

Negative-Pressure Wound Therapy - Home-Use

Draft Key Questions: Comment & Response

June 7, 2016

Health Technology Assessment Program (HTA)

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Negative Pressure Wound Therapy – Home-Use

**Response to Public Comments on Topic and
Draft Key Questions**

June 7, 2016

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Response to Public Comments, Topic and Key Questions**Negative Pressure Wound Therapy – Home-Use**

Hayes, Inc. is an independent vendor contracted to produce evidence assessment reports for the Washington Health Technology Assessment (WA HTA) program. For transparency, all comments received during the comments process are included in this response document.

Draft key questions for each WA HTA report are posted online in order to gather public input and any additional evidence to be considered in the evidence review. Since key questions guide the evidence report, WA HTA seeks input on whether the questions are appropriate to address its mandate to gather evidence on safety, efficacy, and cost-effectiveness relevant to coverage determinations. Input about the following is especially helpful:

- Are appropriate populations or indications identified?
- Are appropriate comparators identified?
- Are appropriate patient-oriented outcome measures included?
- Are there special policy or clinical considerations that could affect the review?

Comments related to program decisions, process, or other matters not pertaining to the evidence report are acknowledged through inclusion only. When comments cited evidence, the vendor was encouraged to consider inclusion of this evidence in the report.

This document responds to comments from the following parties:

Topic:

- Ron Silverman, MD (Kinetic Concepts, Inc. (KCI), an Acelyty company)
- Robin Martin, PhD and Elizabeth Huddleston, PhD (Smith & Nephew Advanced Wound Management)

Key Questions:

- Sharon Whalen, RN, MS (Kinetic Concepts, Inc. (KCI), an Acelyty company)

Table 1 provides a summary of comments with responses.

Table 1. Public Comments on Topic and Key Questions, *Negative Pressure Wound Therapy – Home-Use*

Comment and Source	Response
Comments on Topic	
March 11, 2015 letter and enclosures submitted electronically from Ron Silverman, MD (Kinetic Concepts, Inc./Acelity)	
<p>KCI, an Acelity company, is writing in response to the Washing State Health Care Authority’s Health Technology Assessment (HTA) program selection of Negative Pressure Wound Therapy (NPWT) in the home setting for a health technology assessment.</p> <p>KCI is the leader in negative pressure wound therapy (NPWT) and a division within Acelity, a global wound care and regenerative medicine company. Acelity is focused on developing products and therapies that improve clinical outcomes while helping reduce the overall cost of patient care. Acelity is a company devoted to understanding, developing and commercializing innovative, high-technology transformational healing solutions for patients with wounds.</p> <p>For your review during the HTA process, we are providing you and the HTA committee a document summarizing the current clinical evidence for Negative Pressure Wound Therapy for wounds in the home. We have also provided some background information on wounds and NPWT.</p> <p>Key to any evidence and study design is the understanding of what is effective wound healing. Effective wound healing is dependent upon removal of barriers to wound healing and development of a wound environment that supports the healing process such as removal of exudate, inflammatory mediators (cytokines, proteases) and infectious material; presence of metabolically active cells to produce granulation tissue; and protection of the peri-wound tissue. Wound healing also goes through a series of phases (inflammatory, proliferative, and remodeling). NPWT addresses these key wound healing factors especially in the inflammatory and proliferative phases of wound healing.</p> <p>Several of the presented studies show improved outcomes of wound healing with NPWT in various chronic wounds, such as diabetic foot ulcers (DFUs), pressure ulcers (PrUs) and venous leg ulcers (VLUs).</p> <p>In a quantitative meta-analysis of 10 randomized controlled trials (RCTs) evaluating the effectiveness of NPWT vs the standard of care in chronic wounds, Suissa et al found that NPWT wounds had a significantly larger decrease in wound size (relative change ratio, 0.77; 95% CI, 0.63-0.96) and a significantly shorter time to healing (ratios of median time to healing, 0.74; 95 percent confidence interval, 0.70 to 0.78), compared to wounds treated with standard of care.¹ Based on their analyses, the authors concluded “negative-pressure therapy seems to offer a significant benefit over standard wound care for the treatment of chronic wounds.”¹</p> <p>DFUs, which have the potential for ongoing care and risk of amputation, are a major concern for diabetic patients and their physician providers. Diabetes is the leading cause of non-traumatic lower extremity amputations in the United</p>	<p>Thank you for your comments, evidence summary, and citations for several publications regarding negative pressure wound therapy. The references will be considered for inclusion in the report.</p>

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<p>States,² and approximately 14-24 percent of patients with diabetes who develop a foot ulcer will require an amputation.³ Foot ulceration precedes 85% of diabetes-related amputations.⁴ In a multicenter RCT comparing advanced bet al found a greater percentage of foot ulcers attained complete closure with NPWT (73/169, 43.2%) compared to AMWT (48/166, 28.9%; $p=0.007$).⁵ Additionally, significantly fewer amputations were reported for NPWT patients compared to AMWT patients (7/169 versus 17/166, respectively; $p=0.035$).⁵</p> <p>NPWT clinical evidence has been reviewed by many organizations. Currently, all US payers, including both commercial health plans and Medicare, cover NPWT in some capacity for a variety of disease states. In the body of this document, we highlight some of these health plans and their coverage.</p> <p>Acelity is committed to ongoing research and development, and we work with both physician care providers and government agency health plans. Currently, there is an ongoing Level 1 RCT comparing NPWT vs. standard of care that was initiated for determination of Home Care coverage in Germany. This RCT is evaluating the use of NPWT (V.A.C.® Therapy) for treatment of postsurgical subcutaneous abdominal wound healing impairments. Patients are initially treated in the acute setting then transitioned to “ambulatory care.” More than 300 of the planned 552 patients have been enrolled to date. Other ongoing research includes a retrospective analysis of data from the RCT by Armstrong et al⁶ that compared NPWT to Advanced Moist Wound Therapy for the treatment of partial foot amputation wounds in patients with diabetes. In addition to efficacy, this analysis evaluates the impact of both treatments on the lengths of stay, costs, and quality-of-life metrics of 162 patients.</p> <p>HTA evaluation and evidence-based medicine are important factors in health care delivery. In evaluation of the evidence for wounds, it is especially important to consider all evidence including RCTs as well as prospective, retrospective, comparative, and non-comparative studies. This broad approach is important in chronic wound care, because this patient population frequently has multiple comorbidities, varying severity of wounds, need for comprehensive management with multiple overlapping interventions; and care delivered in various healthcare settings by a wide range of clinical caregivers. All these factors can present a challenge in constructing and conducting RCTs and other studies on chronic wounds.</p> <p>We appreciate the opportunity to provide you and the HTA committee this information on the safety and efficacy of NPWT. Please feel free to contact us, if there is any additional material you wish us to provide.</p> <ol style="list-style-type: none"> 1. Suissa, D., Danino, A., Nikolis, A. Negative-Pressure Therapy versus Standard Wound Care: A Meta-Analysis of Randomized Trials. <i>Plast Reconstr Surg.</i> 2011; 128: 5, 498e-503e. 2. Brem, H., Sheehan, P., Rosenberg, H.J. et al. Evidence-based protocol for diabetic foot ulcers. <i>Plast Reconstr Surg.</i> 2006; 117: 7S, 193S-209S. 3. American Diabetes Association. Consensus Development Conference on Diabetic Foot Wound Care: 7-8 April 	

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<p>Comments on Topic</p>	
<p>1999, Boston, Massachusetts. American Diabetes Association. Diabetes Care. 1999; 22: 8, 1354-1360.</p> <p>4. Lavery, L.A., Boulton, A.J., Niezgodna, J.A., Sheehan, P. A comparison of diabetic foot ulcer outcomes negative using pressure wound therapy versus historical standard of care. International Wound Journal. 2007; 4: 2, 103-113.</p> <p>5. Blume, P.A., Walters, J., Payne, W. et al. Comparison of negative pressure wound therapy using vacuum-assisted closure with advanced moist wound therapy in the treatment of diabetic foot ulcers: a multicenter randomized controlled trial. Diabetes Care. 2008; 31: 4, 631-636.</p> <p>6. Armstrong, D.G., Lavery, L.A., Diabetic Foot Study Consortium. Negative pressure wound therapy after partial diabetic foot amputation: a multicentre, randomised controlled trial. Lancet. 2005; 366: 9498, 1704-1710</p> <p>An overview of clinical evidence was enclosed with the letter.</p>	
<p>March 12, 2015, letter and summary of evidence submitted by Drs. Robin Martin and Elizabeth Huddleston (Smith & Nephew Advanced Wound Management)</p>	
<p>Background</p> <p>While NPWT has been widely adopted in a range of clinical disciplines and searches in the peer review literature now yield in excess of 2,400 articles (November 2013), there remain some authors who consistently express doubts over the strength of the evidence for NPWT over conventional wound care. Following systematic reviews or meta-analyses of randomized NPWT studies (Ubbink et al. 2008) (Vikatmaa et al. 2008) (Gregor et al. 2008) concluded their papers arguing against its wider adoption. In response in 2009 Smith & Nephew convened an International NPWT Expert panel of clinicians to take a fresh and independent look at the evidence. All published evidence was considered objectively in studies using any type of NPWT device. Three papers were published reviewing the evidence and making a series of evidence based recommendations: in trauma and reconstructive surgery (Krug et al. 2011), in chronic wounds (Vig et al. 2011) and in reviewing the evidence for variables in NPWT such as choice of filler and pressure setting (Birke-Sorensen et al. 2011). Critical to the views of these articles were the identification of consensus in treatment goals for different wound types, as it is abundantly clear that NPWT is a tool to assist clinicians in achieving a desirable clinical outcomes; for example to protect a wound before closure or to assist the efficiency of a skin graft, rather than a magic bullet that just “makes things go faster.’ The purpose of the present paper is to provide an update of where the development of NPWT evidence has progressed and what significant trends are evident.</p> <p>Evidence streams</p> <p>a. Systematic reviews: Acute, Sub-acute and Chronic wounds</p> <p>(Ubbink et al. 2008) searched for any RCTs where NPWT had been compared to conventional therapy. They found 13</p>	<p>Thank you for your comments, evidence summary, and citations for several publications regarding negative pressure wound therapy. The references will be considered for inclusion in the report.</p>

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<p>trials totaling 573 wounds in 554 patients (as of June 2007). Pooling of data across all trials was not found to be possible given the variety of wound types and the different ways in which NPWT had been used to assist in the treatment process. (Ubbink et al. 2008) considered the trials in groups of similar wound types; mixed chronic wounds (4 trials); diabetic wounds (3 trials); pressure ulcers (2 trials); skin grafts (3 trials) and acute wounds (1 trial). Overall, (Ubbink et al. 2008) conclude “there is little evidence to support the use of NPWT in the treatment of wounds.” They base this conclusion largely on the inability to conduct multiple pooled analyses across several independent studies, small numbers of patients and non-blinded protocols. (Vikatmaa et al. 2008) present a very similar analysis to (Ubbink et al. 2008). Their conclusions were not as negative reviewing essentially the same data. They concede there are needs for much larger studies to show statistically significant effects in each of the different wound indications, but that there are indications that show positive effects of NPWT: chronic leg wounds, skin grafts, and diabetic wounds show reasonable evidence for a positive effect of NPWT. Pressure ulcers show the least convincing evidence. (Gregor et al. 2008) famously and cleverly titled their paper “a vacuum of evidence.” Although they conclude by advising against widespread adoption by government (in Germany in this case), they did acknowledge mostly positive studies in favor of NPWT, although only 2 of 5 RCTs and 2 of 4 comparative cohort studies were statistically significant. s 2</p> <p>Subsequent to the 2008 publications and the Expert Panel articles in 2011, a number of new papers are pertinent to update this discussion. (Peinemann and Sauerland 2011) were able to identify 21 randomized studies although the different methods and wound types again precluded pooling the data. They acknowledge that most published studies show effects in the direction of NPWT, but still worry about possible bias in the execution of the studies and the potential for studies unfavorable to NPWT to have not been published. (Suissa et al. 2011) found 10 randomized trials on just chronic wounds and their conclusions were generally positive for NPWT with some caveats about publication bias. (Yao et al. 2012) conducted a large comparative cohort study using electronic medical records in Boston USA, to find 171 standard wound care patients matched with 171 who received NPWT. The significance of the retrospective nature of the study is that this is real-world data outside of a trial. The outcome was that NPWT patients were 2.6 times more likely to achieve wound closure than non NPWT patients and if anything the co-morbidities of the NPWT patients were greater. (Dumville et al. 2013) provided the Cochrane review update of RCTs in diabetic wounds. In essence no further large DFU NPWT studies have been completed since the KCI funded studies by (Armstrong and Lavery 2005) and (Blume et al. 2008). The conclusion once again is that there is a probable benefit of NPWT but bias might have been present, so endorsement is very qualified. There are now large institutional funded studies underway in Germany in the DFU indication.</p> <p>b. Health Economic analyses</p> <p>While there are few attempts at meta-analysis of health economic outcomes from NPWT use, individual economic analyses have been completed as part of published RCTs. (Braakenburg et al. 2006) conducted an RCT on a mixed group</p>	

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<p>of chronic and acute wounds in which 32 patients received NPWT (V.A.C.®) and 33 patients were treated with control dressings. The study was insufficiently large to identify differences in the endpoints of secondary intention closure or readiness for grafting (although there were positive trends), but there were significant differences in the nursing time taken to treat each patient and the materials used. This study concluded that while time to healing was a little faster overall with NPWT (although not statistically significant at this sample size), patient comfort was improved (reduction in odor, fluid leakage) and the reduction in nursing labor was statistically significant. Overall, costs were not significantly different between the two treatment groups. In a nutshell: the NPWT devices cost more – but saved nursing time. The conventional treatments took more nursing time but cost less in materials.</p> <p>A similar analysis was conducted by (Mouës et al. 2007). In a mixed group of chronic, trauma and delayed healing dehisced wounds, patients were prospectively randomized into NPWT (29) and conventional (25) groups. Here NPWT was used to prepare the wound for surgical closure by primary intention, grafts or flaps. There was no significant difference in the time to take wounds to a point where it was ready for closure (although there were positive trends in favor of NPWT). There were also improvements in the rate of reduction of wound area in favor of NPWT (again not quite significant). However, there were reductions in nursing time (statistically significantly lower for NPWT $p < 0.0001$) which were balanced by higher costs of the NPWT therapy itself.</p> <p>(Apelqvist et al. 2008) reported on an economic analysis of the post-surgical healing of diabetic foot ulcers RCT published earlier by Armstrong and Lavery (2005). In this study containing 77 (NPWT) and 85 (conventional) wounds the treatment costs were lower for NPWT (\$27,270) than for conventional (\$36,096) therapy. These costs were strongly linked to the fewer outpatient visits, dressing changes and antibiotics used in the NPWT group.</p> <p>To summarize the current clinical and health economic literature on the use of NPWT, it appears that differences in the rate of wound progression to healing can be demonstrated, with sufficient numbers of patients in prospective RCTs, but few studies have reached the appropriate numbers. Some wound indications appear easier to demonstrate significant differences in healing rates than others (skin grafts>diabetic foot ulcers> post-surgical dehiscence> pressure ulcers for example). However, economic differences appear much more easily demonstrated with NPWT replacing the nursing resources needed to achieve comparable wound healing outcomes from conventional (non NPWT) therapies.</p> <p>c. Closed incisions</p> <p>A significant development in the clinical use of NPWT which did not feature in the 2008 systematic reviews or the Smith & Nephew NPWT Expert panel publications, is the emerging use of NPWT on the closed incision. First reported by (Stannard et al. 2006) and (Gomoll et al. 2006) in high risk orthopedic incisions, a Smith & Nephew initiative to collaborate with a small panel of orthopedic surgeons has resulted in a systematic review of incisional NPWT detailing 33 articles across many different surgical disciplines which is imminently to be published (Karlakki et al. 2013). The rate</p>	

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<p>of publications is increasing and 26 of the 33 articles on closed incision NPWT have been published in the last 3 years. At present there have been RCTs showing significant reductions in surgical site complications in orthopedic trauma (Stannard et al. 2012) and in cardiothoracic surgery (Grauhan et al. 2013). There has been one smaller RCT which did not show a reduction (Masden et al. 2012). Several comparative cohorts show statistically significant reductions in surgical site complications. Although most articles describe the use of traditional durable NPWT devices (tNPWT) on the closed incision, the introduction of lower cost single use NPWT devices such as PICO™ (Smith & Nephew) or Prevena® (KCI) seems likely to stimulate the completion of larger numbers of studies in the coming years.</p> <p>d. Equivalence of different NPWT devices</p> <p>A distinguishable trend amongst the NPWT clinical evidence is the realization that randomized studies have been performed which show equivalence in outcomes between different devices delivering NPWT. RENASYS™ GO (Smith & Nephew) was shown to be equivalent to V.A.C.® (KCI) by (Rahmanian-Schwarz et al. 2012) in the treatment of acute and chronic wounds and skin grafts. V.A.C. (KCI) with foam was shown to be equivalent to gauze based NPWT with wall suction in reducing area and volume in large surgical dehisced wounds (Dorafshar et al. 2012). V.A.C. (KCI) using foam, was shown to be non-inferior to SNaP® (Spiracur) using gauze, in a study of lower extremity ulcers (Armstrong et al. 2012).</p> <p>e. Development of single use (disposable) NPWT devices</p> <p>Since their introduction into the wound care market single use disposable NPWT devices have been utilized in a wide variety of wound indications and evidence supporting their efficacy has grown. We refer here specifically to the single use NPWT system PICO™ developed by Smith & Nephew, but identical principles apply to single use devices from other manufacturers (Grauhan et al. 2013; Khanbhai et al. 2012; Gabriel et al. 2012; Marston et al. 2014). The evidence for PICO has developed in two distinct areas, firstly, as a means of preventing wound related complications in high risk closed incisions, and secondly, as a therapy to manage and help close complex or non-healing, open chronic wounds. Both groups of evidence will be discussed as this shows how single use devices are being proved to have equivalent efficacy to their durable medical equipment (traditional NPWT) counterparts</p> <p>Following the publication of the first clinical study using PICO (Hudson et al 2013) reported earlier, a similar non-comparative study of 22 patients also showed that PICO was readily deployed across many different wound types (Canonico et al. 2012). These non-randomized studies represent a series of cases with what was described as encouraging results within one of four wound challenges; preventing surgical complications in high risk patients; gaining better control of post-surgical edema after revision arthroplasty; concomitant treatment with compression therapy in venous leg ulcers, and enhancing skin graft take in lower extremities.</p>	

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<p>Concentrating on high risk closed incisions, PICO was used in a (non-randomized) comparison within 50 patients undergoing bowel surgery for Crohn’s disease, a population who have a much greater risk of developing post-surgical complications.(Pellino et al. 2013; Selvaggi et al. 2014) Typically applied for 4-7 days, the PICO treated group experienced significantly less post-operative wound complications in the closed abdominal incision, resulting in shorter hospital stays and fewer readmissions. The study also demonstrated that patients discharged with the system managed the therapy well in an outpatient setting with few issues.</p> <p>More recently, the same authors have reported a similar study with 50 patients undergoing colorectal surgery and another 50 patients undergoing breast surgery (Pellino et al 2014). PICO was assigned to 25 patients in each surgery group while the remaining 25 received standard care. PICO was routinely applied for 7 days with a dressing change at 3 days if necessary. The study again demonstrated that PICO resulted in a positive effect on reducing i) length of stay (almost by half), ii) rate of seroma formation (8% v 40%), iii) lower rates of surgical site events (SSEs) or complications (8% v 44%), and iv) lower ASEPSIS scores following colorectal surgery. Additionally PICO significantly reduced the rate of SSEs following breast surgery from 36% to 8% as well as reduced ASEPSIS scores.</p> <p>Similarly PICO was used as part of a treatment protocol to address high infection rates in women following caesarean sections, particularly in high BMI patients. Before implementation of the new protocol, infection rates were 12%. Over a 10 month period, PICO was applied to 50 high risk patients (high BMI >35kg/m2) immediately after surgery and left <i>in situ</i> for 7 days, and OPSITE™ Post-Op Visible was given to all other patients (610 patients) and again left <i>in situ</i> for 7 days. The introduction of OPSITE Post-Op Visible reduced Perspectives on infection rates to 6.3%, while those patients treated with PICO™ had 0% infection rates, despite data that suggests that high BMI patients are much more likely to suffer post-surgical infections following C-sections (Bullough et al. 2014).</p> <p>A retrospective comparative study demonstrated a significant reduction in wound dehiscence and surgical site infections using PICO compared to standard dressings following spine fusion surgery (Adogwa et al. 2014). The authors retrospectively reviewed the first 46 cases of using single use NPWT (PICO) to their immediately preceding 114 cases without NPWT to assess the incidence of wound infection and dehiscence. A 50% decrease in the incidence of wound dehiscence was observed in the NPWT patient cohort (6.38% vs. 12.28%, p=0.02). Similarly, compared to the non-NPWT cohort, the incidence of post-operative SSIs was significantly decreased in the NPWT cohort (10.63% vs. 14.91%, p=0.04).</p> <p>With regards to open or chronic wounds, Payne and Edwards describe the use of PICO on a collection of 21 cases of traumatic wounds or post-operative wound complications. They demonstrated how PICO can benefit a wide range of clinical wounds by optimizing patient care, promoting rapid wound healing and offering significant savings in bed days by facilitating early discharge from hospital (Payne and Edwards 2014). Additional peer review papers have also been</p>	

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<p>published describing case examples (Ahmad et al. 2013; Dowsett et al. 2013). Dowsett developed a treatment pathway for non-healing venous leg ulcers which incorporated the use of PICO in conjunction with compression bandaging systems. The guidelines offer a decision making pathway and case examples to assist clinicians dealing with patients who have non-healing venous leg ulcers to decide if NPWT may be an appropriate additional treatment option. Other publications include case examples of treating challenging, non-healing wounds and guidelines for incorporating PICO into treatment pathways for use in outpatient settings (Dowsett and Timmons 2012; Murphy and Powell 2013; Narayan <i>et al.</i> 2014; Timmons and Russell 2012). Independent comparisons on the usability of PICO versus other portable NPWT systems in the clinical setting have also been published. (Gillespie et al. 2013).</p> <p>A larger study that merits particular attention, is a recently published non-comparative evaluation carried out in North American in which a total of 326 patients were treated with PICO in a community setting in Ontario, Canada (Hurd <i>et al</i> 2014). The mean age of patients evaluated was 57 years and 49.5% were male. The mean duration of the wound was 8.9 weeks with a range from 1 week to 68 weeks and mean baseline wound area was 19.9cm². The wounds were mostly surgical wounds (68%) that had become infected and split open (dehiscid) and were delaying the patient’s return to normal living.</p> <p>The results from the PICO patients were compared retrospectively with patients previously treated with traditional full-sized traditional NPWT (tNPWT) in the same institutions. Patients were matched on the basis of age, sex and wound characteristics. Patients with wounds greater than 100cm² and/or high levels of exudate were excluded on the basis that these would be unsuitable candidates for treatment with PICO. The final cohort included in the analysis comprised 304 patients treated with PICO and 539 patients treated with NPWT. Wound area and volume were marginally greater in the tNPWT arm although patients treated with PICO™ were older and had longer wound duration prior to treatment. When the healing was analyzed it was found that the reduction of wound area was very similar between PICO and full sized NPWT (Hurd <i>et al</i> 2014). In order to manage a full range of wound types within hospital and in homecare environments, protocols employing both device types could in principle allow the most economical solution to wound management needs.</p> <p>f. Active ongoing clinical research</p> <p>Clinical research activity to assess the effects of NPWT continues in many global locations. A selection of current large scale clinical trials can be identified from www.clinicaltrials.gov. Example include:</p> <p style="padding-left: 40px;">NCT01640366 RCT bilateral breast reduction single use NPWT vs standard care 200 patients; NCT01480362 RCT DFU traditional portable NPWT vs standard care 360 patients;</p>	

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<p>Summary of themes</p> <p>A review of NPWT clinical data suggests that it is rather easy to show reduced nursing costs for the same level of wound healing efficacy, whereas only a few larger randomized studies have shown superiority in wound healing.</p> <p>As more NPWT systems become available, the evidence suggests that different NPWT devices on the whole offer equivalent clinical efficacy.</p> <p>As the adoption of single use NPWT devices widens in various wound indications and patient settings, a growing body of evidence suggests that on appropriate wounds, single use systems can provide equivalent clinical outcomes to traditional durable NPWT systems.</p> <p>Dr Robin Martin (PhD) Senior Director, Global Medical & Clinical Affairs Dr Elizabeth Huddleston (PhD) Clinical Science Program Director, Global Medical & Clinical Affairs Smith & Nephew Advanced Wound Management</p> <p>References</p> <p>Adogwa, O. et al., 2014. Negative Pressure Wound Therapy Reduces Incidence of Post-Operative Wound Infection and Dehiscence After Long-Segment Thoracolumbar Spinal Fusion: A Single Institutional Experience. <i>The spine journal : official journal of the North American Spine Society</i>.</p> <p>Ahmad, Z., Davis, M. & Das-Gupta, R., 2013. PICO: a revelation in topical negative pressure therapy? <i>The international journal of lower extremity wounds</i>, 12(1), pp.16–7.</p> <p>Apelqvist, J. et al., 2008. Resource utilization and economic costs of care based on a randomized trial of vacuum-assisted closure therapy in the treatment of diabetic foot wounds. <i>American journal of surgery</i>, 195(6), pp.782–8.</p> <p>Armstrong, D.G. et al., 2012. Comparative effectiveness of mechanically and electrically powered negative pressure wound therapy devices: a multicenter randomized controlled trial. <i>Wound repair and regeneration : official publication of the Wound Healing Society [and] the European Tissue Repair Society</i>, 20(3), pp.332–41.</p> <p>Armstrong, D.G. & Lavery, L. a, 2005. Negative pressure wound therapy after partial diabetic foot amputation: a multicentre, randomised controlled trial. <i>Lancet</i>, 366(9498), pp.1704–10.</p> <p>Birke-Sorensen, H. et al., 2011. Evidence-based recommendations for negative pressure wound therapy: Treatment variables (pressure levels, wound filler and contact layer) - Steps towards an international consensus. <i>Journal of</i></p>	

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<p><i>plastic, reconstructive & aesthetic surgery : JPRAS</i>, 64 Suppl, pp.S1–S16.</p> <p>Blume, P.A. et al., 2008. Comparison of negative pressure wound therapy using vacuum-assisted closure with advanced moist wound therapy in the treatment of diabetic foot ulcers: a multicenter randomized controlled trial. <i>Diabetes care</i>, 31(4), pp.631–6.</p> <p>Braakenburg, A. et al., 2006. The clinical efficacy and cost effectiveness of the vacuum-assisted closure technique in the management of acute and chronic wounds: a randomized controlled trial. <i>Plastic and reconstructive surgery</i>, 118(2), pp.390–7; discussion 398–400.</p> <p>Bullough, L. et al., 2014. Changing wound care protocols to reduce postoperative and readmission. <i>Wounds UK</i>, 10(1), pp.84–89.</p> <p>Canonico, S. et al., 2012. Therapeutic possibilities of portable NPWT. <i>Acta Vulnologica</i>, 10(2), pp.57–64.</p> <p>Dorafshar, A.H. et al., 2012. A Prospective Randomized Trial Comparing Subatmospheric Wound Therapy With a Sealed Gauze Dressing and the Standard Vacuum-Assisted Closure Device. <i>Annals of plastic surgery</i>, 69(1), pp.79–84.</p> <p>Dowsett, C. et al., 2013. Venous leg ulcer management : single use negative pressure wound therapy. <i>British Journal of Community Nursing</i>, (March). s 8</p> <p>Dowsett, C. & Timmons, J., 2012. NPWT in the community how to guide. <i>Wounds UK</i>, 7(1), pp.1–3.</p> <p>Dumville, J.C. et al., 2013. Negative pressure wound therapy for treating foot wounds in people with diabetes mellitus. <i>The Cochrane database of systematic reviews</i>, 10(10), p.CD010318.</p> <p>Gabriel, A. et al., 2012. Evaluation of an ultra-lightweight, single-patient-use negative pressure wound therapy system over dermal regeneration template and skin grafts. <i>International wound journal</i>, pp.1–8.</p> <p>Gillespie, B.M. et al., 2013. end-users ' assessment of prophylactic negative pressure wound therapy products. <i>Wound Practice & Research</i>, 21(2), pp.74–81.</p> <p>Gomoll, A.H., Lin, A. & Harris, M.B., 2006. Incisional vacuum-assisted closure therapy. <i>Journal of orthopaedic trauma</i>, 20(10), pp.705–9.</p> <p>Grauhan, O. et al., 2013. Prevention of poststernotomy wound infections in obese patients by negative pressure wound therapy. <i>The Journal of thoracic and cardiovascular surgery</i>, 145(5), pp.1387–92.</p> <p>Gregor, S. et al., 2008. Negative pressure wound therapy: a vacuum of evidence? <i>Archives of surgery (Chicago, Ill. : 1960)</i>, 143(2), pp.189–96.</p> <p>Hurd, T., Trueman, P. & Rossington, A., 2014. Use of a Portable, Single Use Negative Pressure Wound Therapy Device in Home Care Patients with Low to Moderately Exuding Wounds: A Case Series. <i>Ostomy wound management</i>, 60(3), pp.30–36.</p>	

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<p>Karlakki, S. et al., 2013. Negative pressure wound therapy for management of the surgical incision in orthopaedic surgery A REVIEW OF EVIDENCE AND MECHANISMS FOR AN EMERGING INDICATION. <i>Bone and Joint Research</i>, 2(X), pp.1–9.</p> <p>Khanbhai, M. et al., 2012. Disposable NPWT device to facilitate early patient discharge following complex DFU. <i>Journal of wound care</i>, 21(4), pp.180, 182.</p> <p>Krug, E. et al., 2011. Evidence-based recommendations for the use of Negative Pressure Wound Therapy in traumatic wounds and reconstructive surgery: steps towards an international consensus. <i>Injury</i>, 42 Suppl 1, pp.S1–12.</p> <p>Marston, W. a. et al., 2014. A Multicenter Randomized Controlled Trial Comparing Treatment of Venous Leg Ulcers Using Mechanically Versus Electrically Powered Negative Pressure Wound Therapy. <i>Advances in Wound Care</i>, 00(00), p.141016081615000.</p> <p>Masden, D. et al., 2012. Negative pressure wound therapy for at-risk surgical closures in patients with multiple comorbidities: a prospective randomized controlled study. <i>Annals of surgery</i>, 255(6), pp.1043–1047. s 9</p> <p>Mouës, C.M. et al., 2007. Comparing conventional gauze therapy to vacuum-assisted closure wound therapy: a prospective randomised trial. <i>Journal of plastic, reconstructive & aesthetic surgery : JPRAS</i>, 60(6), pp.672–81.</p> <p>Murphy, S. & Powell, G., 2013. Pilonidal sinus wounds : Successful use of the novel negative pressure wound therapy device PICO TM. <i>Wounds UK</i>, 9(4), pp.80–83.</p> <p>Narayan, N., Edwards, D. & Ragoowansi, R.H., 2014. Glove and PICO: a novel technique for treatment of chronic wound due to osteomyelitis of the hand. <i>BMJ case reports</i>, June 2.</p> <p>Payne, C. & Edwards, D., 2014. Application of the Single Use Negative Pressure Wound Therapy Device (PICO) on a Heterogeneous Group of Surgical and TraumaticWounds. <i>eplasty</i>, 14(e20), pp.152–166.</p> <p>Peinemann, F. & Sauerland, S., 2011. Negative-pressure wound therapy: systematic review of randomized controlled trials. <i>Deutsches Ärzteblatt international</i>, 108(22), pp.381–9.</p> <p>Pellino, G. et al., 2013. Effects of a New Pocket Device for Negative Pressure Wound Therapy on Surgical Wounds of Patients Affected With Crohn’s Disease: A Pilot Trial. <i>Surgical innovation</i>, In Press.</p> <p>Rahmanian-Schwarz, A. et al., 2012. A novel option in negative pressure wound therapy (NPWT) for chronic and acute wound care. <i>Burns : journal of the International Society for Burn Injuries</i>, 38(4), pp.573–7.</p> <p>Selvaggi, F. et al., 2014. New Advances in Negative Pressure Wound Therapy (NPWT) for Surgical Wounds of Patients Affected with Crohn’s Disease. <i>Surgical technology international</i>, 24, pp.83–9.</p> <p>Stannard, J.P. et al., 2012. Incisional negative pressure wound therapy after high-risk lower extremity fractures. <i>Journal of orthopaedic trauma</i>, 26(1), pp.37–42.</p>	

Comment and Source	Response
Comments on Topic	
<p>Stannard, J.P. et al., 2006. Negative pressure wound therapy to treat hematomas and surgical incisions following high-energy trauma. <i>The Journal of trauma</i>, 60(6), pp.1301–6.</p> <p>Suissa, D., Danino, A. & Nikolis, A., 2011. Negative-pressure therapy versus standard wound care: a meta-analysis of randomized trials. <i>Plastic and reconstructive surgery</i>, 128(5), p.498e–503e.</p> <p>Timmons, J. & Russell, F., 2012. Introducing a new portable negative pressure wound therapy. <i>Wounds UK</i>, 8(1), pp.47–52.</p> <p>Ubbink, D.T. et al., 2008. A systematic review of topical negative pressure therapy for acute and chronic wounds. <i>The British journal of surgery</i>, 95(6), pp.685–92.</p> <p>Vig, S. et al., 2011. Evidence-based recommendations for the use of negative pressure wound therapy in chronic wounds: steps towards an international consensus. <i>Journal of tissue viability</i>, 20 Suppl 1, pp.S1–18. s 10</p> <p>Vikatmaa, P. et al., 2008. Negative pressure wound therapy: a systematic review on effectiveness and safety. <i>European journal of vascular and endovascular surgery : the official journal of the European Society for Vascular Surgery</i>, 36(4), pp.438–48.</p> <p>Yao, M. et al., 2012. A retrospective cohort study evaluating efficacy in high-risk patients with chronic lower extremity ulcers treated with negative pressure wound therapy. <i>International wound journal</i>, pp.1–8.</p>	
Comments on Draft Key Questions	
May 16, 2016 e-mail from Sharon Whalen (Kinetic Concepts Inc (KCI)/Acelity)	
<p>“Please accept these comments on Health Technology Assessment (HTA) for NPWT from Kinetic Concepts Inc (KCI). KCI is the leader in negative pressure wound therapy (NPWT) and a division within Acelity, a global wound care and regenerative medicine company. Acelity is focused on developing products and therapies that improve clinical outcomes while helping reduce the overall cost of patient care.</p> <p>Recently the draft questions for NPWT HTA were announced. We have two comments regarding these research questions. One is that evidence of effectiveness for wound care products and services is not limited to clinical research but can be established through a combination of scientific evidence and expert knowledge. This approach is consistent with evidence-based medicine (EBM), which is the integration of best research evidence with clinical expertise. The EBM approach is particularly important in chronic wound care. Patients with wounds typically have multiple co-morbidities, which present in varying degrees of severity. Comprehensive chronic wound care frequently involves the use of multiple interventions, often in conjunction with each other.</p>	<p>Thank you for your comments. Articles cited in the two overviews of clinical evidence provided with your email will be reviewed and considered for inclusion. The HTA will follow established internationally recognized best practices to independently and objectively evaluate peer-reviewed literature on NPWT. The review will include a systematic search for literature that meets pre-determined inclusion and exclusion criteria to best answer the key questions. The quality of included studies as well as the overall quality of the body of</p>

Comment and Source	Response
Comments on Topic	
<p>NPWT has been a treatment option for patients for over 20 years. Over that time evidence began with randomized clinical studies and prospective studies providing valuable outcome data to providers. NPWT has become a standard of care for some wound therapy and the evidence and utilization of NPWT has shifted to development of meta-analysis reviews and consensus statements and organizational treatment guidelines.</p> <p>For this reason, we believe there should be inclusion of all forms of evidence for review is imperative.</p> <p>In addition, for many patients NPWT therapy begins in the hospital setting and is then transferred to the home setting. This occurs because wounds may take several weeks to achieve their therapy healing goal, and it is logical that patients would be discharged from the hospital to the home setting. It is also logical that clinical research studies also follow that path of a beginning in the inpatient setting and ending in the home setting.</p> <p>For this reason we believe it is important that the HTA program review of the outcome literature include research studies that begin in the hospital setting and continue in the home setting.</p> <p>We provided clinical evidence last year on NPWT was this topic was first placed on the HTA Director list. I am providing the program additional clinical evidence for review. The additional evidence are in two documents. The first document is NPWT over surgical incisions which include procedures post trauma or with patient with high co-morbidities. The clinical endpoints with the use of NPWT on these patients are decrease in seroma, decrease in infection and decrease of time in the hospital setting. Again, these patients begin the NPWT in the inpatient setting; often require continued use of NPWT in the home setting.</p> <p>The second document is clinical evidence on disposable NPWT device. One of the key studies in this dossier is a RCT study by Armstrong which provides statistical significant outcomes that disposable NPWT is equivalent to DME NPWT.</p> <p>If there is any additional information or questions you may have, please let me know.”</p> <p>Two documents which provided overviews of clinical evidence were also submitted.</p>	<p>evidence will be assessed to determine the strength and direction of the evidence. A summary of existing guidelines and payer policies will be summarized but will not contribute to the assessment of the strength and direction of the evidence. When completed the draft report will be available for comment for 30 days.</p>



Josh Morse, MPH
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Electronically submitted to: shtap@hca.wa.gov.

Dear Mr. Morse

KCI, an Acelity company, is writing in response to the Washing State Health Care Authority's Health Technology Assessment (HTA) program selection of Negative Pressure Wound Therapy (NPWT) in the home setting for a health technology assessment.

KCI is the leader in negative pressure wound therapy (NPWT) and a division within Acelity, a global wound care and regenerative medicine company. Acelity is focused on developing products and therapies that improve clinical outcomes while helping reduce the overall cost of patient care. Acelity is a company devoted to understanding, developing and commercializing innovative, high-technology transformational healing solutions for patients with wounds.

For your review during the HTA process, we are providing you and the HTA committee a document summarizing the current clinical evidence for Negative Pressure Wound Therapy for wounds in the home. We have also provided some background information on wounds and NPWT.

Key to any evidence and study design is the understanding of what is effective wound healing. Effective wound healing is dependent upon removal of barriers to wound healing and development of a wound environment that supports the healing process such as removal of exudate, inflammatory mediators (cytokines, proteases) and infectious material; presence of metabolically active cells to produce granulation tissue; and protection of the peri-wound tissue. Wound healing also goes through a series of phases (inflammatory, proliferative, and remodeling). NPWT addresses these key wound healing factors especially in the inflammatory and proliferative phases of wound healing.

Several of the presented studies show improved outcomes of wound healing with NPWT in various chronic wounds, such as diabetic foot ulcers (DFUs), pressure ulcers (PrUs) and venous leg ulcers (VLUs).

In a quantitative meta-analysis of 10 randomized controlled trials (RCTs) evaluating the effectiveness of NPWT vs the standard of care in chronic wounds, Suissa et al found that NPWT wounds had a significantly larger decrease in wound size (relative change ratio, 0.77; 95% CI, 0.63-0.96) and a significantly shorter time to healing (ratios of median time to healing, 0.74; 95 percent confidence interval, 0.70 to 0.78), compared to wounds treated with standard of care.¹ Based on their analyses, the authors concluded “negative-pressure therapy seems to offer a significant benefit over standard wound care for the treatment of chronic wounds.”¹

DFUs, which have the potential for ongoing care and risk of amputation, are a major concern for diabetic patients and their physician providers. Diabetes is the leading cause of non-traumatic lower extremity amputations in the United States,² and approximately 14-24 percent of patients with diabetes who develop a foot ulcer will require an amputation.³ Foot ulceration precedes 85% of diabetes-related amputations.⁴ In a multicenter RCT comparing advanced bet al found a greater percentage of foot ulcers attained complete closure with NPWT (73/169, 43.2%) compared to AMWT (48/166, 28.9%; $p=0.007$).⁵ Additionally, significantly fewer amputations were reported for NPWT patients compared to AMWT patients (7/169 versus 17/166, respectively; $p=0.035$).⁵

NPWT clinical evidence has been reviewed by many organizations. Currently, all US payers, including both commercial health plans and Medicare, cover NPWT in some capacity for a variety of disease states. In the body of this document, we highlight some of these health plans and their coverage.

Acelity is committed to ongoing research and development, and we work with both physician care providers and government agency health plans. Currently, there is an ongoing Level 1 RCT comparing NPWT vs. standard of care that was initiated for determination of Home Care coverage in Germany. This RCT is evaluating the use of NPWT (V.A.C.® Therapy) for treatment of postsurgical subcutaneous abdominal wound healing impairments. Patients are initially treated in the acute setting then transitioned to “ambulatory care.” More than 300 of the planned 552 patients have been enrolled to date. Other ongoing research includes a retrospective analysis of data from the RCT by Armstrong et al⁶ that compared NPWT to Advanced Moist Wound Therapy for the treatment of partial foot amputation wounds in patients with diabetes. In addition to efficacy, this analysis evaluates the impact of both treatments on the lengths of stay, costs, and quality-of-life metrics of 162 patients.

HTA evaluation and evidence-based medicine are important factors in health care delivery. In evaluation of the evidence for wounds, it is especially important to consider all evidence

including RCTs as well as prospective, retrospective, comparative, and non-comparative studies. This broad approach is important in chronic wound care, because this patient population frequently has multiple comorbidities, varying severity of wounds, need for comprehensive management with multiple overlapping interventions; and care delivered in various healthcare settings by a wide range of clinical caregivers. All these factors can present a challenge in constructing and conducting RCTs and other studies on chronic wounds.

We appreciate the opportunity to provide you and the HTA committee this information on the safety and efficacy of NPWT. Please feel free to contact us, if there is any additional material you wish us to provide.

Sincerely,



Ron Silverman, MD

Chief Medical Officer, Acelyty

Associate Professor of Surgery, University of Maryland School of Medicine

Associate Professor of Plastic Surgery (adjunct), Johns Hopkins School of Medicine

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Negative Pressure Wound Therapy (NPWT) in the Home Setting

Kinetic Concepts, Inc. (KCI), an Acely company, respectfully submits the following comments in response to the Health Technology Assessment (HTA) on Negative Pressure Wound Therapy (Home Use). The stated goal of this HTA is to systematically review the safety, efficacy, and cost-effectiveness of negative pressure wound therapy (NPWT) for treatment of wounds in the home setting. Acely is a company devoted to understanding, developing and commercializing innovative, high-technology transformational healing solutions for patients with wounds.

We commend the Washington State Health Care Authority on the efforts to conduct this HTA. Evidence of effectiveness for wound care products and services is not limited to clinical research but can be established through a combination of scientific evidence and expert knowledge.¹ This approach is consistent with evidence-based medicine (EBM), which is the integration of best research evidence with clinical expertise.¹ The EBM approach is particularly important in chronic wound care. Patients with wounds typically have multiple co-morbidities, which present in varying degrees of severity. Comprehensive chronic wound care frequently involves the use of multiple interventions, often in conjunction with each other.

Effective wound healing is dependent upon removal of barriers to wound healing and development of a wound environment that supports the healing process. Issues to be addressed include removal of exudate, inflammatory mediators (cytokines, proteases) and infectious material; adequate perfusion to the wound bed; presence of metabolically active cells to produce granulation tissue; and protection of the peri-wound tissue. NPWT addresses these key factors especially in the inflammatory and proliferative phases of wound healing.

Negative Pressure Wound Therapy

NPWT creates an environment that promotes wound healing by secondary or tertiary (delayed primary) intention, preparing the wound bed for closure, reducing edema, promoting granulation tissue formation and perfusion and by removing exudate and infectious material. NPWT is indicated for patients with chronic, acute, traumatic, sub-acute and dehisced wounds, partial-thickness burns, ulcers (ie, diabetic, pressure or venous insufficiency), flaps, and grafts. NPWT can be used in acute, long term care and home care settings. The basic elements of NPWT generally include a dressing, an adhesive drape, connective tubing, a negative pressure source, and an exudate collection container.

While various forms of NPWT have been developed since the 1980s, the NPWT system commercialized in 1997 (V.A.C.[®] Therapy, KCI, an Acely company, San Antonio, TX) is the system used in the majority of published studies. This integrated wound management system consists of three main components: V.A.C.[®] Therapy unit, SensaT.R.A.C.[™] technology, and V.A.C. GranuFoam[™] Dressing. The therapy unit provides either intermittent or continuous

negative pressure to the wound bed. SensaT.R.A.C.™ technology signals the therapy unit when a change in target pressure is detected by sensors at the wound site, so the unit can adjust negative pressure settings to compensate. The reticulated, hydrophobic, open-cell foam dressing is cut to fill the entire wound bed and sealed with a semi-occlusive drape.

NPWT safety in the homecare setting

In 2013 Kaufman-Rivi et al reported the results of the FDA-mandated survey² that gathered information from wound care specialists and professional home healthcare providers. In the first phase, a semi-structured questionnaire was administered to 22 participants who either responded during in-depth telephone interviews (n=17) or completed self-administered questionnaires (n=5). During the second phase of the study, participants (n=342) responded to a Web survey based on the original questionnaire. Survey results highlighted the need for prescriber training regarding the types of patients appropriate for NPWT as well as clarification as to when to begin and discontinue therapy. More than half (61%) of home healthcare professionals who took the Web survey had not experienced complications with NPWT systems. Problems identified by home health care providers included inadequate seal (93%) or suction (52%), pain (29%), infection (24%), odor (18%), and bleeding (22%). The majority (96%) of this group, however, stated these events occurred “only occasionally or rarely.” Respondents emphasized the need for ongoing or expanded NPWT training for physicians, nurses, and other home healthcare providers. The authors concluded that “Overall, respondents thought that there was a definite benefit to NPWT, regardless of the care setting, and that it was a safe therapy when prescribed and administered appropriately.”²

Based on survey results, training and support provided by manufacturers are important factors in optimal use of NPWT in the home. For example, in addition to product labeling and instructions for use materials, KCI provides 24/7/365 phone support by clinicians trained to respond to customers’ questions regarding safe product use. KCI’s provider medical education programs in support of safe and effective use of NPWT in all care settings.

The literature also provides evidence that NPWT is safe in the home setting, when used and monitored appropriately. The majority of patient therapy days in 2 NPWT randomized controlled trials (RCTs) occurred in the home care setting. In the RCT by Blume et al that compared NPWT (n=169) to Advanced Moist Wound Therapy (AMWT; n=166) for treatment of diabetic foot ulcers (DFUs), approximately 90% of therapy days occurred in the home setting: NPWT, 9,471 of 10,579 days (89.5%) and AMWT, 12,210 of 12,810 days (95.3%).³ In this study significantly ($p=0.035$) fewer secondary amputations were reported in NPWT patients (n=7 of 169, 4.1%) compared to AMWT patients (17 of 166, 10.2%). There were no significant differences between the groups for other adverse events (eg, edema, wound infection, cellulitis) at 6 months.³ In the second RCT, Armstrong et al compared NPWT (n=77) to Moist

Wound Therapy (MWT; n=85) for the treatment of partial diabetic foot amputations.⁴ Of 10,908 total therapy days in this RCT, 89.1% (9,719 days) were in the home setting.⁵ In the NPWT group 2 of 77 (3%) patients had secondary amputations compared to 9 of 85 (11%) in the AMWT group ($p=0.060$).⁴ There was no difference between the groups in overall number of adverse events: 40 of 77 (52%) NPWT patients vs 46 of 88 (54%) AMWT patients ($p=0.875$).⁴ In both studies the majority of therapy days occurred in the home setting and the safety profiles were similar between the groups.

Evolution of NPWT Systems

Expanding use of NPWT has led to system modifications. Alarms and alerts are incorporated to notify clinicians and patients about issues that may affect delivery of therapy (eg, critical battery levels, tube blockages, leaks). Dressings have been developed to address specific wound needs (eg, the V.A.C.® GranuFoam™ Bridge Dressing, which places the SensaT.R.A.C.™ Pad away from the wound site and facilitates use of NPWT in diabetic foot wounds requiring off-loading therapy). Changes in the way health care is delivered have also influenced NPWT development. Patients – especially those with chronic wounds – may transition through several care settings during the treatment of a non-healing wound. The need for increased portability has resulted in smaller units that facilitate patient mobility and provide ongoing NPWT during transitions among care settings.

Evolution of NPWT literature

In 2007, Willy et al conducted a systematic review of NPWT literature on NPWT and reported “a veritable flood of publications starting from the year 2000 onwards.”⁶ Their review of 550 peer-reviewed articles demonstrated the marked expansion in the types of wounds treated with NPWT between 2000 and 2006.⁶ The literature also reflects the expansion of NPWT use to include long-term care and home care as well as acute care. Early NPWT RCTs (especially those dealing with chronic wounds) were small; however, growing emphasis on EBM has led to larger studies such as those by Blume et al (n=342)³ and Armstrong et al (n=162).⁴ Currently there are more than 40 NPWT RCTs among over 1,000 peer-reviewed articles related to NPWT. The majority of these publications report results using one type of NPWT.

Evidence supporting NPWT treatment of chronic wounds in the home setting

Adjunctive NPWT has been shown to be effective in removing exudate and infectious materials and promoting granulation tissue formation^{3,7} in different types of chronic wounds, including DFUs, pressure ulcers (PrUs), and venous leg ulcers (VLUs). Used in conjunction with irrigation and debridement, NPWT mechanisms of action assist physicians and clinicians in preparing the wound for closure. Key chronic wound studies have been summarized below with additional detail provided in tables.

Chronic wounds

Suissa et al conducted a quantitative meta-analysis of 1993-2010 RCTs to evaluate the effectiveness of NPWT compared to standard wound care for the management of chronic wounds.⁸ The 10 NPWT RCTs analyzed included DFUs, PrUs, VLU, and diabetic foot amputation wounds. Standard wound care included wet-to-dry dressings as well as advanced moist wound therapy (AMWT) with alginates, hydrocolloids, foams or hydrogels.

- Based on analyses, NPWT wounds had a significantly larger wound size reduction compared to wounds treated with standard wound care (relative change ratio, 0.77; 95% CI, 0.63-0.96).
- Time to healing was also significantly shorter in the NPWT group compared to the standard wound care group (median time to healing ratio, 0.74; 95% CI, 0.70 to 0.78).
- Suissa et al concluded that “negative-pressure therapy seems to offer a significant benefit over standard wound care for the treatment of chronic wounds.”⁸

Table 1 summarizes key points from some of the systematic reviews, consensus statements and practice guidelines for chronic wounds.

Table 1. NPWT Systematic Reviews, Consensus Statements, and Practice Guidelines for Chronic Wounds

Document	Key Points
<p>Advanced wound care therapies for nonhealing diabetic, venous, and arterial ulcers: a systematic review. Greer N et al. <i>Ann Intern Med.</i> 2013 Oct 15;159(8):532-42.⁹</p>	<p><i>Summary:</i> Nonhealing ulcers affect patient quality of life and impose a substantial financial burden on the health care system.</p> <ul style="list-style-type: none"> • This review systematically evaluated benefits and harms of advanced wound care therapies for nonhealing diabetic, venous, and arterial ulcers. • For diabetic ulcers, 35 trials (9 therapies) met eligibility criteria. There was moderate-strength evidence for improved healing with a biological skin equivalent (relative risk [RR], 1.58 [95% CI, 1.20 to 2.08]) and negative pressure wound therapy (RR, 1.49 [CI, 1.11 to 2.01]) compared with standard

Document	Key Points
	<p>care and low-strength evidence for platelet-derived growth factors and silver cream compared with standard care.</p> <ul style="list-style-type: none"> • For venous ulcers, 20 trials (9 therapies) met eligibility criteria. There was moderate-strength evidence for improved healing with keratinocyte therapy (RR, 1.57 [CI, 1.16 to 2.11]) compared with standard care and low-strength evidence for biological dressing and a biological skin equivalent compared with standard care. One small trial of arterial ulcers reported improved healing with a biological skin equivalent compared with standard care. Overall, strength of evidence was low for ulcer healing and low or insufficient for time to complete healing. <p><i>Conclusion:</i> Compared with standard care, some advanced wound care therapies may improve the proportion of ulcers healed and reduce time to healing, although evidence is limited.</p>
<p>Evidence-based recommendations for the use of negative pressure wound therapy in chronic wounds: steps towards an international consensus. Vig S et al. <i>J Tissue Viability</i>. 2011 Dec;20 Suppl 1:S1-18.¹⁰</p>	<p><i>Summary:</i> Negative Pressure Wound Therapy (NPWT) has become widely adopted over the last 15 years and over 1000 peer-reviewed publications are available describing its use. Despite this, there remains uncertainty regarding several aspects of usage.</p> <ul style="list-style-type: none"> • In order to respond to this gap a global expert panel was convened to develop evidence-based recommendations describing the use of NPWT. • In this communication the results of the study of evidence in chronic wounds including pressure ulcers, diabetic foot ulcers (DFU), venous leg ulcers (VLU), and ischaemic lower limb wounds are reported.

Document	Key Points
	<ul style="list-style-type: none"> • Evidence-based recommendations were obtained by a systematic review of the literature, grading of evidence, drafting of the recommendations by a global expert panel followed by a formal consultative consensus development program in which 422 independent healthcare professionals were able to agree or disagree with the recommendations. The criteria for agreement were set at 80% agreement. Evidence and recommendations were graded according to the SIGN (Scottish Intercollegiate Guidelines Network) classification system. • The primary treatment goal of NPWT in most chronic wounds is to achieve wound closure (either by secondary intention or preparing the wound for surgical closure). • Secondary goals commonly include: to reduce wound dimensions, and to improve the quality of the wound bed. Thirteen evidence based recommendations were developed in total to address these treatment goals; 4 for pressure ulcers, 4 for DFU, 3 for ischaemic lower limb wounds and 2 for VLU. <p><i>Conclusion:</i> The present evidence base is strongest for the use of NPWT in non-ischaemic DFU and weakest in VLU. The development of evidence-based recommendations for NPWT with direct validation from a large group of practicing clinicians offers a broader basis for consensus than work by an expert panel alone.</p>

Document	Key Points
<p>The clinical effectiveness of negative pressure wound therapy: a systematic review. Xie X et al. <i>J Wound Care.</i> 2010 Nov;19(11):490-5.¹¹</p>	<p><i>Summary:</i> This review estimated the efficacy of NPWT on the basis of a systematic review of reported RCTs.</p> <ul style="list-style-type: none"> • A systematic literature search for relevant RCTs was carried out. The credibility of the outcome of each study was evaluated using a specially constructed instrument. • We identified 17 RCTs, of which five had not been included in previous reviews or health technology assessments. For diabetic foot ulcers (seven RCTs), there was consistent evidence of the benefit of NPWT compared with control treatments. For pressure ulcers (three RCTs), results were conflicting. In trials involving mixed wounds (five RCTs), evidence was encouraging but of inadequate quality. Significant complications were not increased. <p><i>Conclusion:</i> There is now sufficient evidence to show that NPWT is safe and effective, to justify its use in the treatment of diabetes-associated chronic leg wounds. There is also evidence, though of poor quality, to suggest that healing of other wounds may also be effective.</p>
<p>Vacuum assisted closure: recommendations for use. A consensus document. Harding K et al. <i>Int Wound J.</i> 2008 Jul;5 Suppl 4:iii-19.¹²</p>	<p><i>Summary:</i> Vacuum assisted closure (VAC) Therapy has helped to improve wound care outcomes and has led to a number of dramatic changes in clinical practice over the past decade.</p> <p><i>Conclusion:</i> VAC therapy must be used as part of an individualized, comprehensive treatment plan and is indicated for both acute and chronic wounds.</p>

Document	Key Points
<p>Position document: Topical negative pressure in wound management. European Wound Management Association (EWMA). London: MEP Ltd, 2007.¹³</p>	<p>This position document reviews the literature reporting results with topical negative pressure (TNP) therapy (V.A.C.® Therapy) and indicates areas where TNP should be used with caution or avoided completely. The authors show the need for accurate wound assessment and a precise application technique. This collection of articles reviews the pathophysiological effects of TNP and presents a European perspective on the practical issues of successfully integrating TNP therapy into clinical practice</p>

Diabetic foot ulcers and partial amputations

A multicenter RCT (n=342) by Blume et al examined the safety and efficacy of NPWT compared with AMWT (predominately hydrogels and alginates) for treating diabetic patients with a stage 2 or 3 calcaneal, dorsal, or plantar foot ulcer $\geq 2 \text{ cm}^2$ in area.³ As mentioned earlier, approximately 90% of therapy days for both groups occurred in the homecare setting. All wounds were treated until ulcer closure or completion of the 112-day active treatment period.³

- A greater percentage of foot ulcers attained complete closure with NPWT (73/169, 43.2%) compared to AMWT (48/166, 28.9%; $p=0.007$).
- Based on Kaplan Meier analyses, the median time to complete ulcer closure was 96 days for NPWT (95% CI 75.0-114.0) ($p=0.001$) and could not be determined for AMWT.
- Additionally, significantly fewer amputations were reported for NPWT patients compared to AMWT patients (7/169 versus 17/166, respectively; $p=0.035$).
- According to the authors, “NPWT appears to be as safe as and more efficacious than AMWT in the treatment of diabetic foot ulcers.”³

Diabetes is the leading cause of non-traumatic lower extremity amputations in the United States,¹⁴ and approximately 14-24 percent of patients with diabetes who develop a foot ulcer will require an amputation.¹⁵ Foot ulceration precedes 85% of non-traumatic amputations in patients with diabetes.⁷ Armstrong et al conducted a multicenter RCT comparing NPWT (n=77)

and MWT (n=85) for the treatment of partial foot amputations in patients with diabetes.⁴ MWT consisted of alginates, hydrocolloids, foams or hydrogels. Wounds were treated until complete wound closure or completion of the 112-day active treatment phase, and the majority of therapy days (9,719/10,908 days; 89.1%) were in the home setting.⁵

- Significantly more wounds healed in the NPWT group than in the Control group: 43 (56%) vs 33 (39%); $p=0.005$.
- Based on time to complete closure, the rate of wound healing was faster in the NPWT group compared to the Control group ($p=0.005$). Time to 76-100% granulation tissue formation was also significantly shorter in the NPWT group ($p=0.002$).
- The safety profiles were similar for both groups, demonstrating that NPWT was safe and effective in treating diabetic foot amputations.⁴

Additional DFU studies are summarized in **Table 2**, and **Table 3** lists systematic reviews, consensus statements and practice guidelines related to NPWT treatment of DFUs.

Table 2. Diabetic foot ulcer studies

Author	Study Type and Patients	Results/Conclusions
Blume PA et al ³ (2008)	<ul style="list-style-type: none"> • RCT comparing NPWT and advanced moist wound therapy (AMWT) • A total of 342 patients were enrolled and received either NPWT (V.A.C.® Therapy; n=169) or AMWT (n=166) 	<ul style="list-style-type: none"> • Greater proportion of foot ulcers achieved complete ulcer closure with NPWT (73/169, 43.2%) compared to AMWT (48/166; 28.9%) within 112 days of active treatment (p=0.007) • Kaplan-Meier median estimate to 100% closure was 96 days (95% CI 75.0-114.0) for NPWT and not determinable for AMWT (p=0.001) • NPWT patients experienced significantly (p=0.035) fewer secondary amputations <p>No significant difference between the groups was observed in treatment-related complications such as infection, cellulitis or osteomyelitis at 6 months</p>
Eginton MT et al ¹⁶ (2003)	<ul style="list-style-type: none"> • RCT comparing NPWT (V.A.C.® Therapy) and conventional moist dressings (total of 10 patients were enrolled) 	<ul style="list-style-type: none"> • The wound depth was significantly decreased over the weeks of the trial to 1.2 cm (p<0.05) • NPWT dressing decreased the wound volume and depth significantly more than the moist gauze dressings (59% vs. 0% and 49% vs. 8%, respectively)

Author	Study Type and Patients	Results/Conclusions
McCallon SK et al ¹⁷ (2000)	<ul style="list-style-type: none"> • RCT comparing NPWT (V.A.C.® Therapy; n=5) and saline-moist gauze (n=5) 	<ul style="list-style-type: none"> • Satisfactory healing was noted in the NPWT group (22.8 days versus 42.8 days for control) • Average decrease in surface area for the NPWT group was 28.4% compared to an average increase of 9.5% for the control
Kim BS et al ¹⁸ (2011)	<ul style="list-style-type: none"> • Prospective cohort study of patients (n=45) with septic diabetic feet with limb-threatening infection that were treated with NPWT 	<ul style="list-style-type: none"> • Thirty-two cases (71%) were infected with two or more organisms. NPWT was applied for 26.2 ± 14.3 days • The median time to achieve more than 75% wound area granulation was 23 (range, 4 to 55) days and 104 (range, 38 to 255) days to complete wound healing • Successful limb salvage was achieved in 44 cases (98%); 14 (31%) without any amputation and 30 (67%) with partial foot amputations • Total number of operations per limb was 2.4±1.3 • One case of repeated infection and necrosis was managed with a transtibial amputation • There were no complications associated with NPWT

Table 3. Systematic reviews, consensus statements and practice guidelines related to NPWT treatment of diabetic foot ulcers

Document	Key Points
<p>Negative pressure wound therapy in the treatment of diabetic foot ulcers: a systematic review of the literature. Guffanti A. <i>J Wound Ostomy Continence Nurs.</i> 2014 May-Jun;41(3):233-7.¹⁹</p>	<p><i>Summary:</i> NPWT is an option for management of complex wounds such as diabetic foot ulcers.</p> <ul style="list-style-type: none"> • The nursing literature from 2000 to 2010 was reviewed for studies comparing clinical outcomes for DFUs treated with NPWT and those treated with standard moist wound therapy (SMWT). • PubMed and OVID databases were explored using the following search terms: vacuum-assisted closure, NPWT, diabetic wounds, and standard moist wound therapy. Research studies to judge efficacy were limited to the results from studies of experimental studies with RCTs on patients with diabetic foot wounds as the inclusion criteria. • Four studies were identified that met the established criteria. <p><i>Conclusion:</i> Despite variations in patient population, methodology, and additional outcome variables studied, NPWT systems were shown to be more effective than SMWT with regard to proportion of healed wounds and rate of wound closure.</p>
<p>A systematic review of the effectiveness of negative pressure wound therapy in the management of diabetes foot ulcers. Noble-Bell G and Forbes A. <i>Int Wound J.</i> 2008 Jun;5(2):233-42.²⁰</p>	<p><i>Summary:</i> Foot ulcers are a common complication in patients with diabetes.</p> <ul style="list-style-type: none"> • Negative pressure wound therapy (NPWT) is a wound care therapy that is being increasingly used in the management of foot ulcers. • This article presents a systematic review examining the effectiveness of this therapy. The review question is how effective is NPWT in achieving wound

Document	Key Points
	<p>healing in diabetes foot ulcers?</p> <ul style="list-style-type: none"> • The primary outcome for this study was the number of patients achieving complete wound healing (secondary outcomes, other markers of wound healing, adverse events and patient satisfaction). A systematic literature review and tabulative synthesis of RCTs was performed. • The review identified four RCTs of weak to moderate quality. Only one study examining NPWT in post-amputation wound healing reported data on the primary outcome. These data show a 20% improvement in wound healing [odds ratios = 2.0%, confidence interval (CI) -1.0 to 4.0] and number needed to treat = 6 (CI 4-64). No serious treatment-related complications were reported by any of the studies. • One study suggested a reduction in the risk of secondary amputation (absolute risk reduction = 7.9%, CI 0.5-15.43). • Studies also reported an increase in granulation and wound-healing rates in patients treated with NPWT therapy. No data on patient satisfaction or experience were reported. <p><i>Conclusion:</i> While all the studies included in the review indicated that the NPWT therapy is more effective than conventional dressings, the quality of the studies were weak and the nature of the inquiries in terms of outcome and patient selection divergent. There is a strong need for larger trials to assess NPWT therapy in diabetes care with different groups of patients and in relation to different clinical objectives and parameters.</p>

Document	Key Points
<p>Consensus statement on negative pressure wound therapy (V.A.C. Therapy) for the management of diabetic foot wounds. Andros G et al. <i>Ostomy Wound Manage.</i> 2006 Jun;Suppl:1-32.²¹</p>	<p><i>Summary:</i> In 2004, a multidisciplinary expert panel convened at the Tucson Expert Consensus Conference (TECC) to determine appropriate use of negative pressure wound therapy as delivered by a Vacuum Assisted Closure device (V.A.C. THERAPY, KCI, San Antonio, Texas) in the treatment of diabetic foot wounds.</p> <ul style="list-style-type: none"> • These guidelines were updated by a second multidisciplinary expert panel at a consensus conference on the use of V.A.C. THERAPY, held in February 2006, in Miami, Florida. This updated version of the guidelines summarizes current clinical evidence, provides practical guidance, offers best practices to clinicians treating diabetic foot wounds, and helps direct future research. • The Miami consensus panel discussed 12 key questions regarding V.A.C. THERAPY and its use for the treatment of a diabetic foot wound. <p><i>Conclusion:</i> While proper debridement, infection control, and adequate blood supply are required for successful limb salvage or foot reconstruction, the use of the V.A.C. THERAPY System has enabled clinicians to solve complex wound problems with more simple solutions.</p>
<p>Guidelines regarding negative pressure wound therapy (NPWT) in the diabetic foot. Armstrong DG et al. <i>Ostomy Wound Manage.</i> 2004 Apr;50(4B Suppl):3S-27S.²²</p>	<p><i>Summary:</i> The purpose of these guidelines is to summarize consensus of a multidisciplinary expert advisory panel convened to determine appropriate use of NPWT (Vacuum-Assisted Closure or V.A.C. Therapy) in the treatment of diabetic foot wounds.</p> <ul style="list-style-type: none"> • The Tucson Expert Consensus Conference (TECC) on V.A.C. Therapy was convened in an effort to guide the direction for future research either to confirm or refute current

Document	Key Points
	<p>consensus while providing practical guidance to the clinician currently treating diabetic foot wounds. The consensus committee discussed and commented on the ten key questions regarding NPWT and its use in the treatment of a diabetic foot wound.</p> <p><i>Conclusion:</i> NPWT has revolutionized soft-tissue reconstruction of the foot and ankle because it has enabled the clinician to close wounds by simple techniques that in the past would have required complex pedicled microsurgical free flaps.</p>

Pressure ulcers

In a prospective randomized trial by Joseph et al, NPWT was compared to traditional saline-wet-to-moist (WM) dressings for the treatment of chronic wounds.²³ Twenty-four patients with 36 chronic wounds (mostly pressure ulcers) were randomized to receive either NPWT (n=18 wounds) or WM (n=18 wounds). Blinded, independent wound evaluators measured wounds by volume displacement of alginate impression molds and performed punch biopsies for histology and culture.

- The most significant difference in volume was the change in depth of 66% for NPWT compared to 20% for WM (p<0.00001).
- Furthermore, there was granulation tissue formation in 64% of the wounds treated with NPWT (n=9).
- The authors recommended that NPWT be applied to chronic, non-healing wounds that are deep and complicated.²³

Table 4 provides details on additional PrU studies. Several clinical guidelines and consensus statements are summarized in **Table 5**.

Table 4. Pressure ulcer studies

Author	Study Type and Patients	Results/Conclusions
Wild T et al ²⁴ (2008)	<ul style="list-style-type: none"> • RCT comparing NPWT (V.A.C.® Therapy; n=5) and Redon Bottles (n=5) • Study was terminated after post-hoc analysis revealed significantly better results when using NPWT 	<ul style="list-style-type: none"> • 54% increase in granulation tissue formation observed in NPWT group, while a reduction in granulation tissue was observed in the Redon group (p=0.001) • NPWT group showed a 27% reduction of fibrin tissue at the wound base, Redon group showed a 21.8% increase (p= 0.035) • NPWT had significantly better results, whereas the Redon group required substantially larger care effort
Ford CN et al ²⁵ (2002)	<ul style="list-style-type: none"> • RCT comparing NPWT (V.A.C.® Therapy; n=20) and Wound Gel (n=15) 	<ul style="list-style-type: none"> • NPWT group had a higher mean percent reduction in ulcer volume compared to Wound Gel group (51.8% vs. 42.1%, p=0.46) • NPWT group showed a decrease in the mean number of PMNs and lymphocytes per high-power field; Wound gel group showed an increase (p=0.13, p= 0.41 respectively) • Antibiotics were prescribed for patients whose ulcers had underlying osteomyelitis. Ulcers with osteomyelitis that were treated with NPWT improved, while there was no improvement in similar

Author	Study Type and Patients	Results/Conclusions
Joseph E et al ²³ (2000)	<ul style="list-style-type: none"> • RCT of 24 patients with 36 wounds • NPWT (V.A.C.® Therapy; n=18 wounds) was compared to a control group of wet-to-moist dressings (control; n=18 wounds) 	<p>wounds in the Wound Gel group (p=0.25)</p> <ul style="list-style-type: none"> • NPWT group had a significantly higher % change in wound volume (p= 0.038), as well as a higher % change in wound depth compared to control (p<0.00001) • Groups displayed different histological characteristics, NPWT group displaying granulation tissue formation in 64% of wounds, and control group presented with inflammation and fibrosis in 81% of wounds
Baharestani MM et al ²⁶ (2008)	<ul style="list-style-type: none"> • Non-randomized retrospective analysis of the Outcome Assessment and Information Set (OASIS) database from patient data between July 2002 and September 2004 • Patients with a prior Stage III or IV pressure ulcers treated with NPWT were included • Early NPWT: within the first 30 days of start of home health care • Late NPWT: 30 days after standard of care 	<ul style="list-style-type: none"> • Median duration of NPWT was 31 days (range 3 to 169) for pressure ulcers • Median lengths of stay in early NPWT group for pressure ulcers was 85 days (range: 11 to 239) compared to 166 days (range: 60 to 657) for late NPWT group (p<0.0001) • After controlling demographic patient variables, regression analysis indicated that for each day NPWT initiation was delayed, almost 1 day was added to the total length of stay ($\beta=0.96$, $p<0.0001$ [pressure ulcers]) • Early initiation of NPWT may be associated with

Author	Study Type and Patients	Results/Conclusions
		shorter length of stay for patients receiving home care for Stage III or Stage IV pressure ulcers

Table 5. Pressure ulcer guidelines

Document	Key Points
<p>Prevention & Treatment of Pressure Ulcers: Quick Reference Guide NPUAP, EPUAP, PPIA. Haesler E, editor. 1-72. 2014. Perth, Australia, Cambridge Media.²⁷</p>	<p><i>Summary:</i> This document provides a summary of the recommendations and excerpts of the supporting evidence for pressure ulcer prevention and treatment.</p> <ul style="list-style-type: none"> • The purpose of the prevention recommendations is to guide evidenced based care to prevent the development of pressure ulcers • The purpose of the treatment focuses recommendations is to provide evidence-based guidance on the most effective strategies to promote pressure ulcer healing. <p><i>Conclusion:</i> NPWT should be considered as an early adjuvant for the treatment of deep, Category/Stage III and IV pressure ulcers (as discussed on pages 48-49).</p>
<p>Consensus Statement: A Practical Guide for Managing Pressure Ulcers with Negative Pressure Wound Therapy Utilizing Vacuum-Assisted Closure- Understanding the Treatment Algorithm. Baharestani et al. <i>Adv Skin Wound Care.</i> 2008.21:1-20.²⁸</p>	<p><i>Summary:</i> This article provides a practical guide for the use of Vacuum-Assisted Closure in the management of pressure ulcers.</p> <ul style="list-style-type: none"> • The information and opinions expressed were agreed upon by a consensus group with representation from a multidisciplinary advisory panel. • The recommendations are to help clinicians establish treatment protocols for the use of the system in the management of pressure ulcers.

Document	Key Points
	<ul style="list-style-type: none"> • NPWT has been shown to heal pressure ulcers in both randomized and nonrandomized studies. <p><i>Conclusion:</i> Created by a panel of wound care experts, this algorithm provides guidance on how to best to integrate NPWT when a patient has a Stage III or Stage IV pressure ulcer.</p>
<p>Guidelines for the treatment of pressure ulcers. Whitney J et al. <i>Wound Repair Regen.</i> 2006; 14: 6, 663-679.²⁹</p>	<p><i>Guideline #7b.1:</i> Consider using negative pressure wound therapy (NPWT) for stage III or IV pressure ulcers that fail to progress in healing with conventional therapy. (Level I)</p> <p><i>Principle:</i> NPWT applies negative pressure to the wound removing wound exudates and debris. Current evidence indicates that NPWT may support pressure ulcer healing by increasing wound perfusion and formation of granulation tissue and by reducing bacterial load.</p>
<p>Guidelines for managing pressure ulcers with negative pressure wound therapy. Gupta S et al. <i>Adv Skin Wound Care.</i> 2004 Nov-Dec;17 Suppl 2:1-16.³⁰</p>	<p><i>Summary:</i> Pressure ulcers are a serious health issue, leading to clinical, financial, and emotional challenges</p> <ul style="list-style-type: none"> • Numerous treatment modalities are available to promote wound healing, yet clinicians may be unsure how to incorporate these treatment options into an overall plan of care for the patient with a pressure ulcer • A consensus panel of experienced wound care clinicians convened in July 2004 to review the mechanisms of action and research basis for one such treatment modality: NPWT • After answering key questions about this modality, they developed an algorithm to assist the clinician in making decisions about using NPWT appropriately when a patient has a Stage III or Stage IV pressure ulcer

Document	Key Points
	<p><i>Conclusion:</i> The current body of literature, coupled with anecdotal reports and clinical experience, suggests that NPWT can be an important part of Stage III and Stage IV pressure ulcer care</p>

Venous leg ulcers

An RCT by Vuerstaek et al prospectively studied the efficacy of NPWT compared to conventional wound care (control) for the treatment of VLUs.³¹ A total of 60 patients (30 NPWT and 30 Control) were randomized; the primary endpoint was time to complete healing. Data revealed a significantly shorter time to achieve complete healing using NPWT with a median time of 29 days (95% CI, 25.5 to 32.5) for the NPWT group as compared to 45 days (95% CI, 36.2 to 53.8) with control therapy (p=0.0001). Additionally, wound bed preparation was significantly shorter in the NPWT group than the control group (7 days versus 17 days, respectively; p=0.005). The authors recommended that NPWT “should be considered as the treatment of choice for chronic leg ulcers owing to its significant advantages in the time to complete healing and wound bed preparation time compared with conventional wound care.”³¹

Additional studies are presented in **Table 6**.

Table 6. Venous leg ulcer studies

Authors	Study Type and Patients	Results/Conclusions
Vuerstaek JD et al ³¹ (2006)	<ul style="list-style-type: none"> • RCT comparing NPWT (V.A.C.® Therapy; n=30) and modern wound dressings (control; n= 30) 	<ul style="list-style-type: none"> • NPWT group had a significantly shorter median healing time compared to control group (29 days vs. 45 days, p=0.0001) • Wound bed preparation was also significantly shorter for the NPWT group (7 days) than the control group (17 days), p=0.005
Dini V et al ³² (2011)	<ul style="list-style-type: none"> • RCT comparing NPWT (n=15) and moist wound dressings (control; n=15) 	<ul style="list-style-type: none"> • There was no significant difference in the mean number of immunohistochemical markers and edema between the NPWT group and control • Granulation tissue formation of the wound bed was significantly higher in the NPWT group than the control at the end of the first week (p<0.001)
Loree S et al ³³ (2004)	<ul style="list-style-type: none"> • Prospective cohort study of 15 patients who were treated with NPWT (V.A.C.® Therapy) 	<ul style="list-style-type: none"> • Percentage of fibrinous tissue reduction was 28% on day three and 40% three days later • NPWT promoted healthy tissue formation

Authors	Study Type and Patients	Results/Conclusions
Egemen O et al ³⁴ (2012)	<ul style="list-style-type: none"> • Prospective cohort study of 20 patients who were treated with NPWT 	<ul style="list-style-type: none"> • Mean number of dressing changes of silver-impregnated foam prior to grafting was 2.9 (range 1-8 changes) • Mean number of dressing changes after skin grafting was 2.6 (range 2-5 changes) • Mean length of hospital stay was 16.9 (range 10-43 days) • All wounds healed completely without more debridement or regrafting

Cost Effectiveness of NPWT

In today’s outcome-oriented healthcare arena, cost effectiveness analysis plays a critical role in determining efficacy of medical technologies.³⁵ Major cost drivers for wound care include time to healing, staff time, length of stay (LOS), number of dressings, rate of infections and long waiting time from diagnosis to treatment.³⁶ Only a small portion of costs involve wound treatment products. For instance, the cost of materials typically accounts for 10-20% of the total cost of treating a patient.^{36, 37}

Another important consideration in the cost equation concerns the ease of transitioning patients from high cost care settings to lower cost care settings. There is a growing focus within the US healthcare system to seek quality outcomes and value-based purchasing. Studies have demonstrated that NPWT can result in fewer hospitalizations, emergent care incidents, complications, reduced amputations, fewer dressing changes, decreased personnel commitments, shorter hospitalization, and reduced treatment times.³⁸⁻⁴³ By minimizing these factors that contribute to direct and indirect wound care costs, NPWT has emerged in many cases as a cost-effective option for wound healing in various care settings.²⁶ Disposable, single-patient NPWT systems have also been developed to facilitate the delivery of NPWT during transitions across the continuum of care.

NPWT Cost-effectiveness Study Results

Results of economic studies that address costs associated with the use of NPWT in treating wounds are summarized below:

Cost-effectiveness studies such as Schwien et al⁴⁴ and Apelqvist et al,⁵ used economic models to compare the standard medical costs of traditional wound care dressings with the costs of using NPWT, including hospitalization and medical procedures performed.

- Schwien et al retrospectively compared hospitalization rates for home-care patients with Stage III and IV pressure ulcers treated with NPWT versus other wound care modalities. NPWT patients had lower rates for hospitalization (35% vs 48%, $p<0.05$), hospitalization due to wound complications (5% vs 14%, $p<0.01$) and wound-related emergent care (0% vs 8%, $p=0.01$). In this study, home-care patients treated with NPWT had significantly reduced hospital admissions.⁴⁴
- Using clinical data from the RCT conducted by Armstrong et al comparing NPWT to MWT for treatment of partial diabetic foot amputations⁴, Apelqvist et al calculated resource utilization and direct economic costs for clinical outcomes.⁵ The average direct cost per patient treated for ≥ 8 weeks (independent of outcome) was lower for the NPWT group compared to the MWT group: \$27,270 vs \$36,096, respectively. For wounds that achieved healing, the average total cost for NPWT patients ($n=43$) was lower by a third compared that of MWT patients ($n=33$): \$25,954 vs \$38,806, respectively.⁵ According to this cost-effectiveness study, more NPWT patients achieved healing of their partial diabetic foot amputations at a lower overall cost of care.

Three additional published studies have examined the clinical efficacy of NPWT versus traditional wound-care dressings in reducing incidence of amputations. Frykberg et al,⁴⁵ Blume et al,³ and Armstrong et al⁴ reported a reduction in amputations with adjunctive use of NPWT (5.8%, 6.1%, and 8.0%, respectively).

In the RCT conducted by Vuerstaek et al, NPWT ($n=30$) was compared to conventional wound care (Control; $n=30$) for the treatment of chronic VLU. Compared to the Control group, the NPWT group had a significantly shorter median healing time (45 days vs. 29 days, respectively; $p=0.0001$) and a significantly shorter time to wound bed preparation (17 days vs 7 days; $p=0.005$). The authors reported that total wound care costs for hospitalized patients with VLUs were 25% to 30% lower for the NPWT group compared to the standard care group ($p=0.001$).³¹

Driver and Blume conducted a cost analysis⁴⁶ of post-hoc retrospective data from the RCT by Blume et al that compared NPWT ($n=162$) to AMWT ($n=162$) for treatment of patients with DFUs. The average per-patient cost (independent of closure) was lower for the NPWT group (\$11,984.40) compared to the AMWT group (\$13,557.51). The median wound area reduction

from baseline was 85.0% for NPWT patients compared to 61.8% for AMWT patients. The median cost per 1 cm² of closure (regardless of closure status) was lower for NPWT patients (\$1,460.42 vs. \$2,566.17, respectively).⁴⁶

Studies have also shown that when NPWT is initiated in the course of wound treatment can have cost implications.

- In a retrospective study Baharestani et al analyzed the effect of early vs late initiation of NPWT on home care length of stay (LOS) for Stage III or Stage IV (n=98) PrUs.²⁶ After controlling for demographic patient variables, regression analysis showed that for every day NPWT initiation was delayed, almost 1 day was added to total LOS ($\beta=0.96$; $p<0.001$).²⁶
- A retrospective cohort study by Yao et al reported that patients with chronic lower extremity ulcers that were treated with NPWT within 3 months of ulcer onset had 3.38 (95% CI 1.68-6.82) times greater likelihood of achieving wound healing than those with late NPWT initiation (≥ 1 year post ulcer onset).⁴⁷

In the US, NPWT has been covered by all types of health plans and government agencies. A high-level overview of some of the provider policies that include coverage for NPWT is presented in **Table 7. Appendix 1** contains a bibliography of these policies.

Table 7. Health plans and Medicare administrators that cover NPWT

List of payers who cover NPWT (see **Appendix 1**). Medical Necessity and other specific criteria exist; see specific policy for full details.

Covered NPWT – Various Disease States in the Home					Covered NPWT in Home (Initially Encountered in Hospital)		
Health Plan or Agency	Diabetic Foot Ulcers (DFUs)	Venous/ Arterial Ulcers (VLUs)	Pressure Ulcers (PrUs - Stage III – IV)	General Chronic (over 30 days)	All Wounds Encountered in Hospital (DFU-VLU-PrU)	Surgically Created Wounds /Traumatic Wounds /Pre-operative Grafts	Other
Noridian (Medicare)	Covered	Covered	Covered	Covered	Covered	Covered	
WPS (Medicare)	Covered	Covered	Covered	Covered	Covered	Covered	
CGS (Medicare)	Covered	Covered	Covered	Covered	Covered	Covered	
Aetna	Covered	Covered	Covered	Covered	Covered	Covered	
Cigna	Covered	Covered	Covered	Covered	Covered	Covered	
AmeriHealth	Covered	Covered	Covered	Covered	Covered	Covered	
BCBS NC	Covered	Covered	Covered	Covered	Covered	Covered	Enterocutaneous fistulas
BC Idaho	Covered	Covered	Covered	Covered	Covered	Covered	Wound in patients with underlying conditions*
Excellus BCBS	Covered	Covered	Covered	Covered	Covered	Covered	
Health Partners	Covered	Covered	Covered	Covered	Covered	Covered	

Table 7. Health plans and Medicare administrators that cover NPWT

List of payers who cover NPWT (see **Appendix 1**). Medical Necessity and other specific criteria exist; see specific policy for full details.

Covered NPWT – Various Disease States in the Home					Covered NPWT in Home (Initially Encountered in Hospital)		
Health Plan or Agency	Diabetic Foot Ulcers (DFUs)	Venous/ Arterial Ulcers (VLUs)	Pressure Ulcers (PrUs - Stage III – IV)	General Chronic (over 30 days)	All Wounds Encountered in Hospital (DFU-VLU-PrU)	Surgically Created Wounds /Traumatic Wounds /Pre-operative Grafts	Other
Medica	Covered	Covered	Covered	Covered	Covered	Covered	
WellCare	Covered	Covered	Covered	Covered	Covered	Covered	Wound in patients with underlying conditions*
United Health	Covered	Covered	Covered	Covered	Covered	Covered	

*Wounds in patients with underlying clinical conditions which are known to negatively impact wound healing, which are nonhealing (at least 30 days), despite optimal wound care. (Examples of underlying conditions include, but are not limited to diabetes, malnutrition, small vessel disease, and morbid obesity. Malnutrition, while a risk factor, must be addressed simultaneously with the negative pressure wound therapy.)

CONCLUSION

As demonstrated in the literature, NPWT has been used safely and effectively to treat chronic wounds in the home. Coverage of this adjunctive therapy by a wide variety of health care providers also indicates recognition of the value of NPWT. According to Kaufman-Rivi et al, respondents in their survey of NPWT home usage concluded that “there was a definite benefit to NPWT, regardless of the care setting, and that it was a safe therapy when prescribed and administered appropriately.”² Acelity is committed to providing educational opportunities for NPWT prescribers and users, clinical phone support for NPWT patients, and ongoing NPWT research to support the safe and effective use of NPWT.

Appendix 1. Bibliography of provider policies

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Perspectives on NPWT Evidence for Health Technology Assessments

Background

While NPWT has been widely adopted in a range of clinical disciplines and searches in the peer review literature now yield in excess of 2,400 articles (November 2013), there remain some authors who consistently express doubts over the strength of the evidence for NPWT over conventional wound care. Following systematic reviews or meta-analyses of randomized NPWT studies (Ubbink et al. 2008) (Vikatmaa et al. 2008) (Gregor et al. 2008) concluded their papers arguing against its wider adoption. In response in 2009 Smith & Nephew convened an International NPWT Expert panel of clinicians to take a fresh and independent look at the evidence. All published evidence was considered objectively in studies using any type of NPWT device. Three papers were published reviewing the evidence and making a series of evidence based recommendations: in trauma and reconstructive surgery (Krug et al. 2011), in chronic wounds (Vig et al. 2011) and in reviewing the evidence for variables in NPWT such as choice of filler and pressure setting (Birke-Sorensen et al. 2011). Critical to the views of these articles were the identification of consensus in treatment goals for different wound types, as it is abundantly clear that NPWT is a tool to assist clinicians in achieving a desirable clinical outcomes; for example to protect a wound before closure or to assist the efficiency of a skin graft, rather than a magic bullet that just ‘makes things go faster.’ The purpose of the present paper is to provide an update of where the development of NPWT evidence has progressed and what significant trends are evident.

Evidence streams

a. Systematic reviews: Acute, Sub-acute and Chronic wounds

(Ubbink et al. 2008) searched for any RCTs where NPWT had been compared to conventional therapy. They found 13 trials totaling 573 wounds in 554 patients (as of June 2007). Pooling of data across all trials was not found to be possible given the variety of wound types and the different ways in which NPWT had been used to assist in the treatment process. (Ubbink et al. 2008) considered the trials in groups of similar wound types; mixed chronic wounds (4 trials); diabetic wounds (3 trials); pressure ulcers (2 trials); skin grafts (3 trials) and acute wounds (1 trial). Overall, (Ubbink et al. 2008) conclude “there is little evidence to support the use of NPWT in the treatment of wounds.” They base this conclusion largely on the inability to conduct multiple pooled analyses across several independent studies, small numbers of patients and non-blinded protocols. (Vikatmaa et al. 2008) present a very similar analysis to (Ubbink et al. 2008). Their conclusions were not as negative reviewing essentially the same data. They concede there are needs for much larger studies to show statistically significant effects in each of the different wound indications, but that there are indications that show positive effects of NPWT: chronic leg wounds, skin grafts, and diabetic wounds show reasonable evidence for a positive effect of NPWT. Pressure ulcers show the least convincing evidence. (Gregor et al. 2008) famously and cleverly titled their paper “a vacuum of evidence.” Although they conclude by advising against widespread adoption by government (in Germany in this case), they did acknowledge mostly positive studies in favor of NPWT, although only 2 of 5 RCTs and 2 of 4 comparative cohort studies were statistically significant.

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Subsequent to the 2008 publications and the Expert Panel articles in 2011, a number of new papers are pertinent to update this discussion. (Peinemann and Sauerland 2011) were able to identify 21 randomized studies although the different methods and wound types again precluded pooling the data. They acknowledge that most published studies show effects in the direction of NPWT, but still worry about possible bias in the execution of the studies and the potential for studies unfavorable to NPWT to have not been published. (Suissa et al. 2011) found 10 randomized trials on just chronic wounds and their conclusions were generally positive for NPWT with some caveats about publication bias. (Yao et al. 2012) conducted a large comparative cohort study using electronic medical records in Boston USA, to find 171 standard wound care patients matched with 171 who received NPWT. The significance of the retrospective nature of the study is that this is real-world data outside of a trial. The outcome was that NPWT patients were 2.6 times more likely to achieve wound closure than non NPWT patients and if anything the co-morbidities of the NPWT patients were greater. (Dumville et al. 2013) provided the Cochrane review update of RCTs in diabetic wounds. In essence no further large DFU NPWT studies have been completed since the KCI funded studies by (Armstrong and Lavery 2005) and (Blume et al. 2008). The conclusion once again is that there is a probable benefit of NPWT but bias might have been present, so endorsement is very qualified. There are now large institutional funded studies underway in Germany in the DFU indication.

b. Health Economic analyses

While there are few attempts at meta-analysis of health economic outcomes from NPWT use, individual economic analyses have been completed as part of published RCTs. (Braakenburg et al. 2006) conducted an RCT on a mixed group of chronic and acute wounds in which 32 patients received NPWT (V.A.C.™) and 33 patients were treated with control dressings. The study was insufficiently large to identify differences in the endpoints of secondary intention closure or readiness for grafting (although there were positive trends), but there were significant differences in the nursing time taken to treat each patient and the materials used. This study concluded that while time to healing was a little faster overall with NPWT (although not statistically significant at this sample size), patient comfort was improved (reduction in odor, fluid leakage) and the reduction in nursing labor was statistically significant. Overall, costs were not significantly different between the two treatment groups. In a nutshell: the NPWT devices cost more – but saved nursing time. The conventional treatments took more nursing time but cost less in materials.

A similar analysis was conducted by (Mouës et al. 2007). In a mixed group of chronic, trauma and delayed healing dehisced wounds, patients were prospectively randomized into NPWT (29) and conventional (25) groups. Here NPWT was used to prepare the wound for surgical closure by primary intention, grafts or flaps. There was no significant difference in the time to take wounds to a point where it was ready for closure (although there were positive trends in favor of NPWT). There were also improvements in the rate of reduction of wound area in favor of NPWT (again not quite significant). However, there were reductions in nursing time (statistically significantly lower for NPWT $p < 0.0001$) which were balanced by higher costs of the NPWT therapy itself.

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(Apelqvist et al. 2008) reported on an economic analysis of the post-surgical healing of diabetic foot ulcers RCT published earlier by Armstrong and Lavery (2005). In this study containing 77 (NPWT) and 85 (conventional) wounds the treatment costs were lower for NPWT (\$27,270) than for conventional (\$36,096) therapy. These costs were strongly linked to the fewer outpatient visits, dressing changes and antibiotics used in the NPWT group.

To summarize the current clinical and health economic literature on the use of NPWT, it appears that differences in the rate of wound progression to healing can be demonstrated, with sufficient numbers of patients in prospective RCTs, but few studies have reached the appropriate numbers. Some wound indications appear easier to demonstrate significant differences in healing rates than others (skin grafts>diabetic foot ulcers> post-surgical dehiscence> pressure ulcers for example). However, economic differences appear much more easily demonstrated with NPWT replacing the nursing resources needed to achieve comparable wound healing outcomes from conventional (non NPWT) therapies.

c. Closed incisions

A significant development in the clinical use of NPWT which did not feature in the 2008 systematic reviews or the Smith & Nephew NPWT Expert panel publications, is the emerging use of NPWT on the closed incision. First reported by (Stannard et al. 2006) and (Gomoll et al. 2006) in high risk orthopedic incisions, a Smith & Nephew initiative to collaborate with a small panel of orthopedic surgeons has resulted in a systematic review of incisional NPWT detailing 33 articles across many different surgical disciplines which is imminently to be published (Karlakki et al. 2013). The rate of publications is increasing and 26 of the 33 articles on closed incision NPWT have been published in the last 3 years. At present there have been RCTs showing significant reductions in surgical site complications in orthopedic trauma (Stannard et al. 2012) and in cardiothoracic surgery (Grauhan et al. 2013). There has been one smaller RCT which did not show a reduction (Masden et al. 2012). Several comparative cohorts show statistically significant reductions in surgical site complications. Although most articles describe the use of traditional durable NPWT devices (tNPWT) on the closed incision, the introduction of lower cost single use NPWT devices such as PICO^o (Smith & Nephew) or PrevenaTM (KCI) seems likely to stimulate the completion of larger numbers of studies in the coming years.

d. Equivalence of different NPWT devices

A distinguishable trend amongst the NPWT clinical evidence is the realization that randomized studies have been performed which show equivalence in outcomes between different devices delivering NPWT. RENASYS^o GO (Smith & Nephew) was shown to be equivalent to V.A.C.TM (KCI) by (Rahmanian-Schwarz et al. 2012) in the treatment of acute and chronic wounds and skin grafts. V.A.C. (KCI) with foam was shown to be equivalent to gauze based NPWT with wall suction in reducing area and volume in large surgical dehisced wounds (Dorafshar et al. 2012). V.A.C. (KCI) using foam, was shown to be non-inferior to SNaPTM (Spiracur) using gauze, in a study of lower extremity ulcers (Armstrong et al. 2012).

e. Development of single use (disposable) NPWT devices

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Since their introduction into the wound care market single use disposable NPWT devices have been utilized in a wide variety of wound indications and evidence supporting their efficacy has grown. We refer here specifically to the single use NPWT system PICO[®] developed by Smith & Nephew, but identical principles apply to single use devices from other manufacturers (Grauhan et al. 2013; Khanbhai et al. 2012; Gabriel et al. 2012; Marston et al. 2014). The evidence for PICO has developed in two distinct areas, firstly, as a means of preventing wound related complications in high risk closed incisions, and secondly, as a therapy to manage and help close complex or non-healing, open chronic wounds. Both groups of evidence will be discussed as this shows how single use devices are being proved to have equivalent efficacy to their durable medical equipment (traditional NPWT) counterparts

Following the publication of the first clinical study using PICO (Hudson et al 2013) reported earlier, a similar non-comparative study of 22 patients also showed that PICO was readily deployed across many different wound types (Canonico et al. 2012). These non-randomized studies represent a series of cases with what was described as encouraging results within one of four wound challenges; preventing surgical complications in high risk patients; gaining better control of post-surgical edema after revision arthroplasty; concomitant treatment with compression therapy in venous leg ulcers, and enhancing skin graft take in lower extremities.

Concentrating on high risk closed incisions, PICO was used in a (non-randomized) comparison within 50 patients undergoing bowel surgery for Crohn's disease, a population who have a much greater risk of developing post-surgical complications.(Pellino et al. 2013; Selvaggi et al. 2014) Typically applied for 4-7 days, the PICO treated group experienced significantly less post-operative wound complications in the closed abdominal incision, resulting in shorter hospital stays and fewer readmissions. The study also demonstrated that patients discharged with the system managed the therapy well in an outpatient setting with few issues.

More recently, the same authors have reported a similar study with 50 patients undergoing colorectal surgery and another 50 patients undergoing breast surgery (Pellino et al 2014). PICO was assigned to 25 patients in each surgery group while the remaining 25 received standard care. PICO was routinely applied for 7 days with a dressing change at 3 days if necessary. The study again demonstrated that PICO resulted in a positive effect on reducing i) length of stay (almost by half), ii) rate of seroma formation (8% v 40%), iii) lower rates of surgical site events (SSEs) or complications (8% v 44%), and iv) lower ASEPSIS scores following colorectal surgery. Additionally PICO significantly reduced the rate of SSEs following breast surgery from 36% to 8% as well as reduced ASEPSIS scores.

Similarly PICO was used as part of a treatment protocol to address high infection rates in women following caesarean sections, particularly in high BMI patients. Before implementation of the new protocol, infection rates were 12%. Over a 10 month period, PICO was applied to 50 high risk patients (high BMI >35kg/m²) immediately after surgery and left *in situ* for 7 days, and OPSITE[®] Post-Op Visible was given to all other patients (610 patients) and again left *in situ* for 7 days. The introduction of OPSITE Post-Op Visible reduced

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infection rates to 6.3%, while those patients treated with PICO[®] had 0% infection rates, despite data that suggests that high BMI patients are much more likely to suffer post-surgical infections following C-sections (Bullough et al. 2014).

A retrospective comparative study demonstrated a significant reduction in wound dehiscence and surgical site infections using PICO compared to standard dressings following spine fusion surgery (Adogwa et al. 2014). The authors retrospectively reviewed the first 46 cases of using single use NPWT (PICO) to their immediately preceding 114 cases without NPWT to assess the incidence of wound infection and dehiscence. A 50% decrease in the incidence of wound dehiscence was observed in the NPWT patient cohort (6.38% vs. 12.28%, $p=0.02$). Similarly, compared to the non-NPWT cohort, the incidence of post-operative SSIs was significantly decreased in the NPWT cohort (10.63% vs. 14.91%, $p=0.04$).

With regards to open or chronic wounds, Payne and Edwards describe the use of PICO on a collection of 21 cases of traumatic wounds or post-operative wound complications. They demonstrated how PICO can benefit a wide range of clinical wounds by optimizing patient care, promoting rapid wound healing and offering significant savings in bed days by facilitating early discharge from hospital (Payne and Edwards 2014). Additional peer review papers have also been published describing case examples (Ahmad et al. 2013; Dowsett et al. 2013). Dowsett developed a treatment pathway for non-healing venous leg ulcers which incorporated the use of PICO in conjunction with compression bandaging systems. The guidelines offer a decision making pathway and case examples to assist clinicians dealing with patients who have non-healing venous leg ulcers to decide if NPWT may be an appropriate additional treatment option. Other publications include case examples of treating challenging, non-healing wounds and guidelines for incorporating PICO into treatment pathways for use in outpatient settings (Dowsett and Timmons 2012; Murphy and Powell 2013; Narayan *et al.* 2014; Timmons and Russell 2012). Independent comparisons on the usability of PICO versus other portable NPWT systems in the clinical setting have also been published. (Gillespie et al. 2013).

A larger study that merits particular attention, is a recently published non-comparative evaluation carried out in North America in which a total of 326 patients were treated with PICO in a community setting in Ontario, Canada (Hurd *et al.* 2014). The mean age of patients evaluated was 57 years and 49.5% were male. The mean duration of the wound was 8.9 weeks with a range from 1 week to 68 weeks and mean baseline wound area was 19.9cm². The wounds were mostly surgical wounds (68%) that had become infected and split open (dehiscence) and were delaying the patient's return to normal living.

The results from the PICO patients were compared retrospectively with patients previously treated with traditional full-sized traditional NPWT (tNPWT) in the same institutions. Patients were matched on the basis of age, sex and wound characteristics. Patients with wounds greater than 100cm² and/or high levels of exudate were excluded on the basis that these would be unsuitable candidates for treatment with PICO. The final cohort included in the analysis comprised 304 patients treated with PICO and 539 patients treated with tNPWT. Wound area and volume were marginally greater in the tNPWT arm although

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patients treated with PICO^o were older and had longer wound duration prior to treatment. When the healing was analyzed it was found that the reduction of wound area was very similar between PICO and full sized NPWT (Hurd *et al* 2014). In order to manage a full range of wound types within hospital and in homecare environments, protocols employing both device types could in principle allow the most economical solution to wound management needs.

f. Active ongoing clinical research

Clinical research activity to assess the effects of NPWT continues in many global locations. A selection of current large scale clinical trials can be identified from www.clinicaltrials.gov. Example include:
NCT01640366 RCT bilateral breast reduction single use NPWT vs standard care 200 patients;
NCT01480362 RCT DFU traditional portable NPWT vs standard care 360 patients;

Summary of themes

A review of NPWT clinical data suggests that it is rather easy to show reduced nursing costs for the same level of wound healing efficacy, whereas only a few larger randomized studies have shown superiority in wound healing.

As more NPWT systems become available, the evidence suggests that different NPWT devices on the whole offer equivalent clinical efficacy.

As the adoption of single use NPWT devices widens in various wound indications and patient settings, a growing body of evidence suggests that on appropriate wounds, single use systems can provide equivalent clinical outcomes to traditional durable NPWT systems.

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Masters, Christine V. (HCA)

From: Whalen, Sharon <Sharon.Whalen@Acelity.com>
Sent: Monday, May 16, 2016 9:27 AM
To: HCA ST Health Tech Assessment Prog
Subject: Submission comments and evidence regarding HTA: NPWT
Attachments: NPWT Clinical Literature on Incision Management.doc; Disposable NPWT -SNAP-Clinical and Economic Evidence.doc

John Morse, MPH
Program Director
Washington State Health Care Authority
Health Technology Assessment
PO Box 42712
Olympia, WA 98504-2712

Electronically submitted to: shtap@hca.wa.gov.

Dear Mr. Morse

Please accept these comments on Health Technology Assessment (HTA) for NPWT from Kinetic Concepts Inc (KCI). KCI is the leader in negative pressure wound therapy (NPWT) and a division within Acelity, a global wound care and regenerative medicine company. Acelity is focused on developing products and therapies that improve clinical outcomes while helping reduce the overall cost of patient care.

Recently the draft questions for NPWT HTA were announced. We have two comments regarding these research questions. One is that evidence of effectiveness for wound care products and services is not limited to clinical research but can be established through a combination of scientific evidence and expert knowledge. This approach is consistent with evidence-based medicine (EBM), which is the integration of best research evidence with clinical expertise. The EBM approach is particularly important in chronic wound care. Patients with wounds typically have multiple co-morbidities, which present in varying degrees of severity. Comprehensive chronic wound care frequently involves the use of multiple interventions, often in conjunction with each other.

NPWT has been a treatment option for patients for over 20 years. Over that time evidence began with randomized clinical studies and prospective studies providing valuable outcome data to providers. NPWT has become a standard of care for some wound therapy and the evidence and utilization of NPWT has shifted to development of meta-analysis reviews and consensus statements and organizational treatment guidelines.

For this reason, we believe there should be inclusion of all forms of evidence for review is imperative.

In addition, for many patients NPWT therapy begins in the hospital setting and is then transferred to the home setting. This occurs because wounds may take several weeks to achieve their therapy healing goal, and it is logical that patients would be discharged from the hospital to the home setting. It is also logical that clinical research studies also follow that path of a beginning in the inpatient setting and ending in the home setting.

For this reason we believe it is important that the HTA program review of the outcome literature include research studies that begin in the hospital setting and continue in the home setting.

We provided clinical evidence last year on NPWT was this topic was first placed on the HTA Director list. I am providing the program additional clinical evidence for review. The additional evidence are in two documents. The first document is NPWT over surgical incisions which include procedures post trauma or with patient with high co-morbidities. The clinical endpoints with the use of NPWT on these patients are decrease in seroma, decrease in infection and decrease of

time in the hospital setting. Again, these patients begin the NPWT in the inpatient setting; often require continued use of NPWT in the home setting.

The second document is clinical evidence on disposable NPWT device. One of the key studies in this dossier is a RCT study by Armstrong which provides statistical significant outcomes that disposable NPWT is equivalent to DME NPWT .

If there is any additional information or questions you may have, please let me know.

Sharon

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Advanced Wound Therapies



Acelity is a global wound care and regenerative medicine company created by uniting the strengths of KCI, LifeCell and Systagenix. Acelity employees now have **acelity.com** email addresses but will still receive emails sent to their previous KCI, LifeCell or Systagenix email. Learn more about us by visiting **acelity.com**.

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NPWT and Incisional Management

Scientific and Clinical Outcomes Overview

In recent years there have been several publications highlighting the efficacy of Negative Pressure Wound Therapy placed over closed surgical incisions at the conclusion of a surgical procedure. In general, this application of NPWT is used for patients or specific surgical procedures where there is an elevated risk of post operative wound complication. Note that unlike traditional use of NPWT, which is placed on an open wound, this application places the NPWT device over the top of the suture or staple line of a closed incision. NPWT has been associated with a reduction in post operative wound complications in a variety of incision types in certain high risk patient populations. There is clinical evidence that supports the expansion of use of NPWT over incisions in the areas of abdominal surgery, orthopedic surgery, sternotomy incisions, and vascular surgery of the groin.

Below are highlights of various peer review papers on this topic.

Abdominal Surgery

- Gassman, et al⁽¹⁾ conducted a retrospective comparative review of patients who underwent ventral hernia operations.
 - A total of 63 patients (31 primary closure alone; 22 primary closure with 7 days of overlying NPWT; and 10 secondary closure with NPWT)
 - Compared to patients treated with primary closure alone, patients treated with primary closure with overlying NPWT had:
 - Shorter average LOS: 7 vs. 10 days ($p>0.05$)
 - Fewer surgical site infections (SSI): 18% vs 55% ($p<0.01$)
 - Lower recurrence rates: 5% vs. 23% ($p<0.05$)
 - Compared to primary closure alone, primary and secondary closures with NPWT were associated with a 2-fold and 8.5-fold decreased odds ratio for SSI, respectively ($p<0.02$).
 - Authors concluded: the use of NPWT was associated with lower rates of SSI and recurrence.

- Condé-Green, et al⁽²⁾ published the results of a retrospective review of patients who underwent abdominal wall reconstruction to repair large ventral hernias. Overall impact on complications, dehiscence, infection and seroma rates was measured.



- Total of 56 patients treated (23 patients with incisional NPWT and 33 patients with dry gauze dressings). Incisional NPWT dressing was applied intraoperatively and removed after 5 days.
- Incisional NPWT patients had significantly better overall wound complication rates as compared to standard dressing patients: 63.6% (5/23) vs. 22%,(21/33) respectively (p=0.020), and skin dehiscence rates: 39% (2/23) vs. 9%,(13/33) respectively (p=0.014)
- Vargo, et al⁽³⁾ conducted a retrospective review of abdominal wounds with NPWT (30 patients) vs historical control of patients who were at high risk of infection.
 - Results showed 0% incidence of infection for the NPWT group vs 20% on the historical control group
 - Authors concluded: NPWT can be successfully applied to closed surgical incisions. Initial results showed a statistically significant reduction in wound infection rate compared to historical controls.
- Bonds, et al,⁽⁴⁾ in a retrospective chart review evaluated the effect of risk factors and the use of incisional NPWT on surgical site infection (SSI) rates in all patients undergoing open colectomy.
 - All 254 patients received standard wound closure through the use of staples or sutures. Over the incisions, patients received either postoperative dressings (occlusive dressing) or the placement of incisional NPWT device.
 - Sixty-nine patients (27%) experienced an SSI, four (12.5%) from the incisional NPWT patients group vs 65 (29.3%) for the patients without incisional NPWT.
 - Logistic regression showed two significant factors: diabetes mellitus increased the chance of surgical site infection (OR, 1.98; p=0.031 or 0.05), and the use of incisional NPWT was associated with a decreased rate of SSI (OR, 0.317; p=0.041).
 - Authors concluded: the use of incisional NPWT appeared to reduce SSIs in open colorectal surgery.

Orthopedic Surgery

- Stannard, et al⁽⁵⁾ in a prospective multicenter RCT compared the use of incisional NPWT against standard postoperative dressings (SOC) over clean closed surgical incisions after high-energy fractures.
 - A total of 249 patients with 263 calcaneus, pilon, or tibial plateau fractures were studied. 130 patients with 141 fractures were randomized to incisional NPWT vs 119 patients with 122 fractures were randomized to SOC.
 - Results revealed 23 total infections in the SOC group compared to 14 in the NPWT group (p=0.049) and 20 cases of dehiscence in the SOC group compared to only 12 in the NPWT group (p=0.044).
 - Author concluded: . NPWT should be considered for high risk wounds after severe skeletal trauma.



- Pachowsky, et al⁽⁶⁾ studied 19 consecutive patients treated with NPWT vs standard postoperative dressings (SOC) over closed incisions following total hip arthroplasty.
 - Ten patients were randomized to the SOC group and 9 to the NPWT group.
 - Results showed significantly decreased volume of postoperative seromas in the NPWT group versus the SOC group on day 10 (1.97 vs. 5.08 ml; p=0.021). Seroma was present in 44% of the NPWT patients and 90% of SOC patients.
 - The NPWT group required significantly fewer days of antibiotics (8.44 ± 2.24 vs 11.8 ± 2.82 days, p =0.005).
 - .
 - Authors concluded: the use of NPWT decreased the development of postoperative seromas and improved wound healing.
- Paucer, et al⁽⁷⁾ in a prospective randomized comparison of NPWT vs Standard Wound Dressing (SWD) for incisions after hemiarthroplasty for femoral neck fractures measured the reduction of wound complications. Seroma and secretions were measured. Total of 21 patients (11 NPWT and 10 patients with SWD)
 - Seroma: after 5 days, the NPWT Group had $0.257 \pm 0.75 \text{ cm}^3$ and the SWD Group developed $3.995 \pm 5.01 \text{ cm}^3$ after 5 days
 - Secretion: the NPWT Group had 0.9 ± 1.0 days and the SWD Group had 4.3 ± 2.45 days
 - Authors concluded: NPWT demonstrated decreased development of postoperative seroma, reduction of total wound secretion days and reduction in time for needed dressing changes.
- Reddix, et al⁽⁸⁾ in a retrospective patient chart review evaluated morbidly obese patients with acetabular fractures and the application of NPWT to clean, closed surgical incisions.
 - 19 patients were enrolled with a mean follow-up period of 21 months.
 - There were no wound complications or infections during the perioperative and follow-up period.
 - Authors concluded that NPWT over clean closed incisions may be a useful adjunctive therapy for reducing post-operative complications in morbidly obese patients with acetabular fractures.
- Reddix, et al⁽⁹⁾ published the results of a retrospective comparison of wound infection and dehiscence rates in patients with acetabular fracture surgery. Patients received either standard of care (SOC) or NPWT over incisions.
 - Non-NPWT group of 66 patients had 4 (6.06%) deep wound infections and 2 (3.03%) dehiscences.
 - NPWT group of 235 patients had 3 (1.27%) deep wound infections and 1 (0.426%) dehiscence.
 - Authors concluded: NPWT infection rate of 1.27% represented a significant decrease in comparison to other groups (infection rates of 4.2%, 4%, and 5% of



similar size ($p = 0.0282$; reference rate =4%), and that the application of NPWT decreased their incidence of perioperative incision complications.

- The current postoperative protocol calls for NPWT placed over acetabular fracture surgery incisions.

Sternotomy Incisions

- Grauhan, et al⁽¹¹⁾ reported on a prospective comparative study that analyzed 150 obese cardiac surgery patients, whose sternotomy wound incisions were treated with either NPWT ($n=75$) or conventional sterile wound dressings (Control; $n=75$). Wound infection within 90 days was the primary study endpoint.
 - NPWT group had significantly fewer wound infections than the Control group: 3/75 (4%) vs. 12/75 (16%), respectively; $p= 0.0266$; odds ratio, 4.57; 95% confidence interval (CI), 1.23-16.94.
 - NPWT group had significantly fewer Gram-positive skin flora wound infections: 1 vs. 10, respectively; $p= 0.0090$
 - NPWT group, 71/75 (95%) of the incisions were primarily closed when the dressing was removed in 6 to 7 days. The authors concluded that NPWT over clean, closed surgical incisions for the first 6 to 7 postoperative days significantly reduced the likelihood of wound infection after median sternotomy for high-risk obese cardiac surgery patients.
- Grauhan, et al,⁽¹⁰⁾ conducted a prospective comparative study of patients undergoing cardiac surgery via median sternotomy with conventional dressings changed every 1–2 days vs NPWT therapy for 6–7 days.
 - Conventional dressings: 3,508 patients (historical cohort) and NPWT therapy 237 patients (prospective cohort)
 - The post-sternotomy infection rate was significantly less in patients treated with NPWT Therapy. Infection rates were Conventional dressings: 3.4% (119 of 3,508 patients) vs NPWT Therapy: 1.3% (3 of 237 patients) $p < 0.05$.
 - For the NPWT Therapy group 98.7% (234/237) of patients without infection, the incision was primarily closed at removal of the NPWT.
 - Author Conclusion: NPWT over clean-closed incisions the first 6 to 7 postoperative days significantly reduced the incidence of wound infection after median sternotomy in a high risk group of obese patients.

Vascular Surgery

- Matatov, et al⁽¹²⁾ in a retrospective comparative study evaluated the rate of wound infections in vascular surgery patients whose closed groin incisions were treated with either NPWT therapy or other dressings (skin adhesives or absorbent dressings) as the Control.



- Ninety patients' records with 115 groin incisions were reviewed: the Control group (49 patients) and the NPWT group (41 patients) with wound evaluations at postoperative days 7 and 30.
- Significantly more wound infections were reported in Control versus NPWT therapy incisions: 30% (19/63) vs. 6% (3/52); $p=0.0011$.
- Incision infections were also more severe in the control group; 16% (10/63) Szilagyi grade I, 11% (7/63) grade II, and 3% (2/63) grade 3 infections vs only 6% (3/52) Szilagyi grade I infections were reported for NPWT Therapy incisions.
- Author conclusions: incisions treated with NPWT had a significantly lower incidence of groin wound infection.

Footnotes:

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7. Pauser J, Nordmeyer M, Biber R, et al. Incisional negative pressure wound therapy after hemiarthroplasty for femoral neck fractures - reduction of wound complications. *Int Wound J*. 2014 Aug 14.
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**SMART NEGATIVE PRESSURE™ (SNAP™)
Therapy System:
Scientific and Clinical Outcomes Overview**



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Executive Summary

Wound healing progression involves removal of barriers to wound healing such as exudate and infectious material, inadequate perfusion to the wound bed and lack of healthy granulation tissue. Successful healing involves addressing wounds that may be stalled in the inflammatory and proliferative phases of wound healing. Many passive and active therapies have been developed to address those barriers of wound healing. This includes Negative Pressure Wound Therapy, which is the application of sub-atmospheric pressure to create an environment that promotes wound healing by drawing wound edges together, removing exudate and infectious material, reducing edema and promoting perfusion and granulation tissue formation.

For over 35 years, KCI has provided new technologies and therapies designed to facilitate wound healing, while being more manageable for caregivers and comfortable for patients around the world. KCI's V.A.C.® Therapy was the first powered NPWT system to be commercialized in the US in 1995 following clearance by FDA under 510(k) K945062. A large body of clinical evidence (the majority reporting results using the V.A.C.® Therapy System) has demonstrated the value of using NPWT for the treatment of wide variety of wounds.

With the increased treatment of wounds in the outpatient settings, a variety of portable NPWT systems have been developed for use across the continuum of care. The majority of these are electrically powered; however, recently a mechanically powered NPWT, SMART NEGATIVE PRESSURE™ (SNAP™) Therapy, has been cleared by FDA (under initial 510(k) K111393) for treatment of wounds that would benefit from the use of NPWT to promote healing through the removal of small amounts of exudate, infectious material, and tissue debris (**Figure 1**). This therapy is indicated for patients with chronic, acute, traumatic, sub-acute and dehisced wounds, partial-thickness burns, ulcers (such as diabetic, pressure or venous insufficiency), flaps and grafts, and surgically closed incisions.

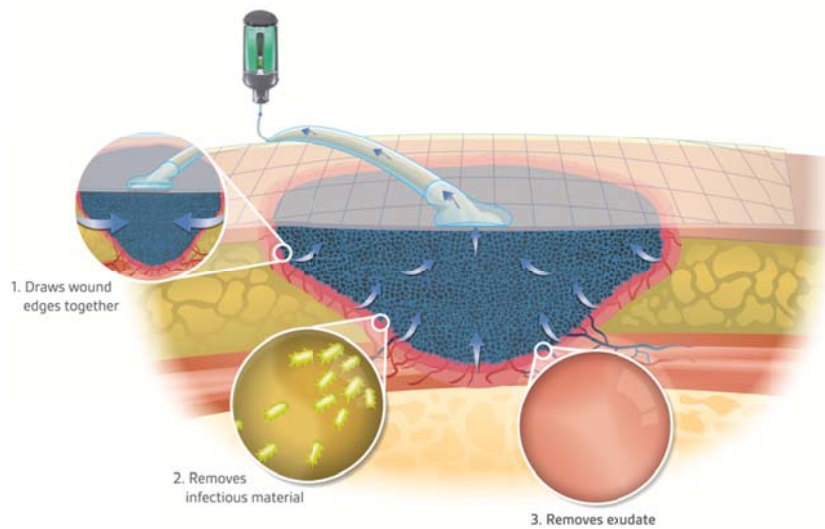


Figure 1. SNAP™ Therapy promotes wound healing by drawing wound edges together and removing small amounts of infectious material and exudate.

This document provides an overview of the SNAP™ Therapy System and the scientific, clinical, and economic evidence reporting positive outcomes using this innovative non-powered NPWT system in the outpatient setting.

Background

Powered negative pressure wound therapy (NPWT) has been used for almost 20 years across the continuum of care. Its application on a variety of acute and chronic wounds speaks to the versatility of NPWT in wound care. V.A.C.® Therapy was introduced commercially in 1995¹; since then, the number of other manufacturers with similar FDA-cleared devices has increased substantially.

Important considerations when choosing an NPWT system include wound characteristics (type, size, and severity), care setting, treatment cost, and patient mobility. While the majority of NPWT systems are electrically powered, the SMART NEGATIVE PRESSURE™ (SNAP™) Therapy System is a mechanically powered NPWT device specifically designed to promote wound healing through the removal of small amounts of exudate, infectious material, and tissue debris.



SNAP Therapy consists of the following elements (see **Figures 2A and 2B**):

- Disposable cartridge which delivers negative pressure at -125 mmHg
- Wound interface layer of either antimicrobial gauze or reticulated open-cell foam
- Advanced hydrocolloid dressing with integrated microport
- Cut-to-length tubing
- One-way flow valve
- Strap.²

The single-use SNAP™ Therapy System is lightweight (< 3 ounces) to enhance patient mobility, quiet (no electrical components), and designed for wounds that are less than 13 x 13 cm in area and are low exudating (≤ 180 cc/week) (see **Figure 1B**).³

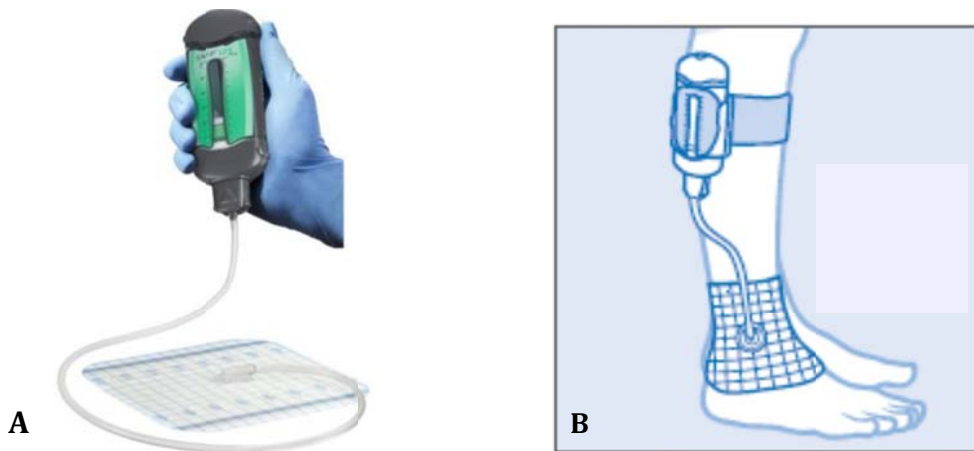


Figure 2. SNAP™ Therapy System: A) Cartridge and advanced hydrocolloid dressing B) Illustration of application to a lower extremity wound

SNAP™ Therapy System – Scientific and Clinical Evidence

Scientific studies have been conducted to evaluate the ability of SNAP™ Therapy to deliver NPWT. A set of specialized constant force springs creates forced air expansion that produces the predetermined level of negative pressure used by SNAP Therapy.⁴ Because maintenance of a prescribed level of negative pressure is critical for NPWT, a scientific bench study compared the



ability of both SNAP™ Therapy and V.A.C.® Therapy to maintain target negative pressure (-125 mmHg) with and without exudate inflow in a simulated wound model. Results indicated that with and without fluid in the model, SNAP Therapy delivered negative pressure (at -125 mmHg set point) similar to that delivered by V.A.C. Therapy over a 24-hour period.⁴ An animal study was used to evaluate SNAP Therapy's ability to produce granulation tissue. Rats with surgically created 2.5 x 3 cm wounds were treated with either SNAP Therapy at -125 mmHg or the SNAP Dressing without negative pressure. Animals treated with SNAP Therapy at -125 mmHg had a significantly greater wound size reduction at 7 days compared to those treated with the SNAP Therapy dressing and no negative pressure: 51%. vs. 12%, respectively, $p < 0.05$.⁴ This rodent study was modeled on a previous study in which animals treated with a V.A.C. Therapy Dressing and negative pressure at -125 mmHg achieved a 40% decrease in wound size.⁵ According to the authors, the similarity of results in these animal studies "suggests that the SNAP system may have efficacy equal to that of vacuum assisted closure for some wounds."⁴

Clinical Evidence

A number of clinical studies have been published on SNAP Therapy (**Table 1**) The studies provide the results from over 150 patients with a variety of wounds, including venous leg ulcers and diabetic foot ulcers), The studies include randomized controlled trials (RCTs) as well as a number of case series and case studies reporting experience using the system.

While complete (100%) wound closure is the endpoint usually required by regulatory agencies to determine product efficacy, percentage of wound size reduction at certain time points can provide important information as to whether a treatment is likely to heal a wound.^{6,7} Studies have shown that diabetic foot ulcers achieving $\geq 50\%$ wound size reduction in 4 weeks (30 days)⁸ and $\geq 90\%$ wound size reduction in 8 weeks⁹ were more likely to achieve healing in 12 weeks. Some SNAP Therapy studies report complete wound closure data, while others focus on percent wound size reduction at specific time points.



Table 1: Key Clinical Evidence Supporting Use of SNAP™ Therapy

Author	Study Type	Patients	Results/Conclusions
DG Armstrong et al ¹⁰ <i>(Wound Repair and Regeneration; 2012)</i>	Randomized controlled trial (RCT) SNAP Therapy vs V.A.C. Therapy	<ul style="list-style-type: none"> • 132 patients (pts) with noninfected, nonischemic, nonplantar lower extremity diabetic and venous wounds were enrolled • 115/132 pts had follow-up data available for analysis • 83 pts finished the study with either healing or 16 weeks of therapy: <ul style="list-style-type: none"> ○ SNAP Therapy: 41 pts ○ V.A.C. Therapy: 42 pts 	<ul style="list-style-type: none"> • Primary endpoint was wound size reduction • Baseline wound size: SNAP Therapy: 5.37 ± 6.14 vs V.A.C. Therapy : 9.95 ± 11.38 (p < 0.05) • Study was powered to demonstrate comparative efficacy, noninferiority • In terms of wound size reduction , SNAP Therapy pts demonstrated noninferiority to V.A.C. Therapy pts at 4, 8, 12 and 16 weeks (p=0.0030, 0.0130, 0.0051, and 0.0044, respectively) • There was no significant difference in complete wound closure at all time points • Device-related adverse events and complications (eg, infection) also similar between groups • Study demonstrated similar wound healing outcomes between SNAP Therapy and V.A.C. Therapy in the study population

Author	Study Type	Patients	Results/Conclusions
<p>WA Marston et al¹¹</p> <p><i>(Advances in Wound Care, 2015)</i></p>	<p>Sub-analysis of the previously published 2012 RCT¹⁰</p> <p>SNAP Therapy vs V.A.C. Therapy</p>	<ul style="list-style-type: none"> • 40 patients (pts) with venous leg ulcers <ul style="list-style-type: none"> ○ SNAP Therapy (n=19) ○ V.A.C. Therapy (n=21) 	<ul style="list-style-type: none"> • Primary endpoint: wound size reduction • Initial wound sizes; SNAP Therapy: 4.85 ± 4.49 cm² vs V.A.C. Therapy: 11.60 ± 12.12 cm². • SNAP Therapy: Significantly greater wound size reduction at 4, 8, 12, and 16 weeks (<i>p</i>=0.0039, 0.0086, 0.0002, and 0.0005, respectively), compared to V.A.C. Therapy • 50% wound closure at 30 days: SNAP Therapy: 52.6% (10/19) vs V.A.C. Therapy: 23.8% (5/21) (odds ratio [OR] 3.56, 95% confidence interval [CI] of [0.923, 13.699]) • Complete wound closure at 90 days: SNAP Therapy: 57.9% (11/19) vs V.A.C. Therapy: 38.15% (8/21) (OR, 2.23, 95% CI [0.63, 7.93])

Author	Study Type	Patients	Results/Conclusions
<p>B Lerman et al¹²</p> <p><i>(Plastic and Reconstructive Surgery; 2010)</i></p>	<p>Prospective comparative study</p> <p>SNAP Therapy vs patient-matched controls</p>	<ul style="list-style-type: none"> Prospective Study: 21 wound care center pts with refractory lower extremity ulcers treated with SNAP Therapy over a period lasting up to 4 months Retrospective matched controls (2 unique matches per SNAP Therapy patient): 42 pts treated over the preceding 4 years at the same clinic with modern wound care protocols including skin substitutes and skin grafting. 	<ul style="list-style-type: none"> Primary endpoint: Evaluate safety and efficacy of SNAP Therapy for treatment of refractory lower extremity ulcers. SNAP Therapy group: <ul style="list-style-type: none"> 100% (21/21) pts demonstrated reduced wound size 86% (18/21) had a statistically significant healing trend ($p < 0.05$) Based on Kaplan-Meier estimates, mean time to healing for SNAP Therapy pts vs matched control pts was 74.25 ± 20.1 vs 148.73 ± 63.1 days, respectively; $p < 0.0001$ The difference represented a 50% absolute reduction in time to healing for SNAP Therapy pts.

Author	Study Type	Patients	Results/Conclusions
<p>S Bradbury et al¹³</p> <p><i>(Advances in Wound Care; 2015)</i></p>	<p>Case series</p> <p>SNAP Therapy</p>	<ul style="list-style-type: none"> • 37 evaluable pts were treated with SNAP Therapy and appropriate standard care for up to 6 weeks for 1 of 3 types of chronic wounds: <ul style="list-style-type: none"> ○ Venous leg ulcers (n=15) ○ Mixed etiology leg ulcers (n=13) ○ Neuropathic foot ulcers (n=9) 	<ul style="list-style-type: none"> • Primary endpoint of percentage change in wound size was met: <ul style="list-style-type: none"> ○ 42.64% mean percentage decrease in wound area across the study population between weeks 1 and 8 ○ Mean reduction in wound size was 64% for venous leg ulcers and 55% for neuropathic foot ulcers • 15 (41%) pts developed wound infection <ul style="list-style-type: none"> ○ Skin-related adverse events were more likely to occur in the leg ulcer groups.
<p>KD Fong et al¹⁴</p> <p><i>(WOUNDS; 2010)</i></p>	<p>Case Series</p> <p>SNAP Therapy</p>	<ul style="list-style-type: none"> • 12 consecutive adult pts with chronic wounds were followed biweekly for complications and wound healing over a 4-week period • First clinical experience using SNAP Therapy on pts 	<ul style="list-style-type: none"> • All 12 pts experienced wound healing after SNAP Therapy treatment • The 6/12 pts who met all study requirements had a statistically significant ($p<0.01$) mean wound area reduction of 97.2% at 4 weeks post SNAP Therapy initiation. • Five of these 6 pts achieved complete wound healing



Author	Study Type	Patients	Results/Conclusions
B Lerman et al ³ <i>(Journal of Diabetes Science and Technology; 2010)</i>	Case Series SNAP Therapy	<ul style="list-style-type: none"> • 4 diabetic pts with refractory lower extremity wounds were treated with SNAP Therapy in the outpatient WCC setting 	<ul style="list-style-type: none"> • SNAP™ Therapy duration was 4 weeks in 3 pts and 6 weeks in 1 patient. • After use of SNAP Therapy for wound bed preparation: <ul style="list-style-type: none"> ○ 2 wounds achieved complete wound closure ○ 1 wound was closed with a single application of Apligraf® (Organogenesis, Inc., Canton, MA) ○ 1 wound was closed with a skin graft.

Author	Study Type	Patients	Results/Conclusions
<p>T Awad and M Butcher¹⁵</p> <p><i>(Wounds International; 2012)</i></p>	<p>Case Study</p> <p>SNAP Therapy</p>	<ul style="list-style-type: none"> • Middle-aged male with Type 2 diabetes and a history of 2 ulcerations on the lateral border of his left foot presented with a new ulceration on his left foot. Both previous ulcerations had been treated with portable NPWT devices • This third ulceration was extensive and presented over his previous ray amputation. Wound had slough, high exudate levels, and heavy bacterial colonization. There was exposed tendon in the base of the wound 	<ul style="list-style-type: none"> • Antibiotic therapy was commenced • SNAP Therapy was applied with a moistened antimicrobial gauze-interface layer beneath the hydrocolloid dressing • NPWT was initiated at -125 mmHg. Cartridge was attached to pt's leg to facilitate movement • Although advised to be non-weight-bearing, pt returned to "light duties" following discharge from the hospital. • There was significant wound size reduction during and after discontinuation of SNAP Therapy. Wound achieved full closure. • Compared to the prior different 2 battery-powered NPWT devices, pt preferred SNAP Therapy because it was light, portable, and easy to use. <ul style="list-style-type: none"> ○ Silent system did not disturb sleep and coworkers did not realize he was undergoing treatment.



Health Economics

In 2011 Hutton and Sheehan¹⁶ analyzed costs and effectiveness of 3 therapies for treatment of diabetic lower extremity wounds: modern wound dressings, powered NPWT, and SNAP Therapy. An economic model using peer-reviewed data was used to simulate outcomes for the different treatments. The proportion of patients expected to heal over a period of 16 weeks was used to measure costs and effectiveness, because the 16-week time period was standard for NPWT trials. Healing progress was modeled as “exponential decay of individuals remaining in therapy each week.”¹⁶ The model incorporated healing and complication rates in the literature for diabetic foot wounds and recent SNAP Therapy studies. The model also assumed equal efficacy between SNAP Therapy and powered NPWT based on clinical study results.¹⁶

Based on the model, the authors reported that, compared to modern dressings, SNAP Therapy saved over \$9,000 per wound treated by avoiding longer treatment times and costs for complications and healed more wounds. Healing time was similar for NPWT and SNAP Therapy; however, Medicare and private payer costs were \$2300 and \$2800 less, respectively, for SNAP Therapy patients. The authors concluded that, in addition to cost savings, SNAP Therapy also allowed patients greater mobility.¹⁶

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