Technology Assessment

Technology Assessment Program

Negative Pressure Wound Therapy Technologies For Chronic Wound Care in the Home Setting

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Negative Pressure Wound Therapy Technologies for Chronic Wound Care in the Home Setting

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Peer Reviewers

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Negative Pressure Wound Therapy Technologies for Chronic Wound Care in the Home Setting

Structured Abstract

Objectives: To systematically review the efficacy and safety of negative pressure wound therapy (NPWT) for treatment of chronic wounds in the home setting.

Data Sources: On June 2014, we searched MEDLINE®, Embase®, the Cochrane Central Register of Controlled Trials, and the Cumulative Index to Nursing and Allied Health Literature (CINAHL®).

Review Methods: Two independent reviewers screened search results. We included studies examining the use of NPWT in patients with chronic wounds, including venous leg ulcers, arterial leg ulcers, diabetic foot ulcers, pressure ulcers, and mixed etiology chronic wounds. We searched for comparative trials that followed subjects in the home setting. We extracted data into standardized forms and summarized results qualitatively.

Results: We retrieved 5,912 citations, and found seven studies which met our criteria for inclusion. Six of the studies compared NPWT devices to other wound care methods. One study compared two different NPWT devices. Data were limited by variability in the types of comparator groups, variable quality in study design, and limited reporting of outcomes.

Conclusions: We were unable to draw conclusions about the efficacy or safety of NPWT for the treatment of chronic wounds in the home setting due to insufficient evidence. Though NPWT has been used across the wound care spectrum, significant research gaps remain. Standardization of wound care research protocols, such as providing consistency in comparator groups, robust randomized study designs, larger trials, and common definitions of outcomes, would be helpful in providing evidence to inform decisions about the use of NPWT.

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Introduction

Chronic wounds are wounds that have failed to proceed through the normal process of healing.[1] There are varying etiologies of chronic wounds in the U.S. population, which all create a burden upon the health care system. The health care expenditures for chronic wounds have been estimated to be up to $25 billion dollars per year.[2, 3]

Common types of chronic wounds include venous insufficiency ulcers, arterial leg ulcers, diabetic foot ulcers, and pressure ulcers.[4] These wounds can affect a large number of people with varying degrees of severity. Venous insufficiency ulcers are a large proportion of chronic wounds as a whole, with over 50% of chronic leg ulcers occurring as a result of a venous etiology.[5] Amputations related to diabetic foot wounds have been associated with high cumulative mortality – up to 70 percent within 10 years from the first amputation due to a diabetic foot ulcer.[6] Annual prevalence of venous insufficiency ulcers in those 65 and older has been estimated to be 1.69 per 100 person-years.[7] The prevalence of pressure ulcers varies between 0.31 to 0.70 percent per year, with increasing incidence with advancing age.[8] Given the aging population in the United States and the growing incidence of cardiovascular disease, diabetes, and obesity,[9, 10] the prevalence of chronic wounds, and the associated burdens, can only be expected to grow.

There are a variety of modalities available for chronic wound treatment, with some targeted toward specific types of wounds, such as compression for venous insufficiency ulcers. Routine wound care may involve any or all of the following: debridement (removal of material from the wound bed to permit healing), wound dressings (including gauzes, films, hydrogels, hydrocolloids, alginates, and foams), barrier products, and topical or systemic antimicrobials. In addition to these various wound dressings and medications, there are other adjunctive treatment modalities, such as skin substitutes, hyperbaric oxygen, and negative pressure wound therapy (NPWT).[4] This last modality is the focus of our review.

NPWT refers to the application of negative pressure across a wound. The technology emerged in the 1980s[11] and consists of the application of a dressing, usually foam or gauze, on the wound, which is then connected through tubing to a vacuum pump. The area is sealed with an adhesive film and the pump delivers a controlled negative pressure across the wound bed.[12] The Centers for Medicare and Medicaid Services (CMS) defines NPWT as the "application of subatmospheric pressure to a wound to remove exudate and debris, via an integrated system consisting of a suction pump, separate exudate collection chamber, and dressing, over specific wounds".[13] The aim of NPWT is to facilitate wound healing, promote granulation of the wound bed, and provide a bridge to surgical closure.

There are many mechanisms by which these devices may promote wound healing. Mechanisms of action include removing excess fluid while improving circulation to the wound bed,[14] reducing bacterial load on the wound surface, providing a mechanical effect that aids wound healing,[15] promoting cell proliferation and synthesis,[16, 17] and increasing the level of angiogenic and stimulatory cytokines,[18] and endothelial cell mobilization.[19-22]

With the potential benefits, there are also potential harms associated with NPWT. Reported adverse effects include pain, retention of foreign bodies from the dressing, bleeding, infection, death from infection or bleeding, and even complications stemming from power outages, which results in unrecognized interruption of therapy.[23-29] In 2011, the U.S. Food and Drug Administration (FDA) issued a safety communication regarding serious complications associated with NPWT systems. Their report included 174 reports of injury and 12 deaths that have occurred since 2007. Of significant concern was the number of events happening in the home

setting. Infection was the most common; however, bleeding was the most severe adverse event, and it led to significant morbidity and mortality. As a result, the FDA issued recommendations regarding patient selection, monitoring, contraindications, and risk factors that should be followed by clinicians. Additionally, the FDA endorsed education of the patient and caregivers to improve safety monitoring in the home setting.[30]

The devices range in price and in type; many different devices are available, and each offers a variety of options, including the ability to: add instillation fluids, vary the negative pressure settings, vary the dressing applied to the wound base from foams to gauzes, and use multiple types of overlying wound dressings. In traditional systems the electronic pump is continually used and the dressings are disposable. There are also systems where both the pump and dressings are disposable.

NPWT devices are usually applied by a variety of clinicians, but patients can apply some of the newer technologies. A number of manufacturers produce these devices, though the majority of the devices used in the U.S. come from just a few vendors.[31]

The NPWT technology has been widely adopted for the management of surgical wounds, especially those which need to heal by secondary intention. NPWT devices are marketed for wounds such as open abdominal incisions, dehisced surgical wounds, burns, preparation for skin graft sites, and traumatic wounds.[32-36]

In addition to treatment of acute surgical wounds, NPWT has been used to treat multiple types of chronic wounds (i.e., wounds that have failed to heal, or those that do not respond to treatment). These types of wounds are typically managed in the home or outpatient setting, or nonacute care facilities such as rehabilitation or skilled nursing units.

The common chronic wounds treated with NPWT are those referenced above: venous insufficiency ulcers, diabetic foot ulcers, and pressure ulcers.[23, 37-42] It is in these chronic nonhealing wounds for which further evaluation of the efficacy of NPWT in the home environment is needed.[23, 43-45]

Due to a lack of studies, results from previous systematic reviews of NPWT have primarily illustrated limitations in the evidence.[31, 37, 46, 47] For example, a Technology Assessment completed in 2009 supported by the Agency for Healthcare Research and Quality (AHRQ) demonstrated a lack of well-designed comparative studies assessing NPWT for a variety of different types of wounds.[31] In addition, none of these prior reviews examined the use of NPWT specifically in the home environment.

There is a critical need for evidence to guide the appropriate use of NPWT, particularly due to the increase in incidence of chronic wounds, driven by the aging of the U.S. population, as well as by increases in incidence of diabetes and obesity, all risk factors for developing chronic lower extremity wounds.

It is critical to assess the quality and strength of evidence related to the use of NPWT for chronic wounds in the home environment, especially as it applies to the Medicare population (i.e., those over 65 years of age or with disabilities).

Scope and Key Questions

In this systematic review, sponsored by AHRQ, we reviewed the literature on NPWT for chronic wound care in the home environment. We evaluated studies address the following Key Questions which were proposed by the Centers for Medicaid and Medicare (CMS) (Figure 1).

Key Question 1: What are the various NPWT technologies commercially available in the U.S. that are used to treat patients with chronic wounds (i.e., diabetic foot ulcers, arterial ulcers, venous ulcers, or pressure ulcers)?

Key Question 2, Part A: In patients who are similar to Medicare patients (age 65 or older or disabled) with chronic wounds, does the home use of NPWT significantly improve any of the following outcomes as compared with treatment with other wound care methods?

1) Clinical outcomes
    a) Complete wound healing by secondary intention (i.e., healing without surgical repair)
    b) Time to complete wound healing by secondary intention
    c) Time to surgical readiness of the wound bed
    d) Mortality
    e) Wound healing rate (e.g., percent ulcer area reduction or other measurement) for healed wounds
2) Patient-centered outcomes
    a) Return to prior level of functional activity
    b) Pain
    c) Health-related quality of life
3) Adverse events
    a) Infection rates
    b) Extremity amputation
    c) Emergency room visits related to the negative pressure wound therapy or treated wound
    d) Unplanned hospitalization/unplanned surgeries related to the negative pressure wound therapy or treated wound
    e) Blood transfusions/bleeding
    f) Dropout rate of patients and the reason for dropout (e.g., patients who discontinued therapy due to pain, inconvenience, lack of efficacy, another reason, or an unspecified reason)

Key Question 2, Part B: For studies included in Key Question 2, Part A, what wound care modalities were used prior to and concurrently with NPWT?

Key Question 2, Part C: For studies included in Key Question 2, Part A, what specific wound care modalities were used prior to and concurrently in the control groups of the studies?

Key Question 2, Part D: For studies included in Key Question 2, Part A, how do the treatments used prior to and/or concurrently with NPWT or the treatment of the control patients compare with usual care of chronic wounds?

Key Question 3: In patients with chronic wounds, do characteristics of the NPWT administration predict better or worse outcomes compared with other characteristics? Characteristics to be considered are:

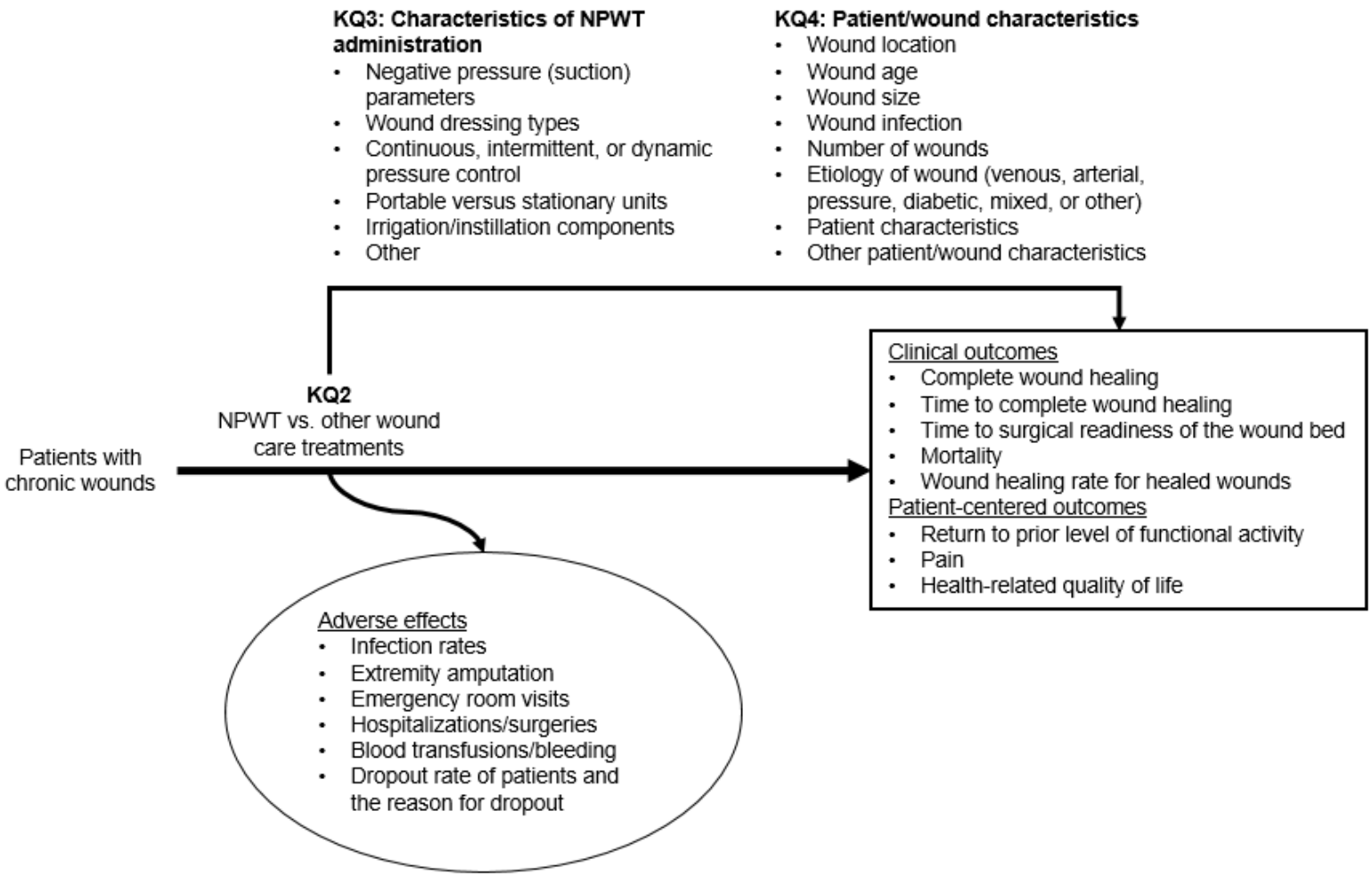
1) Negative pressure (suction) parameters, including amplitude, frequency, duration of suction, and other parameters as specified by the device
2) Wound dressing types

3) Continuous, intermittent, or dynamic pressure control
4) Portable versus stationary units
5) Irrigation/instillation components
6) Other characteristics of NPWT administration

Key Question 4: If any answer to Key Question 2, Part A is yes, are there specific characteristics that predict better or worse outcomes? Characteristics to be considered are:

1) Wound characteristics
    a) Wound location
    b) Wound age
    c) Wound size
    d) Wound infection
    e) Number of wounds
    f) Etiology of wound
        i) Venous
        ii) Arterial
        iii) Pressure
        iv) Diabetic
        v) Mixed
    g) Other wound characteristics
2) Patient characteristics:
    a) Age
    b) Diagnosis/comorbidities (e.g., diabetes/end-stage renal disease)
    c) Nutritional status
    d) Smoking status/history
    e) Vascular status
    f) Glycemic control (as appropriate)
    g) Previous treatment applied
    h) Other patient characteristics

Figure 1. Analytic framework for the treatment of chronic wounds with NPWT in the home setting



KQ = Key Question; NPWT = negative pressure wound therapy

Methods

The Agency for Healthcare Research and Quality (AHRQ) and the Center for Medicare and Medicaid Services (CMS) commissioned the Johns Hopkins University Evidence-based Practice Center to conduct a systematic review on the effectiveness and safety of negative pressure wound therapy (NPWT) for chronic wound care compared with other wound care treatments or other NPWT devices in the home setting.

For KQ1 (the list of NPWT used to treat patients with chronic wounds) we searched the U.S. Food and Drug Administration's Web site for NPWT currently approved for use in the U.S. We supplemented this list by searching manufacturer's Web sites and reviewing the previous technology assessment on NPWT.[31] The following methods refer to KQs 2 through 4.

Protocol Development

Representatives from the Coverage and Analysis Group (CAG) at CMS posed the questions for the review. We drafted a protocol for preparing this systematic review. With feedback from the AHRQ and CAG representatives, we finalized the protocol and registered it on PROSPERO (CRD42014008909).

Search Strategy

In June 2014, we searched the following databases for primary studies: MEDLINE®, Embase®, the Cochrane Central Register of Controlled Trials, and the Cumulative Index to Nursing and Allied Health Literature (CINAHL®). We developed a search strategy for MEDLINE, accessed via PubMed®, based on an analysis of medical subject headings (MeSH) and text words of key articles identified a priori. We had no date or language restrictions in the search strategies, and we hand searched the reference lists of included articles and relevant reviews. Additionally, in March 2014, we searched Clinicaltrials.gov to identify any relevant registered trials. Our search strategies are presented in Appendix A.

Study Selection

Two independent reviewers screened each abstract (see Appendix B). Both reviewers had to agree that the article met at least one of the exclusion criteria to be excluded (see Table 1 for the list of inclusion/exclusion criteria developed a priori and outlined in our protocol). We tracked and resolved differences between reviewers regarding abstract inclusion or exclusion through consensus adjudication.

Articles promoted on the basis of the abstract screen underwent another independent screen by two reviewers using the full-text (see Appendix B for article review form). We tracked and resolved differences between reviewers regarding article inclusion or exclusion through consensus adjudication.

We included studies that evaluated patients with chronic wounds. We considered chronic wounds to be venous insufficiency ulcers, arterial ulcers, diabetic foot ulcers, or ulcers of a mixed etiology. Chronic wounds were defined by the type of wound, without any restrictions on the duration of the wound. We excluded studies of patients with surgical or traumatic wounds. We also excluded studies that included fewer than 20 patients with chronic wounds as studies with 10 or fewer patients per group were considered to not be adequately powered to detect meaningful differences for the clinical outcomes of interest. We considered studies eligible

regardless of whether the population was a Medicare population (i.e., 65 years of age or older; disabled).

We included studies that evaluated a NPWT device commercially available and approved for use in the U.S. We included studies that compared a NPWT device with other wound care methods or with another NPWT device. We considered eligible studies with independent and paired comparison groups.

We included studies that evaluated clinical outcomes (complete wound healing, time to complete wound healing, time to surgical readiness of the wound bed, mortality, or wound healing rate for healed wounds), patient-centered outcomes (return to prior level of functional activity, pain, or health-related quality of life), or adverse events (infection rates, extremity amputation, emergency room visits related to the NPWT or treated wound, unplanned hospitalizations/surgeries related to the NPWT or treated wound, blood transfusions/bleeding, or dropout rates and the reasons for dropout). Generally, closure of the surface of the wound by the growth of epithelium over the defect is healing. If the closure has durability over time it is complete wound healing. Complete wound healing was considered as defined by the study authors and we included their definitions, when provided. We did not include the surrogate outcome wound healing rate (percent ulcer area reduction or other measurement) as an outcome for unhealed wounds. Chronic wounds may not heal in a linear fashion, becoming static at any time, and thus rate cannot be used to accurately predict complete healing.[48]

We focused our review on studies that followed patients in the home setting. We included studies that were described as in "outpatient setting" if it was reported (or we interpreted) that patients were not in assisted living, skilled or maintenance nursing homes.

Table 1. Inclusion and exclusion criteria

PICOTS	Inclusion criteria	Exclusion criteria
Population and condition of interest	• We included studies of human subjects. • We included studies of patients with chronic wounds of any etiology (venous, arterial, diabetic, pressure, or mixed). • We included studies with any population regardless of age or disability.	• We excluded studies of patients with surgical or traumatic wounds.
Interventions	• We included studies of NPWT.	• We excluded studies that did not evaluate an NPWT that is commercially available and approved for use in the U.S.
Comparisons	• We included studies that compared NPWT with other wound care methods. • We included studies that have a comparison group. Comparison groups could be either independent or paired.	• We excluded studies that did not have a comparison group.

Outcomes	• We included studies that evaluated one of the following outcomes:
	o Clinical outcomes
	  • Complete wound healing
	  • Time to complete wound healing
	  • Time to surgical readiness of the wound bed
	  • Mortality
	  • Wound healing rate for healed wounds
	o Patient-centered outcomes
	  • Return to prior level of functional activity
	  • Pain
	  • Health-related quality of life
	o Adverse events
	  • Infection rates
	  • Extremity amputation
	  • Emergency room visits related to the NPWT or treated wound
	  • Unplanned hospitalizations/ unplanned surgeries related to the NPWT or treated wound
	  • Blood transfusions/bleeding
	  • Dropout rate of patients and reasons
		• We excluded studies that reported wound healing rates without also reporting complete wound healing.

Type of study	• Any study design with a comparison group was eligible.	• We excluded articles with no original data (e.g., reviews, editorials, and commentaries). • We excluded studies with less than 20 subjects. • We excluded studies published in languages other than English. • We excluded meeting or conference abstracts.
Timing and setting	• We included studies regardless of the length of followup. • We included studies that are conducted in the home. (We included studies that were described as in "outpatient setting" if it was reported (or we interpreted) that patients were not in assisted living, skilled or maintenance nursing homes.)	• We excluded studies conducted in the hospital, inpatient, or long-term care settings.

NPWT = negative pressure wound therapy

Data Extraction

We created and pilot tested standardized forms for data abstraction (see Appendix B). Each article underwent double data extraction by the study investigators. The second reviewer confirmed the first reviewer's abstracted data for completeness and accuracy. Reviewer pairs were formed to include personnel with both clinical and methodological expertise. For all articles, the reviewers extracted information on general study characteristics (e.g., study design, study period, and followup), study participants (e.g., age, sex, smoking status, vascular status, glycemic control, wound etiology), characteristics of the wound (e.g., location, age, size, infection status, and quantity), interventions (e.g., negative pressure parameters, wound dressing types, type of pressure control [continuous, intermittent, or dynamic], portable or stationary units, irrigation or instillation components), comparisons, outcome measures, definitions, and the results of each outcome, including measures of variability.

We also collected data on treatments used prior to NPWT, whether debridement was conducted prior to NPWT, and the manner in which complete wound healing was classified and confirmed. We collected data on subgroups of interest (e.g., wound location, wound age, wound size, wound infection, number of wounds, age, sex, comorbidities, nutritional status, smoking status, vascular status, glycemic control, prior treatments, and wound etiology).

All information from the data extraction process was entered into the Systematic Review Data Repository (SRDR) database (Systematic Review Data Repository. Accessed at http://srdr.ahrq.gov/ on February 20, 2014) by the individual completing the review. Reviewers entered comments into the system whenever applicable. The SRDR database was used to maintain the data and to create detailed evidence tables and summary tables.

Quality (Risk of Bias) Assessment of Individual Studies

Two reviewers independently assessed individual study quality. We used the Cochrane Collaboration's Risk of Bias Tool[49] to assess the quality of all included studies. For both the RCTs and the nonrandomized studies, the overall study quality was assessed as good, fair, or poor.

Differences between reviewers were resolved through consensus adjudication.

Data Synthesis

Because the different chronic wound populations are not homogenous, we synthesized the results for each wound type separately when possible.

We planned to conduct meta-analyses for an outcome if there were sufficient data (at least three studies) and studies were sufficiently homogenous with respect to key variables (population characteristics, study duration, and treatment (see protocol for planned analyses).

For the randomized controlled trials, we calculated absolute risk differences with 95 percent confidence intervals for the outcome of complete wound healing using STATA 12.1 (College Station, Texas).

We qualitatively synthesized studies, and we summarized the study design and patient population characteristics, including descriptors of the wound (e.g., wound location, age, size, infection status, etiology, and number of wounds).

Strength of the Body of Evidence

At the completion of our review, at least two reviewers independently assigned evidence grades based on the study limitations, directness, consistency, precision, and reporting bias of the evidence body. Conflicts were resolved through consensus or third-party adjudication. We graded the strength of evidence addressing KQs 2 through 4 using the evidence grading scheme recommended in the *Methods Guide*.[50] We applied evidence grades to the bodies of evidence about each intervention comparison for the outcomes determined to be most important in making decisions about use of this therapy. We graded the following outcomes: complete wound healing, time to surgical readiness, pain, infection rates, and dropout rate of patients and reasons.

We classified evidence pertaining to the KQs into four basic categories: 1) "high" grade; 2) "moderate" grade; 3) "low" grade; and 4) "insufficient" grade. Table 2 defines each strength of evidence grade.

Table 2. Strength of evidence grades and definitions

Grade	Definition
High	We are very confident that the estimate of effect lies close to the true effect for this outcome. The body of evidence has few or no deficiencies. We believe that the findings are stable.
Moderate	We are moderately confident that the estimate of effect lies close to the true effect for this outcome. The body of evidence has some deficiencies. We believe that the findings are likely to be stable, but some doubt remains.
Low	We have limited confidence that the estimate of effect lies close to the true effect for this outcome. The body of evidence has major or numerous deficiencies (or both). We believe that additional evidence is needed before concluding either that the findings are stable or that the estimate of effect is close to the true effect.
Insufficient	We have no evidence, we are unable to estimate an effect, or we have no confidence in the estimate of effect for this outcome. No evidence is available or the body of evidence has unacceptable deficiencies, precluding judgment.

Applicability

We assessed the applicability of studies in terms of the degree to which the study population (age, duration of ulcer, comorbidities), interventions (treatment, cointerventions, duration of treatment), and outcomes may be applicable for the treatment of individuals with chronic wounds who are treated with NPWT in the home setting. We also specifically considered and discussed applicability of the evidence to the Medicare population.

Peer Review and Public Commentary

Experts in wound care, dermatology, endocrinology, geriatrics, internal medicine, nursing, plastic surgery, podiatry, and vascular surgery, and representatives from other government agencies were invited to provide external peer review of this Technology Assessment; AHRQ and CAG representatives also provided comments. The draft report was posted on the AHRQ Web site for 3 weeks to allow for public comment. We addressed all reviewer comments, revising the text as appropriate, and documented everything in a "disposition of comments report" that will be made available 3 months after the Agency posts the final Technology Assessment on the AHRQ Web site.

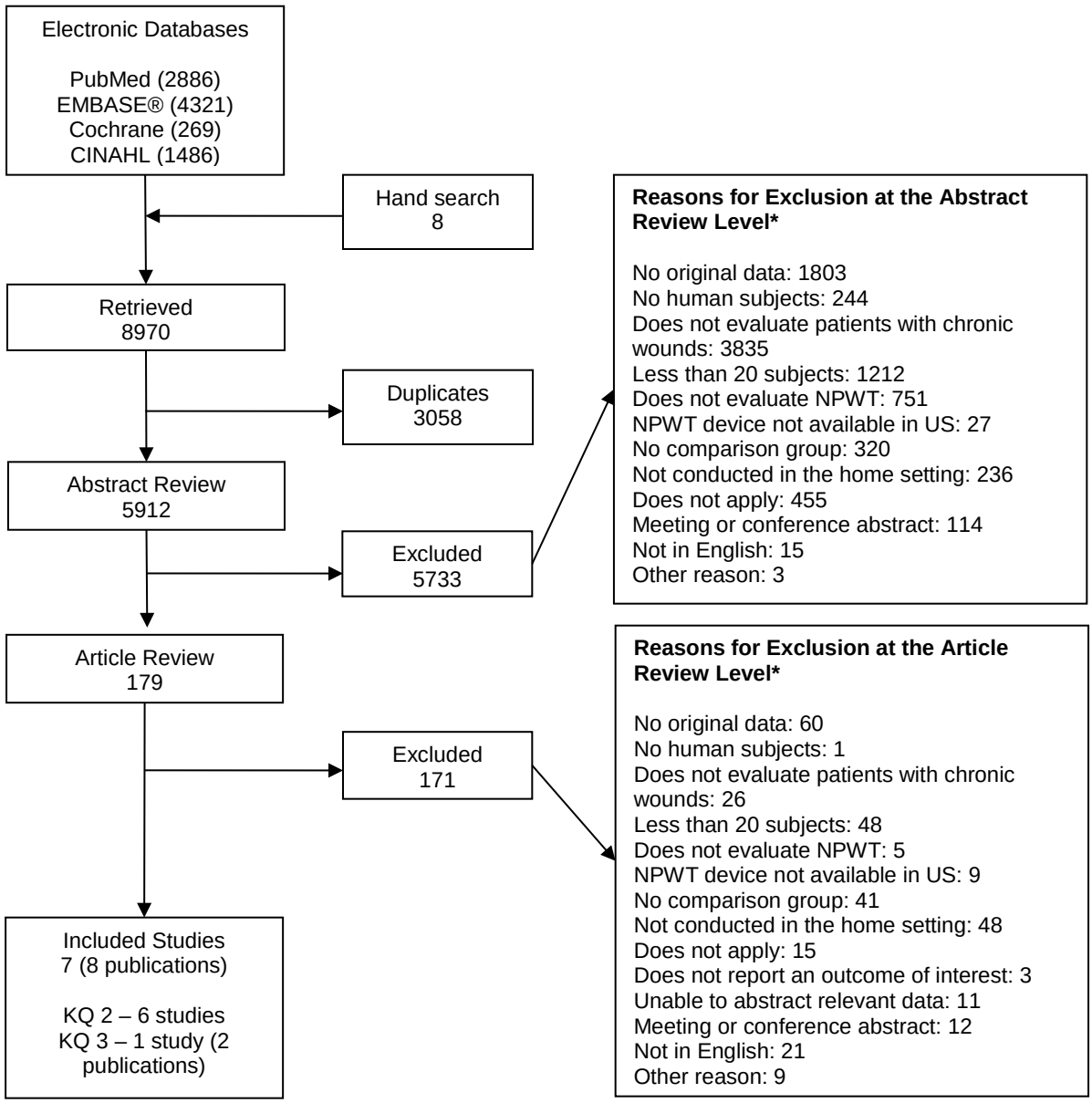
Results

Search Results

We retrieved 5,912 unique citations (Figure 2) and included seven studies (reported in eight publications). We identified six studies that compared NPWT with other wound care methods[51-56] and one study (two publications) that compared two different NPWT devices.[57, 58] Appendix C lists the excluded articles and the reason(s) that they were excluded.

We retrieved 96 protocols from ClinicalTrials.gov. Two protocols were deemed potentially relevant. One of these protocols was for a randomized controlled trial (RCT) that aimed to compare a NPWT with standard dressings among patients with pressure ulcers.[59] This study was terminated because of a low recruitment rate. The second protocol was matched to one of the included studies[57, 58] using the ClinicalTrials.gov registry number (NCT).[60] We identified an additional seven protocols that compared NPWT with either other wound treatments or another NPWT device among patients with chronic wounds.[61-67] However, we were unable to determine if these protocols met our eligibility criteria as information about the setting was not provided.

Figure 2. Summary of the literature search



* Total may exceed number in corresponding box, as articles could be excluded for more than one reason at this level.
CINAHL = Cumulative Index to Nursing and Allied Health Literature; NPWT = negative pressure wound therapy

Negative Pressure Wound Therapy Technologies Commercially Available in the U.S.

We searched the U.S. Food and Drug Administration Web site to identify NPWT technologies (Key Question 1). Supplemental information about available devices was obtained by reviewing the previous technology assessment on NPWT[31] and through each manufacturer's Web sites. Table 3 lists the NPWT technologies commercially available in the U.S. to treat wounds.

Table 3. Negative pressure wound therapy technologies commercially available in the U.S. to treat wounds

Manufacturer/Company	Model	Setting used
Atmos	Wound RX S 041 Wound pump	Hospital and home
Convatec	See IRB/Boehringer	
Genadyne	Genadyne A4 Wound Vacuum System	Hospital and home
Innovative Therapies	SVEDMAN™ and SVED™ Wound Treatment Systems	Hospital and home
Invacare	MoblVac®	Hospital and home
IRB Medical Equipment/ Boehringer Wound Systems/ConvaTec	Engenex® Advanced NPWT System	Hospital and home
Joerns (manufactured by Medela; distributed by Joerns)	Invia® Liberty™ Invia® Vario	Hospital and home
Kalypto Medical (acquired by Smith & Nephew)	NPD 1000™ Negative Pressure Wound Therapy System	Home
KCI (Kinetic Concepts, Inc.)	V.A.C.Via™ Therapy V.A.C.Ulta™ Therapy ActiV.A.C.® Therapy V.A.C. ATS® Therapy V.A.C. Freedom® Therapy V.A.C. Instill® Wound Therapy InfoV.A.C.® Therapy ABThera™ Open Abdomen Negative Pressure Therapy (open abdominal wounds)	Hospital and home Hospital Hospital and home Hospital and home Hospital and home Hospital Hospital and home Hospital Home
MediTop BV/The Medical Company	Exusdex® wound drainage pump	Primarily hospital use but may be used at home
Medela	Invia® Liberty™ Invia® Vario Medela® Invia Liberty pump Invia® Motion™	Hospital and home
Premco Medical Systems	Prodigy™ NPWT System (PMS-800 and PMS-800V)	Hospital and home
Prospera	PRO-I™ (stationary) PRO-II™ (portable) PRO-III™	Hospital and home Home Hospital and home
Smith and Nephew	Renasys EZ Plus Renasys Go PICO V1STA (previously by Blue Sky Medical Group) EZCare (previously by Blue Sky Medical Group)	Hospital and home Hospital and home Hospital and home Hospital and home Hospital
Spiracur	SNaP®	Hospital and home

Home Use of Negative Pressure Wound Therapy Compared With Other Wound Care Methods

Six studies compared NPWT with other wound care therapies (KQ 2, KQ 4).[51-56] Study details are provided in evidence tables (Appendix D).

Study Designs

Only one of the identified studies comparing NPWT with other wound care therapy was a RCT. Ford et al. randomized patients with pressure ulcers to either NPWT (n=20 ulcers) or one of three gel products (n=15 ulcers) over 6 weeks.[56] The three gel products were a papain-urea debridement ointment for necrotic wounds, a cadexomer iodine product for decubitus ulcers, and a papain-urea-chlorophyllin-copper ointment for clean, granulating wounds.

The other five studies were retrospective observational studies. Lavery et al.[54] identified patients on NPWT from a proprietary database (n=1135) and compared these to patients in studies from a meta-analysis (n=586) (Margolis, 2000).[68] Fife et al. identified those on NPWT (n=72) and those not (n=1,299) from a proprietary medical records database from wound care centers in 18 states over 5 years.[53] Lerman et al. identified and followed people on NPWT prospectively, but used a matched historical control identified through chart review, that was matched prior to reviewing outcomes.[52] Schwien et al. identified patients with pressure ulcers using NPWT (n=60) and those not using NPWT (n=2,288) from a data warehouse of home health patient records.[55]Yao et al. identified those on NPWT (n=171) and those not (n=171) through chart review of patient records from a major medical center data warehouse.[51]

Participants

In only one study were patients clearly treated in the home setting.[55] The description of settings was vague in each of the other studies. We included studies that were described as in "outpatient setting" if it was reported (or we interpreted) that patients were not in assisted living, skilled or maintenance nursing homes. In two studies, (Ford, 2002; Yao, 2012)[51, 56] patients were recruited in the inpatient setting but followed up in the outpatient setting. For these studies, we contacted the authors to confirm that the patients were not hospitalized during the followup period. One author (Ford) replied that we interpreted correctly that followup was conducted in the outpatient setting. The other author (Yao) did not respond to our query.

For each of the studies, there was limited information about the participants, including about each of the patient characteristics that we sought to examine (KQ4). There was also limited information about wound characteristics, such as wound age and size (KQ4).

We present the results organized by etiology of the wound. Yao et al. (2012) evaluated wound healing in patients with lower extremity ulcers of different etiologies (diabetic, arterial, pressure, venous insufficiency, and mixed ulcer).[51] Two studies limited participants to those with diabetic foot and arterial ulcers (Lavery, 2007; Fife, 2008).[53, 54] Two studies focused on pressure ulcers (Ford, 2002; Schwien, 2005).[55, 56] One study examined NPWT in participants with mixed ulcers (Lerman, 2010).[52] Table 4 lists the number of studies included for each type of chronic wound.

Table 4. Number of studies comparing NPWT with other wound care methods that evaluated each type of outcome for each type of chronic wound

Type of chronic wound	Total number of studies	Clinical outcomes	Patient-centered outcomes	Adverse events
Diabetic foot ulcers and arterial ulcers	3 retrospective cohorts	2	1	1
Pressure ulcers	1 RCT 2 retrospective cohorts	2	0	2
Venous insufficiency ulcers	1 retrospective cohort	1	0	0
Mixed ulcer population	2 retrospective cohorts	2	0	1

RCT = randomized controlled trial

Interventions

Beyond the brand name, the specifics of the NPWT device were not described in five studies (Lavery, 2007; Yao, 2012, Fife, 2008, Lerman, 2010 and Schwien, 2005).[51-55] In all but one of the studies, a Vacuum Assisted Closure (V.A.C.®) Therapy device (Kinetic Concepts, Inc., San Antonio, TX) was used. Lerman et al. used the Smart Negative Pressure (SNaP®) Wound Care System (Spiracur, Inc., Sunnyvale, CA).[52] Ford et al. stated that the dressings used with the NPWT device were changed on Mondays, Wednesdays, and Fridays.[56]

Details about the therapy provided in the comparison group were not provided in three studies (Yao, 2012, Fife, 2008, and Schwien, 2005).[51, 53, 55] In these studies, the comparison group was usually described as patients who did not receive a NPWT device or received other wound care treatment. The comparison group in Lavery et al. were those in the Margolis, 2000 meta-analysis that received wet-to-moist dressings.[54] The comparison group in Lerman et al. received wound care therapies that included Apligraf® (Organogenesis, Canton, MA), Regranex® (Smith and Nephew, Inc., London, UK), and skin grafting.[52] It was designed that the patients in the comparison group in Ford et al. would receive one of three gel products, depending on the type of wound.[56] The three gel products were a papain-urea debridement ointment for necrotic wounds, a cadexomer iodine product for decubitus ulcers, and a papain-urea-chlorophyllin-copper ointment for clean, granulating wounds. No wounds received the papain-urea product, as they were all surgically debrided. The dressings in the comparison group were changed either once or twice daily.

Outcomes

We sought data about 14 different outcomes categorized as clinical outcomes (five outcomes), patient-centered outcomes (three outcomes), and adverse events (six outcomes). As shown in Table 4, few outcomes were reported across the six studies. The outcomes are discussed in more detail below. However, in general, the outcomes were poorly defined, differentially reported for NPWT and control groups, and in some cases surrogate measures were used. For instance, wound measurements are essential to the evaluation of wound healing and wound healing rates. Only two studies, by Lerman et al. and Ford et al., evaluated wound dimensions by linear measurements, wound photographs, and by obtaining plaster impressions by blinded clinic staff.[52, 56]

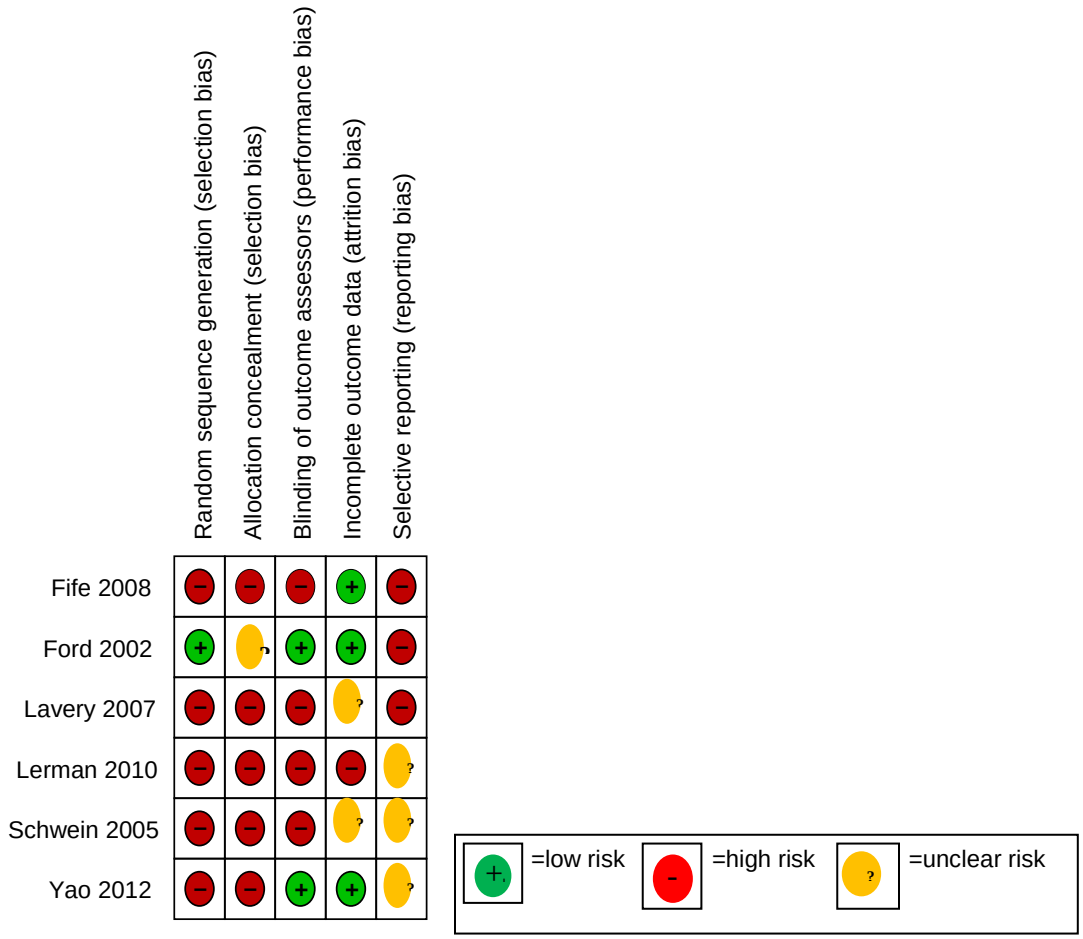
Study Quality

The Ford et al. study was the only RCT and it was judged to be of fair quality.[56] This RCT had adequate randomization sequence generation, but we could not determine if there was adequate concealment of allocation. The clinic staff that performed wound measurements using

plaster molds were blinded to intervention status. However, study participants were not blinded due to the nature of the study. There was incomplete reporting for some of the outcomes, such as osteomyelitis, and incomplete reporting of diabetes mellitus status and control. Lastly, the wounds of the comparison groups were heterogeneous in nature, as some required a cadexomer iodine ointment for potentially infected wound beds related to exudate characteristics while other wounds were considered "clean."

The remaining five studies were observational studies of fair[51] to poor quality.[52-55] These studies had several methodological issues, including inappropriate control groups,[53, 54] high attrition,[52] poor outcome reporting,[51, 53] the potential for data dredging as details about how the comparison group was identified were not reported,[55] and poor reporting of comorbidities or concomitant treatments.[51-53] Figure 3 summarizes the risk of bias for each included study.

Figure 3. Summary of the risk of bias scores for each study that compared a negative pressure wound therapy with other wound care treatment among patients with chronic wounds



Effects of Interventions

Among Patients with Diabetic Foot Ulcers and Arterial Ulcers (3 studies)

Clinical Outcomes

Lavery et al. defined wound healing in the NPWT group as closure by secondary intention or by surgical intervention if adequate granulation for closure was documented. Wound healing in the control group was defined as wounds completely healed (no drainage or full epithelialization).[54] The proportion of wounds achieving complete wound healing was compared at 12 and 20 weeks. The proportion of wounds reaching complete healing was statistically significantly greater in groups treated with NPWT as compared with those in the control group receiving wet-to-moist therapy when measured at 12 weeks (40% versus 24%) and 20 weeks (46% versus 33%) ($P < 0.001$).

Lavery et al. also examined healing in relation to ulcer size and wound duration at 12 and 20 weeks.[54] Wounds were stratified according to wound size and duration. Wounds less than 2 cm^2 were considered small, those 2 to 4 cm^2 were medium in size, and those greater than 4 cm^2 were considered large in size. Wounds that were less than 6 months old were stratified as short duration, those 6 to 12 months old were considered medium duration, and those greater than 12 months old were considered long duration.

The authors reported that wounds of all sizes treated with NPWT were more likely to achieve successful treatment endpoint (closure through secondary intention or through surgical intervention, or if adequate granulation tissue was present) ($P < 0.05$). However, at 12 weeks, wounds in the NPWT group that were less than 6 months duration and those greater than 12 months duration were more likely to achieve closure. At 20 weeks, NPWT healed significantly more wounds only among wounds older than 12 months ($P < 0.05$).[54]

Yao et al. analyzed complete healing as an event but did not define complete healing.[51] Those using NPWT were more likely to achieve wound closure than the those in the control group for both patients with diabetic foot ulcers and arterial ulcers. After adjustment for co-morbidities (including diabetes, peripheral arterial disease, coronary heart disease, chronic kidney disease, congestive heart failure, stroke, smoking) and "other variables associated with disease severity" (undefined), those treated with NPWT had a higher incidence of wound closure compared to the control group among patients with diabetic foot ulcers (adjusted hazard ratio 3.26 (95% confidence interval [CI], 2.21 to 4.83)) and among patients with arterial ulcers (2.27 (95% CI, 1.56 to 3.78)).

None of the studies reported on other clinical outcomes such as time to complete wound healing by secondary intention, time to surgical readiness, or mortality.

Patient-Centered Outcomes

Fife et al. reported no differences in the provision of pain medication between the NPWT and non-NPWT groups (data not reported).[53] None of the other studies reported pain as an outcome and no study reported other patient-centered outcomes, such as functional activity or quality of life.

Adverse Events

Fife et al. reported that patients in the NPWT group compared with those in the control group had fewer infections as indicated by the surrogate measures of fewer antibiotic prescriptions written ($P < 0.05$), and fewer cultures taken ($P < 0.05$).[53] However, the authors did not report any

data for these outcomes nor report the specifics of statistical testing. There were no incidences of bleeding in either group. Additionally, NPWT was not discontinued because of bleeding. The other two studies that included patients with diabetic foot ulcers and arterial ulcers did not report adverse event outcomes.

Among Patients with Pressure Ulcers (3 studies)

Clinical Outcomes

In the Ford et al. study, six ulcers in the NPWT group (30%) and six ulcers in the control group (40%) underwent flap surgery.[56] Two ulcers in each group completely healed (risk difference 3%, 95% CI, -18% to 25%).

Yao et al. reported that those treated with NPWT had a higher incidence of wound closure compared to those in the control group. The adjusted hazard ratio for wound healing was 1.72 (95% CI, 0.43 to 6.95) in the study by Yao et al.[51]

Patient-Centered Outcomes

None of the studies reported on patient-centered outcomes.

Adverse Events

Two studies reported on adverse events. Ford et al. reported one patient with diabetes, hypertension, and vascular insufficiency treated with NPWT developed sepsis related to a lateral malleolar ulcer and required amputation.[56] Twenty-eight patients with 41 full thickness pressure ulcers were enrolled in this trial; however, 22 patients with 35 wounds completed the trial. Although the study reported reasons for drop outs (two patients died, three were lost to followup, and one was deemed noncompliant), they do not report the number of drop outs in each treatment group.

Schwien et al. reported that none of the patients in the NPWT group required an emergent care visit for a wound problem while 189 (8%) of the control group did ($P < 0.01$).[55] Three patients (5%) using NPWT for their stage three or four pressure ulcer experienced hospitalizations for a wound problem versus 310 patients (14%) in control group ($P < 0.05$). The results remained statistically significant when data were stratified by pressure ulcer grade.

Among Patients with Venous Insufficiency Ulcers (1 study)

Clinical Outcomes

One study (Yao, 2012), compared NPWT with a control group among patients with venous insufficiency ulcers.[51] In this study, wounds treated with NPWT had a higher incidence of wound closure than those not treated with NPWT among patients with venous insufficiency ulcers (adjusted hazard ratio, 6.31; 95% CI, 1.49 to 26.6).

Patient-Centered Outcomes

This study did not report on patient-centered outcomes.

Adverse Events

This study did not report on adverse events.

Among Patients with Mixed Ulcer Population (2 studies)

Clinical Outcomes

Yao et al. included patients with different ulcers of the lower extremities (diabetic foot ulcers, arterial ulcers, venous insufficiency ulcers, and pressure ulcers) and reported that all ulcers treated with NPWT had a greater chance of healing first compared with those in the control group (adjusted hazard ratio for all ulcers 2.63 (95% CI, 1.87 to 3.70)).[51]

Yao et al. also evaluated whether the timing of NPWT application had an effect on healing. The authors defined ulcer onset as the date the ulcer was first documented in a clinic note. Early NPWT use was defined as receiving NPWT within 3 months of ulcer onset, intermediate NPWT use was defined as receiving NPWT within 4-12 months of ulcer onset, and late NPWT was defined as receiving NPWT 1 year or later after ulcer onset. The ulcers in the early NPWT treatment group had higher incidence of wound closure compared with those in which NPWT was used later (adjusted hazard ratio 3.38; 95% CI, 1.68 to 6.82).

Lerman et al. conducted a Kaplan-Meier analysis to estimate wound healing and time to complete wound healing. Kaplan-Meier estimates of wound healing at 1, 2, 3, and 4 months was greater in the NPWT group than in the retrospective matched control group.[52] The percent of wounds healed at 1, 2, 3, and 4 months was 0%, 20%, 66%, and 83% in the NWPT group and 0%, 7%, 21%, and 36% in the matched control group. Wounds in the NPWT arm had a significantly reduced time to complete healing compared with the retrospective matched control arm resulting in a 50 percent absolute reduction in time to healing ($P < 0.0001$).[52]

Patient-Centered Outcomes

Neither study (Yao, 2012; Lerman, 2010) reported any patient-centered outcomes.

Adverse Events

Lerman et al. followed patients on NPWT for 13 months and reported that 21 of 35 patients completed the study.[52] Two subjects were removed due to hospitalizations not related to the wound and six subjects were noncompliant with the protocol. Seven subjects had complications related to the study protocol requiring withdrawal: allergic skin reaction to the hydrocolloid dressing (1), wound infection (1), bleeding post debridement (1), worsening lower extremity edema (1), and maceration to periwound skin (3). Data were not reported for the matched historical control group. Yao et al. did not report adverse events.

Strength of Evidence

The strength of the body of evidence comparing NPWT with other wound care treatments (KQ2 and KQ4) is summarized in Table 5. We had pre-defined critical outcomes, those essential for decision making in wound care, for which we determined the strength of evidence. For each of these five critical outcomes, across all wound etiologies, the strength of the evidence is *insufficient* to draw conclusions on the effectiveness and safety of NPWT compared with other wound care treatments. There were few studies addressing each outcome for each wound etiology; for several outcomes, we identified no studies.

Most of the studies were observational studies of poor quality. Only one study was a RCT and it was judged to be fair quality.[56] We downgraded the strength of evidence domain of directness because some studies used inappropriate control groups[53, 54] or used surrogate markers for outcomes.[53] We were rarely able to evaluate consistency. There were not enough studies to use funnel plots to determine if there was reporting bias. However, this seems to be a field where

publication bias may be of concern. Five of the studies reported funding from industry, while Yao et al. did not report funding source. The RCT had a small sample size, and therefore, imprecise results.[56] Some of the observational studies reported limited data on outcomes, so we were unable to determine precision.[52, 53]

Table 5. Negative pressure wound therapy versus other wound therapies for the treatment of chronic wounds: Strength of evidence domains

Population	Outcome	Study design: No. studies (N)	Study limitations	Directness	Consistency	Precision	Reporting bias	Strength of evidence
Diabetic foot ulcers/ arterial ulcers	Complete wound healing	Observational: 2 (1979)[51, 54]	High	Indirect	Consistent	Precise	Undetected	Insufficient
	Time to surgical readiness	0	NA	NA	Unknown	NA	NA	Insufficient
	Pain	Observational: 1 (1331)[53]	High	Indirect	Unknown	Unable to determine	Undetected	Insufficient
	Infection	Observational: 1 (1331)[53]	High	Indirect	Unknown	Unable to determine	Undetected	Insufficient
	Dropout rates	0	NA	NA	Unknown	NA	NA	Insufficient
Pressure ulcers	Complete wound healing	RCT: 1 (35)[56] Observational: 1 (40)[51]	Medium	Direct	Inconsistent	Imprecise	Undetected	Insufficient
	Time to surgical readiness	0	NA	NA	Unknown	NA	NA	Insufficient
	Pain	0	NA	NA	Unknown	NA	NA	Insufficient
	Infection	RCT: 1 (35)[56]	Medium	Direct	Unknown	Imprecise	Undetected	Insufficient
	Dropout rates	0	NA	NA	Unknown	NA	NA	Insufficient
Venous insufficiency ulcers	Complete wound healing	Observational: 1 (33)[51]	High	Direct	Unknown	Imprecise	Undetected	Insufficient
	Time to surgical readiness	0	NA	NA	Unknown	NA	NA	Insufficient
	Pain	0	NA	NA	Unknown	NA	NA	Insufficient
	Infection	0	NA	NA	Unknown	NA	NA	Insufficient
	Dropout rates	0	NA	NA	Unknown	NA	NA	Insufficient
Mixed ulcer population	Complete wound healing	Observational: 2 (527)[51, 52]	High	Direct	Consistent	Precise	Undetected	Insufficient
	Time to surgical readiness	0	NA	NA	Unknown	NA	NA	Insufficient
	Pain	0	NA	NA	Unknown	NA	NA	Insufficient
	Infection	0	NA	NA	Unknown	NA	NA	Insufficient
	Dropout rates	Observational: 1 (36)[52]	High	Direct	Unknown	Unable to determine	Undetected	Insufficient

NA = not applicable; RCT = randomized controlled trial

Wound Care Modalities Used Prior To Or With Intervention

We attempted to abstract and consider the potential impact of wound care therapies used prior to or with intervention in the NPWT group (Key Question 2b) and in the control groups (Key Question 2c) for each of the studies that compared home use of NPWT with other wound care therapies. We also attempted to consider how these prior and concurrent therapies compare with the usual care of chronic wounds (Key Question 2d). However, the six studies addressing NPWT versus other chronic wound care therapies did not discuss specific wound care regimens used prior to or concurrently with NPWT. Instead, nondescript terms such as "complete wound therapy program" or "traditional treatments" were used to define wound care modalities prior to NPWT initiation in some studies.[52, 54] One study, by Schwien et al., described the use of "any other wound care therapy" as inclusion criterion for the comparison group.[55] Most studies mentioned debridement of necrotic tissue as part of their inclusion criteria or pretreatment modalities.[51, 52, 54, 56]

Strict diabetes management and compression therapy for venous ulcers are other important factors in wound healing. Unfortunately, this parameter was not consistently reported, even in studies evaluating healing specific to these wounds. "Comprehensive diabetes management" was an inclusion criterion for the NPWT group only in one study (Lavery, 2007).[54] Pressure reduction of diabetic foot ulcers and pressure ulcers is mentioned in the treatment and control groups of two studies (Lavery, 2007 and Ford, 2002).[54, 56]

In the Ford et al. trial, pretreatment in a pressure ulcer trial included tissue and/or bone cultures plus magnetic resonance imaging (MRI) for suspected osteomyelitis and a 6-week course of antibiotics for confirmed osteomyelitis in the treatment and control groups.[56] Pretreatment tests were repeated at the conclusion of the trial.

Specific reference to the use of "appropriate beds" and repositioning throughout the treatment period was mentioned in the Lavery et al. study evaluating NPWT in stage three and four pressure ulcers, while "reduction in pressure of the affected ulcer, as needed," and "appropriate offloading, as needed," was mentioned by Ford et al. "Wet-to-moist dressings" were the treatment used in the control group of the Lavery et al. study.[54]

Characteristics of Negative Pressure Wound Therapy Compared With Other Characteristics

We identified one study which compared two different NPWT technologies (Key Question 3). The study was reported in two articles: one article, by Armstrong et al., 2011,[57] reported interim analysis of results, while the second, by Armstrong et al., 2012,[58] was the final report. Study details are provided in evidence tables (Appendix D).

Study Design

Participants were randomized to two types of technologies, the Vacuum Assisted Closure (V.A.C.) Therapy System, marketed by KCI (n=68), and the Smart Negative Pressure Wound Care System (SNaP), marketed by Spiracur (n=64). Patients were evaluated at 4, 8, 12, and 16 weeks.

Participants

Patients with either diabetic foot ulcers or venous insufficiency ulcers were enrolled in the outpatient setting. (As noted earlier, we included studies that were described as in "outpatient setting" if it was reported (or we interpreted) that patients were not in assisted living, skilled or maintenance nursing homes.) Patients were excluded if they were under 18 years of age, if their ulcer size was less than 1 cm^2 or greater than 100 cm^2, if there was any clinical sign of active infection as decided upon by the authors, if the ankle/brachial index was less than 0.7 or greater than 1.2, if the wound was greater than 10 cm in the widest diameter, or if the wound was not present for at least 30 days despite appropriate wound care prior to entry. Though the number enrolled and mean age were fairly similar, there appears to be a difference in the mean size of the wound, with the V.A.C. group being used on a larger wound size (9.85 versus 5.37 mean cm^2).

Interventions

The V.A.C. system uses an electric powered pump device, which is re-used, and disposable dressings. Two models of V.A.C. were used: the ActiV.A.C. system and the Freedom V.A.C.. Of the V.A.C. group, 94.6 percent were on the ActiV.A.C. system, with the remaining 5.4 percent placed on the Freedom V.A.C.. The SNaP system is designed to be disposable in its entirety. The negative pressure is generated by a mechanical force, without electricity.

Characteristics of the devices that may play into wound healing such as suction pressure, and the details regarding the two devices were not described in this study (Table 6). Both devices were designed to be portable, however, the dressing type is variable between the two groups. No difference in characteristics between the two V.A.C. devices used was mentioned.

Negative pressure (suction) parameters were not reported. No irrigation/instillation components were reported. There is a description of the time it takes to apply the device in the clinic, however, it is unclear as to who is applying the device to the wound. It may be inferred that the device was placed by the study staff.

Table 6. Characteristics of the negative pressure wound therapy devices used in the randomized controlled trial

Author, year	Group	Suction type	Dressing type*	Pressure control	Portable	Reusable
Armstrong, 2012[58]	SNaP	Continuous	Gauze	Continuous	Yes	Single use
Armstrong, 2012[58]	V.A.C.	Not reported	Foam	Not reported	Yes	Not reported

* Dressing type was reported in the interim analysis publication.[57]

SNaP = Smart Negative Pressure Wound Care System; V.A.C. = Vacuum Assisted Closure Therapy System

Outcomes

Complete wound healing was a secondary outcome in this study but the outcome was not defined. Adverse events and patient-centered outcomes were assessed. Details about the outcomes are discussed below.

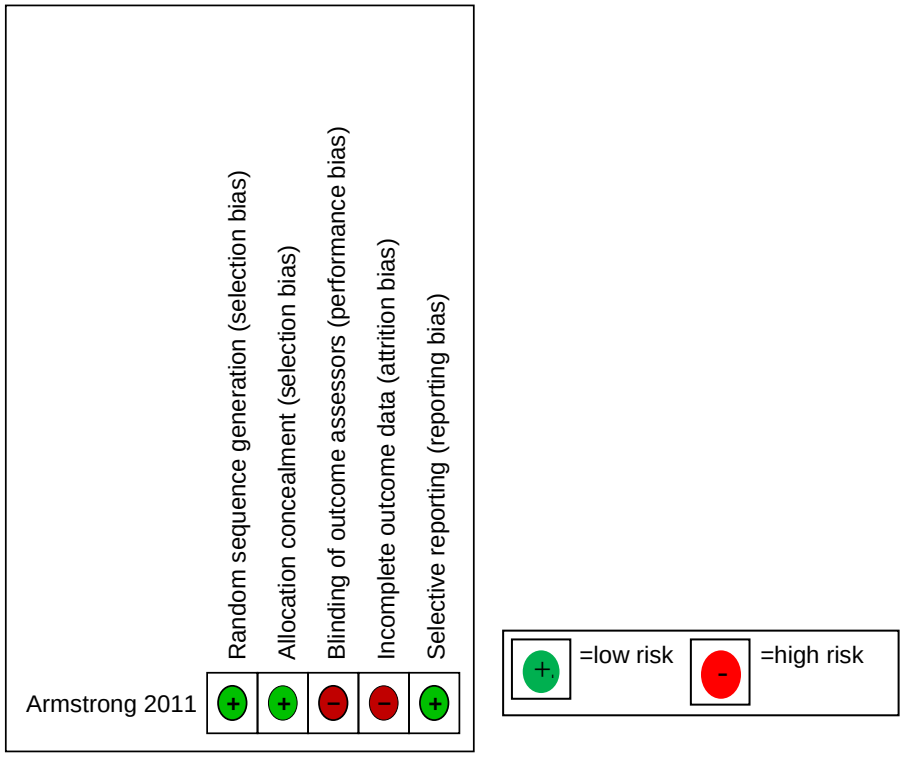
Study Quality

The overall study quality for this RCT was rated as fair. There was adequate random sequence generation and allocation concealment, but participants and study personnel were not blinded (Figure 4).

There were some additional problems with study quality. Some of the baseline characteristics may affect the study, such as the difference in wound size between the two groups. This may

have an impact on full healing, and healing rates to full closure are not discussed. A larger wound may take longer to heal by the nature of the size of the wound. In addition, there are a number of differences between the devices themselves, such as the difference in dressing type (gauze versus foam). The limitation to two specific types of chronic wounds does provide some level of standardization. However, the comparator group utilized two different V.A.C. systems. The number of patients is also small. The assessment of pain level is unclear, as there is a comparison to an expected sum. The use of exit interviews, given that the devices could not be adequately blinded, may have introduced bias in the patient-reported outcomes.

Figure 4. Summary of the risk of bias scores for the study that compared a negative pressure wound therapy device with another negative pressure wound therapy device among patients with chronic wounds



Effects of Interventions

Clinical Outcomes

The percentage of wounds closed at 4, 8, 12, and 16 weeks was assessed. The percent of wounds healed did not differ significantly between the two different NPWT devices (Kaplan-Meier estimates Wilcoxon *P*= 0.9252).[58] Time to surgical readiness of the wound bed and mortality were not reported. Though percent decrease in the wound area was reported, the wound healing rate for healed wounds was not reported. The proportion of wounds healed appears to be similar between the two groups, however, the different V.A.C. devices were not further separated into subgroups.

Patient-Centered Outcomes

Exit surveys to assess user experiences were completed for the 105 of the subjects who finished the study (n=52 V.A.C. and N=53 SNaP). To examine the ability to return to their prior level of functional activity, subjects were asked about their level of activity both during and after device usage. Patients who were treated with the SNaP device were significantly more likely to agree or strongly agree that they were able to perform their normal daily activities than patients treated with the V.A.C. device (79% versus 58%; $P = 0.004$ *calculated by review authors).[58] Additionally, a higher percentage of SNaP-treated subjects than V.A.C.-treated subjects reported that their activity level either increased or stayed the same (83% versus 48%; $P < 0.05$ *calculated by review authors).

The level of pain was examined in the exit interviews, by a summation of pain scores, as compared to what would be the expected sum of scores. It is unclear how the expected score number was obtained, and further description of the definition of the pain scores is not described. Patient-reported pain scores were not statistically significantly different between the two NPWT devices.[58]

Health-related quality of life was not assessed.

Adverse Events

The number of patients who were diagnosed with an active infection while using the devices was five in the V.A.C. group, and two in the SNaP group (7.4 % versus 3.1%, $P = 0.28$* calculated by review authors). Other adverse events including amputation rates, emergency room visits, unplanned hospitalizations/surgeries, and blood transfusions/bleeding were not reported. Of the 132 patients enrolled, 14 subjects were dropped prior to initiation of treatment, and an additional three subjects dropped after baseline, prior to follow up assessments. Eighty-three patients completed the study with healing or for the full 16 weeks of therapy. Reasons for dropout were not reported.

Strength of Evidence

The grading of the strength of evidence of the body of literature comparing different characteristics of NPWT technologies is summarized in Table 7. We determined that the evidence was *insufficient* to make any conclusions about the effect of characteristics of NPWT on chronic wound care.

We found a single RCT of fair quality that compared two different NPWT devices among patients with diabetic foot ulcers and venous insufficiency ulcers. This RCT reported on complete wound healing, pain, infections, and dropout rates. We did not find any studies that evaluated different NPWT characteristics in terms of time to surgical readiness. We rated the study as having a medium level of study limitations because of lack of blinding, imbalanced study groups particularly in terms of wound size, and lack of reporting of intervention details. We downgraded study limitations to “high” for the outcome of pain because of limited reporting of statistical details. All of the outcomes were direct, but the results were imprecise. We were unable to assess consistency or reporting bias. The study was funded by the manufacturer of one of the devices (SNaP) and two of the investigators reported receiving funding from manufacturers of both devices being evaluated.

Table 7. Characteristics of negative pressure wound therapy versus other characteristics for the treatment of chronic wounds: Strength of evidence domains

Outcome	Study design: No. studies (N)	Study limitations	Directness	Consistency	Precision	Reporting bias	Strength of evidence
Complete wound healing	RCT: 1 (132)[57, 58]	Medium	Direct	Unknown	Imprecise	Undetected	Insufficient
Time to surgical readiness	0	NA	NA	Unknown	NA	NA	Insufficient
Pain	RCT: 1 (105)[57, 58]	High	Direct	Unknown	Imprecise	Undetected	Insufficient
Infection	RCT: 1 (132)[57, 58]	Medium	Direct	Unknown	Imprecise	Undetected	Insufficient
Dropout rates	RCT: 1 (132)[57, 58]	Medium	Direct	Unknown	Imprecise	Undetected	Insufficient

NA = not applicable; RCT = randomized controlled trial

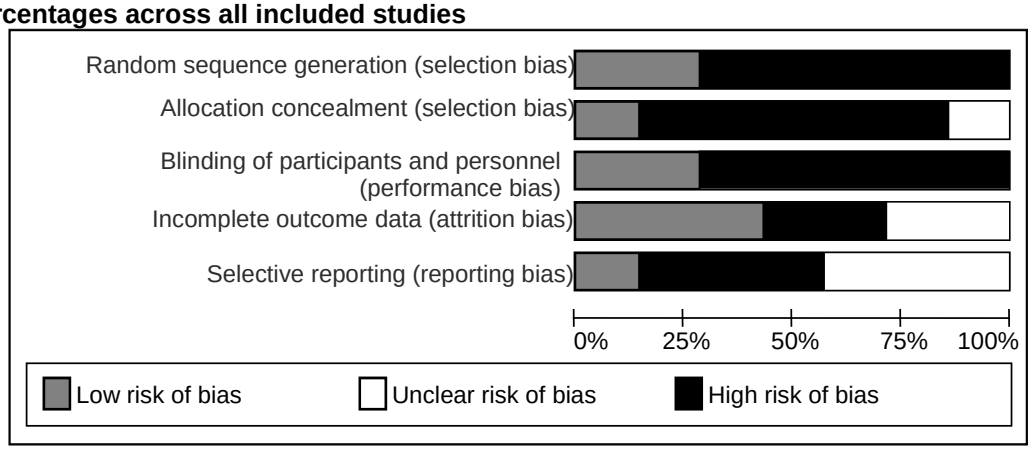
Discussion

Key Findings and the Strength of Evidence

- Key Question 1 did not require a systematic review, but rather a search for NPWT that are approved by the FDA for use in the United States.
- For Key Questions 2, 3, and 4, the evidence was limited and insufficient to draw conclusions regarding the use of NPWT in the home setting.
- In Key Questions 2 and 4, the comparator group was not well defined, and may or may not have included a range of wound healing modalities, all of which may or may not be beneficial for wound healing. The lack of consistency in the reporting of the various parameters important in the wound healing process made it difficult to compare the studies with one another.
- For Key Question 3, we identified only one study that compared two types of NPWT. Though the trial was randomized, the overall numbers were small. No other "outpatient only" studies were identified that compared the various components or characteristics of the devices on the market, despite the numerous devices identified in Key Question 1.

The majority of the studies showed high risk of bias across multiple areas of study design and outcomes (Figure 5), and the high risk added to the difficulty in interpreting the evidence base. We found a profound paucity of well-designed and well-conducted studies evaluating these technologies in the home setting. Though we considered studies that described following patients in the outpatient setting as studies of home use, true confirmation that NPWT was used in the home environment was lacking. The few studies we identified were either small experimental studies, or retrospective studies, which used administrative data from large databases. The studies were further limited by the lack of well-defined comparator groups. The strength of evidence for all comparisons and outcomes of interest was insufficient, which meant that we could not draw conclusions regarding the efficacy or harms associated with NPWT for chronic wounds in the home setting.

Figure 5. Risk of bias graph: review of authors' judgments about each risk of bias, presented as percentages across all included studies



Findings in Relationship to What is Already Known

Studies on NPWT, as well as previous reviews of NPWT, either focus on surgical wounds or were performed in the inpatient setting (Tables 8 and 9). In all of the previous reviews, the same limitations in the available studies were noted. Throughout these reviews, the evidence ranged from "moderate strength" to "no valid evidence," and the need for good quality randomized controlled trials was noted.[31, 37, 47]

There were two studies, which examined the use of NPWT in the care of chronic wounds, which predominantly included patients in the outpatient setting (Table 9).[69, 70] However, as the outpatient data could not be analyzed separately from the inpatient data, these studies were not included in our review, given the difference in care that is provided in inpatient versus outpatient settings. Though two of the studies we included in our review recruited patients from the inpatient setting, the followup was performed in the outpatient setting, on the basis of which we considered that these subjects were not hospitalized during the followup period.[51, 56] Both groups of authors were contacted to confirm, and one replied (Ford, 2002), stating that the study should be interpreted as we had interpreted it and we received no response from the other author (Yao, 2012).

Many other NPWT studies were found that did not meet our eligibility criteria. These included studies considered key in the field, which were excluded primarily because they included inpatients (Table 9).

Table 8. Summary of previous systematic reviews on NPWT

Author, year	Review scope	Setting	Number of articles	Findings
Ubbink, 2008[37]	Effect of NPWT in chronic wound healing	Hospital	9 (7 trials)	There is no valid or reliable evidence that NPWT increases chronic wound healing.
Sullivan, 2009[31]	Technology assessment of NPWT devices	Inpatient and outpatient	143 studies, 22 systematic reviews	Unable to address key questions based on the literature at that time.
Dumville, 2013[47]	Effect of NPWT compared with standard care or adjuvant therapies in diabetic foot wounds	Any setting	5	There is some evidence to suggest that NPWT is more effective in healing postoperative foot wounds and ulcers of the foot in people with DM compared with moist wound dressings.
Greer, 2013[46]	Benefits and harms of advanced wound care therapies for nonhealing diabetic, venous, and arterial ulcers	NR	59 (56 RCTs, 3 RCTs examining NPWT)	There was moderate-strength evidence for improved healing with NPWT compared with standard care.

DM = *diabetes mellitus*; NPWT = negative pressure wound therapy; NR = not reported; RCT = randomized controlled trial

Table 9. Other studies found during search, representing some of the variation in the literature

Author, year	Type of study	Reason for exclusion	Findings
Argenta, 1997[71]	Case series, clinical trial	Inclusion of subacute and acute wounds, no comparison group	Favorable response in majority of the wounds included, descriptive study.
Vuerstaek, 2006[72]	RCT	Inpatient population only	Median time to chronic wound healing was shorter in the NPWT group versus the conventional wound care group.
Frykberg, 2007[70]	Retrospective analysis	Mixed population of inpatient and outpatient	Amputation rates were higher in the control group versus NPWT group.
Blume, 2008[69]	RCT	Mixed population of inpatient and outpatient	43.2% of patients with foot ulcers closed with NPWT versus 28.9% using advanced moist wound therapy

NPWT = negative pressure wound therapy; RCT = randomized controlled trials

Applicability

Given the mixture of wound etiologies, and the lack of details about the patients in each of the studies, it was difficult to generalize the results to the overall population. The populations studied all had chronic wounds, and since the chronic wound treatment modalities can be used across the age spectrum, the data we found could be applicable to the Medicare population. Though some of the studies identified were targeted towards a specific wound type, others were more general in their description, making it difficult to apply the results to specific populations. In addition, given the overall lack of description around what constitutes standard wound care, and the wide variety of wound care products available for standard wound care, robust comparisons could not be made. Finally, the focus of this review was use of NPWT in the home population, thus the results are not necessarily applicable to other health care settings, in which NPWT may be used.

Limitations of the Review Process

NPWT is used to treat a variety of wounds, including acute and chronic, and is used in a variety of settings. However, our review focused specifically on the comparative effectiveness and safety of NPWT to treat chronic wounds in the home setting.

We screened 5,912 citations in our effort to find studies assessing the comparative efficacy and safety of NPWT for chronic wound care in the home or outpatient setting. While we attempted to focus on home use by using outpatient setting as an indicator of home use, many of the studies did not clearly identify the actual patient treatment location, and as a result, we could not confirm that all patients were treated in the home setting.

Only seven studies were identified as using NPWT in the outpatient setting for chronic wounds. Some studies with outcomes of interest were excluded primarily because the populations were mixed and included patients followed in the inpatient setting, which introduces a different level of care, observation, and compliance. In these mixed studies, subgroup analysis was not performed, and therefore, the outpatient subjects' outcomes could not be defined. Wound care is performed in a variety of settings. However, given that our review focus was on the home environment, we excluded studies even if a small portion of the included subjects were followed only in the inpatient environment.

Because treatment with NPWT is often terminated prior to complete wound healing, many studies may not report on complete wound healing, but rather report on an intermediate outcome,

such as the wound healing rate (e.g., percent ulcer area reduction). We excluded studies that evaluated this surrogate outcome only because chronic wounds may not heal in a linear fashion, becoming static at any time. Thus wound healing rate cannot be used to accurately predict complete healing.[48]

We also excluded studies with a sample size less than 20 patients. However, most of these studies were also excluded for other reasons (e.g., no original data, no comparison group, not followed in the home setting). Finally, we limited our review to studies with comparison groups. Studies of other designs, such as case series may provide further information about adverse events, but it may be difficult to interpret the cause of many adverse events without a control group.

Limitations of the Evidence Base

There were few studies that addressed the effectiveness and safety of NPWT to treat chronic wounds in the home environment. Unfortunately, the few studies that we found were of low quality (Table 10).

The prospective, randomized studies had a small sample sizes and short durations of followup.[56, 57] Larger studies were retrospective and based on administrative or patient record databases. The retrospective, administrative or patient record database studies were particularly problematic because they generally lacked details regarding patient characteristics, NPWT devices studied, treatments used by the comparison groups, and prior and concurrent wound treatments. For these studies, we were not able to establish if consistent wound care protocols were being followed. The brand and model of the NPWT device was often not reported, so we were unable to determine if there were any differences in effectiveness and safety across the devices. Similarly, there were limited details reported regarding the comparison group. Often, the control group was simply patients who did not receive NPWT.[51-53, 55] Considering the wide range of treatment options for chronic wounds, we are unable to determine what treatments the comparison groups received.

Six of the seven studies were supported at least partially by manufacturers; the other study did not report a funding source.[51] In the studies that reported industry funding, few reported on the involvement of the sponsor in the design, analysis, and reporting of the study. With this limited information, it is hard to rule out the possibility of publication bias or other reporting bias.

Another limitation was the use of surrogate outcomes. For instance, Fife et al. used number of antibiotic prescriptions as a surrogate measure for infections.[53] However, we do not know how well antibiotic prescriptions correlate with clinical infection.

Patient-centered outcomes were frequently not reported in the studies. When they were reported, studies used either a surrogate marker, such as provision of pain medication[53] or a non-validated exit interview.[57, 58] Considering the burden of having chronic wounds, it is important to understand the effects of NPWT on patient-centered outcomes.

Regardless of the study design, most studies were deficient in reporting key characteristics. Many of the studies did not describe the patient setting and it was unclear who was applying the wound treatments. Furthermore, we often did not know the level of training and expertise of the people applying the wound treatment. NPWT treatments require dressing changes that must occur on a regular basis as set by the manufacturers, and thus may receive a higher level of attention from a provider, making NPWT more provider intense compared with other wound

care regimens. The application of the wound treatments could affect compliance with and the effectiveness of the treatments. Compliance was not assessed in any of the studies.

Many of the studies lacked standardized descriptions of the patient population at baseline. Many patients with chronic wounds often have several comorbidities, which could affect wound healing. However, few studies reported the effect of such comorbidities on the outcomes. Some of the studies failed to report other baseline patient characteristics, such as wound duration or size. Since many of the studies were observational, it is hard to determine if patients were balanced in these key characteristics across NPWT and control groups. Therefore, we are unable to assess how selection bias could have influenced the results.

For many studies, we do not know the prior and concomitant treatments patients received. This includes not only wound care treatments, such as compression, debridement, and dressings, but also treatments to manage the underlying condition, such as diabetes management or off-loading. Due to the limited reporting, we are unable to determine how these other treatments could have influenced results.

We acknowledge that it is difficult to blind study investigators and patients in device studies. In studies where blinding is not feasible, it is important to have objective outcome assessments to minimize bias. Only one of the studies blinded outcome assessors.[56] In this study, blinded staff evaluated wound healing from wound measurements of plaster impressions. Most of the other studies inadequately described how wound healing was defined and determined. The Food and Drug Administration defines complete wound healing as “skin-repithelialization without drainage at two consecutive visits, 2 weeks apart by the end of the study.”[73] None of the studies used this definition.

Table 10. Characteristics of studies comparing NPWT with a control group or other NPWT devices among patients with chronic wounds

	Lerman, 2010[52]	Ford, 2002[56]	Schwien, 2005[55]	Fife, 2008[53]	Lavery, 2007[54]	Yao, 2012[51]	Armstrong, 2011[57]
Study Design Prospective vs. retrospective	Prospective observational, retrospective comparator group	Prospective, randomized	Retrospective	Retrospective	Retrospective	Retrospective	Prospective, randomized
Administrative data	Yes	No	Yes	Yes	Yes	Yes	No
Concurrent comparator group	No	Yes	Yes	Yes	No	Yes	Yes
Patient setting defined	Yes – Outpatient	No	Yes – Home	No	No	No	No
Description of prior wound treatment	No	No	No	No	No	No	No
Description of concurrent wound treatment	No	Yes	No	No	No	No	Yes
Clear wound outcomes definition	No	No	No	No	No	No	Yes
Use of FDA definition of complete wound healing	No	No	No	No	No	No	No
Consistent measurement protocol	Yes	Yes	No	No	No	No	Yes
Blinded outcome assessors	No	Yes	No	No	No	No	No
Identification of people applying wound therapy	No	No	No	No	No	No	No

Shaded items indicate a limitation in the study design.
FDA = Food and Drug Administration

Research Gaps

Our findings identified multiple research gaps, the primary being a need for standardized methods in defining wound eligibility, outcome measures, and interventions. Certainly, a set protocol defining standard wound care for the various types of wounds may be helpful in designing future research protocols, and a standardized method of wound evaluation, including blinded staff and consistent methods of measurements that can be replicated in other studies, may help provide consistency and design more informative studies.

Given that patients with chronic wounds are medically complex, studies should include patients with a specific type of chronic wound and provide details about the characteristics of the wound. This would include reporting on the average number of wounds, the percent of patients with previous wounds, the size and duration of the wound, and the appearance of the wound base. The underlying medical comorbidities play a role in wound healing, thus studies need to clearly describe, and as appropriate, adjust for or provide subgroup analysis based on these characteristics. The patient cohort should be described in terms of other comorbidities using a standardized scale, such as the Charlson index. Other patient characteristics that are relevant to the underlying condition, such as hemoglobin A1c levels for patients with diabetic foot ulcers, should also be reported.

Wound care treatment is complex and future studies should provide details about the treatment protocols for both the NPWT and control groups. Careful descriptions of the care prior to and/or concurrent to NPWT or their comparison groups should be made, given the wide array of available wound care products, modalities, and adjunctive treatments. This would include details about approach to debridement, as well as concomitant treatments such as diabetes management or off-loading. For the NPWT group, details on the brand and model of NPWT, the suction parameters, wound dressing types, type of pressure control, type of units (portable or stationary), and the irrigation/instillation components should be described. Information such as the personnel performing the wound care, and the location of the treatment of the patients should be explicitly described.

Outcomes need to be clearly defined and, at a minimum, should include complete wound healing, time to surgical readiness, pain, infection rates, and dropout rate of patients and reasons. Further, outcome measurements need to be as objective as possible. Ideally, the outcome assessor(s) would be masked to treatment assignment. Several organizations, such as the FDA, and the European Wound Management Association have noted the need for objective outcomes with blinding of outcome assessors, where possible.[48, 74]

Larger, prospective studies are needed for each of the different types of chronic wounds treated by NPWT, and to compare the different components of these devices, if not the devices themselves. Future studies of devices need to have methodological rigor, including attention to enrollment criteria; clear definitions of outcomes that are reproducible and easily measured; the addressing of potential confounding variables; randomized designs which minimize bias; and the studies should be sufficiently powered to determine clinically important effects. Patients need to be followed for an adequate length of time to ensure sustained outcomes. Definitions for adequate follow-up and durable outcomes need to be developed. Details about what data are missing and why need to be clearly reported with appropriate methods for analysis, including intention-to-treat analysis.

In Table 11, we use the PICOS (Population, Intervention, Comparison, Outcomes, and Study design) framework to outline characteristics of an ideal study.

Table 11. Characteristics of an ideal study to compare the effectiveness and safety of negative pressure wound therapy with other wound treatments in patients with chronic wounds

PICOS	Characteristics
Population	• Includes patients with a specific type of chronic wound • Describes the patient cohort in terms of other comorbidities using a standardized scale (e.g., Charlson index) • Describes other patient characteristics that are relevant to the underlying condition (e.g., provides information on HbA1c levels for patients with diabetic foot ulcers) • Describes baseline characteristics of the wound (e.g., number of wounds, previous ulcers, duration of wound, size of wound, size duration, and appearance of the wound base)
Intervention	• Describes a treatment protocol that the NPWT group receives, including details on the brand and model of NPWT, the suction parameters, wound dressing types, type of pressure control (continuous, intermittent, or dynamic), type of units (portable or stationary), and the irrigation/instillation components • Details the treatments used prior to study enrollment, including the types of treatments used and the number of patients that received each treatment • Details other concomitant treatments, such as diabetes management or off-loading
Comparisons	• Describes a treatment protocol that the comparison group receives • Details the treatments used prior to study enrollment, including the types of treatments used and the number of patients that received each treatment • Details other concomitant treatments, such as diabetes management or off-loading, and if debridement is used, the approach to debriding the wound
Outcomes	• Defines and uses an objective measure for complete wound healing • Includes important outcomes, at a minimum: complete wound healing, time to surgical readiness, pain, infection rates, and dropout rate of patients and reasons • Assesses compliance of the subject with the study intervention
Study design	• Follows patients for an adequate length of time, to ensure sustained outcomes • Collects data on patients prospectively • Describes the study setting, including details on who is performing the wound care, their level of training, and their expertise in applying the treatments

HbA1c = hemoglobin A1c; NPWT = negative pressure wound therapy

Conclusion

We performed a systematic review to evaluate the efficacy and safety of NPWT for the treatment of chronic wounds in the home setting, and determined that the existing evidence is insufficient to draw any conclusions. There is a clear need for consensus on study methods, and we believe that the research community involved in NPWT devices should strive to standardize the conduct and reporting of studies, to provide stronger evidence to inform decisions about the utility and safety of these devices.

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List of Abbreviations

Abbreviations	Definitions
AHRQ	Agency for Healthcare Research and Quality
CAG	Coverage and Analysis Group
CI	Confidence interval
CINAHL	Cumulative Index to Nursing and Allied Health Literature
CMS	Centers for Medicare and Medicaid services
CPT	Current Procedural Terminology
FDA	Food and Drug Administration
ICD	International Classification of Diseases
KCI	Kinetic Concepts Inc.
KM	Kaplan-Meier
KQ	Key question
MeSH	Medical subject headings
MRI	Magnetic Resonance Imaging
N	Number
NA	Not available
NPUAP	National Pressure Ulcer Advisory Panel
NPWT	Negative pressure wound therapy
NR	Not reported
PICOTS	Population , intervention, comparison, outcome, timing, setting
RCT	Randomized controlled trial
S&N	Smith and Nephew
SD	Standard deviation
SNaP	Smart Negative Pressure Wound Care System
SRDR	Systematic Review Data Repository
U.S.	United States
V.A.C.	Vacuum Assisted Closure

Appendix A: Detailed Electronic Database Search Strategies

PubMed Strategy

Search	String	Hits
#1	“wound healing”[mh]	91953
#2	“skin ulcer”[mh]	34694
#3	“wounds and injuries”[mh:noexp]	62378
#4	Wound*[tiab]	133934
#5	Ulcer*[tiab]	161431
#6	#1 OR #2 OR #3 OR #4 OR #5	407104
#7	Vacuum[mh]	3623
#8	Suction[mh]	10280
#9	“Negative-pressure wound therapy”[mh]	1292
#10	“negative pressure”[tiab] OR “negative-pressure”[tiab]	5831
#11	“vacuum assisted”[tiab] OR “vacuum-assisted”[tiab]	2081
#12	“subatmospheric”[tiab] OR “sub-atmospheric”[tiab]	467
#13	“vacuum sealing”[tiab] OR “vacuum sealed”[tiab] OR “vacuum-sealed”[tiab]	219
#14	#7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13	20971
#15	Animals[mh] NOT humans[mh]	3900404
#16	(#6 AND #14) NOT #15	2886

Embase Strategy

Search	String	Hits
#1	'wound healing'/exp	118248
#2	'wound care'/exp	65077
#3	'skin ulcer'/exp	50849
#4	Wound*:ti,ab	162317
#5	Ulcer*:ti,ab	204536
#6	#1 OR #2 OR #3 OR #4 OR #5	462438
#7	'Vacuum'/exp	27769
#8	'vacuum assisted closure'/exp	3384
#9	“negative pressure”:ti,ab OR “negative-pressure”:ti,ab	6807
#10	“vacuum assisted”:ti,ab OR “vacuum-assisted”:ti,ab	2580
#11	“subatmospheric”:ti,ab OR “sub-atmospheric”:ti,ab	521
#12	“vacuum sealing”:ti,ab OR “vacuum sealed”:ti,ab OR “vacuum-sealed”:ti,ab	254
#13	#7 OR #8 OR #9 OR #10 OR #11 OR #12	33384
#14	#6 AND #13	4552
#15	'Animal'/exp NOT 'human'/exp	4332414
#16	#14 NOT #15	4321

The Cochrane Central Register of Controlled Trials (CENTRAL) Strategy

Search	String	Hits
#1	MeSH descriptor: [Wound Healing] explode all trees	4431
#2	MeSH descriptor: [Skin Ulcer] explode all trees	1851
#3	MeSH descriptor: [Wounds and Injuries] this term only	1271
#4	Wound*:ti,ab,kw	14058
#5	Ulcer*:ti,ab,kw	15012
#6	#1 OR #2 OR #3 OR #4 OR #5	28134
#7	MeSH descriptor: [Vacuum] explode all trees	131
#8	MeSH descriptor: [Suction] explode all trees	786
#9	MeSH descriptor: [Negative-Pressure Wound Therapy] explode all trees	108
#10	“negative pressure”:ti,ab,kw OR “negative-pressure”:ti,ab,kw	575
#11	“vacuum assisted”:ti,ab,kw OR “vacuum-assisted”:ti,ab,kw	157
#12	“subatmospheric”:ti,ab,kw OR “sub-atmospheric”:ti,ab,kw	22
#13	“vacuum sealing”:ti,ab,kw OR “vacuum sealed”:ti,ab,kw OR “vacuum-sealed”:ti,ab,kw	14
#14	#7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13	1519
#15	(#6 AND #14)	364
	Only trials	269

CINAHL Strategy

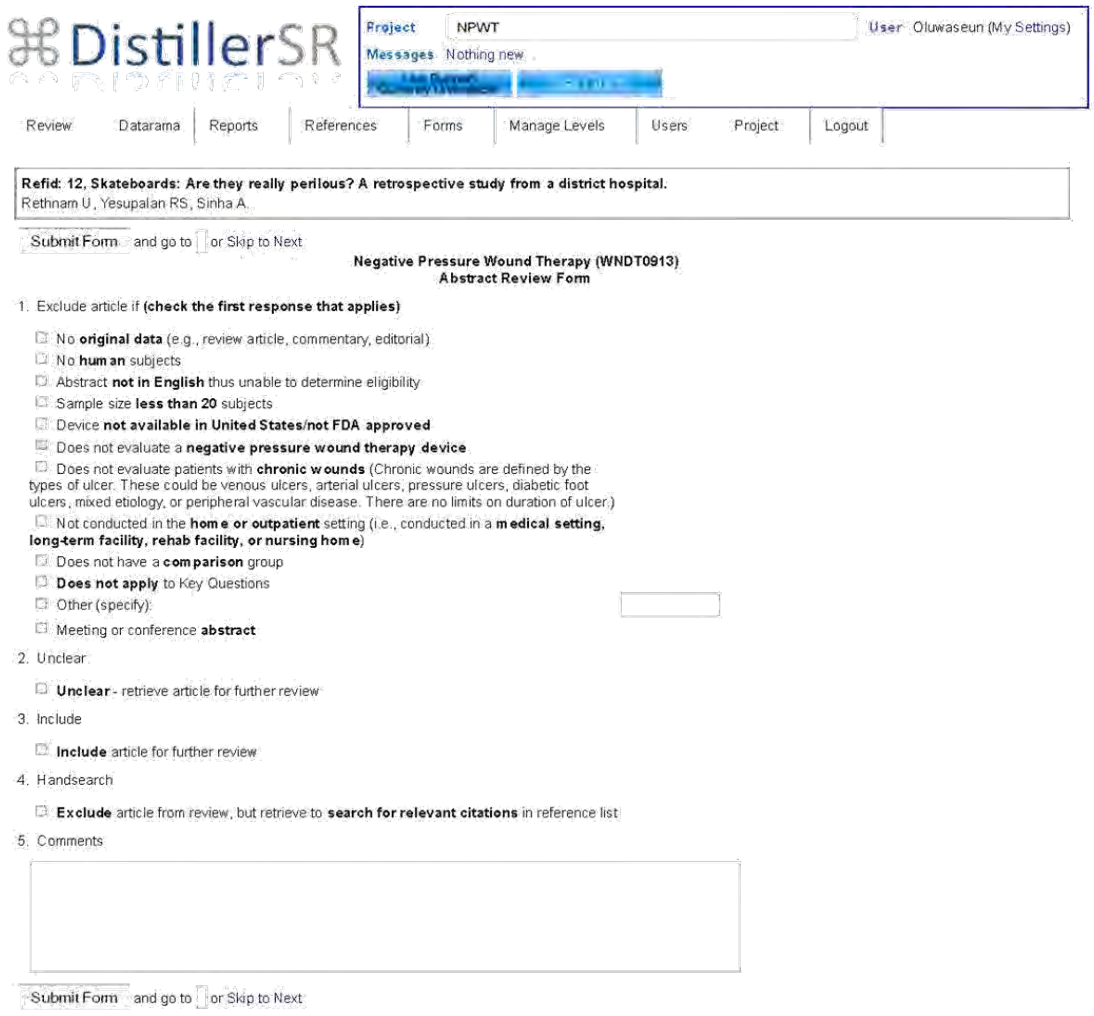
Search	String	Hits
#1	MH “Skin ulcer+”	17319
#2	MH “Wounds, chronic”	1843
#3	TX Wound*	57694
#4	TX Ulcer*	23253
#5	S1 OR S2 OR S3 OR S4	72361
#6	MH Vacuum+	197
#7	MH Suction+	1836
#8	MH “Negative Pressure Wound Therapy”	952
#9	TX “negative pressure” OR TX “negative-pressure”	1615
#10	TX “vacuum assisted” OR TX “vacuum-assisted”	434
#11	TX “subatmospheric” OR TX “sub-atmospheric”	44
#12	TX “vacuum sealing” OR TX “vacuum sealed” OR TX “vacuum-sealed”	6
#13	S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12	3667
#14	(S5 AND S13)	1486

ClinicalTrials.gov Strategy

Search	String	Hits
#1	Negative pressure wound therapy	93

Appendix B: Forms

Abstract Review Form



DistillerSR

Project NPWT User Oluwaseun (My Settings)

Messages Nothing new

Review | Datarama | Reports | References | Forms | Manage Levels | Users | Project | Logout

Refid: 12, Skateboards: Are they really perilous? A retrospective study from a district hospital.
Rethnam U, Yesupalan RS, Sinha A.

Submit Form and go to or Skip to Next

Negative Pressure Wound Therapy (WNDT0913)
Abstract Review Form

1. Exclude article if **(check the first response that applies)**
   - ☐ No **original data** (e.g., review article, commentary, editorial)
   - ☐ No **human** subjects
   - ☐ Abstract **not in English** thus unable to determine eligibility
   - ☐ Sample size **less than 20** subjects
   - ☐ Device **not available in United States/not FDA approved**
   - ☑ Does not evaluate a **negative pressure wound therapy device**
   - ☐ Does not evaluate patients with **chronic wounds** (Chronic wounds are defined by the types of ulcer. These could be venous ulcers, arterial ulcers, pressure ulcers, diabetic foot ulcers, mixed etiology, or peripheral vascular disease. There are no limits on duration of ulcer.)
   - ☐ Not conducted in the **home or outpatient** setting (i.e., conducted in a **medical setting, long-term facility, rehab facility, or nursing home**)
   - ☐ Does not have a **comparison** group
   - ☐ **Does not apply** to Key Questions
   - ☐ Other (specify):
   - ☐ Meeting or conference **abstract**
2. Unclear
   - ☐ **Unclear** - retrieve article for further review
3. Include
   - ☐ **Include** article for further review
4. Handsearch
   - ☐ **Exclude** article from review, but retrieve to **search for relevant citations** in reference list
5. Comments

Submit Form and go to or Skip to Next

Article Review Form

Refid: 12, Skateboards: Are they really perilous? A retrospective study from a district hospital.
Rethnam U, Yesupalan RS, Sinha A.

Submit Form and go to or Skip to Next

Negative Pressure Wound Therapy
Article Review Form

1. Exclude article if **(check the first response that applies)**
   - ☐ No **original data** (e.g., review article, commentary, editorial)
   - ☐ No **human** subjects
   - ☐ Meeting abstract
   - ☐ Not in English and unable to determine eligibility
   - ☐ Sample size **less than 20** subjects
   - ☐ Device **not available in United States/not FDA approved**
   - ☐ Does not evaluate a **negative pressure wound therapy device**
   - ☐ Does not evaluate patients with **chronic wounds**(Chronic wounds is defined by the type of ulcer. This could be venous ulcers, arterial ulcers, pressure ulcers, diabetic foot ulcers, mixed etiology, or peripheral vascular disease. There are no limits on duration of ulcer.)
   - ☐ Not conducted in the **home or outpatient** setting or conducted in a medical setting, long term facility, rehab facility, or nursing home
   - ☐ Does not have a **comparison**group
   - ☐ **Does not apply to key questions**
   - ☐ Does not report an **outcome** of interest
   - ☐ Unable to **abstract** relevant data
   - ☐ Other (specify:)
2. Include
   - ☐ Include article for further review
3. Handsearch
   - ☐ Exclude article from review, but retrieve to search for relevant citations in reference list
4. Comments

Submit Form and go to or Skip to Next

Data Abstraction Form: Key Question 2 and 4

Key Questions

This extraction form was created to answer the following key questions:

2 Part A: In patients who are similar to Medicare patients (age 65 or older or disabled) with chronic wounds, does the home use of negative pressure wound therapy significantly improve any of the clinical, patient-centered or adverse events outcomes as compared with treatment with other wound care methods? Part B: For studies included in Key Question 2, Part A, what wound care modalities were used prior to and concurrently with negative pressure wound therapy? Part C: For studies included in Key Question 2, Part A, what specific wound care modalities were used prior to and concurrently in the control groups of the studies? Part D: For studies included in Key Question 2, Part A, how do the treatments used prior to and/or concurrently with negative pressure wound therapy or the treatment of the control patients compare with usual care of chronic wounds?

4 If any answer to Key Question 2, Part A is yes, are there specific characteristics that predict better or worse outcomes?

Arm Name Suggestions

Arm Title	Arm Description	User Note
NPWT		
Control		
Total		

Arm Details

NPWT Brand

- ☐ KCI
- ☐ Smith and Nephew
- ☐ Other... Please specify
- ☐ Not reported

Model

- ○ Model.....
- ○ Not reported

Dressing types

	Type
Foam	Select...
Guaze	Select...
Other	

Portable Vs Stationary

- ○ Portable
- ○ Stationary

Not reported

Suction

Single setting
Multiple setting
Intermittent
Continuous
Other... Please specify
Not reported

Pressure setting (mmHg)

	mmHg
Min range	
Max range	
Not reported	

Other (please specify):

Recommended changing interval

Every 2 days
Every 3 days
Other... Please specify
Not reported

Reusable

Single use
Multiple use
Not reported

Instillation system

Hypochlorite based solution
Silver based solution
Sulfer based solution
Isotonic solution
Other... Please specify
Not reported

Duration of use(weeks)

Prior to VAC

Debridement
Other... Please specify
Not reported

Control details

Comments

Design Details and Enrollment

What study design was used? (Please check one response)

Randomized controlled trial
Non-randomized controlled trial
Cohort
Case-control
Other...(specify)
Not reported

When was the study enrollment period? (enter the 4-digit year for start and/or end, or indicate not reported)

Start year...
End Year...
Not reported

What was the trial or cohort name?

Trial or cohort name....
Not reported

What was the funding source? (Please check all that apply)

Government
Industry
Non-profit agency
Other(specify)...
None
Not reported

Where did the study occur? (Please check all that apply)

- ☐ Unites States
- ☐ Canada
- ☐ Worldwide
- ☐ Other(specify)...
- ☐ Not reported

What was the total intended followup duration or maximum possible followup?

- ☐ Days... ..
- ☐ Weeks... ..
- ☐ Months... ..
- ☐ Years... ..
- ☐ Not reported

What was the total number at enrollment or cohort inception?

- ○ N....
- ○ Not reported

Which etiologies of chronic wounds did the study include?

- ☐ Arterial ulcers
- ☐ Diabetic foot ulcers
- ☐ Pressure ulcers or pressure sores
- ☐ Venous ulcers
- ☐ Mixed etiology
- ☐ Other(specify)...

Please specify the exclusion criteria. Any inclusion criteria should be entered as exclusion criteria.

- ☐ No patients with chronic wounds
- ☐ Age (years) <... Please specify
- ☐ Age (years) >... Please specify
- ☐ Ulcer duration (weeks) <... Please specify
- ☐ Ulcer duration (weeks) >... Please specify
- ☐ Ulcer size (cm2) <... Please specify
- ☐ Ulcer size (cm2) >... Please specify
- ☐ Clinical infection
- ☐ Ankle/brachial index < ... Please specify
- ☐ Exudate level
- ☐ Comorbid conditions (e.g., vasculitis, rheumatoid arthritis, severe kidney disease, heart disease)
- ☐ Diabetes
- ☐ Treatment with systemic antimicrobials
- ☐ Treatment with corticosteroids
- ☐ Pain... Please specify
- ☐ Other... Please specify
- ☐ Other..... Please specify
- ☐ Other..... Please specify
- ☐ Other..... Please specify

Comments

Baseline Characteristics Fields

N enrolled

- ☐ Persons...
- ☐ Number of ulcers present...
- ☐ Number of ulcers being treated...
- ☐ Not reported

Age (years)

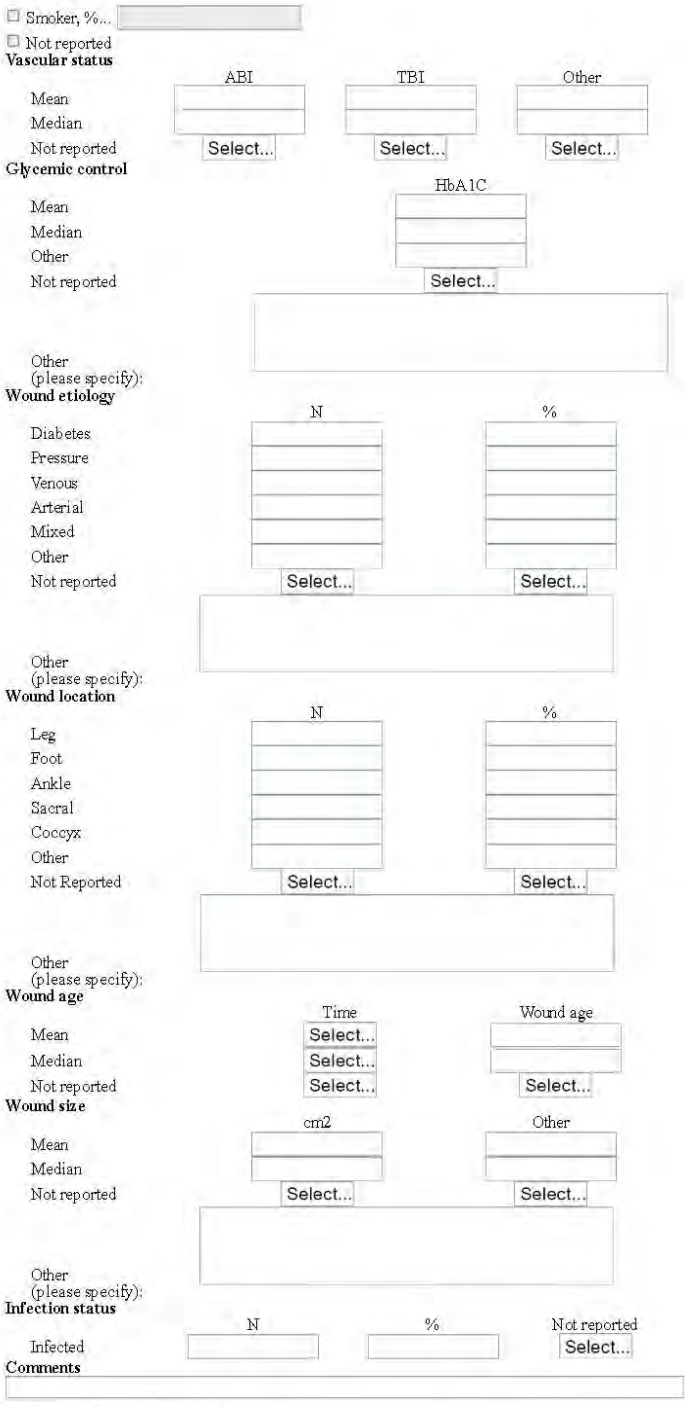
- ☐ Mean...
- ☐ Median...
- ☐ Min range...
- ☐ Max range...
- ☐ Not reported

Gender

- ☐ Male,N...
- ☐ Male,%...
- ☐ Not reported

Smoking status

- ☐ Smoking defined as...
- ☐ Smoker, N...



Outcome Name Suggestions

Outcome Title	Note
Complete wound healing by secondary intention	
Time to complete wound healing by secondary intention	
Time to surgical readiness	
Mortality	
Return to prior level of functional activity	
Pain	
Health-related quality of life	
Infection	
Extremity amputation	
Emergency room visit	
Unplanned hospitalization	
Unplanned surgeries	
Blood transfusions	
Bleeding	
Dropout rate	

Outcome Details

No questions specified.

Adverse Events

Arm or Total	Title	Description
NPWT		
Control		
Total		
Total		

Quality Dimension Fields

Quality Dimension	Value	Notes
What is the risk of selection bias (biased allocation to interventions) due to inadequate generation of a randomized sequence? [Low, Unclear, High]		
What is the risk of selection bias (biased allocation to interventions) due to inadequate concealment of allocations before assignment? [Low, Unclear, High]		
For each main outcome or class of outcomes, what is the risk of performance bias due to knowledge of the allocated interventions by participants and personnel during the study (lack of study participant and personnel blinding)? [Low, Unclear, High]		
For each main outcome or class of outcomes, what is the risk of attrition bias due to amount, nature, or handling of incomplete outcome data? [Low, Unclear, High]		
What is the risk of reporting bias due to selective outcome reporting? [Low, Unclear, High]		
Are there other biases due to problems not covered in 1-5? [Yes, No]		

Overall Rating of Study:
Quality Guideline Used in Assessment:

Data Abstraction Form: Key Question 3

Key Questions

This extraction form was created to answer the following key questions:

3 In patients with chronic wounds, do characteristics of the negative pressure wound therapy administration predict better or worse outcomes compared with other characteristics?

Arm Name Suggestions

No arms specified.

Arm Details

VAC Brand

- ☐ KCI
- ☐ Smith and Nephew
- ☐ Other... Please specify
- ☐ Not reported

Model

- ○ Model.....
- ○ Not reported

Dressing types

	Type
Foam	Select...
Guaze	Select...
Other	

Portable Vs Stationary

- ○ Portable
- ○ Stationary
- ○ Not reported

Suction

- ☐ Single setting
- ☐ Multiple setting
- ☐ Intermittent
- ☐ Continuous
- ☐ Other... Please specify
- ☐ Not reported

Pressure setting (mmHg)

mmHg

Min range
Max range
Not reported
Other (please specify):

Recommended changing interval

- ☐ Every 2 days
- ☐ Every 3 days
- ☐ Other... Please specify
- ☐ Not reported

Reusable

- ○ Single use
- ○ Multiple use
- ○ Not reported

Instillation system

- ☐ Hypochlorite based solution
- ☐ Silver based solution
- ☐ Sulfer based solution
- ☐ Isotonic solution
- ☐ Other... Please specify
- ☐ Not reported

Duration of use(weeks)

Prior to VAC

- ☐ Debridement
- ☐ Other... Please specify
- ☐ Not reported

Comments

Design Details and Enrollment

What study design was used? (Please check one response)

- ○ Randomized controlled trial
- ○ Non-randomized controlled trial
- ○ Cohort
- ○ Case-control
- ○ Other...(specify)
- ○ Not reported

When was the study enrollment period? (enter the 4-digit year for start and/or end, or indicate not reported)

- ☐ Start year... .
- ☐ End Year... .
- ☐ Not reported

What was the trial or cohort name?

- ○ Trial or cohort name....
- ○ Not reported

What was the funding source? (Please check all that apply)

- ☐ Government
- ☐ Industry
- ☐ Non-profit agency
- ☐ Other(specify)...
- ☐ None
- ☐ Not reported

Where did the study occur? (Please check all that apply)

- ☐ Unites States
- ☐ Canada
- ☐ Worldwide
- ☐ Other(specify)...
- ☐ Not reported

What was the total intended followup duration or maximum possible followup?

- ☐ Days... .
- ☐ Weeks... ..
- ☐ Months... ..
- ☐ Years... ..
- ☐ Not reported

What was the total number at enrollment or cohort inception?

- N....
- Not reported

Which etiologies of chronic wounds did the study include?

- Arterial ulcers
- Diabetic foot ulcers
- Pressure ulcers or pressure sores
- Venous ulcers
- Mixed etiology
- Other(specify)...

Please specify the exclusion criteria. Any inclusion criteria should be entered as exclusion criteria.

- No patients with chronic wounds
- Age (years) <... Please specify
- Age (years) >... Please specify
- Ulcer duration (weeks) <... Please specify
- Ulcer duration (weeks) >... Please specify
- Ulcer size (cm2) <... Please specify
- Ulcer size (cm2) >... Please specify
- Clinical infection
- Ankle/brachial index <... Please specify
- Exudate level
- Comorbid conditions (e.g., vasculitis, rheumatoid arthritis, severe kidney disease, heart disease)
- Diabetes
- Treatment with systemic antimicrobials
- Treatment with corticosteroids
- Pain... Please specify
- Other... Please specify
- Other..... Please specify
- Other..... Please specify
- Other..... Please specify

Comments

Baseline Characteristics Fields

N enrolled

- Persons...
- Number of ulcers present...
- Number of ulcers being treated...
- Not reported

Age (years)

- Mean...
- Median...
- Min range...
- Max range...
- Not reported

Gender

- Male,N...
- Male,%...
- Not reported

Smoking status

- Smoking defined as...
- Smoker, N...
- Smoker, %...
- Not reported

Vascular status

	ABI	TBI	Other
Mean			
Median			
Not reported	Select...	Select...	Select...

Glycemic control

	HbA1C
Mean	
Median	
Other	

Not reported Select...

Other (please specify):

Wound etiology

	N	%
Diabetes		
Pressure		
Venous		
Arterial		
Mixed		
Other		
Not reported	Select...	Select...

Other (please specify):

Wound location

	N	%
Leg		
Foot		
Ankle		
Sacral		
Coccyx		
Other		
Not Reported	Select...	Select...

Other (please specify):

Wound age

	Time	Wound age
Mean	Select...	
Median	Select...	
Not reported	Select...	Select...

Wound size

	cm2	Other
Mean		
Median		
Not reported	Select...	Select...

Other (please specify):

Infection status

	N	%	Not reported
Infected			Select...

Comments

Outcome Name Suggestions

Outcome Title	Note
Complete wound healing by secondary intention	
Time to complete wound healing by secondary intention	
Time to surgical readiness	
Mortality	
Return to prior level of functional activity	
Pain	
Health-related quality of life	
Infection	

Outcome Title	Note
Extremity amputation	
Emergency room visit	
Unplanned hospitalization	
Unplanned surgeries	
Blood transfusions	
Bleeding	
Dropout rate	

Outcome Details

No questions specified.

Adverse Events

Arm or Total	Title	Description
Total		

Quality Dimension Fields

Quality Dimension	Value	Notes
What is the risk of selection bias (biased allocation to interventions) due to inadequate generation of a randomized sequence? [Low, Unclear, High]		
What is the risk of selection bias (biased allocation to interventions) due to inadequate concealment of allocations before assignment? [Low, Unclear, High]		
For each main outcome or class of outcomes, what is the risk of performance bias due to knowledge of the allocated interventions by participants and personnel during the study (lack of study participant and personnel blinding)? [Low, Unclear, High]		
For each main outcome or class of outcomes, what is the risk of attrition bias due to amount, nature, or handling of incomplete outcome data? [Low, Unclear, High]		
What is the risk of reporting bias due to selective outcome reporting? [Low, Unclear, High]		
Are there other biases due to problems not covered in 1-5? [Yes, No]		

Overall Rating of Study:
Quality Guideline Used in Assessment:

Appendix C: List of Excluded Studies

1. Ahmed M, Soskova T, Williams DT. Regarding "State-of-the-art treatment of chronic leg ulcers: A randomized controlled trial comparing vacuum-assisted closure (V.A.C.) with modern wound dressings". J Vasc Surg. 2007 Sep;46(3):614-5; author reply 5-6. PMID: 17826260. **No original data**
2. Akbari A, Moodi H, Ghiasi F, et al. Effects of vacuum-compression therapy on healing of diabetic foot ulcers: randomized controlled trial. J Rehabil Res Dev. 2007;44(5):631-6. PMID: 17943674. **Sample size less than 20 subjects**
3. Al-Benna S. Economical negative pressure wound therapy. Ann R Coll Surg Engl. 2012 Apr;94(3):214. PMID: 22507736. **No original data, Sample size less than 20 subjects**
4. Alfano C, Angelisanti M, Calzoni C, et al. [Treatment of ulcer and difficult wounds of the lower limbs: our experience]. Ann Ital Chir. 2012;83(2):135-41. **Not conducted in home setting or outpatient setting**
5. Armstrong DG, Bluman EM, Gould L, et al. Wound care. Foot Ankle Spec. 2008 Jun;1(3):177-9. PMID: 19825713. **No original data**
6. Armstrong DG, Boulton AJ, Banwell P. Negative pressure wound therapy in treatment of diabetic foot wounds: a marriage of modalities. Ostomy Wound Manage. 2004 Apr;50(4A Suppl):9-12. PMID: 15317237. **No original data**
7. Armstrong DG, Lavery LA, Abu-Rumman P, et al. Outcomes of subatmospheric pressure dressing therapy on wounds of the diabetic foot. Ostomy Wound Manage. 2002 Apr;48(4):64-8. PMID: 11993062. **Does not have a comparison group**
8. Ashby R, Dumville J, Soares MO, et al. A pilot study of negative pressure wound therapy for the treatment of grade III/IV pressure ulcers. The 2011 International Nursing Research Conference; 16-18 May, 2011; Harrogate, UK; 2011. p. 95. **Sample size less than 20 subjects**
9. Augustin M, Blome C, Zschocke I, et al. Benefit evaluation in the therapy of chronic wounds from the patients' perspective--development and validation of a new method. Wound Repair Regen. 2012 Jan-Feb;20(1):8-14. PMID: 22150801. **Device not available in the US/not FDA approved, Does not have a comparison group, Does not apply to key questions**
10. Augustin M, Zschocke I. Patient evaluation of the benefit of outpatient and inpatient vacuum therapy. Multicenter study with patient-relevant end points. MMW-Fortschritte der Medizin. 2006;148(SUPPL. 1):25-32. **Not in English and unable to determine eligibility, Does not have a comparison group**
11. Ayala J, Payne W, Keith MS. Time to 50% reduction in wound area as a significant predictor of complete wound closure in patients with partial diabetic foot amputations: results from a randomized controlled trial comparing vacuum assisted closure to standard therapy (ST). SAWC 2006; April 30 - May 3, 2006; San Antonio, Texas; 2006. **Unable to retrieve article**
12. Baharestani MM, Houliston-Otto DB, Barnes S. Early versus late initiation of negative pressure wound therapy: examining the impact on home care length of stay. Ostomy Wound Manage. 2008 Nov;54(11):48-53. PMID: 19037137. **Does not apply to key questions**
13. Baharestani MM. Use of negative pressure wound therapy in the treatment of neonatal and pediatric wounds: a retrospective examination of clinical outcomes. Ostomy Wound Manage. 2007 Jun;53(6):75-85. PMID: 17586874. **Sample size less than 20 subjects, Does not evaluate patients with chronic wounds, Not conducted in home setting or outpatient setting, Other- pediatric data**
14. Bartkowski R, Endrich B. [DRG practice: wound management with vacuum therapy]. Chirurg. 2007 Dec;Suppl:414-6.

PMID: 18546567. **No original data, Not in English and unable to determine eligibility**

15. Beno M, Martin J, Sager P. Vacuum assisted closure in vascular surgery. Bratisl Lek Listy. 2011;112(5):249-52. PMID: 21682077. **Not conducted in home setting or outpatient setting, Unable to abstract relevant data**

16. Beral D, Adair R, Peckham-Cooper A, et al. Chronic wound sepsis due to retained vacuum assisted closure foam. BMJ. 2009;338:b2269. PMID: 19553260. **Sample size less than 20 subjects, Does not evaluate patients with chronic wounds**

17. Blume PA, Sumpio BE. Interim results of a randomized, controlled multicenter trial of vacuum-assisted closure therapy* in the treatment and blinded evaluation of diabetic foot ulcers. 20th Annual Symposium on Advanced Wounds Care and the Wound Healing Society Meeting; 2007, 28 April - 1 May; Tampa, FL; 2007. p. C126. **Meeting abstract, Unable to abstract relevant data**

18. Blume PA, Walters J, Payne W, et al. Comparison of negative pressure wound therapy using vacuum-assisted closure with advanced moist wound therapy in the treatment of diabetic foot ulcers: a multicenter randomized controlled trial. Diabetes Care. 2008 Apr;31(4):631-6. PMID: 18162494. **Not conducted in home setting or outpatient setting**

19. Braakenburg A, Obdeijn MC, Feitz R, et al. The clinical efficacy and cost effectiveness of the vacuum-assisted closure technique in the management of acute and chronic wounds: a randomized controlled trial. Plast Reconstr Surg. 2006 Aug;118(2):390-7; discussion 8-400. PMID: 16874208. **Not conducted in home setting or outpatient setting, Unable to abstract relevant data**

20. Brin YS, Mumcuoglu KY, Massarwe S, et al. Chronic foot ulcer management using maggot debridement and topical negative pressure therapy. J Wound Care. 2007 Mar;16(3):111-3. PMID: 17385586. **Sample size less than 20 subjects, Does not have a comparison group**

21. Carson SN, Overall K, Lee-Jahshan S, et al. Vacuum-assisted closure used for healing chronic wounds and skin grafts in the lower extremities. Ostomy Wound Manage. 2004 Mar;50(3):52-8. PMID: 15206090. **Does not evaluate patients with chronic wounds, Does not have a comparison group**

22. Chien SH, Tan WH, Hsu H. New continuous negative-pressure and irrigation treatment for infected wounds and intractable ulcers. Plast Reconstr Surg. 2008 Jul;122(1):318; author reply 9. PMID: 18594433. **No original data**

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Appendix D: Evidence Tables

Table 1: Study Design Characteristics of Included Studies

Author, Year	Study Design Location	Trial or Cohort Name	Funding Source	Enrollment Followup	N at Enrollment	Etiologies of Wounds	Exclusion Criteria
Armstrong, 2011[1]	RCT United States	NR	Industry	Start year: NR End year: NR Followup: 16 weeks	65	Diabetic foot ulcers; venous ulcers	Age < 18 years; ulcer size < 1cm^2; ulcer size > 100 cm^2; clinical infection; ankle/brachial index < 0.7 or >1.2; ulcer size >10cm in widest diameter. Wounds not present for >30 days despite appropriate wound care prior to entry
Armstrong, 2012[2]	RCT United States	NR	Industry	Start year: NR End year: NR Followup: 16 weeks	132	Diabetic foot ulcers; Venous ulcers	Age < 18 years; ulcer size < 1cm^2; ulcer size > 100 cm^2; clinical infection; ankle/brachial index < 0.7 or >1.2; ulcer size >10cm in widest diameter. Wounds not present for >30 days despite appropriate wound care prior to entry
Fife, 2008[3]	Cohort, but the control group is a mix of pre-NPWT and never users United States	IntelliTrak	Industry	Start year: 2001 End year: 2006 Followup: NR	1331	Diabetic foot ulcers	Not treated in an outpatient setting
Ford, 2002[4]	RCT United States	NR	NR	Start year: NR End year: NR Followup: 10 months	28	Pressure ulcers or pressure sores	Age < 21 year; Age > 80 years; ulcer duration < 4 weeks; clinical infection; comorbid conditions e.g., vasculitis, rheumatoid arthritis, severe kidney disease, heart disease; treatment with corticosteroids; absence of stage III or IV ulcers

Author, Year	Study Design Location	Trial or Cohort Name	Funding Source	Enrollment Followup	N at Enrollment	Etiologies of Wounds	Exclusion Criteria
Lavery, 2007[5]	Cohort United States	NR	Industry	Start year: 1996 End year: 2004 Followup: NR	2677	Diabetic foot ulcers	No patients with chronic wounds; no debridement of necrotic tissue, no comprehensive diabetes management included with the case plan; no reduction in pressure of affected ulcer, no description of wound size and duration prior to NPWT
Lerman, 2010[6]	Prospective observational analysis and retrospective match-controlled comparisons United States	NR	Industry	Start year: 2008 End year: 2009 Followup: 4 months	Total: 78 NPWT: 36 Control: 42	Diabetic foot ulcers; venous ulcers	Age < 18 years; ulcer size < 1.5cm in narrowest diameter; ulcer size > 10cm in greatest diameter; wound surrounded by 2cm or less of intact epithelium around the wound edge; wounds that healed following greater than 14 days of traditional treatments
Schwien, 2005[7]	Retrospective analysis of a database United States	Data from Outcome Concept Systems (OCS) OASIS data warehouse	Industry	Start year 2003; End year 2004 Followup: NR	2348	Pressure ulcers or pressure sores	Clinical infection; patients who died at home, enteral or parenteral nutrition therapy, high risk factor of heavy smoking, alcohol dependency, or drug dependency, poor or unknown overall prognosis, secondary diagnoses of uncontrolled DM, cancer, systemic infections, or related to malnutrition/ anemias/ proteinemia
Yao, 2012[8]	Cohort United States	NR	NR	Start year: 2002 End year: 2010 Followup: 8 years	342	Arterial ulcers; diabetic foot ulcers; pressure ulcers or pressure sores; venous ulcers	Age < 18 years; HIV positive; sickle cell disease; traumatic and burns ulcers; active malignancy with chemotherapy

DM=diabetes mellitus; HIV=Human Immunodeficiency Virus; N=number; NA=not available/not applicable; NPWT=negative pressure wound therapy; NR= not reported; RCT= randomized controlled trial

Table 2: Study Population Characteristics of Included Studies

Author, Year	Arm	Arm Description	N Enrolled	Mean Age (years)	Males, N (%)	Smoker, N (%)	Wound Etiology, %	Wound Location, %	Mean Wound Age (weeks)	Mean Wound Size (cm^2)	Infection Status,%
Armstrong 2011[1]	SNaP	Smart Negative Pressure (SNaP®) Wound Care System	32	65.8	15* (48)	6* (20)	NR	NR	NR	NR	NR
Armstrong 2011[1]	VAC	NA	33	65.1	16* (50)	4*(12.5)	NR	NR	NR	NR	NR
Armstrong 2011[1]	Total	Total	65	NR	31*(48.5*)	10*(15.4*)	NR	NR	NR	NR	NR
Armstrong 2012[2]	SNaP	Smart Negative Pressure (SNaP®) Wound Care System	64	65.0	31* (48.4)	11* (17.2)	NR	NR	52.4	5.37	NR
Armstrong 2012[2]	VAC	NA	68	65.6	43* (63.2)	5* (7.4)	NR	NR	68.8	9.95	NR
Armstrong 2012[2]	Total	Total	132	R	74*(56.1*)	16* (12*)	NR	NR	NR	NR	NR
Fife, 2008[3]	NPWT	Period of time when receiving NPWT therapy	72	NR	NR	NR	Diabetic: 100	NR	NR	NR	NR
Fife, 2008[3]	Control	Non NPWT. Patients who did not receive NPWT or prior to receiving NPWT	1299	NR	NR	NR	Diabetic: 100	NR	NR	NR	NR

Author, Year	Arm	Arm Description	N Enrolled	Mean Age (years)	Males, N (%)	Smoker, N (%)	Wound Etiology, %	Wound Location, %	Mean Wound Age (weeks)	Mean Wound Size (cm^2)	Infection Status,%
Fife, 2008[3]	Total	Total	1331	Mean: 60.4 Min: 1 Max: 104	NR	142*(10.7) Smoking defined as tobacco abuse	Diabetic: 100	NR	NR	NR	NR
Ford, 2002[4]	NPWT	VAC	NR	41.7	NR	NR	NR	NR	NR	NR	NR
Ford, 2002[4]	Control	Healthpoint System HP	NR	54.4	NR	NR	NR	NR	NR	NR	NR
Ford, 2002[4]	Total	Total	28 N of ulcers present : 41 N of ulcers being treated: NR	NR	NR	NR	Pressure: 100	Leg; 2.9* Foot: 11.4* Ankle: 11.4* Sacral: 48.6* Coccyx: 0 Other: 25.7	NR	NR	NR
Lavery, 2007[5]	NPWT	Obtained through KCI database	2091	65.2	1349* (64.5)	NR	Diabetic: 100	NR	22.9	13.5	NR
Lavery, 2007[5]	NPWT-Matched	Excluded patients older than 70 years and those with wounds of less than 1 month in duration	1135	58.5	732*(64.5)	NR	Diabetic: 100	NR	26.5	13.8	NR
Lavery, 2007[5]	Control	Margolis pooled analysis	586	58.0	NR (73.2)	NR	Diabetic: 100	NR	30	1.61	NR
Lavery, 2007[5]	Total	Total	NR	NR	NR	NR	Diabetic: 100	NR	NR	NR	NR

Author, Year	Arm	Arm Description	N Enrolled	Mean Age (years)	Males, N (%)	Smoker, N (%)	Wound Etiology, %	Wound Location, %	Mean Wound Age (weeks)	Mean Wound Size (cm^2)	Infection Status,%
Lerman, 2010[6]	NPWT	SNaP	36	64.0	9 (42.9)	9 (42.9)	Diabetic: 47.6 Venous: 52.4	NR	36.4	NR	NR
Lerman, 2010[6]	Control	Match	42	66.8	19 (45.2)	8 (20.0)	Diabetic: 50 Venous: 50	NR	31.2	NR	NR
Lerman, 2010[6]	Total	Total	NR	NR	28 (44.4)	17 (27.9)	Diabetic: 49.2 Venous: 50.8	NR	NR	NR	NR
Schwien, 2005[7]	NPWT	NA	60	Mean: 65.0 Min range: 21 Max range: 90	28* (47*)	NR	Pressure: 100	NR	NR	NR	NR
Schwien, 2005[7]	Control	NA	2288	Mean: 71.4 Min range: 18 Max range: 106	961* (42*)	NR	Pressure: 100	NR	NR	NR	NR
Schwien, 2005[7]	Total	Total	2348*	NR	989*(42.1*)	NR	Pressure: 100*	NR	NR	NR	NR
Yao, 2012[8]	NPWT		171	60.8	99 (57.9)	67 (40.6)	Diabetic: 81.8 Pressure: 13.45 Venous: 8.8 Arterial: 66.7	Leg: 15.7 Foot: 84.21*	NR	NR	79.5

Author, Year	Arm	Arm Description	N Enrolled	Mean Age (years)	Males, N (%)	Smoker, N (%)	Wound Etiology, %	Wound Location, %	Mean Wound Age (weeks)	Mean Wound Size (cm^2)	Infection Status,%
Yao, 2012[8]	Control	Non NPWT	171	61.3	99 (57.9)	59 (34.5)	Diabetic: 69.4 Pressure: 10.1 Venous: 10.6 Arterial: 34.9	Leg: 29.2 Foot: 70.76*	NR	NR	91.1
Yao, 2012[8]	Total	Total	342	NR	198* (57.9*)	NR	NR	Leg: 22.51* Foot: 77.48*	NR	NR	84.8*

ABI=ankle brachial index; *=calculated; Diabetic= diabetic foot ulcer; Max=maximum range; Min= minimum range; N=number; NPWT=negative pressure wound therapy; NR=not reported; Pressure=pressure ulcer; TBI=toe brachial index; VAC=vacuum assisted closure; Venous=venous stasis ulcer
None of the studies reported on vascular status or glycemic control.

Table 3: Study Intervention Details of Included Studies

Author, Year	Arm Details	NPWT brand Model Portable	Dressing Type Recommended Changing Interval	Suction Pressure Setting (mmHg)	Reusable	Instillation System	Duration of Use (weeks)	Prior to NPWT
Armstrong, 2011[1]	SNaP	Spiracur SNaP® NR	Gauze Every 3 days	NR NR	NR	NR	NR	Debridement
Armstrong, 2011[1]	VAC	KCI ActiV.A.C.® and V.A.C. Freedom® Portable	Foam Every 2 days	NR NR	NR	NR	NR	Debridement
Armstrong, 2012[2]	SNaP	Spiracur SNaP® Portable	NR NR	Continuous NR	Single use	NR	NR	Debridement
Armstrong, 2012[2]	VAC	KCI ActiV.A.C.® system and V.A.C. Freedom™ Portable	NR NR	NR NR	NR	NR	NR	Debridement
Fife, 2008[3]	Control Unspecified wound care treatment either prior to the start of NPWT or among patients who never received NPWT	NA	NA	NA	NA	NA	NA	NA
Fife, 2008[3]	NPWT	KCI V.A.C® Therapy NR	NR NR	NR NR	NR	NR	NR	NR

Author, Year	Arm Details	NPWT brand Model Portable	Dressing Type Recommended Changing Interval	Suction Pressure Setting (mmHg)	Reusable	Instillation System	Duration of Use (weeks)	Prior to NPWT
Ford, 2002[4]	Control The Healthpoint System HP consists of 3 FDA-approved gel products Accuzyme, Iodosorb, and Panafil each targeted to optimize a particular macroscopic phase of wound healing.	NA	NA	NA	NA	NA	NA	NA
Ford, 2002[4]	NPWT	NR NR NR	NR Every 2 days	NR NR	NR	NR	6	Debridement
Lavery, 2007[5]	Control Standard wet-to-moist wound therapy	NA	NA	NA	NA	NA	NA	NA
Lavery, 2007[5]	NPWT	KCI V.A.C.® Therapy NR	NR NR	NR NR	NR	NR	NR	NR
Lavery, 2007[5]	NPWT-Matched	KCI V.A.C® Therapy NR	NR NR	NR NR	NR	NR	NR	NR
Lerman, 2010[6]	Control Modern wound care protocols that included the use of Apligraf, Regranex, and skin grafting.	NA	NA	NA	NA	NA	NA	NA

Author, Year	Arm Details	NPWT brand Model Portable	Dressing Type Recommended Changing Interval	Suction Pressure Setting (mmHg)	Reusable	Instillation System	Duration of Use (weeks)	Prior to NPWT
Lerman, 2010[6]	NPWT	SNaP® NR Portable	Gauze: antimicrobial Other: hydrocolloid dressing layer Twice weekly	Multiple setting 75-125	Single use	NR	7.44	Debridement
Schwien, 2005[7]	Control Any other wound care therapy other than NPWT	NA	NA	NA	NA	NA	NA	NA
Schwien, 2005[7]	NPWT	KCI NR	Foam: Open cell Every 2 days	Intermittent; Continuous NR	NR	NR	NR	NR
Yao, 2012[8]	Control NR	NA	NA	NA	NA	NA	NA	NA
Yao, 2012[8]	NPWT	KCI NR NR	NR NR	NR NR	NR	NR	≥1	NR

FDA=U.S. Food and Drug Administration; KCI= Kinetic Concepts, Inc; NA=not available/not applicable; NPWT=negative pressure wound therapy; NR=not reported

Table 4: Clinical Outcome: Complete wound healing by secondary intention- Arterial Ulcers

Author, Year	Arm	N Enrolled	N Analyzed	N of Events	Person-Years	Event Rate per 100 Person-Years	Within Arm Comparison	Between Arm Comparison
Yao, 2012[8]	Control	NR	59	37	102.89	35.96 (95% CI, 26.05 to 49.63)	NR	
Yao, 2012[8]	NPWT	NR	114	78	99.54	78.36 (95% CI, 62.56 to 97.83)	NR	Unadj HR: 2.33 (95% CI, 1.57 to 3.48) adj HR: 2.27 (95% CI, 1.56 to 3.78) Ref group: control Adj for: DM, peripheral arterial disease, coronary heart disease, CKD, CHF, stroke, smoking etc

adj=adjusted; CHF= congestive heart failure; CI = conflidence interval; CKD=chronic kidney disease; DM=diabetes mellitus; HCL=higher confidence limit; HR=hazard ratio; N=number; unadj=unadjusted

Table 5a: Clinical Outcome: Complete wound healing by secondary intention- Diabetic Foot Ulcers

Author, Year	Arm	Subgroup	Outcome Description	Timepoint	N Enrolled	N Analyzed	Events	Person-Years	Event Rate per 100 Person-Years	Between Arm Comparison
Lavery, 2007[5]	Control	All participants	Wound healing was defined as wound completely healed	12 weeks	586	NR	23.9%	NR	NR	NR
Lavery, 2007[5]	Control	Small ulcers <2 cm^2		12 weeks	347	NR	29.4%	NR	NR	NR
Lavery, 2007[5]	Control	Medium ulcers 2-4 cm^2		12 weeks	123	NR	17.9%	NR	NR	NR
Lavery, 2007[5]	Control	Large ulcers >4 cm^2		12 weeks	116	NR	13.8%	NR	NR	NR
Lavery, 2007[5]	Control	Short duration <6 months		12 weeks	202	NR	30.2%	NR	NR	NR
Lavery, 2007[5]	Control	Medium duration 6-12 months		12 weeks	88	NR	28.4%	NR	NR	NR
Lavery, 2007[5]	Control	Long duration >12 months		12 weeks	189	NR	15.3%	NR	NR	NR
Lavery, 2007[5]	NPWT-Matched	All participants	Wound closure through secondary intention or through surgical intervention of if adequate granulation for closure by these methods were documented	12 weeks	1135	NR	39.5%	NR	NR	NR

Author, Year	Arm	Subgroup	Outcome Description	Timepoint	N Enrolled	N Analyzed	Events	Person-Years	Event Rate per 100 Person-Years	Between Arm Comparison
Lavery, 2007[5]	NPWT-Matched	Small ulcers <2 cm^2		12 weeks	181	NR	43.1%	NR	NR	NR
Lavery, 2007[5]	NPWT-Matched	Medium ulcers 2-4 cm^2		12 weeks	167	NR	43.7%	NR	NR	NR
Lavery, 2007[5]	NPWT-Matched	Large ulcers >4 cm^2		12 weeks	787	NR	37.8%	NR	NR	NR
Lavery, 2007[5]	NPWT-Matched	Short duration <6 months		12 weeks	787	NR	40.3%	NR	NR	NR
Lavery, 2007[5]	NPWT-Matched	Medium duration 6-12 months		12 weeks	169	NR	39.6%	NR	NR	NR
Lavery, 2007[5]	NPWT-Matched	Long duration >12 months		12 weeks	179	NR	35.8%	NR	NR	NR
Lavery, 2007[5]	NPWT	Small ulcers <2 cm^2	Wound closure through secondary intention or through surgical intervention of if adequate granulation for closure by these methods were documented	12 weeks	343	NR	41.4%	NR	NR	NR
Lavery, 2007[5]	NPWT	Medium ulcers 2-4 cm^2		12 weeks	323	NR	40.1%	NR	NR	NR
Lavery, 2007[5]	NPWT	Large ulcers >4 cm^2		12 weeks	1425	NR	37.8%	NR	NR	NR

Author, Year	Arm	Subgroup	Outcome Description	Timepoint	N Enrolled	N Analyzed	Events	Person-Years	Event Rate per 100 Person-Years	Between Arm Comparison
Lavery, 2007[5]	NPWT	Short duration <6 months		12 weeks	1543	NR	39.9%	NR	NR	NR
Lavery, 2007[5]	NPWT	Medium duration 6-12 months		12 weeks	279	NR	36.2%	NR	NR	NR
Lavery, 2007[5]	NPWT	Long duration >12 months		12 weeks	269	NR	35.3%	NR	NR	NR
Yao, 2012[8]	Control	Diabetic ulcer	Healed wounds	NR	NR	118	N: 80	205.65	38.9 (95% CI, 31.25 to 48.43)	
Yao, 2012[8]	NPWT	Diabetic ulcer	Healed wounds	NR	NR	140	N: 94	112.01	83.92 (95% CI, 68.56 to 102.72)	Unadj HR: 2.33 (95% CI, 1.57 to 3.48) adj HR: 2.27 (95% CI, 1.56 to 3.78) Ref group: control Adj for: DM, peripheral arterial disease, coronary heart disease, CKD, CHF, stroke, smoking etc

adj=adjusted; CHF = congestive heart failure; CI = confidence interval; CKD = chronic kidney disease; DM = diabetes mellitus; N=number; NPWT=negative pressure wound therapy; NR= not reported; unadj=unadjusted

Table 5b: Adverse Event: Bleeding-Diabetic Foot Ulcers

Author, Year	Arm	Subgroup	Outcome Description	Timepoint	N Enrolled	N Analyzed	Events	Within Arm Comparison	Between Arm Comparison
Fife, 2008[3]	Control	All Participants	Discontinued NPWT due to bleeding	NR	1299	NR	Count: NR	NR	NR
Fife, 2008[3]	NPWT	All Participants	Discontinued NPWT due to bleeding	NR	72	NR	Count: 0	NR	NR
Fife, 2008[3]	Control	All Participants	Sanguineous drainage	NR	1299	NR	Count: 0	NR	NR
Fife, 2008[3]	NPWT	All Participants	Sanguineous drainage	NR	72	NR	Count: 0	NR	NR

N=number; NPWT=negative pressure wound therapy; NR=not reported

Table 5c: Adverse Event: Infection-Diabetic Foot Ulcers

Author, Year	Arm	Subgroup	Outcome Description	Timepoint	N Enrolled	N Analyzed	Events	Within Arm Comparison	Between Arm Comparison
Fife, 2008[3]	Control	All Participants	N of antibiotic prescriptions	NR	1299	NR	NR	NR	Reference
Fife, 2008[3]	NPWT	All Participants	N of antibiotic prescriptions	NR	72	NR	NR	NR	*P* < 0.05 NPWT vs. Control
Fife, 2008[3]	Control	All Participants	N of cultures	NR	1299	NR	NR	NR	Reference
Fife, 2008[3]	NPWT	All Participants	N of cultures	NR	72	NR	NR	NR	*P* < 0.05 NPWT vs. Control

N=number; NPWT=negative pressure wound therapy; NR=not reported; vs.=versus

Table 5d: Adverse Event: Pain- Diabetic Foot Ulcers

Author, Year	Arm	Subgroup	Outcome Description	Timepoint	N Enrolled	N Analyzed	Events	Within Arm Comparison	Between Arm comparison
Fife, 2008[3]	Control	All Participants	Provision of pain medications	NR	1299	NR	NR	NR	Reference
Fife, 2008[3]	NPWT	All Participants	Provision of pain medications	NR	72	NR	NR	NR	*P* > 0.05 NPWT vs. Control

n=number; NPWT=negative pressure wound therapy; NR=not reported

Table 6a: Clinical Outcome: Complete wound healing by secondary intention- Pressure Ulcers

Author, Year	Arm	Subgroup	Outcome Description	Timepoint	N Enrolled	N Analyzed	Events	Person-Years	Event Rate per 100 Person-Years	Between Arm Comparison
Ford, 2002[4]	Control	All participants	Ulcer healed completely	During the treatment period	NR	15	Count: 2 %: 13	NR	NR	NR
Ford, 2002[4]	NPWT	All participants	Ulcer healed completely	During the treatment period	NR	20	Count: 2 %: 10	NR	NR	NR
Yao, 2012[8]	Control	Pressure ulcer	Healed wounds	NR	NR	17	N: 13	16.77	77.52 (95% CI, 45.01 to 133.51)	Reference
Yao, 2012[8]	NPWT	Pressure ulcer	Healed wounds	NR	NR	23	N: 17	11.96	142.14 (95% CI, 88.36 to 228.65)	Unadj HR: 2.19 (95% CI, 1.03 to 4.66) adj HR: 1.72 (95% CI, 0.43 to 6.95) NPWT vs. Control adj for: DM, peripheral arterial disease, coronary heart disease, CKD, CHF, stroke, smoking etc

adj=adjusted; CHF=congestive heart failure; CKD=chronic kidney disease; DM=diabetes mellitus; HCL=higher confidence limit; HR=hazard ratio; LCL=lower confidence limit; N=number; NPWT=negative pressure wound therapy; NR=not reported; unadj=unadjusted; vs.=versus

Table 6b: Adverse Event: Emergency room visits- Pressure Ulcers

Author, Year	Arm	Subgroup	Outcome Description	Timepoint	N Enrolled	N Analyzed	Events	Within Arm Comparison	Between Arm Comparison
Schwien, 2005[7]	Control	All participants	Instances of emergent care for wound problem	NR	NR	2288	N: 189 %: 8	NR	
Schwien, 2005[7]	NPWT	All participants	Instances of emergent care for wound problem	NR	NR	60	N: 0 %: 0	NR	*P* < 0.01 NPWT vs. Control
Schwien, 2005[7]	Control	Stage III pressure ulcers	Instances of emergent care for wound problem	NR	NR	NR	N: 126 %: 7	NR	
Schwien, 2005[7]	NPWT	Stage III pressure ulcers	Instances of emergent care for wound problem	NR	NR	NR	N: 0 %: 0	NR	*P* < 0.01 NPWT vs. Control
Schwien, 2005[7]	Control	Stage IV pressure ulcers	Instances of emergent care for wound problem	NR	NR	NR	N: 63 %: 11	NR	
Schwien, 2005[7]	NPWT	Stage IV pressure ulcers	Instances of emergent care for wound problem	NR	NR	NR	N: 0 %: 0	NR	*P* < 0.01 NPWT vs. Control

N=number; NPWT=negative pressure wound therapy; NR=not reported; vs.=versus

Table 6c: Adverse Event: Extremity Amputation- Pressure Ulcers

Author, Year	Arm	Subgroup	Outcome Description	Timepoint	N Enrolled	N Analyzed	Events	Within Arm Comparison	Between Arm Comparison
Ford, 2002[4]	Control	All participants	Extremity amputation	NR	NR	NR	N: 0	NR	NR
Ford, 2002[4]	NPWT	All participants	Extremity amputation	NR	NR	NR	N: 1	NR	NR

N=number; NPWT=negative pressure wound therapy; NR=not reported

Table 6d: Adverse Event: Infections- Pressure Ulcers

Author, Year	Arm	Subgroup	Outcome Description	Timepoint	N Enrolled	N Analyzed	Events	Within Arm Comparison	Between Arm Comparison
Ford, 2002[4]	Control	All participants	Sepsis	NR	NR	NR	N: 0	NR	NR
Ford, 2002[4]	NPWT	All participants	Sepsis	NR	NR	NR	N: 1	NR	NR

N=number; NPWT=negative pressure wound therapy; NR=not reported

Table 6e: Adverse Event: Unplanned Hospitalizations- Pressure Ulcers

Author, Year	Arm	Subgroup	Outcome Description	Timepoint	N Enrolled	N Analyzed	Events	Within Arm Comparison	Between Arm Comparison
Schwien, 2005[7]	Control	All participants	Instances of hospitalization for wound problem	NR	NR	2288	N: 310 %: 14	NR	
Schwien, 2005[7]	NPWT	All participants	Instances of hospitalization for wound problem	NR	NR	60	N: 3 %: 5	NR	$P < 0.05$ NPWT vs. Control
Schwien, 2005[7]	Control	Stage III pressure ulcers	Instances of hospitalization for wound problem	NR	NR	NR	N: 194 %: 11	NR	
Schwien, 2005[7]	NPWT	Stage III pressure ulcers	Instances of hospitalization for wound problem	NR	NR	NR	N: 1 %: 3	NR	$P < 0.05$ NPWT vs. Control
Schwien, 2005[7]	Control	Stage IV pressure ulcers	Instances of hospitalization for wound problem	NR	NR	NR	N: 116 %: 20	NR	
Schwien, 2005[7]	NPWT	Stage IV pressure ulcers	Instances of hospitalization for wound problem	NR	NR	NR	N: 2 %: 7	NR	$P < 0.01$ NPWT vs. Control

N=number; NPWT=negative pressure wound therapy; NR=not reported; vs.=versus

Table 7a: Clinical Outcome: Complete wound healing by secondary intention- Venous Stasis Ulcers

Author, Year	Arm	Subgroup	Timepoint	N Enrolled	N Analyzed	Events	Person - Years	Event Rate per 100 Person-Years	Between Arm Comparison

Author, Year	Arm	Subgroup	Timepoint	N Enrolled	N Analyzed	Events	Person - Years	Event Rate per 100 Person-Years	Between Arm Comparison
Yao, 2012[8]	Control	Venous ulcers	NR	NR	18	N: 14	30.69	45.62 (95% CI, 27.02 to 77.03)	Reference
Yao, 2012[8]	NPWT	Venous ulcers	NR	NR	15	N: 12	7.79	154.04 (95% CI, 87.48 to 271.24)	Unadj HR: 4.90 (95% CI, 1.72 to 13.59) adj HR: 6.31 (95% CI, 1.49 to 26.6) NPWT vs. Control adj for: DM, peripheral arterial disease, coronary heart disease, CKD, CHF, stroke, smoking etc

adj=adjusted; CHF=congestive heart failure; CKD=chronic kidney disease; DM=diabetes mellitus; HCL=higher confidence limit; HR=hazard ratio; LCL=lower confidence limit; N=number; NPWT=negative pressure wound therapy; NR=not reported; unadj=unadjusted; vs.=versus

Table 8a: Clinical Outcome: Complete wound healing by secondary intention- Mixed population

Author, Year	Arm	Subgroup	Timepoint	N Enrolled	N Analyzed	Person - Years	Events	Event Rate per 100 Person-Years	Between Arm Comparison
Lerman, 2010[6]	Control	All Participants	1 month	NR	42	NR	KM %: 0	NR	
Lerman, 2010[6]	NPWT	All Participants	1 month	NR	21	NR	KM %: 0	NR	Log-Rank *P* <0.0001 Wilcoxon *P* = 0.0001
Lerman, 2010[6]	Control	All Participants	2 months	NR	42	NR	KM %: 7.1	NR	
Lerman, 2010[6]	NPWT	All Participants	2 months	NR	21	NR	KM %: 20	NR	Log-Rank *P* <0.0001 Wilcoxon *P* = 0.0001
Lerman, 2010[6]	Control	All Participants	3 months	NR	42	NR	KM %: 21.4	NR	
Lerman, 2010[6]	NPWT	All Participants	3 months	NR	21	NR	KM %: 66.2	NR	Log-Rank *P* <0.0001 Wilcoxon *P* = 0.0001
Lerman, 2010[6]	Control	All Participants	4 months	NR	42	NR	KM %: 35.7	NR	
Lerman, 2010[6]	NPWT	All Participants	4 months	NR	21	NR	KM %: 83.1	NR	Log-Rank *P* <0.0001 Wilcoxon *P* = 0.0001
Yao, 2012[8]	Control	All ulcers	NR	171	171	274.36	N: 118	43.01 (95% CI, 35.91 to 51.51)	
Yao, 2012[8]	NPWT	All ulcers	NR	171	171	131.47	N: 119	90.51 (95% CI, 75.63 to 108.32)	Unadj HR: 2.25 (95% CI, 1.73 to 3.96) adj HR: 2.63 (95% CI, 1.87 to 3.70) NPWT vs. Control adj for: DM, peripheral arterial disease, coronary heart disease, CKD, CHF, stroke, smoking etc
Yao, 2012[8]	Control	Grade I ulcers superficial ulcer involving skin only	NR	NR	67	77.41	N: 51	65.88 (95% CI, 50.07 to 86.69)	NR
Yao, 2012[8]	NPWT	Grade I ulcers superficial ulcer involving skin only	NR	NR	85	56.51	N: 61	107.95 (95% CI, 83.99 to 138.74)	NR
Yao, 2012[8]	Control	Grade II ulcers deep ulcer involving muscle/ tendon/bone	NR	NR	100	194.41	N: 65	33.43 (95% CI, 26.22 to 42.63)	NR
Yao, 2012[8]	NPWT	Grade II ulcers deep ulcer involving muscle/ tendon/bone	NR	NR	85	74.96	N: 58	77.96 (95% CI, 59.81 to 100.08)	NR

adj=adjusted; CHF=congestive heart failure; CKD=chronic kidney disease; DM=diabetes mellitus; HCL=higher confidence limit; HR=hazard ratio; KM=Kaplan- Meier estimates; LCL=lower confidence limit; N=number; NPWT=negative pressure wound therapy; NR=not reported; unadj=unadjusted; vs.=versus

Table 8b: Clinical Outcome: Time to complete wound healing by secondary intention- Mixed population

Author, Year	Arm	Subgroup	Timepoint	N Enrolled	N Analyzed	Person-Years	Events	Between Arm Comparison
Lerman, 2010[6]	Control	All participants	NR	NR	NA	NR	Average days per KM: 148.73	
Lerman, 2010[6]	NPWT	All participants	NR	NR	21	NR	Average days per KM: 74.25	Log Rank *P* < 0.0001 NPWT vs. Control

KM= Kaplan-Meier estimates; N=number; NPWT=negative pressure wound therapy; NR=not reported; vs.=versus

Table 8c: Adverse Event: Unspecified- Mixed population

Author, Year	Arm	Subgroup	Outcome Description	Timepoint	N Enrolled	N Analyzed	Events	Within Arm Comparison	Between Arm Comparison
Lerman, 2010[6]	Control	All participants	NR	NR	NA	NR	NR	NR	NR
Lerman, 2010[6]	NPWT	All participants	NR	NR	36	NR	Counts: 7	NR	NR

N=number; NPWT=negative pressure wound therapy; NR=not reported

Table 8d: Adverse Event: Infections- Mixed population

Author, Year	Arm	Subgroup	Outcome Description	Timepoint	N Enrolled	N Analyzed	Events	Within Arm Comparison	Between Arm Comparison
Lerman, 2010[6]	Control	All participants	Wound infection requiring discontinuation of NPWT	NR	NA	NR	NA	NR	NR
Lerman, 2010[6]	NPWT	All participants	Wound infection requiring discontinuation of NPWT	NR	36	NR	Counts: 1	NR	NR

N=number; NA=not available; NPWT=negative pressure wound therapy; NR=not reported

Table 9a: KQ3 Clinical Outcome: Complete wound healing by secondary intention

Author, Year	Arm	Subgroup	Outcome Description	Timepoint	N Enrolled	Events
Armstrong, 2012[2]	SNaP	All participants	NR	0-4 weeks	64	5.3%
Armstrong, 2012[2]	VAC	All participants	NR	0-4 weeks	68	9.2%
Armstrong, 2011[1]	SNaP	All participants	NR	4 weeks	32	0%
Armstrong, 2011[1]	VAC	All participants	NR	4 weeks	33	0%

N=number; NPWT=negative pressure wound therapy; NR=not reported

Table 9b: KQ3 Adverse Event: Infection

Author, Year	Arm	Subgroup	Outcome Description	Timepoint	N Enrolled	N Analyzed	Events
Armstrong, 2012[2]	SNaP	All participants	NR	NR	64	64	Count: 2 %: 3.1
Armstrong, 2012[2]	VAC	All participants	NR	NR	68	68	Count: 5 %: 7.4
Armstrong, 2011[1]	SNaP	All participants	NR	NR	32	32	Count: 2 %: 6.3
Armstrong, 2011[1]	VAC	All participants	NR	NR	33	33	Count: 1 %: 3.0

N=number; NPWT=negative pressure wound therapy; NR=not repo

Table 9c: KQ3 Adverse Event: Pain

Author, Year	Arm	Subgroup	Outcome Description	Timepoint	N Analyzed	Events	Between Arm Comparison
Armstrong, 2012[2]	SNaP	All participants	Pain	NR	64	Count: 1 %: 1.6	NR
Armstrong, 2012[2]	VAC	All participants	Pain	NR	68	Count: 4 %: 5.9	NR
Armstrong, 2012[2]	SNaP	All participants	Pain What was your overall discomfort from using the NPWT device?	Exit survey	53	NR	
Armstrong, 2012[2]	VAC	All participants	Pain What was your overall discomfort from using the NPWT device?	Exit survey	52	NR	Fisher's Exact Test: 0.0432 VAC vs.SNaP
Armstrong, 2012[2]	SNaP	High level of discomfort	Pain What was your overall discomfort from using the NPWT device?	Exit survey	53	Count: 1 %: 1.9	NR
Armstrong, 2012[2]	VAC	High level of discomfort	Pain What was your overall discomfort from using the NPWT device?	Exit survey	52	Count: 4 %: 7.7	NR
Armstrong, 2012[2]	SNaP	Low level of discomfort	Pain What was your overall discomfort from using the NPWT device?	Exit survey	53	Count: 8 %: 15.1	NR
Armstrong, 2012[2]	VAC	Low level of discomfort	Pain What was your overall discomfort from using the NPWT device?	Exit survey	52	Count: 13 %: 25.0	NR
Armstrong, 2012[2]	SNaP	Moderate discomfort	Pain What was your overall discomfort from using the NPWT device?	Exit survey	53	Count: 7 %: 13.2	NR
Armstrong, 2012[2]	VAC	Moderate discomfort	Pain What was your overall discomfort from using the NPWT device?	Exit survey	52	Count: 11 %: 21.2	NR
Armstrong, 2012[2]	SNaP	Minimum discomfort	Pain What was your overall discomfort from using the NPWT device?	Exit survey	53	Count: 16 %: 30.2	NR
Armstrong, 2012[2]	VAC	M inimum discomfort	Pain What was your overall discomfort from using the NPWT device?	Exit survey	52	Count: 16 %: 30.8	NR
Armstrong, 2012[2]	SNaP	No discomfort	Pain What was your overall discomfort from using the NPWT device?	Exit survey	53	Count: 21 %: 39.6	NR
Armstrong, 2012[2]	VAC	No discomfort	Pain What was your overall discomfort from using the NPWT device?	Exit survey	52	Count: 8 %: 15.4	NR

Author, Year	Arm	Subgroup	Outcome Description	Timepoint	N Analyzed	Events	Between Arm Comparison
Armstrong, 2012[2]	SNaP	All participants	What was your level of pain associated with dressing changes for the NPWT device?	Exit survey	53	Sum of scores: 2545.50 Expected sum of scores: 2809.0 SD of sum: 148.52	NR
Armstrong, 2012[2]	VAC	All participants	What was your level of pain associated with dressing changes for the NPWT device?	Exit survey	52	Sum of scores: 3019.50 Expected sum of scores: 2756.0 SD of sum: 148.52	Wilcoxon Test *P* = 0.0795 VAC vs.SNaP
Armstrong, 2012[2]	SNaP	All participants	What was your level of pain associated with just wearing the NPWT device?	Exit survey	53	Sum of scores: 2659.0 Expected sum of scores: 2809.0 SD of sum: 141.84	
Armstrong, 2012[2]	VAC	All participants	What was your level of pain associated with just wearing the NPWT device?	Exit survey	52	Sum of scores: 2906.0 Expected sum of scores: 2756.0 SD of sum: 141.84	Wilcoxon Test *P* = 0.2943 VAC vs.SNaP
Armstrong, 2012[2]	SNaP	All participants	What was your overall level of pain associated with treatment with the NPWT device?	Exit survey	53	Sum of scores: 2588.50 Expected sum of scores: 2809.0 SD of sum: 147.49	
Armstrong, 2012[2]	VAC	All participants	What was your overall level of pain associated with treatment with the NPWT device?	Exit survey	52	Sum of scores: 2976.50 Expected sum of scores: 2756.0 SD of sum: 147.49	Wilcoxon Test *P* = 0.1388 VAC vs.SNaP
Armstrong, 2011[1]	SNaP	All participants	What was your level of pain associated with just wearing the NPWT device?	Exit survey	11	Sum of scores: 102.5 Expected sum of scores: 126.5 SD of sum: 14.434	
Armstrong, 2011[1]	VAC	All participants	What was your level of pain associated with just wearing the NPWT device?	Exit survey	11	Sum of scores: 150.5 Expected sum of scores: 126.5 SD of sum: 14.434	Wilcoxon *P* = 0.1184 t test P-value: 0.0403 VAC vs.SNaP
Armstrong, 2011[1]	SNaP	All participants	Pain What was your overall discomfort from using the NPWT device?	Exit survey	13		

Author, Year	Arm	Subgroup	Outcome Description	Timepoint	N Analyzed	Events	Between Arm Comparison
Armstrong, 2011[1]	VAC	All participants	Pain What was your overall discomfort from using the NPWT device?	Exit survey	12		Fisher's Exact Test: 0.0282 Chi-Squared *P* = 0.0424 VAC vs.SNaP
Armstrong, 2011[1]	SNaP	High level of discomfort	Pain What was your overall discomfort from using the NPWT device?	Exit survey	13	Count: 0 %: 0.0	NR
Armstrong, 2011[1]	VAC	High level of discomfort	Pain What was your overall discomfort from using the NPWT device?	Exit survey	12	Count: 1 %: 8.3	NR
Armstrong, 2011[1]	SNaP	Low level of discomfort	Pain What was your overall discomfort from using the NPWT device?	Exit survey	13	Count: 2 %: 15.4	NR
Armstrong, 2011[1]	VAC	Low level of discomfort	Pain What was your overall discomfort from using the NPWT device?	Exit survey	12	Count: 12 %: 16.7	NR
Armstrong, 2011[1]	SNaP	Moderate discomfort	Pain What was your overall discomfort from using the NPWT device?	Exit survey	13	Count: 1 %: 7.7	NR
Armstrong, 2011[1]	VAC	Moderate discomfort	Pain What was your overall discomfort from using the NPWT device?	Exit survey	12	Count: 3 %: 25.0	NR
Armstrong, 2011[1]	SNaP	Minimum discomfort	Pain What was your overall discomfort from using the NPWT device?	Exit survey	13	Count: 3 %: 23.1	NR
Armstrong, 2011[1]	VAC	Minimum discomfort	Pain What was your overall discomfort from using the NPWT device?	Exit survey	12	Count: 4 %: 33.3	NR
Armstrong, 2011[1]	SNaP	No discomfort	Pain What was your overall discomfort from using the NPWT device?	Exit survey	13	Count: 7 %: 53.9	NR
Armstrong, 2011[1]	VAC	No discomfort	Pain What was your overall discomfort from using the NPWT device?	Exit survey	12	Count: 2 %: 16.7	NR
Armstrong, 2011[1]	SNaP	All participants	What was your overall level of pain associated with treatment with the NPWT device?	Exit survey	12	Sum of scores: 121.5 Expected sum of scores: 150.0 SD of sum: 16.89	

Author, Year	Arm	Subgroup	Outcome Description	Timepoint	N Analyzed	Events	Between Arm Comparison
Armstrong, 2011[1]	VAC	All participants	What was your overall level of pain associated with treatment with the NPWT device?	Exit survey	12	Sum of scores: 178.5 Expected sum of scores: 150.0 SD of sum: 16.89	Wilcoxon *P* = 0.111 t test *P* = 0.0696 VAC vs.SNaP
Armstrong, 2011[1]	SNaP	All participants	What was your level of pain associated with dressing changes for the NPWT device?	Exit survey	13	Sum of scores: 112.5 Expected sum of scores: 144.0 SD of sum: 15.664	
Armstrong, 2011[1]	VAC	All participants	What was your level of pain associated with dressing changes for the NPWT device?	Exit survey	12	Sum of scores: 163.5 Expected sum of scores: 132.0 SD of sum: 15.664	Wilcoxon *P* = 0.0605 t test *P* = 0.0245 VAC vs.SNaP

N=number; NPWT=negative pressure wound therapy; NR=not reported; SD=standard deviation; vs.=versus

Table 9d: KQ3 Patient-centered Outcome: Return to prior level of functional activity

Author, Year	Arm	Subgroup	Outcome Description	Timepoint	N Analyzed	Events	Between Arm Comparison
Armstrong, 2012[2]	SNaP	All participants	After treatment with the NPWT, how did your overall activity level change?	Exit survey	53	Count: NA	
Armstrong, 2012[2]	VAC	All participants	After treatment with the NPWT, how did your overall activity level change?	Exit survey	52	Count: NA	Fisher's Exact Test $P < 0.05$ VAC vs. SNaP
Armstrong, 2012[2]	SNaP	Less active	After treatment with the NPWT, how did your overall activity level change?	Exit survey	53	Count: 9 %: 17.0	NR
Armstrong, 2012[2]	VAC	Less active	After treatment with the NPWT, how did your overall activity level change?	Exit survey	52	Count: 27 %: 51.9	NR
Armstrong, 2012[2]	SNaP	More active	After treatment with the NPWT, how did your overall activity level change?	Exit survey	53	Count: 6 %: 11.3	NR
Armstrong, 2012[2]	VAC	More active	After treatment with the NPWT, how did your overall activity level change?	Exit survey	52	Count: 2 %: 3.9	NR
Armstrong, 2012[2]	SNaP	Stayed the same	After treatment with the NPWT, how did your overall activity level change?	Exit survey	53	Count: 38 %: 71.7	NR
Armstrong, 2012[2]	VAC	Stayed the same	After treatment with the NPWT, how did your overall activity level change?	Exit survey	52	Count: 23 %: 44.2	NR
Armstrong, 2012[2]	SNaP	Agree	I was able to work and do my normal daily activity while being treated with the NPWT?	Exit survey	53	Count: 23 %: 43.4	NR
Armstrong, 2012[2]	VAC	Agree	I was able to work and do my normal daily activity while being treated with the NPWT?	Exit survey	52	Count: 25 %: 48.1	NR
Armstrong, 2012[2]	SNaP	Disagree	I was able to work and do my normal daily activity while being treated with the NPWT?	Exit survey	53	Count: 3 %: 5.7	NR
Armstrong, 2012[2]	VAC	Disagree	I was able to work and do my normal daily activity while being treated with the NPWT?	Exit survey	52	Count: 11 %: 21.2	NR
Armstrong, 2012[2]	SNaP	Neutral	I was able to work and do my normal daily activity while being treated with the NPWT?	Exit survey	53	Count: 7 %: 13.2	NR

Author, Year	Arm	Subgroup	Outcome Description	Timepoint	N Analyzed	Events	Between Arm Comparison
Armstrong, 2012[2]	VAC	Neutral	I was able to work and do my normal daily activity while being treated with the NPWT?	Exit survey	52	Count: 7 %: 13.5	NR
Armstrong, 2012[2]	SNaP	Strongly agree	I was able to work and do my normal daily activity while being treated with the NPWT?	Exit survey	53	Count: 19 %: 35.9	NR
Armstrong, 2012[2]	VAC	Strongly agree	I was able to work and do my normal daily activity while being treated with the NPWT?	Exit survey	52	Count: 5 %: 9.6	NR
Armstrong, 2012[2]	SNaP	Strongly disagree	I was able to work and do my normal daily activity while being treated with the NPWT?	Exit survey	53	Count: 1 %: 1.9	NR
Armstrong, 2012[2]	VAC	Strongly disagree	I was able to work and do my normal daily activity while being treated with the NPWT?	Exit survey	52	Count: 4 %: 7.7	NR
Armstrong, 2011[1]	SNaP	All participants	After treatment with the NPWT, how did your overall activity level change?	Exit survey	13	NR	
Armstrong, 2011[1]	VAC	All participants	After treatment with the NPWT, how did your overall activity level change?	Exit survey	12	NR	Chi-square *P* = 0.0210 Fisher's Exact Test *P* = 0.0179 VAC vs.SNaP
Armstrong, 2011[1]	SNaP	Less active	After treatment with the NPWT, how did your overall activity level change?	Exit survey	13	Count: 1 %: 7.7	NR
Armstrong, 2011[1]	VAC	Less active	After treatment with the NPWT, how did your overall activity level change?	Exit survey	12	Count: 7 %: 58.3	NR
Armstrong, 2011[1]	SNaP	More active	After treatment with the NPWT, how did your overall activity level change?	Exit survey	13	Count: 1 %: 7.7	NR
Armstrong, 2011[1]	VAC	More active	After treatment with the NPWT, how did your overall activity level change?	Exit survey	12	Count: 0 %: 0	NR
Armstrong, 2011[1]	SNaP	Stayed the same	After treatment with the NPWT, how did your overall activity level change?	Exit survey	13	Count: 11 %: 84.6	NR
Armstrong, 2011[1]	VAC	Stayed the same	After treatment with the NPWT, how did your overall activity level change?	Exit survey	12	Count: 5 %: 41.7	NR

Author, Year	Arm	Subgroup	Outcome Description	Timepoint	N Analyzed	Events	Between Arm Comparison
Armstrong, 2011[1]	SNaP	Overall	After treatment with the NPWT, how did your overall activity level change?	Exit survey	13	Count: NR %: NR	NR
Armstrong, 2011[1]	VAC	Overall	After treatment with the NPWT, how did your overall activity level change?	Exit survey	12	Count: NR %: NR	Chi-square *P* = 0.0210 Fisher's Exact Test *P* = 0.0179 VAC vs.SNaP
Armstrong, 2011[1]	SNaP	All participants	I was able to work and do my normal daily activity while being treated with the NPWT?	Exit survey	NR	NR	
Armstrong, 2011[1]	VAC	All participants	I was able to work and do my normal daily activity while being treated with the NPWT?	Exit survey	NR	NR	Chi-square *P* = 0.0068 Fisher's Exact Test : 0.0038 VAC vs.SNaP
Armstrong, 2011[1]	SNaP	Agree	I was able to work and do my normal daily activity while being treated with the NPWT?	Exit survey	13	Count: 6 %: 46.2	NR
Armstrong, 2011[1]	VAC	Agree	I was able to work and do my normal daily activity while being treated with the NPWT?	Exit survey	12	Count: 4 %: 33.3	NR
Armstrong, 2011[1]	SNaP	Disagree	I was able to work and do my normal daily activity while being treated with the NPWT?	Exit survey	13	Count: 0 %: 0	NR
Armstrong, 2011[1]	VAC	Disagree	I was able to work and do my normal daily activity while being treated with the NPWT?	Exit survey	12	Count: 4 %: 33.3	NR
Armstrong, 2011[1]	SNaP	Neutral	I was able to work and do my normal daily activity while being treated with the NPWT?	Exit survey	13	Count: 1 %: 7.7	NR
Armstrong, 2011[1]	VAC	Neutral	I was able to work and do my normal daily activity while being treated with the NPWT?	Exit survey	12	Count: 4 %: 33.3	NR
Armstrong, 2011[1]	SNaP	Strongly agree	I was able to work and do my normal daily activity while being treated with the NPWT?	Exit survey	13	Count: 6 %: 46.2	NR
Armstrong, 2011[1]	VAC	Strongly agree	I was able to work and do my normal daily activity while being treated with the NPWT?	Exit survey	12	Count: 0 %: 0	NR
Armstrong, 2011[1]	SNaP	Strongly disagree	I was able to work and do my normal daily activity while being treated with the NPWT?	Exit survey	13	Count: 0 %: 0	NR

Author, Year	Arm	Subgroup	Outcome Description	Timepoint	N Analyzed	Events	Between Arm Comparison
Armstrong, 2011[1]	VAC	Strongly disagree	I was able to work and do my normal daily activity while being treated with the NPWT?	Exit survey	12	Count: 0 %: 0	NR

N=number; NA= not applicable/not available; NPWT=negative pressure wound therapy; NR=not reported; SD=standard deviation; vs.=versus

Table 10: Study Quality

Author, Year	What is the risk of selection bias biased allocation to interventions due to inadequate generation of a randomized sequence?	What is the risk of selection bias biased allocation to interventions due to inadequate concealment of allocations before assignment?	For each main outcome or class of outcomes, what is the risk of performance bias due to knowledge of the allocated interventions by participants and personnel during the study lack of study participant and personnel blinding?	For each main outcome or class of outcomes, what is the risk of attrition bias due to amount, nature, or handling of incomplete outcome data?	What is the risk of reporting bias due to selective outcome reporting?	Are there other biases?*	Overall Quality
Armstrong, 2011[1]	Low	Low	High	High	Low	Unsure	Fair
Armstrong, 2012[2]	Low	Low	High	High	Low	Unsure	Fair
Fife, 2008[3]	High	High	High	Low	High	Yes	Poor
Ford, 2002[4]	Low	Unclear	Medium	Low	High	Yes	Fair
Lavery, 2007[5]	High	High	High	Unclear	High	Yes	Poor
Lerman, 2010[6]	High	High	High	High	Unclear	Yes	Poor
Schwien, 2005[7]	High	High	High	Unclear	Unclear	Yes	Poor
Yao, 2012[8]	High	High	Low	Low	Unclear	Yes	Fair

*= These include the following: documentation of control of underlying disease such as blood sugar measurements in diabetics, and use of compression device in venous stasis ulcers; clear outcome definition

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