data from a single-centre trial. 220 patients were randomized to treatment with either single-use negative pressure wound therapy or standard care i.e., film dressings of clinician choice and followed for 6 weeks. Outcomes included dressing changes, length of stay (LOS), surgical site complications, cost and quality adjusted life years. The expected complications with standard care were taken from the Karlakki et al. RCT.10 These baseline data were then adjusted to reflect the expected reduction in complications and LOS reported in the same RCT observed in patients treated with sNPWT. The economic model adopted a similar time horizon as the RCT of 6 weeks post-operatively, which was deemed sufficient follow-up to capture the majority of SSI and their associated impact on resource use and outcomes. Given the short time horizon of less than 1 year, no discounting was applied to either costs or outcomes.		220 consecutively enrolled adults aged 18 years or older scheduled to undergo routine hip and knee replacement between October 2012 and October 2013 and patients were followed for 6 weeks after surgery. (Karlakki et al.)	Single-use negative pressure wound therapy [PICO (Smith & Nephew Healthcare Ltd, Hull, UK)]	Standard care	6 weeks	The randomized controlled trial reported a reduction in dressing changes (p=0.002), SSC (p=0.06) and LOS (p=0.07) in favour of single-use negative pressure wound therapy compared with standard care. The model estimated 0.116 and 0.115 QALY gained, 0.98 and 0.92 complications avoided for single-use negative pressure wound therapy and standard care, respectively. The cost/patient was £5,602 ($7,954) and £6,713 ($9,559) for single-use negative pressure wound therapy and standard care respectively resulting in cost-saving of £1,132 ($1,607) in favour of single-use negative pressure wound therapy. Greater savings were observed in subgroups of higher risk patients with BMI□35 and ASA□3 i.e., £7,955 ($11,296) and £7,248 ($10,293), respectively. The findings were robust to a range of sensitivity analyses. **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 maximize efficiency**.**

Evidence Table : **COST-EFFECTIVENESS**
Question : How cost-effective is NPWT as therapeutic dressing for acute and chronic wounds?

Bibliographic citation	Study Design/ Methods	LE	Number of Patients & Patient Characteristics	Intervention	Comparison	Length of Follow-up (If Applicable)	Outcome Measures/Effect Size
17. Costa ML, Achten J, Knight R, et al. Negative-pressure wound therapy compared with standard dressings following surgical treatment of major trauma to the lower limb: the WHiST RCT. Health Technol Assess. 2020;24(38):1-86. **Country** United Kingdom	Cost-effectiveness analysis **Objective:** To investigate the cost-effectiveness, of incisional negative-pressure wound therapy versus standard dressing for wounds associated with major trauma to the lower limbs. **Methods:** The within-trial economic evaluation was conducted in line with the reference case required by the National Institute for Health and Care Excellence for technology appraisal, such that costs were estimated from an NHS and Personal Social Services perspective, and health utilities were derived from the EuroQol-5 Dimensions instrument using UK tariffs. An incremental cost-effectiveness analysis comparing the cost-effectiveness of standard dressing with that of incisional NPWT, expressed in terms of incremental cost-per-QALY gained, was performed from the NHS and PSS perspective for the base-case analysis. Results were presented using incremental cost-effectiveness ratios (ICERs) and cost-effectiveness acceptability curves (CEACs) generated via non-parametric bootstrapping with 1000 replicas. This accommodates sampling (or stochastic) uncertainty and varying levels of willingness to pay for an additional QALY. The ICER was compared with willingness-to-pay thresholds of £20,000 and £30,000 per QALY, which are commonly assumed in the UK by bodies such as the National Institute for Health and Care Excellence. An additional £15,000 cost-effectiveness threshold was also included to reflect recent trends in health-care decision-making. The net monetary benefit (NMB) of standard dressing versus incisional NPWT was also computed and presented in a graph across different cost-effectiveness thresholds, for which a positive incremental NMB indicated that incisional NPWT is cost-effective compared with standard dressing at the given cost-effectiveness threshold.		1548 adult patients presented at the recruitment centres within 72 hours of sustaining major trauma and who required a surgical incision to treat a fractured lower limb.	Incisional NPWT	Standard dressing	6 months post surgery	The incremental cost-effectiveness ratio in the base-case analysis was £396,531 per quality of life-year gained, which indicated that incisional negative-pressure wound therapy had higher costs and marginally better outcomes than standard dressings. The health economic evaluation therefore indicated that incisional negative-pressure wound therapy is very unlikely to be cost-effective. **CONCLUSIONS** There was no difference in the rate of other wound healing complications, nor any difference in the patients' self-report of disability or health-related quality of life. Incisional negative-pressure wound therapy is very unlikely to be cost-effective. In conclusion, and contrary to previous reports, incisional negative-pressure wound therapy did not provide an economic benefit for patients with surgical incisions associated with major trauma to the lower limbs.

Evidence Table : **COST-EFFECTIVENESS**
Question : How cost-effective is NPWT as therapeutic dressing for acute and chronic wounds?

Bibliographic citation	Study Design/ Methods	LE	Number of Patients & Patient Characteristics	Intervention	Comparison	Length of Follow-up (If Applicable)	Outcome Measures/Effect Size
18. Svensson-Björk R, Saha S, Acosta S, et al. Cost-effectiveness analysis of negative pressure wound therapy dressings after open inguinal vascular surgery - The randomised INVIPS-Trial. J Tissue Viability. 2021;30(1):95-101. **Country** Sweden	Cost-effectiveness analysis **Objective:** To evaluate the cost-effectiveness of NPWT compared to standard dressings for the prevention of SSIs after open inguinal vascular surgery **Methods:** Patient data were retrieved from the randomised INVIPS-trial's open arm, which included patients randomised to either NPWT or standard dressings. The patients were surveyed for SSIs for 90 days postoperatively. The patients' individual cost data were included and analysed from a **healthcare perspective.** The patients' quality of life was measured using the Vascuqol-6 questionnaire pre- and 30 days postoperatively. Cost-effectiveness of NPWT was determined by decreased or equal total costs and a significant reduction in SSI incidence.		119 patients underwent elective, open revascularisation procedures in the lower limb via inguinal incisions between November 2013 and October 2018 at Skåne University Hospital in Malmo¨, Sweden.			30 days postoperatively	The mean vascular procedure-related costs at 90 days were €16,621 for patients treated with NPWT (n = 59) and €16,285 for patients treated with standard dressings (n = 60), p = 0.85. The SSI incidence in patients treated with NPWT was 11.9% (n = 7/59) compared to 30.0% (n = 18/60) with standard dressings, p = 0.015. This corresponds to an increased mean cost of €1,853 per SSI avoided. The cost-effectiveness plane of incremental vascular procedure-related costs and difference in Vascuqol-6 score showed that 42% of estimates were in the quadrant where NPWT was dominant. **CONCLUSIONS** NPWT is considered cost-effective over standard dressings in patients undergoing open inguinal vascular surgery due to reduced SSI incidence at no higher costs.

Evidence Table : **COST-EFFECTIVENESS**
Question : How cost-effective is NPWT as therapeutic dressing for acute and chronic wounds?

<table>
<tr><th>Bibliographic citation</th><th>Study Design/ Methods</th><th>LE</th><th>Number of Patients & Patient Characteristics</th><th>Intervention</th><th>Comparison</th><th>Length of Follow-up (If Applicable)</th><th>Outcome Measures/Effect Size</th></tr>
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<td>19. Nicolazzo D, Rusin E, Varese A, et al. Negative Pressure Wound Therapy and Traditional Dressing: An Italian Health Technology Assessment Evaluation. Int J Environ Res Public Health. 2023;20(3).

Country
Italy</td>
<td>Budget impact analysis

Objective:
To assess the added value in implementing advanced wound care in the clinical practice, enhancing not only a higher clinical outcome, but also an economic hospital sustainability

Methods:
The analysis assumed the hospital perspective and considered a 12-month time horizon. To better evaluate the results and demonstrate the true value of the device in reducing the after-surgery infection rate, the study has been restricted to the management of an inguinal incision in the field of vascular and endoprosthetic surgery inside an Italian hospital in Piedmont (Northern Italy).

A budget impact analysis (BIA) was performed to define the economic sustainability of NPWT adoption on the hospital budget, assuming a 12-month time horizon and considering the number of admissions performed within a medium-size hospital for lower limb revascularization surgery with groin injury (N = 811 patients/year).

The budget impact analysis includes the economic evaluation of the potential development of a surgical site infection, as well as re-operation or re-hospitalization.</td>
<td></td>
<td>Patients over 60 affected by PAD who have undergone hospitalization, for vascular surgery for lower limb revascularization.</td>
<td>NPWT</td>
<td>Traditional dressings</td>
<td>12 months</td>
<td>The economic results were in line with scientific evidence on the topic: in high-risk patients and high-risk surgical procedures, ciNPT (closed incision negative pressure) appears to have the potential to reduce surgical incision complications and a surgical cost per patient up to $9000, depending on the type of incision and patient risk factors.

The more the NPWT is implemented in the clinical practice, the higher the economic savings, ranging from a minimum of 1.15% (Scenario 2) to a maximum of 18.56% (Senario 4).

The reduction in hospital stays could have a favourable impact on a decrease in the patients' productivity losses as well as a faster recovery rate, with a positive social impact.

Since NPWT is related to a lower length of stay and requires a lower number of follow-up procedures, it could generate a reduction in the social costs sustained by both the patients and the related caregivers equal to 28% (EUR 710 for traditional dressing vs. EUR 985 for NPWT).

CONCLUSIONS
The economic analysis has demonstrated the capability of NPWT to optimize the overall PAD patients' clinical pathway, with an overall saving per patient equal to 15%.

The BIA confirms the economic sustainability of NPWT for the hospital budget.</td>
</tr>
</table>

	Population Traditional Medication	Population NPWT	Pathway Traditional Medication	Pathway NPWT	Total	Savings %
Base Scenario	100%	0%	EUR 9,058,814	EUR 0	EUR 9,058,814	
Scenario 1	80%	20%	EUR 7,461,150	EUR 1,802,681	EUR 9,263,831	2.26%
Scenario 2	50%	50%	EUR 5,064,655	EUR 3,890,317	EUR 8,954,972	−1.15%
Scenario 3	20%	80%	EUR 2,668,160	EUR 5,977,953	EUR 8,646,112	−4.56%
Scenario 4	0%	100%	EUR 0	EUR 7,369,710	EUR 7,369,710	−18.65%

Evidence Table : **COST-EFFECTIVENESS**
Question : How cost-effective is NPWT as therapeutic dressing for acute and chronic wounds?

Bibliographic citation	Study Design/ Methods	LE	Number of Patients & Patient Characteristics	Intervention	Comparison	Length of Follow-up (If Applicable)	Outcome Measures/Effect Size
20. Nherera LM, Trueman P, Schmoeckel M, et al. Cost-effectiveness analysis of single use negative pressure wound therapy dressings (sNPWT) compared to standard of care in reducing surgical site complications (SSC) in patients undergoing coronary artery bypass grafting surgery. J Cardiothorac Surg. 2018;13(1):103. **Country** German	Cost-effectiveness analysis **Objective:** To estimate the cost-effectiveness of single use negative pressure wound therapy (sNPWT) compared to 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. **Methods:** A decision analytic model was developed from the Germany Statutory Health Insurance payer's perspective over a 12-week time horizon. Baseline data on SSC, revision operations, length of stay, and readmissions were obtained from a prospective observational study of 2621 CABG patients in Germany. Effectiveness data for sNPWT was taken from a randomised open label trial conducted in Poland which randomised 80 patients to treatment with either sNPWT or standard care. Cost data (in Euros) were taken from the relevant diagnostic related groups and published literature.		Patients undergoing CABG surgery. The mean age of patients that were modelled is 65 years	sNPWT	Standard care	12 weeks	The clinical study reported an increase in wounds that healed without complications 37/40 (92.5%) in the sNPWT compared to 30/40 (75%) patients in the SC group p = 0.03. The model estimated sNPWT resulted in 0.989 complications avoided compared to 0.952 and the estimated quality adjusted life years were 0.8904 and 0. 8593 per patient compared to standard care. The estimated mean cost per patient was €19,986 for sNPWT compared to €20,572 for SC resulting in cost-saving of €586. The findings were robust to a range of sensitivity analyses. **CONCLUSIONS** The sNPWT can be considered a cost saving intervention that reduces surgical site complications following CABG surgery compared to standard care. The authors 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.

Evidence Table : **COST-EFFECTIVENESS**
Question : How cost-effective is NPWT as therapeutic dressing for acute and chronic wounds?

Bibliographic citation	Study Design/ Methods	LE	Number of Patients & Patient Characteristics	Intervention	Comparison	Length of Follow-up (If Applicable)	Outcome Measures/Effect Size
21. Petrou S, Parker B, Masters J, et al. Cost-effectiveness of negative-pressure wound therapy in adults with severe open fractures of the lower limb: evidence from the WOLLF randomized controlled trial. Bone Joint J. 2019;101-b(11):1392-1401. **Country** United Kingdom	Cost-effectiveness analysis **Objective:** To estimate the cost-effectiveness of negative-pressure wound therapy (NPWT) in comparison with standard wound management after initial surgical wound debridement in adults with severe open fractures of the lower limb. **Methods:** An economic evaluation was conducted from the perspective of the United Kingdom NHS and Personal Social Services, based on evidence from the 460 participants in the Wound Management of Open Lower Limb Fractures (WOLLF) trial. Economic outcomes were collected prospectively over the 12-month follow-up period using trial case report forms and participant-completed questionnaires. Bivariate regression of costs (given in £, 2014 to 2015 prices) and quality-adjusted life-years (QALYs), with multiple imputation of missing data, was conducted to estimate the incremental cost per QALY gained associated with NPWT dressings. Sensitivity and subgroup analyses were undertaken to assess the impacts of uncertainty and heterogeneity, respectively, surrounding aspects of the economic evaluation.		460 patients, aged 16 years or over and presenting with a severe, open frac- ture of the lower limb, were randomly assigned on a 1:1 basis to NPWT or a standard wound dressing after the first surgical debridement of the open fracture wound.	NPWT	Standard care	12 months	The base case analysis produced an incremental cost-effectiveness ratio of £267 910 per QALY gained, reflecting higher costs on average (£678; 95% confidence interval (CI) -£1082 to £2438) and only marginally higher QALYS (0.002; 95% CI -0.054 to 0.059) in the NPWT group. The probability that NPWT is cost-effective in this patient population did not exceed 27% regardless of the value of the cost-effectiveness threshold. This result remained robust to several sensitivity and subgroup analyses. **CONCLUSIONS** This trial-based economic evaluation suggests that NPWT is unlikely to be a cost-effective strategy for improving outcomes in adult patients with severe open fractures of the lower limb.

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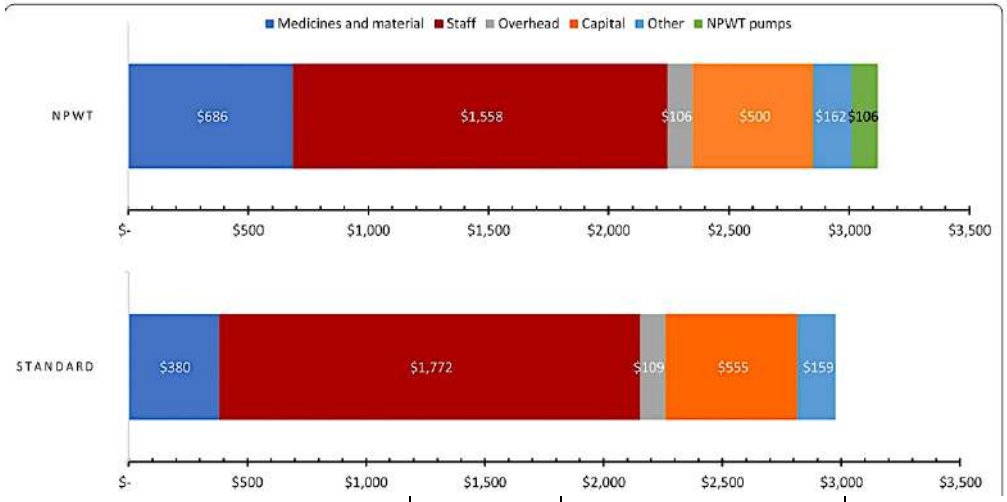
22. Älgå A, Löfgren J, Haweizy R, et al. Cost analysis of negative-pressure wound therapy versus standard treatment of acute conflict-related extremity wounds within a randomized controlled trial. World Journal of Emergency Surgery. 2022;17(1):9. **Countries** Jordan and Iraq	Cost analysis study **Objective:** To estimate treatment-related costs of NPWT in comparison with standard treatment for conflict-related extremity wounds. **Methods:** The authors derived outcome data from a randomized, controlled superiority trial that enrolled adult (≥ 18 years) patients with acute (≤ 72 h) conflict-related extremity wounds at two civilian hospitals in Jordan and Iraq. Primary endpoint was mean treatment-related healthcare costs (adjusted to 2019 US dollars).		165 adult (≥18 years) patients with acute (≤72 h) conflict-related extremity wounds Patients were enrolled from June 9, 2015, to October 24, 2018. 155 men [93.9%]; 10 women [6.1%]; and median [IQR] age, 28 [21–34] years) were included in the analysis.  **Mean costs per treated patient. Currency data are in 2019 US dollars.** **NPWT, negative-pressure wound therapy**	NPWT	Standard treatment (wound dressings with non-adhesive sterile gauze covered with a bandage)		The cost per surgery was $329 in the NPWT group and $250 in the standard treatment group. The cost per day spent at the hospital was $116 and $109 in the NPWT and standard treatment groups, respectively. The mean patient cost for the full hospital period was $3118 in the NPWT group and $2976 in the standard treatment group (Table 2). Consequently, the use of NPWT was associ- ated with an additional $142 (5%) per treated patient compared to standard treatment. Overall, results were robust in a sensitivity analysis. **CONCLUSIONS** With similar clinical outcomes compared to standard care, the results do not support the use of NPWT in routine treatment of conflict-related extremity wounds at civilian hospitals in resource scarce settings

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23. Alipour V, Rezapour A, Ebrahimi M, et al. Cost-Utility Analysis of Negative Pressure Wound Therapy Compared With Traditional Wound Care in the Treatment of Diabetic Foot Ulcers in Iran. Wounds. 2021;33(2):50-56. **Country** Iran	CEA/ Cost-utility study **Objective:** To analyse the cost- utility of NPWT compared with traditional wound care (TWC) for the treatment of patients with diabetic foot ulcers in Iran from the perspective of health care providers. **Methods:** The Markov model was applied, incorporating the 7 health states of uninfected, infected, infected post-amputation, healed, healed post-amputation, amputation, and death for a 1-year time period and monthly cycles (12 cycles). Quality-adjusted life years (QALYs) were calculated from utility weights of each diagnosis, which were derived from the published literature. Costs for each diagnosis were estimated monthly and separately based on inpatient and outpatient care. The analysis of cost-effectiveness and sensitivity for uncertain parameters was carried out using TreeAge Pro 2011 software.		Patients with DFU	NPWT	Traditional wound care	1 year	A total of 200 patient records (NPWT = 100; TWC = 100) were analyzed in this study. The results indicated that annual cost per patient for NPWT and TWC strategies were $5165 ± $3258 and $9833 ± $5861, respectively. In addition, mean effectiveness per patient per year for NPWT and TWC strategies were 8.9026 ± 1.7622 and 8.7974 ± 1.855 QALYs, respectively. When treatment with NPWT was compared with TWC using the ICER of -$44 370 per QALY, NPWT was shown as a more cost-effective treatment strategy than TWC. **Conclusions** The results of the study show that NPWT is less costly and more effective compared with TWC. In addition, NPWT reduces the number of amputations and increases the number of healed wounds, decreasing patients' and payers' costs. The sensitivity analysis of parameters proved the robustness of the Markov model.

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24. Driver VR, Blume PA. Evaluation of wound care and health-care use costs in patients with diabetic foot ulcers treated with negative pressure wound therapy versus advanced moist wound therapy. J Am Podiatr Med Assoc. 2014;104(2):147-153. **Country** US	Costing study **Objective:** To evaluate overall costs of negative pressure wound therapy (NPWT; V.A.C. Therapy; KCI USA, Inc, San Antonio, Texas) versus advanced moist wound therapy (AMWT) in treating grade 2 and 3 diabetic foot wounds during a 12-week therapy course. **Methods:** Data from two study arms (NPWT [n = 169] or AMWT [n = 166]) originating from Protocol VAC2001-08 were collected from patient records and used as the basis of the calculations performed in the cost analysis. Costs were divided into wound therapy costs and nontherapy wound treatment costs. Wound therapy costs consisted of the cost of dressings or the NPWT system, and labor during dressing changes. Nonwound therapy costs encompassed concomi- tant antibiotic therapy, acute inpatient services (including acute-care hospitalizations and wound- related surgical procedures that were performed in an acute-care facility), extended care hospitalisations (ie, stays in skilled nursing facilities (SNFs), rehabilitation clinics, or hospice), and outpatient surgical procedures. Costs were calculated retrospectively based on the observed frequency that trial participants used health-care resources. Estimated hospital costs were derived from data from the Healthcare Cost and Utilization Project Nationwide Inpatient Sample. Mean cost of physician services for lower- limb amputation, debridement, and other wound-related surgical procedures in acute-care and outpatient facilities were estimated using the Medicare Resource-Based Relative Value Scale 2007. The mean cost per inpatient day in extended-care facilities was estimated using the Medicare reimbursement rate for an SNF.		Patient population consisted of diabetic adults 18 years old or older who had a grade 2 or 3 calcaneal, dorsal, or plantar foot ulcer greater than 2 cm2 in area after debridement.	Negative pressure wound therapy was delivered using the V.A.C. Therapy System. Dressing changes were performed every 48 to 72 hours (minimum 3 times per week).	AMWT dressings included use of alginates, hydrocolloids, foams, or hydrogels, according to Wound, Ostomy and Continence Nursing Society guidelines and institutional treatment protocols that follow standards of care for treating DFUs	12 weeks	The total cost for all patients, regardless of closure, was $1,941,472.07 (average per-patient cost: $11,984.40) in the NPWT group compared to $2,196,315.86 (average per-patient cost: $13,557.51) in the AMWT group. The total wound treatment cost was $764,392.30 (average per-patient cost: $4,718.47) in the NPWT group compared to $374,599.14 (average per-patient cost: $2,312.34) in the AMWT group. The total nontherapy wound treatment cost was $1,177,079.77 (average per-patient cost: $7,265.93) in the NPWT group compared to $1,821,716.73 (average per-patient cost: $11,245.17) in the AMWT group. The results showed that NPWT patients had a significantly higher average daily rate of volume reduction compared to the control group (5.02 ± 13.36 versus 0.40 ± 0.88 cm3/day; p = 0.046). Regardless of closure status, the overall median cost to close 1 cm2 of the wound using NPWT was $1,460.42 compared to $2,566.17 using AMWT. The cost-per-cm3 reduction was $11.90/cm3 for NPWT patients versus $30.92/cm3 for the control group. **Conclusion** NPWT is more cost effective than AMWT in recalcitrant wounds because of lower expenditures on resource use and procedures.

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25. Vaidhya N, Panchal A, Anchalia MM. A New Cost-effective Method of NPWT in Diabetic Foot Wound. Indian J Surg. 2015;77(Suppl 2):525-529. **Country** India	Costing study **Objective:** To determine whether NPWT is a cost-saving option compare to saline-moistened gauze in the treatment of diabetic foot wounds. **Methods:** Cost-analysis was conducted. The total number of days till end point achieved, total number of dressings required and average cost of treatment calculated. End point of study was when wound was ready for either skin grafting or secondary suturing.		60 patients having diabetic foot were included. All these patients initially underwent surgical debridement for removal of necrotic patch or slough. All patients were given standard medical therapy for diabetes and anti-microbials were given according to culture sensitivity reports. 30 patients were dressed with NPWT dressing and 30 patients were dressed with conventional dressing. Patients with osteomyelitis, peripheral vascular disease, or malignancy were excluded.	NPWT (VAC^{TM} system, KCI Inc., USA) NPWT system consisted of four components: A usual suction machine generating pressure of −80 to −150 mmHg, Ryle's tube, piece of foam cut according to size and shape of ulcer, and adhesive transparent dressing (OpSite by Smith & Nephews, UK). The suction was applied 30 min on and 30 min off. Dressings changed every 48–72 hours.	Conventional dressing - Saline-moistened gauze Conventional dressing was done by cleaning with povidine iodine solution with or without hydrogen peroxide and applying moist gauze to wound and dressing closed by cotton bandage. Dressing changed twice a day.	-	Satisfactory healing was achieved in mean 7.46 (SD ± 2.25) dressings in NPWT group vs 69.8 (SD ± 11.93) dressings in conventional group (p<0.001). Mean days of dressings were 17.2 (SD ± 3.55) in NPWT group as compared to 34.9 (SD ±5.96) days in conventional group (p < 0.001). Success rates of 90% and 76.66% were achieved in NPWT and conventional groups respectively. Average cost of NPWT was Rs. 500 approximately and conventional dressing costs Rs. 200 approximately per dressing. Therefore, average cost of NPWT and conventional dressing was Rs. 3,750 and 7,000, respectively. If, cost of daily treatment, hospital stay, and morbidity is taken into account, the cost of conventional dressing will significantly increase. The VAC system by KCI Inc., USA costs Rs. 3–4 lacs and dressing costs Rs. 1,100/day. And rental charges are $100/day. Requirement for analgesics and antibiotics was much less in NPWT group. Patient compliance was also better among NPWT group.

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26. Flack S, Apelqvist J, Keith M, et al. An economic evaluation of VAC therapy compared with wound dressings in the treatment of diabetic foot ulcers. J Wound Care. 2008;17(2):71-78. **Country** USA	CEA **Objective:** To determine the cost-effectiveness of Vacuum Assisted Closure (VAC) therapy (KCI Medical), based on a comparison with both traditional and advanced wound dressings, for the treatment of diabetic foot ulcers in the US. **Methods:** A Markov model was designed to estimate the cost per amputation avoided and the cost per quality-adjusted life year (QALY) of VAC therapy, compared with both traditional and advanced dressings. Over a one-year period the Markov model simulated 1000 patients using transition probabilities obtained from the literature. The health states used in the model were: uninfected ulcer; infected ulcer; infected ulcer post-amputation; healed; healed post-amputation; amputation; and death. Patients initially treated with VAC switched to the advanced dressing after three months of treatment if their wound remained unhealed. Patients treated with traditional or advanced dressings were assumed to continue with their treatment for the full 12 months if they remained unhealed. **Perspective** The US payer (national health service or insurer)		The population considered is intended to reflect the population of patients presenting with diabetic foot ulcers in practice. The characteristics of the population include: ● Males and females with diabetic foot ulcers ● Type 1 or type 2 diabetes mellitus ● Aged 50–65 years ● 2.3% of patients presenting with an infected ulcer, with all other patients presenting with an unhealed diabetic foot ulcer.	NPWT (VAC, KCI Medical)	Traditional and advanced wound dressings **Traditional dressing**: Saline gauze **Advanced wound dressings:** Apligraf (Novartis) and Dermagraft (Smith & Nephew).	12 months	The model results demonstrate improved healing rates (61% versus 59%), more QALYs (0.54 versus 0.53) and an overall lower cost of care ($52,830 versus $61,757 per person) for patients treated with VAC therapy compared with advanced dressings. Vacuum Assisted Closure was also shown to be a dominant intervention when compared with traditional dressings. **Conclusion** The model results indicate that VAC therapy is less costly and more effective than both traditional and advanced dressings. The results are robust to changes in key parameters, including the transition probabilities, the cost of VAC therapy and the utility weights applied to health states.

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27. Whitehead SJ, Forest-Bendien VL, Richard JL, et al. Economic evaluation of Vacuum Assisted Closure® Therapy for the treatment of diabetic foot ulcers in France. Int Wound J. 2011;8(1):22-32. **Country** France	CEA **Objective:** To assess the cost-effectiveness of Vacuum Assisted Closure® (V.A.C.®) Therapy compared with advanced wound care (AWC) for the treatment of diabetic foot ulcers (DFUs) in France. **Methods:** The Markov model follows the progression of 1000 hypothetical patients over a 1-year period. The model was populated with French-specific data, obtained from published sources and clinical experts. The analysis evaluated costs and health outcomes, in terms of quality-adjusted life-years (QALYs), wounds healed and amputations, from the perspective of the payer.		The simulated DFU patients have either type 1 or type 2 diabetes and are aged 50–65 years. The model assumes that all patient characteristics other than the treatment regimes are equal, such as wound size and wound duration. It is assumed that on entering the model, patients have not previously undergone an amputation.	V.A.C.® Therapy	Combination of Algosteril® (Laboratoires Brothier, Nanterre, France) alginate with Adaptic® (Systagenix Wound Management, Gargrave, UK) could be considered to be representative of the standard practice for wound management in France	1 year	- The patients treated with V.A.C.® Therapy experienced more QALYs (0·787 versus 0·784) and improved healing rates (50·2% versus 48·5%) at a lower total cost of care (€ 24,881 versus €28,855 per patient per year) when compared with advanced wound care. - Sensitivity analyses conducted around key model parameters indicated that the results were affected by hospital resource use and costs. -DFU treatment using V.A.C.® Therapy in France was associated with lower costs, additional QALYs, more healed ulcers and fewer amputations than treatment with advanced wound care. -V.A.C.® Therapy was therefore found to be the dominant treatment option.