Washington State Health Care Authority

Negative Pressure Wound Therapy – Home Use

Final evidence review

October 14, 2016

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Negative Pressure Wound Therapy – Home Use

A Health Technology Assessment

Prepared for Washington State Health Care Authority

FINAL REPORT

October 14, 2016

Acknowledgement

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List of Abbreviations

AMWT – advanced moist wound therapy

DFU – diabetic foot ulcer

NPWT – negative pressure wound therapy

PU – pressure ulcer

SNaP – Smart Negative Pressure Wound Care System

VAC – vacuum-assisted closure negative pressure wound therapy (generic term)

V.A.C. – Vacuum-Assisted Closure Negative Pressure Wound Therapy System (brand name)

VLU – venous leg ulcer

EVIDENCE SUMMARY

The **EVIDENCE SUMMARY** provides background information, the methods and search results for this report, findings with respect to the Key Questions, and payer policies and practice guidelines. The **EVIDENCE SUMMARY** also includes conclusions and an assessment of the quality of the evidence for each Key Question. In general, references are not cited in the **EVIDENCE SUMMARY**. The **EVIDENCE SUMMARY** ends with an **Overall Summary and Discussion**. The **TECHNICAL REPORT** provides additional detail, with full citation, regarding background information, study results, and payer policies and guidelines, but does not include conclusions or quality assessment.

Summary of Clinical Background

Wound Types of Interest

Chronic wounds, defined within this report by type or etiology and not by duration, include venous insufficiency ulcers, diabetic foot ulcers (DFUs), and pressure ulcers. Although the causes for chronic wounds vary, in all cases, at least 1 of the phases of wound healing is altered and the pathway to healing is impaired. Patients with chronic wounds may experience a range of severity, including substantial limitations in mobility and poor health-related quality of life. Chronic wounds account for an estimated $25 billion dollars in healthcare expenditures per year.

Surgical wounds are defined for this report as incisions made to skin and tissue in the course of a patient's care for an underlying health concern requiring surgical intervention. Surgical wounds that are closed by means such as sutures, staples, tape, or glue that hold the wound edges together are referred to as surgical wounds expected to heal by primary intention. Surgical wounds may also be left open for the healing process; these are referred to as surgical wounds healing by secondary intention. The scope of this report encompasses both types of surgical wounds but does not include surgical repair related to trauma, fractures, or burns, or to procedures utilizing skin flaps or grafts.

Negative Pressure Wound Therapy

Negative pressure wound therapy (NPWT), also referred to as subatmospheric pressure wound therapy or vacuum-assisted wound therapy, involves the application of negative pressure (suction) to the surface of a wound. The technology was introduced in the 1990s and is used for treatment of chronic and acute wounds. NPWT is thought to promote wound healing by providing a warm, moist wound bed while removing wound fluid. The device may remove molecular factors that inhibit cell growth, improve blood flow to the wound, enhance wound oxygenation, and improve the flow of nutrients to the wound. NPWT may also create mechanical forces that draw the wound edges together, and induce cell proliferation, cell migration to the wound, and angiogenesis.

NPWT consists of the application of a foam or gauze-type dressing sealed with an adhesive film and connected via tubing to a vacuum pump. Continuous or intermittent controlled negative pressure is applied across the wound. Wound effluent is collected in a canister.

Among the potential benefits of NPWT are symptom management, reduced frequency of dressing changes, and cost-effectiveness compared with alternative wound therapies because of faster healing times that may lead to lower overall treatment costs. There are also potential harms associated with NPWT. These include pain, retention of foreign bodies from the dressing, bleeding, infection, death from infection or bleeding, and complications stemming from loss of electricity. Safety concerns, particularly those related to home use of NPWT devices, prompted the Food and Drug Administration (FDA) to issue a preliminary Public Health Notification and Advice for Patients communication in November 2009 (click here). An updated safety communication was issued in 2011 (click here). The alerts included recommendations to clinicians regarding patient selection, monitoring, contraindications, and risk factors. Contraindications for NPWT include: inadequately debrided wounds; necrotic tissue with eschar; untreated osteomyelitis; cancer in the wound; untreated coagulopathy; nonenteric and unexplored fistulas; and exposed vital organs. Some devices also list untreated malnutrition as a contraindication.

Policy Context

This topic was selected for review through the Washington state Health Technology Assessment program. State agencies in Washington that purchase health care identify topics and evaluate potential topics based on concerns related to safety, efficacy and cost-effectiveness. NPWT is used in the treatment of slow or nonhealing wounds. Home use of NPWT includes use of a portable device. Participating agencies ranked concerns for NPWT as medium for safety, medium/high for efficacy, and medium for cost-effectiveness. An evidence-based assessment of the comparative effectiveness, safety, and cost is warranted to guide coverage policy.

Summary of Review Objectives and Methods

Review Objectives

Population: Patients diagnosed with chronic wounds (defined as venous leg ulcers, arterial leg ulcers, diabetic foot ulcers, pressure ulcers, and mixed etiology chronic wounds) or nonhealing surgical wounds

Interventions: NPWT

Comparisons: Other wound care methods; comparison of NPWT devices

Outcomes: Clinical outcomes (complete wound healing; time to complete wound healing; time to surgical readiness of the wound bed or time to wound closure; proportion of wounds closed; seroma/hematoma; reoperation; mortality; wound healing rate for healed wounds); patient-centered outcomes (return to prior level of functional activity; pain; health-related quality of life); safety (infection rates; extremity amputation; emergency room visits related to the NPWT

or treated wound; unplanned hospitalizations or surgeries related to the NPWT or treated wound; blood transfusions/bleeding)

Settings: Home or outpatient setting

Key Questions

1a. What is the clinical effectiveness of NPWT in the home or outpatient settings for treatment of chronic wounds (i.e., venous leg ulcers, arterial leg ulcers, diabetic foot ulcers, pressure ulcers, and mixed etiology chronic wounds)?

1b. What is the clinical effectiveness of NPWT in the home or outpatient settings for treatment of nonhealing closed or open surgical wounds (i.e., incisions expected to heal by primary intention or incisions expected to heal by secondary intention)?

2. What are the harms associated with NPWT?

3. Does the effectiveness of NPWT or incidence of adverse events vary by clinical history (e.g., diabetes), wound characteristics (e.g., size, chronicity), duration of treatment, types of device, or patient characteristics (e.g., age, sex, prior treatments, smoking, or other medications)?

4. What are the cost implications and cost-effectiveness of NPWT?

Methods

See the **Methods** section of the **TECHNICAL REPORT**, Appendix I, Appendix II, and Appendix III for additional detail.

Search Strategy and Selection Criteria

Core databases, PubMed, and the websites of relevant specialty societies were searched for systematic reviews, meta-analyses, economic evaluations, and practice guidelines. Systematic reviews were selected if they were of good quality and pertained to 1 or more of the key questions. Three such systematic reviews were identified and used as the source of primary studies and the foundation for update literature searches for this report. Update literature searches and study selection processes were done to update the existing systematic reviews with more recent primary evidence. The PubMed (searched on May 17, 2016, and September 12, 2016) and OVID-Embase (searched on July 1, 2016, and September 12, 2016) databases were searched for primary studies designed to answer the Key Questions.

Inclusion Criteria

- Studies conducted in patients diagnosed with chronic wounds (venous ulcers, arterial ulcers, diabetic ulcers, pressure ulcers, or mixed etiology ulcers) or nonhealing surgical wounds.
- NPWT was intervention.

- Comparative study (randomized controlled trials [RCTs] only for surgical wound studies; other comparative study designs accepted for chronic wounds as long as the number of participants was ≥ 20).
- Studies conducted in the home or outpatient setting (studies were included that were described as in "outpatient setting" if it was reported (or we interpreted) that patients were not in hospitals/acute care settings, assisted living, skilled, or maintenance nursing homes for follow-up care).
- Studies that evaluated at least 1 of the following outcomes:
    - Clinical outcomes (complete wound healing; time to complete wound healing; time to surgical readiness of the wound bed or time to wound closure; proportion of wounds closed; seroma/hematoma; reoperation; mortality; wound healing rate for healed wounds).
    - Patient-centered outcomes (return to prior level of functional activity; pain; health-related quality of life).
    - Safety (infection rates; extremity amputation; emergency room visits related to the NPWT or treated wound; unplanned hospitalizations or surgeries related to the NPWT or treated wound; blood transfusions/bleeding).

More details of these criteria, the rationale for these criteria, and the rationale for using existing systematic reviews to identify primary studies are presented in the **METHODS** section of the **TECHNICAL REPORT**.

Exclusion Criteria

- Patients with traumatic wounds, fractures, skin grafts/flaps, or burns.
- Fewer than 20 patients with chronic wounds (studies with ≤ 10 patients per group would not be adequately powered to detect meaningful differences in clinical outcomes); any-size RCT accepted for nonhealing surgical wounds.
- Studies that evaluated an NPWT that is not commercially available and approved for use in the United States.
- Studies with no comparison with other wound treatments or other NPWT devices.
- Studies that reported wound healing rates without also reporting complete wound healing (wound healing rate is considered a surrogate outcome measure because chronic wounds may not heal in a linear fashion, and cannot be used to accurately predict complete healing).
- Conference abstracts, posters, or presentations.
- Nonhuman studies.

- No original data (e.g., editorials, letters, non–systematic reviews).
- Economic evaluations conducted outside of the United States.

More details of these criteria and the rationale for these criteria are presented in the **METHODS** section of the **TECHNICAL REPORT**.

Quality Assessment

The Assessment of Multiple Systematic Reviews (AMSTAR) tool was employed to determine the quality of selected systematic reviews. The process used by Hayes for assessing the quality of primary studies and bodies of evidence is in alignment with the methods recommended by the Grading of Recommendations Assessment, Development and Evaluation (GRADE) Working Group. Like the GRADE Working Group, Hayes uses the phrase *quality of evidence* to describe bodies of evidence in the same manner that other groups, such as the Agency for Healthcare Research and Quality (AHRQ), use the phrase *strength of evidence*. A tool created for internal use at Hayes was used to guide interpretation and critical appraisal of economic evaluations. The tool for economic evaluations was based on best practices as identified in the literature and addresses issues such as the reliability of effectiveness estimates, transparency of the report, quality of analysis (e.g., the inclusion of all relevant costs, benefits, and harms), generalizability/applicability, and conflicts of interest. The Rigor of Development domain of the Appraisal of Guidelines Research and Evaluation (AGREE) tool, along with a consideration of commercial funding and conflicts of interest among the guideline authors, was used to assess the quality of practice guidelines. See the **Methods** section of the **TECHNICAL REPORT** and Appendix II and Appendix III for details on quality assessment methods.

Summary of Search Results

A total of 24 articles representing 17 primary studies met inclusion criteria. Eleven articles representing 9 primary studies were carried forward from the 3 selected systematic reviews, and 13 additional articles meeting inclusion criteria for this health technology assessment (HTA) were identified from recent literature searches and manual searches of key references. These 13 articles represent 8 newly included studies and 2 recent publications from studies included in the previously published systematic reviews.

See Appendix IV for a list of the 54 studies that were excluded from analysis after full-text review.

Five practice guidelines published in the last 10 years were identified.

Findings

Summary of Findings tables follow each Key Question. See **EVIDENCE SUMMARY, Methods,** *Quality Assessment* and the corresponding section in the **TECHNICAL REPORT**, as well as Appendix II and Appendix III, for details regarding the assessment of bodies of evidence. See Appendix V for full evidence tables.

Key Question #1a: What is the clinical effectiveness of NPWT in the home or outpatient settings for treatment of chronic wounds (venous leg ulcers, arterial leg ulcers, diabetic foot ulcers, pressure ulcers, and mixed etiology chronic wounds)?

Six primary studies meeting inclusion criteria were identified that address KQ1a. There were 2 RCTs and 4 observational studies. The RCTs ranged in size from 28 to 341 patients. The observational studies ranged in size from 78 to 2677 patients. All 6 studies compared NPWT with other types of wound treatment; there was variation across the studies in the types and the level of detail provided about comparison treatments. Wound types in the study populations varied. Three studies included only patients with diabetic foot ulcers (DFUs). One study included only patients with pressure ulcers. The remaining 2 studies included patients with lower extremity ulcers of different etiologies. Half of the studies (3 out of 6) included for KQ1a were rated as poor-quality. Two RCTs and 1 retrospective cohort study were rated as fair-quality. Overall, the quality of the evidence regarding *the clinical effectiveness of the home use of NPWT for treating chronic wounds* was considered to be low due to a lack of evidence for some outcomes, methodological limitations of available studies, few available studies for some types of chronic wounds, and obvious or potential heterogeneity within the body of evidence with respect to aspects such as treatment delivery, comparators, and methods.

Diabetic Foot Ulcers (DFUs)

A total of 4 studies (2 poor-quality and 2 fair-quality) met inclusion criteria for KQ1a and evaluated NPWT for treating DFUs. Three studies assessing NPWT for treating chronic DFUs found benefit with NPWT for complete wound healing or wound closure. Time to wound closure was shorter for patients receiving NPWT in 1 study. No other clinical outcomes eligible for this HTA were reported in these studies. Provision of pain medication as a surrogate measure for pain was reported in 1 study of DFU. Results suggest no difference between groups. The quality of evidence for each of these 3 outcomes ranged from low to very low because of lack of studies, quality of the individual studies, and mixed or uncertain applicability to 1 or more PICOS (population, intervention, comparator, outcomes, setting) elements. No studies reporting on other clinical or patient-centered outcomes were identified; therefore, the evidence is insufficient for other outcomes with respect to the home use of NPWT for treating DFUs. See **Table 1** for a summary of findings from the included studies for DFUs.

Table 1. Summary of Findings, Key Question 1a – Diabetic Foot Ulcers

Key: AMWT, advanced moist wound therapy; DFU(s), diabetic foot ulcer(s); HR, hazard ratio; NPWT, negative pressure wound therapy; NR, not reported; NS, not significant; PICOS, population, intervention, comparator, outcomes, setting; pt(s), patient(s); RCT, randomized controlled trial; tx, treatment

Number, Size, and Quality of Studies	Quality of Evidence	Direction of Findings	Key Study Results
KQ #1a. DFUs – clinical outcomes: complete wound healing/closure			
3 studies (n=3361)	**OVERALL: LOW** **Study quality:** Poor-Fair	Results favor NPWT	***Lavery, 2007 (n=2677)*** *Complete wound healing at 12 wks and 20 wks*

Number, Size, and Quality of Studies	Quality of Evidence	Direction of Findings	Key Study Results
Lavery, 2007 (retrospective cohort, poor) Blume, 2008 (RCT, fair) Yao, 2014 (retrospective cohort, fair)	**Quantity and precision:** Few studies, moderate to large sample sizes **Consistency:** Consistent results in 3 studies in favor of NPWT **Applicability to PICOS:** Mixed **Publication bias:** Unknown		*(NPWT matched; Controls):* *12 wks (all population): 39.5%; 23.9%; P<0.001* *12 wks (small ulcers <2 cm^2): 43.1%; 29.4%; P<0.05* *12 wks (medium ulcers 2-4 cm^2): 43.7%; 17.9%; P<0.05* *12 wks (large ulcers >4 cm^2): 37.8%; 13.8%; P<0.05* *20 wks (all population): 46.3%; 32.8%; P<0.001* *20 wks (small ulcers <2 cm^2): 50.3%; 38.9%; P<0.05* *20 wks (medium ulcers 2-4 cm^2): 46.1%; 48.5%; 25.2%; P<0.05* *20 wks (large ulcers >4 cm^2): 45.3%; 44.9%; 22.4%; P<0.05* ***Blume, 2008 (n=342)*** *(NPWT, AMWT)* *Complete closure during active tx phase:* *73/169 (43%); 48/166 (29%); P=0.007* *Complete closure at end of active tx phase:* *73/120 (61%); 48/120 (40%), P=0.001* *Surgical closure by split-thickness skin grafts, flaps, sutures, or amputations: 16 (10%); 14 (8%), P=*NR ***Yao, 2014 (n=342 total, includes pts with different types of lower extremity ulcers and/or multiple ulcers)*** *Incidence of wound healing for DFU* *Non-NPWT as reference group* *Unadjusted HR: 2.38 (95% CI, 1.75-3.23)* *Adjusted HR: 3.26 (95% CI, 2.21-4.83)*
KQ #1a. DFUs – clinical outcomes: time to complete wound healing/closure			
1 study (n=342) Blume, 2008 (multicenter RCT, fair)	**OVERALL: LOW** **Study quality:** Fair **Quantity and precision:** Single study **Consistency:** Single study **Applicability to PICOS:** Uncertain **Publication bias:** Unknown	Results favor NPWT	***Blume, 2008 (n=342)*** *Kaplan-Meier median estimate for 100% ulcer closure was 96 days (95% CI, 75.0-114.0) for NPWT and not determinable for AMWT (P=0.001)*
KQ1a. DFUs – patient-centered outcomes: pain			
1 study (n=1331) Fife, 2008 (retrospective	**OVERALL: VERY LOW** **Study quality:** Poor **Quantity and precision:** Single study **Consistency:** Single study	No difference	***Fife, 2008 (n=1331)*** *Provision of pain medication as a surrogate measure for pain:* *P=NS*

Number, Size, and Quality of Studies	Quality of Evidence	Direction of Findings	Key Study Results
cohort, poor)	**Applicability to PICOS:** ✓ **Publication bias:** Unknown		
KQ1a. DFUs – other clinical and patient-centered outcomes: *Insufficient, no studies*			

Arterial Ulcers

One fair-quality study reported incidence of wound healing for patients with arterial ulcers; results favored NPWT. The evidence for this outcome was considered to be of very low quality because of the availability and quality of only 1 study. No studies reporting on other clinical or any patient-centered outcomes were identified; therefore, the evidence is insufficient for other outcomes with respect to the home use of NPWT for treating arterial ulcers. See **Table 2** for a summary of the findings.

Table 2. Summary of Findings, Key Question 1a – Arterial Ulcers

Key: HR, hazard ratio; NPWT, negative pressure wound therapy; PICOS, population, intervention, comparator, outcomes, setting; pts, patients

Number, Size, and Quality of Studies	Quality of Evidence	Direction of Findings	Key Study Results
KQ #1a. Arterial ulcers – clinical outcomes: complete wound healing			
1 study (n=342) Yao, 2014 (retrospective cohort, fair)	**OVERALL: VERY LOW** **Study quality:** Fair **Quantity and precision:** Single study **Consistency:** Single study **Applicability to PICOS:** Uncertain **Publication bias:** Unknown	Favors NPWT	***Yao, 2014 (n=342 total, includes pts with different types of lower extremity ulcers and/or multiple ulcers)*** *Incidence of wound healing for arterial ulcers* *Non-NPWT as reference group* *Unadjusted HR: 2.33 (95% CI, 1.57-3.48)* *Adjusted HR: 2.27 (95% CI, 1.56-3.78)*
KQ #1a. Arterial ulcers - other clinical and patient-centered outcomes: *Insufficient, no studies*			

Pressure Ulcers

Two fair-quality studies provided results for complete wound healing with NPWT for patients with pressure ulcers compared with other wound treatments. Results were inconsistent and not statistically significant in either study. The evidence for this outcome was considered to be of very low quality because of imprecision, uncertain applicability to 1 or more PICOS elements, and lack of data. No studies reporting on other clinical or any patient-centered outcomes were identified; therefore, the evidence is

insufficient for these outcomes with respect to the home use of NPWT for treating pressure ulcers. See **Table 3** for a summary of the findings.

Table 3. Summary of Findings, Key Question 1a – Pressure Ulcers

Key: HR, hazard ratio; NPWT, negative pressure wound therapy; NS, not significant; PICOS, population, intervention, comparator, outcomes, setting; pts, patients; RCT, randomized controlled trial

Number, Size, and Quality of Studies	Quality of Evidence	Direction of Findings	Key Study Result
KQ #1a. Pressure ulcers – clinical outcomes: complete wound healing			
2 studies (n=364) Ford, 2002 (RCT, fair) Yao, 2014 (retrospective cohort, fair)	**OVERALL: VERY LOW** **Study quality:** Fair **Quantity and precision:** Few studies, small sample sizes **Consistency:** Inconsistent **Applicability to PICOS:** Mixed **Publication bias:** Unknown	Difference NS	***Ford, 2002 (n=22 pts, 35 wounds; results analyzed per wound)*** *NPWT, Control:* *2/20 (10%); 2/15 (13%) (risk difference 3%; 95% CI, –18% to 25% [calculated by Rhee, 2014])* ***Yao, 2014 (n=342 total, includes pts with different types of lower extremity ulcers and/or multiple ulcers)*** *Incidence of wound healing for pressure ulcers:* *Non-NPWT as reference group:* *Unadjusted HR: 2.19 (95% CI, 1.03-4.66)* *Adjusted HR: 1.72 (95% CI, 0.43-6.95)*
KQ #1a. Pressure ulcers – other clinical and patient-centered outcomes: *Insufficient, no studies*			

Venous Insufficiency Ulcers

One fair-quality study reported complete wound healing for patients with venous ulcers. Results suggest that venous ulcers were more likely to heal among patients who received NPWT than among those who did not receive NPWT. The evidence for this outcome was considered to be of very low quality because of the availability and quality of only 1 study. No studies reporting on other clinical or any patient-centered outcomes were identified; therefore, the evidence is insufficient for these outcomes with respect to the home use of NPWT for treating venous insufficiency ulcers. See **Table 4** for a summary of the findings.

Table 4. Summary of Findings, Key Question 1a – Venous Insufficiency Ulcers

Key: HR, hazard ratio; NPWT, negative pressure wound therapy; PICOS, population, intervention, comparator, outcomes, setting; pts, patients

Number, Size, and Quality of Studies	Quality of Evidence	Direction of Findings	Key Study Results
KQ #1a. Venous insufficiency ulcers – clinical outcomes: complete wound healing			
1 study (n=342) Yao, 2014 (retrospective cohort, fair)	**OVERALL: VERY LOW** **Study quality:** Fair **Quantity and precision:** Single study, small sample size **Consistency:** Single study **Applicability to PICOS:** Uncertain **Publication bias:** Unknown	Favors NPWT	***Yao, 2014 (n=342 total, includes pts with different types of lower extremity ulcers and/or multiple ulcers)*** *Incidence of wound healing for venous ulcers:* *Non-NPWT as reference group:* *Unadjusted HR: 4.90 (95% CI, 1.72-13.59)* *Adjusted HR: 6.31 (95% CI, 1.49-26.6)*
KQ #1a. Venous insufficiency ulcers – other clinical and patient-centered outcomes: *Insufficient, no studies*			

Mixed Ulcer Populations

For populations of patients with different wound types, results from 1 fair-quality and 1 poor-quality study favor NPWT compared with other wound treatments. Both studies suggest that more wounds healed in the NPWT groups than in the non-NPWT groups, and 1 study suggests that wounds healed faster among patients who received NPWT than among those who did not. The evidence for each of these outcomes was considered to be of low to very low quality because of lack of studies, quality of the individual studies, and mixed or uncertain applicability to 1 or more PICOS elements. No studies reporting on other clinical or any patient-centered outcomes were identified; therefore, the evidence is insufficient for these outcomes with respect to the home use of NPWT for treating ulcers of mixed etiology. See **Table 5** for a summary of the findings.

Table 5. Summary of Findings, Key Question 1a – Mixed Ulcer Populations

Key: CND, cannot determine; HR, hazard ratio; NPWT, negative pressure wound therapy; NR, not reported; PICOS, population, intervention, comparator, outcomes, setting; pts, patients

Number, Size, and Quality of Studies	Quality of Evidence	Direction of Findings	Key Study Results
KQ #1a. Mixed ulcer populations – clinical outcomes: complete wound healing			
2 studies (n=420) Lerman, 2010	**OVERALL: LOW** **Study quality:** Poor-Fair **Quantity and precision:** Few studies, small	1 study favors NPWT; trend favors	***Lerman, 2010 (n=78)*** *Complete wound healing* *NPWT, Control (statistical significance NR):* *1 month: 0%; 0%*

Number, Size, and Quality of Studies	Quality of Evidence	Direction of Findings	Key Study Results
(prospective cohort with matched historical controls, poor) Yao, 2014 (retrospective cohort, fair)	sample sizes **Consistency:** CND **Applicability to PICOS:** Mixed **Publication bias:** Unknown	NPWT in 1 study, statistical significance NR	*2 months: 20%; 7.1%* *3 months: 66.2%; 21.4%,* *4 months: 83.1%; 35.7%* ***Yao, 2014 (n=342 total, includes pts with different types of lower extremity ulcers and/or multiple ulcers)*** *Incidence of wound healing for mixed ulcers:* *Non-NPWT as reference group:* *Unadjusted HR: 2.25 (95% CI, 1.73-3.96)* *Adjusted HR: 2.63 (95% CI, 1.87-3.70)*
KQ #1a. Mixed ulcer populations – clinical outcomes: time to complete wound healing			
1 study (n=78) Lerman, 2010 (prospective cohort with matched historical controls, poor)	**OVERALL: VERY LOW** **Study quality:** Poor **Quantity and precision:** Single study, small sample size **Consistency:** Single study **Applicability to PICOS:** ✓ **Publication bias:** Unknown	Favors NPWT	***Lerman, 2010 (n=78)*** *Time to complete wound healing (mean ± SD), days:* *NPWT, Control (analysis based on pts with healed wounds):* *74.25±20.1; 148.73±63.1 (P<0.0001), represents 50% absolute reduction in time to healing*
KQ #1a. Mixed ulcer populations – other clinical and patient-centered outcomes: *Insufficient, no studies*			

Key Question #1b: What is the clinical effectiveness of NPWT in the home or outpatient settings for treatment of nonhealing closed or open surgical wounds (i.e., incisions expected to heal by primary intention or incisions expected to heal by secondary intention)?

Four fair-quality RCTs were identified for Key Question 1b. Each of the studies of surgical wounds included a unique population. The studies included patients with total knee arthroplasty, deep perivascular wound infections, patients requiring surgical treatment for a pilonidal sinus, and patients with wounds from diabetic foot wound–related amputations. In all 4 studies, wound care started in an acute care setting and was continued at home after discharge. Study sizes ranged from 20 to 162. One study was a multicenter RCT conducted in the United States, 1 was a single-center study conducted in Australia, and the other 2 were single-center studies conducted in Europe. In the 3 studies of patients with surgical wounds healing by secondary intention, vacuum-assisted closure (VAC) was compared with alginate dressing in 1 study, compared with silicone dressing in another, and compared with various dressings (moist wound care with alginates, hydrocolloids, foams, or hydrogels) in the third study. The study of patients with surgical wounds healing by primary intention compared the Prevena Incisional Management System (KCI Inc.) with conventional dry dressings.

Two studies conducted in Europe among patients who received different surgical interventions reported conflicting results with respect to median time to wound healing. One study found no difference between NPWT and silicone dressing for patients being treated for pilonidal sinus, and 1 study found that the median number of days to complete wound healing was statistically significantly shorter in the NPWT group compared with a group receiving alginate dressing for deep perivascular wound infections. It should be noted that these studies included different patient populations and evaluated NPWT therapy against different comparisons. The third study was conducted in the United States among patients with diabetic foot wound–related amputations. Results from this study suggest that a higher proportion of wounds were healed in the NPWT therapy group than in the standard moist wound therapy group, and the NPWT group healed faster. Patient-centered outcomes were reported in 3 of the 4 studies. A small RCT in which patients served as their own controls reported better scores for 2 quality-of-life factors (dressing leakage and wound protection) for the NPWT knees than the conventional dry dressing knees, but no other quality-of-life factors were statistically significantly different. Results from 2 of the studies of wound healing by secondary intention suggest no difference between NPWT and alginate dressing for quality of life, return to prior level of activity, and pain outcomes. The quality of the evidence for each of these outcomes ranged from low to very low quality because of lack of studies for specific wound types, quality of the individual studies, small sample sizes, and some inconsistencies in the findings.

The overall quality of the body of evidence for the clinical effectiveness of NPWT in the home or outpatient settings for treatment of surgical wounds healing by secondary intention is considered to be low because of the lack of evidence for some outcomes, methodological limitations of available studies, heterogeneity within the body of evidence with respect to populations, methods, and comparators, and few available studies. With respect to surgical wounds healing by primary intention, the evidence is insufficient based on 1 small RCT and limited results for eligible outcomes. The evidence eligible for this HTA was limited to 1 study each for only 4 different surgical procedures, which may limit its applicability to other types of surgery. Table 6 summarizes the findings for KQ1b.

Table 6. Summary of Findings, Key Question 1b – Surgical Wounds

Key: CDD, conventional dry dressing; EQ(-5D), European Quality of Life (5 Dimensions); IQR, interquartile range; NPWT, negative pressure wound therapy; NR, not reported; NS, not significant; PICOS, population, intervention, comparator, outcomes, setting; RCT, randomized controlled trial; tx, treatment; VAS, visual analog scale (or score)

Number, Size, and Quality of Studies	Quality of Evidence	Direction of Findings	Key Study Results
KQ #1b. Surgical wounds – clinical outcomes: complete wound healing/closure			
1 study (n=162) Armstrong, 2005, Armstrong, 2007, Apelqvist, 2008 (RCT, fair)	**OVERALL: VERY LOW** **Study quality:** Fair **Quantity and precision:** Single study **Consistency:** Single study **Applicability to PICOS:** ✓ **Publication bias:** Unknown	Favors NPWT	***Armstrong, 2005; Apelqvist, 2008 (n=162)*** *NPWT, standard tx* *Proportion of wounds healed: 43 (56%), 33 (39%); P=0.04* *Difference in proportions = 0.1702 (95% asymptotic CI, 0.0184-0.322)* *Wounds healed by secondary intention: 31 (40%), 25 (30%); P=NR* *Wounds healed after surgical closure: 12 (16%), 8 (9%); P=0.244*
KQ #1b. Surgical wounds – clinical outcomes: time to complete wound healing			
3 studies (n=231) Armstrong, 2005, Apelqvist, 2008 (RCT, fair) Biter, 2014 (RCT, fair) Monsen, 2014; Acosta, 2013, Monsen, 2015 (RCT, fair)	**OVERALL: LOW** **Study quality:** Fair **Quantity and precision:** Few studies, small sample sizes **Consistency:** Inconsistent **Applicability to PICOS:** ✓ **Publication bias:** Unknown	No difference or favors NPWT	***Armstrong, 2005; Apelqvist, 2008 (n=162)*** *Time to complete wound healing (median [IQR]), days:* *NPWT, standard tx* *56 (26-92), 77 (40-112); P=0.005* ***Biter, 2014 (n=49)*** *Time to complete wound healing (median [range]), days:* *NPWT, silicone dressing* *84 (34-349), 93 (43-264); P=0.44* ***Monsen, 2014, Acosta, 2013, Monsen, 2015 (n=20)*** *Time to complete wound healing (median [range]), days:* *NPWT, alginate dressing* *57 (25-115) (for n=9); 104 (57-175) (for n=7); P=0.026*
KQ #1b. Surgical wounds – patient-centered outcomes: pain			
2 studies (n=69) Biter, 2014 (RCT, fair) Monsen, 2014; Acosta, 2013, Monsen, 2015 (RCT, fair)	**OVERALL: VERY LOW** **Study quality:** Fair **Quantity and precision:** Few studies, small sample sizes **Consistency:** Consistent **Applicability to PICOS:** ✓ **Publication bias:** Unknown	No difference	***Biter, 2014 (n=49)*** *Pain (VAS, median):* *NPWT, silicone dressing* *Day of surgery: 1.5; 1.7; P=0.24* *14 days after surgery: 2.2; 2.5; P=0.29* ***Monsen, 2014; Acosta, 2013, Monsen, 2015 (n=20 at study start, n=17 at 4 weeks)*** *No difference was shown between the NPWT and the alginate group, in pain intensity or influence on daily life at study start or after 4 weeks of tx.*

Number, Size, and Quality of Studies	Quality of Evidence	Direction of Findings	Key Study Results
KQ #1b. Surgical wounds – patient-centered outcomes: return to prior level of activity			
1 study (n=49) Biter, 2014 (RCT, fair)	**OVERALL: VERY LOW** **Study quality:** Fair **Quantity and precision:** Single study, small sample size **Consistency:** Single study **Applicability to PICOS:** ✓ **Publication bias:** Unknown	No difference	***Biter, 2014 (n=49)*** *Time to return to work or school (median [range]), days:* *NPWT, silicone dressing* *27 (7-126); 29 (6-63); P=0.92*
KQ #1b. Surgical wounds – patient-centered outcomes: quality of life			
2 studies (n=41) Monsen, 2014; Acosta, 2013, Monsen, 2015 (RCT, fair) Manoharan, 2016 (RCT, fair)	**OVERALL: VERY LOW** **Study quality:** Fair **Quantity and precision:** Small sample sizes; 1 study for each wound type; different indicators measured **Consistency:** Single study for each wound type; different indicators measured **Applicability to PICOS:** ✓ **Publication bias:** Unknown	No difference	***Monsen, 2014; Acosta, 2013, Monsen, 2015 (n=20)*** *Quality of life, EQ-5D Index, and EQ-VAS (health status):* *NPWT n=6 with healed wound; alginate dressing n=6 with healed wound* *EQ-5D Index: 0.69 (0.30-0.80), 0.66 (0.52-0.86); P=NS* *EQ-VAS (median [q1-q3]): 70 (63.75-750), 55 (35-85.5)* *Neither scale was statistically significantly different between groups either before or after tx.* ***Manoharan, 2016 (n=21 pts; 42 knees)*** *Quality-of-life factors, mean (SD) (scale 0 = very happy, 5 = very unhappy)* *Dressing leakage: NPWT 0.14 (0.13) vs CDD 0.38 (0.34); P=0.019, ES=1.02* *Wound protection: NPWT 0.16 (0.05) vs CDD 0.33 (0.16); P=0.001, ES=0.0212* *NS differences for odor, itch, movement, body image, self-esteem, personal hygiene, sleep, and pain*
KQ #1b. Surgical wounds – other clinical and patient-centered outcomes: *insufficient, no studies*			

Key Question #2: What are the harms associated with NPWT?

Safety outcomes sought for this HTA were infection rates; extremity amputation; emergency room visits related to the NPWT or treated wound; unplanned hospitalizations or surgeries related to the NPWT or treated wound; and blood transfusions/bleeding. Six studies were identified that reported on adverse events in patients with chronic wounds. These studies evaluated NPWT compared with other wound treatments in patients with DFUs, pressure ulcers, and mixed ulcers. No studies comparing NPWT with other wound treatments reporting adverse events for patients with arterial ulcers or venous insufficiency ulcers were identified. Results from 2 studies favored NPWT with respect to rates of

amputation and a third study favored NPWT with respect to rates of infection among patients with DFUs. For patients with pressure ulcers, 1 study reported statistically significant results in favor of NPWT for emergent care and hospitalization. The study reporting adverse events among a mixed ulcer population did not report data for the comparison group. The evidence for harms associated with the home use of NPWT to treat chronic wounds was considered to be of low quality because of the quality of the individual studies, few studies for specific wound types, and uncertain applicability to 1 or more of the PICOS elements.

Adverse events were reported in 5 studies evaluating NPWT compared with other wound treatments for surgical wounds. None of the studies reported statistically significant differences between groups for the adverse events described in the publications. The evidence for harms associated with the home use of NPWT to treat surgical wound healing by primary intention or secondary intention was considered to be of very low quality because of the quality of the individual studies, few studies for specific wound types, and small sample sizes.

The quality of the overall body of evidence for *harms associated with home use of NPWT for chronic or surgical wounds is considered to be low* because of methodological limitations of available studies, few available studies for specific types of wounds, and uncertain applicability of some of the studies to the home setting. See **Table 7** for a summary of the evidence.

Table 7. Summary of Findings, Key Question #2 – Harms

Key: DFU(s), diabetic foot ulcer(s); iNPWTd , incisional negative pressure wound therapy device; IV, intravenous; NPWT, negative pressure wound therapy; NR, not reported; NS, not significant; OR, odds ratio; PICOS, population, intervention, comparator, outcomes, setting; pts, patients; PU, pressure ulcers; RCT, randomized controlled trial; RR, risk ratio; tx, treatment; VAC, vacuum-assisted closure

Number, Size, and Quality of Studies	Quality of Evidence	Direction of Findings	Key Study Results
KQ #2: Chronic wounds			
6 studies (n=20,445) Blume, 2008 (RCT, fair) Fife, 2008 (retrospective observational, poor) Ford, 2002 (RCT, poor) Frykberg, 2007 (retrospective observational, fair)	**OVERALL: LOW** **Study quality:** Poor-Fair **Quantity and precision:** Few studies for each wound type, small to large study sizes **Consistency:** Consistent **Applicability to PICOS:** Mixed **Publication bias:** Unknown	No difference or favors NPWT	***Blume, 2008 (n=341) – DFUs*** *Complications (NPWT group; AMWT group), n (%):* *Secondary amputations: 7 (4%); 17 (10%); P=0.035* *Edema: 5 (3%); 7 (4%); P=NS* *Wound infection: 4 (2%); 1 (<1%); P=NS* *Cellulitis: 4 (2%); 1 (<1%); P=NS* *Osteomyelitis: 1 (<1%); 0 (0%); P=NS* *Staphylococcus infection: 1 (<1%); 0 (0%); P=NS* *Infected skin ulcer: 1 (<1%); 2 (1%); P=NS* ***Fife, 2008 (n=1331) – DFUs*** *Complications (NPWT group; Control group):* *Bleeding (discontinued NPWT due to bleeding): No DFU pts with the V.A.C. required the discontinuation of the V.A.C. because of bleeding.* *Bleeding (sanguineous drainage): No cases found*

Number, Size, and Quality of Studies	Quality of Evidence	Direction of Findings	Key Study Results
Lerman, 2010 (retrospective observational, poor) Schwien, 2005 (retrospective observational, poor)			*in either group* *Infection (antibiotics): V.A.C. pts had fewer antibiotic prescriptions (numbers NR); P<0.05* *Infection (culture): V.A.C. pts had fewer cultures taken (numbers NR); P<0.05* ***Ford, 2002 (n=28) – PUs*** *Complications (VAC group; Control group), n (%):* *Sepsis: 1 (0.5%); 0 (0%); P=NR* *Extremity amputation: 1 (0.5%); 0 (0%); P=NR* ***Frykberg, 2007 (n=16,319) – DFUs*** *Complications:* *Amputations – Overall, NS differences without stratification or risk adjustment* *Amputations – Overall, cost-based risk-adjusted analysis:* *Commercial dataset: Control group 21.4% vs NPWT group 14.1%; P=0.0951* *Medicare dataset: Control group 16.6% vs NPWT group 10.8%; P=0.0077* *Amputations – Overall, debridement-based risk adjusted analysis:* *Commercial dataset: Control group 21.4% vs 18.3%; P=0.5221* *Medicare dataset: Control group 16.6% vs NPWT group 11.2%; P=0.0128* ***Lerman, 2010 (n=78) – Mixed ulcers*** *7 NPWT pts had complications related to the study protocol requiring withdrawal: allergic skin reaction to the hydrocolloid dressing (n=1), wound infection (n=1), bleeding post debridement (n=1), worsening lower extremity edema (n=1), and maceration to periwound skin (n=3)* *NOTE: Data for these and 8 other pts who withdrew were not included in the final analysis.* ***Schwien, 2005 (n=2348) – PUs*** *Complications (NPWT group; Control group):* *Emergency room visits:* *All pts: 0/60 (0%); 189/2288 (8%); P<0.01* *Stage III PU: 0 (0%); 126 (7%); P<0.01* *Stage IV PU: 0 (0%); 63 (11%); P<0.01* *Wound-related hospitalization:* *All pts: 3/60 (5%); 310/2288 (14%); P<0.01* *Stage III PU: 1 (3%); 194 (11%); P<0.01* *Stage IV PU: 2 (7%); 116 (20%); P<0.01*
KQ #2: Surgical wounds			
5 studies (n=471)	**OVERALL: VERY LOW** **Study quality:** Fair	No difference or favors	***Armstrong, 2005; Apelqvist, 2008 (n=162)*** *Complications (NPWT group; Standard tx group):*

Number, Size, and Quality of Studies	Quality of Evidence	Direction of Findings	Key Study Results
Armstrong, 2005, Apelqvist, 2008 (RCT, fair) Biter, 2014 (RCT, fair) Karlakki, 2016 (RCT, fair) Manoharan, 2016 (RCT, fair) Monsen, 2014; Acosta, 2013, Monsen, 2015 (RCT, fair)	**Quantity and precision:** Few studies, small sample sizes **Consistency:** Consistent **Applicability to PICOS:** ✓ **Publication bias:** Unknown	NPWT	*Second amputation: 2 (3%); 9 (11%); P=0.060; RR 0.225 (95% CI, 0.05-1.1)* *5 (6%) of standard tx group received high-level (above foot) amputation—2 above knee, 3 below knee; no high-level amputations were done in the NPWT group.* *Infections and infestations: 25 (32%); 27 (32%); P=1.000* *Wound infection: 13 (17%); 5 (6%)* *In the NPWT group, 3 infections were classified as mild, 6 as moderate, 4 as severe; none were deemed related to tx. In the Standard tx group, 2 were classified as mild, 1 as moderate, and 2 as severe; 2 of the 5 events were deemed to be related to the tx, 1 of which was serious.* *Tx-related adverse events: 9 (12%); 11 (13%)* *1 event in the NPWT group was classified as serious; 5 events in the Standard tx group were classified as serious.* ***Biter, 2014 (n=49)*** *Complications (NPTW group; Silicone dressing group), n (%):* *Wound infection/abscess: 2 (8%); 2 (8%); P=1.00* ***Karlakki, 2016 (n=220)*** *Overall wound complications: OR 4.0, 95% CI, 0.95-30; P=0.06 (favors NPWT group)* *Readmissions (iNPWTd; Control): 0, 1* *Surgical site infections (iNPWTd; Control): NR; 7 suspected* *Cellulitis: 1 in iNPWTd group, treated by general practitioner* *Blisters (iNPWTd; Control): 11%; 1%* ***Manoharan, 2016 (n=21 pts; 42 knees)*** *Wound complications: NPWT: 1 knee with severe blistering requiring hospital readmission and IV antibiotics Control: 1 knee with persistent wound drainage (treated with NPWT as an inpatient for 2 days)* *Readmissions: 1 pt with blistering on knee receiving NPWT* *Infections: No wound dehiscence or infection during trial* ***Monsen, 2014, Acosta, 2013, Monsen, 2015 (n=20)*** *Complications (NPWT group; dressing group), n (%):*

Number, Size, and Quality of Studies	Quality of Evidence	Direction of Findings	Key Study Results
			Amputation: 3 (30%); 2 (20%) *Mortality, in-hospital: 0; 1 (10%)* *Mortality, total: 2 (20%); 5 (50%) by end of follow-up (P=0.35)*

Key Question #3: Does the effectiveness of NPWT or incidence of adverse events vary by clinical history (e.g., diabetes), wound characteristics (e.g., size, chronicity), duration of treatment, types of device, or patient characteristics (e.g., age, sex, prior treatments, smoking, or other medications)?

Four studies were identified providing information pertaining to KQ3 with respect to patients with chronic wounds and 1 study was included for surgical wounds. Among the studies of chronic wounds, 1 was a fair-quality RCT, 1 was a fair-quality observational study, and 2 were poor-quality observational studies. Two of these studies compared different NPWT devices. An RCT conducted by Armstrong et al. (2011 and 2012) provides a comparison of the V.A.C. Therapy System (KCI Inc.), and the SNaP Wound Care System (Spiracur Inc.), and the Law et al. (2015) study provides a comparison of the V.A.C. Therapy System with non-KCI models. The studies by Lavery et al. (2007) and Yao et al. (2014) provide information about the role of wound size and chronicity when NPWT is compared with other wound treatments. However, the Yao et al. study does not provide information about chronicity for the alternative wound treatment group; therefore, the results are shown here for information only and are not considered in the overall body of evidence. No studies looked at comparative effectiveness in relation to clinical history, duration of treatment, or patient characteristics. A fair-quality study by Armstrong et al. (2005 and 2007) assessed the role of wound chronicity in healing among patients with diabetes who have had partial foot amputations.

Overall, evidence of varying clinical effectiveness or rates of harms is considered to be very low because of a lack of studies for specific wound types and comparisons, methodological limitations of the few available individual studies, and lack of evidence for some outcomes.

Different Types of NPWT Devices Compared with Each Other (SNaP Versus V.A.C.)

In a fair quality RCT enrolling 162 patients with DFUs or venous leg ulcers (VLUs) and evaluating treatment with SNaP compared with V.A.C. for up to 16 weeks, complete wound healing was assessed at 4, 8, 12, and 16 weeks. A Kaplan-Meier survival analysis showed no significant difference between the SNaP and V.A.C. groups for the proportion of wounds healed over time (*P*=0.9620); analyses adjusting for baseline wound size were also not statistically significant. Time to surgical readiness of the wound bed and mortality were not reported. Although percentage decrease in the wound area was reported, the wound healing rate for healed wounds was not reported. Information about return to prior level of activity and pain were also evaluated in this RCT through responses to exit interviews from 105 patients

who completed the study. Patients who were treated with the SNaP device were 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% and 58%, respectively). A higher percentage of SNaP-treated patients than V.A.C.-treated patients reported that their activity level either increased or stayed the same (83% and 48%, respectively). *P* values were calculated for these outcomes by Rhee and colleagues (2014), authors of an AHRQ systematic review. The results were statistically significant. The level of pain was examined by a summation of pain scores, as compared with what would be the expected sum of scores. It is unclear how the expected summary score number was obtained, and further description of the definition of the pain scores is not provided. Patient-reported pain scores were not statistically significantly different between the 2 NPWT devices. In a subanalysis of 40 patients (V.A.C. n=21; SNaP n=19) with VLUs from this same RCT, Kaplan-Meier estimates suggest no significant difference in the proportion of VLU patients who completely healed over time (*P*=0.3547 unadjusted for baseline wound size; *P*=0.4656 adjusted for baseline wound size). Rates of adverse events reported in this RCT for the full patient population were similar between the groups. The rate of clinically determined infection was 3.1% in the SNaP (n=2) and 7.4% in the V.A.C. group (n=5) (*P*=0.28; *P* value calculated by Rhee et al.). In the subanalysis of VLUs, the rate of infection was found to be 5.3% in the SNaP group (n=1) and 9.5% in the V.A.C. group (n=2) (*P*=1.000). Marston et al. (2015) report that rates of adverse events among the subgroup of patients with VLUs were similar between treatment groups and consistent with the larger study population.

Different Types of NPWT Devices Compared with Each Other (V.A.C. Versus non-KCI Models)

In a publication of findings from a poor-quality retrospective national claims database analysis comparing V.A.C. NPWT to non-KCI NPWT devices for patients with chronic and acute wounds (n=13,556), investigators reported hospital readmission rates for the period following an initial NPWT claim in an outpatient setting. At 3 months and 6 months, wound-related readmission rates were statistically significantly lower for the V.A.C. group compared with the non-KCI device group across all wound types. At 3 months, the rates in each group were 5% and 8%, respectively, for the V.A.C. (n=12,843) and non-KCI device (n=713) groups ($P \leq 0.01$). The rates at 6 months were 6% and 11%, respectively, for the V.A.C. (n=11,073) and non-KCI device (n=601) groups ($P \leq 0.01$). Significant differences in favor of V.A.C. were also reported for mean per-patient inpatient stays and emergency room visits at 3 months and 6 months for all wound types. When mean per-patient inpatient stays and emergency room visits at 3 months and 6 months were analyzed by wound category (nonhealing surgical wounds, open wounds, and pressure ulcers) statistical significance did not persist for inpatient stays at 3 months and at 6 months for nonhealing surgical wounds or emergency room visits for pressure ulcers at 3 months and at 6 months.

NPWT Compared with Other Wound Treatments: Wound Size and Chronicity

One poor-quality study among patients with DFUs (n=2677) examined healing in relation to ulcer size and wound duration at 12 and 20 weeks. The authors reported that wounds of all sizes treated with NPWT were more likely than those treated with standard wound care to achieve successful treatment endpoint (closure through secondary intention or through surgical intervention, or if adequate granulation tissue was present) ($P<0.05$). Moreover, 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 than those treated with standard wound care. At 20 weeks, NPWT healed significantly more wounds compared with standard wound care only among wounds older than 12 months ($P<0.05$).

One fair-quality study among patients with mixed etiology chronic wounds (n=342) evaluated whether the timing of NPWT application had an effect on healing. 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 [HR], 3.38; 95% CI, 1.68 to 6.82).

A secondary analysis from a fair-quality RCT (n=162) (Armstrong et al., 2005; Armstrong et al., 2007) assessed the role of wound chronicity in wound healing after partial foot amputation in patients with diabetes. Acute wounds were those < 30 days after amputation and chronic wounds were those > 30 days after amputation. Results indicate no statistically significant difference between the NPWT group and standard wound therapy group in the proportion of acute and chronic wounds achieving complete wound closure (acute $P=0.072$; chronic $P=0.320$). Time to complete closure was significantly different in favor of NPWT compared with the standard wound treatment group for both the acute ($P=0.030$) and chronic wounds ($P=0.033$).

Key Question #4: What are the cost implications and cost-effectiveness of NPWT?

Six studies were found that provided information about the cost of NPWT compared with usual care or other NPWT devices. One study compared the cost of mechanical NPWT (SNaP) with electrically powered NPWT devices and standard of care. Five studies compared the cost of NPWT using V.A.C. with other wound therapies or other NPWT devices. All studies found that the primary NPWT device of interest (SNaP or V.A.C.) resulted in cost savings over usual care or alternative NPWT devices. Cost analyses are limited by the limitations of the available evidence base described within this HTA and the applicability of the evidence selected to set up models for economic analyses.

Practice Guidelines

The search of the core sources and relevant specialty groups identified 5 guidelines regarding NPWT and published within the past 10 years. The general recommendations provided by the guidelines are summarized in **Table 8**. Additional details, by guideline, are presented in **Appendix VI**. See also **Practice Guidelines** in the **TECHNICAL REPORT** for additional background information on guidelines.

Table 8. Summary of Practice Guideline Recommendations
Key: DFU(s), diabetic foot ulcer(s); FDA, Food and Drug Administration; GL(s), guideline(s); NPWT, negative pressure wound therapy; PU(s), pressure ulcer(s); VLU(s), venous leg ulcer(s)

Quantity of Individual GLs	Individual GL Quality	Recommendations
Multiple Wound Types		
1 International Expert Panel on Negative Pressure Wound Therapy (NPWT-EP) (2011)	Fair	PUs: • NPWT may be used until surgical closure is possible/desirable. • Alternatively, NPWT should be considered to achieve closure by secondary intention. • NPWT should be used to reduce wound dimensions. • NPWT should be used to improve the quality of the wound bed. DFUs: • NPWT must be considered as an advanced wound care therapy for postoperative Texas grade 2 and 3 diabetic feet without ischemia. • NPWT must be considered to achieve healing by secondary intention. • Alternatively, NPWT should be stopped when wound has progressed suitably to be closed by surgical means. • NPWT should be considered in an attempt to prevent amputation or re-amputation. Ischemic lower limb wounds: • The cautious use of NPWT in chronic limb ischemia when all other modalities have failed may be considered in specialist hands but never as an alternative for revascularization. • NPWT may be considered as an advanced wound care therapy for lower limb ulceration after revascularization. • The use of NPWT is NOT indicated in acute limb ischemia. VLUs: • If first-line therapy (compression) is not efficacious, NPWT should be considered to prepare the wound for surgical closure as part of a clinical pathway. • Use of gauze may be considered to reduce pain during dressing changes in susceptible patients.
DFUs		
1 International Working Group on the Diabetic Foot (2016)	Good	Topical NPWT may be considered in postoperative wounds, even though the effectiveness and cost-effectiveness of the approach remain to be established. (weak; moderate) It is not possible to make a recommendation on the use of NPWT in nonsurgical wounds because of the lack of available evidence.
PUs		

Quantity of Individual GLs	Individual GL Quality	Recommendations
2 National Pressure Ulcer Advisory Panel (2014) Association for the Advancement of Wound Care (2010)	1, Good 1, Fair	Consider NPWT as an early adjuvant for the treatment of deep, category/stage III and IV PUs. (Strength of Evidence = B; Strength of Recommendation = Weak positive recommendation) ADVANCED OR ADJUNCTIVE INTERVENTIONS IF PU IS UNRESPONSIVE TO A-LEVEL MANAGEMENT: NPWT – No consistent effect on PU healing. Increased granulation, less fibrin compared to Redon drain, earlier use may shorten home care stays. Lower cost than gauze. The FDA has advised caution in selecting patients for this therapy due to serious, occasionally fatal, complications.
VLUs		
1 Society for Vascular Surgery (SVS) and the American Venous Forum (AVF) (2014)	Good	GL 4.24: NPWT – The GL suggests against routine primary use of NPWT for VLUs (Grade = 2; Level of Evidence = C) There is currently not enough information to support the primary use of NPWT for VLUs. Evidence supports positive effects with the use of negative pressure therapy for wound healing in general. Tissue granulation, area and volume reduction, and reductions in bioburden have all been reported. There have been few studies specifically studying negative pressure therapy for VLUs, with most studies reporting on mixed wound causes. There has been an increase in the use of NPWT for wound bed preparation to augment skin graft healing.

Selected Payer Policies

At the direction of WA State HCA, published coverage policies for the following organizations were sought: Aetna, Centers for Medicare & Medicaid Services (CMS), Oregon Health Evidence Review Commission (HERC), Group Health Cooperative, and Regence Blue Cross/Blue Shield. The lack of a published coverage policy does not necessarily mean the payer does not provide coverage.

See **Selected Payer Policies** in the **TECHNICAL REPORT** for additional details and links to policy documents.

Aetna

Aetna considers NPWT pumps medically necessary for ulcers and wounds encountered in an inpatient setting or in the home setting when the criteria are met. An NPWT pump and supplies are considered not medically necessary if any contraindication for use (as identified in the policy) is present.

Centers for Medicare & Medicaid Services (CMS)

No CMS National Coverage Determination (NCD) for NPWT was identified on July 25, 2016 (search National Coverage Documents by keywords *negative pressure* or *wound* or *ulcer* or *e2402* in all

documents at: https://www.cms.gov/medicare-coverage-database/search/advanced-search.aspx). In the absence of an NCD, coverage decisions are left to the discretion of local Medicare carriers. There is a Local Coverage Determination (LCD) for NPWT pumps (L33821) that was effective July 1, 2016. The LCD was issued by Noridian Healthcare Solutions LLC, a Medicare contractor in the state of Washington.

The LCD states that an NPWT pump and supplies are covered when ulcers and wounds are encountered in an inpatient setting or in the home setting when the criteria are met.

Group Health Cooperative

Group Health Cooperative covers NPWT pumps and supplies for wound edema, exudate management, and stimulation of granulation for an initial 14-day course when the criteria are met for ulcers and wounds encountered in an inpatient setting or in the home setting, there is a goal of therapy clearly stated, and there are no contraindications for use (as identified in the policy).

Oregon Health Evidence Review Commission (HERC)

No published evidence-based coverage policy for NPWT was identified on the Oregon HERC website. The Prioritized List of Health Services published by the HERC references a Guideline Note regarding NPWT (Guideline Note 62, Negative Pressure Wound Therapy) for lines 8, 30, 51, 84, 210, 212, 240, 290, 384, and 428. The note states, “Negative pressure wound therapy (CPT 97605-97608, HCPCS G0456, G0457) is included on these lines only for patients who: have wounds that are refractory to or have failed standard therapies; are not suitable candidates for surgical wound closure; or, are at high risk for delayed or non-healing wounds due to factors such as compromised blood flow, diabetic complications, wounds with high risk of fecal contamination, extremely exudative wounds, and similar situations.”

Regence Group

No published evidence-based coverage policy for NPWT was identified on the Regence Group website.

Overall Summary and Discussion

Evidence-Based Summary Statement

The availability and use of NPWT devices for treating a variety of wounds has been increasing across the care spectrum. The aim of this HTA was to identify, assess, and summarize the best available evidence applicable to the home use of NPWT.

Results of the included studies were generally consistent for the few outcomes reported suggesting better or similar outcomes for NPWT compared with other wound treatments. However, with respect to the other domains considered in evaluating the overall body of evidence for each key question, there were few or no studies providing data for some outcomes, the quality of the included studies ranged from poor to fair and there was some uncertainty about the applicability of some of the studies to one or more of the PICOS elements. These factors influenced the assessments for each key question.

Overall, the quality of the evidence regarding the clinical effectiveness of the home use of NPWT for treating chronic wounds was considered to be low. The chronic wound category with the most studies

for this key question was DFUs (n=4). Evidence from 3 studies that compared NPWT with other wound therapies for treating chronic DFUs suggests benefit with NPWT for complete wound healing or wound closure (3 studies) and time to wound closure (1 study). Only 1 study reported results for a patient-centered outcome; this study found no difference between groups for provision of pain medication as a surrogate measure for pain. One study provided evidence for the home use of NPWT for treating arterial ulcers or venous ulcers. The study suggests that complete wound healing is more likely among arterial or venous ulcer patients who receive NPWT than those who do not. Two studies focused on patients with pressure ulcers. Results from these studies were inconsistent and not statistically significant in either study. Results from two studies that evaluated mixed etiology wounds suggests that NPWT heals a higher proportion of wounds than other wound therapies, and one study suggests a shorter time to complete wound healing with the use of NPWT. There were no studies identified that provided evidence for other eligible clinical `outcomes or patient-centered outcomes for chronic wounds.

The overall quality of the body of evidence for the clinical effectiveness of NPWT in the home or outpatient settings for treatment of surgical wounds was considered to be low. Each of the 4 RCTs enrolled patients undergoing different surgical procedures and they compared different alternative wound therapies. Overall, the results favored NPWT for the clinical outcomes reported: complete wound healing (1 study) and time to complete wound healing (3 studies). No differences between groups were found for the patient-centered outcomes of pain (2 studies) and return to prior level of activity (1 study). One study reported better quality-of-life scores for 2 factors (dressing leakage and wound protection) but no differences for other quality-of-life factors; another study found no difference between groups for quality of life.

The quality of the overall body of evidence for harms associated with home use of NPWT for chronic wounds and surgical wounds is considered to be low. Six studies evaluated NPWT compared with other wound treatments in patients with DFUs, pressure ulcers, and mixed ulcers. No eligible studies were identified comparing NPWT with other wound treatments reporting adverse events for patients with arterial ulcers or venous insufficiency ulcers. Results from 2 studies favored NPWT with respect to rates of amputation and a third study favored NPWT with respect to rates of infection among patients with DFUs. For patients with pressure ulcers, 1 study reported statistically significant results in favor of NPWT for emergency care and hospitalization. The study reporting adverse events among a mixed ulcer population did not report data for the comparison group. Adverse events were reported in 5 studies evaluating NPWT compared with other wound treatments for surgical wounds. Three of the studies, which were conducted in populations of patients with surgical wounds healing by secondary intention, reported no statistically significant differences between groups for the adverse events described in the publications. The remaining 2 studies were conducted among patients with closed surgical wounds. One of these reported a statistically significant difference in favor of NPWT with respect to wound complications and the other reported 1 adverse event in each group.

Overall, evidence of varying clinical effectiveness or rates of harms from 4 studies among patients with chronic wounds and 1 study among patients with surgical wounds is considered to be of very low quality. Among the 4 chronic wound studies, 1 study compared the V.A.C. Therapy System (KCI Inc.) with the SNaP Wound Care System (Spiracur Inc.); another compared the V.A.C. Therapy System with

unspecified non-KCI models. Two other studies compared NPWT with other wound therapies and evaluated outcomes based on wound size or chronicity. No studies looked at comparative effectiveness in relation to clinical history, duration of treatment, or patient characteristics. In the study comparing V.A.C. with SNaP, no differences were found for proportion of wounds healed over time or patient-reported pain scores. However, patients in the SNaP group were statistically 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. Also, a higher percentage of SNaP-treated patients than V.A.C.-treated patients reported that their activity level either increased or stayed the same. Rates of adverse events reported in this RCT for the full patient population were similar between the groups. In a comparison of hospital readmission rates for V.A.C. patients compared with patients using a non-KCI NPWT device, readmission rates were lower for the V.A.C. group at 3 and 6 months. Analyses of wound size and chronicity in 1 study favored NPWT over other wound therapies. The remaining study did not provide comparative data between NPWT and other wound treatments. The study of patients with surgical wounds included a secondary analysis that assessed the role of wound chronicity in wound healing after partial foot amputation in patients with diabetes. Results indicate no statistically significant difference between the NPWT group and standard wound therapy group in the proportion of acute and chronic wounds achieving complete wound closure. Time to complete closure was significantly different in favor of NPWT compared with the standard wound treatment group for both the acute and chronic wounds.

Six studies were found that provided information about the cost of NPWT compared with usual care or other NPWT devices. One study compared the cost of mechanical NPWT (SNaP) with electrically powered NPWT devices and standard of care. Four studies compared the cost of NPWT using V.A.C. with other wound therapies or other NPWT devices. All studies found that the primary NPWT device of interest (SNaP or V.A.C.) resulted in cost savings over usual care or alternative NPWT devices.

Gaps in the Evidence

The following evidence is needed to better answer the Key Questions of this report:

- Future work needs to include larger, more rigorous prospective studies conducted by independent researchers designed to evaluate direct evidence of NPWT compared with consistent comparators for treatment of specific wound types in the home setting. Consistent definitions and measurements for outcomes across studies would also be helpful.

- Publications with better reporting of study protocols, including settings and details about who changes wound dressings and details about interventions, comparators, and concomitant treatments are needed. Clear descriptions of inpatient and outpatient care would help identify studies applicable to the questions relevant to home use. This is key for performing future comparative assessments, as wound care is highly dependent on factors such as who performs the wound care. The complex nature of wound care, wide variety of products, and differing backgrounds of providers (nursing, surgical, nonsurgical, etc.) make it very difficult to replicate across various healthcare settings.

- Study methods need to include more details about collecting and analyzing clinical, patient-centered, and harms outcomes.
- There is a need for more studies examining response to treatment according to patient characteristics such as comorbidities, smoking status, and age.

TECHNICAL REPORT

Clinical Background

The purpose of this HTA is to assess the evidence on the use of negative pressure wound therapy (NPWT) in the home setting. The types of wounds of most interest are those likely to be managed in the home setting. These include common chronic wounds such as venous insufficiency ulcers, diabetic foot ulcers (DFUs), and pressure ulcers (Rhee et al., 2014). Also of interest to the Washington State Health Technology Assessment program is the use of NPWT in the home setting to treat surgical wounds.

Wound Types of Interest

Chronic wounds, defined within this report by type or etiology and not by duration, include venous insufficiency ulcers, DFUs, and pressure ulcers. Although the causes for chronic wounds vary, in all cases, at least 1 of the phases of wound healing is altered and the pathway to healing is impaired. Patients with chronic wounds may experience a range of severity, including substantial limitations in mobility and poor health-related quality of life. Chronic wounds account for an estimated $25 billion dollars in healthcare expenditures per year (Rhee et al., 2014).

Surgical wounds are defined for this report as incisions made to skin and tissue in the course of a patient's care for an underlying health concern requiring surgical intervention. Surgical wounds that are closed by means such as sutures, staples, tape, or glue that hold the wound edges together are referred to as surgical wounds expected to heal by primary intention. Surgical wounds may also be left open for the healing process; these are referred to as surgical wounds healing by secondary intention. The scope of this report encompasses both types of wounds but does not include surgical repair of wounds related to trauma, fractures, or burns, or to procedures using skin grafting/flaps.

DFUs

Complications of diabetes include neuropathy and ischemia affecting the feet. These conditions contribute to the formation of 2 types of DFUs—neuropathic and neuroischemic ulcers (Edmonds and Foster, 2006). A DFU is a full-thickness wound penetrating through the skin. DFUs may lead to infection of surrounding tissue and subsequently to foot and lower limb amputations (Frykberg and Williams, 2007). The Centers for Disease Control and Prevention (CDC) reports that approximately 73,000 lower limb amputations were performed in adults with diabetes in 2010 (CDC, 2014). A near 50 percent decrease in the rate of amputations among patients with diabetes from 2010 to 2014 is attributed to advances in clinical care, increased availability of preventive healthcare, control of risk factors, and increased awareness of the potential complications of diabetes. However, the number of people affected by complications of diabetes, including DFUs, is still high and is expected to remain high (CDC, 2015).

Venous Insufficiency Ulcers

A venous leg ulcer (VLU) is an open skin lesion of the leg or foot that occurs in an area affected by venous hypertension and poor blood circulation. Risk factors include older age, obesity, previous leg injuries, deep venous thrombosis, and phlebitis. Open ulcers may persist for a long period of time (Collins and Seraj, 2010). VLUs account for approximately 70 percent of all leg ulcers. Estimates suggest that more than 2 million people in the United States have chronic venous insufficiency, 20 percent of whom may develop VLUs. The recurrence rate of VLUs within 10 years is approximately 50 percent (O'Donnell et al., 2014). Pain, disability, and psychosocial effects from VLUs may be substantial.

Pressure Ulcers

The National Pressure Ulcer Advisory Panel (NPUAP) defines a pressure ulcer (or pressure injury) as "…localized damage to the skin and/or underlying soft tissue usually over a bony prominence or related to a medical or other device. The injury can present as intact skin or an open ulcer and may be painful. The injury occurs as a result of intense and/or prolonged pressure or pressure in combination with shear. The tolerance of soft tissue for pressure and shear may also be affected by microclimate, nutrition, perfusion, co-morbidities and condition of the soft tissue."(NPUAP, 2016) Those most at risk for pressure ulcers include diabetic, obese, and elderly patients, and those who have a medical condition limiting their ability to change positions. The prevalence of pressure ulcers varies between 0.31 to 0.70 percent per year (Rhee et al., 2014). Between 1995 and 2008, the incidence of pressure ulcers increased by as much as 80 percent (Sullivan and Schoelles, 2013).

Surgical Wounds

Surgical incisions are often closed by means such as sutures, staples, tape, or glue that hold the wound edges together. This is called healing by primary intention. Some closed surgical wounds may be slow to heal or fail to heal because of infection or other factors such as the patient's age or presence of co-occurring medical conditions (e.g., diabetes, malnutrition, obesity, cardiovascular disease). Failure to heal may also be caused by separation of the wound edges (dehiscence) because of broken sutures, sutures cutting through the skin, or slipped knots. Infection may also contribute to dehiscence (Webster et al., 2014).

Healing by secondary intention is when wounds are intentionally left open to heal. Healing by secondary intention can be an intended part of postsurgical care, or it can be an approach implemented after the failure of wound closure, such as when there is dehiscence caused by inflammation and edema. A recent systematic review by the Cochrane Collaboration stated that good data on the incidence, prevalence, healthcare expenditures, and quality of life effects related to surgical wounds healing by secondary intention are not readily available (Dumville et al., 2015a).

Negative Pressure Wound Therapy

NPWT, also referred to as subatmospheric pressure wound therapy or vacuum-assisted wound therapy, involves the application of subatmospheric pressure to the surface of a wound. The technology was introduced in the 1990s and is used for treatment of chronic and acute wounds. NPWT is thought to

promote wound healing by providing a warm, moist wound bed while removing wound fluid. The device may remove molecular factors that inhibit cell growth, improve blood flow to the wound, enhance wound oxygenation, and improve the flow of nutrients to the wound. NPWT may also create mechanical forces that draw the wound edges together, and induce cell proliferation, cell migration to the wound, and angiogenesis.

NPWT comprises the application of a foam or gauze-type dressing sealed with an adhesive film and connected via tubing to a vacuum pump. Continuous or intermittent controlled negative pressure (suction) is applied across the wound. Wound effluent is collected in a canister. Figure 1 shows a generalized NPWT system.

Figure 1. Negative Pressure Wound Therapy System

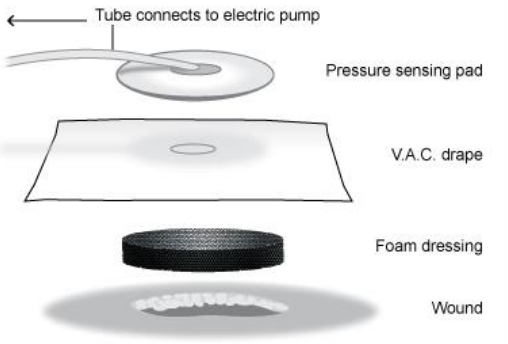


Figure 1. Negative Pressure Wound Therapy System

Food and Drug Administration (FDA)

The V.A.C. Therapy System, manufactured by Kinetic Concepts Inc. (KCI), was the first FDA-approved NPWT device available in the United States. Many other NPWT devices produced by other manufacturers now have FDA clearance. Stationary and portable NPWT systems are available, and recently, a system (SNaP Wound Care System; Spiracur Inc.) that employs a constant force spring to maintain negative pressure rather than relying on electric or battery power has been developed. **Appendix VII** lists some of the NPWT devices that have been or are currently commercially available in the United States. This is not an exhaustive list and is intended to illustrate the variety of options available. Indications as described in the products' 510(k) premarket notifications are also shown in the appendix. Dressing changes are typically performed every 48 to 72 hours during NPWT therapy and no less than 3 times per week for most models; however, some models are designed to stay in place for 7 days. Infected wounds may require more frequent dressing changes. Target pressures and treatment cycling and duration vary according to the type of wound being treated (Argenta and Morykwas, 1997; Mooney et al., 2000; KCI Licensing Inc., 2014). The devices range in price and in type and offer 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 in which 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 (Rhee et al., 2014).

Among the potential benefits of NPWT are symptom management, reduced frequency of dressing changes, and cost-effectiveness compared with alternative wound therapies because of faster healing times that may lead to lower overall treatment costs (Ousey and Milne, 2014).

There are also potential harms associated with NPWT. These include pain, retention of foreign bodies from the dressing, bleeding, infection, death from infection or bleeding, and complications stemming from loss of electricity (Rhee et al., 2014). Safety concerns, particularly those related to home use of NPWT devices, prompted the FDA to issue a preliminary Public Health Notification and Advice for Patients communication in November 2009 (FDA, 2009a; FDA, 2009b) (click here) and an updated notice in 2011 (click here). The purpose of this initial public health notification in 2009 was to alert healthcare providers, patients, and caregivers regarding the risk of death and serious complications, especially bleeding and infection, associated with the use of NPWT systems, and to provide recommendations to reduce the risk. The alert stated that complications are rare but can occur wherever NPWT systems are used. Most of the reports of deaths (n=6) and serious injuries (n=77) received by the FDA between 2007 and 2009 occurred at home or in a long-term care facility. Bleeding was the most serious complication, occurring in 6 death and 17 injury reports most commonly in patients with vascular grafts or sternal and groin wounds, those receiving anticoagulant therapy, and during removal of dressings that adhered to or were embedded in the tissues. Infection was identified in 27 reports and retention of foam dressing pieces and foam adhering to tissues or imbedded in the wound were noted in 32 injury reports. The recommendations included in the 2009 alert set forth the following contraindications and listed the following patient risk factors to be considered before NPWT use:

Contraindications:

- Necrotic tissue with eschar present
- Untreated osteomyelitis
- Nonenteric and unexplored fistulas
- Malignancy in the wound
- Exposed vasculature
- Exposed nerves
- Exposed anastomotic site
- Exposed organs

Patient Risk Factors:

- Patients at high risk for bleeding and hemorrhage
- Patients on anticoagulants or platelet aggregation inhibitors
- Patients with:

  - Friable vessels and infected blood vessels
  - Vascular anastomosis
  - Infected wounds
  - Osteomyelitis
  - Exposed organs, vessels, nerves, tendon, and ligaments
  - Sharp edges in the wound (i.e., bone fragments)
  - Spinal cord injury (stimulation of sympathetic nervous system)
  - Enteric fistulas
- Patients requiring
  - Magnetic resonance imaging
  - Hyperbaric chamber
  - Defibrillation
- Patient size and weight
- Use near vagus nerve (bradycardia)
- Circumferential dressing application
- Mode of therapy – intermittent versus continuous negative pressure

The updated safety communication issued in 2011 was meant to inform healthcare providers, patients, and caregivers about FDA activities since issuing the 2009 alert; additional death and injury reports received by the FDA; new recommendations regarding patient selection, education, and monitoring; and information about pediatric use. Between publication of the 2009 and 2011 alerts, the FDA received reports of 6 more deaths and 97 more injuries (total between 2007 and 2011 of 12 deaths and 174 injuries). Three of the additional death reports indicated that the patients were receiving NPWT at home or in a nursing home. Also, in more than half of the additional injury reports identifying the location of care, adverse events occurred either at home or in a long-term care facility. Infection was the most commonly reported injury, and bleeding continued to be the most serious adverse event and was reported in 3 of the additional deaths. The contraindications and patient risk factors provided in the 2009 alert remained the same.

A recent search of the FDA's Manufacturer and User Facility Device Experience (MAUDE) database for reports of injuries or deaths associated with NPWT powered devices yielded 28 death and 500 injury reports for the date range January 1, 2007 to August 31, 2016. Details regarding the specific devices, circumstances, and care settings for the reported events were not extracted.

Washington State Agency Utilization and Costs

Negative pressure wound therapy

PARAMETERS: Negative pressure wound therapy analysis includes utilization data from PEBB/UMP (Public Employees Benefit Board Uniform Medical Plan), PEBB Medicare, the Department of Labor and Industries (L&I) Workers' Compensation Plan (forthcoming), and Medicaid Fee for Service and Managed Care. The analysis period for agency utilization covers 2011 to 2015. Primary population inclusion criteria: age greater than 17 years old at time of service AND one of the following CPT/HCPCS codes:

A6550	E2402	K0743	K0746	97607
A7000	G0456	K0744	97605	97608
A9272	G0457	K0745	97606	

PEBB/UMP

TABLE 1
PEBB/UMP
2011 – 2015 UTILIZATION AND COSTS*: Negative Pressure Wound Therapy
(*Does not include Medicare*)

Year	Unique Patients (Pt.)	Total Days*	Avg Days/Pt	Sub Amt	Allw Amt	Pd Amt	Avg Pd/ Day
2011	51	3,654	72	$297,983	$199,936	$188,411	$52
2012	48	4,061	85	$486,153	$263,070	$250,875	$62
2013	55	5,591	102	$408,264	$242,822	$228,493	$41
2014	40	6,477	162	$558,671	$360,554	$355,058	$55
2015	48	6,078	127	$451,207	$263,407	$241,807	$40

**The Health Care Authority pays secondary to Medicare for PEBB/UMP members; including Medicare utilization and costs would skew results*

CHART 1 HISTOGRAM
PEBB/UMP and Medicare
2011 – 2015 Distribution of Patients and Days of Service for Negative Pressure Wound Therapy
NOTE: Claims reflect a change in billing methodology: billing daily v. billing

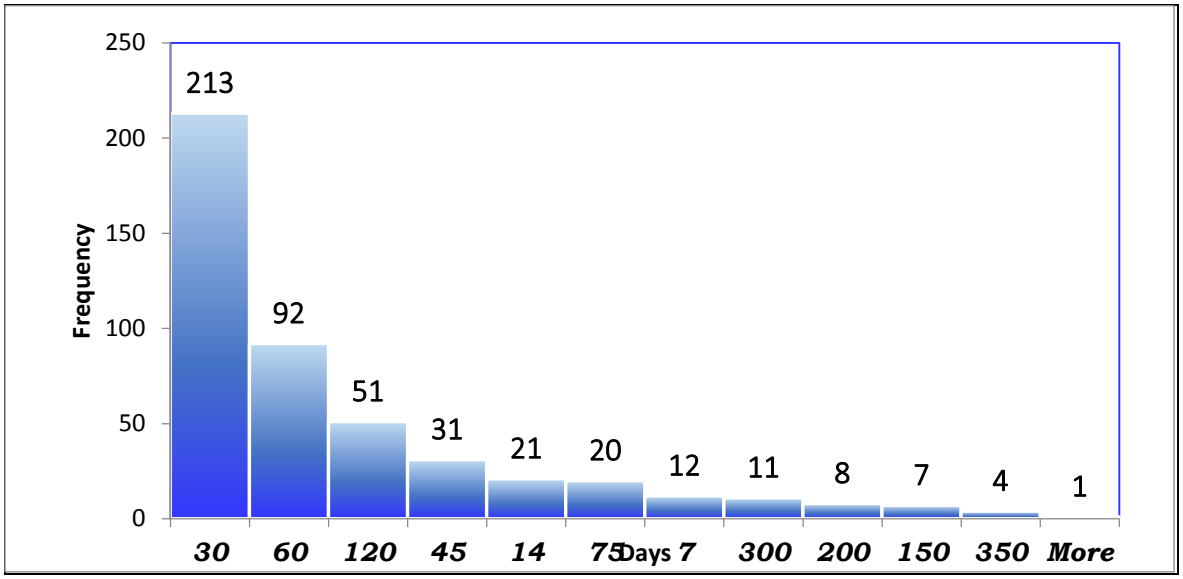


TABLE 2
PEBB/UMP
2011 – 2015 Negative Pressure Wound Therapy
Distribution of Service by Place of Service/Type of Facility and Dx Non-Healing Surgical Wounds *Does Not include Medicare*

Place of Service/ Type of Facility	PEBB/ UMP Distribution
Home/Office	92%
Inpt Hospital	*7%*
Other*	*1%*
	100%

* SKILLED NURSING FACILITY, AMBULATORY SURGERY CENTER, EMERGENCY ROOM

TABLE 3
PEBB UMP/MEDICARE
2011 – 2015 Negative Pressure Wound Therapy by Top 10 Diagnoses by Count and Place of Service/Type of Facility

	Place of Service/Type of Facility				
Diagnosis - Primary	ASC	ER	Home	Inpt. Hospital	Office
NON-HEALING SURGCL WOUND	10		263	6	16
PRESSURE ULCER, BUTTOCK			173	2	13
INFECTED POSTOP SEROMA			7	3	135
OPN WND ANT ABDOMEN-COMP	11		100	1	14
ATTN REM SURG DRESSING		1	115	1	
CHRONIC SKIN ULCER NEC			96		
ATTN REM NONSURG DRESSNG			95		
OPEN WND KNEE/LEG-COMPL	2		67	9	4
PRESSURE ULCER, LOW BACK			64		10
DISRUP-EXTERNAL OP WOUND			63	9	2

MEDICAID FEE-FOR-SERVICE AND MEDICAID MANAGED CARE

TABLE 4
MEDICAID MANAGED CARE AND MEDICAID FEE-FOR-SERVICE
2011 – 2015 Negative Pressure Wound Therapy
Place of Service/Type of Facility by Top 10 Diagnoses by Days of Services

Claim - Short Primary Dx	ASC	Home	Inpt Hospital	Office	Outpt. Hosp.	SNF
NON-HEALING SURGCL WOUND	2	1216	12	12	467	9
DISRUP-EXTERNAL OP WOUND		253	28	6	144	
ULCER OTHER PART OF FOOT		100	3		108	
PRESSURE ULCER, LOW BACK	2	97	6		48	19
DMII OTH NT ST UNCNTRLD		61	9	2	185	
OTHER POSTOP INFECTION		61	33	3	88	
CHRONIC SKIN ULCER NEC		39			173	
OPN WND ANT ABDOMEN-COMP		38	6		117	
ATTN REM NONSURG DRESSNG		2			212	
ATTN REM SURG DRESSING			2		240	

CHART 2
MEDICAID MANAGED CARE AND MEDICAID FEE-FOR-SERVICE
2011 – 2015 Negative Pressure Wound Therapy by Place of Service
By Member by Month

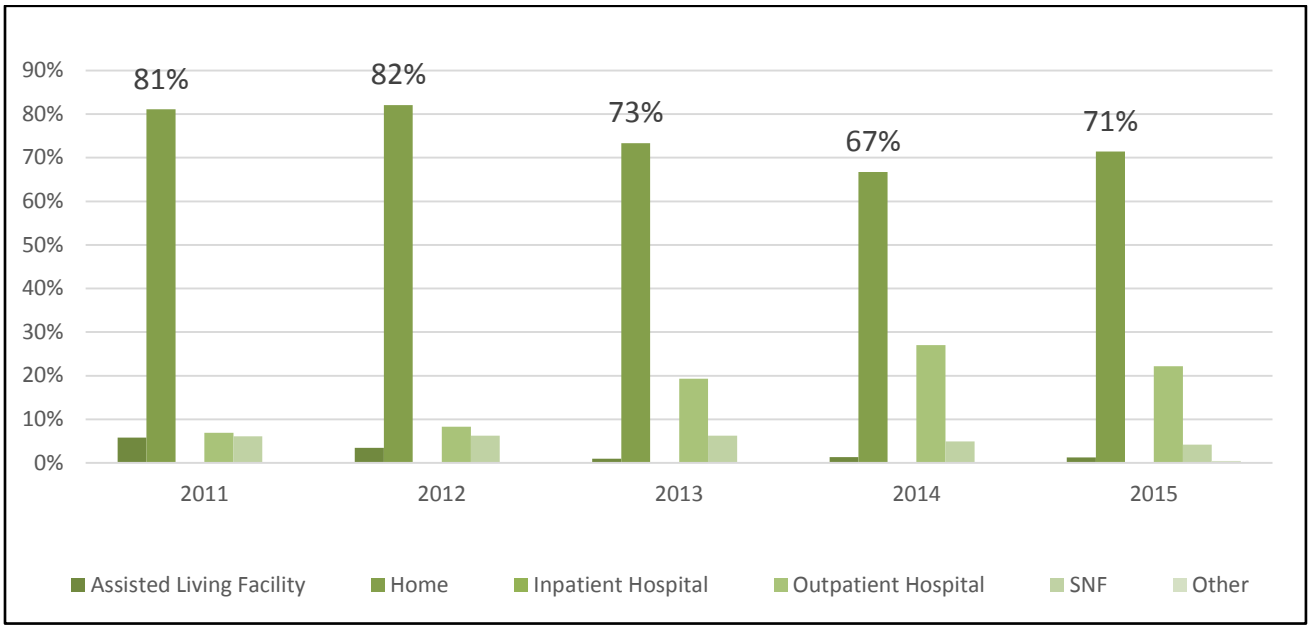


TABLE 5
MEDICAID MANAGED CARE
2011 – 2015 UTILIZATION AND COSTS*: Negative Pressure Wound Therapy

Year	Unique Patients (Pt.)	Total Days*	Avg Days/Pt	Sub Amt	Average Submitted/ Unique Pt.
2011	205	22,540	110.0	$35,920	$175
2012	183	17,342	94.8	$31,048	$170
2013	158	19,362	122.5	$126,405	$800
2014	124	15,819	127.6	$34,204	$276
2015	141	16,478	116.9	$35,765	$254

** Medicaid Managed Care Organizations bill a 'shadow amount" which may, or may not, reflect the true cost of a patient encounter. Allowed and paid dollars omitted from Medicaid Managed Care Analysis*

TABLE 6
MEDICAID FEE-FOR-SERVICES
2011 – 2015 UTILIZATION AND COSTS Negative Pressure Wound Therapy

Year	Unique Patients (Pt.)	Total Days*	Avg Days/Pt	Sub Amt	Avg Submitted/ Unique Patient
2011	51	7,647	149.9	$12,892	$253
2012	53	11,325	213.7	$30,624	$578
2013	137	18,011	131.5	$163,977	$1,197
2014	333	36,323	109.1	$270,734	$813
2015	548	66,724	121.8	$686,369	$1,252

LNI

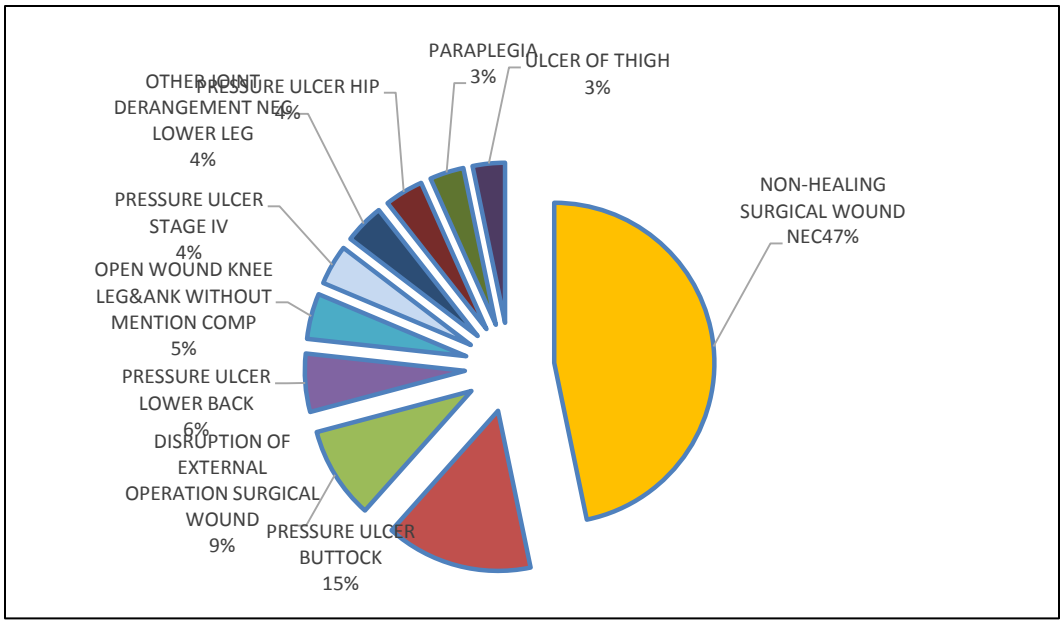
TABLE 7
LNI
2011 – 2015 UTILIZATION AND COSTS
Negative Pressure Wound Therapy – Dx Non-Healing Surgical Wound
NOTE: During 2013, billing units changed from months to days-
NOTE: For analysis months converted to days based on dates of service

Year	Unique Patients (Pt.)	Total Days*	Avg Days/Pt	Charged Amt	Allw Amt/Paid Amt	Avg Allw / Day
2011	21	962	46	$134,069	$78,464	$81.56
2012	9	450	50	$69,592	$47,609	$105.80
2013	25	1,257	50	$202,875	$135,252	$107.60
2014	22	770	35	$276,182	$61,725	$80.16
2015	13	598	46	$92,418	$56,925	$95.19

TABLE 8
LNI
2011 – 2015 Utilization
Negative Pressure Wound Therapy By Average Number of Days by Year
Including Minimum Days, Maximum Days, Mode of Days and Standard Deviation

Days	2011	2012	2013	2014	2015
Average	46	50	50	35	46
Min	30	30	1	5	6
Max	120	90	210	85	162
Mode	30	30	30	24	#N/A
Standard Dev	28	26	39	20	45

CHART 3
L N I
2011 – 2015 Distribution of Top 10 Diagnosis Determined by Days of Service
For Negative Pressure Wound Therapy Claims



Review Objectives

Scope

The scope of this report is defined as:

Population: Patients diagnosed with chronic wounds, defined specifically as venous leg ulcers, arterial leg ulcers, diabetic foot ulcers (DFUs), pressure ulcers, and mixed etiology chronic wounds; or nonhealing surgical wounds (either closed or open)

Interventions: Negative pressure wound therapy (NPWT)

Comparisons: Other wound care methods; comparison of NPWT devices

Outcomes: Clinical outcomes (complete wound healing; time to complete wound healing; time to surgical readiness of the wound bed or time to wound closure; proportion of wounds closed; seroma/hematoma; reoperation; mortality; wound healing rate for healed wounds); patient-centered outcomes (return to prior level of functional activity; pain; health-related quality of life); safety (infection rates; extremity amputation; emergency room visits related to the NPWT or treated wound; unplanned hospitalizations or surgeries related to the NPWT or treated wound; blood transfusions/bleeding)

Settings: Home or outpatient setting

Key Questions

The following key questions will be addressed:

1a. What is the clinical effectiveness of NPWT in the home or outpatient settings for treatment of chronic wounds (i.e., venous leg ulcers, arterial leg ulcers, DFUs, pressure ulcers, and mixed etiology chronic wounds)?

1b. What is the clinical effectiveness of NPWT in the home or outpatient settings for treatment of nonhealing closed or open surgical wounds (i.e., incisions expected to heal by primary intention or incisions expected to heal by secondary intention)?

2. What are the harms associated with NPWT?

3. Does the effectiveness of NPWT or incidence of adverse events vary by clinical history (e.g., diabetes), wound characteristics (e.g., size, chronicity), duration of treatment, types of devices, or patient characteristics (e.g., age, sex, prior treatments, smoking, or other medications)?

4. What are the cost implications and cost-effectiveness of NPWT?

Search Strategy and Selection Criteria

See **Appendix I** for additional search details.

Systematic Reviews and Guidelines

During the period of topic scoping, it was determined that the volume of available literature on NPWT was very large. To accommodate this large body of literature and in recognition of recent systematic review work conducted both by the Agency for Healthcare Research and Quality (AHRQ) and the Cochrane Collaboration, a decision was made to conduct a targeted search for high-quality systematic reviews to identify primary studies for inclusion in this report. In other words, the search strategy, inclusion and exclusion criteria, and eligible studies from the selected systematic reviews were included as primary data for the current report. A systematic search for additional primary data was conducted to ensure that all of the highest-quality available evidence was included in the report. All of the eligible studies (both from the selected systematic reviews and update searches) were abstracted, quality rated, and synthesized for this HTA. The following sources for systematic reviews were searched on March 15, 2016, and May 11, 2016:

- Core online databases such as AHRQ and the Centre for Reviews and Dissemination (York University)
- PubMed, using filters for systematic reviews

Systematic reviews were selected if they were of good quality and pertained to ≥ 1 of the key questions. Three such systematic reviews (Rhee et al., 2014; Webster et al., 2014; Dumville et al., 2015a) were identified and used as the source of some of the included primary studies and the foundation for update literature searches for this report.

Primary Studies and Practice Guidelines

The PubMed (searched on March 15, 2016, May 17, 2016, and September 12, 2016) and OVID-Embase (searched on March 15, 2016, July 1, 2016, and September 12, 2016) databases were searched for primary studies designed to answer the Key Questions. The searches were designed to be update literature searches of selected systematic reviews (Rhee et al., 2014; Webster et al., 2014; Dumville et al., 2015a). Beginning search dates were set to overlap slightly with the most recent search dates of selected systematic reviews to capture new evidence published since the last search of the reviews. The National Guidelines Clearinghouse (https://guideline.gov/) and websites of relevant professional societies were searched for practice guidelines. Specific search strings are documented in **Appendix I**.

Inclusion/Exclusion Criteria

Detailed inclusion and exclusion criteria, along with their rationale, are presented in **Table 9**. The inclusion and exclusion criteria were derived from previously published systematic reviews and in conjunction with the WA-HTA program personnel based on feedback from the participating agencies. Adopting the inclusion and exclusion criteria from the selected systematic reviews allowed for continuity in reviewing and selecting recent literature to add to the evidence base.

Table 9. Inclusion/Exclusion Criteria

Key: NPWT, negative pressure wound therapy; RCT(s), randomized controlled trial(s)

Inclusion Criteria	Exclusion Criteria
Population: Patients diagnosed with chronic wounds defined as venous, arterial, diabetic, pressure, or mixed etiology chronic wounds; or patients with nonhealing surgical wounds	Patients with traumatic wounds, fractures, burns, or skin grafts/flaps
Intervention: NPWT	Studies that evaluated an NPWT device that is not commercially available and approved for use in the United States
Comparator: Other wound care methods; comparison of NPWT devices	Studies with no comparison with other wound treatments or other NPWT devices
Outcomes: Clinical outcomes – complete wound healing; time to complete wound healing; time to surgical readiness of the wound bed or time to wound closure; proportion of wounds closed; seroma/hematoma; reoperation; mortality; wound healing rate for healed wounds Patient-centered outcomes – return to prior level of functional activity; pain; health-related quality of life Safety – infection rates; extremity amputation; emergency room visits related to the NPWT or treated wound; unplanned hospitalizations or surgeries related to the NPWT or treated wound; blood transfusions/bleeding	Studies that reported wound healing rates without also reporting complete wound healing (this is considered a surrogate outcome measure because chronic wounds may not heal in a linear fashion, and cannot be used to accurately predict complete healing)
Study Design: Comparative studies (RCTs only for surgical wounds; other comparative study designs accepted for chronic wounds as long as the total number of participants was ≥ 20). Studies with mixed inpatient/outpatient populations that did not provide separate analyses for the different groups were included if they provided data on the proportion of patients and/or the proportion of therapy days treated in the inpatient versus outpatient/home setting, or if it can be interpreted that the majority of patients were treated in the outpatient/home setting.	Fewer than 20 patients with chronic wounds (studies with ≤ 10 patients per group would not be adequately powered to detect meaningful differences in clinical outcomes); conference abstracts or posters; nonhuman studies; no original data (e.g., editorials, letters, non–systematic reviews), economic analyses conducted outside the United States NOTE: Any-size RCT was accepted for surgical wounds.

Inclusion Criteria	Exclusion Criteria
Setting: Home or outpatient setting NOTE: Studies were included if they were described as in "outpatient setting" or if it was reported (or was interpreted) that patients were not receiving care in long-term care facilities, including assisted living, skilled, or maintenance nursing homes.	Studies in which NPWT was applied only in inpatient (acute or long-term care) settings or that did not provide enough detail about the setting of care to determine whether outpatient or home-based care was provided during the study period.

Quality Assessment

Clinical Studies

The Assessment of Multiple Systematic Reviews (AMSTAR) tool was employed to determine the quality of selected systematic reviews (Shea et al., 2007; Appendix II). Appendix III outlines the process used by Hayes for assessing the quality of individual primary studies and the quality of bodies of evidence. This process is in alignment with the methods recommended by the Grading of Recommendations Assessment, Development and Evaluation (GRADE) Working Group. Quality checklists for individual studies address study design, integrity of execution, completeness of reporting, and the appropriateness of the data analysis approach. Individual studies are labeled as *good*, *fair*, *poor*, or *very poor*.

Like the GRADE Working Group, Hayes uses the phrase *quality of evidence* to describe bodies of evidence in the same manner that other groups, such as AHRQ, use the phrase *strength of evidence*. The Hayes Evidence-Grading Guides ensure that assessment of the quality of bodies of evidence takes into account the following considerations:

- Methodological quality of individual studies, with an emphasis on the risk of bias within studies.
- Applicability to the population(s), intervention(s), comparator(s), outcome(s), and settings of interest, i.e., applicability to the PICOS statement.
- Consistency of the results across studies.
- Quantity of data (number of studies and sample sizes).
- Publication bias, if relevant information or analysis is available.

NOTE: Two terms related to applicability are *directness* and *generalizability*. *Directness* refers to how applicable the evidence is to the outcomes of interest (i.e., health outcomes versus surrogate or intermediate outcomes) or to the comparator of interest (indirect comparison of 2 treatments versus head-to-head trials). *Generalizability* usually refers to whether study results are applicable to real-world practice. If the setting is not specified in a PICOS (population-interventions-comparator-outcomes-setting) statement, the issue of generalizability to real-world settings is not typically treated as an evidence quality issue. Another term used by some organizations is *imprecision*, which refers to findings based on such a small quantity of data that the CI surrounding a pooled estimate includes both clinically

important benefits and clinically important harms, or such a small quantity of data that any results other than large statistically significant effects should be considered unreliable.

Bodies of evidence for particular outcomes are labeled as being of *high*, *moderate*, *low, or very low quality*. These labels can be interpreted in the following manner:

High: Suggests that we can have high confidence that the evidence found is reliable, reflecting the true effect, and is very unlikely to change with the publication of future studies.

Moderate: Suggests that we can have reasonable confidence that the results represent the true direction of effect but that the effect estimate might well change with the publication of new studies.

Low: We have very little confidence in the results obtained, which often occurs when the quality of the studies is poor, the results are mixed, and/or there are few available studies. Future studies are likely to change the estimates and possibly the direction of the results.

Very Low: Suggests no confidence in any result found, which often occurs when there is a paucity of data or the data are such that we cannot make a statement on the findings.

Economic Evaluations

A tool created for internal use at Hayes was used to guide interpretation and critical appraisal of economic evaluations. The tool for economic evaluations was based on best practices as identified in the literature and addresses issues such as the reliability of effectiveness estimates, transparency of the report, quality of analysis (e.g., the inclusion of all relevant costs, benefits, and harms), generalizability/applicability, and conflicts of interest. Sources are listed in **Appendix III**.

Guidelines

The Rigor of Development domain of the Appraisal of Guidelines Research and Evaluation (AGREE) tool (AGREE Next Steps Consortium, 2013), along with a consideration of the items related to commercial funding and conflicts of interest among the guideline authors, was used to assess the quality of practice guidelines. Use of the AGREE tool was limited to these areas because they relate most directly to the link between guideline recommendations and evidence.

Search Results

The 17 studies included in this HTA consist of 9 primary studies identified from 3 good-quality systematic reviews, and 8 additional studies that were added through update searches of electronic databases and manual searches of key publications.

The authors of the previously published systematic reviews screened a large volume of literature and found few eligible publications for evidence synthesis. The literature search conducted for the AHRQ systematic review on NPWT technologies for wound care in the home yielded 5912 unique citations, and the final number of included studies was 7 (published in 8 articles) (Rhee et al., 2014). The literature search done for the Cochrane Collaboration systematic review on NPWT for surgical wounds healing by secondary intention yielded 586 records, and the final number of included studies was 2 (Dumville et al.,

2015a). The systematic review on NPWT for surgical wounds healing by primary intention was an update of a 2012 review; the literature search performed by the authors of the updated review yielded 177 new, unique records, and resulted in a total of 9 included studies (5 of which were part of the 2012 review). Out of the 18 studies (published in 20 articles) in these 3 systematic reviews, 9 studies (11 articles) met inclusion criteria for this HTA. The remaining 9 studies were excluded because of ineligible setting.

In addition to identifying 9 studies (11 articles) from previously published systematic reviews, update literature searches and manual searches of key references yielded 1441 unique citations for review; 67 of these were selected for full-text review. Eight additional studies (published in 11 articles) and 2 recent publications from older studies were selected for inclusion. See **Figure 2** for a summary of the update literature search results.

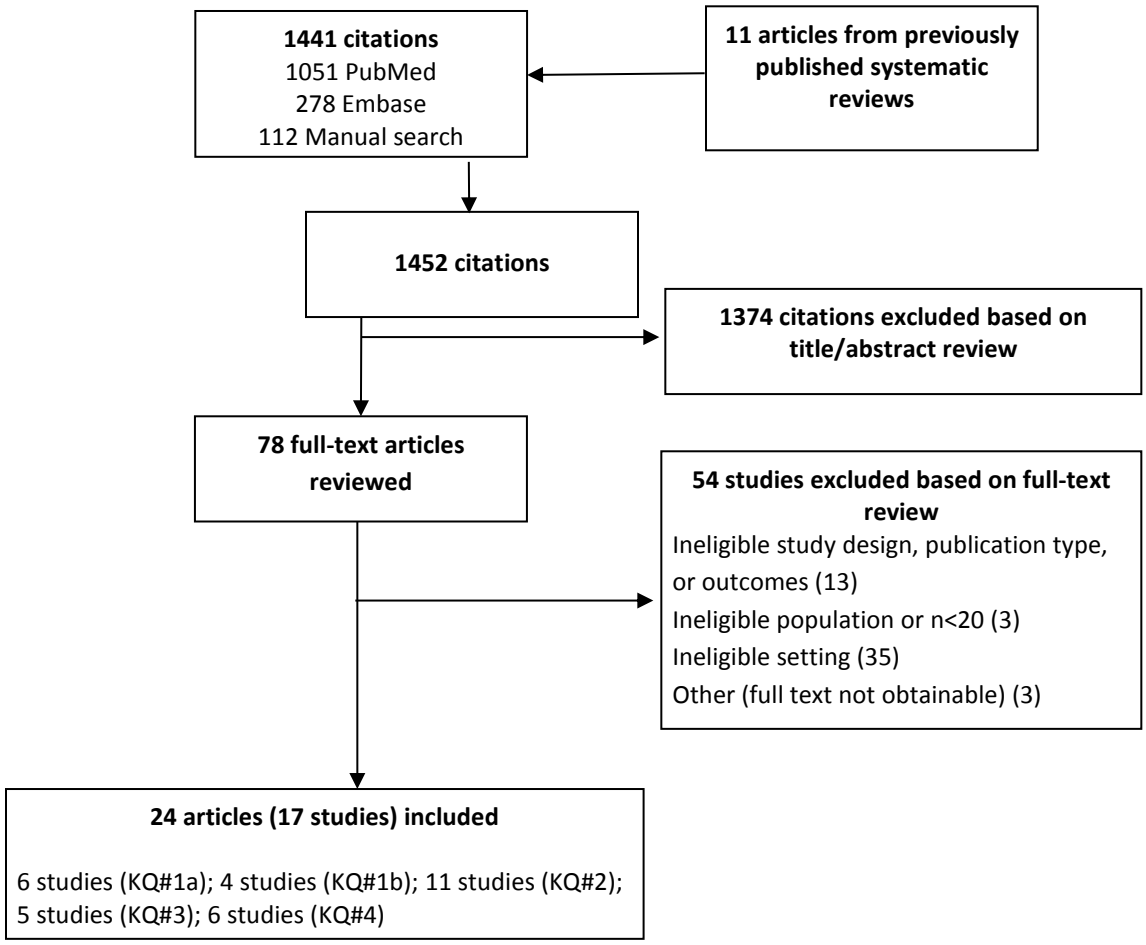
Included Studies

The 17 included primary studies consist of 12 studies (published in 15 articles) of populations with chronic wounds (Ford et al., 2002; Schwien et al., 2005; Frykberg and Williams, 2007; Lavery et al., 2007; Blume et al., 2008; Fife et al., 2008; Flack et al., 2008; Lerman et al., 2010; Armstrong et al., 2011; Hutton and Sheehan, 2011; Armstrong et al., 2012; Driver and Blume, 2014; Yao et al., 2014; Law et al., 2015; Marston et al., 2015) and 5 studies (9 articles) of populations with surgical wounds (Armstrong et al., 2005; Armstrong et al., 2007; Apelqvist et al., 2008; Acosta et al., 2013; Biter et al., 2014; Monsen et al., 2014; Monsen et al., 2015; Karlakki et al., 2016; Manoharan et al., 2016). The studies of chronic wounds include 3 randomized controlled trials (RCTs), 7 observational studies, and 2 economic modeling studies. All 5 studies of surgical wounds were RCTs per the inclusion criteria. **Figure 2** shows the distribution of the included studies across the Key Questions. Some studies may apply to more than 1 Key Question.

Excluded Studies

See **Appendix IV** for a listing of the 54 studies that were excluded from analysis after full-text review.

Figure 2. Summary of Search Results



Literature Review

Key Question #1a: What is the clinical effectiveness of NPWT in the home or outpatient settings for treatment of chronic wounds (i.e., venous leg ulcers, arterial leg ulcers, diabetic foot ulcers, pressure ulcers, and mixed etiology chronic wounds)?

Study characteristics

A good-quality systematic review on NPWT for chronic wound care in the home setting (Rhee et al., 2014) was selected to identify primary studies for inclusion in this HTA. The search strategy by Rhee and colleagues was subsequently updated, through searches of electronic databases and manual searches of other relevant publications, to identify additional new studies since publication of the Rhee systematic review. In all, 6 primary studies meeting inclusion criteria were identified that address Key Question 1a; 5 of these were included in the review by Rhee and colleagues, and 1 additional study was identified for this HTA. **Table 10** includes brief descriptions of the study characteristics. See **Appendix V** for more details. There were 2 RCTs and 4 observational studies. The RCTs ranged in size from 28 to 341 patients

(Ford et al., 2002; Blume et al., 2008). The observational studies ranged in size from 78 to 2677 patients (Lavery et al., 2007; Fife et al., 2008; Lerman et al., 2010; Yao et al., 2014). All 6 studies compared NPWT with other types of wound treatment. One of the studies included both inpatients and outpatients and did not provide separate analyses for each group (Blume et al., 2008). This study was included in this HTA because the publication provided information about the proportion of home care days in each group (89.5% for the NPWT group and 95.3% for the comparison group) and it is one of the few RCTs identified (Blume et al., 2008). While the lack of separate analyses for patients who may have received only inpatient care while receiving NPWT is a limitation of this study, information that both groups received a majority of care in the home setting suggests some applicability to patient populations using NPWT at home.

Wound types in the study populations varied. Patients with DFUs were the focus of 3 studies (Lavery et al., 2007; Blume et al., 2008; Fife et al., 2008). One study included only patients with pressure ulcers (Ford et al., 2002). The remaining 2 studies included patients with lower extremity ulcers of different etiologies (Lerman et al., 2010; Yao et al., 2014).

Not all studies reported details of the NPWT devices used. The 1 study that did report details evaluated the SNaP (Spiracur) device (Lerman et al., 2010). The remaining studies reported the brand name only; in all cases this was the V.A.C. Therapy System (Kinetic Concepts Inc.). Details of comparison treatments were also lacking.

Studies were selected if authors reported, or it was possible to interpret with some certainty, that NPWT was utilized in the home setting. Studies of patients in acute or long-term care facilities such as hospitals, skilled or maintenance nursing facilities, or assisted living were excluded. Studies with patients recruited as inpatients but who received follow-up care in outpatient settings were eligible if all other eligibility criteria were met. The Blume et al. study includes both inpatients and outpatients; it reports proportion of outpatient days but does not report outcome results for each group of patients separately (Blume et al., 2008). In the remaining 5 studies, the setting was not explicitly described, but “outpatient setting” was interpreted as home because it appeared that the patients were not in assisted living or skilled or maintenance nursing homes.

Study Quality

Half of the studies (3 out of 6) included for KQ1a were rated as poor-quality (Lavery et al., 2007; Fife et al., 2008; Lerman et al., 2010). Two RCTs and 1 retrospective cohort study were rated as fair-quality (Ford et al., 2002; Blume et al., 2008; Yao et al., 2014). The 3 fair-quality studies were limited by poor reporting and potentially meaningful differences between groups at baseline. The observational study (Yao et al., 2014) provided stratified and adjusted analyses, which contributed to its rating as fair-quality. Poor-quality ratings were assigned because of methodological weaknesses, including potential for differential concomitant treatments between intervention and control groups (Fife et al., 2008; Lerman et al., 2010); inappropriate or poorly described control groups (Lavery et al., 2007; Fife et al., 2008); high overall attrition (Lerman et al., 2010); poor or selective reporting on comparative treatments, potential confounders, and outcomes (Fife et al., 2008); quality of data source not clear (Fife

et al., 2008); and surrogate data used to assess outcomes (Fife et al., 2008). All studies were limited by the lack of blinding, and all of the observational studies were limited by the lack of randomization. The lack of blinding caregivers and patients to the treatment is primarily because of the nature and obvious differences between the treatments delivered and the unethical practice of delivering a sham or placebo treatment in this patient population (FDA, 2006). The Ford et al. study reported that personnel who measured wounds and obtained plaster impressions were blinded to treatment status. No other study reported blinding of outcome assessors.

Table 10. Study Characteristics of Studies Included for KQ1a

Key: NPWT, negative pressure wound therapy; RCT, randomized controlled trial

Study Study Design (n), Quality	Wound Type			Comparisons	NPWT Devices	
	DFU	PU	Mixed		SNaP (Spiracur)	V.A.C. (KCl)
Blume et al. (2008) RCT (341), Fair	X			Advanced moist wound therapy of primarily hydrogels and alginates consistent with standards of care		X
Fife et al. (2008) Retrospective observational (1331), Poor	X			Unspecified wound care treatment either prior to the start of NPWT or among patients who never received NPWT		X
Ford et al. (2002) RCT (28), Fair		X		Three gel products – Accuzyme, Iodosorb, and Panafil, each targeted to optimize a particular macroscopic phase of wound healing		X
Lavery et al. (2007) Retrospective observational (2677), Poor	X			Matched and unmatched groups of NPWT patients were compared with a control group receiving standard wound care; the control group was identified from a meta-analysis of 5 RCTs published between 1992 and 1998.		X
Lerman et al. (2010) Retrospective observational (78), Poor			X	Matched controls treated at the same center with modern wound care protocols that included the use of Apligraf, Regranex, and skin grafting.	X	

Study Study Design (n), Quality	Wound Type			Comparisons	NPWT Devices	
	DFU	PU	Mixed		SNaP (Spiracur)	V.A.C. (KCI)
Yao et al. (2014) Retrospective observational (342), Fair			X	Matched controls who did not receive NPWT.		X

Clinical and Patient-Centered Outcomes

For Key Question 1a, information on the following clinical outcomes were sought: complete wound healing; time to complete wound healing; time to surgical readiness of the wound bed or time to wound closure; proportion of wounds closed; mortality; and wound healing rate for healed wounds. In line with decisions made by Rhee and colleagues for inclusion in their systematic review, the surrogate outcome of wound healing rate (percent ulcer area reduction or other measurement) was not eligible as an outcome if studies did not also report complete wound healing. 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 (Rhee et al., 2014). Patient-centered outcomes of interest were: return to prior level of functional activity, pain, and health-related quality of life. Only 1 of the studies included for KQ1a reported an eligible patient-centered outcome (Fife et al., 2008).

DFUs

Lavery et al. and Yao et al. reported results for complete wound healing. Blume at al. reported results for wound closure. One of these studies was rated poor-quality (Lavery et al., 2007) and 2 (Blume et al., 2008; Yao et al., 2014) were rated fair-quality. All 3 studies found benefit with NPWT for complete wound healing or wound closure (Lavery et al., 2007; Blume et al., 2008; Yao et al., 2014). Blume et al. also reported time to wound closure; results suggest that wounds treated with NPWT are closed sooner. None of the studies on DFU reported on other eligible clinical outcomes. Provision of pain medication as a surrogate measure for pain was reported in 1 study of DFU; results suggest no difference between groups (Fife et al., 2008). No other patient-centered outcomes were reported in the DFU studies.

Lavery et al. defined wound healing differently for each group. In the NPWT group, it was described as closure by secondary intention or by surgical intervention, or if adequate granulation for closure was documented. Surgical interventions included flaps, grafts, and primary closure. Wound healing in the control group was defined as wounds completely healed (no drainage or full epithelialization). 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 the matched NPWT group compared with the control group at 12 weeks (39.5% versus 23.9%); the results remained significant at 20 weeks (46.3% versus 32.8%) (P<0.001) (Lavery et al., 2007).

Complete healing was not explicitly defined in the Yao et al. study, although it was analyzed as an event. Unadjusted and adjusted hazard ratio (HR) analyses suggest that patients with DFUs who received NPWT (n=140) had a higher incidence of wound healing than those who did not receive NPWT (n=118) (unadjusted HR, 2.38 [95% CI, 1.75 to 3.23] and adjusted HR, 3.26 [95% CI, 2.21 to 4.83]). Analyses were adjusted for comorbidities (including diabetes, peripheral arterial disease, coronary heart disease, chronic kidney disease, congestive heart failure, stroke, smoking) and "other variables associated with disease severity" (Yao et al., 2014).

Blume et al. defined complete ulcer closure as skin closure (100% re-epithelization) without drainage or dressing requirements. During the 112-day active treatment phase, a higher proportion of patients who received NPWT achieved complete closure compared with those who received advanced moist wound therapy (AMWT) (NPWT, 73 out of 169 [43.2%]; AMWT, 48 out of 166 [28.9%]; *P*=0.007). Surgical closure was performed in 9.5% of the NPWT wounds and 8.4% of the AMWT wounds (statistical significance not reported). With respect to time to wound closure, the Kaplan-Meier median estimate for 100 percent ulcer closure was 96 days (95% CI, 75.0 to 114.0) for NPWT and not determinable for AMWT (*P*=0.001). The study investigators state that 89.5 percent of total therapy days for the NPWT group were home care days, and 95.3 percent of total therapy days were home care days for the AMWT group (Blume et al., 2008). Despite the fact that the vast majority of care was provided in the home setting, it should be noted that this study may have included patients who received care only in the inpatient setting, which may have somewhat confounded the results since the inpatient population may have received different levels of care.

Provision of pain medication as a surrogate measure for pain was reported in 1 study of DFU (Fife et al., 2008). This study was rated poor-quality and found no difference between the NPWT and non-NPWT groups.

Arterial Ulcers

One fair-quality study reported incidence of wound healing for patients with arterial ulcers; results favored NPWT. Yao et al. found that patients with arterial ulcers who received NPWT (n=114) had a higher incidence of wound healing than those who did not receive NPWT (n=59) (NPWT unadjusted HR, 2.33 [95% CI, 1.57 to 3.48] and non-NPWT adjusted HR, 2.27 [95% CI, 1.56 to 3.78]) (Yao et al., 2014).

Pressure Ulcers

Two fair-quality studies represent inconsistent results in the direction of their results for complete wound healing with NPWT for patients with pressure ulcers compared with other treatments. The results were not statistically significant in either study. Of note, in the Ford et al. study, 21 patients had 35 wounds and results are reported per wound and not per patient. Complete wound healing results from the Ford et al. and Yao et al. studies are summarized in the Rhee et al. systematic review as follows. In the Ford et al. study, 6 ulcers in the NPWT group (30%) and 6 ulcers in the control group (40%) underwent flap surgery. Two ulcers in each group completely healed (risk difference 3%; 95% CI, –18% to 25% [calculated by Rhee et al.]) (Ford et al., 2002; Rhee et al., 2014). Yao et al. reported that those treated with NPWT had a higher incidence of wound healing compared with those in the control

group. The adjusted HR for wound healing was 1.72 (95% CI, 0.43 to 6.95) in the study by Yao et al (Rhee et al., 2014; Yao et al., 2014).

Venous Insufficiency Ulcers

The fair-quality study by Yao et al. also reported complete wound healing for patients with venous ulcers. Similar to the DFU, arterial ulcer, and pressure ulcer patients evaluated in this study, patients with venous ulcers who received NPWT had a higher incidence of wound healing than those who did not receive NPWT (unadjusted HR, 4.90 [95% CI, 1.72 to 13.59]; adjusted HR, 6.31 [95% CI, 1.49 to 26.6]) (Yao et al., 2014).

Mixed Ulcer Populations

For populations of patients with different wound types, results from 1 fair-quality (Yao et al., 2014) and 1 poor-quality (Lerman et al., 2010) study favor NPWT compared with other wound treatments. When all wound types (DFUs, arterial ulcers, venous insufficiency ulcers, and pressure ulcers) were analyzed together in the Yao et al. study, patients in the NPWT group had a greater likelihood of wound closure compared with patients who did not receive NPWT (unadjusted HR, 2.25 [95% CI, 1.73 to 3.96], adjusted HR, 2.63 [95% CI, 1.87 to 3.70]) (Yao et al., 2014). In the study by Lerman et al., estimates of wound healing at 1, 2, 3, and 4 months of treatment were 0%, 20%, 66.2%, and 83.1%, respectively, for the SNaP (NPWT) group, and 0%, 7.1%, 21.4%, and 35.7%, respectively, in the matched control group that received modern dressings. Time to complete healing was statistically significantly shorter in the NPWT group than the control group (50% absolute reduction; $P<0.0001$). In those reporting wound healing, the SNaP (NPWT)-treated patients healed in an average of 74.25 ± 20.1 days from the start of SNaP treatment, and the matched controls healed in an average of 148.73 ± 63.1 days from the start of conventional treatment ($P<0.0001$) (Lerman et al., 2010).

Key Question #1b: What is the clinical effectiveness of NPWT in the home or outpatient settings for treatment of nonhealing closed or open surgical wounds (i.e., incisions expected to heal by primary intention or incisions expected to heal by secondary intention)?

Study Characteristics

Two good-quality systematic reviews were found that assessed evidence from RCTs on the use of NPWT to treat surgical wounds. One of the systematic reviews evaluated NPWT for surgical wounds healing by secondary intention (Dumville et al., 2015a) and the other (Webster et al., 2014) evaluated NPWT for surgical wounds healing by primary intention. These systematic reviews did not limit their evidence to studies within the home setting; primary studies included in these reviews were screened for eligibility for this HTA on home use of NPWT, and only those with information about outpatient treatment were selected. Update literature searches were conducted to find recently published primary literature to add to the RCT evidence included in these reviews. Four primary studies were identified for Key Question 1b. Two of the RCTs were included in the previously published systematic review on surgical wounds healing by secondary intention (Dumville et al., 2015a); no eligible studies were carried forward from the systematic review on surgical wounds healing by primary intention because none of them were

conducted in the home setting (Webster et al., 2014). No eligible studies were identified in which closed surgical wounds were described as slow or nonhealing prior to the application of NPWT or other wound treatments. In the 2 recent studies on closed surgical wounds identified for inclusion in this HTA, the investigators applied wound treatments immediately after surgery to clean closed incisions (Karlakki et al., 2016; Manoharan et al., 2016). See **Table 11** for a brief summary of study characteristics. Details of included studies are presented in **Appendix V**.

Each of the studies of surgical wounds includes a unique population. Populations include patients with deep infected wounds (Acosta et al., 2013; Monsen et al., 2014; Monsen et al., 2015), patients requiring surgical treatment for a pilonidal sinus (Biter et al., 2014), patients with wounds from diabetic foot wound–related amputations (Armstrong et al., 2005; Armstrong et al., 2007; Apelqvist et al., 2008), and patients undergoing total knee arthroplasty (Manoharan et al., 2016). Three studies were single-center studies conducted in Europe (Sweden and the Netherlands) (Acosta et al., 2013; Biter et al., 2014; Monsen et al., 2014; Monsen et al., 2015) and Australia (Manoharan et al., 2016), and 1 was a multicenter study conducted in the United States (Armstrong et al., 2005; Armstrong et al., 2007; Apelqvist et al., 2008). In all 4 studies, wound care started in an acute care setting and was continued at home after discharge. The specific brands and models of the devices used in the Monsen et al. and Biter et al. studies were not specified; it is unclear whether they are devices commercially available in the United States. Because of the relative dearth of information from home care/outpatient settings, these 2 studies were included in this HTA despite the lack of details about the specific devices used.

Study Quality

A fair-quality rating was assigned to all 4 studies included for Key Question 1b. Limitations of the Monsen et al. study included possible selection bias during recruitment, lack of adequate randomization technique, unclear method for calculating time to wound healing, use of different types of alginate dressings in comparison group, and unclear mean length of follow-up in each group (Acosta et al., 2013; Monsen et al., 2014; Monsen et al., 2015). The investigators in this study performed power calculations, which determined that enrollment of 42 patients was needed; however, the investigators preplanned an interim analysis with 20 patients, and if NPWT was shown to be superior to alginate dressings, they planned to discontinue the trial. Limitations of the Biter et al. (2014) study included lack of power calculations and unclear data analysis methods for the primary outcome, time to complete wound healing. The Armstrong et al. study was limited by the use of different wound dressings in the comparison group based on provider discretion, and potential for bias in treatment/assessment decisions due to lack of blinding of providers and outcome assessors. The Manoharan et al. (2016) study limitations included small sample size and lack of blinding.

Table 11. RCTs Included for KQ1b

Key: NPWT, negative pressure wound therapy; N/S, not specified; VAC, vacuum-assisted closure

Study n, Quality	Patient Population	Comparisons	NPWT Devices
Armstrong et al. (2005); Apelqvist et al. (2008) n=162, Fair	Patients with a wound from a diabetic foot wound amputation to the transmetatarsal level, and evidence of adequate perfusion	NPWT vs standard care (moist wound care with alginates, hydrocolloids, foams, or hydrogels)	V.A.C. Therapy System (KCI Inc.)
Biter et al. (2014) n=49, Fair	Patients requiring surgical treatment for a pilonidal sinus	NPWT for 14 days, then regular wound care was started vs standard open wound therapy (a silicone wound dressing with an absorbent bandage on top)	VAC (N/S)
Monsen et al. (2014); Acosta et al. (2013); Monsen et al. (2015) n=20, Fair	Patients with deep perivascular groin infections (Szilagyi grade III) that had been surgically revised and left open for healing by secondary intention	Vacuum-assisted wound closure (VAC) vs alginate (Sorbalgon or Melgisorb), a soft, highly absorbent dressing that quickly forms a hydrophilic gel	VAC (N/S)
Manoharan et al. (2016), n=21 pts, 42 knees	Patients with closed surgical wounds after bilateral total knee arthroplasty	NPWT for 8 days vs conventional dry dressing	Prevena Incision Management System (Acelity [KCI Inc.])

Clinical and Patient-Centered Outcomes

Three of the studies included for Key Question 1B reported median time to wound healing, and 1 of these also reported proportion of wounds healed. Two studies conducted in Europe among patients who received different surgical interventions reported conflicting results with respect to median time to wound healing. One study (Biter et al., 2014) found no difference between NPWT and silicone dressing for patients being treated for pilonidal sinus, and 1 study (Monsen et al., 2014) found that the median number of days to complete wound healing was statistically significantly shorter in the NPWT group compared with a group receiving alginate dressing for deep perivascular wound infections. It should be noted that these studies included different patient populations and evaluated NPWT against different comparisons. The third study was conducted in the United States among patients with diabetic foot wound–related amputations. Results from this study suggest that a higher proportion of wounds were healed in the NPWT group than in the standard moist wound therapy group, and the NPWT group

healed faster. Patient-centered outcomes were reported in 2 of these 3 studies; the results suggest no difference between NPWT and alginate dressing for quality of life (QOL), return to prior level of activity, and pain outcomes. In 1 study of patients with closed surgical wounds after total knee arthroplasty (Manahoaran et al., 2016), 2 QOL factors (dressing leakage and wound protection) were statistically significantly better for knees with NPWT than those with conventional dry dressings; no other QOL factors were statistically significantly different.

In the Biter et al. trial comparing NPWT (n=24) to silicone dressings (n=25), time to complete wound healing was defined as the number of days until full skin closure was achieved. Median time to complete healing was similar between groups (median: NPWT 84 [range, 34-349] days, control 93 [range, 43-264] days; *P*=0.44). The number of wounds healed was not reported. The median time to resume work or school was also similar between groups (median: NPWT 27 [range, 7-126], control 29 [range, 6-63]; *P*=0.92). Pain was assessed by the visual analog scale (VAS) score on the day of surgery and at 14 days after surgery. The groups were similar at both time points. The scores were higher at postoperative day 14 than on the day of surgery in both groups; the statistical significance of the change from baseline was not reported (Biter et al., 2014).

Monsen et al. compared NPWT to alginate dressing in patients with deep perivascular groin infections subsequent to vascular surgery. Patients were treated in the hospital until the arterial reconstruction was covered with granulation tissue, then patients well enough to be discharged continued treatment at home. In this study, complete wound healing was defined as full skin epithelialization. Median number of days to complete wound healing was statistically significantly shorter in the NPWT group compared with the alginate group (median: NPWT 57 [range, 25-115], control 104 [range, 57-175]; *P*=0.026). The number of wounds healed was not analyzed; however, the median number of days to complete wound healing was calculated using 9 patients in the NPWT group and 7 patients in the alginate dressing group. This does not completely agree with the analysis provided for the number of wounds not healed (defined as no-healed wounds in the groin after 4 months, visible graft material or femoral artery after 1 month of treatment, or amputation or death as a consequence of the groin infection), which was reported as 1 (10%) in the NPWT group and 5 (50%) in the control group (*P*=0.034). It is not clear how many patients in the control group achieved complete wound healing; therefore, this result from this study was not considered in the body of evidence. The NPWT group had fewer in-hospital days (median: NPWT, 13 [range, 5-93], control 20 [range, 6-76]; *P*=0.79), and statistically significantly fewer wound treatment days outside the hospital (median: NPWT 42 [range, 18-81], control 79 [range, 32-171]) (Monsen et al., 2014). At the study start and when the wound was healed, QOL was assessed via the European Quality of Life-5 Dimensions (EQ-5D) questionnaire, which included a VAS for health status (EQ-VAS). Pain was measured at study start, the day after surgical wound revision, and at 4 weeks of treatment (or sooner if wound healing happened before 4 weeks) using the short form of the Brief Pain Inventory (BPI). Six patients in each group completed the EQ-5D at the time of wound healing, and 9 patients in the NPWT group and 8 in the control group completed the BPI at 4 weeks. No difference was shown in EQ-5D and EQ-VAS between the 2 groups at study start or after wound healing; similarly, no difference was shown between the NPWT and the alginate groups in pain intensity or influence on daily life at study start or after 4 weeks of treatment (Monsen et al., 2015).

Patients received either NPWT or standard moist wound care after partial diabetic foot amputation in the study by Armstrong et al. (2005). The study enrolled 162 patients from 18 centers in the United States and treated wounds until they were closed or until the completion of the 112-day assessment. Complete wound closure was defined as 100 percent re-epithelialization without drainage. There was a greater proportion of healed wounds in the NPWT group compared with the control group (NPWT 43 [56%] versus control 33 [39%]; *P*=0.040). Patients in the NPWT group healed faster than those in the control group (*P*=0.005). The median time to complete wound closure for 43 patients in the NPWT group was 56 days. For the 33 patients in the control group who reached complete wound closure, the median time was 77 days. No patient-centered outcomes were reported (Armstrong et al., 2005).

Twenty-one patients who underwent bilateral knee arthroplasty were randomized to either NPWT or conventional dry dressing (CDD) on each knee (Manoharan et al., 2016). Of note, this publication also includes a group of 12 patients who were not randomized to treatment; all 12 patients received CDDs. This group of 12 was evaluated separately for a cost analysis; however, the baseline study demographics include this group of patients and demographics are not provided separately for the 21 patients who were randomized. In this study, the average length of stay for all 33 patients was 4.1 days and it is not clear what proportion of home care days the randomized group received. This study reported eligible QOL outcomes. Results indicate that mean dressing leakage scores were statistically significantly better for the NPWT knees than for the CDD knees (NPWT 0.14 [0.13] vs CDD 0.38 [0.34]; *P*=0.0019; effect size (ES)=1.02). Similarly, wound protection scores were also better for the NPWT knees (NPWT 0.16 [0.05] vs CDD 0.33 [0.16]; *P*=0.001; ES=0.0212) but no other QOL factors were statistically significantly different. The other factors included odor, itch, movement, body image, self-esteem, personal hygiene, sleep, and pain.

Key Question #2: What are the harms associated with NPWT?

Harms Reported in Studies of Chronic Wounds

Safety outcomes sought for this HTA were infection rates; extremity amputation; emergency room visits related to the NPWT or treated wound; unplanned hospitalizations or surgeries related to the NPWT or treated wound; and blood transfusions/bleeding. Six studies (Ford et al., 2002; Schwien et al., 2005; Frykberg and Williams, 2007; Blume et al., 2008; Fife et al., 2008; Lerman et al., 2010) were identified that reported on adverse events in patients with chronic wounds (see **Table 12**). These studies evaluated NPWT compared with other wound treatments in patients with DFUs, pressure ulcers, and mixed ulcers. No studies comparing NPWT with other wound treatments reporting adverse events for patients with arterial ulcers or venous insufficiency ulcers were identified. Results from 2 studies favored NPWT with respect to rates of amputation, and a third study favored NPWT with respect to rates of infection among patients with DFUs. For patients with pressure ulcers, 1 study reported statistically significant results in favor of NPWT for emergency care and hospitalization. The study reporting adverse events among a mixed ulcer population did not report data for the comparison group.

DFUs

Adverse events were reported in 3 studies of patients with DFUs (Frykberg and Williams, 2007; Blume et al., 2008; Fife et al., 2008). Study characteristics and quality ratings for the Blume et al. and Fife et al. studies are summarized under Key Question 1a; this information appears below for the Frykberg and Williams study.

Results from a fair-quality retrospective analysis of data from 2 administrative claims databases evaluating the incidence of lower extremity amputations in patients with DFUs suggest lower amputation rates among patients who received NPWT compared with those who received traditional wound therapies (Frykberg and Williams, 2007). Patients included in this analysis were a mix of inpatient and outpatient populations and they were not analyzed separately. This study was nonetheless included in the report because the authors suggest that patients who received NPWT in acute care settings but not in the outpatient setting are likely to be a small group within their study. It should be noted, however, that measured proportions of inpatients and outpatients or proportion of outpatient care days were not reported. This study employed stratified and adjusted analyses, which contributed to its fair-quality rating. Limitations of this study include retrospective analyses using administrative claims databases and potentially meaningful differences in patient demographics between the groups not accounted for in adjusted analyses.

Frykberg and Williams used a commercial payer database that provided 2 years of data, and a Medicare database that provided 1 year of data. Groups of patients who received NPWT were compared with control groups for each database. No statistical difference was seen in amputation rates between groups in either dataset prior to stratifying by total cost of treatment and depth of debridement, and adjusting for these risk categories within the NPWT group. Comparisons within risk categories between the control group with the unadjusted NPWT group in the commercial dataset showed a trend toward lower amputation rates in the NPWT group in most of the risk categories. The differences were statistically significantly in favor of the NPWT group for the highest total cost category (> $150,000), with an amputation rate of 45.7 percent in the control group and 27.3 percent in the NPWT group (P<0.0001), and in the deepest debridement category (bone) with an amputation rate of 52.7 percent in the controls and 26.3 percent in the NPWT group (P<0.0001). Overall amputation rates in the control group compared with the risk-adjusted cost and debridement NPWT group were not statistically significantly different in the commercial dataset (cost: control group 21.4% versus NPWT group 14.1%; P=0.0951; debridement: control group 21.4% versus NPWT group 18.3%; P=0.5221). With respect to the Medicare dataset, there was also a trend toward lower amputation rates in the NPWT groups for most of the risk categories. In the deepest debridement category, NPWT was associated with a statistically significantly lower amputation rate than the control group (18.3% versus 53.3%; P<0.0001). The NPWT group also had a statistically significantly lower amputation rate compared with the controls in the highest cost category (9.1% versus 44.7%; P<0.0001). The overall amputation rate was also statistically significantly lower in the cost and debridement risk-adjusted NPWT groups compared with the control group (cost: control group 16.6% versus NPWT group 10.8%; P=0.0077; debridement: control group 16.6% versus NPWT group 11.2%; P=0.0128).

Blume et al. reported significantly fewer amputations in the NPWT group in their study when compared with the group that received AMWT (NPWT, 7 out of 169 [4.1%]; AMWT, 17 out of 166 [10.2%];

P=0.035) (Blume et al., 2008). There were no statistically significant differences in other adverse events (edema, wound infection, cellulitis, osteomyelitis, *staphylococcus* infection, and infected skin ulcer) reported in this RCT. However, more patients in the NPWT group experienced wound infection (4 versus 1), cellulitis (4 versus 1), osteomyelitis (1 versus 0), and *staphylococcus* infection (1 versus 0) compared with the AMWT group. The AMWT group had more cases of edema (7 versus 5) and infected skin ulcers (2 versus 1) than the NPWT group.

The cohort study conducted by Fife et al. used surrogate measures such as antibiotic prescriptions and number of cultures taken for estimating rates of infection. Specific data were not reported; however, the investigators concluded that the NPWT group experienced fewer infections based on significantly fewer antibiotic prescriptions (*P*<0.05) and cultures (*P*<0.05) found in the database for this group compared with the control group. Bleeding was not reported in either group, and none of the NPWT patients discontinued treatment because of bleeding (Fife et al., 2008).

Pressure Ulcers

Two studies reported adverse events for patients with pressure ulcers. Study characteristics and quality rating are summarized in Key Question 1a for the Ford et al. study; these are summarized below for the Schwien et al study. In 1 RCT of patients with pressure ulcers, 28 patients with 41 full-thickness pressure ulcers were enrolled; however, 22 patients with 35 wounds completed the trial. Reasons for the 6 patients who did not complete the trial include 2 deaths, 3 lost to follow-up, and 1 noncompliant. It is not clear to which groups each of these patients were randomized; the final numbers for each group were 20 in the NPWT group and 15 in the comparison group. One case of sepsis requiring amputation was reported in the NPWT group (Ford et al., 2002).

Schwien et al. conducted a retrospective analysis of data from home health care agencies. This study was rated poor because of the following limitations: inappropriate or poorly described control groups; poor or selective reporting on comparative treatments, potential confounders, and outcomes. The investigators found a statistically significant difference between the NPWT group and the control group for emergency care visits for wound-related problems. No patients in the NPWT group (n=60) needed emergency care compared with 189 (8%) patients in the comparison group (n=2348) (*P*<0.01). However, 3 (5%) NPWT patients required hospitalization for a wound-related problem, but this was also significantly fewer than the 310 (14%) patients in the comparison group who required hospitalization (*P*<0.01). The results remained statistically significant when data were stratified by pressure ulcer grade (Schwien et al., 2005).

Mixed Ulcer Populations

Adverse events as they were related to study withdrawal were reported only for the NPWT group in the Lerman et al. article. Comparison with the control group is not possible as the data are not provided. Two patients were removed due to hospitalizations not related to the wound and 6 were noncompliant with the protocol. Seven patients had complications related to the study protocol requiring withdrawal: allergic skin reaction to the hydrocolloid dressing (n=1), wound infection (n=1), bleeding post

debridement (n=1), worsening lower extremity edema (n=1), and maceration to periwound skin (n=3). Data for these dropped patients were not included in the final analysis (Lerman et al., 2010).

Table 12. Study Characteristics of Studies Included for KQ2 (Harms) – Chronic Wounds

Key: DFU, diabetic foot ulcer; NPWT, negative pressure wound therapy; PU, pressure ulcer; RCT, randomized controlled trial

Study Study Design (n), Quality	Wound Type			Comparisons	NPWT Devices	
	DFU	PU	Mixed		SNaP (Spiracur)	V.A.C. (KCI)
Blume et al., (2008) RCT (341), Poor	X			Advanced moist wound therapy of primarily hydrogels and alginates consistent with standards of care		X
Fife et al., (2008) Retrospective observational (1331), Poor	X			Unspecified wound care treatment either prior to the start of NPWT or among patients who never received NPWT		X
Ford et al., (2002) RCT (28), Fair		X		Three gel products – Accuzyme, Iodosorb, and Panafil each targeted to optimize a particular macroscopic phase of wound healing		X
Frykberg and Williams (2007) Retrospective observational (16,319), Fair	X			Non-NPWT controls identified from administrative claims databases		X
Lerman et al., (2010) Retrospective observational (78), Poor			X	Matched controls treated at the same center with modern wound care protocols that included the use of Apligraf, Regranex, and skin grafting	X	
Schwien et al., (2005) Retrospective observational (2348), Poor		X		Matched controls receiving any other wound care therapy		X

Harms Reported in Studies of Surgical Wounds

Adverse events were reported in 5 studies evaluating NPWT compared with other wound treatments for surgical wounds (Armstrong et al., 2005; Apelqvist et al., 2008; Acosta et al., 2013; Biter et al., 2014; Monsen et al., 2014; Monsen et al., 2015; Karlakki et al., 2016; Manoharan et al., 2016). Study characteristics and quality ratings are summarized in Key Question 1b (see **Table 11**) for 4 of these studies; details for the fifth study (Karlakki et al., 2016) are described in Appendix Vb. None of the studies reported statistically significant differences between groups for the adverse events described in the publications.

Monsen et al. reported a total of 5 amputations during a median follow-up period of 14 months—3 out of 10 in the NPWT group and 2 out of 10 in the alginate dressing group (no *P* value reported; the Cochrane Review authors calculated a risk ratio [RR] of 1.5 [95% CI, 0.32-7.14] in favor of alginate dressings) (Monsen et al., 2014; Dumville et al., 2015a). One death occurred in the alginate dressing group during in-hospital stay; no deaths occurred in the NPWT patients while they were in the hospital (the Cochrane Review authors calculated an RR of 0.33 [95% CI, 0.02-7.32] in favor of NPWT) (Monsen et al., 2014; Dumville et al., 2015a). Overall, there were 2 deaths in the NPWT group and 5 in the alginate dressing group (*P*=0.35) (Monsen et al., 2014).

Among patients requiring surgical treatment for a pilonidal sinus, Biter et al. reported no differences in wound infection rate between the NPWT group and the standard open wound care group. There were 2 (8%) events in each group (the Cochrane Review authors calculated an RR of 1.04 [95% CI, 0.16-6.81]) (Biter et al., 2014; Dumville et al., 2015b). One patient in the NPWT group visited the emergency room because of a malfunctioning device that needed to be reconnected properly. No other adverse events were reported (Biter et al., 2014).

Armstrong et al. evaluated NPWT compared with standard moist wound therapy in patients after partial diabetic foot amputation. The proportion of patients undergoing a second amputation was higher in the standard therapy group, but the difference was not statistically significant (NPWT 2 [3%], control 9 [11%]; *P*=0.060). Wound infection rates were 17 percent and 6 percent in the NPWT and control groups, respectively (*P* value not reported). In the NPWT group, 3 of the 13 wound infections were classified as mild, 6 were moderate, and 4 were severe. Out of the 5 wound infections in the control group, 2 were mild, 1 was moderate, and 2 were severe. The authors state that none of the 13 wound infections among patients who received NPWT were related to treatment, and 2 of the 5 among the control group were related to treatment. Treatment-related adverse events occurred in 9 (12%) NPWT patients and 11 (13%) control patients. One treatment-related adverse event in the NPWT was classified as serious, and 5 treatment-related adverse events in the control group were classified as serious in the control group (Armstrong et al., 2005).

Two studies (Karlakki et al., 2016 and Manoharan et al., 2016) of patients with closed surgical wounds after total hip or knee arthroplasty reported wound complications. In the Manoharan et al. study, 1 NPWT-treated knee experienced severe blistering requiring hospital readmission and prophylactic intravenous antibiotics. One knee treated with CDD experienced persistent drainage; this knee was treated with NPWT in the hospital for 2 days. No wound dehiscence or infections for either treatment were observed during the 10- to 12-day follow-up period. The study by Karlakki et al. included 220

patients who underwent either elective total hip arthroplasty or total knee arthroplasty. Patients were randomized to either NPWT (Pico; Smith & Nephew Healthcare Ltd.) or conventional dressings. Immediately after surgery the control group received either Mepore (Mölnlycke Health Care AB) or Tegaderm (3M Health Care Ltd.), depending on the surgeon's preference. Two days later, the control group's dressings were changed to Opsite Post-op Visible dressing (Smith & Nephew). In this study, > 50% of patients in each group were discharged within 3 days of surgery; however, some patients may have been in the hospital for the duration of their wound treatment. With respect to wound complications, 2 (2%) patients in the NPWT group experienced wound complications after discharge compared with 9 (8.4%) in the conventional dressing group. The number of wound complications in the conventional dressing group included 2 patients with prolonged wound exudate requiring surgical washout while in hospital, and 7 who were treated for suspected surgical site infections with antibiotics in the community. The odds ratio (OR) for overall wound complications indicates a 4-fold reduction for the NPWT group compared with the conventional dressing group (OR 4.0; 95% CI, 0.95-30; *P*=0.06). Factors such as diabetes, obesity, and smoking status increased the risk of wound complications in both groups. The rate of blisters was 11% in the NPWT group compared with 1% in the control group (statistical significance not reported).

Key Question #3: Does the effectiveness of NPWT or incidence of adverse events vary by clinical history (e.g., diabetes), wound characteristics (e.g., size, chronicity), duration of treatment, types of devices, or patient characteristics (e.g., age, sex, prior treatments, smoking, or other medications)?

Chronic Wounds

Four studies were identified providing information pertaining to KQ3 with respect to patients with chronic wounds, and 1 study provided information for patients with surgical wounds. Among the studies of chronic wounds, 1 was a fair-quality RCT (Armstrong et al., 2011; Armstrong et al., 2012; Marston et al., 2015), 1 was a fair-quality observational study (Yao et al., 2014), and 2 were poor-quality observational studies (Lavery et al., 2007; Law et al., 2015). Two of these studies compared different NPWT devices. An RCT conducted by Armstrong et al. provides a comparison of the V.A.C. Therapy System (KCI Inc.), and the SNaP Wound Care System (Spiracur Inc.), and the Law et al. study provides a comparison of the V.A.C. Therapy System with non-KCI models. The studies by Lavery et al. and Yao et al. provide information about the role of wound size and chronicity when NPWT is compared with other wound treatments. No studies looked at comparative effectiveness in relation to clinical history, duration of treatment, or patient characteristics. A secondary analysis from a fair-quality study of surgical wounds (Armstrong et al., 2005; Armstrong et al., 2007) assessed the role of wound chronicity in wound healing after partial foot amputation in patients with diabetes.

Different Types of NPWT Devices Compared with Each Other (SNaP Versus V.A.C.)

The RCT conducted by Armstrong et al. is presented in 3 publications. The first was an interim analysis (Armstrong et al., 2011), the second is an analysis of the full study population (Armstrong et al., 2012), and the third (Marston et al., 2015) is a subanalysis of patients with venous leg ulcers. Treatment was evaluated for up to 16 weeks, and the full study enrolled 132 patients from 17 wound care centers and analyzed 115 patients (SNaP n=59; V.A.C. n=56). Eighty-three patients completed the study with either healing or 16 weeks of therapy. Complete wound healing was a secondary outcome in this study; the outcome was not defined. Adverse events and patient-centered outcomes were also assessed. The study was rated fair because of potentially meaningful differences in wound size between groups at baseline, the utilization of 2 different V.A.C. (KCI) systems in the comparison group without presenting separate analyses for each device, differential treatment between groups with respect to personnel who changed wound dressings, and patient outcome data obtained from an exit interview and subject to recall and attrition bias, as well as the potential for bias because of the lack of blinding to which device was used. Complete wound healing was assessed at 4, 8, 12, and 16 weeks. A Kaplan-Meier survival analysis showed no significant difference between the SNaP and V.A.C. groups for the proportion of wounds healed over time (P=0.9620); analyses adjusting for baseline wound size were also not statistically significant. 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 (Armstrong et al., 2012).

Information about return to prior level of activity and pain were also evaluated in this RCT through responses to exit interviews. Additionally, rates of pain were reported by the authors as an adverse event; rates were similar between the groups (SNaP n=1 [1.6%]; V.A.C. n=4 [5.9%]). Rhee and colleagues summarized the results of the exit surveys as reported in the Armstrong et al. (2012) publication, and calculated *P* values for the between-group differences. Their summary and calculations are as follows. Exit surveys to assess user experiences were completed for the 105 patients 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, patients 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 Rhee et al.]). Additionally, a higher percentage of SNaP-treated patients than V.A.C.-treated patients reported that their activity level either increased or stayed the same (83% versus 48%; P<0.05 [calculated by Rhee et al.]) (Armstrong et al., 2012; Rhee et al., 2014).

The level of pain was examined by a summation of pain scores, as compared with what would be the expected sum of scores. It is unclear how the expected summary score number was obtained, and further description of the definition of the pain scores is not provided. Patient-reported pain scores were not statistically significantly different between the 2 NPWT devices (Armstrong et al., 2012; Rhee et al., 2014).

In a subanalysis of patients with venous leg ulcers (VLUs) from this same RCT, Marston et al. analyzed 40 patients (V.A.C. n=21; SNaP n=19) from 13 wound care centers who completed the study. VLUs were

defined as those patients who had a leg ulcer in the gaiter region with evidence of venous disease on physical examination, and who were not diabetic. The authors did not state whether this was a preplanned or post hoc analysis. There was a notable difference in wound size between the 2 groups at baseline (mean ± SD: 4.85 ± 4.49 square centimeters [cm^2] for SNaP versus 11.6 ± 12.12 cm^2 for V.A.C.). Kaplan-Meier estimates suggest no significant difference in the proportion of patients who completely healed over time (*P*=0.3547 unadjusted for baseline wound size; *P*=0.4656 adjusted for baseline wound size) (Marston et al., 2015).

Rates of adverse events reported in the Armstrong et al. (2012) publication for the full patient population were similar between the groups. The rate of clinically determined infection was 3.1% in the SNaP (n=2) and 7.4% in the V.A.C. group (n=5) (*P*=0.28 [*P* value calculated by Rhee et al.]) (Armstrong et al., 2012; Rhee et al., 2014). In the subanalysis of VLUs, the rate of infection was found to be 5.3% in the SNaP group (n=1) and 9.5% in the V.A.C. group (n=2) (*P*=1.000) (Marston et al., 2015). Marston et al. report that rates of adverse events among the subgroup of patients with VLUs were similar between treatment groups and consistent with the larger study population.

Different Types of NPWT Devices Compared with Each Other (V.A.C. Versus non-KCI Models)

In a publication of findings from a poor-quality retrospective national claims database analysis comparing V.A.C. NPWT with non-KCI NPWT devices, Law and colleagues evaluated hospital readmission rates for the period following an initial NPWT claim in an outpatient setting. This study was rated poor because of the following methodological limitations: retrospective analysis; heterogeneous patient population and separate analyses were provided for only some of the included wound types; potentially meaningful baseline differences in 3-month analysis group and patient demographic results not presented for 6- and 12-month populations; methods state that data were analyzed at 12 months, but results were not provided; different group sizes; and methods do not indicate that analyses were adjusted to control for confounding variables. Multiple wound types were included in the dataset. Patients with chronic wounds, defined as DFUs (with and without amputation), pressure ulcers, VLUs, and nonhealing surgical wounds, comprised 82.1 percent of the wounds; the remaining wounds were categorized as acute wounds and included open wounds, cellulitis, and necrotizing fasciitis.

Claims data were analyzed at 3 months, 6 months, and 12 months after the index date of the first NPWT claim (patients included at each analysis point changed over time). There was a statistically significant difference in age between the 2 groups for the study sample analyzed at 3 months. Patients in the V.A.C. group (n=12,843 at 3 months) were younger (mean age 59.2 years) than the group treated with non-KCI devices (n=713 at 3 months; mean age 63.6 years) (*P*<0.01). The statistical significance of differences in the rates of individual comorbid conditions was not reported. Instead, the mean Charlson Comorbidity Index score was reported. This was similar between groups (*P* value not significant [NS]). At 3 months and at 6 months, wound-related readmission rates were statistically significantly lower for the V.A.C. group compared with the non-KCI device group across all wound types. At 3 months the rates in each group were 5 percent and 8 percent, respectively, for the V.A.C. (n=12,843) and non-KCI device (n=713) groups (*P*≤0.01). The rates at 6 months were 6 percent and 11 percent, respectively, for the V.A.C. (n=11,073) and non-KCI device (n=601) groups (*P*≤0.01). Significant differences in favor of V.A.C. were

also reported for mean per-patient inpatient stays and emergency room visits at 3 months and at 6 months for all wound types. When mean per-patient inpatient stays and emergency room visits at 3 months and 6 months were analyzed by wound category (nonhealing surgical wounds, open wounds, and pressure ulcers), statistical significance did not persist for inpatient stays at 3 months and 6 months for nonhealing surgical wounds and emergency room visits for pressure ulcers at 3 months and 6 months. Results at 12 months were not reported (Law et al., 2015).

NPWT Compared with Other Wound Treatments: Wound Size and Chronicity

In their systematic review of home use of NPWT for treating chronic wounds, Rhee and colleagues summarized the methods and findings with respect to wound size and chronicity from the Lavery et al. and Yao et al. studies as follows (Rhee et al., 2014). Lavery et al. examined healing in relation to ulcer size and wound duration at 12 and 20 weeks. Wounds were stratified according to wound size and duration. Wounds < 2 cm^2 were considered small, those 2 to 4 cm^2 were medium in size, and those > 4 cm^2 were considered large in size. Wounds that were < 6 months old were stratified as short duration, those 6 to 12 months old were considered medium duration, and those > 12 months old were considered long duration. The authors reported that wounds of all sizes treated with NPWT were more likely than those treated with standard wound care 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 < 6 months duration and those > 12 months duration were more likely to achieve closure. At 20 weeks, NPWT healed significantly more wounds compared with standard wound care only among wounds older than 12 months (P<0.05) (Lavery et al., 2007; Rhee et al., 2014).

Yao et al. also evaluated whether the timing of NPWT application had an effect on healing; however, they did not examine timing with respect to other wound treatments, so no comparison between NPWT and other wound treatments is possible with the data provided. Because no comparison with alternative treatments is provided, these results are shown here for information only and were not considered in the overall body of evidence. 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 to 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 HR, 3.38; 95% CI, 1.68 to 6.82).

Surgical Wounds

A secondary analysis from 1 of the included studies (Armstrong et al., 2005; Armstrong et al., 2007) assessed the role of wound chronicity in wound healing after partial foot amputation in patients with diabetes. Acute wounds were those < 30 days after amputation and chronic wounds were those > 30 days after amputation. Results indicate no statistically significant difference between the NPWT group and standard wound therapy group in the proportion of acute and chronic wounds achieving complete wound closure (acute P=0.072; chronic P=0.320). Time to complete closure was significantly different in

favor of NPWT compared with the standard wound treatment group for both acute (*P*=0.030) and chronic wounds (*P*=0.033).

Key Question #4: What are the cost implications and cost-effectiveness of NPWT?

Six studies were found that provided information about the cost of NPWT compared with usual care or other NPWT devices (Lavery, 2007; Apelqvist, 2008; Flack et al., 2008; Hutton and Sheehan, 2011; Driver and Blume, 2014; Law et al., 2015). One study compared the cost of mechanical NPWT (SNaP) with electrically powered NPWT devices and standard of care. Five studies compared the cost of NPWT using V.A.C. with other wound therapies or other NPWT devices. All studies found that the primary NPWT device of interest (SNaP or V.A.C.) resulted in cost savings over usual care or alternative NPWT devices.

Cost Comparison of Mechanical SNaP Wound Care System with Powered NPWT Devices and Usual Care from Medicaid and Private Payer Perspectives

Hutton and Sheehan (2011) used decision-analytic modeling to compare the cost of the SNaP device with standard care and electrically powered NPWT devices over a 16-week therapy period. Authors assumed equal wound healing efficacy between SNaP and powered NPWT devices based on preliminary studies and ongoing clinical trials (both heal 83.1 percent of patients). Modern dressings were assumed to heal 35.7 percent of patients. Costs of treatment included direct costs and other healthcare costs for diabetic lower extremity wounds. Costs were based on the literature comparing NPWT with modern dressings and Medicare reimbursement rates. SNaP cost $4445 more for the equipment and supplies than modern dressings but saved $1853 in dressing changes, $1846 in additional healthcare costs, $3425 in costs of complications, and $7020 in long-term costs for patients who did not heal. The SNaP Wound Care System saved $9699 (42%) over modern dressings, $2774 (17%) over powered NPWT for a private payer, and $2296 (15%) over powered NPWT for Medicare. Compared with powered NPWT devices, the SNaP system saves $659 in wound dressings for a private payer, and $2612 in dressings and home visits for Medicare. A sensitivity analysis assuming more conservative healing rates (37.9% for modern dressing and 53.7% for powered NPWT and SNaP) still resulted in cost savings in favor of SNaP of $420 versus modern dressings, $3928 versus powered NPWT for private payer, and $2201 versus powered NPWT for Medicare. This economic evaluation was funded by the SNaP device manufacturer (Hutton and Sheehan, 2011). Limitations of this economic study include the limitations of the data on which the model is based and missing parameters for concurrent or consecutive treatments such as pain medication or switching to other wound care methods.

Cost Comparison of Vacuum-Assisted Closure Therapy (V.A.C.) with Other Wound Therapies

Driver and Blume (2014) conducted a post-hoc analysis of patient records from an RCT (Blume et al., 2008) to compare healthcare costs between patients with DFUs receiving V.A.C. and those receiving AMWT. Data were obtained from the medical records of 324 (162 NPWT, 162 AMWT) out of the 335 patients with diabetic ulcers who were analyzed in the original RCT. Wound therapy costs included dressings and labor costs to change dressings. Nonwound therapy consisted of antibiotic therapy, inpatient services, extended care hospitalizations, and surgical procedures. Costs were calculated from patients' healthcare utilization, including hospital costs (Healthcare Cost and Utilization Project

Nationwide Inpatient Sample), physical services for surgical procedures (Medicare Resource-Based Relative Value Scale 2007), and extended-care facility cost per day (Medicare reimbursement rate). The average cost per patient regardless of wound closure was $11,984 for NPWT and $13,557 for AMWT. For patients who achieved wound closure, average cost was $10,172 for NPWT and $9505 for AMWT. For patients who did not achieve wound closure, average cost was $13,262 for NPWT and $15,068 for AMWT. Nonwound treatment costs were higher for patients undergoing AMWT than NPWT. For patients who achieved wound closure, average nonwound treatment cost was $10,716 for NPWT and $13,525 for AMWT. For patients who did not achieve wound closure, average nonwound treatment cost was $13,694 for NPWT and $17,927 for AMWT (Driver and Blume, 2014).

Lavery et al. (2007) aimed to assess the differential cost of care in the outpatient setting between NPWT and wet-to-moist therapy to treat DFUs. The 20-week expected cost of care was calculated using weekly costs of nursing visits, supplies, and physician costs. One to 2 nursing visits per day at a cost of $112 per visit were assumed for the wet-to-moist therapy group. The cost of wet-to-moist therapy supplies was based on an estimated 3 dressing changes per day. Cost estimates for the NPWT group were based on dressing changes every 48 hours and 3 nursing visits per week, with supply costs of $3.50 per dressing and $107 per day rental for the device. Physician costs in both groups were estimated at $66 per visit with an expected visit every 2 weeks. Calculations included the probability of successful treatment in a specified number of weeks; information for this estimate came from outcomes obtained from the retrospective observational study conducted by the authors and reported in the same publication. The 20-week expected cost of care for the NPWT group was $16,733. Twenty-week expected cost for the wet-to-moist therapy group based on 1 nursing visit per day was $15,258; based on 2 nursing visits per day the expected cost was $28,691. The expected 20-week costs for NPWT were similar to those for wet-to-moist therapy when 1 nursing visit per day was assumed. When 2 nursing visits per day were assumed for the wet-to-moist therapy group, the 20-week expected costs of NPWT were 42% less (Lavery, 2007).

In an economic analysis based on data from patients who completed at least 8 weeks of treatment in an RCT of diabetic patients with postamputation wounds, investigators aimed to evaluate resource utilization and direct economic costs of care for patients treated with NPWT (V.A.C.; KCI) compared with those who received moist wound therapy (Armstrong et al., 2005; Apelqvist et al., 2008). Clinical results from the RCT are summarized in key question 1b (Armstrong et al., 2005). Direct costs were calculated retrospectively using data on resource use for each patient. Costs included inpatient care, antimicrobial agents, outpatient treatment visits, surgical procedures, and topical dressing treatment of foot ulcers. The cost of each item or procedure was based on mean costs derived from a national commercial claims dataset (Milliman's Health Cost Guidelines). The cost of the V.A.C. Therapy Unit was based on an average daily rate of $70. Costs for V.A.C. dressing materials were based on $40 material cost applied at each dressing change. All costs are quoted as 2005 figures. The cost analysis concluded that the average direct cost per patient treated for 8 weeks or longer (regardless of clinical outcome) was $27,270 and $36,096 in the NPWT and moist wound therapy groups, respectively. The average total cost to achieve healing was $25,954 for patients treated with NPWT (n=43) compared with $38,806 for the moist wound therapy group (n=33). Sensitivity analyses suggest consistency of the study results.

A Markov model analysis was conducted by Flack et al. (2008) to estimate the cost per amputation avoided and the cost per quality-adjusted life-year (QALY) of V.A.C. (KCI) therapy compared with traditional and advanced wound care dressings. Using a simulated population of patients (n=1000), the model aimed to show how a patient with a DFU treated with each of the options would progress over a 1-year period. Data from published sources were used to define progression, and selected clinical trials provided information about the effectiveness of V.A.C. therapy and the alternative treatments with respect to healing rates. The alternative dressings included traditional dressings (e.g., saline gauze) and advanced wound care dressings (e.g., Apligraf [Novartis] and Dermagraft [Smith & Nephew]). U.S. cost data were applied to the resources used during treatment and Medicare reimbursement schedules for services were derived from a nationally representative database. Costs for traditional, advanced, and V.A.C. dressings were obtained from reimbursement data and expert opinion. Costs for antibiotics and utility weights for QALYs came from published literature. Nondressing unit charges accounted for outpatient costs such as office visit and home health charges. The authors conclude that V.A.C. therapy results in more wounds healed, more QALYs gained, and fewer amputations at a lower cost than traditional dressings. Similarly, NPWT results in fewer amputations and more QALYs gained at a lower overall cost than advanced wound care treatments. Sensitivity analyses suggest overall robustness of the findings (Flack et al., 2008).

Cost Comparison of NPWT V.A.C. with Other NPWT Devices

Law et al. (2015) conducted a retrospective claims database analysis on all patients who had submitted a claim to a major insurance company (Optum Life Sciences) for NPWT in an outpatient setting in the United States at 3-month and 12-month treatment periods. Chronic wounds comprised the majority of wounds (81%); acute wounds were also assessed. NPWT with V.A.C. (KCI) (n=12,843 at 3 months, n=7860 at 12 months) was compared with non-KCI model NPWT devices (n=713 at 3 months, n=378 at 12 months). At 3 months, the per-patient cost for NPWT with V.A.C. ($35,498) was $4224 (11%) lower than NPWT with other devices ($39,722) (*P*=0.08). At 12 months, the per-patient cost for NPWT with V.A.C. ($80,768) was significantly lower ($30,444 [27%]) than NPWT with other devices ($111,212) (*P*=0.03) (Law et al., 2015). This economic evaluation was funded by the device manufacturer.

Practice Guidelines

Five practice guidelines with relevant recommendations were identified. **Appendix VI** presents the recommendations of each guideline.

International Expert Panel on Negative Pressure Wound Therapy (NPWT-EP)

An international panel assembled and funded by NPWT device manufacturer Smith & Nephew Co. met to develop international guidelines concerning NPWT without reference to any particular NPWT device. The group developed evidence-based recommendations using a systematic literature review process including grading of evidence. Draft recommendations were followed by a formal consultative consensus development program involving 422 healthcare professionals. Individual recommendations do not specifically address home use of NPWT; however, the preamble to the recommendations

discusses the use of NPWT as a bridge to surgical closure or for healing by secondary intention, and notes the potential for home use of NPWT for wounds such as chronic wounds that may take a long time to heal. Some disadvantages of using NPWT for long periods are also noted, such as potential detriment on patients' QOL as the result of the devices limiting activity, making noise, being heavy, or causing self-consciousness. Thirteen evidence-based recommendations regarding the general use (regardless of setting) of NPWT were developed: 4 for pressure ulcers, 4 for DFUs, 3 for ischemic lower limb wounds, and 2 for VLUs.

- Pressure ulcers:
    - NPWT may be used until surgical closure is possible/desirable.
    - Alternatively, NPWT should be considered to achieve closure by secondary intention.
    - NPWT should be used to reduce wound dimensions.
    - NPWT should be used to improve the quality of the wound bed.
- DFUs:
    - NPWT must be considered as an advanced wound care therapy for postoperative Texas grade 2 and 3 diabetic feet without ischemia.
    - NPWT must be considered to achieve healing by secondary intention.
    - Alternatively, NPWT should be stopped when wound has progressed suitably to be closed by surgical means.
    - NPWT should be considered in an attempt to prevent amputation or re-amputation.
- Ischemic lower limb wounds:
    - The cautious use of NPWT in chronic limb ischemia when all other modalities have failed may be considered in specialist hands but never as an alternative for revascularization.
    - NPWT may be considered as an advanced wound care therapy for lower limb ulceration after revascularization.
    - The use of NPWT is NOT indicated in acute limb ischemia.
- VLUs:
    - If first line therapy (compression) is not efficacious, NPWT should be considered to prepare the wound for surgical closure as part of a clinical pathway.
    - Use of gauze may be considered to reduce pain during dressing changes in susceptible patients.

Association for the Advancement of Wound Care

The most recent guidelines on pressure ulcer therapy from the Association for the Advancement of Wound Care (AAWC), updated in October 2010, do not specifically mention home use of NPWT. Regarding general guidance on the use of NPWT, the AAWC places NPWT under advanced or adjunctive interventions for pressure ulcers not responsive to "A-level" care. The guidelines state that NPWT shows no consistent effect on pressure ulcer healing, although it may increase granulation. The document includes a statement about the FDA notice issued in 2009 regarding patient selection (FDA, 2009a; AAWC, 2010).

National Pressure Ulcer Advisory Panel

In 2014, the National Pressure Ulcer Advisory Panel (NPUAP), the European Pressure Ulcer Advisory Panel (EPUAP), and the Pan Pacific Pressure Injury Alliance updated their guidelines on the treatment of pressure ulcers (NPUAP et al., 2014). The group recommended the following regarding the use of NPWT for the treatment of pressure ulcers:

1. Consider NPWT as an early adjuvant for the treatment of deep, stage III and IV pressure ulcers.
2. Debride the pressure ulcer of necrotic tissue prior to the use of NPWT.
3. Follow a safe regimen in applying and removing the NPWT system.
4. Evaluate the pressure ulcer with each dressing change.
5. If pain is anticipated or reported, consider placing a nonadherent interface dressing on the wound bed, underneath the foam; lowering the level of pressure and/or changing type of pressure (continuous or intermittent); or using a moist gauze filler instead of foam.
6. Educate the patient and caregivers about NPWT when used in the community setting.

International Working Group on the Diabetic Foot

In its 2016 guidance, the International Working Group on the Diabetic Foot (IWGDF) concluded that it was not possible to make a recommendation on the use of NPWT with respect to chronic, nonsurgical wounds because of a lack of available evidence. Regarding postoperative wounds of the diabetic foot, the group recommends that NPWT may be considered even though the effectiveness and cost-effectiveness remain to be established. The group labeled the strength of this recommendation "weak" with moderate quality of evidence. No specific mention of the use of NPWT in the home setting is included in the guidance (Game et al., 2016).

Society for Vascular Surgery (SVS) and the American Venous Forum (AVF)

The SVS/AVF Joint Clinical Practices Guidelines Committee published recommendations for the management of VLUs in 2014. The only recommendation specific to NPWT is a recommendation against the routine primary use of NPWT for VLUs. The committee cites a lack of evidence to support the primary use of NPWT for VLUs even though there is some evidence supporting positive effects of NPWT for wound healing in general. These clinical practice guidelines do not discuss home use of NPWT (O'Donnell et al., 2014).

Selected Payer Policies

At the direction of WA State HCA, published coverage policies for the following organizations were sought: Aetna, Centers for Medicare & Medicaid Services (CMS), Oregon Health Evidence Review Commission (HERC), GroupHealth, and Regence Blue Cross/Blue Shield. The lack of a published coverage policy does not necessarily indicate that a payer does not provide coverage.

The terms used in searching the payer databases were *negative pressure or wound or e2402.*

Aetna

Aetna considers NPWT pumps medically necessary for ulcers and wounds encountered in an inpatient setting or in the home setting when the criteria are met. An NPWT pump and supplies are considered not medically necessary if any contraindication for use (as identified in the policy) is present.

For ulcers and wounds in the home setting, the member has a chronic stage III or IV pressure ulcer, neuropathic ulcer (e.g., diabetic ulcer), venous or arterial insufficiency ulcer, or a chronic ulcer of mixed etiology, present for at least 30 days. A complete wound therapy program as applicable depending on the type of wound (outlined in the policy), has been tried or considered and ruled out prior to application of NPWT.

Criteria for continued medical necessity, discontinuation, and maximum supply coverage are outlined in the policy.

Aetna considers NPWT experimental and investigational for the treatment of deep sternal wound infection, partial-thickness burns, tibial fractures, for use following surgical excision of pilonidal sinus disease and for recurrent pilonidal disease, and all other indications, because its effectiveness for these indications has not been established.

Aetna considers the use of chemotherapeutic agents in continuous-instillation or intermittent-instillation NPWT experimental and investigational because its effectiveness has not been established.

Aetna considers the use of nonpowered (mechanical) NPWT devices (Smart Negative Pressure [SNaP] Wound Care System) experimental and investigational because their effectiveness has not been established.

Aetna considers the use of single-use NPWT devices (PICO Single Use Negative Pressure Wound Therapy System; Prevena Incision Management System) experimental and investigational for all indications because of insufficient evidence of their effectiveness.

See Negative Pressure Wound Therapy (Aetna Clinical Policy Bulletin No. 0334: http://www.aetna.com/cpb/medical/data/300_399/0334.html.

Centers for Medicare & Medicaid Services (CMS)

No CMS National Coverage Determination (NCD) for NPWT was identified on July 25, 2016 (search National Coverage Documents by keywords *negative pressure* or *wound* or *ulcer* or *e2402* in all documents at: https://www.cms.gov/medicare-coverage-database/search/advanced-search.aspx). In the absence of an NCD, coverage decisions are left to the discretion of local Medicare carriers. There is a Local Coverage Determination (LCD) for NPWT pumps (L33821) that was effective July 1, 2016. The LCD was issued by Noridian Healthcare Solutions LLC, a Medicare contractor in the state of Washington.

The LCD states that an NPWT pump and supplies are covered when ulcers and wounds are encountered in an inpatient setting or in the home setting when the criteria are met.

For ulcers and wounds in the home setting, the beneficiary has a chronic stage III or IV pressure ulcer, neuropathic (e.g., diabetic) ulcer, venous or arterial insufficiency ulcer, or a chronic (present for at least 30 days) ulcer of mixed etiology. A complete wound therapy program as applicable depending on the type of wound (outlined in the LCD), has been tried or considered and ruled out prior to application of NPWT.

An NPWT pump and supplies will be denied at any time as not reasonable or necessary if 1 or more of the exclusions (as identified in the LCD) are present.

See LCD for Negative Pressure Wound Therapy Pumps (L33821).

Group Health Cooperative

Group Health Cooperative covers NPWT pumps and supplies for wound edema, exudate management, and stimulation of granulation for an initial 14-day course when the criteria are met for ulcers and wounds encountered in an inpatient setting or in the home setting, there is a goal of therapy clearly stated, and there are no contraindications for use (as identified in the policy).

For ulcers and wounds in the home setting, the patient has a stage III or IV pressure ulcer, neuropathic/diabetic ulcer, venous insufficiency or arterial ulcer, or a chronic ulcer of mixed etiology. These wounds should have exudate, size, and depth to require this specialized therapy.

A complete wound therapy program as applicable depending on the type of wound (outlined in the policy), should have been tried for 30 days unless edema and/or exudate mandates NPWT.

Criteria for continued coverage, denied coverage, and maximum supply coverage are outlined in the policy.

Group Health Cooperative does not cover nonpowered NPWT (SNaP, PICO) because there is insufficient evidence in the published medical literature to show that this service/therapy is as safe as standard services/therapies and/or provides better long-term outcomes than current standard services/therapies.

See Negative Pressure Wound Therapy: Clinical Review Criteria: https://provider.ghc.org/all-sites/clinical/criteria/pdf/negative_pressure_wound_therapy.pdf.

Oregon Health Evidence Review Commission (HERC)

No published coverage policies for NPWT were identified on the Oregon HERC website (Oregon HERC Coverage Guidances: http://www.oregon.gov/oha/herc/Pages/CoverageGuidances.aspx). The Prioritized List of Health Services published by the HERC references a Guideline Note regarding NPWT (Guideline Note 62, Negative Pressure Wound Therapy) for lines 8, 30, 51, 84, 210, 212, 240, 290, 384, and 428. The note states, “Negative pressure wound therapy (CPT 97605-97608, HCPCS G0456, G0457) is included on these lines only for patients who: have wounds that are refractory to or have failed standard therapies; are not suitable candidates for surgical wound closure; or, are at high risk for delayed or non-healing wounds due to factors such as compromised blood flow, diabetic complications,

wounds with high risk of fecal contamination, extremely exudative wounds, and similar situations." The Oregon Medical Fee and Payment Rules provide a maximum limit for monthly rentals under code E2402 in the absence of a contract that specifies a different rate.

Regence

No published coverage policy for NPWT was identified on the Regence Group website (Regence Group Medical Policies: http://blue.regence.com/policy/).

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APPENDICES

APPENDIX I. Search Strategy

INITIAL SEARCH, SYSTEMATIC REVIEWS (conducted March 15, 2016, and May 11, 2016)

Initially, evidence for this report was obtained by searching for systematic reviews, meta-analyses, practice guidelines, and economic evaluations that had been published in the past 10 years. Searches were conducted in the following databases using the term *negative pressure wound therapy*: Agency for Healthcare Research and Quality (AHRQ), Blue Cross Blue Shield TEC Assessments, Canadian Agency for Drugs and Technology in Health (CADTH), Centre for Reviews and Dissemination (CRD) (York University), Hayes Knowledge Center, Institute for Clinical Systems Improvement (ICSI), National Institute for Health Research Health Technology Assessment (NIHR HTA) Programme (UK), United States Preventive Services Task Force (USPSTF), National Institute for Health and Care Excellence (NICE), and Veterans Affairs Technology Assessment Program (VA TAP). (NOTE: The CRD search strategy includes a search for Cochrane Reviews.) Additional systematic reviews were sought from a search of the PubMed database using filters for Systematic Reviews.

SEARCH FOR PRIMARY CLINICAL STUDIES AND ECONOMIC EVALUATIONS

Three systematic reviews were identified that were relevant to the Key Questions for this report; these systematic reviews were used to identify primary studies for this health technology assessment. Subsequent searches for additional primary studies were designed to update the literature searches from the selected systematic reviews.

PubMed search on May 17, 2016 and September 12, 2016

Search	Query
#26	Search #23 NOT #24 Filters: Publication date from 2013/12/01 to 2016/05/17
#25	Search #23 NOT #24
#24	Search (animals[MeSH Terms]) NOT humans[MeSH Terms]
#23	Search #22 AND #9
#22	Search #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21
#21	Search vacuum-sealed[Title/Abstract]
#20	Search vacuum sealed[Title/Abstract]
#19	Search vacuum-sealing[Title/Abstract]
#18	Search sub-atmospheric[Title/Abstract]
#17	Search subatmospheric[Title/Abstract]

#16 Search vacuum-assisted[Title/Abstract]

#15 Search vacuum assisted[Title/Abstract]

#14 Search negative-pressure[Title/Abstract]

#13 Search negative pressure[Title/Abstract]

#12 Search negative-pressure wound therapy[MeSH Terms]

#11 Search suction[MeSH Terms]

#10 Search vacuum[MeSH Terms]

#9 Search #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8

#8 Search infections, surgical wound[MeSH Terms]

#7 Search dehiscence, surgical wound[MeSH Terms]

#6 Search ulcer*[Title/Abstract]

#5 Search wound*[Title/Abstract]

#4 Search (wounds and injuries[MeSH Terms])

#3 Search skin ulcer[MeSH Terms]

#2 Search wound healing[MeSH Terms]

OVID-Embase search on July 1, 2016 and September 12, 2016

The following search was run in both the Embase and MEDLINE databases. Only nonduplicated search results were reviewed.

1. Wound healing. ab,kw,sh,ti.
2. Wound care. ab,kw,sh,ti.
3. Skin ulcer. ab,kw,sh,ti.
4. "ulcer". ab,kw,sh,ti.
5. Wound. ab,kw,sh,ti.
6. 1 or 2 or 3 or 4 or 5
7. Vacuum. ab,kw,sh,ti.
8. Vacuum assisted closure. ab,kw,sh,ti.
9. (negative pressure or negative-pressure). ab,kw,sh,ti.

10. (vacuum assisted or vacuum-assisted). ab,kw,sh,ti.
11. (subatmospheric or sub-atmospheric). ab,kw,sh,ti.
12. (vacuum sealing or vacuum sealed or vacuum-sealed). ab,kw,sh,ti.
13. 7 or 8 or 9 or 10 or 11 or 12
14. Surgical wound infection. ab,kw,sh,ti.
15. Surgical wound dehiscence. ab,kw,sh,ti.
16. 14 or 15
17. 6 or 16
18. 13 and 17
19. Limit to English language
20. Limit 19 to humans
21. Limit 20 to yr="2014-current"
22. Remove duplicates from 21

Searches 23-34 removed ineligible publication types (e.g., conference abstracts, reviews, letters, editorials)

SEARCH FOR GUIDELINES

The National Guidelines Clearinghouse (https://guideline.gov/) and websites of professional organizations were searched using the term *negative pressure wound therapy*. Professional organizations included Association for the Advancement of Wound Care, the International Working Group on the Diabetic Foot, and the National Pressure Ulcer Advisory Panel.

APPENDIX II. The Assessment of Multiple Systematic Reviews (AMSTAR) Tool

The following key steps describe the AMSTAR tool (Shea et al., 2007):

Step 1	Systematic Review Appraisal Rate the quality of each systematic review using the Assessment of Multiple Systematic Reviews (AMSTAR) tool (Shea et al., 2007). This step is only necessary when data synthesis such as meta-analysis is conducted within the review and used in addition to or in place of individual study data.
Step 2	Individual Study Appraisal a. Initial rating according to study design *Good:* Randomized controlled trials *Fair:* Nonrandomized trial (controlled, parallel-group, quasirandomized) *Poor:* Observational analytic studies (prospective or retrospective trials involving historical controls, pretest-posttest control trial [patients legitimately serve as their own controls], case-control, registry/chart/database analysis involving a comparison group) *Very poor:* Descriptive uncontrolled studies (case reports, case series, cross-sectional surveys [individual-level data], correlation studies [group-level data]) a. Consider the methodological rigor of study execution according to items in a proprietary Quality Checklist b. Repeat for each study
Step 3	Evaluation of Each Body of Evidence by Outcome, Key Question, or Indication a. Initial quality designation according to *best* study design in a body of evidence Downgrade/upgrade *Downgrade factors:* Study weaknesses (Quality Checklists), lack of applicability, inconsistency of results, small quantity of data, publication bias (if adequate information is available) *Possible upgrade factors:* Strong association, dose-*response* effect, bias favoring no effect b. Assign final rating: High-Moderate-Low-Very Low c. Repeat for each outcome/question/application
Step 4	Evaluation of Overall Evidence a. Rank outcomes by clinical importance b. Consider overall quality of the evidence for each *critical* outcome c. Assign overall rating based on lowest-quality body: High-Moderate-Low-Very Low
Step 5	Evidence-Based Conclusion Overall quality of the evidence + balance of benefits and harms

APPENDIX III. Overview of Evidence Quality Assessment Methods

Clinical Studies

Tools used include internally developed Quality Checklists for evaluating the quality (internal validity) of different types of studies, a checklist for judging the adequacy of systematic reviews used instead of de novo analysis, and Hayes Evidence-Grading Guides for evaluating bodies of evidence for different types of technologies. Hayes methodology is in alignment with the GRADE (Grading of Recommendations, Assessment, Development, and Evaluation) system, which was developed by the GRADE Working Group, an international collaborative body.

Step 1	Individual study appraisal: a. Initial rating according to study design *Good:* Randomized controlled trials *Fair:* Nonrandomized trial (controlled, parallel-group, quasirandomized) *Poor:* Observational analytic studies (prospective or retrospective trials involving historical controls, pretest-posttest control trial [patients legitimately serve as their own controls], case-control, registry/chart/database analysis involving a comparison group) *Very poor:* Descriptive uncontrolled studies (case reports, case series, cross-sectional surveys [individual-level data], correlation studies [group-level data]) b. Consider the methodological rigor of study execution according to items in a proprietary Quality Checklist c. Repeat for each study
Step 2	Evaluation of each body of evidence by outcome, key question, or application: a. Initial quality designation according to *best* study design in a body of evidence b. Downgrade/upgrade *Downgrade factors:* Study weaknesses (Quality Checklists), small quantity of evidence, lack of applicability, inconsistency of results, publication bias *Possible upgrade factors:* Strong association, dose-response effect, bias favoring no effect c. Assign final rating: High-Moderate-Low-Very Low d. Repeat for each outcome/question/application
Step 3	Evaluation of overall evidence: a. Rank outcomes by clinical importance b. Consider overall quality of evidence for each *critical* outcome c. Assign overall rating based on lowest-quality body: High-Moderate-Low-Very Low
Step 4	Evidence-based conclusion: Overall quality of evidence + Balance of benefits and harms

Practice Guidelines (checklist taken from AGREE Tool and approach to scoring used in this report)

Rank each item on a scale of 1-7.

Decide on overall quality (1 = lowest to 7 = highest), giving strongest weight to items 7-14 (Rigor of Development Domain) and items 22-23 (Editorial Independence).

For qualitative labels:

Very poor = 1
Poor = 2-3
Fair = 4-5
Good = 6-7

1. The overall objective(s) of the guideline is (are) specifically described.
2. The health question(s) covered by the guideline is (are) specifically described.
3. The population (patients, public, etc.) to whom the guideline is meant to apply is specifically described.
4. The guideline development group includes individuals from all relevant professional groups.
5. The views and preferences of the target population (patients, public, etc.) have been sought.
6. The target users of the guideline are clearly defined.
7. Systematic methods were used to search for evidence.
8. The criteria for selecting the evidence are clearly described.
9. The strengths and limitations of the body of evidence are clearly described.
10. The methods for formulating the recommendations are clearly described.
11. The health benefits, side effects, and risks have been considered in formulating the recommendations.
12. There is an explicit link between the recommendations and the supporting evidence.
13. The guideline has been externally reviewed by experts prior to its publication.
14. A procedure for updating the guideline is provided.
15. The recommendations are specific and unambiguous.
16. The different options for management of the condition or health issue are clearly presented.
17. Key recommendations are easily identifiable.

18. The guideline describes facilitators and barriers to its application.
19. The guideline provides advice and/or tools on how the recommendations can be put into practice.
20. The potential resource implications of applying the recommendations have been considered.
21. The guideline presents monitoring and/or auditing criteria.
22. The views of the funding body have not influenced the content of the guideline.
23. Competing interests of guideline development group members have been recorded and addressed.

Economic Evaluations

A tool developed by Hayes for internal use guides interpretation and critical appraisal of economic evaluations. The tool includes a checklist of items addressing issues such as the reliability of effectiveness assumptions, transparency of reporting, quality of analysis, generalizability/applicability, and conflicts of interest. The following publications served as sources of best practice.

Brunetti M, Shemilt I, Pregno S, et al. GRADE guidelines: 10. Considering resource use and rating the quality of economic evidence. *J Clin Epidemiol*. 2013;66(2):140-150. PMID: 22863410.

Drummond MF, Jefferson TO. Guidelines for authors and peer reviewers of economic submissions to the BMJ. The BMJ Economic Evaluation Working Party. *BMJ*. 1996;313(7052):275-283. PMID: 8704542.

Drummond M, Sculpher M. Common methodological flaws in economic evaluations. *Med Care*. 2005;43(7 Suppl):5-14. PMID: 16056003.

Evers S, Goossens M, de Vet H, van Tulder M, Ament A. Criteria list for assessment of methodological quality of economic evaluations: Consensus on Health Economic Criteria. *Int J Technol Assess Health Care*. 2005;21(2):240-245. PMID: 15921065.

Gerkens S, Crott R, Cleemput I, et al. Comparison of three instruments assessing the quality of economic evaluations: a practical exercise on economic evaluations of the surgical treatment of obesity. *Int J Technol Assess Health Care*. 2008;24(3):318-325. PMID: 18601800.

Hutubessy R, Chisholm D, Edejer TT. Generalized cost-effectiveness analysis for national-level priority-setting in the health sector. *Cost Eff Resour Alloc*. 2003;1(1):8. PMID: 14687420.

Shemilt I, Thomas J, Morciano M. A web-based tool for adjusting costs to a specific target currency and price year. *Evid Policy*. 2010;6(1):51-59.

Smith KA, Rudmik L. Cost collection and analysis for health economic evaluation. *Otolaryngol Head Neck Surg*. 2013;149(2):192-199. PMID: 23641023.

Ubel PA, Hirth RA, Chernew ME, Fendrick AM. What is the price of life and why doesn't it increase at the rate of inflation? *Arch Intern Med*. 2003;163(14):1637-1641. PMID: 12885677.

Books

Drummond MF, O'Brien BJ, Stoddart GL, Torrance GW. *Methods for the Economic Evaluation of Health Care Programmes.* 2nd Edition. Oxford, UK: Oxford University Press; 1997.

Gold MR, Siegel JE, Russell LB, Weinstein MC, eds. *Cost-Effectiveness in Health and Medicine.* Oxford, UK: Oxford University Press; 1996.

Other

Canadian Agency for Drugs and Technologies in Health (CADTH). *Guidelines for the Economic Evaluation of Health Technologies: Canada*. 3rd Edition. Ottawa, Canada: Canadian Agency for Drugs and Technologies in Health; 2006. Available at: http://www.cadth.ca/media/pdf/186_EconomicGuidelines_e.pdf. Accessed October 5, 2016.

APPENDIX IV. Excluded Studies

The following 54 studies were excluded during full-text review.

Ineligible study design, publication type, comparison, or outcomes (13)

1. Anthony H. Efficiency and cost effectiveness of negative pressure wound therapy. *Nurs Stand*. 2015;30(8):64-70.
2. Brinkert D, Ali M, Naud M, Maire N, Trial C, Téot L. Negative pressure wound therapy with saline instillation: 131 patient case series. *Int Wound J*. 2013;(10 Suppl 1):56-60.
3. Chang EI. Discussion: the economic impact of closed-incision negative-pressure therapy in high-risk abdominal incisions: a cost-utility analysis. *Plast Reconstr Surg*. 2016;137(4):1290-1291.
4. Chatterjee A, Macarios D, Griffin L, et al. Cost-utility analysis: sartorius flap versus negative pressure therapy for infected vascular groin graft management. *Plast Reconstr Surg Glob Open*. 2015;3(11):e566.
5. Egemen O, Ozkaya O, Ozturk MB, Aksan T, Orman Ç, Akan M. Effective use of negative pressure wound therapy provides quick wound-bed preparation and complete graft take in the management of chronic venous ulcers. *Int Wound J*. 2012;9(2):199-205.
6. Hurd T, Trueman P, Rossington A. Use of a portable, single-use negative pressure wound therapy device in home care patients with low to moderately exuding wounds: a case series. *Ostomy Wound Manage*. 2014;60(3):30-36.
7. Jeffery SL. Non-adherent and flexible -using Cutimed Sorbact as a filler and liner with NPWT. *J Wound Care*. 2014;23(5 Suppl):S3-S15.
8. Lavery LA, La Fontaine J, Thakral G, Kim PJ, Bhavan K, Davis KE. Randomized clinical trial to compare negative-pressure wound therapy approaches with low and high pressure, silicone-coated dressing, and polyurethane foam dressing. *Plast Reconstr Surg*. 2014;133(3):722-726.
9. Pellino G, Sciaudone G, Candilio G, Campitiello F, Selvaggi F, Canonico S. Effects of a new pocket device for negative pressure wound therapy on surgical wounds of patients affected with Crohn's disease: a pilot trial. *Surg Innov*. 2014;21(2):204-212.
10. Selvaggi F, Pellino G, Sciaudone G, et al. New advances in negative pressure wound therapy (NPWT) for surgical wounds of patients affected with Crohn's disease. *Surg Technol Int*. 2014;24:83-89.
11. Serena TE, Buan JS. The use of a novel canister-free negative-pressure device in chronic wounds: A retrospective analysis. *Adv Skin Wound Care*. 2016;29(4):165-168.
12. Stapleton H. Wound healing in obese women following caesarean section. *Aust Nurs Midwifery J*. 2015;23(3):34.
13. Vassallo IM, Formosa C. Comparing calcium alginate dressings to vacuum-assisted closure: a clinical trial. *Wounds*. 2015;27(7):180-190.

Ineligible population or n < 20 (3)

1. Ashby RL, Dumville JC, Soares MO, et al. A pilot randomised controlled trial of negative pressure wound therapy to treat grade III/IV pressure ulcers [ISRCTN69032034]. *Trials*. 2012;13:119.
2. de Laat EH, van den Boogaard MH, Spauwen PH, van Kuppevelt DH, van Goor H, Schoonhoven L. Faster wound healing with topical negative pressure therapy in difficult-to-heal wounds: a prospective randomized controlled trial. *Ann Plast Surg*. 2011;67(6):626-631.
3. Ousey KJ, Milne J, Cook L, Stephenson J, Gillibrand W. A pilot study exploring quality of life experienced by patients undergoing negative-pressure wound therapy as part of their wound care treatment compared to patients receiving standard wound care. *Int Wound J*. 2014;11(4):357-365.

Ineligible setting or comparison (35)

1. Chio EG, Agrawal A. A randomized, prospective, controlled study of forearm donor site healing when using a vacuum dressing. *Otolaryngol Head Neck Surg*. 2010;142(2):174-178.
2. Chopra K, Gowda AU, Morrow C, Holton L 3rd, Singh DP. The economic impact of closed-incision negative-pressure therapy in high-risk abdominal incisions: a cost-utility analysis. *Plast Reconstr Surg*. 2016;137(4):1284-1289.
3. Correa JC, Mejia DA, Duque N, J MM, Uribe CM. Managing the open abdomen: Negative pressure closure versus mesh-mediated fascial traction closure: a randomized trial. *Hernia*. 2016;20(2):221-229.
4. Dalla Paola L, Carone A, Ricci S, Russo A, Ceccacci T, Ninkovic S. Use of vacuum-assisted closure therapy in the treatment of diabetic foot wounds. *J Diabetes Complications*. 2010;2(2):33-44.
5. Dorafshar AH, Franczyk M, Gottlieb LJ, Wroblewski KE, Lohman RF. A prospective randomized trial comparing subatmospheric wound therapy with a sealed gauze dressing and the standard vacuum-assisted closure device. *Ann Plast Surg*. 2012;69(1):79-84.
6. Dwivedi MK, Srivastava RN, Bhagat AK, et al. Pressure ulcer management in paraplegic patients with a novel negative pressure device: a randomised controlled trial. *J Wound Care*. 2016;25(4):199-200, 200-204, 207-207.
7. Fulco I, Erba P, Valeri RC, Vournakis J, Schaefer DJ. Poly-N-acetyl glucosamine nanofibers for negative-pressure wound therapies. *Wound Repair Regen*. 2015;23(2):197-202.
8. Ghatak PD, Schlanger R, Ganesh K, et al. A wireless electroceutical dressing lowers cost of negative pressure wound therapy. *Adv Wound Care (New Rochelle)*. 2015;4(5):302-311.

9. Gillespie BM, Rickard CM, Thalib L, et al. Use of negative-pressure wound dressings to prevent surgical site complications after primary hip arthroplasty: a pilot RCT. *Surg Innov*. 2015;22(5):488-495.

10. Gunal O, Tuncel U, Turan A, Barut S, Kostakoglu N. The use of vacuum-assisted closure and GranuFoam Silver® dressing in the management of diabetic foot ulcer. *Surg Infect (Larchmt)*. 2015;16(5):558-565.

11. Heard C, Chaboyer W, Anderson V, Gillespie BM, Whitty JA. Cost-effectiveness analysis alongside a pilot study of prophylactic negative pressure wound therapy. *J Tissue Viability*. 2016. Epub ahead of print. June 8, 2016. Available at: http://www.sciencedirect.com/science/article/pii/S0965206X16300249. Accessed October 5, 2016.

12. Hermans MH, Kwon Lee S, Ragan MR, Laudi P. Results of a retrospective comparative study: material cost for managing a series of large wounds in subjects with serious morbidity with a hydrokinetic fiber dressing or negative pressure wound therapy. *Wounds*. 2015;27(3):73-82.

13. Honnegowda TM, Kumar P, Padmanabha Udupa EG, et al. Effects of limited access dressing in chronic wounds: a biochemical and histological study. *Indian J Plast Surg*. 2015;48(1):22-28.

14. Howell RD, Hadley S, Strauss E, Pelham FR. Blister formation with negative pressure dressings after total knee arthroplasty. *Curr Orthop Pract*. 2011;22(2):176-179.

15. Ikura K, Shinjyo T, Kato Y, Uchigata Y. Efficacy of negative pressure wound therapy for the treatment of diabetic foot ulcer/gangrene. *Diabetology Int*. 2014;5(2):112-116.

16. Kakagia D. How to close a limb fasciotomy wound: an overview of current techniques. *Int J Low Extrem Wounds*. 2015;14(3):268-276.

17. Kakagia D, Karadimas EJ, Drosos G, Ververidis A, Trypsiannis G, Verettas D. Wound closure of leg fasciotomy: comparison of vacuum-assisted closure versus shoelace technique. a randomised study. *Injury*. 2014;45(5):890-893.

18. Kim PJ, Attinger CE, Oliver N, et al. Comparison of outcomes for normal saline and an antiseptic solution for negative-pressure wound therapy with instillation. *Plast Reconstr Surg*. 2015;136(5):657e-664e.

19. Kirkpatrick AW, Roberts DJ, Faris PD, et al. Active negative pressure peritoneal therapy after abbreviated laparotomy: the intraperitoneal vacuum randomized controlled trial. *Ann Surg*. 2015;262(1):38-46.

20. Leclercq A, Labeille B, Perrot JL, Vercherin P, Cambazard F. Skin graft secured by VAC (vacuum-assisted closure) therapy in chronic leg ulcers: a controlled randomized study. *Ann Dermatol Venereol*. 2016;143(1):3-8.

21. Lewis LS, Convery PA, Bolac CS, Valea FA, Lowery WJ, Havrilesky LJ. Cost of care using prophylactic negative pressure wound vacuum on closed laparotomy incisions. *Gynecol Oncol*. 2014;132(3):684-689.

22. Li PY, Yang D, Liu D, Sun SJ, Zhang LY. Reducing surgical site infection with negative-pressure wound therapy after open abdominal surgery: a prospective randomized controlled study. *Scand J Surg*. 2016. Epub ahead of print. September 8, 2016. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27609528. Accessed October 5, 2016.

23. Liu X, Liang J, Zao J, et al. Vacuum sealing drainage treatment combined with antibiotic-impregnated bone cement for treatment of soft tissue defects and infection. *Med Sci Monit*. 2016;22:1959-1965.

24. Llanos S, Danilla S, Barraza C, et al. Effectiveness of negative pressure closure in the integration of split thickness skin grafts: a randomized, double-masked, controlled trial. *Ann Surg*. 2006;244(5):700-705.

25. Masden D, Goldstein J, Endara M, Xu K, Steinberg J, Attinger C. Negative pressure wound therapy for at-risk surgical closures in patients with multiple comorbidities: a prospective randomized controlled study. *Ann Surg*. 2012;255(6):1043-1047.

26. McCallon SK, Frilot C. A retrospective study of the effects of clostridial collagenase ointment and negative pressure wound therapy for the treatment of chronic pressure ulcers. *Wounds*. 2015;27(3):44-53.

27. Mody GN, Nirmal IA, Duraisamy S, Perakath B. A blinded, prospective, randomized controlled trial of topical negative pressure wound closure in india. *Ostomy Wound Manage*. 2008;54(12):36-46.

28. Moues CM, van den Bemd GJ, Heule F, Hovius SE. Comparing conventional gauze therapy to vacuum-assisted closure wound therapy: a prospective randomised trial. *J Plast Reconstr Aesthet Surg*. 2007;60(6):672-681.

29. Osterhoff G, Zwolak P, Kruger C, Wilzeck V, Simmen HP, Jukema GN. Risk factors for prolonged treatment and hospital readmission in 280 cases of negative-pressure wound therapy. *J Plast Reconstr Aesthet Surg*. 2014;67(5):629-633.

30. Pachowsky M, Gusinde J, Klein A, et al. Negative pressure wound therapy to prevent seromas and treat surgical incisions after total hip arthroplasty. *Int Orthop*. 2012;36(4):719-722.

31. Petkar K, Dhanraj P, Sreekar H. Vacuum closure as a skin-graft dressing: a comparison against conventional dressing. *Eur J Plast Surg*. 2012;35(8):579-584.

32. Sajid MT, Mustafa Q, Shaheen N, Hussain SM, Shukr I, Ahmed M. Comparison of negative pressure wound therapy using vacuum-assisted closure with advanced moist wound therapy in the treatment of diabetic foot ulcers. *J Coll Physicians Surg Pak*. 2015;25(11):789-793.

33. Skrinjar E, Duschek N, Bayer GS, et al. Randomized controlled trial comparing the combination of a polymeric membrane dressing plus negative pressure wound therapy against negative pressure wound therapy alone: the WICVAC study. *Wound Repair Regen*. 2016;24(5):928-935.

34. Stannard JP, Volgas DA, McGwin G 3rd, et al. Incisional negative pressure wound therapy after high-risk lower extremity fractures. *J Orthop Trauma*. 2012;26(1):37-42.

35. Vaidhya N, Panchal A, Anchalia MM. A new cost-effective method of NPWT in diabetic foot wound. *Indian J Surg*. 2015;77(Suppl 2):525-529.

Other (full text not obtainable) (3)

1. Abdalla S, Rolph R, Rampersad A, Patel G, Oke T. Application of the Prevena™ incision management system following complex ventral hernia repairs with abdominal wall reconstruction. *Surg Technol Int*. 2016;XXIX.

2. Niezgoda JA. A comparison of vacuum assisted closure therapy to moist wound care in the treatment of pressure ulcers: Preliminary results of a multicenter trial [abstract X001]. 2nd World Union of Wound Healing Societies Meeting, Paris, France. July 8-13, 2004.

3. Uchino M, Hirose K, Bando T, Chohno T, Takesue Y, Ikeuchi H. Randomized controlled trial of prophylactic negative-pressure wound therapy at ostomy closure for the prevention of delayed wound healing and surgical site infection in patients with ulcerative colitis. *Dig Surg*. 2016;33(6):449-454.

APPENDIX V. Evidence Tables

APPENDIX Va. Studies of Chronic Wounds

Key: AMWT, advanced moist wound therapy; DFU(s), diabetic foot ulcer(s); DM, diabetes mellitus; EE, economic evaluation; ER, emergency room; f/u, follow-up; grp(s), group(s); HCPCS, Healthcare Common Procedure Coding System; HIV, human immunodeficiency virus; HR, hazard ratio; hx, history; KCI, Kinetic Concepts Inc.; mmHg, millimeter of Mercury; NPWT, negative pressure wound therapy; NA, not applicable; NR, not reported; prep, preparation; pt(s), patient(s); PU(s), pressure ulcer(s); QALY, quality-adjusted life-years; RCT, randomized controlled trial; tx, treatment (or therapy); USD, United States dollars; VAC, vacuum-assisted closure

Authors/Study Design	Study Population	Treatment	Results	Quality/Comments
Ford et al. (2002) Boston University School of Medicine, Boston, MA RCT *F/u:* 10 mos *Time frame:* NR *Funding source:* Supported in part by an Alpha Omega Alpha Student Research Fellowship. Plastic Surgery Education Foundation Scientific Essay Award Winner (CNF). Supported in part by grants from the Plastic Surgery	n=28 pts, 41 wounds (# of wounds treated NR); 22 pts with 35 wounds completed the trial # wounds in NPWT grp: 20 # wounds in control grp: 15 *Inclusion criteria:* PU or pressure sores *Exclusion criteria:* Aged <21 or > 80 yrs; ulcer duration <4 wks; clinical infection; comorbid conditions (e.g., vasculitis, rheumatoid arthritis, severe kidney disease, heart disease); tx with corticosteroids; absence of stage III or IV ulcers *Clinical hx/pt characteristics (VAC grp; Control grp):*	Tx setting: Plastic surgery clinic and inpatient referral at Boston Medical Center VAC tx: Brand NR; dressing type NR; recommended changing interval, every 2 days; suction and pressure setting (mmHg) NR; reusable NR; instillation system NR; duration of use, 6 wks Comparator tx: HealthPoint System HP Accuzyme, Iodosorb, and Panafil each targeted to optimize a particular macroscopic phase of wound healing; dressing type NR; change interval, once or twice daily; suction and pressure	*Clinical outcomes (VAC grp; Control grp) (% wounds):* Complete wound healing: 2/20 (10%); 2/15 (13%) (risk difference 3%, 95% CI, –18% to 25% [calculated by Rhee et al.]) *Complications (VAC grp; Control grp) (# pts) (% pts):* Sepsis: 1 (0.5%); 0 (0%) Extremity amputation: 1 (0.5%); 0 (0%)	*Limitations:* Incomplete reporting for some of the outcomes, such as osteomyelitis, and incomplete reporting of DM status and control; wounds of the comparison grps were heterogeneous in nature; pts who dropped out were not included in final analysis; baseline differences in age. *Study quality:* Fair *Conflicts of interest:* NR for individual investigators; study partially funded by industry (KCI).

Authors/Study Design	Study Population	Treatment	Results	Quality/Comments
Education Foundation and KCI, San Antonio, TX.	Mean age (yrs): 41.7; 54.4 % men: NR % smoker: NR Wound etiology: PU Wound location (%): Leg (2.9%); foot (11.4%); ankle (11.4%); sacral (48.6%); other (25.7%) Mean wound age (wks): NR Mean wound size (cm^2): NR Infection status (%): NR Wound prep prior to study txs: Debridement as necessary	(mmHg) NA; reusable NA; instillation system NA; duration of use, 6 wks *Outcome measures:* Complete wound healing by secondary intention		
Schwien et al. (2005) Outcome Concept Systems Inc., Seattle, WA Retrospective analysis of a database *F/u:* NR *Time frame:* 2003-2004 *Funding source:* Industry	n=2348 pts NPWT: n=60 Control: n=2288 *Inclusion criteria:* PU or pressure sores *Exclusion criteria:* Clinical infection; pts who died at home; enteral or parenteral nutrition tx; 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 *Clinical hx/pt characteristics (NPWT grp; Control grp):* Mean age (yrs): 65.0; 71.4	Tx setting: Home healthcare setting NPWT tx: Brand, KCI; dressing type, foam, open cell; recommended changing interval, every 2 days, suction and pressure (mmHg), intermittent and continuous; reusable NR; instillation system NR; duration of use NR Control tx: Any other wound care tx other than NPWT; brand NA; dressing type NR; recommended changing interval NA; suction and pressure NA; reusability NA; instillation ystem NA; duration of use NA	No efficacy outcomes. *Complications (NPWT grp, Control grp) (# pts) (% pts):* Emergency room visits, all pts: 0/60 (0%), 189/2288 (8%); *P*<0.01 Stage III PU: 0 (0%), 126 (7%); *P*<0.01 Stage IV PU: 0 (0%), 63 (11%); *P*<0.01 Wound-related hospitalization, all pts: 3/60 (5%); 310/2288 (14%) Stage III PU: 1 (3%), 194 (11%); *P*<0.01 Stage IV PU: 2 (7%), 116 (20%); *P*<0.01	*Limitations:* Inappropriate or poorly described control grps; poor or selective reporting on comparative txs, potential confounders, and outcomes. *Study quality:* Poor *Conflicts of interest:* The authors disclose that KCI funded this study through data consulting arrangements with Outcome Concept Systems Inc.

Authors/Study Design	Study Population	Treatment	Results	Quality/Comments
	% men: 47; 42 % smoker: NR Wound etiology: Pressure (100%; 100%) Wound location: NR Mean wound age (wks): NR Mean wound size (cm^2): NR Infection status (%): NR Wound prep prior to study txs: NR; NA	*Outcome measures:* Adverse events		
Frykberg and Williams (2007) Carl T. Hayden Veterans Administration Medical Center, Phoenix, AZ; Milliman Inc., Windsor, CT Retrospective claims review *F/u:* NR *Time frame:* Medicare claims from 2003, private claims from 2002-2003 data *Funding source:* Partial funding by KCI, maker of the	n=16,319 NPWT: n=380 (281 Medicare, 99 commercial) Control: n=15,939 (12,514 Medicare, 3425 commercial) *Inclusion criteria:* Identified in databases as NPWT or Control for DFU using ICD-9 codes and criteria presented in next column *Exclusion criteria:* Pts in Medicare database who had NPWT and amputation in same quarter, as unclear which came first *Clinical hx/pt characteristics (NPWT grp, Control grp):* Mean age (yrs): In commercial sample, 55; 56 (NR for Medicare)	Tx setting: NR; pts included in this analysis were a mix of inpatient and outpatient populations and they were not analyzed separately. The authors suggest that pts who received NPWT in acute care settings but not in the outpatient setting are likely to be a small grp within their study; however, measured proportions of inpatients and outpatients or proportion of outpatient care days are NR. NPWT: Identified by scanning pt claims involving NPWT device or supplies, HCPCS code, and medical equipment	*Complications (Commercial NPWT grp; Commercial control grp; Medicare NPWT grp; Medicare control grp) (# pts) (% pts):* Amputations: Overall, without stratification or risk adjustment. Toes to foot: 66 (67%); 2466 (72%); 169 (60%); 6507 (52%) Ankle to knee: 25 (25%); 788 (23%); 79 (28%); 3504 (28%) Above knee: 8 (8%); 171 (5%); 34 (12%); 2503 (20%)	*Limitations:* Retrospective analyses using administrative claims databases and potentially meaningful differences in pt demographics between the grps not accounted for in adjusted analyses. *Study quality:* Fair *Conflicts of interest:* One author has research funding and is a speaker for KCI, maker of the studied VAC system.

Authors/Study Design	Study Population	Treatment	Results	Quality/Comments
studied VAC system; source of remaining funding NR.	% men: In commercial sample: 61; 62; in Medicare sample: 47; 55 % smoker: NR Wound etiology: DM-related, per inclusion criteria Wound location: Foot, per inclusion criteria Mean wound age (wks): NR Mean wound size (cm^2): NR Infection status (%): NR Wound prep prior to study txs: NR	charges. No information about administration available. Control: Identified as all other standard wound txs and no claim or code indicating use of NPWT. Controls selected after adjustment for risk for more severe cases (more comparable to NPWT cases) using cost of care and depth of debridement. No information about administration available. *Outcome measure:* Amputation		
Lavery et al. (2007) Texas A&M Health Science Center College of Medicine; Scott and White Hospital, Temple, TX Cohort *F/u:* NR *Time frame:* 1996-2004 *Funding source:*	n=2677 pts NPWT: n=2091 NPWT matched: n=1135 Control: n=586 *Inclusion criteria:* DFUs *Exclusion criteria:* No pts with chronic wounds; no debridement of necrotic tissue; no comprehensive DM management included with the case plan; no reduction in pressure of affected	Tx setting: Outpatient NPWT tx: VAC tx; brand, KCI; dressing type NR; recommended changing interval NR; suction and pressure setting (mmHg) NR; reusability NR; instillation system NR; duration of use NR NPWT matched tx: VAC tx; brand, KCI; dressing type NR; recommended	*Clinical outcomes (% pts):* Complete wound healing: NPWT matched grp; Control grp: 12 wks (all population): 39.5%; 23.9%; *P*<0.001 20 wks (all population) 46.3%; 32.8%; *P*<0.001 Unmatched NPWT grp; NPWT matched grp; Control grp: 12 wks (small ulcers <2 cm^2): 41.4%; 43.1%; 29.4%; *P*<0.05 20 wks (small ulcers <2 cm^2): 46.6%; 50.3%; 38.9%; *P*<0.05 for matched	*Limitations:* Inappropriate or poorly described control grps. *Study quality:* Poor *Conflicts of interest:* Research was sponsored in part by KCI. In addition, 2 investigators reported receiving grants from and 2 investigators reported professional relationships with KCI.

Authors/Study Design	Study Population	Treatment	Results	Quality/Comments
Industry	ulcer; no description of wound size and duration prior to NPWT *Clinical hx/pt characteristics (NPWT grp; Matched grp; Control grp):* Mean age (yrs): 65.2; 58.5; 58.0 % men: 64.5%; 64.5%; 73.2% % smoker: NR Wound etiology: DM (100%; 100%; 100%) Wound location: NR Mean wound age (wks): 22.9; 26.5; 30 Mean wound size (cm^2): 13.5; 13.8; 1.61 Infection status (%): NR Wound prep prior to study txs: NR; NR; NA	changing interval NR; suction and pressure setting (mmHg) NR; reusability NR; instillation system NR; duration of use NR Comparator tx: Standard wet-to-moist wound tx; brand NR; dressing type NR; recommended changing interval NR; suction and pressure (mmHg) NA; reusability NA; instillation system NA; duration of use NA *Outcome measures:* Complete wound healing by secondary intention	NPWT vs control 12 wks (medium ulcers 2-4 cm^2): 40.1%; 43.7%; 17.9% 20 wks (medium ulcers 2-4 cm^2): 46.1%; 48.5%; 25.2%; *P*<0.05 12 wks (large ulcers >4 cm^2): 37.8%; 37.8%; 13.8% 20 wks: (large ulcers >4 cm^2): 45.3%; 44.9%; 22.4%; *P*<0.05 12 wks (short duration <6 mos): 39.9%; 40.3%; 30.2% 12 wks (medium duration 6-12 mos): 36.2%; 39.6%; 28.4% 12 wks (long duration >12 mos): 35.3%; 35.8%; 15.3% *Economic analysis*: 20-week expected cost of care: NPWT grp; Control grp: One nursing visit per day for both grps: $16,733; $15,258 One nursing visit per day for NPWT compared with 2 nursing visits per day for wet-to-moist wound care grp: $16,733; $28,691 *Complications:* NR	
Blume et al. (2008) Multicenter (initiated at 37 diabetic foot and wound clinics; enrolled pts from 1	n=342 pts enrolled n=341 randomized n=335 analyzed NPWT: n=169	Tx setting: Pts treated in both acute and home care settings (~90% of tx days in home care) NPWT: VAC tx brand, KCI	*Clinical outcomes (NPWT grp; AMWT grp) (# pts) (% pts):* Complete closure during active tx phase: 73/169 (43%); 48/166 (29%); *P*=0.007 Complete closure at end of active	*Limitations:* Potentially meaningful baseline differences between grps; potential for

Authors/Study Design	Study Population	Treatment	Results	Quality/Comments
Canadian and 28 U.S. sites) RCT *F/u:* 9 mos *Time frame:* NR *Funding source:* Industry (KCI USA International, manufacturer of the NPWT device studied)	AMWT: n=166 *Inclusion criteria:* Aged ≥18 yrs; DM; stage 2 or 3 calcaneal, dorsal, or plantar foot ulcer ≥2 cm^2 after debridement; adequate blood perfusion *Exclusion criteria:* Active Charcot's disease or ulcers from electrical, chemical, or radiation burns; collagen vascular disease; ulcer malignancy; untreated osteomyelitis; cellulitis; uncontrolled hyperglycemia; inadequate lower extremity perfusion; ulcer tx with normothermic or hyperbaric oxygen tx; concomitant medication; recombinant or autologous growth factor products; skin and dermal substitutes within 30 days of study start; use of enzymatic debridement; pregnant or breastfeeding *Clinical hx/pt characteristics (NPWT grp, AMWT grp):* Mean age (yrs): 58; 59 % men: 83%; 73% % smoker: 34%; 32% Wound etiology: DM-related,	USA; electrically powered; dressing type, open cell sterile polyurethane or dense open-pore polyvinyl alcohol foam dressing; recommended changing interval NR; suction and pressure setting (mmHg) NR; reusability, pump device is reusable; instillation system NR; duration of use mean 64 days AMWT: Advanced moist wound tx of primarily hydrogels and alginates consistent with standards of care; recommended changing interval NR; duration of use, mean 78 days *Outcome measures:* Complete ulcer closure: 100% re-epithelization, without drainage or dressing requirements; time to closure; complications	tx phase: 73/120 (61%); 48/120 (40%); *P*=0.001 Surgical closure by split-thickness skin grafts, flaps, sutures, or amputations: 16 (10%); 14 (8%); *P*=NR Time to closure, median days: 96 (95% CI, 75-114); not determinable for AMWT (*P*=0.001) *Complications (NPWT grp; AMWT grp) (# pts) (% pts):* Secondary amputations: 7 (4%); 17 (10%); *P*=0.035 Edema: 5 (3%); 7 (4%); *P*=NS Wound infection: 4 (2%); 1 (<1%); *P*=NS Cellulitis: 4 (2%); 1 (<1%); *P*=NS Osteomyelitis: 1 (<1%); 0; *P*=NS *Staphylococcus* infection: 1 (<1%); 0 (0%); *P*=NS Infected skin ulcer: 1 (<1%); 2 (1%); *P*=NS	differential concomitant txs between intervention and control grps; potential performance bias due to lack of blinding. *Study quality:* Fair *Conflicts of interest:* Financial relationships with KCI International, including study support.

Authors/Study Design	Study Population	Treatment	Results	Quality/Comments
	per inclusion criteria Wound location: Foot, per inclusion criteria Mean wound age (days before tx): 198; 206 Mean wound size (cm^2): 13.5; 11.0 Infection status (%): 30%; 27% Wound prep prior to study txs: All debridement within 2 days to random allocation per study protocol			
Flack et al. (2008) York Health Economics Consortium, University of York, UK Cost-effectiveness (Markov model) *Perspective:* Payer (e.g., national health service or insurer) *F/u:* Model assumes 12 mos of tx if wounds not healed by 3 mos *Time frame:* All costs are presented in 2006 USD *Funding source:* KCI USA Inc.	Simulated 1000 pts intended to represent population of pts presenting with DFUs in practice. *Pt characteristics:* Males and females with DFUs; type 1 or 2 DM; aged 50-65 yrs; 2.3% presenting with an infected ulcer, all others with unhealed DFU Selected health states: Uninfected ulcer Infected ulcer Infected ulcer postamputation Healed Healed postamputation Amputation Dead	VAC tx compared with advanced and traditional dressings. Data to populate the model came from comparative studies or RCTs comparing VAC with traditional or advanced wound dressings or comparing advanced wound dressings with traditional dressings (advanced dressings = Apligraf [Novartis] or Dermagraft [Smith & Nephew]; traditional dressing = saline gauze) Relative healing rate used to establish effectiveness and determine risk of progression between	*QALYs (VAC; traditional dressing) per cohort of 1000 (per pt):* 531 (0.53); 523 (0.52) *Amputations (VAC; traditional dressing) per cohort of 1000 (per pt):* 4.24 (0.0042); 4.63 (0.0046) *# healed (VAC; traditional dressing) per cohort of 1000 (per pt):* 542 (0.54); 517 (0.52) *% wounds completely healed in 1 yr (VAC; traditional dressing) per cohort of 1000 (per pt):* 54; 52 *Total cost, 2006 USD (VAC; traditional dressing) per cohort of 1000 (per pt):* $57,944,365 ($57,944); $79,950,692 ($79,951) *QALYs (VAC; advanced dressing) per*	*Limitations:* The authors noted the dearth of high-quality studies of wound care interventions and their use of indirect comparisons of data from multiple studies; analysis limited by quality and directness of available data.

Authors/Study Design	Study Population	Treatment	Results	Quality/Comments
		health states. Resources included (per mon): Inpatient costs: days in hospital, antibiotics, orthopedic appliance Outpatient costs: # of consultations, # of home care visits Dressing costs: VAC dressing, advanced dressing, traditional dressing Costs: U.S. cost data were applied to the resources used during tx. Medicare reimbursement schedules for services were derived from a nationally representative administrative database. Utility weights: Utility weights needed to calculate QALYs were derived from published literature	*cohort of 1000 (per pt):* 540 (0.54); 534 (0.53) *Amputations (VAC; advanced dressing) per cohort of 1000 (per pt):* 1.1 (0.0011); 1.21 (0.0012) *# healed (VAC; advanced dressing) per cohort of 1000 (per pt):* 614 (0.61); 591 (0.59) *% wounds completely healed in 1 yr (VAC; advanced dressing) per cohort of 1000 (per pt):* 61%; 59% *Total cost, 2006 USD (VAC; advanced dressing) per cohort of 1000 (per pt):* $52,829,888 ($52,830); $61,756,764 ($61,757) *Incremental analysis, cohort of 1000 (per pt):* Incremental cost, USD (VAC vs traditional dressing): –$22,006,327 (–$22,006) Incremental cost, USD (VAC vs advanced dressing): –$8,926,877 (–$8927) Amputations averted (VAC vs traditional dressing): 0.4 (0.0004) Amputations averted (VAC vs advanced dressing): 0.10 (0.00) Additional ulcers healed (VAC vs	

Authors/Study Design	Study Population	Treatment	Results	Quality/Comments
			traditional dressing):25 (0.025) Additional ulcers healed (VAC vs advanced dressing): 23 (0.023) Incremental QALYs (VAC vs traditional dressing): 7 (0.007) Incremental QALYs (VAC vs advanced dressing): 6 (0.006) *Authors' conclusions:* VAC vs traditional dressings: Over 1 yr, use of VAC tx results in more wounds healed, more QALYs gained, and fewer amputations at a lower cost than traditional dressings VAC vs advanced dressings: VAC tx results in fewer amputations and an increase in QALYs at an overall lower cost of care; VAC results in additional ulcer-free mos (5.79 vs 5.11 per person) Sensitivity analysis demonstrates the overall robustness of the model findings. Variations to the cost of VAC tx had relatively little impact on the incremental cost-effectiveness ratio.	
Fife et al. (2008) University of Texas Health Science Center, Houston, TX Cohort *F/u:* NR	n=1331 pts NPWT: n=72 Control: n=1299 *Inclusion criteria:* DFU *Exclusion criteria:* Not treated in	Tx setting: Outpatient NPWT tx: VAC tx; brand, KCI; dressing type NR; recommended changing interval NR; suction and pressure setting (mmHg) NR; reusability NR;	*Efficacy outcomes:* NR *Complications (NPWT grp; Control grp):* Bleeding (discontinued NPWT due to bleeding): No DFU pts with the V.A.C. required the discontinuation of the V.A.C. because of bleeding.	*Limitations:* Controls not matched; potential selection bias; retrospective data analysis; quality of data source not clear; surrogate/indirect data used to measure

Authors/Study Design	Study Population	Treatment	Results	Quality/Comments
Time frame: 2001-2006 *Funding source:* Industry	an outpatient setting *Clinical hx/pt characteristics (NPWT grp; Control grp):* Mean age (yrs): NR % men: NR % smoker: NR Wound etiology: DM (100%) Wound location: NR Mean wound age (wks): NR Mean wound size (cm^2): NR Infection status (%): NR Wound prep prior to study txs: NA; NR	instillation system NR; duration of use NR Comparator tx: Unspecified wound care tx either prior to the start of NPWT or among pts who never received NPWT; brand NA; dressing type NA; recommended changing interval NA; suction and pressure (mmHg) NA; reusability NA; instillation system NA; duration of use NA *Outcome measure:* Adverse events	Bleeding (sanguineous drainage): No cases found in either grp Infection (antibiotics): V.A.C. pts had fewer antibiotic prescriptions (#s NR); *P*<0.05 Infection (culture): V.A.C. pts had fewer cultures taken (#s NR); *P*<0.05 Pain (measured by provision of pain medication): *P*=NS	outcomes. *Study quality:* Poor *Conflicts of interest:* Project funded by KCI. Three of the authors report financial interests associated with Intellicure.
Lerman et al. (2010) O'Connor Wound Care Clinic; O'Connor Hospital; Stanford University School of Medicine; Spiracur Inc.; San Jose, Stanford, and Sunnyvale, CA Prospective cohort and retrospective matched-control comparisons *F/u:* 4 mos *Time frame:* 2008-2009	n=78 pts SNaP: n=36 Control: n=42 *Inclusion criteria:* DFUs; venous ulcers *Exclusion criteria:* Aged <18 yrs; ulcer size <1.5 cm in narrowest diameter; ulcer size >10 cm in greatest diameter; wound surrounded by 2 cm or less of intact epithelium around the wound edge; wounds that healed following >14 days of traditional	Tx setting: Outpatient NPWT tx: SNaP (Smart Negative Pressure) Wound Care System (portable); brand Spiracur, Inc; dressing type, gauze, antimicrobial/hydrocolloid dressing layer; recommended changing interval, twice wkly; suction and pressure setting (mmHg), multiple setting 75-125; reusability, single use; instillation system NR; duration of use 7.44 wks	*Clinical outcomes (NPWT grp; Control grp):* Complete wound healing: 1 mo (all population): 0%; 0% 2 mos (all population): 20%; 7.1% 3 mos (all population): 66.2%; 21.4%, 4 mos (all population): 83.1%; 35.7% Time to complete wound healing (mean ± SD) (days): 74.25±20.1; 148.73±63.1; *P*<0.0001 *Complications (NPWT grp; Control grp) (# pts):* Unspecified: 7 pts; NR Infection requiring discontinuation of	*Limitations:* Potential for differential concomitant txs between intervention and control grps; high overall attrition. *Study quality:* Poor *Conflicts of interest:* Work supported by a research grant from Spiracur and 2 authors report professional relationship with Spiracur.

Authors/Study Design	Study Population	Treatment	Results	Quality/Comments
Funding source: Industry	tx *Clinical hx/pt characteristics (SNaP grp; control grp):* Mean age (yrs): 64.0; 66.8 % men: 42.9%; 45.2% % smoker: 42.9%; 20.0% Wound etiology: DM: 47.6%; 50% Venous: 52.4%; 50% Wound location: NR Mean wound age (wks): 36.4; 31.2 Mean wound size (cm^2): NR Infection status (%): NR Wound prep prior to study txs: Debridement in NPWT grp	Comparator tx: Modern wound care protocols that included the use of Apligraf, Regranex, and skin grafting; brand NA; dressing type NA; recommended changing interval NA; suction and pressure (mmHg) NA; reusability NA; instillation system NA; duration of use NA *Outcome measures:* Complete wound healing by secondary intention; time to complete wound healing; adverse events	NPWT: 1; NA	
Armstrong et al. (2011) Southern Arizona Limb Salvage Alliance (SALSA); University of Arizona College of Medicine, Tucson, AZ RCT (interim analysis of study presented in Armstrong et al., 2012) *F/u:* 16 wks *Time frame:* NR	n=65 pts SNaP: n=32 VAC: n=33 *Inclusion criteria:* DFUs; venous ulcers *Exclusion criteria:* Aged <18 yrs; ulcer size <1 cm^2; ulcer size >100 cm^2; clinical infection; ankle/brachial index <0.7 or >1.2; ulcer size >10 cm in widest diameter; wounds present for <30 days	Tx setting: 12 outpatient clinics NPWT tx: SNaP (Smart Negative Pressure) Wound Care System; brand, Spiracur (portable); mechanically powered; dressing type, gauze; recommended changing interval, every 3 days; suction and pressure setting (mmHg) NR; reusability, no; instillation system NR; duration of use	*Clinical outcomes (SNaP grp; VAC grp) (% pts):* Complete wound healing: 4 wks: 0%; 0% 8 wks: 11.8%; 13.6% 12 wks: 38.2%; 36.7% 16 wks: 59.7%; 64.8% There was no significant difference (*P*=0.99) in the proportion of pts healed over time, indicating that the effect of the SNaP System was not significantly different than that of the VAC System in promoting complete wound closure in the population studied.	*Limitations:* See Armstrong et al. (2012) *Study quality:* See Armstrong et al. (2012) *Conflicts of interest:* Study was sponsored by a grant from Spiracur Inc., manufacturer of the SNaP device. Two authors have received research funding from both Spiracur and KCI.

Authors/Study Design	Study Population	Treatment	Results	Quality/Comments
Funding source: Industry (Spiracur Inc., manufacturer of the SNaP device)	*Clinical hx/pt characteristics (SNaP grp; VAC grp):* Mean age (yrs): 65.8; 65.1 % men: 48%; 50% % smoker: 20%; 12.5% Wound etiology: NR Wound location: NR Mean wound age (wks): NR Mean wound size (cm^2): NR Infection status (%): NR Wound prep prior to study txs: Debridement in both grps	NR Comparator tx: VAC tx system; electrically powered; brand, KCI, ActiV.A.C. and V.A.C. models (portable); dressing type, foam; recommended changing interval, every 2 days; suction and pressure (mmHg) NR; reusability, pump device is reusable; instillation system NR; duration of use NR *Outcome measures:* Complete wound healing by secondary intention	*Patient-centered outcomes:* Pain – exit interview responses (n=25): The study investigators reported that there were no differences in reported pain, perceived effectiveness, and pt satisfaction between the devices used to apply negative pressure. However, the SNaP System interfered less with overall activity, sleep, and social interactions than the VAC System. Change in overall activity after NPWT – exit interview response (n=25, VAC grp vs SNaP grp): Chi-square *P*=0.0210 Fisher's exact test *P*=0.0179 *Complications (SNaP grp; VAC grp) (# pts) (% pts):* Infection: 2(6.3%); 1(3%)	
Hutton et al. (2011) University of Michigan, Ann Arbor, MI *Type of EE:* Cost comparison of SNaP device compared with standard care and electrically powered NPWT devices *Design:* Decision-analytic modeling	Decision-analytic modeling approach using an economic model with peer-reviewed data to simulate outcomes for tx with different txs	Tx setting: Home NPWT device: SNaP Wound Care System Powered device: Not specified Assumptions: Authors assumed equal efficacy between SNaP and powered NPWT devices based on preliminary studies and ongoing clinical trials (83.1%	Base case results: The SNaP Wound Care System saved $9699 (42%) over modern dressings, $2774 (17%) over powered NPWT for a private payer, and $2296 (15%) over powered NPWT for Medicare. Cost by category: SNaP costs $4445 more for the equipment and supplies than modern dressings but saves $1853 in dressing changes, $1846 in additional healthcare costs, $3425 in costs of complications, and $7020 in long-term costs for pts who do not heal.	*Limitations:* Limitations of this economic study include the limitations of the data on which the model is based and missing parameters for concurrent or consecutive treatments such as pain medication or switching to other wound care methods.

Authors/Study Design	Study Population	Treatment	Results	Quality/Comments
Perspective: Medicare; private payers *Time horizon:* 16 wks *Funding source:* Spiracur Inc.		healed). Modern dressings are assumed to be 35.7% effective in healing. Base case analysis was based on a single study directly comparing the SNaP system with modern dressing protocols. Costs: Costs of tx include direct costs and other healthcare costs for individuals with diabetic lower extremity wounds. Costs are based on the literature comparing NPWT to modern dressings and Medicare reimbursement rates.	NOTE: Costs are in 2010 USD.	*Conflicts of interest:* 1 author was paid consultant of Spiracur Inc.
Armstrong et al. (2012) Southern Arizona Limb Salvage Alliance (SALSA); University of Arizona College of Medicine, Tucson, AZ RCT *F/u:* 16 wks *Time frame:* NR	n=132 pts SNaP: n=64 VAC: n=68 *Inclusion criteria:* DFUs; venous ulcers *Exclusion criteria:* Aged <18 yrs; ulcer size <1 cm^2; ulcer size >100 cm^2; clinical infection; ankle/brachial index <0.7 or >1.2;	Tx setting: 17 outpatient clinics NPWT tx: SNaP (Smart Negative Pressure) Wound Care System; brand, Spiracur (portable); dressing type NR; recommended changing interval NR; suction and pressure setting (mmHg), continuous; reusability, no;	*Clinical outcomes (SNaP grp; VAC grp) (% pts):* Complete wound healing: 4 wks: 9.2%; 5.3% *Patient-centered outcomes:* <u>Pain – exit interview responses (n=53)</u>: The authors report no significant difference between the grps for perceived pain associated with tx. Pain was measured against an expected sum; the authors do not explain how the	*Limitations:* Potentially meaningful differences in wound size between grps at baseline; the utilization of 2 different V.A.C. (KCI) systems in the comparison grp without presenting separate analyses for each device; differential tx between grps with respect to personnel who

Authors/Study Design	Study Population	Treatment	Results	Quality/Comments
Funding source: Industry	ulcer size >10 cm in widest diameter. Wounds not present for >30 days despite appropriate wound care prior to entry *Clinical hx/pt characteristics (SNaP grp; VAC grp):* Mean age (yrs): 65.8; 65.1 % men: 48.4%; 63.2% % smoker: 17.2%; 7.4% Wound etiology: NR Wound location: NR Mean wound age (wks): 68.8 Mean wound size (cm^2): 9.95 Infection status (%): NR Wound prep prior to study txs: Debridement in both grps	instillation system NR; duration of use NR Comparator tx: VAC tx system; brand, KCI, ActiV.A.C. and V.A.C. models (portable); dressing type NR; recommended changing interval NR; suction and pressure (mmHg) NR; reusability NR; instillation system NR; duration of use NR *Outcome measure:* Complete wound healing by secondary intention	expected sum was determined. <u>Able to work and do normal activities while being treated with NPWT device</u>: VAC grp % agree + strongly agree: 48.1% + 9.6% = 57.7% SNaP grp % agree + strongly agree: 43.4% + 35.9 = 79.3% <u>Return to prior level of functional activity – exit interview response (n=53; VAC grp vs SNaP grp) (% pts)</u>: Less active: 17.0% vs 51.9% More active: 11.3% vs 3.9% Stayed the same: 71.7% vs 44.2% Fisher's exact test $P<0.05$ <u>Able to work – exit interview response (n=53; VAC grp vs SNaP grp) (% pts)</u>: Agree: 43.4% vs 48.1% Disagree: 5.7% vs 21.2% Neutral: 13.2% vs 13.5% Strongly agree: 35.9% vs 9.6% Strongly disagree: 1.9% vs 7.7% *Complications (SNaP grp; VAC grp) (# pts) (% pts):* Infection: 5 (7.4%); 2 (3.1%) Pain: 4 (5.9%); 1 (1.6%)	changed wound dressings, and pt outcome data were obtained from an exit interview and subject to recall and attrition bias, as well as the potential for bias because of the lack of blinding to which device was used. *Study quality:* Fair *Conflicts of interest:* Sponsored through a grant from Spiracur Inc. In addition, 2 investigators have reported receiving research funding from both Spiracur and KCI.
Yao et al. (2014) Center for Restorative Medicine, Boston Medical Center; Boston University School of Medicine; Boston, MA	n=342 pts NPWT: n=171 Control: n=171 *Inclusion criteria:* Arterial ulcers;	Tx setting: continuum of care settings (real world) NPWT tx: Model NR; brand, KCI; dressing type NR; recommended changing	*Clinical outcomes (NPWT grp; Control grp):* Complete wound healing: Arterial ulcers (person yrs): 99.54; 102.89 Arterial ulcers (event rate/100 person	*Limitations:* Poor reporting of outcomes, potentially meaningful differences between grps at baseline.

Authors/Study Design	Study Population	Treatment	Results	Quality/Comments
Cohort study *F/u:* 8 yrs *Time frame:* 2002-2010 *Funding source:* NR	DFUs; PUs or pressure sores; venous ulcers *Exclusion criteria:* Aged <18 yrs; HIV positive; sickle cell disease; traumatic and burns ulcers; active malignancy with chemotherapy *Clinical hx/pt characteristics (NPWT grp; Control grp):* Mean age (yrs): 60.8; 61.3 % men: 57.9%; 57.9% % smoker: 40.6%; 34.5% Wound etiology (% pts): DM: 81.8%; 69.4% Pressure: 13.45%; 10.1% Venous: 8.8%; 10.6% Arterial: 66.7%; 34.9% Wound location (% pts): Leg: 15.7%; 29.2% Foot: 84.21%; 70.76% Mean wound age (wks): NR Mean wound size (cm^2): NR Infection status (%): 79.5%; 91.9% Wound prep prior to study txs: NR; NA	interval NR; suction and pressure setting (mmHg) NR; reusability, no; instillation system NR; duration of use, ≥1 wks Comparator tx: NR; brand NA; dressing type NR; recommended changing interval NA; suction and pressure (mmHg) NA; reusable NA; instillation system NA; duration of use NA *Outcome measures:* Complete wound healing by secondary intention (arterial, diabetic, pressure, venous stasis)	yrs): 78.36 (95% CI, 62.56-97.83); 35.96 (95% CI, 26.05-49.63) Arterial ulcers (unadjusted HR): 2.33 (95% CI 1.57-3.48) Arterial ulcers (adjusted HR): 2.27 (95% CI, 1.56-3.78) Diabetic ulcers (person yrs): 112.01; 205.65 Diabetic ulcers (event rate/100 person yrs): 83.92 (95% CI, 68.56-102.72); 38.9 (95% CI, 31.25-48.43) Diabetic ulcers (unadjusted HR): 2.38 (95% CI, 1.75-3.23) Diabetic ulcers (adjusted HR): 3.26 (95% CI, 2.21-4.83) PUs (person yrs): 11.96; 16.77 PUs (event rate/100 person yrs): 142.14 (95% CI, 88.36-228.65); 77.52 (95% CI, 45.01-133.51) PUs (unadjusted HR): 2.19 (95% CI, 1.03-4.66) PUs (adjusted HR): 1.72 (95% CI, 0.43-6.95) Venous stasis ulcers (person yrs): 7.79; 30.69 Venous stasis ulcers (event rate/100 person yrs): 154.04 (95% CI, 87.48-271.24); 46.62 (95% CI, 27.02-77.03) Venous stasis ulcers (unadjusted HR): 4.90 (95% CI, 1.72-13.59) Venous stasis ulcers (adjusted HR): 6.31	*Study quality:* Fair *Conflicts of interest:* NR

Authors/Study Design	Study Population	Treatment	Results	Quality/Comments
			(95% CI, 1.49-26.6) All ulcers (person yrs): 131.47; 274.36 All ulcers (event rate/100 person yrs): 90.51 (95% CI, 75.63-108.32); 43.01 (95% CI, 35.91-51.51) All ulcers (unadjusted HR): 2.25 (95% CI, 1.73-3.96) All ulcers (adjusted HR): 2.63 (95% CI, 1.87-3.70) Grade I ulcers (person yrs): 56.61; 77.41 Grade I ulcers (event rate/100 person yrs): 107.95 (95% CI, 83.99-138.74); 65.88 (95% CI, 50.07-86.69) Grade I ulcers (unadjusted HR): NR Grade I ulcers (adjusted HR): NR Grade II ulcers (person yrs): 74.96; 194.41 Grade II ulcers (event rate/100 person yrs): 77.96 (95% CI, 59.81-100.08); 33.43 (95% CI, 26.22-42.63) Grade II ulcers (unadjusted HR): NR Grade II ulcers (adjusted HR): NR	
Driver and Blume (2014) Veterans Affairs New England Health Care Division, Providence, RI	n=324 pts NPWT: n=162 AMWT: n=162 *Inclusion criteria:* See Blume et al. (2008)	Tx setting: See Blume et al. (2008); proportion of inpatient/outpatient days were NR for the cost analysis population NPWT: See Blume et al. (2008)	*Results:* Avg cost per pt regardless of wound closure: $11,984 for NPWT and $13,557 for AMWT Pts who achieved wound closure, avg cost: $10,172 for NPWT and $9505 for AMWT	*Limitations:* Post hoc retrospective analysis; also see Blume et al. (2008) for assessment of original RCT. *Conflict of interest:*

Authors/Study Design	Study Population	Treatment	Results	Quality/Comments
Post-hoc retrospective medical records review of pts enrolled in an RCT for cost analysis (pts were enrolled in the Blume et al. [2008] article) *F/u*: 112 days *Timeframe:* NR *Funding source:* NR	*Exclusion criteria:* See Blume et al. (2008); pts with missing data for hospitalizations during which a split- or full-thickness skin graft or flap was performed were excluded from the cost analysis (n=7 NPWT; n=4 AMWT) *Clinical hx/pt characteristics (NPWT grp, AMWT grp):* Mean ± SD age (yrs): 58±12; 59±12 % men: 84%; 74% % smoker: 20.4%; 19.8% Wound etiology: DM Wound location: Foot Mean wound age (days): NR Mean wound size (cm^2): NR Infection status (%): NR Wound prep prior to study txs: All debridement within 2 days to random allocation per study protocol	AMWT: See Blume et al. (2008) *Economic analysis:* Wound tx costs: Dressings or the NPWT system, and labor during dressing changes Nonwound tx costs: Concomitant antibiotic tx, acute inpatient services (including acute care hospitalizations and wound-related surgical procedures performed in an acute care facility), extended care hospitalizations (i.e., stays in skilled nursing facilities, rehabilitation clinics, or hospice), and outpatient surgical procedures Costs were calculated from pts' healthcare utilization, including hospital costs (Healthcare Cost and Utilization Project Nationwide Inpatient Sample), physical services for surgical	Pts who did not achieve wound closure, avg cost: $13,262 for NPWT and $15,068 for AMWT Nonwound tx costs were higher for pts undergoing AMWT than NPWT. Pts who achieved wound closure, avg nonwound tx cost: $10,716 for NPWT and $13,525 for AMWT Pts who did not achieve wound closure, avg nonwound tx cost: $13,694 for NPWT and $17,927 for AMWT	personnel at KCI provided data analysis and medical writing support. No conflicts of interest or financial disclosures were stated.

Authors/Study Design	Study Population	Treatment	Results	Quality/Comments
		procedures (Medicare Resource-Based Relative Value Scale 2007), and extended-care facility cost per day (Medicare reimbursement rate).		
Law et al. (2015) Claims data assessed by KCI and Optum Life Sciences Retrospective claims database analysis *F/u:* NR *Time frame:* Claim submitted between January 2009 and June 2012 *Funding source:* Study sponsored by KCI	n=13,556 pts with chronic (81%) or acute wounds NPWT-V: n=12,843 NPWT-O: n=713 *Inclusion criteria:* ≥1 NPWT claims during time frame in outpatient setting in U.S. from an insurance company; had continuous medical and pharmacy benefits at least 12 mos before index tx and 3 mos post-tx *Exclusion criteria:* NR *Clinical hx/pt characteristics (NPWT-V grp; NPWT-O grp):* Mean age (yrs): 59; 64 % men: 48%; 48% % smoker: NR Wound etiology: NR Wound location: NR Mean wound age (wks): NR Mean wound size (cm^2): NR Infection status (%): NR Wound prep prior to study txs:	Tx setting: Outpatient NPWT-V: NPWT with VAC (KCI). No information about administration available. NPWT-O: NPWT with all other models from other manufacturers. No other information available. *Outcome measures:* Readmission; inpatient stays; ER visits	*Economic analysis:* NPWT-V (n=12,843 at 3 mos, n=7860 at 12 mos) was compared with NPWT-O (n=713 at 3 mos, n=378 at 12 mos). At 3 mos: Per-pt cost for NPWT-V: $35,498 ($4224 [11%] lower than NPWT-O; *P*=0.08) Per-pt cost for NPWT-O: $39,722. At 12 mos: Per-pt cost for NPWT-V: $80,768 ($30,444 [27%] lower than NPWT-O; *P*=0.03) Per-pt costs for NPWT-O: $111,212 *Complications (NPWT-V grp, NPWT-O grp) (# pts) (% pts):* Readmission, any, 3 mos: 2954 (23%), 221 (31%) Readmission, wound-related, 3 mos: 642 (5%), 57 (8%) Readmission, any, 6 mos: 3433 (31%); 258 (43%) Readmission, wound-related, 6 mos: 664 (6%); 66 (11%)	*Limitations:* Retrospective analysis; heterogeneous pt population and separate analyses were provided for only some of the included wound types; potentially meaningful baseline differences in 3-mo analysis grp and pt demographic results were not presented for 6- and 12-mo populations; methods state that data were analyzed at 12 mos, but results were not provided; different grp sizes; methods do not indicate that analyses were adjusted to control for confounding

Authors/Study Design	Study Population	Treatment	Results	Quality/Comments
	NR		Inpatient stay, 3 mos: All, wound-related: 64 (0.5%), 8 (1.1%); *P*<0.0001 Nonhealing surgical: 51 (0.4%), 4 (0.6%); *P*=0.14 Open: 51 (0.4%), 9 (1.2%); *P*=0.03 PU: 128 (1.0%), 15 (2.1%); *P*=0.002 Inpatient stay, 6 mos: All, wound-related: 89 (0.8%), 102 (1.7%); *P*<0.0001 Nonhealing surgical: 55 (0.5%), 5 (0.8%); *P*=0.13 Open: 66 (0.6%), 9 (1.5%); *P*=0.04 PU: 188 (1.7%), 20 (3.3%); *P*=0.01 ER visit, 3 mos: All, wound-related: 13 (0.1%), 4 (0.6%); *P*<0.0001 Nonhealing surgical: 13 (0.1%), 4 (0.5%); *P*=0.0007 Open: 13 (0.1%), 8 (1.2%); *P*=0.0005 PU: 51 (0.4%), 5 (0.7%); *P*=0.11 ER visit, 6 mos: All, wound-related: 22 (0.2%), 5 (0.9%); *P*<0.0001 Nonhealing surgical: 11 (0.1%), 4 (0.7%); *P*=0.002 Open: 11 (0.1%), 10 (1.6%); *P*=0.0001 PU: 66 (0.6%), 7 (1.1%); *P*=0.16	variables. *Study quality:* Poor (for adverse events) *Conflicts of interest:* Lead author was employee of KCI; other 2 authors were paid consultants of KCI.
Marston et al. (2015)	n=40 pts	Tx setting: Outpatient	*Clinical outcomes (SNaP grp; VAC grp):*	*Limitations:* In addition to the

Authors/Study Design	Study Population	Treatment	Results	Quality/Comments
University of North Carolina, Chapel Hill, NC Multicenter RCT; subanalysis of Armstrong et al. (2012), assessing venous lesion ulcer pts who had 16 wks of tx or healing recruited from 13 sites in the U.S. *F/u:* 16 wks *Time frame:* July 2009 – March 2011 (according to ClinicalTrials.gov database) *Funding source:* Industry (Spiracur Inc., manufacturer of the SNaP device)	SNaP: n=19 VAC: n=21 *Inclusion criteria (for full study population):* DFUs; lower extremity venous ulcers; in location amenable to creation of airtight seal using study dressings; adequate blood perfusion *Exclusion criteria:* Aged <18 yrs; ulcer size <1 cm^2; ulcer size >100 cm^2; clinical infection; ankle/brachial index <0.7 or >1.2; ulcer size >10 cm in widest diameter; wounds not present for >30 days despite appropriate wound care prior to entry; active infection; untreated osteomyelitis; pregnancy; allergies to study materials; cause of wound included cancer, burn, collagen vascular disease, sickle cell, vasculopathy or pyoderma gangrenosum; active Charcot arthropathy; on renal dialysis; active chemotherapy; previous tx with NPWT, growth factors, hyperbaric oxygen, or bioengineered tissue product within 30 days of enrollment;	SNaP: Mechanically powered SNaP (Smart Negative Pressure) Wound Care System; brand, Spiracur (portable); mechanically powered; dressing type, gauze; recommended changing interval, every 3 days; suction and pressure setting (mmHg) NR; reusability, no; instillation system NR; duration of use NR VAC: Electrically powered VAC tx system; brand, KCI, ActiV.A.C. and V.A.C. models (portable); dressing type, foam; recommended changing interval, every 2 days; suction and pressure (mmHg) NR; reusability, pump device is reusable; instillation system NR; duration of use NR *Outcome measures (SNaP grp; VAC grp):* Complete wound healing by secondary intention	Complete wound healing: Data NR, but authors reported no significant difference in healing rates among study completers between grps whether or not adjusted for baseline wound size. (Data on this outcome for a larger population appear to have been reported in Armstrong et al. [2012].) *Complications (SNaP grp; VAC grp) (# pts) (% pts):* Infection: 1 (5%); 2 (10%) (infection also reported in Armstrong et al. [2011] among more pts) Maceration: 3 (16%); 3 (14%) Allergic reaction to dressing: 1 (5%); 3 (14%) Pain: 1 (5%); 3 (14%) Blisters: 3 (16%); 2 (10%) Other: 2 (11%); 2 (10%) The authors wrote that these were not significantly different between grps and were similar to the total pt pool in Armstrong et al. (2012).	limitations of the main study, this subanalysis is limited by having conducted a completers' analysis; it is unclear whether this was a preplanned analysis or post-hoc analysis. *Study quality:* See Armstrong (2012) *Conflicts of interest:* This study was sponsored by a grant from Spiracur Inc., manufacturer of the SnAP device. Two authors have received research funding from both Spiracur and KCI.

Authors/Study Design	Study Population	Treatment	Results	Quality/Comments
	>30% reduction in wound surface area during wk prior to enrollment *Clinical hx/pt characteristics (SNaP grp; VAC grp):* Mean age (yrs): 67.5; 66.8 % men: 42%; 52% % smoker: 21%; 10% Wound etiology: Diabetic venous ulcers, per inclusion criteria Wound location: Foot, per inclusion criteria Mean wound age (days): <30, per inclusion criteria Mean (SD) wound size (cm^2): 4.85 (±4.49); 11.60 (±12.12) Infection status (%): NR Wound prep prior to study txs: Debridement in both grps			

APPENDIX Vb. Studies of Surgical Wounds

Key: BMI, body mass index; BPI, Brief Pain Inventory; ES, effect size; EQ-5D, European Quality of Life-5 Dimensions; f/u, follow-up; grp(s), group(s); HbA1c, hemoglobin A1c; hx, history; iNPWTd, incisional negative pressure wound therapy dressings; IQR, interquartile range; KCI, Kinetic Concepts Inc.; mmHg, milliliter of Mercury; NA, not available; NPWT, negative pressure wound therapy; NR, not reported; NS, not statistically significant; OR, odds ratio; prep, preparation; pt(s), patient(s); RCT, randomized controlled trial; RR, risk ratio; SSI, surgical site infection; THA, total hip arthroplasty; TKA, total knee arthroplasty; tx, treatment (or therapy); VAC, vacuum-assisted closure; VAS, visual analog scale

Authors/Study Design	Study Population	Treatment	Results	Quality/Comments
Armstrong et al. (2005) **Armstrong et al. (2007)** **Apelqvist et al. (2008)** Scholl's Center for Lower Extremity Ambulatory Research (CLEAR), Rosalind Franklin University of Medicine and Science; Chicago, IL RCT (multicenter, n=18) *F/u:* 16 wks (112 days) *Time frame:* NR *Funding source:* KCI	n=162 NPWT: n=77 Standard tx: n=85 *Inclusion criteria:* Aged ≥18 yrs; wound from diabetic foot amputation to the transmetatarsal level; adequate perfusion; all wounds correspond to University of Texas grade 2 or 3 depth *Exclusion criteria:* Active Charcot arthropathy of the foot;	Tx setting: Inpatient and home care; 89.1% of days were home care, 10.9% were inpatient (Apelqvist et al., 2008); % for each grp NR NPWT: VAC system (KCI); electrically powered; dressing type NR; recommended changing interval, changes of VAC dressings were performed every 48 hrs; suction and pressure setting (mmHg) NR; reusability NR; instillation system NR; duration of use NR Standard tx: Dressing type, moist wound tx with alginates, hydrocolloids, foams, or hydrogels; recommended changing interval, changed every day unless otherwise	*Clinical outcomes (NPWT grp, Standard tx grp):* Proportion of wounds healed: 43 (56%), 33 (39%); *P*=0.04; difference in proportions = 0.1702 (95% asymptotic CI, 0.0184-0.322) Healed by secondary intention: 31 (40%), 25 (30%); *P*=NR Healed wounds after surgical closure: 12 (16%), 8 (9%); *P*=0.244 Time to complete wound healing (median [IQR]): 56 days (26-92), 77 (40-112); *P*=0.005 *Pt-centered outcomes:* NR *Complications (NPWT grp; Standard tx grp):* Second amputation: 2 (3%), 9 (11%); *P*=0.060; RR 0.225 (95% CI, 0.05-1.1); 5 (6%) of Standard tx grp received high-level (above foot) amputation—2 above knee, 3 below knee; no high-level amputations were done in the NPWT grp	*Limitations:* Use of different wound dressings in the comparison grp based on provider discretion and potential for bias in tx/assessment decisions due to lack of blinding of providers and outcome assessors to tx. *Study quality:* Fair *Conflicts of interest:* Authors received research funding and are members of the speaker's bureau for KCI, the manufacturer of the device used in the study.

Authors/Study Design	Study Population	Treatment	Results	Quality/Comments
	wounds resulting from burns; venous insufficiency; untreated cellulitis or osteomyelitis (after amputation); collagen vascular disease; malignant disease in the wound or uncontrolled hyperglycemia (HbA1c >12%) *Clinical hx/pt characteristics (NPWT grp, Standard tx grp):* Mean (SD) age (yrs): 57.2 (13.4), 60.1 (12.3), 59 (12.8) overall % men: 86%, 78% % currently use tobacco: 5%, 13% Wound etiology: Diabetic foot amputation	recommended by treating clinician; duration of use NR All pts received off-loading tx as indicated. *Outcome measures:* Primary: Proportion of wounds with complete closure (100% epithelialization without drainage assessed based on data from wound assessments and photographs taken by treating clinician) Secondary: Rates of wound healing or facilitation of surgical wound closure; foot salvage; tx-related complications *Economic analysis:* The analysis included inpatient stays for acute care, extended care, and other inpatient hospital care initiated or caused by foot lesion during the study. Cost estimates for surgical procedures are based on the minimum commercial fee according to Medicare and include	Infections and infestations: 25 (32%), 27 (32%); *P*=1.000 Wound infection: 13 (17%), 5 (6%) In the NPWT grp, 3 infections were classified as mild, 6 as moderate, 4 as severe; none were deemed related to tx. In the Standard tx group, 2 were classified as mild, 1 as moderate, and 2 as severe; 2 of the 5 events were deemed to be related to the tx, 1 of which was serious. Tx-related adverse events: 9 (12%), 11 (13%). 1 event in the NPWT grp was classified as serious; 5 events in the Standard tx grp were classified as serious. *Cost analysis results (NPWT grp, Standard tx grp):* Avg direct cost per pt treated for 8 wks or longer (regardless of clinical outcome): $27,270, $36,096 Avg total cost to achieve healing: $25,954 (n=43); $38,806 (n=33) *Secondary analysis (Armstrong et al., 2007): Role of wound chronicity in healing:* Proportion of wounds closed (NPWT vs Standard tx): No significant difference in the proportion of acute or chronic wounds achieving complete closure (acute, *P*=0.072; chronic, *P*=0.320) Time to complete closure (NPWT vs	

Authors/Study Design	Study Population	Treatment	Results	Quality/Comments
	Wound location: Foot Mean (SD) wound age (mos): 1.2 (3.9), 1.8 (5.9) Mean (SD) wound size (cm^2): 22.3 (23.4), 19.2 (17.6) Infection status (%): NR Wound prep prior to study txs: Amputation to transmetatarsal level foot	only those costs accumulated during the 112-day study period. Costs for oral and systemic antibiotics were calculated using duration of tx and # of courses. Outpatient tx visits included clinic visits and visits to pts' homes. The cost per visit included estimated cost for personnel time and estimated cost of a clinic visit. Topical wound dressing costs were based on avg use of primary topical txs. Calculations for these costs included actual # of dressing changes, estimated material costs based on primary dressing material, estimated time for each dressing change, and cost per hr of personnel performing the dressing change. Dressing changes done by pts or family members were treated separately.	Standard tx): Statistically significantly different in favor of NPWT for both acute and chronic wounds (acute, *P*=0.030; chronic, *P*=0.033)	
Biter (2014) Sint Franciscus	n=49	Tx setting: Outpatient	*Clinical outcomes (NPWT grp; Silicone dressing grp):*	*Limitations:* No power calculations reported

Authors/Study Design	Study Population	Treatment	Results	Quality/Comments
Gasthuis, Rotterdam, the Netherlands RCT *F/u:* 6 mos *Time frame:* Surgery occurred between October 2009 and May 2012 *Funding source:* NR, but authors noted no financial disclosures	NPWT: n=24 Dressing: n=25 Does not include 4 early terminations (see *Complications*) or 2 losses to f/u after completion of 2-wk examination *Inclusion criteria:* Symptomatic pilonidal sinus with or without a previous abscess of the sinus *Exclusion criteria:* Aged <16 yrs; previous attempt at surgical excision of pilonidal disease; inability to undergo frequent f/u; pilonidal sinus situated <3 cm from anus	NPWT: Brand NR; NR if powered; dressing type, open-pore foam covered by adhesive semipermeable dressing; recommended changing interval, sponge replaced at 3, 7, 10 days postsurgery; suction and pressure setting (mmHg), 125; reusability NR; instillation system NR; duration of use, 14 days Silicone dressing: Dressing type, silicone wound dressing applied to wound and topped with absorbent bandage; recommended changing interval, pts advised to rinse wound 3× daily for 2 wks after excision; duration of use NR. Special dressings applied only if the wound appeared sloughy and/or retained pus. All: Same prewound care surgical technique. For pain, paracetamol or if necessary nonsteroidal anti-inflammatory drugs	Time to complete wound healing (median) (range) (days): 84 (34-349), 93 (43-264); *P*=0.44 Wound volume (cm^3): Day of surgery: 60, 56 (*P*=0.61) 14 days later: 24, 40 (*P*=0.10) Wound size reduction (ratio): 0.30; 0.57 (*P*=0.02) Recurrence <6 mos after wound closure (# pts) (% pts): 3 (13%); 1 (4%) (*P*=0.30) *Pt-centered outcomes (NPWT grp n=24; Silicone dressing grp n=25):* Pain (median): Day of surgery: 1.5; 1.7 (*P*=0.24) 14 days after surgery: 2.2; 2.5 (*P*=0.29) Walk without pain (14 days): 16 (67%); 21 (84%) (*P*=0.13) Sit without pain (14 days): 12 (50%); 14 (56%) (*P*=0.67) Time to return to work or school (days) (median) (range): 27 (7-126); 29 (6-63) (*P*=0.92) None of the pt-oriented outcomes were statistically significantly different between grps. *Complications (NPTW grp; Silicone dressing grp):* Wound infection/abscess (# pts) (% pts): 2 (8%), 2 (8%) (*P*=1.00)	and unclear data analysis methods for primary outcome. *Study quality:* Fair *Conflicts of interest:* The authors reported no conflicts of interest.

Authors/Study Design	Study Population	Treatment	Results	Quality/Comments
	Clinical hx/pt characteristics (NPWT grp; Silicone dressing grp): Median age (range) (yrs): 23 (16-44); 29 (16-65) % men: 75%; 92% % smoker: 25%; 24% Wound etiology: Pilonidal sinus disease Wound location: Pilonidal sinus (cleft at top of buttocks) Mean wound age (wks): NR Mean wound size (cm^2): NR. Mean wound volume ($cm^{3)}$: 60; 56 (*P*=0.61) Infection status (%): NR Wound prep prior to study txs: Surgical excision	recommended. *Outcome measures:* Time to achieve wound healing (days until full skin closure); wound infection (pain and redness of the wound); pain (mean score on VAS); time to return to daily activities such as work or school	Early termination of NPWT: 4 (17% of 24 randomly allocated): Due to pain (n=2), bad odor (n=1), or unspecified "practical considerations" (n=1) Any "concerns": 16 (67%), 19 (76%)	
Monsen et al. (2014)	n=20	Tx setting: Hospital as	*Clinical outcomes (NPWT grp; Dressing*	*Limitations:* Possible

Authors/Study Design	Study Population	Treatment	Results	Quality/Comments
Monsen et al. (2015) **Acosta et al. (2013)** Vascular Center, Malmo-Lund, Skane University Hospital; Malmo and Lund, Sweden RCT *F/u:* Median 14 mos *Time frame:* February 13, 2007 – November 24, 2011 *Funding source:* NR	NPWT: n=10 Dressing: n=10 Does not include 4 additional randomized pts who were excluded from time to wound healing outcome due to skin transplantation (n=1 from NPWT grp), secondary skin closure (n=1 from Dressing grp) or death prior to healed wound (n=2 from Dressing grp) *Inclusion criteria:* Deep perivascular groin infections (Szilagyi grade III) that occurred after arterial surgery *Clinical hx/pt characteristics (NPWT grp,*	long as graft material or native artery was visible, then outpatient NPWT: VAC system (KCl); electrically powered; dressing type, silicone-based (Mepitel; Mölnycke Health Care AB); recommended changing interval, changes of VAC dressings were performed 3×/wk; suction and pressure setting (mmHg) 125; reusability, pump is reusable; instillation system NR; duration of use NR Dressing: Dressing type, Alginate dressing (Sorbalgon [Hartmann ScandiCare AB], Anderstorp or Melgisorb [Mölnlycke Health Care AB]); recommended changing interval, as often as indicated clinically; duration of use NR All pts received the same debridement prior to wound tx of either type *Outcome measure:*	*grp):* Time to complete wound healing (median) (range) (days): 57 (25-115) (for n=9); 104 (57-175) (for n=7); *P*=0.026 Tx failure (visible graft material or femoral artery after 1 mo of tx or amputation or death due to groin infection) (# pts) (% pts): 1 (10%), 5 (50%) *Pt-centered outcomes:* Quality of Life, EQ-5D (NPWT grp n=6 with healed wound; Dressing grp n=6 with healed wound) (Monsen et al., 2015): EQ-D – Index: 0.69 (0.30-0.80), 0.66 (0.52-0.86); *P*=NS EQ-5D – VAS (median [q1-q3]): 70 (63.75-750), 55 (35-85.5) Neither scale was statistically significantly different between grps either before or after tx. Pain, BPI (NPWT grp n=9 after 4 weeks; Dressing grp n=8 after 4 weeks) (Monsen 2015): NS differences between grps before or after tx. Overall summary scores NR. *Complications (NPWT grp; Dressing grp):* Amputation: 3 (30%), 2 (20%) In NPWT grp, 3 transfemoral amputations due to groin infection (n=1) or worsening of critical limb ischemia (n=2). In Dressing grp, 1 underwent transfemoral amputation due to groin infection and 1	selection bias during recruitment; lack of adequate randomization technique; unclear method for calculating time to wound healing; use of different types of alginate dressings in comparison grp; unclear mean length of f/u in each grp. *Study quality:* Fair *Conflicts of interest:* The authors report no conflicts of interest.

Authors/Study Design	Study Population	Treatment	Results	Quality/Comments
	Dressing grp): Mean Age (yrs): 71; 73 % men: 80%, 50% % smoker: NR Wound etiology: Arterial surgery, per inclusion criteria Wound location: Groin, per inclusion criteria Wound age (wks): Time of index procedure to randomization, median 16 days each grp Wound size (median) (range) (cm^2): 13 (7.6-37.6); 20.5 (4.6-44.5) Infection status: All, per inclusion criteria Wound prep prior to study txs: All had debridement, per inclusion criteria	Time to complete wound healing; EQ-5D; BPI; quality of life; adverse events	underwent metatarsal amputation because of worsening of critical limb ischemia. Mortality, in-hospital: 0, 1 (10%) 1 pt in Dressing grp died during hospital stay. Mortality, total: 2 (20%), 5 (50%) by end of f/u (*P*=0.35) In an "early interim analysis" (Acosta et al., 2013), adverse events were reported at median 29.5 mos (range 4-51) for the first 5 pts enrolled in each grp (NPWT grp n=5 with healed wound; Dressing grp n=5 with healed wound). Tx failures: 1 (due to re-bleeding); 3 (2 failures to heal within 2 mos, 1 visible interposition bypass graft in the groin after 1-mo tx requiring wound closure with sutures) Erysipelas of groin, late: 1, 0	

Authors/Study Design	Study Population	Treatment	Results	Quality/Comments
Karlakki et al. (2016) Robert Jones and Agnes Hunt Orthopaedic Hospital; Oswestry, UK RCT (single center, n=220) *F/u*: 6 wks *Time frame*: October 2012 through October 2013 *Funding source*: Smith & Nephew UK	n=220 randomized (209 per protocol population) iNPWTd: n=107 (102 per-protocol population) Control: n=108 (107 per-protocol population) 116 THAs and 93 TKAs *Inclusion criteria:* All consecutive pts undergoing routine THAs and TKAs with participating surgeons *Exclusion criteria*: Known allergies to dressings; undergoing revision joint surgery; unwilling to attend additional clinics; on warfarin	Tx setting: Inpatient and outpatient (>50% of pts discharged within 3 days of surgery in both grps) iNPWTd: Smith & Nephew Pico dressing; recommended changing interval, 1 wk; suction and pressure setting (mmHg) NR; reusability, no; no instillation system; duration of use, 1 wk Control: Dressing type, conventional dressings: either Mepore (Mölnlycke Health Care AB) or Tegaderm (3M Health Care Ltd.) as per the surgeon's preferred practice. Dressing changed to OPSITE Post-Op Visible dressing (Smith & Nephew) on the second postoperative day as per the usual routine practice; recommended changing interval, a minimum of 1 dressing change and further changes based on the extent and amount of wound exudate (exudate filling more than 50% of the dressing); duration of	*Clinical outcomes:* No eligible clinical outcomes reported *Pt-centered outcomes:* NR *Wound complications:* iNPWTd: 2 (2%) pts experienced wound complications after discharge Control: 9 (8.4%), includes 2 pts with prolonged wound exudate requiring surgical washout while in hospital; 7/9 treated as suspected SSI with antibiotics in the community iNPWTd grp vs control grp: Overall wound complications: OR 4.0; 95% CI, 0.95-30; *P*=0.06 Confounding factors analyses: BMI: OR 1.2; 95% CI, 1.04-1.3; *P*=0.007 Obesity (BMI ≥35): OR 4.5; 95% CI, 1.1-16; *P*=0.03 Morbid obesity (BMI ≥40): OR 68; 95% CI, 6.7-1904; *P*<0.001 Diabetes: OR 4.9; 95% CI, 1.0-2.0; *P*=0.05 Smoking OR NR, *P*=0.006 Procedure (TKA vs THA): OR 3.5; 95% CI, 0.84-16; *P*=0.07 Anesthetic: OR NR; *P*=0.05 Wound closure method (suture vs staple): OR 0.0; 95% CI, 0.0-0.9; *P*=0.04 *Readmissions (iNPWTd grp; Control grp)*: 0, 1 (pain and stiffness, treated with arthroscopic washout)	*Limitations:* Use of different types of dressings in comparison grp immediately after surgery; different f/u and assessment procedures for each grp; lack of blinding; not all pts received f/u care outside the hospital; use of drains was not analyzed as a confounding factor for wound complications. *Study quality:* Fair *Conflicts of interest:* Two of the authors (Karlakki and Whitall) report receiving payment and funding for consultancy work, lectures, and other projects unrelated to this paper. The study was funded through a grant from Smith & Nephew UK, to cover the cost of NPWT dressings and data collection costs.

Authors/Study Design	Study Population	Treatment	Results	Quality/Comments
	Clinical hx/pt characteristics (iNPWTd grp, control grp): Mean (SD) age (yrs): 69.0 (9.0), 69.2 (9.0) % men: 48%, 51% % current or previous use of tobacco: 22%, 22% % obese (BMI ≥35): 17%, 8% % morbidly obese (BMI≥40): 3%, 1% % diabetic: 5%, 11% Wound etiology: THA 52%, 59%; TKA 48%, 41% Wound location: hip or knee Mean (SD) wound age (mos): NA Mean (SD) wound size (cm^2): NR Infection status (%): NR Wound prep	use NR For both grps the dressing was changed earlier or again if there was progressive exudate filling 50% or more of the dressing *Outcome measures:* Primary: Impact of iNPWTd on wound healing and effect on length of hospital stay Secondary: Wound complications, # of dressing changes, and the overall cost-effectiveness of the dressing Cost-effectiveness: Overall cost-effectiveness of the dressing. Cost of Pico system (costs of hospital stays are reported in British pound sterling)	*Infections (iNPWTd; Control)*: SSI: NR; 7 (suspected SSI) 1 pt in iNPWTd grp was treated for cellulitis by general practitioner *Blisters (iNPWTd grp; Control grp)*: 11%; 1% Blisters were inspected in the iNPWTd grp at 1-wk clinic visit and noted in control grp at 2-wk phone call	

Authors/Study Design	Study Population	Treatment	Results	Quality/Comments
	prior to study txs: Wound closure with staples, 75%, 68% Wound closure with sutures, 25%, 32%			
Manoharan et al., 2016 The Orthopaedic Research Institute of Queensland, Pimlico, Australia RCT (single center, n=21 pts, 42 knees) *F/u*: <2 wks *Time frame*: February through December 2014 *Funding source*: NR; Acelity provided dressings for the study	n=21pts, 42 knees NPWT: n=21 Control: n=21 *Inclusion criteria:* NR *Exclusion criteria*: <18 yrs old; pregnant *Clinical hx/pt characteristics:* NOTE: Pt characteristics are reported for 33 pts; 12 of them received standard wound dressings and were not included in the randomized grp who received either standard dressing or NPWT	Tx setting: Inpatient and outpatient; avg inpatient stay for all 33 pts was 4.1 (range 3-7) days NPWT: Acelity KCI Prevena Incision Management System; recommended changing interval, 1 wk; suction and pressure setting (mmHg) 125; reusability, no; no instillation system; duration of use, 8 days with suction, in place until 10-12 days post operation f/u visit Control: Dressing type, conventional dry dressings; recommended changing interval, as needed per amount of discharge on the dressings; duration of use NR	*Clinical outcomes:* No eligible clinical outcomes reported *Pt-centered outcomes:* Quality of life (mean) (±SD) (NPWT grp; Control grp): Dressing leakage: 0.14 (0.13); 0.38 (0.34) *P*=0.019; ES =1.02 Wound protection: 0.16 (0.05); 0.33 (0.16) *P*=0.001, ES=0.0212 NS differences for other quality-of-life factors. *Wound complications:* NPWT: 1 knee with severe blistering requiring hospital readmission and intravenous antibiotics Control: 1 knee with persistent wound drainage (treated with NPWT as an inpatient for 2 days) Readmissions: 1 pt with blistering on knee receiving NPWT Infections: No wound dehiscence or infection during trial	*Limitations:* Lack of blinding and small sample size. *Study quality:* Fair *Conflicts of interest:* Manufacturer provided equipment for the study; 1 or more of the authors of this paper have disclosed potential or pertinent conflicts of interest which may include receipt of payment, either direct or indirect, institutional support, or association with an entity in the biomedical field which may be perceived to have potential conflict of interest with this work. For full

Authors/Study Design	Study Population	Treatment	Results	Quality/Comments
	on each knee. Overall (n=33) Mean (range) age (yrs): 66 (45-80) % men: 58% % current or previous use of tobacco: NR Mean (range) BMI: 29.79 (23-44) Mean (range) Charlson Comorbidity Index: 2.33 (0-5) Wound etiology: TKA Wound location: knee	*Outcome measures:* Primary: Cost of dressings, wound complications, and quality-of-life factors (the following were assessed via wound diary: odor, dressing leakage, itch, movement, body image, self-esteem, personal hygiene, wound protection, sleep, and pain) Secondary: Evidence of maceration, evidence of blistering		disclosure statements refer to http://dx.doi.org/10.1016/j.arth.2016.04.016

APPENDIX VI. Summary of Practice Guidelines

Key: DFU, diabetic foot ulcer; FDA, Food and Drug Administration; NPWT, negative pressure wound therapy; PU, pressure ulcer; VLU, venous leg ulcer

Sponsor, Title	Relevant Recommendations	Quality*/Main Limitations

International Expert Panel on Negative Pressure Wound Therapy (NPWT-EP) (Vig et al., 2011)
 	
Evidence-based recommendations for the use of NPWT in chronic wounds: steps towards an international consensus
	• PU
	  ○ NPWT may be used until surgical closure is possible/desirable.
	  ○ Alternatively, NPWT should be considered to achieve closure by secondary intention.
	  ○ NPWT should be used to reduce wound dimensions.
	  ○ NPWT should be used to improve the quality of the wound bed.
	• DFU
	  ○ NPWT must be considered as an advanced wound care therapy for postoperative Texas grade 2 and 3 diabetic feet without ischemia.
	  ○ NPWT must be considered to achieve healing by secondary intention.
	  ○ Alternatively, NPWT should be stopped when wound has progressed suitably to be closed by surgical means.
	  ○ NPWT should be considered in an attempt to prevent amputation or re-amputation.
	• Ischemic lower limb wounds
	  ○ The cautious use of NPWT in chronic limb ischemia when all other modalities have failed may be considered in specialist hands but never as an alternative for revascularization.
	  ○ NPWT may be considered as an advanced wound care therapy for lower limb ulceration after revascularization.
	  ○ The use of NPWT is NOT indicated in acute limb ischemia.
	• VLUs
	  ○ If first-line therapy (compression) is not efficacious, NPWT should be considered to prepare the wound for surgical closure as part of a clinical pathway.
	  ○ Use of gauze may be considered to reduce pain during dressing changes in susceptible patients.
		5.3 – Fair (more discussion of the strengths and limitations of body of evidence needed; the expert panel, literature review, and guideline development and writing was funded and led by Smith & Nephew; membership in the Expert Panel is not described; authors state that the manuscript was not unfairly influenced by the funder and that the recommendations reflect the independent and unbiased views of the expert panel)

Association	D. ADVANCED OR ADJUNCTIVE INTERVENTIONS IF PU IS	4.0 – Fair (criteria for

Sponsor, Title	Relevant Recommendations	Quality*/Main Limitations
for the Advancement of Wound Care (AAWC, 2010) *Association for the Advancement of Wound Care (AAWC) Guideline of Pressure Ulcer Guidelines*	UNRESPONSIVE TO A-LEVEL MANAGEMENT 3. Negative Pressure Wound Therapy—No consistent effect on PU healing. Increased granulation, less fibrin compared to Redon drain, earlier use may shorten home care stays. Lower cost than gauze. The FDA has advised caution in selecting patients for this therapy due to serious, occasionally fatal, complications. Please read the FDA notice at: http://www.fda.gov/MedicalDevices/Safety/AlertsandNotices/PublicHealthNotifications/ucm190658.htm	selecting evidence not described, methods for formulating recommendations not described, guideline review and update process not described)
National Pressure Ulcer Advisory Panel (NPUAP, 2014) *Treatment of pressure ulcers. In: Prevention and treatment of pressure ulcers: clinical practice guideline*	NPWT 1. Consider NPWT as an early adjuvant for the treatment of deep, category/stage III and IV pressure ulcers. (Strength of Evidence = B; Strength of Recommendation = Weak positive recommendation) *Caution: NPWT is not recommended in inadequately debrided, necrotic or malignant wounds; where vital organs are exposed; in wounds with no exudate; or in individuals with untreated coagulopathy, osteomyelitis or local or systemic clinical infection. Cautious use by an experienced health professional is recommended for individuals on anticoagulant therapy; in actively bleeding wounds; or where the wound is in close proximity to major blood vessels.* 2. Debride the PU of necrotic tissue prior to the use of NPWT. (Strength of Evidence = C; Strength of Recommendation = Strong positive recommendation) 3. Follow a safe regimen in applying and removing the NPWT system. (Strength of Evidence = C; Strength of Recommendation = Strong positive recommendation) 4. Evaluate the PU with each dressing change. (Strength of Evidence = C; Strength of Recommendation = Weak positive recommendation) 5. If pain is anticipated or reported consider: 1. Placing a nonadherent interface dressing on the wound bed, underneath the foam 2. Lowering the level of pressure, and/or changing type of pressure (continuous or intermittent) 3. Using a moist gauze filler instead of foam (Strength of Evidence = C; Strength of	6.4 – Good (procedure for updating not identified)

Sponsor, Title	Relevant Recommendations	Quality*/Main Limitations
	Recommendation = Weak positive recommendation) 6. Educate the individual and his/her significant others about NPWT when used in the community setting. (Strength of Evidence = C; Strength of Recommendation = Strong positive recommendation)	
International Working Group on the Diabetic Foot (Game et al., 2016) *IWGDF guidance on use of interventions to enhance the healing of chronic ulcers of the foot in diabetes*	Topical NPWT may be considered in postoperative wounds even though the effectiveness and cost-effectiveness of the approach remain to be established. (weak; moderate) It is not possible to make a recommendation on the use of NPWT in nonsurgical wounds because of the lack of available evidence.	6 – Good (unclear if guidelines were reviewed externally by experts, a procedure for updating was not identified)
Society for Vascular Surgery (SVS) and the American Venous Forum (AVF) (O'Donnell et al., 2014) *Management of venous leg ulcers: clinical practice guidelines of the Society for Vascular Surgery and the American Venous Forum*	Guideline 4.24: Negative Pressure Therapy [–] We suggest against routine primary use of negative pressure wound therapy for venous leg ulcers. [GRADE - 2; LEVEL OF EVIDENCE - C] There is currently not enough information to support the primary use of NPWT for VLUs. Evidence supports positive effects with the use of negative pressure therapy for wound healing in general. Tissue granulation, area and volume reduction, and reductions in bioburden have all been reported. There have been few studies specifically studying negative pressure therapy for VLUs, with most studies reporting on mixed wound causes. There has been an increase in the use of NPWT for wound bed preparation to augment skin graft healing.	6.2 – Good (criteria for selecting evidence is not clearly described; need to update mentioned, but the method for updating was not identified)

*According to the Rigor of Development domain of the Appraisal of Guidelines Research and Evaluation (AGREE) tool, along with a consideration of commercial funding and conflicts of interest among the guideline authors. Guidelines were scored on a scale of 1 to 7 and judged to be good (6-7), fair (4-5), or poor (1-3).

APPENDIX VII. Examples of NPWT Technologies

Examples of NPWT Technologies Commercially Available in the United States[a]

Key: FDA, Food and Drug Administration; NPWT, negative pressure wound therapy; SNaP, Smart Negative Pressure Wound Care System

Manufacturer/ Company	Model	Care Setting[b]	Indications as Described in the Device or Consumer Information/Instructions Document on the FDA Website
Atmos (K090130, 2009)	ATMOS S041 WOUND	Hospital and home	The ATMOS S041 Wound is a suction device intended for aspiration and collection of secretions and body fluids from wounds, and is indicated for patients who would benefit from a suction device, particularly as the device may promote wound healing. ATMOS S041 is appropriate for use on the following wounds: pressure ulcers, diabetic/neuropathic ulcers, venous insufficiency ulcers, traumatic wounds, postoperative and dehisced surgical wounds, explored fistulas, skin flaps and grafts.
Cardinal Health K150124, 2015 K143016, 2015 K142916, 2015	Cardinal Health NPWT PRO HC Cardinal Health NPWT PRO to GO Cardinal Health NPWT PRO at Home Sved Wound Treatment System	Acute, extended and home care	The Cardinal Health NPWT PRO HC/PRO to GO/PRO at Home/Sved systems are an integrated wound management system indicated for the application of continual or intermittent NPWT to the wound as the device may promote wound healing by the removal of fluids, including wound exudates, irrigation fluids, body fluids, and infectious materials. The system is intended for patients with chronic, acute, traumatic, subacute, and dehisced wounds; partial-thickness burns; ulcers (e.g., diabetic or pressure); flaps; and grafts. The systems are intended for use in acute, extended, and home care settings.
Cork Medical Products LLC (Creo Quality LLC) K140022, 2014	Nisus NPWT	Setting not specified	Patients who would benefit from NPWT, particularly as the device may promote wound healing by the removal of excess exudates, infectious material, and tissue debris.
Devon Medical Products K140634, 2014 K132225, 2014	ExtriCARE 2400 NPWT Extricare 3600 NPWT	Variety of wound care settings	The extriCARE 2400 and extriCARE 3600 NPWT systems are indicated for wound management via the application of negative pressure to the wound by the removal of wound exudate, infectious materials, and tissue debris from the wound bed. It is indicated for the following wound types: chronic, acute, traumatic, subacute and dehisced, partial-thickness burns, ulcers (e.g., diabetic or pressure), flaps, and grafts.
Foryou Medical Electronics Co. Ltd. K113236, 2013	ForYou NPWT Pro/ForYou NPWT NP32	Hospital	Patients who would benefit from NPWT, particularly as the device may promote wound healing by the removal of excess exudates, infectious material, and tissue debris.

Manufacturer/ Company	Model	Care Setting[b]	Indications as Described in the Device or Consumer Information/Instructions Document on the FDA Website
Genadyne Biotechnologies Inc. K082676, 2008 K090638, 2009	Genadyne A4 Wound Vacuum System Genadyne A4 XLR8 Wound Vacuum System	Hospital and home	Patients who would benefit from NPWT, particularly as the device may promote wound healing by the removal of excess exudates, infectious material, and tissue debris.
Innovative Therapies K093564, 2009	SVED Wound Treatment System	Hospital and home	For patients who would benefit from vacuum-assisted drainage and controlled delivery of topical wound treatment solutions and suspensions over the wound bed. The intended use of the Sved Wound Treatment System is for patients with chronic, acute, traumatic, subacute, and dehisced wounds; diabetic ulcers; pressure ulcers; flaps; and grafts.
IRB Medical Equipment/ Boehringer Wound Systems/ ConvaTec K061788, 2006	Boehringer Laboratories Suction Pump System	Hospital and home	For the application of suction (negative pressure) to wounds to promote wound healing and for the removal of fluids, including wound exudate, irrigation fluids, body fluids and infectious materials.
IVT Medical Ltd. K121817, 2013	Vcare α	Setting not specified	For wound management via application of continual or intermittent negative pressure to the wound for removal of fluids, including wound exudate, irrigation fluids, and infectious materials. It is indicated for management of chronic, acute, traumatic, subacute and dehisced wounds; partial-thickness bums; ulcers (such as diabetic or pressure); flaps; and grafts.
Kalypto Medical (acquired by Smith & Nephew) K080275, 2008	NPD 1000 Negative Pressure Wound Therapy System	Home	The NPD 1000 Negative Pressure Wound Therapy System is a portable, low-powered, battery-operated suction pump intended for the application of suction to remove a small amount of fluid from the wound bed, including wound exudate and infectious material, which may promote wound healing.
KCI (Kinetic Concepts Inc.) (KCI, LifeCell, and Systagenix are now Acelity) K100657, 2010	V.A.C. Ulta Therapy	Hospital	The instillation option is indicated for patients who would benefit from vacuum-assisted drainage and controlled delivery of topical wound treatment solutions and suspensions over the wound bed. The V.A.C. Ulta Negative Pressure Wound Therapy System with and without instillation is indicated for patients with chronic, acute, traumatic, subacute and dehisced wounds; partial-thickness burns; ulcers (such as diabetic, pressure, and venous

Manufacturer/ Company	Model	Care Setting[b]	Indications as Described in the Device or Consumer Information/Instructions Document on the FDA Website
K132741, 2013 K120033, 2012 K120499, 2012 K091585, 2009 K150006, 2015			insufficiency); flaps; and grafts.
	ActiV.A.C. Therapy InfoV.A.C. V.A.C. Via V.A.C. ATS Therapy V.A.C. Freedom Therapy	Hospital, extended, and home	The ActiVAC., InfoVAC., V.A.C. ATS, V.A.C. Freedom, V.A.C. Via, and V.A.C. Simplicity Negative Pressure Wound Therapy Systems are integrated wound management systems for use in acute, extended, and home care settings. When used on open wounds, they are intended to create an environment that promotes wound healing by secondary or tertiary (delayed primary) intention by preparing the wound bed for closure, reducing edema, and promoting granulation tissue formation and perfusion; and by removing exudate and infectious material. Open wound types include: chronic, acute, traumatic, subacute, and dehisced wounds; partial-thickness burns; ulcers (such as diabetic, pressure, or venous insufficiency); flaps; and grafts. When used on closed surgical incisions, they are also intended to manage the environment of surgical incisions that continue to drain following sutured or stapled closure by maintaining a closed environment and removing exudates via the application of NPWT.
	V.A.C. Instill Wound Therapy	Hospital	The V.AC. Instill Therapy System is indicated for patients who would benefit from V.A.C. Therapy coupled with controlled delivery of topical wound treatment solutions and suspensions over the wound bed. It is intended for patients with chronic, acute, traumatic, subacute, and dehisced wounds; partial-thickness burns; ulcers (such as diabetic, pressure, or venous insufficiency); flaps; and grafts.
	ABThera Open Abdomen Negative Pressure Therapy	Hospital	The ABThera Open Abdomen Negative Pressure Therapy System is indicated for temporary bridging of abdominal well openings where primary closure is not possible and/or repeat abdominal entries are necessary. The intended use of this system is in open abdominal wounds with exposed viscera, including, but not limited to, abdominal compartment syndrome. The intended care setting is a closely monitored area within the acute care hospital, such as the intensive care unit. The abdominal dressing will most often be applied in the operating theater.
	Prevena Incision Management System	Hospital and home	The Prevena Incision Management System is intended to manage the environment of surgical incisions that continue to drain following sutured or stapled closure by maintaining a closed environment and removing exudate via the application of NPWT.

Manufacturer/ Company	Model	Care Setting[b]	Indications as Described in the Device or Consumer Information/Instructions Document on the FDA Website
MediTop BV/The Medical Company K082311, 2008	Exsudex Wound Drainage Pump	Primarily hospital use but may be used at home	The Exsudex Wound Drainage Device is a compact, portable device indicated for patients who would benefit from the application of negative pressure to the area of a wound, for the aspiration and removal of surgical fluids, irrigation fluids, tissue (including bone), gases, bodily fluids, or infectious materials either during surgery or at the patient's bedside, particularly as the device may promote wound healing.
Medela K142626, 2015 K113678, 2012	Invia Liberty	Hospital and home	The Medela Invia Liberty Negative Pressure Wound Therapy System is indicated to help promote wound healing through means that include drainage and removal of infectious material or other fluids under the influence of continuous and/or intermittent negative pressures, particularly for patients with chronic, acute, traumatic, subacute, or dehisced wounds; partial-thickness burns; ulcers (such as diabetic or pressure); flaps; and grafts.
	Invia Motion	Hospital and home	The portable Medela Invia Motion NPWT system is indicated to create an environment that promotes wound healing by secondary or tertiary (delayed primary) intention by preparing the wound bed for closure, reducing edema, and promoting granulation tissue formation and perfusion; and by removing exudates and infectious material. It is intended for use in hospitals, clinics, long-term care and home care settings on adult patients with chronic, acute, subacute, traumatic, dehisced wounds; partial-thickness burns; ulcers (such as diabetic, neuropathic, pressure, or venous insufficiency); flaps; and grafts.
Premco Medical Systems K082415, 2008	Prodigy™ NPWT System (PMS-800 and PMS-800V)	Hospital and home	The Prodigy 800V NPWT System is indicated for use in patients that would benefit from a suction device, particularly as the device may promote wound healing, or for aspiration and removal of surgical fluids, tissue (including bone), gases, bodily fluids, or infectious material from a patient’s airway or respiratory support system either during surgery or at the patient’s bedside.
Prospera K112458, 2012	PRO-I (stationary) PRO-II (portable) PRO-III	Hospital and home	The Prospera Negative Pressure Wound Therapy System is indicated for patients that would benefit from a suction device, particularly as the device may promote wound healing by removal of wound exudate, debris, and infectious material, or for the aspiration and removal of surgical fluids, tissue (including bone), gases, bodily fluids, or infectious material from the patient's airway or respiratory support system. The Prospera Negative Pressure Wound Therapy may be used during surgery or at the patient's bedside and is indicated for home use.
Smith & Nephew (includes subsidiary Blue Sky Medical)	Renasys EZ Plus	Hospital and home	The Renasys EZ Plus NPWT is indicated for patients who would benefit from a suction device (NPWT) as it may promote wound healing via removal of fluids, including irrigation and body fluids, wound exudates, and infectious materials. Appropriate

Manufacturer/ Company	Model	Care Setting[b]	Indications as Described in the Device or Consumer Information/Instructions Document on the FDA Website
K151326, 2015 K083375, 2009 K151436, 2016 K061919, 2007			wound types include: chronic, acute, traumatic, subacute, and dehisced wounds; ulcers (e.g., pressure or diabetic); partial-thickness burns; and flaps and grafts. The Renasys EX Plus professional healthcare facility model (REF 66800697) is intended for use in acute care settings and other professional healthcare environments where product use is conducted by or under the supervision of a qualified healthcare professional.
	Renasys Go	Hospital and home	Renasys GO is indicated for patients who would benefit from a suction device (negative pressure) to help promote wound healing by removing fluids, including irrigation and body fluids, wound exudates, and infectious materials. Examples of appropriate wound types include: chronic, acute, traumatic, subacute, and dehisced wounds; ulcers (e.g., pressure or diabetic); partial-thickness burns; and flaps and grafts.
	PICO Single Use Negative Pressure Wound Therapy System	Hospital and home	PICO is indicated for patients who would benefit from a suction device (NPWT) as it may promote wound healing via removal of low to moderate levels of exudate and infectious materials. Appropriate wound types include: chronic, acute, traumatic, subacute, and dehisced wounds; ulcers (e.g., pressure or diabetic); partial-thickness burns; flaps and grafts; and closed surgical incisions. PICO Single Use Negative Pressure Wound Therapy System is suitable for use in both hospital and home care setting.
	EZCare (previously by Blue Sky Medical Group)	Hospital and home	The Versatile 1 EZCare Wound Vacuum System is indicated for patients who would benefit from a suction device, particularly as the device may promote wound healing.
Spiracur (SNaP Therapy System acquired by Acelity in 2015) K151710, 2015	SNaP	Hospital and home	SNaP System with SNaP Cartridge (60 cc) or SNaP Plus Cartridge (150cc): The SNaP Wound Care System is indicated for patients who would benefit from wound management via the application of negative pressure, particularly as the device may promote wound healing through the removal of excess exudate, infectious material, and tissue debris. The SNaP Wound Care System is indicated for removal of small amounts of exudate from chronic, acute, traumatic, subacute, and dehisced wounds; partial-thickness burns; ulcers (such as diabetic, venous, or pressure); surgically closed incisions; flaps; and grafts.
Talley Group Ltd. K080897, 2008 K143004, 2016	Venturi Negative Pressure Wound Therapy	Hospital	Use of the Venturj Negative Pressure Wound Therapy system is indicated for use for patients with acute or chronic wounds who may be benefited by the application of negative pressure therapy and the potential wound healing effects of removal of fluids, including wound exudates, irrigation fluids, body fluids, and infectious materials. Venturi is intended for use in acute care settings only.

Manufacturer/ Company	Model	Care Setting[b]	Indications as Described in the Device or Consumer Information/Instructions Document on the FDA Website
	Venturi MiNO TG600/14	Healthcare environment	The Talley Venturi MiNO TG600/14 is intended for use for patients with acute or chronic wounds who may be benefited by the application of continual NPWT to the wound for removal of fluids, including wound exudate, irrigation fluids, and infectious materials. The device is intended for use by qualified healthcare professionals in a healthcare environment.
Wound Rx Medical LLC K142385, 2015	Whisper Pump System	Hospital, transitional, or nursing facility	The Whisper Pump System is a suction device intended for aspiration and collection of secretions and body fluids from wounds and is indicated for patients who would benefit from a suction device, particularly as the device may promote wound healing. The Whisper Pump System is appropriate for use on the following wounds: pressure ulcers, diabetic/neuropathic ulcers, venous insufficiency ulcers, traumatic wounds, postoperative and dehisced surgical wounds, explored fistulas, and skin flaps and grafts.

[a]The table from Rhee et al. (2014) titled "Negative Pressure Wound Therapy Technologies Commercially Available in the U.S." was updated using the following strategy: After confirming that NPWT does not require a premarket authorization (PMA), the term "negative pressure wound therapy" was used to search the following website: http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmnsimplesearch.cfm.
[b]Supplemental information (e.g., care setting) was obtained from manufacturers' websites; the care setting is not always specified in the 510(k) premarket notification materials found on the FDA website.