Washington State Health Care Authority

Negative pressure wound therapy – Home use

Draft evidence report: Comments and response

October 14, 2016

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Negative Pressure Wound Therapy – Home Use
Response to Public Comments on Draft Report

October 14, 2016

Prepared by:

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Response to Public Comments, Draft Report

Negative Pressure Wound Therapy – Home Use

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

Comments related to program decisions, processes, or other matters not pertaining to the evidence report are acknowledged through inclusion only. When comments cite evidence, the information is forwarded to the vendor for consideration in the evidence report.

This document responds to comments from the following parties:

- Scott Fannin, DO, and Kathie Itter, Executive Director (Washington Osteopathic Medical Association [WOMA])
- Sharon Whalen, RN, MS, Sr. Director, Reimbursement & Health Policy (Acelity [KCI])
- Robin Martin, PhD (Smith & Nephew, Inc.)
- Greg Devereux, Executive Director Washington Federation of State Employees (AFSCME)

Table 1 provides a summary of the comments with corresponding responses.

Table 1. Public Comments on Draft Report, Negative Pressure Wound Therapy – Home Use

Key: FDA, Food and Drug Administration; HTA, health technology assessment; NPWT, negative pressure wound therapy; RCT, randomized controlled trial

Comment and Source	Response
September 13, 2016, letter from Scott Fannin, DO (Washington Osteopathic Medical Association)	
Comment: "The WOMA found that Aetna, Noridian (Medicare local carrier), the Oregon Health Evidence Review Commission, Group Health and Regence all cover, subject to criteria, outpatient NPWT. In contrast, we found that Regence and the Oregon Health Evidence Review Commission were described as not having a "Coverage Policy". This causes us concern about the due diligence practices of the preparer. WOMA is aware of the health technology assessment program's reliance on randomized controlled trials and similar data. We feel that far more reliable benchmarks are the coverage policies of health plans. In this era of cost-effective outcomes, the health plans simply do not cover technologies that do not improve patient outcomes and are cost effective in achieving those improved outcomes. The clinical committee's decisions are much more likely to achieve cost effective and improved outcomes if more weight is given to health plan coverage policies than on trials and studies that are of a low quality. NPWT is an excellent example of where an inaccurate coverage decision could be made if it is based on the relied upon evidence. When one reads the Hayes Report's Overall Summary and Discussion there are eleven negative comments. Relying on the "evidence" it would be possible to reduce access to NPWT whereas every plan we know of provides coverage to selected patients. WOMA appreciates the efforts of the clinical committee to make cost effective coverage decisions. We strongly believe, however, that the evidence that is most relevant is not a significant part of the current process. WOMA urges the health technology assessment program to place much more weight on health plan coverage than it currently does."	Thank you for your comment and review of the HTA. All statements in the report regarding coverage polices for home use of NPWT are correct and up-to-date. The results of the original search for published evidence-based policies regarding coverage of NPWT specifically for the Oregon Health Evidence Review Commission (HERC) and Regence Group were verified and found to be correct. No coverage policies were identified that outline clinical criteria required for coverage. Absence of a published policy is not meant to imply that a therapy is not covered. A Guideline Note regarding NPWT associated with Oregon's July 1, 2016, Prioritized List of Health Services (search for "Guideline Note 62" within this PDF) and an entry for NPWT in the Oregon Medical Fee and Payment Rules (code E2402) was identified. This section of the report has been updated to add further explanation regarding the Guideline Note. No additional published policy information was found to add to the results for the Regence Group search. The report on NPWT provides a systematic evaluation of the available scientific literature that describes how the technology affects specific and hopefully meaningful patient outcomes. Coverage or payment policy decisions from health plans are not considered the same level of evidence as peer-reviewed published scientific studies and are not considered as part of the evidence-base for the report, though they are described in the report.
September 19, 2016, comments from Greg Devereux, Executive Director, Washington Federation of State Employees (AFSCME)	
Comment: "it is my understanding that the Uniform Medical Plan administered	Thank you for your comment and review of the HTA. All statements in the

Comment and Source	Response
by Regence currently covers NPWT without restrictions, and Group Health covers NPWT with some restrictions. We are concerned that as a result of the cited low quality evidence in the Hayes report, it is possible that the Clinical Committee could further restrict or end access to NPWT on an outpatient basis. We express concern based on the understanding that Clinical Committee is to review the evidence from the research group, Hayes, and make coverage decisions based on that evidence. In reviewing the Overall Summary and Discussion of the Hayes report (pages 20-22) we note eleven (11) quotes where the evidence is of low quality, one neutral observation and two (2) positive references. Based on the preponderance of low quality evidence one would expect limited, if any, coverage. The Health Technology Assessment Program by-laws describe a hierarchy of evidence that does not include market practices. This, in our opinion, may lead to a scenario where PEBB subscribers have no coverage for a technology or device that is commonly covered in other plans. We base this concern on the definition found in the Appendix to the Clinical Committee's by-laws: [see attachment for quote from by-laws] WFSE contends that broad adoption of health plan policies covering NPWT is its own evidence and should be considered as such. We would draw attention to the following coverage decisions of national and regional health plans of NPWT: – The local Medicare carrier, Noridian, has issued a Local Coverage Decision (LCD) which covers NPWT with conditions on an outpatient basis. The effective date of the most recent review is October 1, 2015. – The Hayes report investigation was limited to a website review of Regence and states, "No coverage policy for NPWT was identified on their website." Further investigation would show that NPWT is a covered benefit. – Similarly, the Hayes report lists the Oregon Health Evidence Review Commission (HERC) as "No coverage guidance for NPWT" as determined by a website review, which does not actually express whether it or is not covered benefit.	report regarding coverage polices for home use of NPWT are correct and up-to-date. Please refer to the responses in reply to other comments regarding payer coverage policies. The purpose of the HTA program is to help determine what works and to ensure that state resources are used more effectively for care that is shown to provide value. Similar to the response above, the report on NPWT provides an evaluation of the available scientific literature that describes how the technology affects specific and hopefully meaningful patient outcomes. Coverage, payment policies, or market practices are not considered the same level of evidence as peer-reviewed published scientific studies and are not considered when assessing the strength of the evidence for the use of NPWT.

Comment and Source	Response
– Group Health follows the NPWT LCD criteria for its Medicare members (not mentioned in the Hayes report), and uses difference criteria for its non-Medicare population (described in the report). – The Blue Cross Blue Shield Association issued the following in January 2016: [see attachment for quoted excerpt from Blue Cross Blue Shield policy]. We also take this opportunity to respectfully raise concerns about the level of due diligence in reporting coverage policies of the selected health plans, limiting research to mere website review. The impression we were left with was NPWT was not covered by plans when, in fact, it appears that NPWT is a standard of care for certain patients with wounds that are not healing and needs no further evidence to merit coverage. Reliance on the HTAP evidence hierarchy could likely result in coverage policies that would negatively impact patient outcomes. As expressed above, we are concerned about this leading to a scenario where multitudes of non-PEBB subscribers have NPWT as a covered benefit, and PEBB-subscribers do not."	
September 16, 2016, e-mail from Sharon Whalen (Sr. Director, Reimbursement & Health Policy, Acelity)	
Comment: "KCI developed the first NPWT device and it has been an evidence based therapy for the last 27 years. NPWT has been a valuable therapy for many years and currently, all managed care organizations and Medicare cover the use of NPWT for a variety of indications in a variety of care settings, including outpatient and the home. As you are aware, each of the various insurance programs and companies has their own evidence-based review process. The clinical evidence for NPWT has been reviewed many times by many insurance plans, and each of them has reached the conclusion that NPWT is a covered benefit for their beneficiaries and members. It is important to note that the Hayes report was not entirely accurate in their review of current payer policies. Medicare (Noridian), Aetna, Cigna, Group Health, cover NPWT. Regence and Premera follow the Noridian policy and cover NPWT. In addition, the Blue Cross Blue Shield Association in 2016 reviewed NPWT in the home setting and found there was moderate level of evidence for NPWT with individuals with chronic wounds and co-morbidities affecting wound healing who are treated with NPWT. This was the same conclusion since 2014.	Thank you for your comment and review of the HTA. As stated above, all statements in the report regarding coverage polices for home use of NPWT are correct and up-to-date. Please see the response above regarding payer policies for Regence. Premera is not on the list of plans included in the report because it is not on the WA HTA Program's list of major health plans for which coverage policy information is required to be included in the report. The commentator did not provide a reference to the Blue Cross Blue Shield 2016 review mentioned in their comments; a search for the reference uncovered the following document with the subject "Negative Pressure Wound Therapy in the Outpatient Setting" from the Blue Cross Blue Shield Federal Employee Program, with a last review date of June 2016 and an effective date of July 15, 2016 (https://media.fep**blue**.org/-/media/7DDAD02646C24EA08BCE4C8F7 E3466C3.pdf). The document describes conditions for initiation and continuation of the use of powered NPWT devices. Citations include several systematic reviews from various organizations such as Blue Cross Blue Shield (2000), the Agency for Healthcare

Comment and Source	Response
They stated, *"The evidence is sufficient to determine qualitatively that the technology results in a meaningful improvement in the net health outcome."*	Research and Quality (2004, 2009, 2014), and the Cochrane Collaboration (2008, 2013, 2014, and 2015), as well as several primary studies. Conclusions stated in the summary of evidence section vary depending on wound type. The summary of evidence states that evidence is insufficient to determine effects of the technology on health outcomes for the following wound types: chronic pressure ulcers; traumatic or surgical wounds (acute or nonhealing), partial-thickness burns, and full-thickness burns. With respect to patients with chronic wounds and comorbidities affecting wound healing (further described as diabetic lower extremity ulcers of unknown duration, amputation wounds, and nonhealing lower extremity ulcers due to venous insufficiency), the evidence summary states that: "The largest body of evidence is for foot ulcers in patients who have diabetes, showing a higher rate of wound healing and fewer amputations with NPWT. A single RCT in patients with non-healing leg ulcers who were treated with skin grafts found a faster rate of healing with NPWT." The conclusion is that the evidence from systematic reviews and RCTs is sufficient to determine qualitatively that the technology results in a meaningful improvement in the net health outcome. The detailed description of the evidence in this policy document mentions the dearth of high-quality, direct or indirect evidence for the home/outpatient use of NPWT. This assessment of the quality of the evidence is consistent with those presented in the current HTA. This summary statement has not been added to the report because a summary of Blue Cross Blue Shield Association policies for independent entities other than for Regence Blue Cross Blue Shield was not requested by the WA HCA.
Comment: "We would like to make comments on the clinical evidence and conclusions from the Hayes group. Hayes identified only selected clinical studies to conduct their review and eliminated a vast majority of clinical evidence that has been accumulated over the years. In their review, Hayes generally concludes that the evidence was low for NPWT in various conditions. This is in vast contrast to the evidence-based reviews completed by Medicare and insurance companies that provides coverage for NPWT. Therefore we disagree with the "low" quality statement on evidence for NPWT. Below are	Thank you for your comments and additional citations. Hayes employed a systematic approach to the search and selection of studies for inclusion in this report and these are outlined in the report. The report was focused on the use of NPWT in the home setting; therefore, setting was an important factor in the selection of the best available evidence to answer the key questions outlined in the report. All of the citations provided by the commentator were reviewed and considered for eligibility in this HTA. Beyond those studies already cited and assessed in the draft report, no additional studies cited in the comment

Comment and Source	Response
specific comments we would like to provide to the Authority on the Hayes evaluation of clinical evidence. Once you review the additional clinical evidence and recognize the full list of payers that cover NPWT in the home setting, the Authority will appreciate the positive impact NPWT has had on patients."	met the inclusion criteria.
Comment: "The articles listed in the HTA report for diabetic foot ulcers (DFU), arterial ulcers, pressure ulcers (PU), venous insufficiency leg ulcers (VLU) and mixed ulcers provide evidence of effectiveness. For example, the study conducted by Blume is among the first large RCTs published utilizing V.A.C.® Therapy on DFUs with the majority of the patients being treated in the home care setting. However, we believe that additional smaller RCTs should also have been considered for inclusion in this HTA review since they represent higher levels of evidence than some of the large retrospective case series utilized in this report."	Thank you for your comment and review of the HTA. For key question 1a (chronic wounds), studies with fewer than 20 patients were excluded because they are likely to lack statistical power to detect meaningful differences in the outcomes of interest. Studies with small enrollments may also not be generalizable and may be at risk of unbalanced distribution between groups, depending on the randomization method employed. Because of the dearth of evidence from RCTs of any size for surgical wounds (key question 1b, surgical wounds), all RCTs were accepted if other inclusion criteria were met. However, the serious limitations of small sample sizes were noted and considered when assessing the strength of the evidence.
Comment: "We disagree with the HTA authors that state that the evidence available is of poor quality. We believe that the clinical outcome evidence from publications for DFUs provides a sufficient amount of clinical evidence supporting use of NPWT. However, the evidence for pressure ulcers and venous insufficiency ulcers is robust with several randomized control trials for each category."	Thank you for your comment and review of the HTA. Methods for assessing the quality of individual studies, bodies of evidence for specific outcomes, and overall bodies of evidence for each key question are described in the HTA.
Comment: "There are clinical effectiveness studies for NPWT on non-healing surgical wounds and surgical incisions. Table 2 illustrates many studies that have been published on the use V.A.C.® Therapy in the surgical arena. Table 3 reports the use of NPWT and disposable NPWT, PREVENA™ Therapy, over surgical incisions. For over 10 years, NPWT has been reported as a viable method to manage patient surgical incisions at risk for a surgical site infection (SSI). These studies include five randomized controlled trials, one meta-analysis, three prospective case controlled studies, eight retrospective patient record reviews, multiple case series and individual case studies. Table 2 is a partial listing of currently published studies. In 2009, Stannard et al first reported on the relationship	Thank you for your comment. We reviewed the citations provided. Two of the studies listed in Table 2 were already included in the draft HTA (Biter et al., 2014; and Armstrong et al., 2005). The other citations were reviewed and determined to not meet the inclusion criteria for this key question. Any-sized RCT was included for key question 1b if all other inclusion criteria were met.

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between patient related risk factors and the use of NPWT for prevention of SSI.[12;13] Recently, Willy et al concluded that both patient and wound related risk factors should be included in the decision making for managing surgical incisions prior to prescribing NPWT.[14] In conclusion, we believe that there is substantial evidence to support the use of NPWT in surgical wounds and surgical site incisions. As mentioned above, we also conclude that some of the smaller RCTs should be considered for inclusion since they represent higher levels of evidence than a large retrospective case series."	
Comment: "The harms for NPWT are well defined in the literature and manufacturer's Instructions for Use. Conversely, the incidence of these events is relatively low or unreported."	Thank you for your comment.
Comment: "Key Question #3 is asking for NPWT effectiveness or incidence of adverse events based on clinical history, wound characteristic, etc. The authors of this report provided clinical evidence of comparative reports of one type of NPWT compared to other NPWT systems. The reports emphasis was more on similar demographics and wound size of studies rather than reporting any adverseve events. The RCTs, such as Armstrong and Lavery (2005)[61], Blume et al (2008)[62], Armstrong (2012)[63], and Marston (2015)[64] reported on adverse events. Chronic wounds are complex in complex patients with multiple comorbidities [*sic*]. Therefore, the clinical evidence is usually presented by wound type with comorbid conditions as a subset analyses."	Thank you for your comment. One of the comparisons of interest for Key Question 3 was types of devices; therefore, we included studies that compared different NPWT devices with each other in this section of the report. Eligible clinical, patient-centered, and harms outcomes were presented if the studies reported them in a manner applicable to Key Question 3. Information about the role of wound chronicity from a 2007 publication of a subanalysis from the Armstrong et al. (2005) study has been added to the report. Also, a statement about adverse events in the venous leg ulcer subgroup analysis from Marston et al. (2015) was added.
Comment: "*Other NPWT Systems vs V.A.C.® Therapy* Although the vast majority of NPWT literature is reported using V.A.C.® Therapy, the number of alternative NPWT systems has increased over the years. Therefore, it is important to understand the differences that may exist among the different NPWT systems, such as ability to remove fluid in short amounts of time and to maintain target pressure from the wound site (Figure 2)."	Thank you for your comment.
Comment: "*Health economic retrospective review of Armstrong and Lavery 2005*	Thank you for your comment. Results from the Apelqvist et al. (2008) and Driver and Blume (2014) publications were included in the draft and final report. The Flack et al. (2008) analysis was added to the final report after

Comment and Source	Response
In 2008, Apelqvist et al published their findings on resource utilization and direct economic cost of care for patients treated with V.A.C.® Therapy compared to standard moist wound therapy (MWT). The analyses were based on the published RCT by Armstrong and Lavery. Apelqvist et al found that more surgical procedures, including debridement, were required for the MWT group (120 vs 43 V.A.C.® Therapy, p <.001). The average dressing change performed per patient was 118 (range 12-226) for MWT versus 41 (6-140) for V.A.C.® Therapy (p=0.0001). Outpatient treatment visits were 11 (range 0-106) for the MWT group versus 4 (range 0-47) in the NPWT group (p<0.05). The average total cost to achieve healing was $25,954 for V.A.C.® Therapy (n=43) compared to $38,806 for MWT group (n=33). The authors concluded that V.A.C.® Therapy-treated diabetic patients with post amputation wounds resulted in lower resource utilization and a greater number of patients obtaining wound healing at a lower overall cost of care compared to MWT. *Health economic retrospective review of Blume et al 2008* Recently , Driver and Blume (2014) published their findings on a post-hoc retrospective analysis of patients enrolled in an RCT (Blume et al, 2008) to evaluate overall costs of V.A.C.® Therapy (n=169) versus advanced moist wound therapy (AMWT; n=166) in treating grade 2 and 3 diabetic foot wounds during a 12-week therapy course. A total of 324 patient records (NPWT = 162; AMWT = 162) were analyzed. There was a median wound area reduction of 85.0% from baseline for V.A.C.® Therapy treated patients and 61.8% reduction in those treated with AMWT. Total cost for all patients, regardless of closure, was $1,941,472.07 for V.A.C.® Therapy group compared to $2,196,315.86 for AMWT group. For patients achieving complete wound closure, the mean cost per patient for V.A.C.® Therapy group was $10,172 compared to $9,505 for the AMWT group. The median cost per 1 cm^2 of closure was $1,227 for V.A.C.® Therapy and $1,695 for AMWT. In patients not achieving complete wound closure, the mean total wound care cost per patient was $13,262 for V.A.C.® Therapy group, compared to $15,069 for AMWT group. The median cost to close 1 cm^2 in non-healing wounds for V.A.C.® Therapy was $1,633, compared to $2,927 for AMWT. They concluded that the results show a greater cost effectiveness for V.A.C.® Therapy versus AMWT.	assessing the publication for eligibility. The Law and Beach (2014) citation referred to in the comment does not meet inclusion criteria; however, a publication titled, “Comparison of Health Care Costs and Hospital Readmission Rates Associated With Negative Pressure Wound Therapies” by Law et al. (2015) was included in the draft and final report.

Comment and Source	Response
Other health economics review In 2008, Flack et al reported on the cost-effectiveness of V.A.C.® Therapy compared to advanced wound dressings, for the treatment of diabetic foot ulcers in the US. They used a Markov model designed to estimate the cost per amputation avoided and the cost per quality-adjusted life year (QALY) of V.A.C.® Therapy, compared with both traditional and advanced dressings. The Markov model simulated 1000 patients over a one year period using transition probabilities obtained from the literature. The model analyzed health states, such as: uninfected ulcer; infected ulcer; infected ulcer post-amputation; healed; healed post-amputation; amputation; and death. Simulated patients initially treated with V.A.C.® Therapy switched to the advanced dressing after three months of treatment if their wound remained unhealed. Simulated patients treated with traditional or advanced dressings were assumed to continue with their treatment for the full 12 months if they remained unhealed. The model results demonstrate improved healing rates (61% versus 59%), more QALYs (0.54 versus 0.53) and an overall lower cost of care ($52,830 versus $61,757 per person) for V.A.C.® Therapy-simulated patients compared with advanced dressings. V.A.C.® Therapy was reported to be the dominant intervention when compared with traditional dressings. The model results indicate that V.A.C.® Therapy was less costly and more effective than both traditional and advanced dressings. The results were reported to be robust to changes in key parameters, including the transition probabilities. This evidence reports that V.A.C.® Therapy and the utility weights applied to health states are cost effective. *Large retrospective review of Optum database* An analysis was reported by Law and Beach (2014) who performed a retrospective observational database analysis, which was conducted by Premier Research Services (Charlotte, NC), that identified and followed to discharge hospitalization visits where NPWT was provided to patients.[65] The objective of this study was to assess hospital charges and readmission rates for patients who were treated with V.A.C.® Therapy versus other NPWT systems. De-identified hospital database records of patients treated between 01-Jul-2011 and 30-Jun-2013 with at least one NPWT claim were retrospectively analyzed. The analysis included 18,385 V.A.C.® Therapy discharges and 3,253 other NPWT	

Comment and Source	Response
discharges from 144 and 24 hospitals, respectively. Results showed V.A.C.® Therapy patients had 10% shorter LOS (13.0 vs. 14.5 days, respectively; *p*<0.0001)."	
September 19, 2016, comments from Robin Martin, PhD (Smith & Nephew, Inc.)	
Comment: "The Hayes review of the published evidence for NPWT used in the home has been professionally conducted using recognized methodology. The literature surveys cut off dates have been reported as mid-2016."	Thank you for your comment. An update literature search was conducted on September 12, 2016, for the final draft of the HTA. Three studies were added for the final report.
Comment: "It is refreshing to see the review attempt to examine the impact of NPWT on the burden of surgical wounds in the home care setting. A very significant proportion of wounds managed by NPWT in outpatient clinics or in the home setting are dehisced surgical wounds with delayed healing (Baharestani, Houliston-Otto, & Barnes, 2008). (Dowsett, Davis, Henderson, & Searle, 2012) There was some confusion as regards the description of what a relevant surgical wound is for the purpose of the review. The authors use a definition: *"….incisions made to initially closed skin and tissue in the course of a patient's care for an underlying health concern requiring surgical intervention. Surgical wounds that are closed by means such as sutures, staples, tape, or glue that hold the wound edges together are referred to as surgical wounds expected to heal by primary intention. Surgical wounds may also be left open for the healing process; these are referred to as surgical wounds healing by secondary intention"* This definition implies that surgical wounds have been intentionally left unclosed. Whilst this may sometimes occur in traumatic or military wounds, it is much more likely that surgical wounds in the home care setting will have been the result of Surgical Site infections or dehiscence. It is important that these two kinds of wounds are not confused."	Thank you for the comment and clarification that there are different types of wounds that may heal by secondary intention. Three of the studies included in the HTA for surgical wounds described the wounds as being left open after surgical intervention.
Comment: "The assessment of published studies has been well conducted in this review. It must be acknowledged however that using established assessment tools the NPWT evidence for closure and is frequently described as "low quality" whereas a descriptor of "low volume" might be a better summary. Although the number of studies using randomization is low, those that have been conducted favour NPWT and are of fair quality (Armstrong & Lavery, 2005) (Blume, Walters, Payne, Ayala, & Lantis, 2008). One of the	Thank you for your comment and review of the HTA. The quality assessment methods used in this HTA are described in detail within the report. Three levels of quality assessment are conducted. First, the quality of individual studies is rated using established methods. Second, the quality of a body of evidence for specific outcomes is assessed. Lastly, the overall body of evidence for a key question is determined. A number of factors are considered in determining the quality of the overall body of evidence for a specific outcome or for a key

Comment and Source	Response
attributes that increases the likelihood that a study is deemed of lower quality is the lack of blinding. This is much harder to accommodate in studies with devices which will leave marks on the skin that indicate the type of therapy than in pharmaceutical trials where a placebo medication is readily available. Although one must be aware of publication bias; the relative tendency for trials which demonstrate no significant effects to go unpublished, it is notable that no substantive and properly powered randomized studies have been conducted and reported that show no benefit of NPWT, when the interest in such a subject would almost certainly be published and guarantee the reputation of the investigators."	question; these include the quality of individual studies, the consistency of results, the directness of the results to the outcomes of interest, and the precision of the results. Applicability of the results to the population of interest is also assessed. In the draft and final report, we acknowledge the challenges of conducting double-blind studies for this technology and cite the FDA Guidance to Industry in this matter.
Comment: "At several places the review cites the non-specific details of the NPWT device used in a clinical trial, particularly a study conducted outside the US, as a reason to give less weight to its finding. In general, it seems to be accepted that NPWT devices are equivalent when studied in a randomized protocol. (Rahmanian-Schwarz, Willkomm, Gonser, Hirt, & Schaller, 2012), (Dorafshar, Franczyk, Gottlieb, Wroblewski, & Lohman, 2012), (Armstrong, Marston, Reyzelman, & Kirsner, 2012): each of these studies showed no difference between different NPWT systems. Lack of payer coverage was also cited for some of the newer single use systems: Prevena (Acelity) and PICO (Smith & Nephew) on the grounds that these devices have a poor evidence base. Large randomized studies in chronic wounds may not have been published using these single use devices – although one such study has already been conducted with the SNaP single use device which demonstrated non-inferiority with traditional reusable NPWT pumps (Armstrong et al., 2012). On the contrary the RCT evidence base for use of single use Prevena or PICO devices on closed surgical incisions is growing rapidly and has been the subject of recent systematic reviews (Hyldig et al., 2016) (De Vries et al., 2016) and publications (De Vries et al., 2016) (Karlakki et al., 2016). Other studies are ongoing and recorded in www.clinicaltrials.gov (NCT02470806) PICO vs traditional NPWT."	Thank you for your comment and review of the HTA. Details about which devices are used may be relevant when considering applicability to U.S. settings. Without those details, there is uncertainty with regard to applicability. However, this does not affect the internal validity of the study. Regarding evidence showing no difference between devices, only 1 of the studies (Armstrong et al., 2012) listed in the comment was evaluated in this review; the others did not meet inclusion criteria. Statements regarding lack of coverage for specific devices because they have a poor evidence base were extracted from the payer policies. One of the newer studies (Karlakki et al., 2016) referenced in the comments was identified in the update literature search and added to the HTA.
Comment: "Using the same methodology for the incidence of adverse events in randomized studies as used for outcomes, there is little evidence for an increased safety risk using NPWT compared to standard care."	Thank you for this comment.
Comment: "In a professional assessment of the evidence for NPWT in Chronic	Thank you for your comment and review of the HTA. The quality assessment

Comment and Source	Response
and Delayed healing infected or dehisced surgical wounds a Hayes Inc. review found more evidence in favour of the use of NPWT in these wound types, than against it. Whilst the evidence is undoubtedly of low volume, the best conducted studies find in favour of NPWT. Evidence generation is active, in particular for single use devices that have substantially changed the economics of the deployment of NPWT in homecare settings since the first days of commercial NPWT using more expensive reusable devices."	methods used in this HTA are described in detail within the report. Three levels of quality assessment are conducted. First, the quality of individual studies is rated using established methods. Second, the quality of a body of evidence for specific outcomes is assessed. Lastly, the overall body of evidence for a key question is determined. A number of factors are considered in determining the quality of the overall body of evidence for a specific outcome or for a key question; these include the quality of individual studies, the consistency of results, the directness of the results to the outcomes of interest, and the precision of the results. Applicability of the results to the population of interest is also assessed.

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September 19, 2016

Mr. Josh Morse, Director
Josh.morse@hca.wa.gov
Washington State Health Technology Assessment Program

Dear Mr. Morse,

The Washington Osteopathic Medical Association (WOMA) welcomes the opportunity to submit comments on the Hayes report relating to negative pressure wound therapy (NPWT). The WOMA believes that NPWT can be a valuable adjunct to wound therapy in patients with underlying comorbidities and other complications which compromises wound healing. We are aware that virtually all health plans our members deal with cover NPWT for such patients and we are confused by the Hayes Report's characterization of some health plans as not having coverage policies.

The WOMA found that Aetna, Noridian (Medicare local carrier), the Oregon Health Evidence Review Commission, Group Health and Regence all cover, subject to criteria, outpatient NPWT. In contrast, we found that Regence and the Oregon Health Evidence Review Commission were described as not having a "Coverage Policy". This causes us concern about the due diligence practices of the preparer.

WOMA is aware of the health technology assessment program's reliance on randomized controlled trials and similar data. We feel that far more reliable benchmarks are the coverage policies of health plans. In this era of cost-effective outcomes, the health plans simply do not cover technologies that do not improve patient outcomes and are cost effective in achieving those improved outcomes. The clinical committee's decisions are much more likely to achieve cost effective and improved outcomes if more weight is given to health plan coverage policies than on trials and studies that are of a low quality.

NPWT is an excellent example of where an inaccurate coverage decision could be made if it is based on the relied upon evidence. When one reads the Hayes Report's Overall Summary and Discussion there are eleven negative comments. Relying on the "evidence" it would be

possible to reduce access to NPWT whereas every plan we know of provides coverage to selected patients.

WOMA appreciates the efforts of the clinical committee to make cost effective coverage decisions. We strongly believe, however, that the evidence that is most relevant is not a significant part of the current process. WOMA urges the health technology assessment program to place much more weight on health plan coverage than it currently does.

Again, we appreciate the opportunity to comment.

Sincerely yours,

Scott Fannin, DO
President

Pc/BOG
File 31b

Council 28
AFSCME
Washington Federation of State Employees

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September 19, 2016

Josh Morse, Director
Josh.morse@hca.wa.gov
Washington Health Technology Assessment Program

Dear Mr. Morse,

The Washington Federation of State Employees (WFSE) welcomes the opportunity to submit comments on the Hayes report relating to negative pressure wound therapy (NPWT). It is my understanding that the Uniform Medical Plan administered by Regence currently covers NPWT without restrictions, and Group Health covers NPWT with some restrictions. We are concerned that as a result of the cited low quality evidence in the Hayes report, it is possible that the Clinical Committee could further restrict or end access to NPWT on an outpatient basis.

We express this concern based on the understanding that the Clinical Committee is to review the evidence from the research group, Hayes, and make coverage decisions based on that evidence. In reviewing the ***Overall Summary and Discussion*** of the Hayes report (pages 20-22) we note eleven (11) quotes where the evidence is of low quality, one (1) neutral observation and two (2) positive references. Based on the preponderance of low quality evidence one would expect limited, if any, coverage.

The Health Technology Assessment Program by-laws describe a hierarchy of evidence that does not include marketplace practices. This, in our opinion, may lead to a scenario where PEBB subscribers have no coverage for a technology or device that is commonly covered in other plans. We base this concern on the definition found in the Appendix to the Clinical Committee's by-laws:

> "Evidence-based" means the objective, ordered, and explicit use of the best available evidence when making a coverage or reimbursement determination. Greatest weight is given to the evidence determined, based on objective factors, to be the most valid and reliable, considering the nature and source of the evidence, the empirical characteristic of the studies or trials upon which the evidence is based, and the consistency of the outcome with comparable studies. Additional evidentiary valuation factors such as recency (date of information); relevance (the applicability of the information to the key questions presented or participating agency programs and clients); and bias (conflict of interest or political considerations) may also be considered.

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WFSE contends that the broad adoption of health plan policies covering NPWT is its own evidence and should be considered as such. We would draw attention to the following coverage decisions of national and regional health plans of NPWT:

- The local Medicare carrier, Noridian, has issued a Local Coverage Decision (LCD) which covers NPWT with conditions on an outpatient basis. The effective date of the most recent review is October 1, 2015.

- The Hayes report investigation was limited to a website review of Regence and states, "No coverage policy for NPWT was identified on their website." Further investigation would show that NPWT is a covered benefit.

- Similarly, the Hayes report lists the Oregon Health Evidence Review Commission (HERC) as "No coverage guidance for NPWT" as determined by a website review, which does not actually express whether it or is not a covered benefit.

- Group Health follows the NPWT LCD criteria for its Medicare members (not mentioned in the Hayes report), and uses different criteria for its non-Medicare population (described in the report).

- The Blue Cross Blue Shield Association issued the following in January 2016:

    - From Blue Cross Blue Shield Association is an association of independent Blue Cross and Blue Shield companies. © 2016 Blue Cross Blue Shield Association. Original Review Date: Jul 1998 Current Review: Jan 2016 Next Review: Jan 2017

Indication 2: Individuals with chronic wounds and co-morbidities affecting wound healing who are treated with negative pressure wound therapy. **The evidence is sufficient to determine qualitatively that the technology results in a meaningful improvement in the net health outcome. (Emphasis added)**	Evidence Level Moderate for 2014 2015 2016 2017

We also take this opportunity to respectfully raise concerns about the level of due diligence in reporting coverage policies of the selected health plans, limiting research to mere website review. The impression we were left with was NPWT was not covered by plans when, in fact, it appears that NPWT is a standard of care for certain patients with wounds that are not healing and needs no further evidence to merit coverage. Reliance on the HTAP evidence hierarchy could likely result in coverage policies that would negatively impact patient outcomes. As

expressed above, we are concerned about this leading to a scenario where multitudes of non-PEBB subscribers have NPWT as a covered benefit, and PEBB-subscribers do not.

Thank you for your consideration.

Sincerely,

[redacted]

Greg Devereux
Executive Director

c: Alia Griffing, Director of Research & Policy

John Morse, MPH
Program Director
Washington State Health Care Authority
Health Technology Assessment
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Electronically submitted to: shtap@hca.wa.gov.

Dear Mr. Morse

We appreciate the opportunity to provide comments to the Heath Care Authority on the Hayes Health Technology Assessment of Negative Pressure Wound Therapy (NPWT) in the Home Setting. Acelity is a global wound care and regenerative medicine company that is is focused on developing products and therapies that improve clinical outcomes while helping reduce the overall cost of patient care. Kinetic Concepts Inc (KCI) is a division within Acelity, Inc. and is the leader in NPWT.

KCI developed the first NPWT device and it has been an evidence based therapy for the last 27 years. NPWT has been a valuable therapy for many years and currently, all managed care organizations and Medicare cover the use of NPWT for a variety of indications in a variety of care settings, including outpatient and the home. As you are aware, each of the various insurance programs and companies has their own evidence-based review process. The clinical evidence for NPWT has been reviewed many times by many insurance plans, and each of them has reached the conclusion that NPWT is a covered benefit for their beneficiaries and members. It is important to note that the Hayes report was not entirely accurate in their review of current payer policies. Medicare (Noridian), Aetna, Cigna, Group Health, cover NPWT. Regence and Premera follow the Noridian policy and cover NPWT.

In addition, the Blue Cross Blue Shield Association in 2016 reviewed NPWT in the home setting and found there was moderate level of evidence for NPWT with individuals with chronic wounds and co-morbidities affecting wound healing who are treated with NPWT. This was the same conclusion since 2014. They stated, *"The evidence is sufficient to determine qualitatively that the technology results in a meaningful improvement in the net health outcome.'*

We would like to make comments on the clinical evidence and conclusions from the Hayes group. Hayes identified only selected clinical studies to conduct their review and eliminated a vast majority of clinical evidence that has been accumulated over the years. In their review, Hayes generally concludes that the evidence was low for NPWT in various conditions. This is in vast contrast to the evidence-based reviews completed by Medicare and insurance companies that provides coverage for NPWT. Therefore we disagree with the "low" quality statement on evidence for NPWT. Below are specific comments we would like to provide to the Authority on the Hayes evaluation of clinical evidence.

Once you review the additional clinical evidence and recognize the full list of payers that cover NPWT in the home setting, the Authority will appreciate the positive impact NPWT has had on patients.

If you have any questions or if we could provide any additional materials please feel free to contact me.

Sincerely,
Sharon Whalen, RN MS

Clinical Evidence and Review of the Washington State Health Care Authority HTA-Negative Pressure Wound Evidence Report prepared by Hayes.

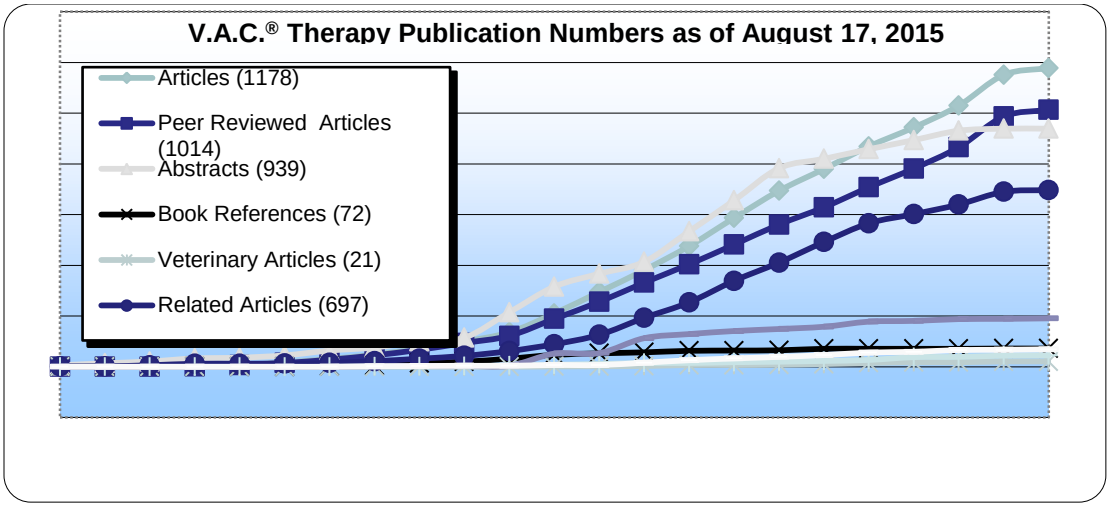
Executive Summary

Wound healing progression involves removal of barriers to wound healing such as exudate, adequate perfusion to the wound bed and production of 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 (NPWT). NPWT is utilized across the continuum of care and has substantial amounts of clinical outcome data to demonstrate efficacy to create an environment that promotes healing in a wide variety of wounds.

For over 35 years, KCI has led the way in the development of new technologies and therapies designed to make wound healing more efficacious and economical, as well as manageable for caregivers and more comfortable for patients around the world. The first NPWT system was available in 1997 with the introduction of the V.A.C.® Therapy System. The V.A.C.® Therapy System (V.A.C.® Therapy) is FDA cleared and 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.

Out of all the NPWT products, KCI's V.A.C.® Therapy has the largest body of evidence to date, including over 1000 peer reviewed articles, of which 44are randomized controlled trials (RCT) (Figure 1). These studies have demonstrated several benefits of NPWT, as well as the effectiveness of V.A.C.® Therapy in helping to manage diabetic foot wounds, chronic wounds (eg, pressure ulcers and lower extremity ulcers), and a variety of acute wounds.

Figure 1: V.A.C.® Therapy Publication Numbers



Key Question 1a: What is the clinical effectiveness of NPWT in the home or outpatient settings for treatment of chronic wounds?

The clinical effectiveness of NPWT for wounds, specifically the use of V.A.C.® Therapy, has been published in over 100 articles for chronic wounds (Table 1). These articles include 8 RCTs, 1 meta-analysis and a prospective clinical trial.

Table 1: Literature review of V.A.C.® Therapy and Chronic Wounds

Wound Type	Number of Articles	Key References
Chronic Wounds		
Ulcers		
Pressure	44	[1]Wanner et al 2003 (RCT) [2]Ford et al 2002 (RCT) [3]Joseph et al 2000 (RCT) [4]Wild et al 2008 (RCT) [5]Ashby et al 2012 (RCT)
Diabetic Foot	49	[6]Suissa et al 2011 (Meta Analysis) [7]Blume et al 2008 (RCT)
Venous Insufficiency	16	[8]Egemen et al 2012 (PCT; Level 2) [9]Vuerstaek et al 2006 (RCT) [10]Dini et al 2010 (RCT)

Authors Suissa, Danimo and Andreas published a meta-analysis of randomized trials of NPWT vs standard wound care. Their results demonstrated that NPWT appears to be an effective treatment for chronic wounds.[11]

The articles listed in the HTA report for diabetic foot ulcers (DFU), arterial ulcers, pressure ulcers (PU), venous insufficiency leg ulcers (VLU) and mixed ulcers provide evidence of effectiveness. For example, the study conducted by Blume is among the first large RCTs published utilizing V.A.C.® Therapy on DFUs

with the majority of the patients being treated in the home care setting. However, we believe that additional smaller RCTs should also have been considered for inclusion in this HTA review since they represent higher levels of evidence than some of the large retrospective case series utilized in this report. We disagree with the HTA authors that state that the evidence available is of poor quality. We believe that the clinical outcome evidence from publications for DFUs provides a sufficient amount of clinical evidence supporting use of NPWT. However, the evidence for pressure ulcers and venous insufficiency ulcers is robust with several randomized control trials for each category.

Key Question 1b: What is the clinical effectiveness of NPWT in the home or outpatient settings for treatment of non-healing closed or open surgical wounds (eg, surgical incisions to heal by primary or secondary intention)?

Surgical wounds

There are clinical effectiveness studies for NPWT on non-healing surgical wounds and surgical incisions. Table 2 illustrates many studies that have been published on the use V.A.C.® Therapy in the surgical arena. Table 3 reports the use of NPWT and disposable NPWT, PREVENA™ Therapy, over surgical incisions.

For over 10 years, NPWT has been reported as a viable method to manage patient surgical incisions at risk for a surgical site infection (SSI). These studies include five randomized controlled trials, one meta-analysis, three prospective case controlled studies, eight retrospective patient record reviews, multiple case series and individual case studies. Table 2 is a partial listing of currently published studies. In 2009, Stannard et al first reported on the relationship between patient related risk factors and the use of NPWT for prevention of SSI.[12;13] Recently, Willy et al concluded that both patient and wound related risk factors should be included in the decision making for managing surgical incisions prior to prescribing NPWT.[14]

In conclusion, we believe that there is substantial evidence to support the use of NPWT in surgical wounds and surgical site incisions. As mentioned above, we also conclude that some of the smaller RCTs should be considered for inclusion since they represent higher levels of evidence than a large retrospective case series.

Table 2: Literature review of V.A.C.® Therapy and Acute Wounds

Wound Type	Number of Articles	Key References
Acute Wounds		
Surgical Wounds	333	[15]Biter et al 2014 (RCT; Level 1) [16]Long et al 2014 (PCT; Level 2)long [17]Falagas et al 2013 (CRS, Level 3) [18]Sziklavari et al 2011 (PCT; Level 3) [19;20]Zannis et al 2009 (PCT; Level 3) [21]Siegel et al 2007 (CRS; Level 3) [22]De Feo et al 2011 (CRS; Level 3) [23]Fuchs et al 2005 (CRS; Level 3) [24]Song et al 2003 (CRS; Level 3) [25]Bickels et al 2005 (CRS; Level 3) [26]de Leon et al 2009 (CRS; Level 3) [27]Yang et al 2006 (CRS; Level 3)
General Trauma	28	[28]Milcheski et al 2014 (PCT; Level 2) [29]Babiak et al 2012 (PCT; Level 2) [30]Stannard et al 2006 (RCT; Level 1) [31]Machen et al 2007 (CSE; Level 4) [32]Labler et al 2007 (CST; Level 4)
Grafts	99	[33]Blume et al 2010 (CRS; Level 3) [34]Vidrine et al 2005 (CRS; Level 3) [35]Stone et al 2004 (CRS; Level 3) [36]Moisidis et al 2004 (RCT; Level 1) [37]Scherer et al 2002 (CSE; Level 3) [38]Jeschke et al 2004 (RCT; Level 1) [39]Eisenhardt et al 2012 (RCT; Level 1)
Diabetic Foot Amputations	15	[40]Lavery et al 2008 (CRS; Level 3) [41]Armstrong and Lavery 2005 (RCT; Level 1) [42]Dalla Paola 2010 (RCT; Level 1) [43]Eginton et al 2003 (RCT; Level 1)

Table 3: Literature review of NPWT and disposable NPWT Prevena Therapy over surgical incisions

Author	Study Type	Patients	Results/Conclusions
JP Stannard et al[44] *(Journal of Orthopaedic Trauma, 2012)*	RCT V.A.C.® Therapy (NPWT) vs Standard Postoperative Dressings®	• 249 patients with 263 calcaneus, pilon and tibial plateau fractures • Randomization: NPWT, 130 patients (141 fractures) vs Control, 119 patients (122 fractures).	• Significant decrease for incidence of dehiscence (12 cases [NPWT] vs 20 cases [Control]; P = 0.044) • Significant decrease for total infections (14 cases [NPWT] vs 23 cases [Control]; P = 0.049) • Incidence of acute infection trended lower with NPWT (1 case) vs control (5 cases)

JP Stannard et al[45] *(Journal of Trauma, 2006)*	RCT (Interim Analysis) V.A.C. Therapy (NPWT) vs Standard Postoperative Dressings	• 44 patients with high-energy trauma wounds with draining hematomas (31 Control and 13 NPWT) • 44 patients with high-energy fractures (24 Control and 20 NPWT)	• High-energy trauma wounds: Control group drained a mean of 3.1 days compared to only • 1.6 days for NPWT (P = 0.03) • High-energy fractures: Control group drained a mean of 4.8 days compared to only 1.8 days for NPWT (P = 0.02)
Masden et al[46] *(Annals of Surgery, 2012)*	RCT NPWT vs Standard dry silver dressings (Control) [1]	• 81 high-risk patients with multiple comorbidities whose closed sur- gical incisions with treated with: • NPWT (n=44) • Control (n=37) • Majority (74/81) of patients underwent lower extremity wound closure post amputation. • All incisions were evaluated on postoperative day 3, at first out- patient visit, and at subsequent visits. Average follow-up period was 113 days.	• No differences in demographic, preoperative, and operative variables between groups • Wound complication rates did not achieve statistical significance between the groups: ○ Infection: NPWT, 3/44 (6.8%) vs. Control, 5/37 (13.5%), p = 0.46 ○ Dehiscence: NPWT, 16/44 (36.4%) vs. ○ Control, 11/37 (29.7%), p = 0.53 ○ Reoperation: NPWT, 9/44 (21%) vs.Control, 8/37 (22%), p = 0.89 ○ Overall, 40% of NPWT and 35% of Control groups experienced wound infection, dehiscence, or both.
M Pachowsky et al[47] *(International Orthopaedics, 2011)*	RCT Disposable NPWT Prevena Incision Management System (NPWT) vs Standard Postoperative Dressings [1]	• 19 patients (10 Control and 9 NPWT) with closed incisions after total hip arthroplasty. • Postoperative seromas were mea- sured in both groups on the fifth and tenth postoperative days.	• Significantly decreased development of postoperative seromas in the NPWT group on postoperative day 10 (average volume of 1.97 ml) compared to Control (5.08 ml) (P = 0.021) • A seroma was present in 44% of the NPWT patients and 90% of the Control patients • The NPWT group received significantly fewer days of antibiotics (8.44 ± 2.24 vs 11.8 ± 2.82 days, P = 0.005) • A secretion in the wound after day 5 was reported in fewer patients in the NPWT group (1 vs 5 patients)
J Pauser et al[48] *(International Wound Journal, 2014)*	RCT Disposable NPWT Prevena Incision Management System (NPWT) vs. Standard Postoperative Dressings	• 21 patients with femoral neck fractures (FNF) treated with hip hemiarthroplasty (HA) who were randomized to receive either incision NPWT (iNPWT) or standard postoperative dressings (Control) over clean sutured wounds. ○ Control: 10 patients ○ iNPWT (Prevena Therapy): 11 patients • There were no differences in patient age, coagulation time, postoperative wound size, or wound secretion volume.	• Compared to the Control, iNPWT patients had: ○ Reduced seroma volume at postoperative day 5 (0.257 ± 0.75 cm^3 vs. 3.995 ± 5.01 cm^3, respectively; $p<0.05$); at postoperative day 10, no difference was reported ○ Fewer days of wound secretions (0.9 ± 1.0 days vs. 4.3 ± 2.45 days, respectively; $p=0.0005$) ○ Fewer dressing changes (5.4 vs. 9.5, respectively; $p<0.0001$) ○ Reduced time (and materials) for dressing changes (14.9 ± 3.9 minutes vs. 42.9 ± 11.0 minutes, respectively; $p<0.0001$) • The authors concluded that using iNPWT for closed wounds in the HA setting "might help to reduce complications of prolonged wound healing and postoperative seroma in the wound…and save time needed for wound care"

DP Singh et al *(Plastic and Reconstructive Surgery, 2015)*	Retrospective Review of Patient Records V.A.C. Therapy (NPWT)	• Meta-analysis of 14 studies comprising 4,631 patients that compared the effectiveness of closed incision negative pressure therapy (ciNPT) versus standard dressings (control) on SSI occurrence and wound dehiscence ○ Control: 3,526 patients ○ ciNPT: 1,105 patients	• Compared to the Control, ciNPT patients had: ○ Decreased rates of surgical site infections (6.61% vs. 9.36%, respectively) ○ Reduced rates of dehiscence (5.32% vs. 10.68%, respectively). However, because the statistical heterogeneity among these studies was too high, further investigation is required. • The results of this meta-analysis support ciNPT as a valid approach for reducing SSIs. • The authors "…recommend considering the use of ciNPT over surgical incisions at relatively high risk of wound infection and dehiscence and in patients with multiple comorbidities."
O Grauhan et al[49] *(Journal of Thoracic and Cardiovascular Surgery, 2013)*	Prospective Comparative Study Disposable NPWT Prevena Incision Management System (NPWT) vs conventional sterile wound dressings (Control)	• 150 consecutive obese (BMI 30) patients, whose sternotomy wound incisions were treated with: • Prevena Therapy (n=75) • Control (n=75) ○ Primary study endpoint: Wound infection within 90 days ○ Patients allocated to treatment groups by alternating based on time of operation. ○ Patients with diabetes assigned "half and half to both groups, with priority." • Dressing changes: ○ Prevena Therapy: Placed under sterile OR conditions; kept at 125mmHg for the first 6 to 7 postoperative days. • Control: Changed on the first or second postoperative day and every 1-2 days thereafter. • No significant preoperative patient differences between groups. • All patients followed for at least 90 days.	• Prevena Therapy group, compared to Control group, had significantly fewer ○ Wound infections: 3/75 (4%) vs. 12/75 (16%), respectively; P= 0.0266; odds ratio,4.57; 95% confidence interval (CI), 1.23-16.94. ○ Patients whose wound infections had Gram-positive skin flora: 1 vs. 10, respec- tively; P= .0090; odds ratio, 11.39; 95% CI, 1.42-91.36. • Timing of wound infection incidence: ○ Prevena Therapy group: 71/75 (95%) of the incisions were primarily closed when the dressing was removed in 6 to 7 days. No wound infections occurred after post- operative day 7. ○ Control group: 9/12 wound infections occurred beyond postoperative day 7 and up to day 35. • Authors concluded that Prevena Therapy over clean, closed surgical incisions for the first 6 to 7 postoperative days significantly reduced wound infection after median sternotomy for high-risk obese cardiac surgery patients

G Weir[50] *(International Wound Journal, 2014)*	Prospective Case-Control Pilot Study Disposable NPWT Prevena Incision Management System (NPWT) vs. conventional postoperative wound dressings (Control)	• 8 patients undergoing vascular bypass procedures • Patients required bilateral femoral access. • Prevena was placed on one femoral area; contralateral femoral area received standard postoperative dressing (Control). • Patients required intra-operative heparin and postoperative anti-coagulation therapy. • Patients had at least one of the following risk factors for development of wound complications: obesity, diabetes, hypertension, hypercholesterolemia, smoking within 6 weeks prior to surgery, and HIV/AIDS.	• Wound complications requiring surgical intervention occurred in three of the control wounds, while no wound complications occurred where Prevena Therapy was applied. • The authors suggested that using Prevena Therapy in high-risk patients undergoing vascular surgery potentially reduced wound complications with no observable increase in hemorrhage.

O Grauhan et al[51]
 	
(International Wound Journal, 2014)
	Prospective Comparative Study
	
	Disposable NPWT Prevena Incision Management System (NPWT) vs. conventional sterile wound dressings (Control)
		• 3745 cardiac surgery patients undergoing sternotomy
		  ○ Prevena Therapy (n=237)
		  ○ Control (n=3,508)
		• Primary study endpoint: Wound infection within 30 days
		• Dressing changes
		  ○ Prevena Therapy: Applied immediately after skin suturing and remained in place for 6-7 days.
		  ○ Control: Changed on the first or second postoperative day and every 1-2 days thereafter.
		• All patients followed for at least 30 days
			• The Prevena Therapy group had a significantly lower infection rate than the Control group: 3/237 (1.3%) vs. 119/3508 (3.4%), respectively; p<0.05; odds ratio 2.74.
			• In the Prevena Therapy group, 234/237 (98.7%) of the incisions were primarily closed when the dressing was removed 6-7 days after application.
			• The authors concluded that using Prevena Therapy for the first 6-7 days over clean, closed surgical incisions reduced the incidence of postoperative wound infections, and the reduced rate in wound infections may be cost effective for patients, hospitals, and health insurance companies.

SH Swift et al[52]
 	
(Journal of Reproductive Medicine, 2015)
	Retrospective Review of Patient Records
	
	Dispsaobe NPWT Prevena Incision Management System Therapy (NPWT)
		• 319 women at increased risk for infectious morbidity and wound complications after cesarean delivery
		  ○ Control: 209 patients
		  ○ NPWT: 110 patients
		• Patients were followed as part of postpartum care or were followed up at 6 weeks postpartum.
			• Compared to the Control, NPWT patients had:
			  ○ Fewer postoperative complications (21.0% vs. 6.4%, respectively; p=0.0007)
			  ○ Fewer wound infections (11.5% vs. 2.7%, respectively; p=0.008)
			  ○ Fewer cases of endometritis (6.7% vs. 0.9%, respectively; p=0.023)
			  ○ Approximately the same number of wound separation cases (3.8% vs. 2.7%, respectively; p=0.754)
			• The NPWT group, who were at increased risk for postoperative infections and wound complications, had significant reductions in deep and superficial infectious morbidity after the NPWT system was applied to closed cesarean section incisions.

DP Singh et al[53] *(Plastic and Reconstructive Surgery, 2015)*	Retrospective Review of Patient Records V.A.C. Therapy (NPWT)	• Meta-analysis of 14 studies comprising 4,631 patients that compared the effectiveness of closed incision negative pressure therapy (ciNPT) versus standard dressings (control) on SSI occurrence and wound dehiscence ○ Control: 3,526 patients ○ ciNPT: 1,105 patients	• Compared to the Control, ciNPT patients had: ○ Decreased rates of surgical site infections (6.61% vs. 9.36%, respectively) ○ Reduced rates of dehiscence (5.32% vs. 10.68%, respectively). However, because the statistical heterogeneity among these studies was too high, further investigation is required. • The results of this meta-analysis support ciNPT as a valid approach for reducing SSIs. • The authors "…recommend considering the use of ciNPT over surgical incisions at relatively high risk of wound infection and dehiscence and in patients with multiple comorbidities."
RN Reddix et al[54] *(Journal of Surgical Orthopaedic Advances, 2010)*	Retrospective Review of Patient Records V.A.C. Therapy (NPWT) vs Standard Postoperative Dressings (Control)	• 66 patients with acetabular fractures treated with standard postoperative care (Control) • 235 patients with acetabular fractures treated with NPWT	• The authors noted that their infection rate of 1.27% represented a significant decrease in comparison to other groups (infection rates of 4.2%,[55]4%,[56] and 5%[57]) of similar size (P=0.0282; reference rate =4%). • Application of NPWT over incisions decreased incidence of perioperative incision complications at the author's institution.
R Tauber et al[58] *(Journal of Plastic, Recon- structive and Aesthetic Surgery, 2013)*	Retrospective Review of Patient Records V.A.C. Therapy (NPWT) vs Conventional Compres- sion Dressings (Control)	• 24 patients who underwent 45 inguinal lymph node dissections (LNDs) as treatment for penile or urethral cancer o NPWT: 8 patients (15 LNDs) o Control: 16 patients (30 LNDs)	• NPWT was applied using V.A.C.® WhiteFoam Dressing, and NPWT dressings remained in place for up to 7 days • Compared to NPWT, Control patients tended to have: ○ Higher levels of maximum drained fluid per day (P=0.496) ○ Longer duration of drainage (P=0.632). ○ More reinterventions (7 vs 1, respectively; P=0.631). ○ NPWT patients had significantly fewer wound complications (p= 0.032) than Control pa tients: • 20% vs 62% incidence of lymphoceles, respectively • 7% vs 45% persistent lymphorrhoea • 0% vs 46% lower extremity lymphoedema ○ Along with shorter hospital stay, the authors commented that NPWT patients benefitted because ". . . further oncological treatments could be administered without delay."

T Matatov et al[59] *(Journal of Vascular Surgery, 2013)*	Retrospective Review of Patient Records V.A.C. Therapy (NPWT) vs Skin Adhesive or Absorbent (Control)	• 90 vascular surgery patients with 115 groin incisions for longitudinal or transverse femoral cut-down ○ Prevena Therapy: 41 patients (52 incisions) ○ Control: 49 patients (63 incisions)	• Used Szilagyi scale to rate degree of infection from grade I (lowest) to grade 3 (highest) • Prevena Therapy was applied intraoperatively and removed after 5-7 days. • Mean times of wound evaluation: Prevena Therapy, 7 and 33 days postoperatively vs Control: 10 and 40 days • Prevena Therapy-treated incisions had sig- nificantly lower overall rate of infection: 3/52 (6%) vs 19/63 (30%), p=0.0011 • Incidence and severity of infections by group: • Prevena Therapy: 3 infections, all Szilagyi grade I ○ Control: 19 infections, 10 (16%) Szilagyi grade I, 7 (11%) grade II, and 2 (3%) grade III ○ According to the authors, Prevena Therapy "significantly decreased the incidence of groin wound infection in patients after vascular surgery"
AU Blackham et al[60] *(American Journal of Surgery, 2013)*	Retrospective Review of Patient Records V.A.C. Therapy (NPWT) vs standard sterile dress- ings (Control)	• 189 patients underwent 191 surgical procedures for pancre- atic, colorectal, or peritoneal surface malignancies ○ NPWT: 104 cases ○ Control: 87 cases	• Patients evaluated as being at risk for develop- ment of SSIs were treated with NPWT • Compared to Control patients, NPWT patients had significantly: ○ More neoadjuvant chemotherapy (P=0.024) ○ More clean-contaminated operations (P<0.001) ○ Longer operation times (P<0.001) ○ Greater intraoperative blood loss (P<0.001) o More frequent blood transfusions (P=0.002) • NPWT patients had significantly fewer inci- sional SSIs compared to SSD patients • In a subset analysis of clean-contaminated cases, NPWT was associated with significantly fewer: • Superficial incisional SSIs (6.0% vs 27.4%, P=0.001) • Total SSIs (16.0% vs 35.5%, P=0.011) • Wound openings for any reason (16.0% vs 35.5%, P=0.011) • In this study, NPWT decreased incidence of SSIs in surgical oncology patients • An RCT is planned to further evaluate the efficacy of incisional NPWT in this patient population.

KEY QUESTION #2 WHAT ARE THE HARMS ASSCOIATED WITH NPWT?

The harms for NPWT are well defined in the literature and manufacturer's Instructions for Use.

Conversely, the incidence of these events is relatively low or unreported.

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

Key Question #3 is asking for NPWT effectiveness or incidence of adverse events based on clinical history, wound characteristic, etc. The authors of this report provided clinical evidence of comparative reports of one type of NPWT compared to other NPWT systems. The reports emphasis was more on similar demographics and wound size of studies rather than reporting any adverseve events. The RCTs, such as Armstrong and Lavery (2005)[61], Blume et al (2008)[62], Armstrong (2012)[63], and Marston (2015)[64] reported on adverse events. Chronic wounds are complex in complex patients with multiple comorbiities. Therefore, the clinical evidence is usually presented by wound type with comorbid conditions as a subset analyses.

Other NPWT Systems vs V.A.C.® Therapy

Although the vast majority of NPWT literature is reported using V.A.C.® Therapy, the number of alternative NPWT systems has increased over the years. Therefore, it is important to understand the differences that may exist among the different NPWT systems, such as ability to remove fluid in short amounts of time and to maintain target pressure from the wound site (Figure 2).

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

Health economic retrospective review of Armstrong and Lavery 2005

In 2008, Apelqvist et al published their findings on resource utilization and direct economic cost of care for patients treated with V.A.C.® Therapy compared to standard moist wound therapy (MWT). The analyses were based on the published RCT by Armstrong and Lavery. Apelqvist et al found that more surgical procedures, including debridement, were required for the MWT group (120 vs 43 V.A.C.® Therapy, $p < .001$). The average dressing change performed per patient was 118 (range 12-226) for MWT versus 41 (6-140) for V.A.C.® Therapy ($p=0.0001$). Outpatient treatment visits were 11 (range 0-106) for the MWT group versus 4 (range 0-47) in the NPWT group ($p<0.05$). The average total cost to achieve healing was $25,954 for V.A.C.® Therapy (n=43) compared to $38,806 for MWT group (n=33). The authors concluded that V.A.C.® Therapy-treated diabetic patients with post amputation wounds resulted in lower resource utilization and a greater number of patients obtaining wound healing at a lower overall cost of care compared to MWT.

Health economic retrospective review of Blume et al 2008

Recently , Driver and Blume (2014) published their findings on a post-hoc retrospective analysis of patients enrolled in an RCT (Blume et al, 2008) to evaluate overall costs of V.A.C.® Therapy (n=169) versus advanced moist wound therapy (AMWT; n=166) in treating grade 2 and 3 diabetic foot wounds during a 12-week therapy course. A total of 324 patient records (NPWT = 162; AMWT = 162) were analyzed. There was a median wound area reduction of 85.0% from baseline for V.A.C.® Therapy treated patients and 61.8% reduction in those treated with AMWT. Total cost for all patients, regardless of closure, was $1,941,472.07 for V.A.C.® Therapy group compared to $2,196,315.86 for AMWT group. For patients achieving complete wound closure, the mean cost per patient for V.A.C.® Therapy group was $10,172 compared to $9,505 for the AMWT group. The median cost per 1 cm^2 of closure was $1,227 for V.A.C.® Therapy and $1,695 for AMWT. In patients not achieving complete wound closure, the mean

total wound care cost per patient was $13,262 for V.A.C.® Therapy group, compared to $15,069 for AMWT group. The median cost to close 1 cm^2 in non-healing wounds for V.A.C.® Therapy was $1,633, compared to $2,927 for AMWT. They concluded that the results show a greater cost effectiveness for V.A.C.® Therapy versus AMWT.

Other health economics review

In 2008, Flack et al reported on the cost-effectiveness of V.A.C.® Therapy compared to advanced wound dressings, for the treatment of diabetic foot ulcers in the US. They used a Markov model designed to estimate the cost per amputation avoided and the cost per quality-adjusted life year (QALY) of V.A.C.® Therapy, compared with both traditional and advanced dressings. The Markov model simulated 1000 patients over a one year period using transition probabilities obtained from the literature. The model analyzed health states, such as: uninfected ulcer; infected ulcer; infected ulcer post-amputation; healed; healed post-amputation; amputation; and death. Simulated patients initially treated with V.A.C.® Therapy switched to the advanced dressing after three months of treatment if their wound remained unhealed. Simulated patients treated with traditional or advanced dressings were assumed to continue with their treatment for the full 12 months if they remained unhealed. The model results demonstrate improved healing rates (61% versus 59%), more QALYs (0.54 versus 0.53) and an overall lower cost of care ($52,830 versus $61,757 per person) for V.A.C.® Therapy-simulated patients compared with advanced dressings. V.A.C.® Therapy was reported to be the dominant intervention when compared with traditional dressings. The model results indicate that V.A.C.® Therapy was less costly and more effective than both traditional and advanced dressings. The results were reported to be robust to changes in key parameters, including the transition probabilities. This evidence reports that V.A.C.® Therapy and the utility weights applied to health states are cost effective.

Large retrospective review of Optum database

An analysis was reported by Law and Beach (2014) who performed a retrospective observational database analysis, which was conducted by Premier Research Services (Charlotte, NC), that identified and followed to discharge hospitalization visits where NPWT was provided to patients.[65] The objective of this study was to assess hospital charges and readmission rates for patients who were treated with V.A.C.® Therapy versus other NPWT systems. De-identified hospital database records of patients treated between 01-Jul-2011 and 30-Jun-2013 with at least one NPWT claim were retrospectively analyzed. The analysis included 18,385 V.A.C.® Therapy discharges and 3,253 other NPWT discharges from 144 and 24

hospitals, respectively. Results showed V.A.C.® Therapy patients had 10% shorter LOS (13.0 vs. 14.5 days, respectively; $p<0.0001$).

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Commentary on: Negative Pressure Wound Therapy – Home Use: A Health Technology Assessment Prepared for Washington State Health Care Authority

Conduct of the review

The Hayes review of the published evidence for NPWT used in the home has been professionally conducted using recognized methodology. The literature surveys cut off dates have been reported as mid-2016.

Included wound types

It is refreshing to see the review attempt to examine the impact of NPWT on the burden of surgical wounds in the home care setting. A very significant proportion of wounds managed by NPWT in outpatient clinics or in the home setting are dehisced surgical wounds with delayed healing (Baharestani, Houliston-Otto, & Barnes, 2008). (Dowsett, Davis, Henderson, & Searle, 2012) There was some confusion as regards the description of what a relevant surgical wound is for the purpose of the review. The authors use a definition:

> *"….incisions made to initially closed skin and tissue in the course of a patient's care for an underlying health concern requiring surgical intervention. Surgical wounds that are closed by means such as sutures, staples, tape, or glue that hold the wound edges together are referred to as surgical wounds expected to heal by primary intention. Surgical wounds may also be left open for the healing process; these are referred to as surgical wounds healing by secondary intention"*

This definition implies that surgical wounds have been intentionally left unclosed. Whilst this may sometimes occur in traumatic or military wounds, it is much more likely that surgical wounds in the home care setting will have been the result of Surgical Site infections or dehiscence. It is important that these two kinds of wounds are not confused.

What the evidence says

The assessment of published studies has been well conducted in this review. It must be acknowledged however that using established assessment tools the NPWT evidence for closure and is frequently described as “low quality” whereas a descriptor of “low volume” might be a better summary. Although the number of studies using randomization is low, those that have been conducted favour NPWT and are of fair quality (Armstrong & Lavery, 2005) (Blume, Walters, Payne, Ayala, & Lantis, 2008) . One of the attributes that increases the likelihood that a study is deemed of lower quality is the lack of blinding. This is much harder to accommodate in studies with devices which will leave marks on the skin that indicate the type of therapy than in pharmaceutical trials where a placebo medication is readily available. Although one must be aware of publication bias; the relative tendency for trials which demonstrate no significant effects to go unpublished, it is notable that no substantive and properly powered randomized studies have been conducted and reported that show no benefit of NPWT, when the interest in such a subject would almost certainly be published and guarantee the reputation of the investigators.

Use of named devices

At several places the review cites the non-specific details of the NPWT device used in a clinical trial, particularly a study conducted outside the US, as a reason to give less weight to its finding. In general, it seems to be accepted that NPWT devices are equivalent when studied in a randomized protocol. (Rahmanian-Schwarz, Willkomm, Gonser, Hirt, & Schaller, 2012), (Dorafshar, Franczyk, Gottlieb, Wroblewski, & Lohman, 2012), (Armstrong, Marston, Reyzelman, & Kirsner, 2012): each of these studies showed no difference between different NPWT systems. Lack of payer coverage was also cited for some of the newer single use systems: Prevena (Acelity) and PICO (Smith & Nephew) on the grounds that these devices have a poor evidence base. Large randomized studies in chronic wounds may not have been published using these single use devices – although one such study has already been conducted with the SNaP single use

device which demonstrated non-inferiority with traditional reusable NPWT pumps (Armstrong et al., 2012). On the contrary the RCT evidence base for use of single use Prevena or PICO devices on closed surgical incisions is growing rapidly and has been the subject of recent systematic reviews (Hyldig et al., 2016) (De Vries et al., 2016) and publications (De Vries et al., 2016) (Karlakki et al., 2016). Other studies are ongoing and recorded in www.clinicaltrials.gov (NCT02470806) PICO vs traditional NPWT.

On the evidence for NPWT generated adverse events

Using the same methodology for the incidence of adverse events in randomized studies as used for outcomes, there is little evidence for an increased safety risk using NPWT compared to standard care.

Summary

In a professional assessment of the evidence for NPWT in Chronic and Delayed healing infected or dehisced surgical wounds a Hayes Inc. review found more evidence in favour of the use of NPWT in these wound types, than against it. Whilst the evidence is undoubtedly of low volume, the best conducted studies find in favour of NPWT. Evidence generation is active, in particular for single use devices that have substantially changed the economics of the deployment of NPWT in homecare settings since the first days of commercial NPWT using more expensive reusable devices.

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