Vacuümgeassisteerde Wondbehandeling: een Rapid Assessment

KCE reports 61A

Federaal Kenniscentrum voor de Gezondheidszorg
Centre fédéral d'expertise des soins de santé
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Disclaimer:	De experts en validatoren werkten mee aan het wetenschappelijk rapport maar werden niet betrokken in de aanbevelingen voor het beleid. Deze aanbevelingen vallen onder de volledige verantwoordelijkheid van het KCE.
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Voorwoord

Simultaan met de toename van bepaalde chronische ziekten zoals diabetes en met de progressieve veroudering worden beleidsmakers meer en meer geconfronteerd met vragen omtrent kwaliteit en terugbetaling van wondzorg. Op zich is dit misschien een weinig spectaculair onderwerp, maar daarom niet minder belangrijk gezien het aantal patiënten – naar schatting een 150.000 – dat in België met een chronische vaak traag helende huidwonde geconfronteerd wordt. Zo nu en dan zien we in de geschreven en audiovisuele media één of ander wondermiddel opduiken, meestal met een patiëntengetuigenis erbij. Ook het KCE wordt met deze interesse in wondzorg geconfronteerd, getuige de vraag van het RIZIV om een 'rapid assessment' te doen over vacuümgeassisteerde wondbehandeling (het onderwerp van dit rapport) en binnenkort hyperbare zuurstoftherapie.

Vacuümgeassisteerde wondbehandeling lijkt een eenvoudig gegeven: door middel van onderdruk wordt het wondvocht afgezogen en wordt de doorbloeding bevorderd, waardoor de wonde sneller zou genezen. Deze technologie werd recent gecommercialiseerd. Gezien het potentieel groot aantal patiënten met chronische wonden lijkt het logisch dat vooraleer een dergelijke veelbelovende technologie wijdverspreid wordt toegepast, de bewijzen over de klinische werkzaamheid en de economische aspecten even objectief op een rijtje worden gezet. De resultaten daarvan kan u in onderliggend rapport terugvinden.

Tijdens dit 'rapid assessment' kon het KCE eens te meer rekenen op enthousiaste externe experten en heel wat informatie van de producenten van deze technologie, waarvoor onze welgemeende dank. Chronische wondzorg is een toenemend medisch en maatschappelijk probleem. Klinisch onderzoek naar mogelijke innovatieve interventies kan dan ook alleen maar sterk aangemoedigd worden.

Jean-Pierre Closon
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Executive summary

ACHTERGROND

Chronische wonden – zoals doorligwonden, diabetische voetwonden en vasculaire ulcera – en acute wonden (hoofdzakelijk veroorzaakt door traumata of chirurgie) vormen een belangrijk gezondheidsprobleem, niet alleen door hun epidemiologie, maar ook door hun tijdsintensieve en dure behandeling. Volgens recente richtlijnen van de Wound Healing Society zijn de hoekstenen van chronische wondzorg: vochtige verbanden, behandelen van infecties (door middel van debridering, lokale en/of systemische antimicrobiële behandeling), voorbereiding van het wondbed, chirurgie en adequate voeding. Afhankelijk van het wondtype zijn bovendien meer specifieke interventies nodig.

Vacuümgeassisteerde wondbehandeling (Negative Pressure Wound Therapy - NPWT) vormt een nieuw alternatief voor de behandeling van chronische en acute wonden. Tijdens NPWT wordt een onderdruk of vacuüm gebruikt om de wonde te draineren. De wonde wordt op deze manier gestimuleerd om granulatieweefsel te vormen wat de genezing ten goede komt.

DOELSTELLING

Het doel van deze 'rapid assessment' is de beschikbare klinische en economische evidence samen te vatten over NPWT voor de behandeling van chronische en acute wonden in vergelijking met standaard wondbehandeling.

METHODOLOGIE

In meerdere electronische databanken werd gezocht naar HTA-rapporten, systematische reviews, gerandomizeerde studies (RCT) en economische evaluaties. De grijze literatuur werd doorzocht via Google en via contacten met de industrie.

Relevante studies werden o.b.v. titel en abstract geselecteerd door 1 onderzoeker. De geselecteerde studies werden vervolgens o.b.v. de full-text beoordeeld op hun kwaliteit door 1 onderzoeker, en nadien door een 2^{e} onafhankelijke onderzoeker en een groep van externe experten. Studies van lage kwaliteit werden niet in aanmerking genomen voor de eindconclusies.

Van de geïncludeerde klinische studies werden de volgende gegevens geëxtraheerd: studie design, aantal en type patiënten, interventie, comparator, uitkomstvariabelen en resultaten.

Voor de economische evaluatie werden de Belgische materiaalprijzen vergeleken met de internationale prijzen, rekening houdende met de koopkrachtpariteit. Tenslotte werd er ook een beknopte kostenanalyse gedaan.

RESULTATEN

KLINISCHE EFFECTIVITEIT EN VEILIGHEID

Van de 10 HTA-rapporten, 5 systematische reviews en 15 RCTs die beoordeeld werden op hun kwaliteit, werden er respectievelijk zeven, twee en twee studies als kwalitatief goed of matig goed bevonden. Er werden ook 5 lopende RCTs gevonden.

Over het algemeen verwijzen de HTA-rapporten en systematische reviews naar dezelfde evidence, en wordt deze evidence als onvoldoende beschouwd om een veralgemeend gebruik van NPWT te verantwoorden. De meeste auteurs van deze rapporten benadrukken de nood aan bijkomende goede RCTs.

Sinds het meest recente HTA-rapport werden nog 4 RCTs gepubliceerd, waarvan er slechts 1 van matige kwaliteit bleek te zijn. Bovendien bleken de 2 RCTs die als kwalitatief matig goed beoordeeld werden toch nog belangrijke methodologische tekorten te hebben, wat het moeilijk maakt om een ongenuanceerde uitspraak te doen over de klinische effectiviteit en veiligheid van NPWT. Hoewel NPWT een veilige behandeling lijkt, zijn er weinig gegevens over eventuele nevenwerkingen of complicaties. Zelfs voor specifieke indicaties, zoals diabetische voetwonden of huidgreffen, is de evidence schaars doch veelbelovend.

ECONOMISCHE EVALUATIE

Van de 4 kosteneffectiviteitstudies en 3 kostenanalyses was er slechts 1 kostenanalyse die als kwalitatief matig goed werd beoordeeld, terwijl de andere studies van slechte kwaliteit bleken te zijn. Tot nog toe werden er geen adequate kosteneffectiviteitanalyses uitgevoerd. Op zich was dit ook niet mogelijk bij gebrek aan kwalitatief goede gegevens over de klinische effectiviteit.

De Belgische prijzen voor NPWT materiaal liggen in de lijn van de buitenlandse prijzen. Gebaseerd op de prijzen voor kant-en-klaar materiaal zoals toegepast door de marktleider, komt de materiaalkost voor 1 week NPWT binnen het ziekenhuis op meer dan €500. Een hoge winstmarge is een mogelijke verklaring voor deze prijzen, gezien ze niet te verklaren zijn door belangrijke R&D uitgaven. Sommige concurrenten bieden nu reeds vergelijkbaar materiaal aan voor minder dan een derde van deze prijs. Hospitaalmateriaal dat vrij verkrijgbaar is in de handel zou de prijzen nog verder kunnen drukken.

In tegenstelling tot Nederland is er geen specifieke terugbetaling van NPWT in België. Andere landen zoals Frankrijk verwierpen een dergelijke aanvraag tot terugbetaling bij gebrek aan klinische evidence.

CONCLUSIES

- **Gebaseerd op de huidige evidence is de klinische effectiviteit van vacuümgeassisteerde wondbehandeling (Negative Pressure Wound Therapy - NPWT) niet bewezen. Deze veelbelovende nieuwe technologie kan dan ook niet als routinebehandeling beschouwd worden voor chronische en acute wonden. Enkel voor diabetische voetwonden en huidgreffen is er beperkte evidence voor de effectiviteit van NPWT.**
- **Hoewel NPWT een veilige technologie lijkt, zijn gegevens over de veiligheid schaars.**
- **Er is een gebrek aan goede kosteneffectiviteitanalyses. Op dit moment kunnen er geen conclusies getrokken worden over de kosteneffectiviteit van deze technologie, hetgeen ook verband houdt met de onzekerheid over de klinische effectiviteit ervan.**
- **Gezien NPWT een ogenschijnlijk veilige technologie is, is er geen reden om dit type van behandeling af te raden. Toch dienen ziekenhuizen geïnformeerd te worden over het gebrek aan evidence voor de klinische effectiviteit, veiligheid en kosteneffectiviteit van NPWT. Bovendien dienen ze zich bewust te zijn van de winstmarge voor de verdeler van deze technologie, die vermoedelijk ruimte laat voor verdere onderhandeling.**
- **Volgens klinische experten lijkt NPWT effectief bij een kleine groep van zorgvuldig geselecteerde patiënten. Een beperking van (de terugbetaling van) NPWT tot deze geselecteerde patiënten lijkt op dit moment echter onmogelijk, gezien de huidige evidence niet duidelijk toelaat om de patiëntengroepen die de meeste baat hebben bij de technologie op een correcte manier af te lijnen.**
- **Er is een duidelijke nood aan goede RCTs voor specifieke wondtypes (bvb. diabetische voetwonden, doorligwonden, traumatische wonden of veneuze ulcera) als onderdeel van het R&D proces. NPWT is echter nu reeds een courante technologie in meerdere ziekenhuizen.**

SCIENTIFIC SUMMARY

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ABBREVIATIONS

FDA	Food and Drug Administration
HTA	Health technology assessment
INAHTA	International Network of Agencies for Health Technology Assessment
LOS	Length of stay
NPWT	Negative pressure wound therapy
TNP	Topical negative pressure
ICER	Incremental cost-effectiveness ratio
RCT	Randomized controlled trial
SD	Standard deviation
SE	Standard error
VAC	Vacuum-assisted wound closure

1 INTRODUCTION

Chronic wounds – such as pressure ulcers, diabetic foot ulcers and vascular ulcers – represent a major health problem, not only because of their epidemiology, but also because of their time- and resource-consuming management. In 2000, the prevalence of pressure ulcers was estimated to be 10.7% in the Belgian hospitals and 11.4% in the Belgian nursing homes [1]. However, this is probably an underestimation. The prevalence of pressure ulcers in 2001/2002 varied from 8.3% (Italy) to 22.9% (Sweden) in the Summary Report on the Prevalence of Pressure Ulcers of the EPUAP, European Pressure Ulcer Advisory Panel. The Belgian prevalence was estimated to be more than 20%, based however on the combined results of two hospitals only (http://www.epuap.org/review4_2/page7.html). Fifteen percent of persons admitted to long-term care facilities already present a pressure ulcer at admission [2]. Twenty percent of patients admitted without a pressure ulcer will develop one within 2 years. Nine percent of hospitalized patients develop pressure ulcers [2].

According to the IKED report of 2004 [3], 5% and 8.3% of the type 1 and type 2 diabetic patients respectively have a history of a diabetic foot ulcer. Worldwide the prevalence of diabetes was estimated to be 2.8% in 2000, and the risk of developing a foot ulcer between 12% and 25% for diabetic patients. Such ulcers cause 84% of all non-traumatic amputations in diabetic patients [4].

Acute wounds are usually caused by trauma (e.g. degloving injuries, contusions, lacerations, etc.), surgery (fasciotomy wounds for compartment syndrome, wounds after surgical debridement, etc.) or burns. In contrast to chronic wounds, few information is available on the incidence of acute wounds.

In general, there is a lack of very concrete evidence-based guidelines about the use of wound therapy. According to recent guidelines published by the Wound Healing Society, the mainstay of chronic wound treatment consists of moist dressings (of which a large variety exists), infection control (through debridement, topical and/or systemic antimicrobial treatment), wound bed preparation, surgery and adequate nutrition [5-8]. Depending on the type of the wound, more specific interventions are used, such as compression for venous ulcers [8], positioning and support surfaces for pressure ulcers [7], offloading for diabetic ulcers [6], and restoration of blood flow for arterial insufficiency ulcers [5]. Other treatment options include hyperbaric oxygen therapy (which is the subject of a separate rapid assessment by the KCE), topical warming [9], laser therapy [10], etc.

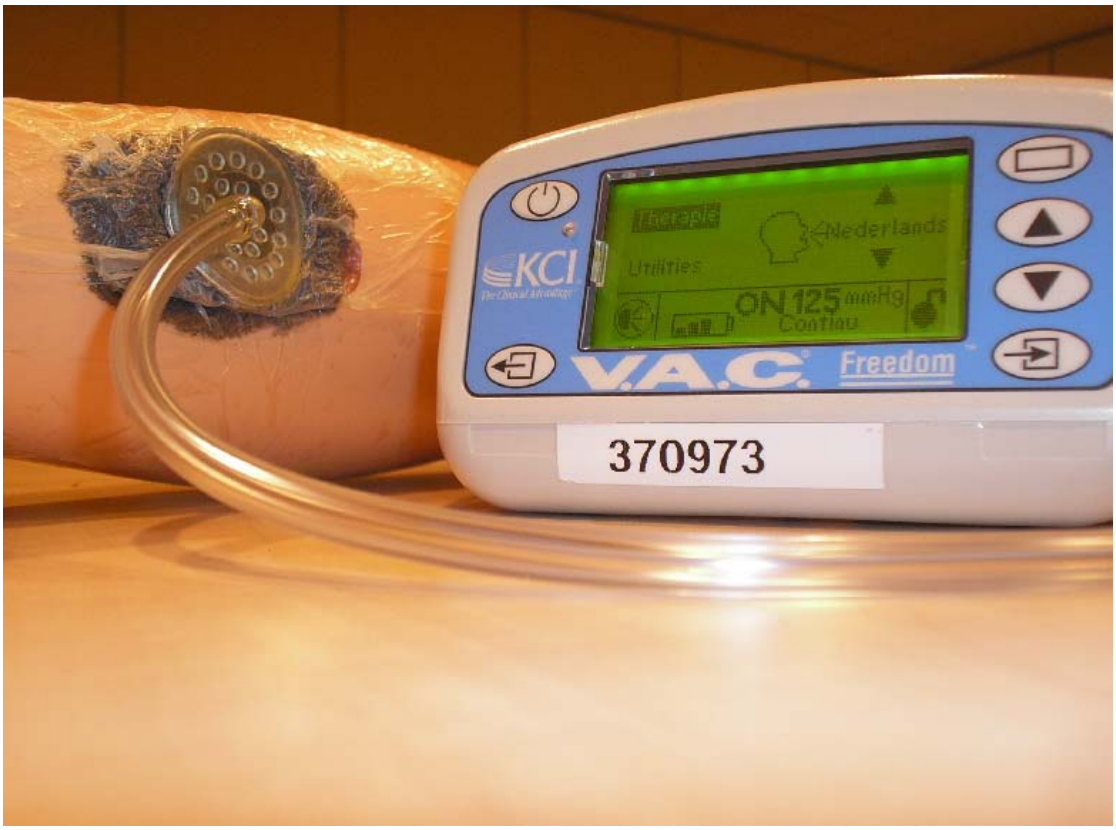
This report presents a rapid assessment of an emerging technology for the treatment of chronic and acute wounds: negative pressure wound therapy. Based on other existing HTA reports, systematic reviews and clinical trials, the objective is to provide a clear synthesis of the evidence on clinical effectiveness, safety and cost-effectiveness of the technology. The report follows the standard methodology of HTA reports of the KCE. However, in contrast to full HTA reports, patient issues, ethical issues and organisational issues will not be addressed extensively.

2 TECHNOLOGY DESCRIPTION

Negative pressure wound therapy (NPWT) (Syn. vacuum-assisted wound closure, topical negative pressure, subatmospheric pressure) was pioneered in the late eighties [11]. A pressure below the atmospheric pressure (i.e. a relative vacuum) is used to create suction, which drains the wound and influences the shape and growth of the surface tissues in a way that promotes healing. By draining the fluid from the wound, the substrate for growth of micro-organisms is removed, leading to a reduction of the microbial load. Negative pressure may also accelerate granulation tissue formation and improve blood flow in the tissue at the wound edges. Above this, the mechanical stimulation of cells by tensile forces may also play a role, by increasing cell proliferation and protein synthesis [12].

During the procedure, a sterile foam dressing is cut to fit the shape and size of the wound (figure 1). This foam is placed into the wound bed and held in place with an overlying airtight adhesive polyurethane drape secured to surrounding normal skin. A non-collapsible drain tube is embedded in the foam dressing and included under the adhesive drape with a mesentery technique used to maximize the seal obtained. The tube is connected to a vacuum source, and fluid is drawn from the wound through the foam into a disposable canister. The device can be programmed to provide varying degrees of pressure (usually a subatmospheric pressure in a range of -25 to -200 mmHg) either continuously or intermittently. The foam dressing collapses and its open-cell nature allows equal levels of subatmospheric pressure to be transmitted to all surfaces in contact with the foam. When an air leak is present, often due to an insufficient seal by the adhesive drape, some NPWT devices provide an alarm sound. The applied dressing can be left for 2 to 7 days. The vacuum foam can be changed under inpatient conditions, in the operating theatre or under outpatient conditions.

Figure 1: Negative pressure wound therapy device (Source: KCI, with permission).



3 CLINICAL EFFECTIVENESS

3.1 METHODS

3.1.1 Search strategy

An iterative search strategy was performed, first searching for existing health technology assessments (HTA) and systematic reviews, and subsequently for randomized controlled trials (RCTs) not included in the retrieved HTAs and systematic reviews. The following electronic databases were searched: HTA database, Cochrane Library [OVID], Medline [OVID], Pre-Medline [OVID], Embase [Embase.com], Cinahl [OVID] and British Nursing Index [OVID]. Finally, as indexing and MeSH terms are often not developed yet for emerging technologies, a complementary search was done of the grey literature via Google and via contacts with suppliers and manufacturers of vacuum-assisted wound closure devices. References of the retrieved studies were also checked.

The search date was from February 12th, 2007 onwards.

3.1.2 Search terms

During a pre-assessment of the literature, some RCTs were identified that were not included in the identified HTAs. Therefore it was decided to do a sensitive search. The search algorithms for the HTA database, Cochrane Library, Medline, Pre-Medline, Cinahl and British Nursing Index are provided in appendix. For Embase the following search string was used:

(wound* OR ulcer* OR burn* OR 'degloving injury' OR 'degloving injuries' OR 'skin transplantation' OR 'skin transplantation'/exp OR 'skin graft' OR 'free flap'/exp OR 'free flap' OR incision* OR 'skin transplantations' OR 'free flaps' OR 'skin grafts' OR decubit* OR 'diabetic foot'/exp OR 'diabetic foot' OR 'diabetic feet') AND ('suction dressing' OR 'negative pressure' OR 'sub-atmospheric' OR subatmospheric OR 'npwt' OR 'tnp'/exp OR 'tnp' OR 'vac' OR 'vacuum'/exp OR 'vacuum') AND [<1966-2007]/py

For the Google search the following search terms were used in combination: vacuum-assisted wound closure, VAC, NPWT, TNP, subatmospheric, sub-atmospheric, negative pressure, technology assessment, systematic review, randomized.

The title and abstract of citations were reviewed for relevance by one reviewer. Quality control of the search was performed by another reviewer. In case the abstract could not provide enough information, the full-text article was retrieved. No date or language restriction was used. The following in and exclusion criteria were used to select relevant papers:

Inclusion: HTA, systematic review, meta-analysis, RCT; use of subatmospheric pressure for the treatment of acute or chronic wounds; major outcomes of interest: wound closure, adverse events, health-related quality of life.

Exclusion: narrative reviews, letters, commentaries, case series, case studies; articles on primary closed wound drainage, the sandwich-vacuum pack technique etc., and target conditions other than mentioned above.

3.1.3 Quality assessment

The quality of the selected papers was assessed by one reviewer on the basis of the full-text and quality controlled by a second internal reviewer and a group of external experts. To assess the quality of HTA reports, the INAHTA checklist was used (www.inahta.org) (see appendix). The quality of systematic reviews and RCTs was assessed using the checklists of the Dutch Cochrane Centre (www.cochrane.nl) (see appendix).

Quality assessment was summarized as good, average or poor quality (according to the quality of evidence grading for interventional procedures as described in the KCE report 44 on emerging technologies) [13]. HTA reports or systematic reviews received a poor quality appraisal when the search of the literature was insufficient and no quality assessment of included studies was reported. For the quality assessment of the RCTs, three major criteria were the randomization process, the blinding of the assessors and intention-to-treat analysis. An RCT received a poor quality appraisal when at least one of these three criteria was negative.

Poor quality studies were not considered for the final recommendations.

3.1.4 Data extraction strategy

As for clinical trials, information was captured about the study design, number and type of patients included, intervention, comparator, outcome variables and results. Data extraction was done by one reviewer (JV) and quality controlled by a second internal reviewer and a group of external experts.

3.2 RESULTS

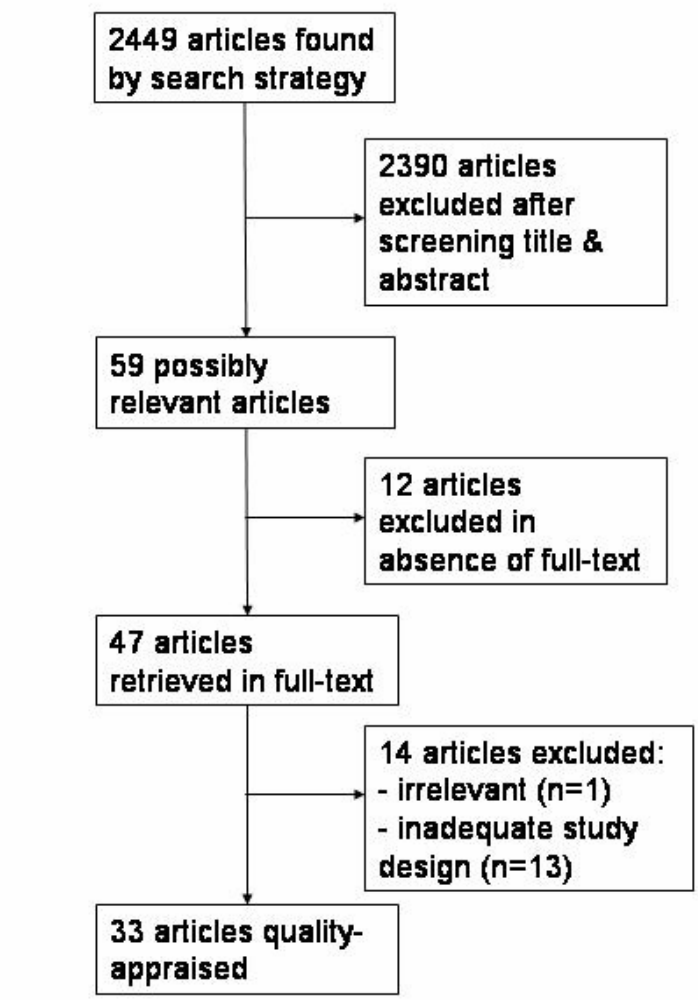
3.2.1 Literature search results

The literature search yielded the following results:

- Medline: 1692 articles
- Pre-Medline: 45 articles
- Embase: 1540 articles
- Cochrane Database of Systematic Reviews: 33 articles
- Cochrane Central Register of Controlled Trials: 107 articles
- Cinahl: 284 articles
- British Nursing Index: 74 articles
- HTA database: 25 articles (HTA 12 articles, NHS EED 7 articles, DARE 6 articles)

After removal of the duplicate articles, 2449 papers were withheld (figure 2). On the basis of title and abstract, 2390 papers were excluded because of irrelevance or inadequate study design. Of the 59 possibly relevant papers, 12 could not be retrieved in full-text (mainly conference proceedings), and were therefore excluded from further review [14-25]. Based on the full-text, another 14 were excluded because of irrelevance (n = 1) [26] or inadequate study design (n = 13) [27-39].

Figure 2: Flow diagram of search results.



3.2.2 HTA reports

In total, 13 possible HTA reports were identified. However, based on the full-text, the report of the NHS [39] was not considered as a real HTA report, and was therefore excluded. Above this, the report of the Medical Advisory Secretariat (MAS) of Ontario prepared in 2004 [40] was updated in 2006 [41]. Finally, the report of Hayes Inc. [24] could not be retrieved in full-text.

In appendix an overview is provided of the quality appraisal of the 10 selected HTA reports. Only one report was considered to be of good quality [42], 6 reports were of moderate quality [10, 41, 43-46], and 3 reports were excluded because of a poor quality [47-49]. Only those of good or moderate quality are discussed below (see appendix for evidence tables).

3.2.2.1 Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen (IQWiG) 2006 [42]

The authors of this high-quality report – written in German – performed a very thorough literature search until May 2005, including Medline, Pre-Medline, Cinahl, the Cochrane database, Embase, DARE, the HTA database, and an extensive search of the grey literature. The search yielded 9 published RCTs (of which 2 were excluded from further analysis) and 11 non-randomized controlled trials. Above this, 19 (at that time) unpublished RCTs were identified, of which 5 were interrupted, 3 finished but not yet published, and 7 ongoing. Of 4 of these unpublished RCTs the status was unclear. All published RCTs were judged to be of bad quality. The authors concluded that the available evidence did not justify a widespread use of NPWT. They advised a new assessment in 2 – 3 years.

3.2.2.2 Medical Advisory Secretariat (MAS) Ontario 2006 [41]

In this report, the results of a thorough literature search (until March 2006, restricted to English) are presented. The authors identified 6 HTA reports, 1 systematic review, and 8 RCTs (of which 2 were excluded because of a small sample size). Only one RCT was judged to be of moderate quality (based on the GRADE criteria), the other included RCTs were found to be of low or very low quality. Based on the retrieved evidence, the authors concluded the clinical effectiveness of NPWT to be unproven at that time.

3.2.2.3 McGill University Health Centre Montreal 2005 [43]

The authors of this report identified 5 HTA reports, 1 systematic review, and 13 clinical studies, of which 6 were RCTs. The quality of the evidence was found to be poor, with small studies and inconsistent study methodology. No statistical or clinical difference in meaningful health outcomes was found between NPWT and other therapies. The authors therefore concluded that the available evidence at that time did not support the routine use of NPWT.

3.2.2.4 Axencia de Avaliación de Technoloxías Sanitarias de Galicia (Avalia-T) 2005 [44]

This report – written in Spanish – included 4 HTA reports, 1 systematic review and 8 RCTs. Overall, the available evidence was considered to be of poor methodological quality and to have too low power to detect differences between NPWT and conventional wound therapy. The authors therefore concluded that NPWT could not be considered as a treatment for chronic wounds at that time.

3.2.2.5 Agency for Healthcare Research and Quality (AHRQ) 2004 [10]

This HTA report, prepared by the Blue Cross Blue Shield for the AHRQ, included 6 RCTs, which were all found to be of small sample size and poor quality. The authors concluded this evidence to be insufficient to support conclusions about the effectiveness of NPWT in the treatment of wounds.

3.2.2.6 Centre for Clinical Effectiveness (CCE) 2003 [45]

The authors of this report identified 1 systematic review and 2 RCTs published since the systematic review. However, these RCTs were found to have serious methodological drawbacks. Therefore, the authors stressed the need for well designed, adequately powered, multi-centre RCTs to evaluate the contribution of NPWT in the management of wounds.

3.2.2.7 Australian Safety and Efficacy Register of New Interventional Procedures – Surgical (ASERNIP-S) 2003 [46]

In this 'accelerated review', the authors reported on 6 RCTs, 4 non-randomized comparative studies, and 7 case series. Although the authors acknowledged that most studies were too small to detect significant differences, they stated that some results did show NPWT to result in better healing than standard methods, with few serious complications. However, they also concluded that more rigorous studies with larger sample sizes were required.

3.2.3 Systematic reviews

Through our search, 5 systematic reviews were identified. In appendix an overview is provided of the quality appraisal of these reviews. Only one report was considered to be of good quality [50], 1 reports was of moderate quality [51], and 3 reports were excluded because of a poor quality [52-54].

The systematic review of Pham et al. [51] is in fact an update of the HTA report of ASERNIP-S [46]. The authors did a thorough search of the literature until October 2004, with an update until July 2005 to include any new RCTs. Apart from two systematic reviews, the authors identified 10 RCTs, preliminary analyses of 2 RCTs in progress, 4 non-randomized comparative studies and 7 case series. In line with the conclusions of ASERNIP-S, the authors claimed the need for high-quality RCTs, but nevertheless considered NPWT to be a promising alternative for the management of various wounds.

Evans et al. [50] performed a search until November 2002 and identified 2 small RCTs that fulfilled their selection criteria. Because of the small sample sizes and methodological limitations of these RCTs, the authors concluded that the findings must be interpreted with caution. They also stressed the need for well designed, adequately powered, multi-centre RCTs.

3.2.4 Randomized clinical trials

In total, 18 RCTs were identified. Another trial that was considered as an RCT by other investigators [46, 51] was not included as an RCT in the present report, because no statement was found about actual randomization [37]. This is in line with the reports of IQWiG [42] and Evans et al. [50]. Of the 18 identified RCTs, one RCT could not be retrieved in full-text [25], but turned out to be a preliminary report of the RCT of Moisidis et al. [55] (personal communication with E. Moisidis). One other RCT was written in Russian, and was therefore not further analysed [56]. Finally, another RCT was excluded because biochemical markers of the inflammatory response were the only reported outcomes [57].

The remaining 15 RCTs were quality appraised (see appendix for quality scores and evidence tables). Of these RCTs, only 2 were found to be of moderate quality [58, 59],

and no RCTs were considered as good quality. Two studies were excluded from further review because they used a quasi-randomization procedure [60, 61]. Only 4 RCTs explicitly used blinded assessors of the wounds [55, 58, 62, 63], and 2 other RCTs used planimetry measurements from digital photographs [59, 64]. Four RCTs reported an intention-to-treat analysis [58, 59, 65, 66].

Of the 13 RCTs (excluding the 2 quasi-RCTs), 7 were funded at least partly by Kinetic Concepts, Inc. (KCI) [52, 59, 63, 65, 67-69]. For four RCTs financial involvement of KCI was unclear [55, 58, 66, 70].

Most studies used NPWT with the equipment provided by KCI as the experimental therapy. Only Llanos et al. used a 'modified' NPWT, i.e. a less dense polyurethane dressing and a vacuum provided by connecting to the central aspiration system of the hospital [58]. The provided negative pressure varied across the studies, although the majority used a continuous pressure of – 125 mmHg [52, 63-65, 67, 68, 70]. The standard wound care in the control group also varied across the 13 RCTs (see evidence tables). Most studies were conducted in a hospital setting, while only three studies used a mixed setting (inpatient – outpatient) [52, 63, 64]. In one study, the setting was unclear [59]. Overall, the number of included patients is low, ranging from 10 to 65. The only exception is the RCT of Armstrong et al., who included 162 patients [59].

Since the most recent HTA report [42], 4 new RCTs were published [58, 65, 67, 69]. Only one of these was of moderate quality [58]. Below, a discussion is provided of the results of all included RCTs per indication.

3.2.4.1 Pressure ulcers

Three RCTs were found that exclusively included patients with pressure ulcers [52, 62, 70]. Greer et al. [52] reported on preliminary results of an RCT that was discontinued [42]. Ford et al. also presented an interim analysis of an RCT comparing NPWT and three FDA-approved gel products (Accuzyme, Iodosorb and Panafil) for the treatment of pressure ulcers [62]. Wanner et al. compared NPWT with a traditional wet-to-moist gauze dressing [70]. Both RCTs showed no significant differences in mean wound size and wound-healing parameters between the NPWT and control groups (see evidence tables). Both studies were of low quality.

3.2.4.2 Diabetic foot ulcers and wounds

Two RCTs were found that evaluated the treatment of diabetic foot ulcers/wounds with NPWT [59, 64] (the 2 excluded quasi-RCTs also addressed diabetic foot wounds). The RCT of Eginton et al. was a very small cross-over study (only 10 diabetic patients with 11 foot wounds included in the study, only 6 patients with 7 wounds included for analysis) of low quality [64]. Significant changes in wound depth and volume but not wound area were found, although these results should of course be interpreted with caution.

The moderate-quality RCT of Armstrong et al. included 162 patients with a wound from a partial diabetic foot amputation [59]. Seventy-seven patients were randomized to receive NPWT, 85 patients to standard moist wound care. However, some patients also underwent surgical wound closure (12 patients in the NPWT group [15.6%] vs. 8 patients in the control group [9.4%]), while other patients didn't. The decision to undergo surgery was not randomized, but taken by the physician based on his clinical impression. The addition of a second, non-randomized intervention adds a confounding variable to the study that makes it impossible to analyze the effect of NPWT alone (for the patients who underwent surgery and had complete wound closure, it is difficult to assess the effect of NPWT compared with standard care because it cannot be separated from the effect of surgery on complete wound closure) (see also MAS [41]). Observers were not blinded for the intervention, but planimetry measurements from digital photographs were used. The authors did not provide a statistical comparison of the baseline characteristics of the 2 groups, but reported that the groups were equal in a response to The Lancet regarding comments from readers [71].

Overall, complete wound closure was achieved in significantly more patients treated with NPWT than with the control treatment (56% vs. 39%, p = 0.04). Also, the time to reach 76 – 100% granulation tissue was significantly shorter in the NPWT group (42 vs. 84 days, p = 0.002). However, the authors did not report a sub-analysis of those patients not treated with surgery.

The rate of secondary amputations did not differ significantly between the two groups, nor did the rate of adverse events. The most frequently reported adverse event was wound infection, which also didn't differ significantly.

3.2.4.3 Skin grafts

Four RCTs were identified that evaluated the effect of NPWT on skin grafts [55, 58, 65, 66], of which two weren't included in previous HTA reports [58, 65].

Moisidis et al. did not find a significant difference in the degree of epithelialisation with NPWT compared with bolster dressings after 2 weeks, although qualitative measurements of graft take (subjectively rated as poor, satisfactory, good or excellent by a blinded clinician) were significantly better with NPWT [55]. Jeschke et al. compared the graft take rate after conventional Integra grafting and Integra grafting plus fibrin glue plus negative-pressure therapy [66]. Mean graft-take rate was significantly higher in the interventional group compared with the control group (98% vs. 78%, p < 0.003), and the period from temporary wound coverage to skin transplantation was significantly less in the interventional group (24 vs. 10 days, p < 0.002). However, it is possible that part of these effects is attributable to the fibrin glue. Both the studies of Moisidis et al. and Jeschke et al. were of low methodological quality.

In the study of Vuurstaek et al., 60 patients with chronic leg ulcers were randomized to either NPWT (n = 30) or standard wound care (n = 30) before and after skin grafting [65]. All patients received skin grafting once 100% granulation was achieved and wound secretion was minimal. The time to complete healing (primary end point) was significantly shorter in the NPWT group compared with the control group (29 vs. 45 days, p = 0.0001). The authors reported a median percentage of successful skin grafts of 83% in the NPWT group vs. 70% in the control group (p = 0.011). Recurrence rate at 1 year was similar (52% vs. 42%, p = 0.47). The complication rate was higher in the NPWT group compared with the control group, but did not differ significantly (40% vs. 23%, p = 0.17). These results should be interpreted with caution, because the assessors were not blinded for the intervention.

Llanos et al. randomized 60 patients with acute traumatic injuries and skin loss that had undergone surgical cleaning and skin grafting to either NPWT (n = 30) or control (n = 30) [58]. Randomization was done using computer-generated random numbers in permuted blocks of 6. The treatment allocation was performed by the nurse of the operating room, who was not blinded for the corresponding assignment, but probably had no influence on treatment decisions. The surgeon was notified of the corresponding treatment once the skin graft had been performed. Wound assessment and data analysis was done by blinded persons. The median percentage of graft loss in the NPWT group was 0% vs. 13% in the control group (p < 0.001). Regrafting was required in 12 patients in the control group vs. 5 patients in the NPWT group (p = 0.045). Total length of stay was shorter in the NPWT group compared with the control group (14 vs. 17 days, p = 0.01). No information was found on complication rate.

3.2.4.4 Complex and traumatic wounds

In the article of Stannard et al. [69], which was not included in previous HTA reports, the preliminary results of 2 RCTs are reported. The first study evaluates the use of NPWT to assist in the evacuation of a draining haematoma and in the closure of the surgical incision following high-energy trauma. At the time of this preliminary analysis, 44 patients were randomized to either NPWT (n = 13) or a pressure dressing (n = 31). A mean drainage time of 1.6 days was found in the NPWT group vs. 3.1 days in the control group (p = 0.03). Surgical irrigation for an infected haematoma was required in 5 patients in the control group vs. 1 patient in the NPWT group (NS). In the second

study, NPWT is evaluated as an adjunct to the healing of surgical incisions after fractures that are at high risk for wound healing problems. At the time of the analysis, 44 patients were randomized to either NPWT (n = 20) or a standard postoperative dressing (n = 24). A mean drainage time of 1.8 days was found in the NPWT group vs. 4.8 days in the control group (p = 0.02). In both groups, 3 patients developed wound infections (NS). The results of these studies need to be interpreted with high caution because of the preliminary character, and because no information was found on the blinding of the assessors or on an intention-to-treat analysis.

Moues et al. randomized 54 patients with a full-thickness wound of various causes to either NPWT (n = 29) or conventional moist gauze therapy (n = 25) [68]. The median time to reach a clean granulating wound bed did not differ between the two treatment groups (6 days in the NPWT group vs. 7 days in the control group, p = 0.19). Wound surface reduction was significantly faster in the NPWT group than in the control group (3.8% vs. 1.7%/day, p < 0.05). However, this trial was hampered by serious methodological flaws (no blinding, no intention-to-treat analysis).

3.2.4.5 Other

Braakenburg et al. investigated the role of NPWT in the treatment of acute and chronic wounds of several etiologies [67]. Sixty-five patients were randomized to either NPWT (n = 32) or conventional therapy (n = 33), which was described as 'various types of dressings from the local wound protocol'. The median healing time did not differ between the 2 groups (16 days in the NPWT group vs. 20 days in the control group, p = 0.32), nor did the other clinical outcomes. The authors reported a higher patient comfort in the NPWT group, although this was not objectively measured. This trial was also of low methodological quality (no blinding, no intention-to-treat analysis).

Joseph et al. randomized 24 patients with 36 chronic non-healing wounds to either NPWT (12 patients, 18 wounds) or traditional wet-to-moist gauze dressings (12 patients, 18 wounds) [63]. About 80% of these patients had a pressure ulcer. After 6 weeks of treatment, the mean % change in wound volume was 78% in the NPWT group vs. 30% in the control group (p = 0.038). Complication rate was lower in the NPWT group than in the control group (17% vs. 44%, p =0.0028).

No RCTs were found on other indications, such as burn injuries, sternal wounds, abdominal compartment syndrome, etc.

3.2.5 Harms and complications

Of the 13 RCTs discussed above (excluding the two quasi-RCTs), 5 studies did not provide information on adverse events [52, 55, 58, 64, 70]. Above this, of the 8 other studies, only 3 authors provided some statistical information [59, 63, 65]. Because of this heterogeneous reporting of adverse events, it is impossible to do a meta-analysis of these results.

Both Armstrong et al. [59] and Vuurstaek et al. [65] did not find a statistically significant difference in the overall incidence of adverse events between the NPWT group and the control group. Only Joseph et al. found a lower complication rate in the NPWT group (see above) [63]. The most commonly reported adverse event in the studies of Armstrong et al. and Joseph et al. was wound infection (17% and 0% in the NPWT group respectively vs. 6% and 33% in the control group respectively), although it is not clear whether the difference between the two study groups was statistical significant [59, 63]. Armstrong et al. reported an incidence of 12% of treatment-related adverse event in the NPWT group compared with 13% in the control group (again, statistical significance unclear) [59]. However, it is unclear what was meant by a treatment-related adverse event.

Vuurstaek et al. reported an incidence of wound infection of only 3% in the control group vs. 0% in the NPWT group (NS) [65]. On the other hand, cutaneous damage secondary to therapy was reported to be more frequent in the NPWT group (23% vs. 7%, p < 0.05).

Although NPWT seems to be a safe procedure, reports other than the identified RCTs clearly indicate the need for systematic reporting of harms and complications. Some studies report pain during dressing changes or during NPWT, even causing NPWT cessation [72]. In the RCT of Braakenburg et al., NPWT was discontinued for that reason in two patients (out of 26) [67]. Philbeck also reported NPWT discontinuation due to pain [73]. Necessity of sedation has also been reported to relieve the pain when NPWT is applied or dressings are changed. Pain may also result from tissue granulating inside the foam when the dressing is not changed soon enough [74, 75].

Correct application of the therapy is crucial to reach desired outcomes, and can be accomplished by appropriate training of nurses. Indeed, pressure sores and skin erosion were observed in the first patients treated in the Braakenburg study [67], and were attributed to the learning curve involved with applying the technology. Above this, a good patient selection is important to ensure that the therapy is applied to the right patient (e.g. excluding catabolic patients, necrotic wounds, etc.).

Mobility is impaired for patients who are not able to use the portable VAC® device and therefore being bound to the pump for 22 hours each day [46]. This 'bond' to the device may also hamper its use in patients suffering from mental disability [47].

In 2006, 48 incidents related to pumps used for NPWT were reported in the US to the Manufacturer and User Facility Device Experience Database (MAUDE) of the FDA, against 53 in 2005 and 15 in 2004 (http://www.fda.gov/cdrh/maude.html accessed on March 21st 2007). According to the medical reports of 51 paediatric patients [76], NPWT therapy was stopped in 3 adolescents due to device malfunction, and then reapplied after temporary appliance of saline-soaked gauze.

3.2.6 Ongoing and unpublished trials

Through the website of ClinicalTrials.gov only one ongoing trial (sponsored by manufacturer KCI) was identified, examining the effect of NPWT on angiogenesis markers in patients with post-surgical dehisced wounds of the lower extremity and tissue ischemia related to arterial insufficiency (NCT00234559). However, KCI provided us with general information on 4 additional ongoing KCI-sponsored RCTs. One RCT included 338 patients with complex diabetic foot ulcers, comparing NPWT to standard wound care. Another RCT included 258 patients with draining haematomas following surgical stabilization of skeletal trauma. Finally, two ongoing RCTs respectively included 348 and 258 patients with soft tissue management needs following fractures. However, no further information was retrieved.

3.3 DISCUSSION

A rather high amount of eligible articles was identified through our literature search. Most included HTA reports and systematic reviews identified a similar body of evidence, and rated the identified RCTs as low quality. In general, the authors of these reports concluded the available evidence to be unsatisfactory to justify a widespread use of NPWT. Since the most recent HTA report, 4 new RCTs were published of which only one was of acceptable quality [58]. Of all identified RCTs in the present report, only 2 had an acceptable level of methodological quality, and even these 2 RCTs had some important flaws. In the study of Armstrong et al. some patients also underwent surgical wound closure (apart from NPWT or standard wound care), but this intervention was not randomized [59]. This confounding variable makes it impossible to analyze the effect of NPWT alone. The study of Llanos et al. was a rather small study (60 patients included) reporting results in favour of a modified NPWT technique [58]. However, no information on complication rates was provided.

Overall, the comparator differed across the identified RCTs, making comparisons difficult. Also, the reported outcomes were very heterogeneous, again making comparisons and meta-analysis difficult.

In conclusion, the newly available evidence does not permit to make a clear statement about the clinical efficacy and safety of NPWT. Even for specific indications, such as

diabetic foot or skin grafting, the available evidence is scarce, but nevertheless promising.

Key points

- **Most identified HTA reports and systematic reviews concluded the available evidence to be unsatisfactory to justify a widespread use of NPWT.**
- **The newly available evidence does not permit to make a clear statement about the clinical efficacy and safety of NPWT.**
- **NPWT seems to be a safe procedure, but harms and complications are underreported.**
- **Improper application of NPWT may cause adverse events.**

4 ECONOMIC EVALUATION

Chronic wound care is expensive both in materials and nursing time. For example, pressure ulcers cost the US about $5 billion, equivalent to €3.8 billion annual health care expenditures, affecting between 1.5 and 3 million inhabitants [2].

NPWT requires an expensive pump that can be purchased or rented. In addition, disposables, such as drapes, dressings, canisters, connectors and drains need to be purchased. The alleged cost savings are hospitalization cost savings due to a shorter length of stay, reduction in nursing time due to less frequent dressings changes, or avoided interventions.

NPWT is emerging in Belgium, mostly in the hospital setting. NPWT portable pumps are still marginally used in Belgium, but as the home wound care setting is growing, the use of portable devices could theoretically rise.

4.1 METHODOLOGY

As far as interventions and indications are concerned, the search strategy included the core of the search for clinical papers. Specific filters were applied in order to retrieve only economic or cost-related articles (see appendix for complete search strategies). Neither date nor language restrictions were imposed. The following electronic databases were searched: HTA database, Medline [OVID], Pre-Medline [OVID], Embase [Embase.com], Cinahl [OVID], British Nursing Index and Archive [OVID] and Econlit [OVID]. Grey literature was retrieved via Google and via contacts with suppliers and manufacturers of vacuum-assisted wound closure devices.

Studies comparatively assessing costs without comparing outcomes were included for review considering the paucity of economic evaluation studies. Full or partial economic evaluations were quality assessed using the Drummond checklist for economic evaluations [77] (see appendix).

Searches were executed on 2nd and 5th February 2007. Auto-alerts were created in order to retrieve more recent papers.

Currencies were converted to euros based on the rates on 19th Februari 2007 (1 CAD = 0.65 EUR, 1 AUD = 0.60 EUR, 1 GBP = 1.48 EUR, 1 USD = 0.76 EUR and 1 ARS = 0.25 EUR). Belgian prices are expressed with inclusion of the value added tax (VAT included).

An international price comparison was made, taking Belgian prices as a baseline and correcting international prices found in the literature by comparative price levels published by the OECD for Februari 2007. The following equation gives the price differential C, which is negative if the Belgian price is cheaper:

$$C = price_B - price_F \cdot \frac{CPI_B}{CPI_F}$$ or C/$price_B$ =percentage of difference, where

$price_B$ = Belgian price

$price_F$ = Foreign country price

CPL_B = Comparative price level for Belgium = 100

CPL_F = Comparative price level for foreign country

Information on prices and costs was also obtained by contacting hospitals using NPWT.

4.2 RESULTS

4.2.1 Results of the literature search

The literature search yielded the following results:

- Medline: 117 articles
- Pre-Medline: 6 articles
- Embase: 107 articles
- Econlit: 0 articles
- Cinahl: 38 articles
- British Nursing Index and Archive: 3
- HTA database: 25 articles (HTA 12 articles, NHS EED 7 articles, DARE 6 articles)

After removal of the duplicate articles (after which 220 papers were kept) 118 papers were selected based on title and abstract. Two English abstracts of Chinese articles reported on global cost reduction in favour of NPWT, but full-text in Chinese was not reviewed. Based on full-text, 6 papers were considered relevant. One additional study was retrieved manually [78].

Since no RCTs were found on certain specific conditions, such as abdominal compartment syndrome or sternitis, partial economic evaluations on patients suffering from these conditions were not taken.

Four cost-effectiveness studies [73] [79] [67] [80] and three cost analyses [43] [78] [81] were selected for further review. Only the cost analysis of Costa was found to be of moderate quality [43]. All other studies were assessed as poor quality.

The most recent cost-effectiveness study is based on a Dutch RCT by Braakenburg et al. [67], which was funded by the industry. Sixty-five consecutive patients suffering from any type of wounds were randomly assigned to NPWT (n=26) or conventional treatment (n=21), after an eventual surgical debridement. Conventional dressings consisted of various dressings from the hospital protocol in function of the underlying infection. The conventional dressings were changed one or more times a day, while NPWT dressings were changed three times a week. No difference was observed between both arms neither in healing time nor in wound surface area changes. Costs included materials and personnel. Daily costs were significantly higher in the case of NPWT treatment (€24 vs. €14), but the overall treatment costs did not differ significantly. More than 3 hours of nursing time were reported to be saved with NPWT treatment in comparison to conventional treatment. Neither detailed cost calculations nor unit costs were given and, as stated before, the quality of the trial methodology was poor.

A second Dutch cost-effectiveness study compared NPWT (n=25) with moist gauze therapy (n=29) on a 30-day basis in patients with open full-thickness wounds before surgical closure [79]. Based on an academic Dutch hospital average for staff costs and inpatient accommodation, the global costs in case of NPWT amounted to €2235 (SD=€1301) against €2565 (SD=€1384) for moist gauze therapy. The median length of stay was not significantly different, although the wound surface reduction was faster in the NPWT group. The authors concluded that both therapies were equally expensive. However, the study presents some important flaws. The costs of patients that withdrew were added to the costs of patients that did reach the endpoint in order to take costs of failure into account. Costs of therapy (other than NPWT or comparator) and operation costs were excluded from the calculation, while reduced wound surface area has an impact on the complexity of surgery or can even make it unnecessary. Finally, the study was funded by the industry.

In their 2004 cost-effectiveness analysis, Stone et al compared NPWT (n=21 wounds in 17 patients) with saline solution-irrigated cotton bolster (n=25 wounds in 23 patients) based on a retrospective chart review. The 40 patients had been admitted to level I trauma centre and treated with split-thickness skin grafting. Main outcome was survival or failure (including re-grafting), .the outcomes were mean graft size, mean duration of dressing and length of stay. None was found to be statistically significant. The average cost of NPWT was $1000 (more or less €761), which was significantly higher than the average cost of the cotton bolster which amounted to $18.5 (€14.1). Authors concluded that - NPWT may not be cost-effective. They advice to use cotton bolster in small routine wounds with a contour that is not complex as it is clinically as effective as NPWT and substantially more cost effective. Finally they pleaded for RCT comparing both treatments in treating grafts with high associated failure rates, in at least 250 patients. This retrospective study has flaws as different wound types in different areas (face, torso, extremities) were pooled and the size of the population was small.

Between 1995 and 1998, Philbeck et al. retrospectively reviewed 1032 Medicare home care patients with 1170 wounds that failed to response to previous interventions [73]. The results in wound area reduction and average costs were broken down per patients group (according to population characteristics and type of wounds) and compared to published costs and outcomes of therapies treating the same wounds (trunk or trochanteric pressure ulcers). Costs included material costs and nursing visit costs estimated at €65 per visit. For 43 pressure ulcers with a wound area of 22.2 cm^2, NPWT combined with a low-air-loss bed took 97 days to reach full closure for an average total cost of €11 075. These results were compared to a study published by Ferrell et al., according to which full closure with treatment by saline-soaked gauze combined with a low-air-loss bed would take 247 days for an average of €17 866. Philbeck et al. concluded that NPWT had superior clinical effectiveness (68% faster healing time) and a clear economical advantage (38% globally cheaper) over saline-soaked gauze for a 22.2 cm^2 pressure ulcer [73]. No other comparisons were done due to the absence of comparable literature.

Some important remarks have to be made on the study of Philbeck et al. Data collection was originally intended for submission to Medicare by the manufacturer K.C.I., and not intended for a clinical study. No details or demographics were provided to assess the comparability with Ferrell's groups of patients. Moreover, the Philbeck study included home healthcare patients [73], while the Ferrell study included nursing home residents. Moreover, no volume comparison was done between both groups of patients. Last but not least, another important flaw of the study lies in the comparison of healing rates: in the Ferrell study, wounds measured 4.3 cm^2 and healed at the rate of 0.09 cm^2. The theoretic number of days for a 22.2 cm^2 wound healing at this rate was calculated. The costs corresponding to this number of days of treatment were compared to the costs really observed for the 43 pressure ulcers wound.

In the first Canadian cost analysis [43], the costs of NPWT were compared to those of advanced moist dressing for one week of treatment at the McGill University Health Centre in Québec. No particular wound type was selected. Costs included nursing fees, material costs and a five-year equipment amortization, but neither overheads nor physician fees were included. Three NPWT dressing changes a week were assumed. The purchase pump price was €13 000, and the price of 10 dressings was €248 to €372 (according to size), plus €2.3 per change of the disposables (gauze, saline solution, syringe, ...). The authors assumed an absence of difference in the length of stay between both alternative treatments. The NPWT therapy costs were estimated at €235 per patient for one week of treatment, ranging from €197 to €290 according to nature and size of the wound, versus €217 (ranging from €145 to €290) for the moist dressing therapy. Due to the lack of evidence in the literature, costs of additional procedures in case of complications or failure could not be taken into account. In absence of published evidence of effectiveness and considering the enthusiasm in buying the technology (15 pumps purchased by the hospital in 2004), the authors recommended against further purchasing and to urgently undertake studies designed to establish the value of this treatment in the different clinical situations in which it is employed. Assumptions were

opinion-based, mostly from hospital staff, which can be considered consistent from a hospital perspective.

In the second Canadian cost analysis, Phillips et al. retrospectively assessed costs and outcomes of 81 patients suffering from all kind of wounds treated by NPWT in a home care setting in 2002/2003 [78]. The only reported clinical outcome was a 50.6% of complete closure or wound ready for skin graft in patients treated with NPWT, varying according to the wound type. The cost of NPWT was $162 150, including equipment rental, dressings, canisters and nursing time. The authors estimated that a week of NPWT would cost €493 against €454 for normal saline-soaked gauze dressings, labour cost savings somewhat offsetting the difference between €404 for NPWT pump rental and supplies vs. €88 for the comparator. Neither details of cost calculation nor statistical analysis were given.

The third cost analysis was done by Herscovici et al. [81] based on a prospective cohort study in an American hospital in 1999-2000. Twenty-one consecutive patients with open high-energy soft tissue injuries were given NPWT after surgical debridement until complete wound closure, and followed up for 6 months for healing and complications after definitive soft tissue coverage. Average length of stay was 19.3 days. Twelve patients did not need further treatment (such as skin graft or free tissue transfer). Overall, partial costs – including materials and nursing fees–amounting to €1520 per patient or €76 per day per patient, were estimated to be similar to those of 20 wounds that required wet-to-dry dressings. These 19 patients (20 wounds) were probably retrieved from the hospital trauma register. No cost comparison with 7 other patients requiring a free tissue transfer was given, as the surgical fee (Medicare) alone averaged €4600. Neither details on patients' comparability or cost calculations nor other statistics than average were given.

The grey literature search revealed an unpublished economic opinion-based model by the Weinberg Group [82]. The authors concluded that NPWT was dominant in comparison with standard care (average cost saving of €1466 from a Medicare perspective to treat 100 patients: 68 patients healed and 28 patients with wounds processing towards healing versus 12 patients healed and 69 patients with healing wounds). The lack of details and many assumptions based on expert opinion makes this study unexploitable.

If the clinical effectiveness was found to be comparable between NPWT and standard treatment, the following question would arise: do the alleged diminution of nursing costs and length of stay offset the equipment costs? Regardless of the quality of economic evaluation, no conclusive cost-effectiveness analyses have been and could have been performed due to the lack of good quality effectiveness data.

4.2.2 Marketing of NPWT and cost analysis

Most studies concern products from Kinetic Concepts Inc (KCI), also present on the Belgian market, with two available products: the V.A.C. ATS® (http://www.kci-medical.com/kci/corporate/kcitherapies/vactherapy/products/vacats/) and the portable V.A.C. Freedom®, which is only marginally used in Belgium yet. The V.A.C.® therapy system was cleared by the F.D.A. for wound healing on May 1995. Portable models were cleared in 2004. On the US market other manufacturers are present, e.g. Blue Sky Medical with the product Versatile One, which was approved by the FDA on August 2004. In the US, about one-third of teaching hospitals and slightly more rehabilitation facilities were using V.A.C. devices in 2000. [47].

In 2003, according to the manufacturer NPWT was used in Canada in approximately 200 hospitals, 195 long-term care facilities and 70 home care programs. In 2004, 800 NPWT systems were rented in Canada, and a few systems were owned [40] [43].

Between 1995 and 2000, more than 15 000 patients with acute and chronic wounds were treated with NPWT worldwide [73]. In 2000, about 2000 V.A.C. devices were in operation worldwide [47].

As purchasing prices or rentals are considered to be costs for the hospital, both terms are indifferently used here. In the case of coverage policies, these prices are only equal to the health insurer costs if the reimbursement amounts to 100% of hospital costs.

Table 1 presents the material prices retrieved from the literature from 2003. Canisters and dressings come in packages of 5 or 10 units. Dressings vary in size and shape.

Table 1 : International NPWT material prices or costs per patient (in Euros).

	USA (2005) [83], [49], [84]	CANADA (2003-05) / 2005) [48], [78] [43] [40]	AUSTRALIA (2003) [46]	UK (2006) [85]	GALICIA (SP) (2005) [44]	NETHERLANDS [79]	GERMANY (2005) [86] [87]	SWITZERLAND (2005) [88]
Pump purchase		7513 (13000 portable)			Free (*)			
Pump rental per day	53 to 65	42 to 62 (39 to 54 portable)	35 (portable) - 39			39		
Canister (1 item)		24 to 41			107	20		
Dressing (1 item)	46	25 to 37 (cf. size)			84 to 128 (cf. size)	26 to 37 (cf. size)		
Costs of disposables per patient per day				37				
Costs per patient per day	76 - 81			67			64-77 (**) (portable)	61
Costs per patient per week					359 to 451 (cf. size)			

(*) Pumps are given by the distributor in Galicia.

When no price ranges are given for the disposables, dressings were considered to be medium-sized and canisters to have a 500 ml capacity. Hospital setting served as comparison. However, the inclusion of drapes, gels and tubing in these costs is unclear. Prices were corrected with comparative price levels in order to be compared with Belgian ones (presented infra in Table 2).

Canadian pump purchase price, canisters and dressings are cheaper than Belgian prices (respectively -9%, -18% and -50%) and rental is similar. USA prices are more expensive than Belgian ones: +19% to +45% for the rental, + 27% for the dressings. Galician prices of disposables are expensive (+88% than Belgian canisters and from +118% to +133% for dressings) but pumps are provided by the distributor and prices of disposables are in return higher than in other countries. Rental in the Netherlands is cheaper than in Belgium (-25%) as well as canisters (-61%) and dressings (-24%). Prices applicable in 2007 in France were retrieved from the website of Estad - FHF (Evaluation des Technologies de Santé pour la Fédération Hospitalière de France) (http://etsad.fhf.fr/etsad/index.php?module=dmi&action=acquisition&p1=58). Rental, canisters and dressings are respectively 11%, 16% and 32% more expensive in France than in Belgium. Caution is required as publication year differ between countries and differ from the date of comparative price levels (February 2007).

Interestingly, the HTA report of McGill University Health Centre is the only source reporting a maintenance cost of €1030 per pump bought at a price of €13000, which represents almost 8% of the purchase price [43]. No details are given on the required maintenance, the sole information is that pumps were still in function five years after their purchase. Maintenance in most countries like Belgium and France are included in the rental.

In Belgium, hospitals rent or buy pumps and buy disposables from K.C.I. One pump is rented for €52 per day. This amount is a catalog rental; actual rental differs from one hospital to another depending on commercial agreements. Pumps can also be bought at €9000, maintenance excluded (personal communication from hospital). Disposables come in sets of 5 or 10 pieces. Canisters each cost €50.4 (500 ml) or €96 (1000 ml). The price of one dressing is €34, €42 or €79 respectively for small, medium or large items, except for specific shapes (e.g. the special abdominal one that costs €318). Prices for drapes (€8.4), gels (€5.3) and connectors (€10 or €14 for a 2- or 4-way connector respectively) must be added. In the home care setting, the package of pump and disposables is rented for an all-inclusive rental of €98 a day (in this case, canister volume is 300 ml).

Costs of NPWT were compared to the costs of an alternative therapy. Moist gauze dressing therapy was chosen as comparator, as it is recommended in the recent guidelines published by the Wound Healing Society [5, 6]. This therapy is also used as comparator in the majority of the identified RCTs (see above). No sensitivity analysis was done but a conservative choice was applied on every post (the lowest costs for NPWT against the highest costs for the comparator).

General assumptions:

- Both therapies were used to treat a medium-sized wound in hospital setting.
- Nursing labour costs were excluded because they are financed through the global budgets of hospitals.
- Costs of saline solution and disinfecting agent were considered marginal for both therapies.
- In the common Belgian practice, NPWT dressings are changed 2 times a week (rather than the 3 times advised by the manufacturer). The smallest canister (500ml) was chosen.
- Saline-soaked sterile gauze dressings are changed 3 times a day.

Table 2 : Material costs of one week treatment : NPWT versus moist-gauze dressing therapy

Material	Unit prices	One week NPWT	One week moist gauze dressing therapy
Pump rental	€52	x 7=€ 364	
Dressing	€42	x 2= €84	
Sterile gauze (a)	€0.163		x 3 x 7 = €3.4
Canister	€50.4	x1=€50.4	
Drape	€8.4	x1=€8.4	
Gel	€5.3	x1=€5.3	
Connector	€10	x1=€10	
TOTAL		**€ 522.1**	**€3.4**

Source: K.C.I. V.A.C.® catalog prices 2007 except (a) expert opinion

As presented in Table 2, one NPWT week would amount to €522 versus €3.4 for moist gauze dressing therapy.

Prices of sterile gauze may be lower than the price assumed: e.g. one pack of 100 sterile 20x20cm 17-threads gauze dressings is sold at €6 on the Belgian medical supplies market (from www.medistore.be). However, heavy exudating wounds demand much more material than this approach while the use of NPWT device is relatively independent of the wound type (expert opinion).

A large Belgian hospital communicated the costs of NPWT based on more than 100 patients treated between 2004 and 2006. The average pump rental amounted to €275 (corresponding to 6.3 days of treatment) added to €425 for the patient disposables, which means that the therapy costs for one patient may amount to €700, which confirms the conservative character of the simulation above.

In order to cut costs from a hospital perspective, some authors advise to return rented devices as quickly as possible, or to use bridging or Y-connecting that, allows to treat simultaneously several wounds from the same patients [84]. It must be noted that, in the latter case, a same negative pressure must be required by all wounds.

In Belgium, Haromed BVBA (www.haromed.be) produces wound and skin care supplies, offering solutions in function of the hospital needs. Wound drainage pumps can be rented or acquired in combination with (Haromed or not) disposables in order to drain wounds. The highest rental price is for a portable Exsudex® pump, that can drain 4 wounds and has an alarm, amounting to €30.3 per day. Including disposables from the same manufacturer (drain, antibacterial filter, canister, dressing, etc.) one day of ambulatory therapy would cost €37.75 (versus the €98 mentioned above). Fixed pumps without alarm can already be rented at €18.2 or purchased at €1450.

Some experimental homemade NPWT systems using readily available materials are used in some hospitals, hence reducing the cost of acquiring or renting commercial noisy and complex systems [88-93]. In a recent US paper, 40 patients were treated with a system requiring off-the-shelf sponges, drape, tubing and a connector to the hospital wall suction apparatus [90]. This system led to more than 40% savings in material costs. Another system requiring weight-loaded syringes reduced the material costs from €61 to less than €5 [88]. It should be noted that in those cases, the system is not equipped with an alarm. Other clinicians have adapted the initial commercial system in order to treat less accessible areas of the body, irregular surfaces or multiple wounds, or a hand that needs to hold its mobility [94] [2].

Off-the-shelf dressings are cheaper than those coming with package solutions claiming the NPWT appellation. Based on prices actually paid by a hospital that has communicated us purchase details, foam dressings are sold between €3 and €5 for a small or medium size (10x10 cm), being tenfold cheaper than €34 to €49 for a small or medium K.C.I. Granufoam® dressing. A similar comparison is also striking for the pump device. For example, the Laerdal Suction Unit (LSU) with Abbott Disposable System is a first aid pump used to remove mucus from the respiratory system. According to the

commercial site (http://www.laerdal.be/document.asp?subnodeid=16628995), the pump insures negative pressure from 80 to more than 500 mmHg (+/- 5%) with 4-hour autonomy, is quiet and comes with filter, tubing, connector and canister. Disposables are sold separately. The pump has also an automatic power saver going off after 2 minutes of negative pressure higher than 200mmHg. The price of this device is €1140, which is almost eight times cheaper than the NPWT device from the V.A.C. ® system.

KCI Medical Belgium is a subsidiary of KCI employing between 4 and 5 full-time equivalents to administrate services and sales systems to Belgian customers. The parent company also produces other products, such as therapeutic surfaces, but VAC rentals and sales represented 78% of the total revenue in 2006 ($1.4 billion or €1 billion). Based on the annual report of 2006, Research and Development (including financing of clinical trials) only amounts to 2.7% of these annual revenues (sales and rentals), while sales, marketing and advertising accounted for 22.1%.

According to KCI, products offered by other producers of suction units should not be considered as vacuum-assisted wound closure devices (personal communication from KCI). Of course, newcomers in the market may influence prices and cut the considerable profit margin of this current almost monopolistic market.

Manufacturers of NPWT systems already present in the US include the following:

- The market leader: Kinetic Concepts Inc (KCI): Classic V.A.C. System, V.A.C. Advanced Therapy System (ATS), Mini V.A.C., and V.A.C. Freedom.
- Blue Sky Medical: Versatile 1 Wound Care
- Neo-Gen Technologies Inc: Neo-Gen One, Closed Wound Drain
- Vital Needs International: Voyager, a portable wound care system

Considerable profit margins probably explain the US trial launched and won by Blue Sky Medical against its competitor in 2006 and in the Netherlands by Haromed in 2004.

4.2.3 Coverage policies

Materials for NPWT are not separately reimbursed in Belgium. Each ambulatory wound nursing visit in the home setting is covered by a fee-for-service system, depending on the surface area and the complexity of the wound. In the hospital setting, medical devices are financed through the global budgets of hospitals.

In the US, NPWT devices are covered by Medicare (but Medicare patients pay 20% of Medicare allowable fee), some Medicaid plans, the Veterans Affairs Healthcare System, and some private insurers for the treatment of chronic wounds. For example, since 1999 for Aetna, and 2004 for Cigna and Harvard Pilgrim, NPWT pumps are covered according to a series of conditions (in home setting or inpatient setting). Approval processes can induce obstacles or delay to obtain reimbursement for the NPWT therapy, taking days to be completed. For some insurance therapy approvals, a form from the manufacturer has to be filled in. For Medicaid patients, as NPWT therapy must be proven to be a 'last resort' therapy, other alternatives have to be documented [84].

In Canada, NPWT therapy and nursing care are publicly paid through the global budgets of hospitals, home care agencies, and long-term care homes [40]. In the Netherlands, almost all health insurers reimburse NPWT. In Italy, where reimbursement is organized by regions, NPWT is only covered in Piemonte and under consideration by the newly established (2005) Regional Council for further reimbursement.

In 2005, the French Commission that rules on reimbursement applications from the industry (Commission d'évaluation des produits et prestations - HAS (Haute Autorité de Santé)) rejected the KCI application for an inscription of NPWT systems on the Liste des Produits et Prestations Remboursables (LPPR) due to the lack of clinical evidence in the scientific literature [95].

In Germany, NPWT is reimbursed in the hospital setting only. A reimbursement of NPWT in the home setting is awaited since 1999. Based on literature related to wound healing speed, a study estimated the budget impact of a switch from traditional wound care for diabetic foot ulcers, decubitus ulcers and leg ulcers to NPWT [96]. Based on (1) the German estimated prevalence of these three conditions, (2) a material cost of €64 for the conservative treatment, (3) a material cost of €71 for NPWT and (4) the estimated number of days needed by each therapy, a 50% substitution could potentially save €700 million out of €5000 million in material for the sickness funds if NPWT was approved [96]. Notwithstanding, the Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen (IQWiG) did not find sufficient evidence to support the financing of NPWT in the ambulatory setting, as mentioned in its recent assessment update (28 March 2007).

4.3 DISCUSSION

Cost-effectiveness studies based on well-designed trials are definitely needed. As often is the case for emerging technologies and due to the enthusiasm that is raised amongst physicians and their patients by premature marketing, RCTs may be difficult to conduct due to the reluctance of patients to enter the conventional arm. However, the search for clinical evidence still yielded 15 RCTs, although the majority of these trials had serious methodological flaws.

Generally, therapy costs or surgery costs (surgery may be less complicated or even avoided after TNP) were not included in the identified cost calculations. Above this, costs of disposables were not always included, nor were costs of sedation (in case analgesia was needed). Ideally, outcomes and costs of the whole hospitalisation episode should be taken into account, including surgery. A long-term follow-up of all included patients should be available, without exclusion of newly infected or deceased patients. Moreover, this follow-up should include treatment of discharged patients who continue their therapy with a portable device, who receive nursing care afterwards or who are even readmitted to the hospital. As NPWT may emerge in the home care setting in Belgium, where NPWT is now primarily used in the hospital setting, economic evaluation will also have to take nurse travel costs into account, considering the number of dressing changes. In case of future foreign studies, results should be transposed cautiously to the Belgian situation as nursing labour costs represent an important component of the comparisons. Training of nurses should also be included in an economic evaluation. The NPWT learning curve influences outcomes and costs as the cumulated number of patient increases over time. Shorter duration of NPWT application as well as shorter hospital stay have been observed as nurses get more and more used to apply NPWT [97].

Key points

- **No conclusive cost-effectiveness analysis has been and could have been performed due to the lack of good quality effectiveness data.**
- **Compared to other countries, Belgium seems to belong to the medium range prices class of NPWT materials**
- **Profit margin may explain the high costs of NPWT, especially on the oligopolistic Belgian market, which cannot be due to important research and development expenses.**
- **Some US insurers allow NPWT reimbursement if strict patient conditions are met. In Canada, NPWT therapy is paid through the global hospitals budget.**
- **In Germany, the NPWT material is reimbursed in hospital setting but home care setting did not obtain reimbursement due to the lack of clinical evidence. In the Netherlands NPWT is reimbursed by almost all health insurers. In Italy, NPWT is only covered in one region. In France, reimbursement has been refused due to the lack of evidence.**
- **There is no specific public financing of NPWT in Belgium.**

5 GENERAL DISCUSSION

The body of evidence that was found on the clinical effectiveness of NPWT was rather large, comprising 10 HTA reports (of which 7 were included), 5 systematic reviews (of which 2 were included) and 15 randomised controlled trials. However, the overall methodological quality of the primary studies was low, which explains the uniform conclusion that the routine use of NPWT is not supported by good evidence. Since the most recent HTA report (IQWIG), 4 new RCTs were published. However, this new evidence does not permit to change this conclusion, even not for specific indications such as diabetic foot or skin grafting.

The comparator in the control group ("standard wound care") varied across the identified RCTs. A majority of the studies compared NPWT to moist gauze dressings, which is advocated as a part of the treatment of chronic wounds by the guidelines of the Wound Healing Society [5-8]. However, in a meta-analysis of 12 controlled trials, identified through a Medline search in 2001, a higher ulcer healing rate was found with hydrocolloid dressings than with conventional gauze dressings (odds ratio with random effect model 1.73, 95%CI 1.08 – 2.78) [98].

There is a clear underreporting of adverse events. However, as was stated in chapter 3.2.5, important harms are possible during the application of NPWT, especially in the hands of inexperienced health care providers. Even if correctly applied, complications related to the therapy are possible, e.g. wound infection, but the exact incidence of these complications is difficult to state based on the data from RCTs.

The FDA published a guidance on the design of clinical trials on the treatment of chronic wounds and ulcers [99]. Besides the importance of randomization and an adequate comparator arm, the FDA stresses the importance of blinding subjects and investigators. However, the FDA acknowledges that in some cases, especially for trials of some medical devices, it is impractical or unethical to implement a control treatment that mimics the test product for the purposes of blinding. In these situations, blinded assessment by a third-party evaluator should be considered [99]. Even this recommendation was hardly followed by most of the identified RCTs in this rapid assessment.

NPWT was found to be a rather expensive treatment with a considerable profit margin for the manufacturer. A search of the literature identified some cheaper alternatives to the commercial NPWT devices [88-93]. Even the RCT of Llanos et al., which was found to be of moderate quality, used a modified NPWT technique by using a less dense polyurethane dressing and providing a vacuum by connecting to the central aspiration system of the hospital, instead of connecting to a designated vacuum pump [58]. According to the authors, the designed dressing only costs around $4 per unit. Although most of these cheaper alternatives have not proven their efficacy and safety in well-designed RCTs (except in the case of Llanos et al.), they prove the profit margin of the technique and open perspectives to lower the current prices.

Based on the discussion above, the following conclusions can be made:

- **In general, based on the current evidence, the efficacy of NPWT is not proven. Therefore, this promising emerging technology cannot be considered routine practice for the treatment of chronic or acute wounds at present. Only for diabetic foot ulcers and skin grafts, some evidence exists on the efficacy of NPWT.**
- **Although NPWT seems to be a safe technology, safety data are scarce.**
- **There is a lack of well-conducted cost-effectiveness analyses. At present, no conclusions can be drawn on the cost-effectiveness of this technology, which is also related to the uncertainty of the clinical efficacy of this technology.**
- **Since NPWT is an apparently safe technology, there is no reason to disallow this type of treatment. However, hospitals should be well-informed about the lack of evidence on the clinical efficacy, safety and cost-effectiveness of NPWT. Above this, they should be made aware of the profit margin of the manufacturer, probably leaving room for further negotiation.**
- **According to clinical experts, NPWT seems to be efficacious in a small group of highly selected patients. However, restriction of (the reimbursement of) NPWT to these selected patients seems impossible at present because those patients who would benefit the most from the technology cannot be defined clearly with the current evidence.**
- **There is a clear need for well-designed RCTs, conducted for well-defined wound types (e.g. diabetic ulcers, pressure ulcers, traumatic wounds or venous ulcers) as part of the R&D process. It is however, already an established technology in several hospitals.**

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7 APPENDICES

SEARCH STRATEGY FOR MEDLINE

1. vacuum.mp. (10486)
2. VAC.mp. (1557)
3. TNP.mp. (2668)
4. NPWT.mp. (9)
5. sub-atmospheric.mp. (25)
6. subatmospheric.mp. (276)
7. negative pressure.mp. (3699)
8. suction dressing.mp. (2)
9. wound$.mp. (183533)
10. ulcer$.mp. (152752)
11. decubit$.mp. (3155)
12. incision$.mp. (29784)
13. free flap.mp. (2784)
14. skin graft$.mp. (9629)
15. skin transplantation$.mp. (25354)
16. degloving injur$.mp. (150)
17. burn$.mp. (56102)
18. diabetic feet.mp. (83)
19. diabetic foot.mp. (3760)
20. exp "Wounds and Injuries"/ (497034)
21. Sutures/ (9556)
22. or/1-8 (18151)
23. or/9-21 (787316)
24. 22 and 23 (1692)

SEARCH STRATEGY FOR PRE-MEDLINE

1. vacuum.mp. (1651)
2. VAC.mp. (38)
3. TNP.mp. (20)
4. NPWT.mp. (0)
5. sub-atmospheric.mp. (4)
6. subatmospheric.mp. (8)
7. negative pressure.mp. (83)
8. suction dressing.mp. (1)
9. wound$.mp. (2134)
10. ulcer$.mp. (1703)
11. decubit$.mp. (40)
12. incision$.mp. (852)
13. free flap.mp. (74)
14. skin graft$.mp. (190)
15. skin transplantation$.mp. (6)
16. degloving injur$.mp. (3)
17. burn$.mp. (1229)
18. diabetic feet.mp. (5)
19. diabetic foot.mp. (98)
20. or/1-8 (1779)
21. or/9-19 (5643)
22. 20 and 21 (45)

SEARCH STRATEGY FOR CDSR

1. vacuum.mp. (70)
2. VAC.mp. (9)
3. TNP.mp. (2)
4. NPWT.mp. (0)
5. sub-atmospheric.mp. (2)
6. subatmospheric.mp. (1)
7. negative pressure.mp. (39)
8. suction dressing.mp. (2)
9. wound$.mp. (475)
10. ulcer$.mp. (492)
11. decubit$.mp. (35)
12. incision$.mp. (217)
13. free flap.mp. (1)
14. skin graft$.mp. (22)
15. skin transplantation.mp. (2)
16. degloving injur$.mp. (0)
17. burn$.mp. (270)
18. diabetic foot.mp. (30)
19. diabetic feet.mp. (3)
20. or/1-8 (108)
21. or/9-19 (1087)
22. 20 and 21 (33)

SEARCH STRATEGY FOR CCRCT

1. vacuum.mp. (490)
2. VAC.mp. (137)
3. TNP.mp. (12)
4. NPWT.mp. (2)
5. sub-atmospheric.mp. (2)
6. subatmospheric.mp. (14)
7. negative pressure.mp. (292)
8. suction dressing.mp. (0)
9. or/1-8 (912)
10. wound$.mp. (8074)
11. ulcer$.mp. (10670)
12. decubit$.mp. (276)
13. incision$.mp. (2364)
14. free flap.mp. (18)
15. skin graft$.mp. (216)
16. skin transplantation.mp. (230)
17. degloving injur$.mp. (0)
18. burn$.mp. (2130)
19. exp "Wounds and Injuries"/ (7393)
20. Sutures/ (410)
21. diabetic foot.mp. (316)
22. diabetic feet.mp. (11)
23. or/10-22 (27030)
24. 9 and 23 (107)

SEARCH STRATEGY FOR CINAHL

1. vacuum.mp. (638)
2. VAC.mp. (111)
3. TNP.mp. (19)
4. NPWT.mp. (21)
5. sub-atmospheric.mp. (1)
6. subatmospheric.mp. (17)
7. negative pressure.mp. (391)
8. suction dressing.mp. (1)
9. wound$.mp. (21054)
10. ulcer$.mp. (11069)
11. decubit$.mp. (299)
12. incision$.mp. (998)
13. free flap.mp. (82)
14. skin graft$.mp. (418)
15. skin transplantation$.mp. (854)
16. degloving injur$.mp. (9)
17. burn$.mp. (9348)
18. SUTURES/ (330)
19. diabetic feet.mp. (19)
20. diabetic foot.mp. (2351)
21. or/1-8 (1031)
22. or/9-20 (38519)
23. 21 and 22 (284)

SEARCH STRATEGY FOR BNI

1. vacuum.mp. (88)
2. VAC.mp. (13)
3. TNP.mp. (5)
4. NPWT.mp. (0)
5. sub-atmospheric.mp. (1)
6. subatmospheric.mp. (0)
7. negative pressure.mp. (49)
8. suction dressing.mp. (0)
9. wound$.mp. (3539)
10. ulcer$.mp. (2114)
11. decubit$.mp. (16)
12. incision$.mp. (22)
13. free flap.mp. (4)
14. skin graft$.mp. (48)
15. degloving injur$.mp. (1)
16. burn$.mp. (815)
17. diabetic foot.mp. (186)
18. diabetic feet.mp. (1)
19. skin transplantation$.mp. (1)
20. or/1-8 (125)
21. or/9-19 (6038)
22. 20 and 21 (74)

SEARCH STRATEGY FOR CRD

Date	**20070202**
Database	**DARE, NHS EED, HTA (CRD)**
Date covered	**YR DARE 1994-2007, NHS EED1995-2007, HTA 1998-2007**
Search Strategy	

# 1	vacuum	63
# 2	VAC	10
# 3	TNP	3
# 4	NPWT	2
# 5	"sub-atmospheric"	0
# 6	subatmospheric	0
# 7	"negative pressure"	16
# 8	"suction dressing"	0
# 9	#11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18	79
# 10	wound*	1098
# 11	ulcer*	919
# 12	decubit*	34
# 13	incision*	168
# 14	"free flap"	9
# 15	"skin graft"	9
# 16	"skin graft*"	22
# 17	"skin transplantation*"	28
# 18	"degloving injur*"	1
# 19	burn*	269
# 20	"diabetic f*"	119
# 21	#10 OR#11 OR #12 OR #13 OR #14 OR #16 OR #17 OR #18 OR #19 OR #20	2158
# 22	#9 AND #21	25

DARE: 6 hits NHS EED:7 hits HTA: 12 hits

SEARCH STRATEGIES WITH ECONOMIC / COST FILTERING

Date	**20070202**
Database	**Ovid MEDLINE(R)**
Date covered	**<1950 to January Week 4 2007>**
Search Strategy	

1 ec.fs. (220024)
2 cost$.tw. (183877)
3 exp "Quality of Life"/ (56734)
4 exp "Costs and Cost Analysis"/ (126225)
5 exp Life Tables/ (8050)
6 exp Survival Analysis/ (73522)
7 or/1-6 (486799)
8 vacuum.mp. (10453)
9 VAC.mp. (1555)
10 TNP.mp. (2665)
11 NPWT.mp. (9)
12 sub-atmospheric.mp. (25)
13 subatmospheric.mp. (276)
14 negative pressure.mp. (3688)
15 suction dressing.mp. (2)
16 or/8-15 (18105)
17 wound$.mp. (183255)
18 ulcer$.mp. (152485)
19 decubit$.mp. (3153)
20 incision$.mp. (29723)
21 free flap.mp. (2780)
22 skin graft$.mp. (9619)
23 skin transplantation$.mp. (25333)
24 degloving injur$.mp. (150)
25 burn$.mp. (56038)
26 suture$.mp. (53879)
27 Sutures/ (9529)
28 diabetic f$.mp. (0)
29 exp "Wounds and Injuries"/ (496422)
30 or/17-29 (813355)
31 16 and 30 (1724)
32 31 and 7 (117)

NOTE: [mp=title, original title, abstract, name of substance word, subject heading word]

Date	20070202
Database	Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations
Date covered	<February 02, 2007>
Search Strategy	

1 cost$.tw. (6690)

2 quality.tw. (11475)

3 survival.tw. (9215)

4 econom$.tw. (3211)

5 or/1-4 (27920)

6 vacuum.mp. (1634)

7 VAC.mp.(36)

8 TNP.mp.(22)

9 NPWT.mp.(0)

10 sub-atmospheric.mp.(3)

11 subatmospheric.mp.(9)

12 negative pressure.mp.(78)

13 suction dressing.mp.(1)

14 or/6-13 (1757)

15 wound$.mp.(2092)

16 ulcer$.mp.(1645)

17 decubit$.mp.(39)

18 incision$.mp.(835)

19 free flap.mp.(73)

20 skin graft$.mp.(185)

21 skin transplantation$.mp.(6)

22 degloving injur$.mp.(3)

23 burn$.mp.(1154)

24 suture$.mp.(681)

25 diabetic f$.mp. (0)

26 or/15-25 (5953)

27 14 and 26 (45)

28 5 and 27 (6)

NOTE: [mp=title, original title, abstract, name of substance word]

Date	**20070202**
Database	**Embase**
Date covered	**[<1966-2007]/py**
Search Strategy	

#4. 'vacuum'/exp OR 'vacuum'	13,410
#5. vac	1,653
#6. 'tnp'/exp OR 'tnp'	4,310
#7. npwt	12
#8. 'sub-amospheric'	0
#9. subatmospheric	283
#10. 'negative pressure'	3,726
#11. 'suction dressing'	4
#12. #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11	22,830
#13. wound*	145,819
#14. ulcer*	180,076
#15. decubit*	10,637
#16. incision*	38,315
#17. 'free flap'/exp OR 'free flap'	6,388
#30. 'skin graft' OR 'skin grafts'	16,898
#31. 'degloving injury' OR 'degloving injuries'	208

#32. #31 AND (**'quality of life'/**) OR ((((**fiscal**:ab,ti,de OR **financial**:ab,ti,de OR **finance**:ab,ti,de OR **funding**:ab,ti,de) OR ((**variable***:ab,ti,de OR **unit***:ab,ti,de OR **estimate***:ab,ti,de) AND **cost***:ab,ti,de) OR (**'socioeconomics'/** OR **'cost benefit analysis'/** OR **'cost effectiveness analysis'/** OR **'cost of illness'/** OR **'cost control'/** OR **'economic aspect'/** OR **'financial management'/** OR **'health care cost'/** OR **'health care financing'/** OR **'health economics'/** OR **'hospital cost'/** OR **'cost minimization analysis'/**)) OR (**'economic evaluation'/** OR **'cost'/** OR **'reimbursement'/** OR **'cost utility analysis'/** OR **'drug cost'/** OR **'energy cost'/** OR **'hospital cost'/** OR **'hospital running cost'/** OR **'biomedical technology assessment'/**)))
107

Date	20070205
Database	Database: British Nursing Index and Archive
Date covered	<1985 to January 2007>
Search Strategy	

1 vacuum.mp. (88)

2 VAC.mp. (13)

3 TNP.mp. (5)

4 NPWT.mp. (0)

5 sub-atmospheric.mp. (1)

6 subatmospheric.mp. (0)

7 negative pressure.mp. (49)

8 suction dressing.mp. (0)

9 or/1-8 (125)

10 wound$.mp. (3539)

11 ulcer$.mp. (2114)

12 decubit$.mp. (16)

13 incision$.mp. (22)

14 free flap.mp. (4)

15 skin graft$.mp. (48)

16 skin transplantation$.mp. (1)

17 degloving injur$.mp. (1)

18 burn$.mp. (815)

19 diabetic foot.mp. (186)

20 diabetic feet.mp. (1)

21 or/10-20 (6038)

22 9 and 21 (74)

23 cost$.tw. (2184)

24 quality.tw. (5668)

25 survival.tw. (421)

26 econom$.tw. (767)

27 exp "Quality of life"/ (36890)

28 or/23-27 (43546)

29 22 and 28 (3)

NOTE: [mp=tw]

Date	20070205
Database	Database: CINAHL - Cumulative Index to Nursing & Allied Health Literature
Date covered	<1982 to December Week 2 2006>
Search Strategy	

1 1 vacuum.mp. (619)
2 VAC.mp. (108)
3 TNP.mp. (19)
4 NPWT.mp. (20)
5 sub-atmospheric.mp. (1)
6 subatmospheric.mp. (17)
7 negative pressure.mp. (379)
8 suction dressing.mp. (1)
9 or/1-8 (1002)
10 wound$.mp. (20696)
11 ulcer$.mp. (10901)
12 decubit$.mp. (296)
13 incision$.mp. (966)
14 free flap.mp. (81)
15 skin graft$.mp. (409)
16 skin transplantation$.mp. (844)
17 degloving injur$.mp. (9)
18 burn$.mp. (9195)
19 diabetic foot.mp. (2303)
20 diabetic feet.mp. (19)
21 or/10-20 (37662)
22 9 and 21 (276)
23 cost$.tw. (29391)
24 quality.tw. (49431)
25 survival.tw. (9985)
26 econom$.tw. (11025)
27 exp "Costs and Costs Analysis"/ (21161)
28 exp "Quality of life"/ (16344)
29 Life Table Method/ (220)
30 exp Survival Analysis/ (9740)
31 or/23-30 (113177)
32 22 and 31 (38)

NOTE: [mp=title, subject heading word, abstract, instrumentation]

Date	**20070205**
Database	**Database: Econlit**
Date covered	**1969 to November 2006 (OVID)**
Search Strategy	

1	vacuum.mp.	95
2	VAC.mp.	1
3	TNP.mp.	0
4	NPWT.mp.	0
5	sub-atmospheric.mp.	0
6	subatmospheric.mp.	0
7	negative pressure.mp.	0
8	suction dressing.mp.	0
9	or/1-8	96
10	wound$.mp.	38
11	ulcer$.mp.	33
12	decubit$.mp.	0
13	incision$.mp.	1
14	free flap.mp.	0
15	skin graft$.mp.	0
16	skin transplantation.mp.	0
17	degloving injur$.mp.	0
18	burn$.mp.	448
19	suture$.mp.	1
20	or/10-18	519
21	9 and 19	0
22	vacuum.mp.	95
23	VAC.mp.	1
24	TNP.mp.	0
25	NPWT.mp.	0
26	sub-atmospheric.mp.	0
27	subatmospheric.mp.	0
28	negative pressure.mp.	0
29	suction dressing.mp.	0
30	or/22-29	96
31	wound$.mp.	38
32	ulcer$.mp.	33
33	decubit$.mp.	0
34	incision$.mp.	1
35	free flap.mp.	0
36	skin graft$.mp.	0
37	skin transplantation.mp.	0
38	degloving injur$.mp.	0

39	burn$.mp.	448
40	suture$.mp.	1
41	diabetic f$.mp.	0
42	or/31-39	519
43	30 and 40	0

NOTE: [mp=heading words, abstract, title, country as subject]

QUALITY CHECKLIST FOR ECONOMIC EVALUATIONS APPRAISAL

Study design
The research question is stated
The economic importance of the research question is stated
The viewpoints of the analysis are clearly stated and justified
The rationale for choosing the alternative programmes or interventions compared is stated
The alternatives being compared are clearly described
The form of economic evaluation used is stated
The choice of form of economic evaluation is justified in relation to the questions addressed
Data collection
The sources of effectiveness estimates used are stated
Details of the design and results of effectiveness study are given (if based on a single study)
Details of the method of synthesis or meta-analysis of estimated are given (if based on an overview of a number of effectiveness studies)
The primary outcome measure(s) for the economic evaluation are clearly stated
Methods to value health states and other benefits are stated
Details of the subjects from whom valuations were obtained are given
Productivity changes (if included) are reported separately
The relevance of productivity changes to the study question is discussed
Quantities of resources are reported separately from their unit costs
Methods for the estimation of quantities and unit costs are described
Currency and price data are recorded
Details of currency of price adjustments for inflation or currency conversion are given
Details of any model used are given
The choice of model used and the key parameters on which it is based are justified
Analysis and interpretation of results
Time horizon of costs and benefits is stated
The discount rate(s) is stated
The choice of rate(s) is justified
An explanation is given if costs or benefits are not discounted
Details of statistical tests and confidence intervals are given for stochastic data
The approach to sensitivity analysis is given
The choice of variables for sensitivity analysis is justified

The ranges over which the variables are varied are stated
Relevant alternatives are compared
Incremental analysis is reported
Major outcomes are presented in a disaggregated as well as aggregated form
The answer to the study question is given
Conclusions follow from the data reported
Conclusions are accompanied by the appropriate caveats

QUALITY APPRAISAL OF CLINICAL STUDIES

Table 1 : HTA reports

INAHTA checklist	MAS 2006	IQWiG 2006	McGill 2005	Avalia-T 2005	HPHC 2005	AHRQ 2004	CCOHTA 2003	CCE 2003	ASERNIP 2003	ECRI 2000
Are contact details available for further information?	Y	Y	Y	Y	N	Y	Y	Y	Y	Y
Authors identified?	P	Y	Y	Y	N	Y	Y	Y	Y	N
Statement regarding conflict of interest?	N	Y	N	N	N	N	N	N	N	N
Statement on whether report externally reviewed?	N	Y	N	N	N	Y	Y	N	N	Y
Short summary in non-technical language?	P	N	P	P	N	Y	Y	N	P	P
Reference to the question that is addressed and context of assessment?	Y	Y	Y	N	N	P	N	Y	N	N
Scope of the assessment specified?	Y	Y	P	Y	Y	Y	P	P	Y	Y
Description of the health technology?	Y	Y	P	Y	Y	P	Y	N	Y	Y
Details on sources of information?	Y	Y	Y	Y	N	Y	N	Y	Y	Y
Information on selection of material for assessment?	P	Y	Y	Y	N	Y	N	Y	Y	P
Information on basis for interpretation of selected data?	Y	Y	Y	Y	N	Y	N	Y	Y	N
Results of assessment clearly presented?	Y	Y	Y	Y	N	Y	Y	Y	Y	Y
Interpretation of assessment results included?	Y	Y	Y	Y	N	Y	Y	Y	Y	Y
Findings of the assessment discussed?	Y	Y	Y	Y	N	Y	Y	Y	Y	Y
Medico-legal implications considered?	Y	N	N	N	N	N	N	N	N	N
Conclusions from assessment clearly stated?	Y	Y	Y	Y	N	Y	Y	Y	Y	Y
Suggestions for further action?	Y	Y	Y	Y	N	P	Y	P	N	Y
Overall appraisal	**Moderate**	**Good**	**Moderate**	**Moderate**	**Poor**	**Moderate**	**Poor**	**Moderate**	**Moderate**	**Poor**

Table 2 : Systematic reviews

Cochrane checklist	Willy 2006	Mendonca 2006	Pham 2006	Gupta 2004	Evans 2006
Adequate research question?	Y	N	Y	N	Y
Adequately performed search?	Y	P	Y	P	Y
Adequate selection of articles?	Y	?	Y	?	Y
Adequate quality appraisal of articles?	?	N	P	Y	Y
Adequate description of the data extraction procedure?	N	N	Y	N	Y
Description of the most important characteristics of the included articles?	P	P	Y	N	Y
Adequate handling of clinical and statistical heterogeneity?	N	N	P	N	P
Adequate statistical pooling?	NA	NA	NA	NA	NA
Overall appraisal	**Low**	**Low**	**Moderate**	**Low**	**High**

Table 3 : Randomized controlled trials (first part)

Cochrane checklist	Vuurstaek 2006	Stannard 2006	Llanos 2006	Braakenburg 2006	Armstrong 2005	Etoz 2004	Jeschke 2004	Moisidis 2004
Randomization?	Y	Y	Y	Y	Y	Pseudo	Y	Y
Blinding of randomization?	Y	Y	P	Y	Y	Y	?	?
Blinding of patients?	N	?	N	N	N	?	?	?
Blinding of care provider?	N	?	P	N	N	?	?	?
Blinding of outcome assessor?	N	?	Y	N	P	?	?	Y
Similar groups at baseline?	Y	?	Y	N	P	Y	N	Y
Follow-up long enough?	Y	Y	?	Y	Y	?	?	N
Intention-to-treat-analysis?	Y	?	Y	N	Y	?	Y	N
Comparable treatment of groups?	Y	Y	Y	Y	Y	Y	Y	Y
Overall appraisal	**Low**	**Low**	**Moderate**	**Low**	**Moderate**	**Low**	**Low**	**Low**

Table 4 : Randomized controlled trials (second part)

Cochrane checklist	Moues 2004	Eginton 2003	Wanner 2003	Ford 2002	Joseph 2000	McCallon 2000	Greer 1999
Randomization?	Y	Y	Y	Y	Y	Pseudo	Y
Blinding of randomization?	Y	Y	?	Y	Y	Y	?
Blinding of patients?	N	N	?	?	?	?	?
Blinding of care provider?	N	N	?	?	?	?	?
Blinding of outcome assessor?	N	P	?	Y	Y	?	?
Similar groups at baseline?	N	?	?	N	N	?	?
Follow-up long enough?	Y	Y	Y	Y	Y	Y	?
Intention-to-treat-analysis?	N	N	N	N	?	?	?
Comparable treatment of groups?	Y	Y	Y	Y	Y	Y	?
Overall appraisal	**Low**	**Low**	**Low**	**Low**	**Low**	**Low**	**Low**

EVIDENCE TABLES

Table 5 : HTA reports.

Study ID	Scope	Search strategy	Results	Conclusions	Remarks
MAS 2006	Procedure: Negative pressure wound therapy Patients: patients with wounds (including pressure or diabetic ulcers, sternal wounds, and skin grafts)	Date: March 2006 Sources: Medline, Embase, Pre-Medline, INAHTA, CDSR, www.vacuumtherapy.co.uk Restrictions: RCTs with sample size of ≥ 20; English only	Retrieved evidence: 6 HTA reports 1 SR 6 RCTs (exclusion of 2 other RCTs with < 20 patients) Quality appraisal: GRADE 1 RCT of moderate quality, rest of low or very low quality	Based on the evidence, the clinical effectiveness of NPWT to heal chronic wounds is unproven.	Update of 2004 report
IWQiG 2006	Procedure: Vacuum-assisted wound closure Patients: patients with acute or chronic wounds	Date: May 2005 (update October 2005) Sources: Medline, Pre-Medline, Embase, Cinahl, CCRCT, CDSR, DARE, HTA database, grey literature Restrictions: controlled studies	Retrieved evidence: 9 RCTs (2 excluded from analysis) 11 non-RCTs 19 unpublished RCTs Quality appraisal: All RCTs of bad quality	No strong evidence on superiority of NPWT to conventional wound therapy. No justification for widespread use of NPWT. Assessment to be repeated in 2 – 3 years.	Written in German
McGill 2005	Procedure: Vacuum-assisted wound closure Patients: patients with acute or chronic wounds	Date: March 2005 Sources: Medline, Embase, CDSR, HTA sources Restrictions: English or French	Retrieved evidence: 5 HTAs 1 SR 6 RCTs Quality appraisal: All RCTs of bad quality	The available evidence does not support the routine use of NPWT.	

Study ID	Scope	Search strategy	Results	Conclusions	Remarks
Avalia-T 2005	Procedure: Negative pressure wound therapy Patients: patients with chronic wounds	Date: January 2005 Sources: Medline, Pre-Medline, Embase, HTA database, Cochrane Library, DARE, Spanish databases, Google Restrictions: systematic reviews, meta-analyses, and clinical studies; Spanish, Catalan, Portuguese, French or English language	Retrieved evidence: 4 HTAs 1 SR 8 RCTs Quality appraisal: One RCT with Jadad score 4, three RCTs with Jadad score 3, and 4 RCTs with Jadad score 2	The available evidence has poor methodological quality and too low power to detect differences between NPWT and conventional wound therapy. NPWT cannot be considered as a treatment for chronic wounds.	Written in Spanish
AHRQ 2004	Procedure: Negative pressure wound therapy Patients: patients with chronic wounds	Date: June 2004 Sources: Medline, Embase, CCTR Restrictions: studies on human subjects with English abstracts	Retrieved evidence: 6 RCTs (exclusion of 2 other RCTs) Quality appraisal: All RCTs were rated as poor quality	Insufficient body of evidence to support conclusions about the effectiveness of vacuum-assisted closure in the treatment of wounds.	
CCE 2003	Procedure: Negative pressure wound therapy Patients: patients with acute and chronic wounds	Date: August 2003 Sources: The Cochrane Library, Biological Abstracts, Medline, Pre-Medline, EBM Reviews, DARE, CINAHL, Australasian Medical Index, National Guideline Clearinghouse, SIGN, www.vacuumtherapy.co.uk Restrictions: English only	Retrieved evidence: 1 systematic review 2 RCTs not included in the SR Quality appraisal: All RCTs were rated as poor quality	The addition of two further primary studies in this report that were not included in the systematic review of Evans et al. does not change their conclusion. Therefore, whilst NPWT may offer advantages over other forms of wound dressings, these findings are presently not confirmed in controlled studies identified by this report. There remains a need for well designed, adequately powered, multi-centre randomised trials to evaluate the contribution of NPWT in the management of wounds. Patient relevant outcomes such as mobility and quality of life associated with different treatments should also be collected to further inform clinicians in the management of patients with wounds.	

Study ID	Scope	Search strategy	Results	Conclusions	Remarks
ASERNIP 2003	Procedure: Negative pressure wound therapy Patients: patients with non-healing wounds	Date: July 2003 Sources: Medline, Pre-Medline, Embase, Current Contents, Cochrane Library, CRD databases, grey literature Restrictions: RCTs and observational studies	Retrieved evidence: 2 systematic reviews 6 RCTs 4 non-randomised comparative studies 7 case series Quality appraisal: All RCTs were rated as poor quality	Although most studies were probably too small to detect significant differences, some results did show NPWT to result in better healing than standard methods, with few serious complications. More rigorous studies with larger sample sizes assessing the use of NPWT therapy on different wound types are required. With proper training to ensure appropriate and competent use, NPWT is simple to use and appears to be a promising alternative for the management of various wound types.	

Table 6 : Systematic reviews.

Study ID	Scope	Search strategy	Results	Conclusions	Remarks
Willy 2006	Procedure: Vacuum-assisted wound closure Patients: all wounds	Date: unclear Sources: Medline, Embase, Cochrane library (1980-2005) Restrictions: no reported	Retrieved evidence: not clear Quality appraisal: not stated	Harms can be virtually eliminated with correct use of technology.	Written in German
Mendonca 2006	Procedure: Vacuum-assisted wound closure Patients: all wounds	Date: unclear Sources: Medline and CDSR (from 1995 on) Restrictions: unclear	Retrieved evidence: 5 RCTs 10 case series 5 basic science studies Quality appraisal: not stated	The clinical effectiveness of NPWT is unclear.	
Pham 2006	Procedure: Negative pressure wound therapy Patients: patients with non-healing wounds	Date: July 2005 Sources: Medline, Pre-Medline, Embase, Current Contents, Cochrane Library, CRD databases, grey literature Restrictions: RCTs and observational studies of which the abstract contained efficacy and safety data	Retrieved evidence: 2 systematic reviews 10 RCTs + 2 preliminary analyses 4 non-randomised comparative studies 7 case series Quality appraisal: All RCTs were rated as poor quality	There is a paucity of high-quality RCTs. Based on the data from included studies, the technique does appear to result in better wound healing, with few serious complications.	Update of HTA report of ASERNIP-S
Gupta 2004	Procedure: Negative pressure wound therapy Patients: all wounds	Date: unclear Sources: Medline only Restrictions: no restrictions applied	Retrieved evidence: 1 systematic review 3 prospective trials 61 retrospective case studies 37 case reports Quality appraisal: Own rating system.	Although ample anecdotal data support the usefulness of NPWT, the existing published data also support the use of NPWT in multiple clinical situation.	

Study ID	Scope	Search strategy	Results	Conclusions	Remarks
Evans 2006	Procedure: Topical negative pressure Patients: chronic wounds	Date: November 2002 Sources: Cochrane Wounds Group Specialised Trials Register, HTA database on the Cochrane Library, www.vacuumtherapy.co.uk Restrictions: only RCTs, no restrictions applied on the basis of language or publication status	Retrieved evidence: 2 RCTs Quality appraisal: Small sample sizes, poor quality	The two small trials provide weak evidence suggesting that TNP may be superior to saline gauze dressings in healing chronic human wounds. However, due to the small sample sizes and methodological limitations of these trials, the findings must be interpreted with extreme caution. The effect of TNP on cost, quality of life, pain and comfort was not reported. It was not possible to determine which was the optimum TNP regimen.	Update of 2001 review

Table 7 : Randomized controlled trials.

Study ID	Patients	Intervention/ comparator	Quality Assessment	Outcomes	Comments
Vuurstaek 2006	Patients hospitalized with chronic venous, combined venous and arterial, or microangiopathic (arteriolosclerotic) leg ulcers of >6 months duration (after surgical treatment options had been exhausted and extensive ambulatory treatment (>6 months) in an outpatient clinic according to the SIGN guidelines had failed); < 85 years.	Intervention: NPWT pre- and post-grafting, n = 30 Comparator: Daily local wound care according to the SIGN guideline and compression therapy (double-layered, short, stretch bandages), n = 30	Randomization: computer program using random permuted blocks of eight; treatment allocation through telephone calls to the coordinating center. Blinding: no Intention-to-treat: yes Overall: low quality	Median time to complete healing: 29 (95%CI 25.5-32.5) vs 45 (36.2-53.8) days (p=0.0001) Wound bed preparation time: 7 (5.7-8.3) vs 17 (10-24) days (p=0.005) Time to recurrence: 4 months vs 2 months (p=0.47) Recurrence rate at 1y: 52% vs 42% (p=0.47) Median % of successful skin grafts: 83+/-14% vs 70+/-31% (p=0.011) Nursing time consumption: 232+/-267 vs 386+/-178 minutes (p=0.001) Quality of life: lower in NPWT group during 1st week, higher at the end of therapy Pain scores: similar decrease during first weeks, significant better in NPWT group from 5th week on Complication rate higher in NPWT group (p=0.17); one treatment failure in each group	

Study ID	Patients	Intervention/ comparator	Quality Assessment	Outcomes	Comments
Stannard 2006	I. Patients aged > 18 years, involved in traumatic injury with subsequent surgical incision which drained a minimum of 5 days after surgery. II. Patients aged > 18 years with one of three high-risk fractures after high-energy trauma (calcaneus, pilon, and tibial plateau [Schatzker IV through VI]).	Intervention: NPWT applied to surgical incision; I. n = 13, II. n = 20 Comparator: Standard postoperative dressing; I. n = 31, II. n = 24	Randomization: computer-generated Blinding: not clear Intention-to-treat: not clear Overall: low quality	*First study*: Drainage: 1.6 (0-5) vs 3.1 (0-11) days (p=0.03) Need for surgical irrigation: 1 vs 5 (NS) Late infection: 0 vs 1 (NS) *Second study*: Drainage: 1.8 (0-6) vs 4.8 (0-24) days (p=0.02) Wound infections: 3 in each group (NS) Delayed wound breakdown: 1 in each group (NS)	Preliminary report of 2 RCTs
Llanos 2006	Patients admitted at the hospital with acute traumatic injuries and skin loss which hindered primary closure, undergoing a surgical cleaning of their wound, and with a bacterial count lower than 100,000 colony forming units per gram of tissue	Intervention: Modified NPWT procedure (less dense polyurethane dressing, connection to central aspiration system of hospital); n = 30 Comparator: Same 3 sheets of polyurethane as for NPWT, along with a silicone fenestrated tube, translucent adhesive dressing, and flexible gauze; n = 30	Randomization: computer-generated random numbers in permuted blocks of 6; treatment allocation performed by nurse of operating room who knew the corresponding assignment (surgeon notified after skin grafting) Blinding: yes, blinded wound assessment Intention-to-treat: yes Overall: moderate quality	Median graft loss: 0.0 (0-11.8) vs 4.5 (0-52.9) cm^2 (p=0.001) Median % graft loss: 0.0% (0-62) vs 12.8% (0-75.9) (p<0.001) Regrafting rate: 5 vs 12 (p=0.045) Median time grafting - discharge: 8 (7-13) vs 12 (7-23) days (p=0.001) Total LOS: 13.5 (11-22) vs 17 (10-31) days (p=0.01)	

Study ID	Patients	Intervention/ comparator	Quality Assessment	Outcomes	Comments
Braakenburg 2006	Patients with any type of wound, acute or chronic	Intervention: NPWT; n = 32 Comparator: Various types of dressings from the local wound protocol (changed one or more times a day); n = 33	Randomization: block randomization for each 20 patients by closed envelopes Blinding: no Intention-to-treat: no, 18 patients excluded from analysis Overall: low quality	Median healing time: 16 (9-23) vs 20 (16-24) days (p=0.32); HR 1.33 (0.74-2.40) Change in amount of granulation: 1.7 vs 1.6% per day (p=0.64) Change in amount of wound surface area: 0.1 cm^2 per day in each group (p=0.83) Bacterial growth: 84% vs 58% (p=0.06) Total costs: €353 (111-1503) vs €73 (40-1123) (p=0.09) Total nursing time: 2.9 (0.8-10.1) vs 6.3 (0.6-26.8) hours (p=0.04) Discontinuation of NPWT in 2 patients due to pain during dressing changes Learning curve for NPWT: erosion of adjacent tissue and wound edges in first 3 patients	Differences in underlying diseases (CVD) and chronic wounds between two groups
Armstrong 2005	Patients aged 18 years or older, presence of a wound from a diabetic foot amputation to the transmetatarsal level of the foot, and evidence of adequate perfusion (defined as either transcutaneous oxygen measurements on the dorsum of the foot ≥30 mmHg or ankle brachial indices ≥0.7 and ≤1.2, and toe pressure at ≥30 mmHg)	Intervention: NPWT; n = 77 Comparator: Standard wound treatment (moist wound therapy with alginates, hydrocolloids, foams, or hydrogels); n = 85	Randomization: sealed envelopes Blinding: no, but use of planimetry measurements from digital photographs Intention-to-treat: yes Overall: moderate quality	Complete wound closure: 56% vs 39% (p=0.04) Time to reach 76-100% granulation tissue: 42 vs 84 days (p=0.002) Second amputation: 3% vs 11% of patients (p=0.06); RRR 0.225 (95%CI 0.05-1.1) Adverse events: 52% vs 54% (p=0.875)	Few results reported for patients who had complete wound closure but did not undergo surgical wound closure. Statistical comparison between the 2 groups not reported in study; authors reported groups were equal in response to The Lancet regarding comments from other researchers

Study ID	Patients	Intervention/ comparator	Quality Assessment	Outcomes	Comments
Etoz 2004	Patients with surgically debrided diabetic foot ulcers	Intervention: NPWT as delivered by a standard medical aspiration system (Bicakcilar Inc, Istanbul); n = 12 Comparator: Traditional moist gauze dressing (changed 2x/d); n = 12	Randomization: according to last digit of hospital protocol number (given by a blinded official). Odd numbers NPWT, even numbers control. Blinding: not clear Intention-to-treat: not clear, but no patients lost-to-follow-up Overall: low quality	Diabetic wound surface area decrease: 20.4 vs 9.5 cm^2 (p=0.032)	Pseudo-RCT
Jeschke 2004	Patients with acute and chronic wounds	Intervention: Fibrin glue-anchored Integra grafting with postoperative negative-pressure therapy; n = 6 Comparator: Conventional Integra grafting; n = 6	Randomization: yes, but randomization method not stated Blinding: not clear Intention-to-treat: yes Overall: low quality	% take rate of Integra: 78% (SD 8) vs 98% (2) (p<0.003) Wound infection: 1 vs 2 patients Time to skin transplantation: 10 (1) vs 24 (3) days (p<0.002)	Differences in age and wound size between two groups (though not significant)
Moisidis 2004	Patients with wounds 25 cm^2 or larger and judged clinically ready for skin grafting in the operating theatre: various wound types included on different body areas	Intervention: VAC Advance Therapy System; n = 22 Comparator: Bolster dressing consisting of Mepitel, Acriflavine wool (Defries Industries, Keysborough, Victoria, Australia), and foam sponge; n = 22	Randomization: yes, but randomization method not reported; each wound half was randomized Blinding: yes, blinded wound assessment Intention-to-treat: no, 2 patients lost to follow up Overall: low quality	NPWT had greater degree of epithelialization in 30%, same degree in 45% and less degree in 25% of cases	Each patient served as its own control Short follow-up (2 weeks)
Moues 2004	Patients with a full-thickness wound that could not be closed immediately because of infection, contamination, or chronic character	Intervention: NPWT; n = 29 Comparator: Moist gauze therapy two times a day or more; n = 25	Randomization: sealed envelopes Blinding: no Intention-to-treat: no Overall: low quality	Median time to reach 'ready for surgery': 6.0 (SEM 0.52) vs 7.0 (0.81) (p=0.19) Reduction of wound surface area: 3.8 (0.5) vs 1.7 (0.6) %/day (p<0.05)	Differences in underlying diseases between two groups

Study ID	Patients	Intervention/ comparator	Quality Assessment	Outcomes	Comments
Eginton 2003	Diabetics with significant soft tissue defects of the foot, not expected to heal in 1 month	Intervention: NPWT Comparator: Moist dressing Cross-over design. In total 10 patients with 11 wounds included.	Randomization: random number generator (even numbers NPWT - moist dressings, odd numbers moist dressings - NPWT) Blinding: unclear, but computerized planimetry was used for wound assessment Intention-to-treat: no, 4 patients (4 wounds) excluded from analysis Overall: low quality	% change in wound depth: -49% (SD 11.1) vs -7.7 (5.2) ($p<0.05$) % change in wound area: -16.4 (6.2) vs +5.9% (17.4) (NS) % change in wound volume: -59% (9.7) vs -0.1 (14.7) ($p<0.005$)	
Wanner 2003	Patients with a pressure sore of the pelvic region (deeper than grade 2: at least penetration in the subcutaneous fat); all para- or tetraplegic patients	Intervention: NPWT; n = 11 Comparator: Gauze soaked with Ringer's solution; n = 11	Randomization: yes, but randomization method not reported Blinding: unclear Intention-to-treat: no, 2 patients dropped out (1 lack of data, 1 diarrhea) Overall: low quality	Mean time to reach 50% of initial volume: 27 (SD 10) vs 28 (7) days (NS)	Statistical comparison between two groups not reported in study; few characteristics reported
Ford 2002	Patients with a stage III or IV pressure ulcer for 4 or more weeks	Intervention: NPWT; n = 20 wounds Comparator: Healthpoint System dressings (Accuzyme, Iodosorb, and Panafil; changed once or twice daily); n = 15 wounds	Randomization: table of random letters V and H Blinding: yes, blinded wound assessment Intention-to-treat: no, 6 patients excluded from analysis Overall: low quality	% reduction in wound volume: 51.8% vs 42.1% ($p=0.46$) Reduction in wound depth: 33.6 vs 31.0 cm ($p=0.90$) One complication with sepsis requiring amputation in NPWT group	
Joseph 2000	Patients with chronic non-healing wounds	Intervention: NPWT; n = 12 (18 wounds) Comparator: Wet-to-moist gauze dressings; n = 12 (18 wounds)	Randomization: by label colour Blinding: yes, blinded wound assessment Intention-to-treat: not clear Overall: low quality	Change in wound volume: 78% vs 30% ($p=0.038$) Change in wound depth: 66% vs 20% ($p<0.00001$) Complication rate: 17% vs 44% ($p=0.0028$)	Larger wounds in NPWT group ($p = 0.08$)

Study ID	Patients	Intervention/ comparator	Quality Assessment	Outcomes	Comments
McCallon 2000	Diabetic patients with a non-healing foot ulceration present for longer than 1 month	Intervention: NPWT; n = 5 Comparator: Saline-moistened gauze; n = 5	Randomization: using flip of a coin initially and thereafter by alternating groups Blinding: not clear Intention-to-treat: not clear Overall: low quality	Satisfactory healing: 22.8 (+/- 17.4) days vs 42.8 (+/- 32.5) days Decrease in wound surface area: 28.4% (+/- 24.3) vs 9.5% (+/- 16.9)	Pseudo-RCT Statistical comparison not reported in study; few characteristics reported; older age in NPWT group
Greer 1999	Patients with stage 3 and 4 pressure ulcers in the sacrum, ischium, or trochanter	Intervention: NPWT Comparator: Wet-to-moist dressings	Randomization: yes, but randomization procedure not stated Blinding: not clear Intention-to-treat: not clear Overall: low quality	8 SPD-treated ulcers decreased on average 42% in area over an average of 20 days	Preliminary results of 11 patients; abstract

ECONOMIC EVALUATIONS AND COSTS STUDIES SUMMARY SHEETS

Author	**Braakenburg, A. et al** [67]
Year	2006
Country	Netherlands
Design	Cost-effectiveness based on RCT
	funded by industry
Perspective	Hospital
Time window	healing time is an outcome - From date of debridement till endpoint reached (wound totally granulated OR ready to skin graft or healing by secondary intention)
Interventions	NPWT (V.A.C. ®) (n=26) vs various modern wound dressings (n=21) (various)
Population	Consecutive patients w/ any type of wounds in hospital (n=65) NPWT exclusions= 3 dead, 2 early dismissal, 1 refusal Comparator exclusions=5 dead, 6 early dismissal, 1 amputation
Assumptions	
Data source for costs	Hospital - Sum of Material costs at every dressing change (dressings, tapes, reservoirs, foams, connectors, and the depreciation costs of the pump). - Personnel costs: time to change a dressing, measured by stopwatch
Cost items included	Direct Material costs + personnel costs
Data source for outcomes	Evaluation of patients three times a week (same physician two times a week + two wound nurse practitioners), to record granulation rate, change in wound surface, pain, bacterial clearance, adverse events and time involvement of the nursing staff. Measures via visual analogue scale for pain score. Photographs and bacteriologic swabs were taken once a week to assess the progress of the wound, and wound surface measurements were obtained two times per week
Discounting	No (prices 2003)
Costs	Total Nursing time: NPWT 2.9 hours (range:0.8-10.1) versus 6.3(0.6-26.8) p=0.04 Nursing time Per day: 10.2(3.3-50.3) versus 16.8(8.0-73.2)

€(range)	NPWT	Conventional	p
Material costs / day	€19(5-86)	€7(2-25)	<0.0001
Labor costs / day	€5 (2–23)	€8 (4–34)	<0.0001
Total costs /day	€24 (10-110)	€14 (7-59)	<0.0001
Total material costs	€259 (86-1297)	€94 (16-431)	<0.0001
Total Labor costs	€81 (21-282)	€176 (16-750)	<0.04
Total costs	e353 (111-1053)	€273 (40-1123)	<0.09

Outcomes	Healing time: 16 days (IC95% 9-23) versus 20 days (16-24) p=0.32 Healing time for diabetic/cardiovascular patients: 14 (IC95% 9-19) versus 23(18-28) Overall change in wound surface 0.1 cm² per day for both groups
	No reduction in bacterial load
Cost-effectiveness	No ICER (incremental cost ratio) reported
Sensitivity analysis	No
Conclusions	No statistic difference in healing time or reduction of wound surface area. Especially cardiovascular and diabetic patients benefit from this therapy. The total costs of both therapies are comparable, but the advantage is its comfort for patients and nursing staff (odor, leakage, changes)
Remarks	- Number of excluded patients at admission unknown (but list of exclusions clearly stated) - Early dismissal, amputation and death were factors of exclusion after randomization, - comparator=various type of dressings - NPWT in 2 patients because of pain during dressing changes. - Definitive closure achieved by different techniques (skin-grafts or healing by second intention)

Author	**Moues, C. M.. et al** - [79]			
Year	2005			
Country	Netherlands			
Design	Cost-effectiveness based on RCT funded by industry			
Perspective	Hospital			
Time window	30 days			
Interventions	NPWT (V.A.C.) (n=29 wounds in 26 patients) vs moist gauze dressings (n=25 wounds in 23 patients)			
Population	54 patients with full-thickness wounds in need of open-wound management before surgical closure			
Assumptions	- Hospitalisation costs €250/day (=average costs for a hospital bed at a plastic surgery department in Dutch academic hospital including basic nursing care, hotel costs, doctor's visits and management costs and operation costs.) - Staff costs= €31.15 / hour = average in Dutch academic hospitals.			
Data source for costs	Physician recorded per dressing change: - number of dressings (and size), sponges, foam and solvents, - number of changes, number of staff involved per dressing changes, duration of dressing changes			
Cost items included	- Material costs + hospitalisation costs + labour costs			
Data source for outcomes	RCT			
Discounting	No (prices 2003)			
Costs	+/- Standard deviation with IC95%	NPWT	Moist gauze	p
	Mean Material costs	€414 +/- €229	€15 +/- 11€	p<0.0001
	Mean Hospitalisation costs	€1788 +/- €1060	€2467 +/- 1336€	p<0.05
	Mean Nursing costs	€33 +/- €31	€83 +/- 58€	p<0.0001
	TOTAL costs	€2235 +/-€ 1301	€2565 +/- €1384	NS
Outcomes	Wound surface reduction 3.8 NPWT +/- 0.5% (SD) vs 1.7 +/- 0.6% (SD) Median duration NPWT 6 +/- 0.52 (SE) days vs 7+/- 0.81 (SE)			
	Reduction of pain and inconvenience with NPWT (not measured)			
Cost-effectiveness	No ICER (incremental cost ratio) reported			
Sensitivity analysis	One-way analysis on Inpatient accomodation IF = €200/day => total costs =€1878+/- €1089 NPWT vs €2071 +/- €1117 IF = €300/day => total costs =€2593 +/- €1512 vs €3058 +/- €1651			
Conclusions	- Larger reduction in wound surface area with NPWT, no significant difference in LOS - NPWT equally as expensive as conventional moist gauze therapy			
Remarks	- Before and during treatment, necrotic tissue was sharp debrided when considered clinically necessary. - Other comparators replace moist gauze more and more (alginates, hydrogels ...) but moist gauze therapy still on of the most popular treatment in Europe and USA - Neither therapy costs nor surgery post included (may be less complicated or even avoided after NPWT) - Difference in debridement before TNP or moist gauze - Lack of patient details + different pathologies - Patients withdrawn if specis or complications - Exclusion criteria unclear (patients withdrawn if not deemed to be 'ready for surgery' within 30 days of treatment or if therapy was stopped before 30 days). - Addition of withdrawn patients costs to selected patients costs			

Author	**Costa, V. et al**[43]				
Year	2005				
Country	Canada				
Design	Cost analysis				
Perspective	Hospital				
Time window	one week				
Interventions	NPWT (V.A.C. ®)				
	versus advanced moist wound dressing				
Population	No particular specification on theoretic patient				
Assumptions	V.A.C. pump are amortized in 5 years, used 50 weeks per year NPWT dressing are changed 3 times a week versus 1.5 a day for advance moist wound dressings Nursing time is 30 min. per NPWT dressing change and 20 min. per moist wound dressing				
Data source for costs	Hospital finance department, hospital general stores and expert opinions				
Cost items included	Material costs and nursing fees				
Data source for outcomes	n/a				
Discounting	No				
Costs	CAN$	NPWT		advanced moist wound dressing	
		UNIT	1 week/patient	Unit	1 week/patient
	Pump purchase + maintenance	19.900 + 15.575	80 + 31.5	-	
	Dressings (S/M/L)	38 / 47.5 / 57	142.5	15	
	Other material	3.5 / change	10.5	3.5 / change	15.7
	Canister	36	36	-	36.8
	Nursing fees	39.59 / hour	59.4	39.59 / hour	138.6
	TOTAL		359.9		138.6
Outcomes	Mean NPWT LOS 19.3 days (range: 5 - 84) days Twelve patients treated with NPWT did not need further treatment (such as skin graft or free tissue transfer) No outcome comparison was made between three alternatives				
Cost-effectiveness	n/a				
Sensitivity analysis	Yes – Analysis on extremes: MIN NPWT dressing size (small.), nursing time (15 min / change) => NPWT$444.2 MIN comparator: number of moist wound dressing dressings per day(1/day) => moist dressing $ 221.9 MAX NPWT: NPWT dressing size (large), canister number of changes (2) , nursing time (40 min / change) => NPWT $302 MAX comparator: number of moist wound dressing dressings per day (2/day) => moist dressing= $ 221.9				
Conclusions	Although VAC may decrease dressing changes, it may still be more costly than traditional dressings due to materials and a longer time for dressing changes				
Remarks	- Many variables opinion-based, mostly in-hospital which is consistent from the hospital perspective				

Author	**Stone, P et al[80]**			
Year	2004			
Country	USA			
Design	Cost- effectiveness analysis (restrospective chart review)			
Perspective	unclear (probably hospital)			
Time window	2 years			
Interventions	NPWT (V.A.C.® device) (n=21 wounds in 17 patients) versus cotton bolster dressings irrigated with saline solution (n=25 wounds in 23 patients)			
Population	40 patients admitted to a level I trauma centre treated with split-thickness grafting (46 wounds)			
Assumptions	-			
Data source for costs	Chart			
Cost items included	Material cost			
Data source for outcomes	Main endpoint = survival or failure (including revised graft) (source=chart) Mean graft size, LOS or time that dressing was left in place			
Discounting	No			
Costs	US$	NPWT	cotton bolster	
	4 x 3-0 nylon suture		$ 18.44	
	Cotton bolster		$ 0.12	
	2 occlusive dressings	$ 102		
	Large sponge	$ 267		
	Canister 250 ml	$ 190		
	Daily vacuum cost ($90 x 5)	$ 450		
	TOTAL	$ 1 009	$ 18.44	
		NPWT	cotton bolster	p value
	Mean graft size (cm^2) +/- SD	105.6 +/- 88 range: 10-350	150.2+/-78 range: 30-300	0.08
	Mean duration of dressing +/- SD in days	4.8 +/- 0.8 range: 3-7	5.2+/-2.4 range: 2-14	0.36
	Failure (repeat grafting)	0		0.54
Cost-effectiveness	n/a			
Sensitivity analysis	No			
Conclusions	- NPWT may not be cost-effective NPWT is a promising device to secure split-thickness skin grafts, but implies a significantly higher cost => routine wounds that are small and have a contour that is not complex, use of a cotton bolster dressing is clinically as effective as NPWT and substantially more cost effective. A RCT treating grafts with high associated failure rates and these two treatment is needed (minimum size=250 patients)			
Remarks	- different wound type were pooled, with no patient differentiation, - Different wound localizations (face, torso, extremities) - low sample size (46 wounds) - NPWT dressings were			

Author	**Philbeck, T. E. et al[73]**		
Year	1999		
Country	USA		
Design	Cost- effectiveness analysis (restrospective chart review) funded by industry		
Perspective	Medicare		
Time window	30 days		
Interventions	NPWT (portable V.A.C.® device) + low-air-loss bed (n=43 wounds in ? patients) versus saline-soaked gauze dressings + low-air-loss bed (n=84)		
Population	1032 Medicare home healthcare patients w/ 1170 wounds that failed to response to previous interventions – comparison only on 43 22.2 cm² trunk or trochanteric pressure ulcers		
Assumptions	Nursing visits costs estimated at € 65 per visit € 17 866. The authors concluded that NPWT had superior effectiveness (68% faster healing time) and a clear economical advantage (38% globally cheaper) against saline-soaked gauze for a 22.2 cm² pressure ulcer. No other comparisons could be done due to the absence of comparable literature. Data collection was originally intended for submission to Medicare by the manufacturer K.C.I., and not intended for a clinical study. No details or demographics were given to assess the comparability with Ferrell's groups of patients. Moreover, no volume comparison was done between both groups of patients. Last but not least, another important flaw of the study lies in the comparison of healing rates: in the Ferrell study, wounds measured 4.3 cm² and healed at the rate of 0.09 cm². Costs per wound were calculated supposing the wounds measured originally 22.2 cm² healing at this rate.		
Data source for costs	- average calculated cost of wound treatment based on predicted median reimbursement		
Cost items included	Material costs and nursing visit costs		
Data source for outcomes	- Calculated reduction in wound area over time assuming the wound area - Comparison with wound healing time from a study by Ferrell in 1993.		
Discounting	No		
Costs	US$	NPWT + low-air-loss bed	Saline-soaked gauze + low-air-loss bed
	Material costs / day	$ 10	$ 107.46
	Labor costs / day	$ 85	$ 42.5
	Total costs /day	$ 95	$ 149.96
	Total material costs	$ 23 465	$ 14 546
Outcomes	- 22.2cm² pressure ulcer healed at 0.23 cm²/day - Ferrell study: 4.3 cm² wounds closed at an average rate of 0.090 cm²/day		
Cost-effectiveness	- NPWT: closure in 97 days at $ 14 546 versus calculated 247 days at $ 23 465		
Sensitivity analysis	No		
Conclusions	- NPWT is an effective treatment modality for a variety of chronic wounds. It can heal pressure ulcers located on trunk and trochanter 61% faster than similar wounds treated with saline-gauze dressings and can cost payors 38% less.		
Remarks	- selected wounds have failed to response to previous interventions, patient population is not homogeneous: No details or demographics were given to assess the comparability with Ferrell's groups of patients. - Settings of both therapies different (NPWT in home healthcare patients versus nursing home) - No volumetric comparison of wounds - historic comparisons with a study published 6 years earlier - Data collection record designed by device supplier - wounds treated with comparator measured 4.3 cm² and healed at the rate of 0.09 cm². Costs per wound were calculated supposing the wounds measured originally 22.2 cm² healing at this rate.		

Author	**Herscovici, D. et al [81]**			
Year	2003			
Country	USA			
Design	Cost analysis (prospective consecutive)			
Perspective	Unclear (Hospital?)			
Time window	until final wound closure + 6 month follow-up			
Interventions	NPWT (V.A.C. ®) after surgical debridement (changed /48 hours)			
	versus wet-to dry dressing (changed /72 to 96 hours)			
	versus application of a free tissue transfer			
Population	21 patients with 21 open high energy soft tissue injuries recruited consecutively in trauma centre from 1999 to 2001. (falls (5), motor vehicle accidents (8), 4 pedestrians struck by car, one sporting accident / all from different wound area size in various anatomical regions)			
Assumptions	Unclear if Wet-to-dry dressing implies same LOS than NPWT			
Data source for costs	Unclear			
Cost items included	Nursing personnel costs + dressings (only surgical fees for free flap)			
Data source for outcomes	Hospital trauma register Clinical study			
Discounting	No			
Costs	US$ Total costs /day (=material + labor costs) Surgical fees Total costs	NPWT(n=19) $ 103	Wet-to-dry dressing (n=12) $ 100 $ 2 000	Free flap (n=7) $ 6 000
Outcomes	Mean NPWT LOS 19.3 days (range: 5 - 84) days Twelve patients treated with NPWT did not need further treatment (such as skin graft or free tissue transfer) No outcome comparison was made between three alternatives			
Cost-effectiveness	n/a			
Sensitivity analysis	No			
Conclusions	VAC appears to be viable adjunct for open high-energy injuries. It does not replace the need for formal debridement of necrotic tissue, but it may avoid the need for a free tissue tranfer in some patients with large traumatic wounds			
Remarks	- Heterogeneous population suffering from different area size wounds in different anatomical regions. No details on patients comparability were given - No surgical fees or hospitalization costs included - No details on cost calculations or other statistics than average were given.			

Author	**Phillips, D. et al**		
Year	2003		
Country	Canada		
Design	Retrospective cost analysis		
Perspective	Unclear		
Time window	Unclear		
Interventions	NPWT		
	Weekly costs theoretically compared to standard gauze dressing		
Population	81 patients suffering from all kind of wounds		
Assumptions	Unclear if Wet-to-dry dressing implies same duration than NPWT		
Data source for costs	Unclear, probably public payer		
Cost items included	Equipment rental, dressings, canisters and nursing time (excluding travel costs).		
Data source for outcomes	For NPWT : capital Health Home Care Program		
Discounting	No		
Cost	$=Canadian $	NPWT	Standard gauze
	Material costs / week	$135	$206
	Labor costs / week	$560	$135
	Total costs /week	$695	$754
	Total costs	CAD $ 248 200 (n=81)	
Outcomes	Mean NPWT length 30 days (range: 1 to 217) days 50.6% positive outcomes (granulated to skin level, ready for skin graft, or complete closure), Percentage was higher for diabetic ulcers (9/47:77.7), pilonidal sinus (12/26:66.6%) and abdominal wounds (26/29:53.8%) No outcome comparison was made between alternatives		
Cost-effectiveness	n/a		
Sensitivity analysis	No		
Conclusions	Useful information for program-specific guidelines for the use of NPWT.		
Remarks	- Heterogeneous population, different anatomical regions. No details on other outcomes than percentages. - No details on cost calculations, no other statistics than average.		

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Wettelijk depot : D/2007/10.273/30

KCE reports

1. Effectiviteit en kosten-effectiviteit van behandelingen voor rookstop. D/2004/10.273/1.
2. Studie naar de mogelijke kosten van een eventuele wijziging van de rechtsregels inzake medische aansprakelijkheid (fase 1). D/2004/10.273/2.
3. Antibioticagebruik in ziekenhuizen bij acute pyelonefritis. D/2004/10.273/5.
4. Leukoreductie. Een mogelijke maatregel in het kader van een nationaal beleid voor bloedtransfusieveiligheid. D/2004/10.273/7.
5. Het preoperatief onderzoek. D/2004/10.273/9.
6. Validatie van het rapport van de Onderzoekscommissie over de onderfinanciering van de ziekenhuizen. D/2004/10.273/11.
7. Nationale richtlijn prenatale zorg. Een basis voor een klinisch pad voor de opvolging van zwangerschappen. D/2004/10.273/13.
8. Financieringssystemen van ziekenhuisgeneesmiddelen: een beschrijvende studie van een aantal Europese landen en Canada. D/2004/10.273/15.
9. Feedback: onderzoek naar de impact en barrières bij implementatie – Onderzoeksrapport: deel 1. D/2005/10.273/01.
10. De kost van tandprothesen. D/2005/10.273/03.
11. Borstkankerscreening. D/2005/10.273/05.
12. Studie naar een alternatieve financiering van bloed en labiele bloedderivaten in de ziekenhuizen. D/2005/10.273/07.
13. Endovasculaire behandeling van Carotisstenose. D/2005/10.273/09.
14. Variaties in de ziekenhuispraktijk bij acuut myocardinfarct in België. D/2005/10.273/11.
15. Evolutie van de uitgaven voor gezondheidszorg. D/2005/10.273/13.
16. Studie naar de mogelijke kosten van een eventuele wijziging van de rechtsregels inzake medische aansprakelijkheid. Fase II : ontwikkeling van een actuarieel model en eerste schattingen. D/2005/10.273/15.
17. Evaluatie van de referentiebedragen. D/2005/10.273/17.
18. Prospectief bepalen van de honoraria van ziekenhuisartsen op basis van klinische paden en guidelines: makkelijker gezegd dan gedaan.. D/2005/10.273/19.
19. Evaluatie van forfaitaire persoonlijk bijdrage op het gebruik van spoedgevallendienst. D/2005/10.273/21.
20. HTA Moleculaire Diagnostiek in België. D/2005/10.273/23, D/2005/10.273/25.
21. HTA Stomamateriaal in België. D/2005/10.273/27.
22. HTA Positronen Emissie Tomografie in België. D/2005/10.273/29.
23. HTA De electieve endovasculaire behandeling van het abdominale aorta aneurysma (AAA). D/2005/10.273/32.
24. Het gebruik van natriuretische peptides in de diagnostische aanpak van patiënten met vermoeden van hartfalen. D/2005/10.273/34.
25. Capsule endoscopie. D/2006/10.273/01.
26. Medico–legale aspecten van klinische praktijkrichtlijnen. D2006/10.273/05.
27. De kwaliteit en de organisatie van type 2 diabeteszorg. D2006/10.273/07.
28. Voorlopige richtlijnen voor farmaco-economisch onderzoek in België. D2006/10.273/10.
29. Nationale Richtlijnen College voor Oncologie: A. algemeen kader oncologisch kwaliteitshandboek B. wetenschappelijke basis voor klinische paden voor diagnose en behandeling colorectale kanker en testiskanker. D2006/10.273/12.
30. Inventaris van databanken gezondheidszorg. D2006/10.273/14.
31. Health Technology Assessment prostate-specific-antigen (PSA) voor prostaatkankerscreening. D2006/10.273/17.
32. Feedback : onderzoek naar de impact en barrières bij implementatie – Onderzoeksrapport : deel II. D/2006/10.273/19.
33. Effecten en kosten van de vaccinatie van Belgische kinderen met geconjugeerd pneumokokkenvaccin. D/2006/10.273/21.
34. Trastuzumab bij vroegtijdige stadia van borstkanker. D/2006/10.273/23.
35. Studie naar de mogelijke kosten van een eventuele wijziging van de rechtsregels inzake medische aansprakelijkheid (fase III)- precisering van de kostenraming. D/2006/10.273/26.
36. Farmacologische en chirurgische behandeling van obesitas. Residentiële zorg voor ernstig obese kinderen in België. D/2006/10.273/28.
37. HTA Magnetische Resonantie Beeldvorming. D/2006/10.273/32.

38. Baarmoederhalskankerscreening en testen op Human Papillomavirus (HPV). D/2006/10.273/35
39. Rapid assessment van nieuwe wervelzuil technologieën : totale discusprothese en vertebro/ballon kyfoplastie. D/2006/10.273/38.
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44. Een procedure voor de beoordeling van nieuwe medische hulpmiddelen. D/2006/10.273/50.
45. HTA Colorectale Kankerscreening: wetenschappelijke stand van zaken en budgetimpact voor België. D/2006/10.273/53.
46. Health Technology Assessment. Polysomnografie en thuismonitoring van zuigelingen voor de preventie van wiegendood. D/2006/10.273/59.
47. Geneesmiddelengebruik in de belgische rusthuizen en rust- en verzorgingstehuizen. D/2006/10.273/61
48. Chronische lage rugpijn. D/2006/10.273/63.
49. Antivirale middelen bij seizoensgriep en grieppandemie. Literatuurstudie en ontwikkeling van praktijkrichtlijnen. D/2006/10.273/65.
50. Eigen betalingen in de Belgische gezondheidszorg. De impact van supplementen. D/2006/10.273/68.
51. Chronische zorgbehoeften bij personen met een niet- aangeboren hersenletsel (NAH) tussen 18 en 65 jaar. D/2007/10.273/01.
52. Rapid Assessment: Cardiovasculaire Primaire Preventie in de Belgische Huisartspraktijk. D/2007/10.273/03.
53. Financiering van verpleegkundige zorg in ziekenhuizen. D/2007/10 273/06
54. Kosten-effectiviteitsanalyse van rotavirus vaccinatie van zuigelingen in België. D2007/10.273/09
55. Evidence-based inhoud van geschreven informatie vanuit de farmaceutische industrie aan huisartsen. D2007/10.273/12
56. Orthopedisch Materiaal in België: Health Technology Assessment. D2007/10.273/14
57. Organisatie en Financiering van Musculoskeletale en Neurologische Revalidatie inBelgië D/2007/10.273/18
58. De Implanteerbare Defibrillator: een Health Technology Assessment. D/2007/10.273/21
59. Laboratoriumtesten in de huisartsgeneeskunde. D/2007/10.273/24
60. Longfunctietesten bij volwassenen. D/2007/10.273/27
61. Vacuümgeassisteerde Wondbehandeling: een Rapid Assessment. D/2007/10.273/30