3M | V.A.C.® Therapy

3M™ V.A.C.® Therapy

Scientific and clinical outcomes overview

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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 outcomes data demonstrating efficacy in creating an environment that promotes healing in a wide variety of wounds.

The 3M™ V.A.C.® Therapy System was introduced in 1995 as the first commercial NPWT system. 3M™ has continued to lead the way in the development of new technologies and therapies designed to make wound healing manageable for caregivers and more comfortable for patients around the world. The V.A.C.® Therapy System (3M™ V.A.C.® 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.

Negative Pressure Wound Therapy (NPWT) is defined as the application of sub-atmospheric pressure to create an environment that promotes wound healing by secondary or tertiary (delayed primary) intention. NPWT facilitates the continuous removal of exudate and helps prepare the wound bed for closure.

To help promote healing, V.A.C.® Therapy provides mechanical forces at the tissue level to create macrostrain and microstrain. Macrostrain causes the 3M™ Granufoam™ Dressing to contract under a controlled negative pressure setting,[1] drawing the wound edges together, reducing the overall wound area and allowing for granulation tissue to fill in. Microstrain is the transduction of pressure to tissue surfaces, resulting in cell surface deformation as the tissue is being pulled up into the pores (tissue stretch) and the compression of tissue at the struts.[1] Macrostrain and microstrain increase granulation tissue formation. These actions by the application of the V.A.C.® Therapy System are responsible for promoting changes in gene expression, proliferation and protein synthesis, all of which contribute toward the promotion of granulation tissue.[2]

The abundance of clinical evidence for the V.A.C.® Therapy System demonstrates an active, integrated system designed and clinically proven to create an environment that promotes wound healing at the cellular level by preparing the wound bed for closure, reducing edema, promoting granulation tissue formation, promoting perfusion and removing exudate and infectious material. Functions and outcomes of V.A.C.® Therapy are critically linked to the interaction of its component parts. Because other devices use different wound interface materials and do not provide controlled, self-adjusting pressure technology (3M™ SensaT.R.A.C.™ Technology), it cannot be presumed the data from those devices can be pooled and evaluated with V.A.C.® Therapy data, nor can their evidence be construed to represent the same outcomes as V.A.C.® Therapy.

There are numerous studies which have evaluated the cost effectiveness of V.A.C.® Therapy in a variety of settings and indicated wound types. These studies have shown that V.A.C.® Therapy has been associated with fewer hospitalizations[3], fewer complications[4,5], fewer amputations[6,7], fewer dressing changes[8,9], faster time to wound healing[10], shorter hospitalization[6,7], and reduced treatment times[11-13]. By minimizing the factors that contribute to direct and indirect wound care costs, V.A.C.® Therapy has emerged as a cost-effective option for wound management.

This overview document provides both clinical and economic summary of the current peer-reviewed published literature on V.A.C.® Therapy on a wide variety of acute and chronic wound types.

Background

Negative pressure wound therapy (NPWT) has been used for over 25 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 1995[13]; since then, the number of competitor products has increased substantially. However, V.A.C.® Therapy has shown its prevalence in the medical community, being the most published of all the commercial systems with a majority of all NPWT publications utilizing V.A.C.® Therapy.

Wound type, size, and severity, as well as treatment cost and patient mobility, have become important considerations when choosing an NPWT system to improve patient's wound healing outcomes. The V.A.C.® Therapy System is an integrated wound management system for use in acute, long-term care and home care settings. It is intended to create an environment that promotes wound healing by secondary or tertiary (delayed primary) intention by preparing the wound bed for closure, reducing edema, promoting granulation tissue formation and perfusion, and by removing exudate and infectious material. The integrated system includes a pump to provide 3M™ Dynamic Pressure Control™ Therapy, intermittent or continuous negative pressure monitored by SensaT.R.A.C.™ Technology, a separate collection canister, and proprietary dressings.

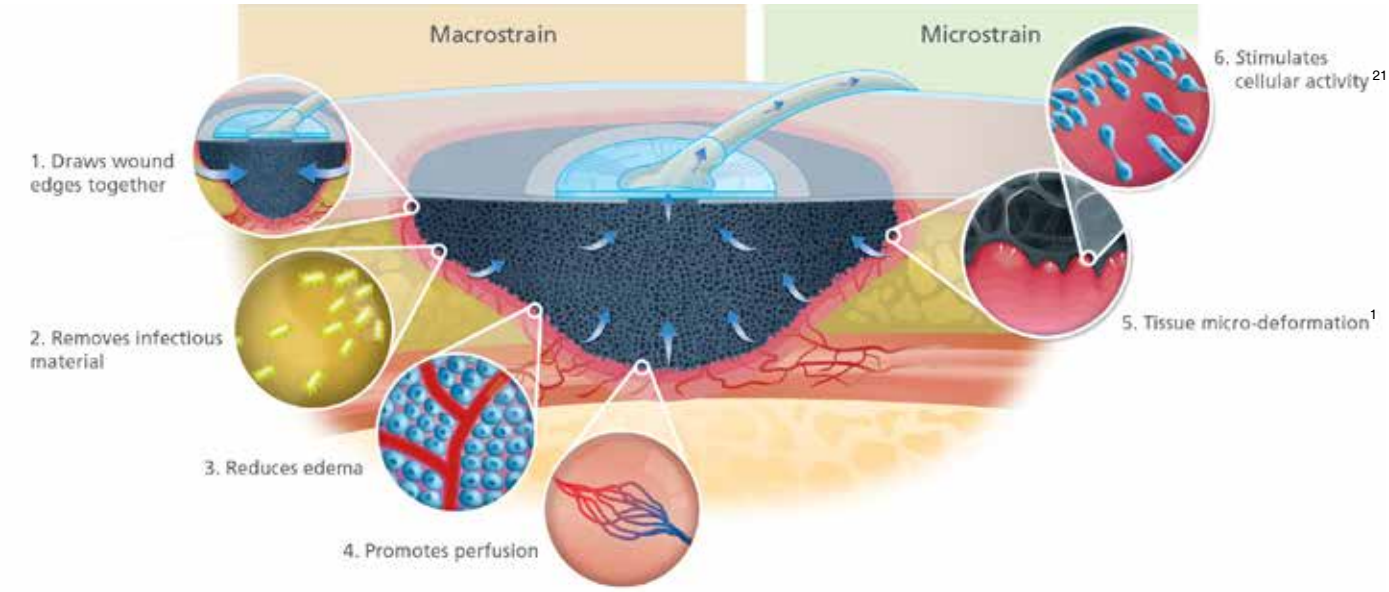
Optimal wound healing occurs when there is:[14,15]

- Effective removal of barriers to wound healing, including exudates, inflammatory mediators (eg, cytokines, proteases) and infectious materials
- Adequate perfusion to the wound bed
- Presence of metabolically active cells to produce granulation tissue
- Protection of the peri-wound tissue

3M™ V.A.C.® Therapy mechanism of action

The integrated V.A.C.® Therapy System has a unique mechanism of action whereby the delivery of negative pressure using the proprietary 3M™ V.A.C.® Granufoam™ Dressing not only maintains a wound environment that promotes healing, but also supports physiologic responses important to wound healing. These responses are observed at the tissue and cellular levels. Macrostrain approximates the tissue edges, minimizing the tissue defect size.[1,19-20] Microstrain stimulates increased cellular proliferation, leading to angiogenesis and granulation tissue formation.[1, 19-20] The adequate delivery of negative pressure can support granulation tissue formation[21], perfusion[22] and removal of wound exudate and infectious materials (**Figure 1**). The scientific foundation for V.A.C.® Therapy forms the basis for the patient outcomes observed in the published clinical literature and supports its use for managing wounds and protecting them from external contamination in all care settings.

Figure 1: Mechanisms of Action



Material matters

Both reticulated open-cell foam (such as V.A.C.® Granufoam™ Dressing) and gauze are currently used with NPWT for the management of wounds. Both dressings create an environment that promotes wound healing by providing a moist wound environment and by removal of exudates. However, due to the differences in dressing interactions, gauze may not offer the same level of granulation tissue formation that is affected through macrostrain and microstrain with V.A.C.® Granufoam™ Dressings.[16, 23-25]

Three bench studies have been published specifically comparing the effect of microstrain on cell proliferation, migration and gene expression. In 2007, McNulty et al.. developed a three-dimensional fibrin matrix to study the effects of negative pressure on fibroblast viability, chemotactic signaling, and proliferation. They found that NPWT utilizing gauze had significant cell death and stimulated less migration and proliferation than V.A.C.® Therapy with V.A.C.® Granufoam™ Dressing treated cells ($p<0.05$).[19] In 2009, Derrick et al.. reported that gene expression profiles for V.A.C.® Therapy with V.A.C.® Granufoam™ Dressing (5,072 genes) were >1.6-fold than moist wound dressings (3,601 genes) and NPWT gauze (3,952 genes).[2] In 2009, McNulty et al. published their finding on the effect of V.A.C.® Therapy with Granufoam Dressing and NPWT gauze on cellular energetics. They found that levels of cytochrome c oxidase, energy charge, and adenosine triphosphate/adenosine diphosphate were significantly increased following the application of V.A.C.® Therapy compared to NPWT gauze ($p<0.05$).[20]

Depending on your goal of therapy such as fluid management and/or fluid management versus granulation tissue formation, 3M has a dressing solution without having to switch between therapy units.

Not all NPWT systems are the same

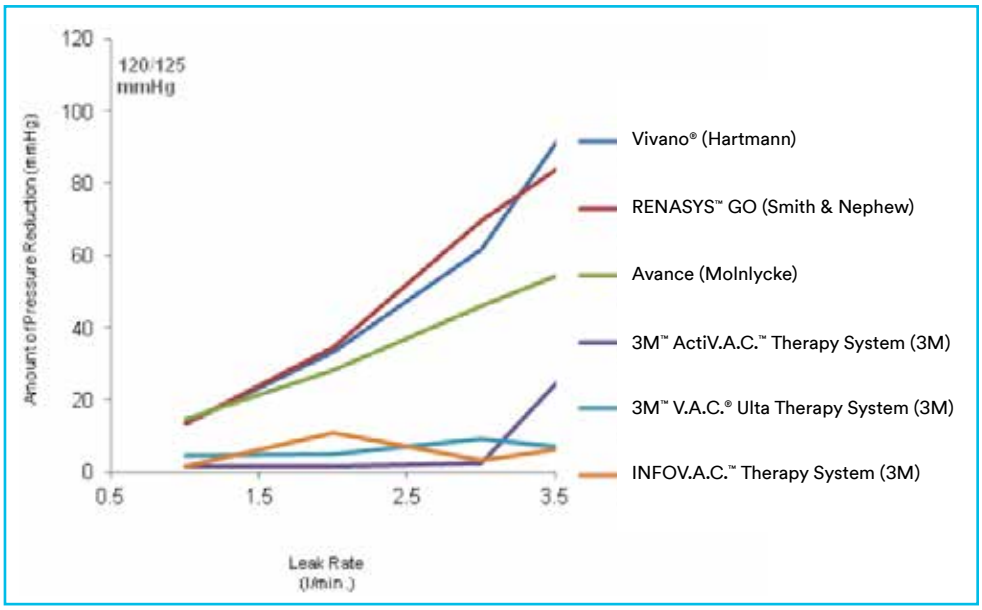
3M™ V.A.C.® Therapy Systems are the only NPWT systems that provide proprietary 3M™ SensaT.R.A.C.™ Technology, a real-time pressure feedback system. This technology continuously monitors, measures, and maintains the set negative pressure at the wound site and adjusts pump output, compensating for wound distance, anatomical wound position, exudates characteristics, and patient movement. The 3M™ SensaT.R.A.C.™ Pad (**Figure 2**) efficiently draws exudates away from the wound through the large inner lumen and independently monitors target pressure at the wound through outer sensing lumens (**Figure 3**). The SensaT.R.A.C. Pad distributes negative pressure to individual sensing lumens and helps reduce tubing blockages and false alarms.

Figure 2: 3M™ SensaT.R.A.C.™ Pad

Figure 3: 3M™ V.A.C.® Tubing

Although the 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. A bench top NPWT study[26], of four cohorts with two units each, compared 3M™ ActiV.A.C.™ Therapy Unit integrated with SensaT.R.A.C. Technology with the RENASYS™ GO Wound Therapy Unit (Smith & Nephew). Therapy units were placed 92cm above dressed simulated wounds with inline canisters for fluid collection 48cm above the simulated wounds. Simulated wound fluid at 30cP viscosity was injected into the dressings, therapy units were started, and wound pressure and fluid volume were measured over 24 hours. Three therapy units per group were tested 3 times each. Under similar test conditions, ActiV.A.C. Therapy maintained a target pressure at the simulated wound site, while RENASYS™ GO was unable to maintain the target negative pressure at the wound site. In addition, it took RENASYS™ GO 24 hours to remove the volume of fluid removed in 15 minutes by ActiV.A.C. Therapy.[26] Correlation of bench results in humans has not been established in specific clinical studies. Similar findings from other bench top studies comparing V.A.C.® Therapy Units with other competitor products have also been reported (**Figure 4**).[27-30] These data demonstrated that the performance of all NPWT systems is not necessarily similar.

Figure 4: Side by side comparative bench test: Tolerance of small-sized air leakage

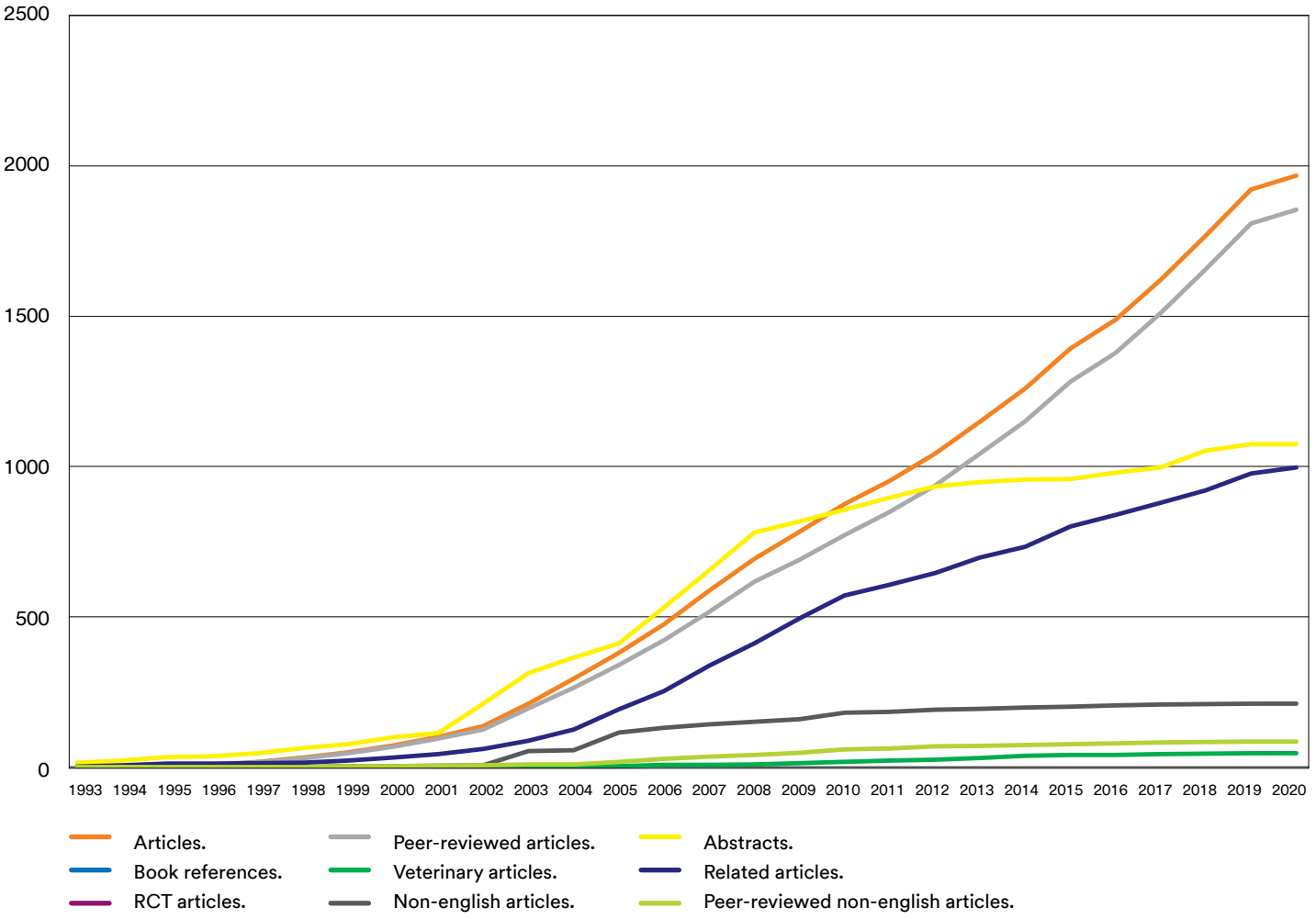


Clinical evidence

Of all the commercialized NPWT products, 3M™ V.A.C.® Therapy has the largest body of evidence to date, including over 1,800 peer-reviewed articles, 97 of which are randomized controlled trials (RCT) (**Figure 5** and **Table 1a-b**).[31] 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. Table 2 lists a number of key references by wound type.

Suissa, Danino and Nikolis published a meta-analysis of randomized trials of NPWT vs standard wound care. Their results suggest that NPWT appears to be effective in the management of chronic wounds.[32]

Figure 5: 3M™ V.A.C.® Therapy publication numbers



Clinical evidence (cont.)

Table 1a: 3M™ V.A.C.® Therapy vs. S&N NPWT vs. Other NPWT manufacturers by evidence type

Type of study	3M™ V.A.C.® Therapy	Smith & Nephew NPWT	Other NPWT manufacturers
RCT	97	24	9
PC	186	34	13
CRS	149	16	3
RS	286	13	13
CST	451	58	24
CSE	307	24	12

Study Type: CRS=Comparative Retrospective Study; CSE= Case Series; CST=Case Study; PC=Prospective Cohort;

RCT=Randomized Controlled Trial; RS=Retrospective Study

Data based on results of a search of 3M internal publication database. (Data as of April 2021)

Table 1b: 3M™ V.A.C.® Therapy vs. Other NPWT evidence numbers by wound type

Type of study	3M™ V.A.C.® Therapy	Smith & Nephew NPWT	Other NPWT manufacturers
Acute Wounds			
Surgical Wounds	788	82	24
General Trauma	154	11	13
Grafts	165	15	2
Chronic Wounds			
Pressure Ulcers	56	3	3
Diabetic Foot	94	9	6
Chronic Leg	23	4	1

Data based on results of a search for Levels 1-5 evidence of the appropriate wound types in a 3M internal publication database. (Data as of April 2021)

Clinical evidence (cont.)

The body of literature provides evidence to 3M™ V.A.C.® Therapy's effectiveness in diabetic foot wounds, chronic wounds such as pressure ulcers and lower extremity ulcers, and a wide variety of acute wounds (**Table 2** below) more evidence can be found at https://www.mykci.com/healthcare-professionals/clinical-evidence.

Table 2: Key publications demonstrating the efficacy of 3M™ V.A.C.® Therapy NPWT

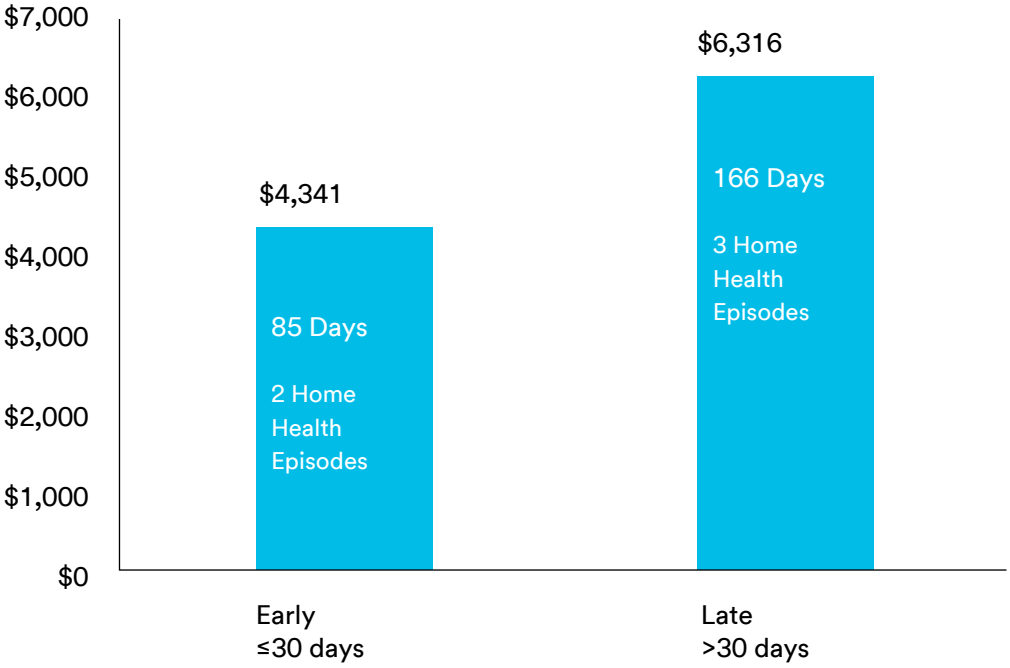
Wound type	Key publications – Acute wounds
Surgical wounds	Zannis et al. 2009 (PCT)[33] Siegel et al. 2007 (CRS)[34] Biter et al. 2014 (RCT)[35] Zenke et al. 2014 (PCT)[36] Seidel et al. 2020 (RCT)[37]
General trauma	Machen et al. 2007 (CSE)[38] Labler et al. 2007 (CST)[39] Raj et al. 2016 (PCT)[40] Maurya et al. 2017 (PC)[41] Burtt et al. 2020 (CRS)[42]
Grafts	Blume et al. 2010 (RS)[43] Ho et al. 2013 (PCT)[44] Eisenhardt et al. 2011(RCT)[45] Joo et al. 2020 (RCT)[46] Vather et al. 2018 (RCT)[47] Halama et al. 2019 (RCT)[48]
Diabetic foot amputations	Lavery et al. 2008 (RS)[49] Armstrong et al. 2005 (RCT)[7] Dalla Paola et al. 2010 (RCT)[12] Eginton et al. 2003 (RCT)[50] De Caridi et al. 2016 (PCT)[51] Sukur et al. 2018 (CRS)[52]

Wound type	Key publications – Chronic wounds
Pressure	Wanner et al. 2003 (RCT)[53] Ford et al. 2002 (RCT)[54] Joseph et al. 2000 (RCT)[55] Wild et al. 2008 (RCT)[56] Fulco et al. 2015 (RCT)[57] Wagstaff et al. 2014 (RCT)[58]
Diabetic foot	Suissa et al. 2011 (Meta Analysis)[32] Blume et al. 2008 (RCT)[6] Cole et al. 2016 (PCT)[59] Skrinjar et al. 2016 (RCT)[60] Maranna et al. 2021 (RCT)[61]
Venous stasis ulcer	Vuerstaek et al. 2006 (RCT)[62] Dini et al. 2011 (RCT)[63] Egemen et al. 2012 (PCT)[64]

Early vs. Late

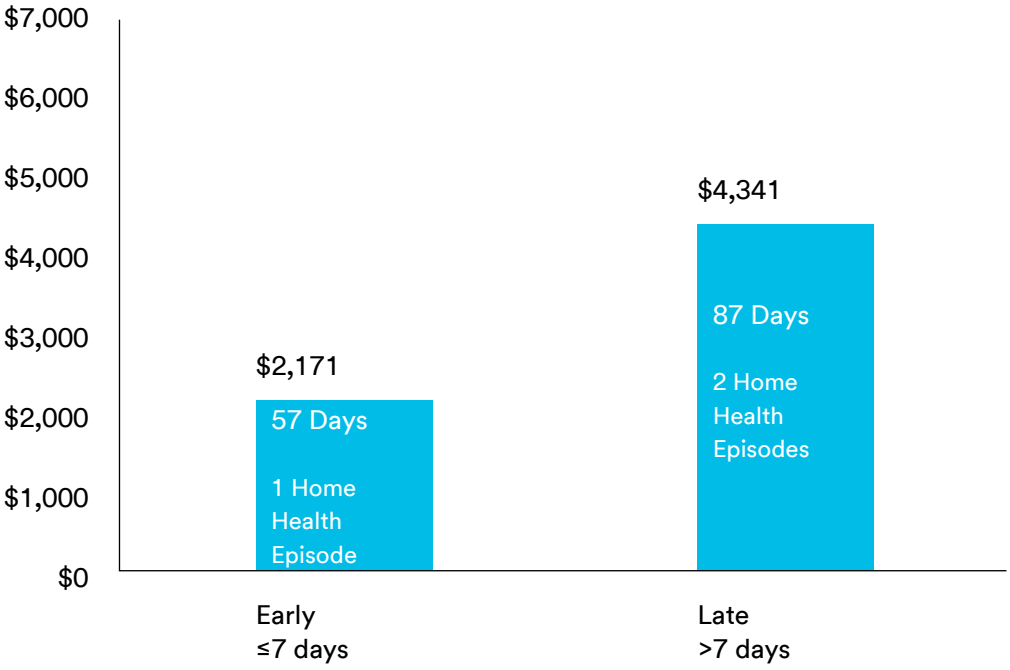
The cost savings associated with the use of 3M™ V.A.C.® Therapy support early initiation of NPWT. A study by Baharestani et al. evaluated how early versus late initiation of NPWT affected the length of stay (LOS) in home healthcare with Stage III or IV pressure ulcers or surgical wounds.[65] The results indicated that early application of NPWT was related to a reduced overall length of home care services (**Figures 6** and **7**). Additionally, higher costs for wound care treatment could result because for each day that NPWT application was delayed, nearly 1 day was added to total LOS.[65] Kaplan et al. further demonstrated the success of early initiation of NPWT for the treatment of traumatic wounds.[66] Records of trauma patients were retrospectively analyzed and divided into two groups: early (Day 1 or 2 of hospital stay) or late group (Day 3 or later). Results showed the early use of NPWT was associated with reduced hospital stays (10.4 vs 20.6 days, $p<0.0001$), ICU stays (5.3 vs 12.4 days, $p<0.0001$), and treatment days, translating into lower total and variable costs. In a third study, de Leon et al. retrospectively investigated the effects of early use of NPWT on LOS in a long-term acute care setting.[67] Records of patients who received NPWT within 14 days of admission (early) or after 15 days of admission (late) were analyzed. Findings from this study favored early initiation of NPWT with a reduction in mean LOS (35.4 vs 56.4 days, $p<0.0001$) and mean time to wound closure (22 vs 34 days, $p=0.0154$) in these patients compared to the late NPWT patients.

Figure 6: Home health comparison of Early vs. Late NPWT on home patients with pressure ulcers[65]



Early vs Late (cont.)

Figure 7: Home health cost comparison of Early vs. Late NPWT on home patients with surgical wounds[65]

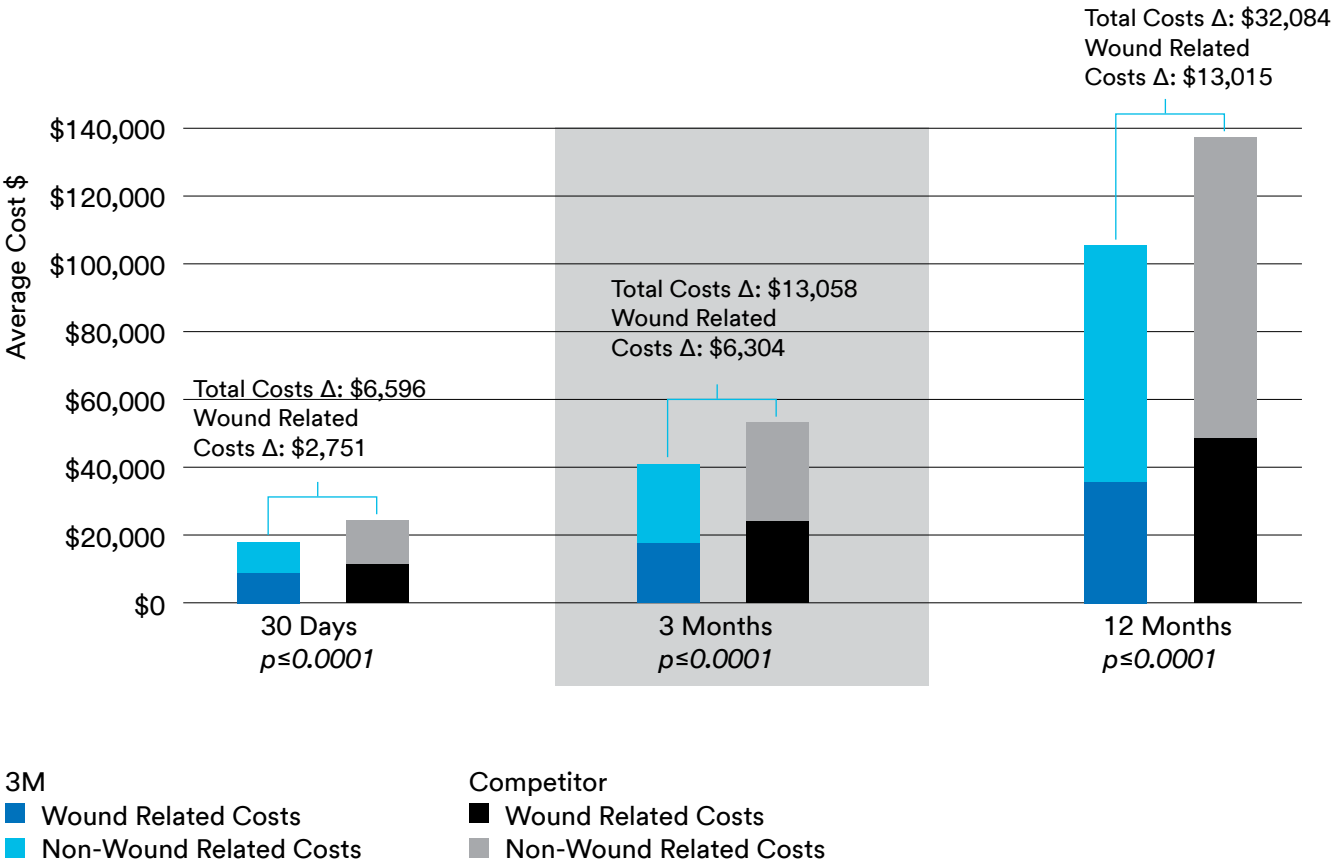


Yao et al. (2014) published findings on their evaluation of the efficacy of negative pressure wound therapy (NPWT) compared to standard of care on wound healing in high-risk patients with multiple significant comorbidities and chronic lower extremity ulcers (LEUs) across the continuum of care setting.[10] This was a retrospective cohort study of 'real-world' high-risk patients conducted using the review of the Boston University Medical Center electronic medical records, along with chart abstraction to capture detailed medical history, comorbidities, healing outcomes and ulcer characteristics. A total of 342 patients (171 NPWT patients with LEUs vs 171 non-NPWT patient matched for age and gender), were included in this cohort from 2002 to 2010. The hazard ratios (HRs) were estimated by COX proportional hazard models after adjusting for potential confounders. The results found that NPWT patients were 2.63 times (95% CI = 1.87-3.70) more likely to achieve wound closure compared to non-NPWT patients. Incidence of wound closure in NPWT patients were increased in diabetic ulcers (HR = 3.26, 95% CI = 2.21-4.83), arterial ulcers (HR = 2.27, CI = 1.56-3.78) and venous ulcers (HR = 6.31, 95% CI = 1.49-26.6) compared to non-NPWT patients. Wound healing appeared to be positively affected by the timing of NPWT application. Compared with later NPWT users (1 year or later after ulcer onset), early NPWT users (within 3 months after ulcer onset) and intermediate NPWT users (4-12 months after ulcer onset) were 3.38 and 2.18 times more likely to achieve wound healing. The authors concluded that despite greater significant comorbidities, patients receiving NPWT experienced a reduced time to healing, and that early use of NPWT demonstrated greater incidence of wound healing. They also determined that the longer the interval before intervention with NPWT, the higher the correlation was to with poor wound healing outcome.

Health economics

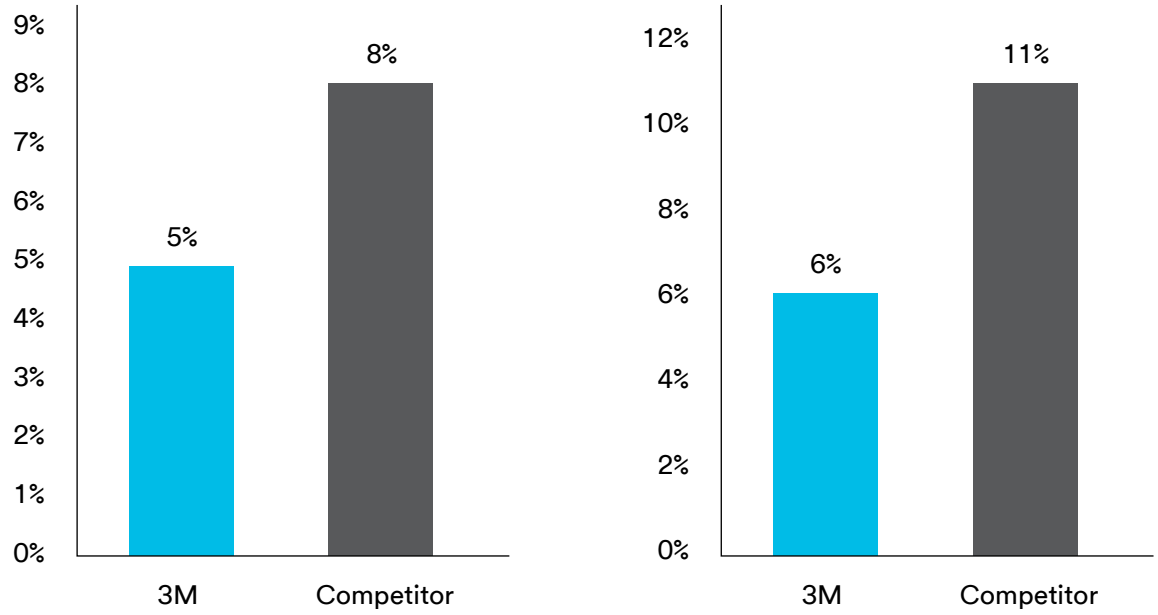
Because not all NPWT systems may be the same and price differences may exist, it is important to understand the comparative effectiveness of these different systems because certain NPWT systems may be associated with potential overall cost savings. Law et al.[68] (2015) analyzed de-identified insurance claim data from a major US insurance company (Optum Life Sciences, Eden Prairie, MN) for patients with chronic wounds who received any type of NPWT model. At 12 months, total costs were significantly lower for 3M™ V.A.C.® Therapy patients (n=7,860) compared to Competitor NPWT patients (n=378) ($80,768 vs $111,212, respectively; p=0.03). A second study by Law et al.[69] retrospectively evaluated a later data set from the same national insurance claims database to assess costs, treatment duration, and multiple sites of care for V.A.C.® Therapy and a case-matched cohort of other NPWT systems. The study found that compared to V.A.C.® Therapy, patients receiving competitor NPWT had a higher cost to treat for all wounds, at all time periods. Compared to V.A.C.® Therapy, competitor NPWT wound-related costs at 30 days were 32% higher ($11,334 vs. $8,583) and total cost to treat at 30 days was 37% higher ($24,405 vs. $17,809). Patients being treated with V.A.C.® Therapy had lower total costs across all time periods, as well as a shorter average length of therapy. These higher competitor costs were driven by statistically significantly higher NPWT, inpatient, home health care, skilled nursing facility, long-term care, and other expenses. The study's findings also reinforce the importance for purchasers and payers to look beyond therapy acquisition price to consider all associated economic outcomes.

Figure 8: Costs at 30 days, 3 months, 12 months: all wounds[69]



Health economics (cont.)

Figure 9: Wound related re-admission rates[70]



A similar analysis was reported by Law and Beach (2014), who performed a retrospective observational database analysis, conducted by Premier Research Services (Charlotte, NC), that identified and followed to discharge hospitalization visits where NPWT was provided to patients.[71] The objective of this study was to assess hospital charges and readmission rates for patients who were treated with 3M™ 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). V.A.C.® Therapy patients also had lower all-cause 30-day readmission rates of 16.1% vs 17.9% (p=0.0145). Average hospital charges were 11% lower ($14,512) for V.A.C.® Therapy patients versus other NPWT patients ($112,759 vs $127,272, p<0.0001). Estimated length of therapy was lower for V.A.C.® Therapy patients versus other NPWT patients (7.1 vs. 7.5, respectively; p<0.0032), and V.A.C.® Therapy patients received NPWT earlier in their stay than patients in facilities using other NPWT (4.6 vs. 5.5 days, respectively; p<0.0001). Percentage of NPWT patients who required an ER visit within 30 and 60 days post discharge was lower for V.A.C.® Therapy patients versus other NPWT patients (16.6% vs 18.1%, respectively, at 30 days, p=0.0456; 23.4% vs 26.2%, respectively, at 60 days, p=0.0012). Based on this analysis, patients treated with V.A.C.® Therapy had shorter lengths of stay and lower hospital readmission rates than patients treated with other NWPT.

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 with standard moist wound therapy (MWT).[71] The analyses were based on the published RCT by Armstrong and Lavery.[7] 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 dressing change average 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 direct cost per patient treated for 8 weeks or longer (independent of clinical outcome) was $27,270 (V.A.C.® Therapy) and $36,096 (MWT). 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.[71]

Health economics (cont.)

In 2014, Driver and Blume[72] published their findings on a post-hoc retrospective analysis of patients enrolled in a randomized controlled trial (Blume et al., 2008)[6] 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 3M™ V.A.C.® Therapy treated patients to 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 1cm^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 1cm^2 in non-healing wounds for V.A.C.® Therapy was $1,633, compared to $2,927 for AMWT. They concluded that the results showed a greater cost effectiveness for V.A.C.® Therapy versus AMWT.[72]

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.[73] 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 1,000 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 demonstrated 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 indicated 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, the cost of V.A.C.® Therapy and the utility weights applied to health states.[73]

In the largest RCT on V.A.C.® Therapy (n=539), Seidel et al. explored both the clinical and health economic outcomes for the use of V.A.C.® Therapy in patients with subcutaneous abdominal wound healing impairment (SAWHI) after surgery compared to conventional wound treatment (CWT).[74] The clinical results showed that V.A.C.® Therapy (n=256), compared to CWT (n=251), in the intent-to-treat population, provided: 1) Significantly higher wound closure rate within 42 days ($p<0.001$); 2) Significantly shorter mean time to wound closure ($p<0.001$); and 3) Significantly greater total reduction of wound surface area ($p=0.007$) and wound volume ($p=0.002$) within 42 days. In the per-protocol population, V.A.C.® Therapy (n=157), compared to CWT (n-174), provided: 1) Significantly higher wound closure rate within 42 days ($p<0.001$), and; 2) Significantly shorter mean time to wound closure ($p<0.001$). In comparing the resource utilization of the per-protocol population[75], V.A.C.® Therapy, as compared to CWT, demonstrated: 1) Significantly shorter treatment length (V.A.C.® Therapy 22.8 days vs. CWT 30.6 days, $p=0.001$); Significantly shorter time for dressing changes per patient (V.A.C.® Therapy 196 minutes vs. CWT 278 minutes, $p<0.001$), and; 3) Significantly shorter time for wound-related procedures per patient (V.A.C.® Therapy 167 minutes vs. CWT 266 minutes, $p<0.001$). However, in this study, due to local infrastructure and reimbursement challenges, many V.A.C.® Therapy patients were prevented from transferring out of the hospital setting which resulted in a longer hospitalization time for V.A.C.® Therapy patients (13.9 days) than CWT patients (11.8 days) ($p=0.047$). The results of this study encouraged a change in out of hospital reimbursement policy for NPWT in Germany.

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