



Veraflo™
Therapy

3M™ Veraflo™ Therapy Clinical Summary



Table of contents

Executive Summary	4
Background.....	4
3M™ Veraflo™ Therapy Mechanism of Action.....	5
Instillation Effect on Granulation Tissue Formation	6
Clinical Evidence	6
Comparison of 3M™ V.A.C.® Therapy versus 3M™ Veraflo™ Therapy	7
Health Economics	8
Early vs. Late.....	10
Conclusion	10
References.....	11
Appendix A: Evidence Summary of Key Publications.....	13

Executive Summary

The management of acute and chronic wounds requires a comprehensive assessment of both the patient and wound to determine the optimal treatment plan for achieving wound care goals. Wound treatment costs can increase when complications such as infection, edema, and poor perfusion develop, and cause delays in wound healing. It is important to consider the direct and indirect costs related to wound care when evaluating advanced therapy options.

The use of advanced technologies, such as negative pressure wound therapy (NPWT) and NPWT with instillation and dwell time (NPWTi-d), have been associated with earlier³⁸ wound closure and more cost-effective treatment compared to lower priced products that require longer treatment times or fail to heal the wound. Over the years wound treatments have progressed from dry gauze products to advanced moist wound therapies and further to active wound management therapies such as 3M™ V.A.C.® Therapy, a clinically evaluated advanced therapy system that was cleared for commercialization in 1995. 3M™ Veraflo™ Therapy, developed in 2011, incorporates both NPWT and wound cleansing features, including a volumetric pump and dressings designed for instillation therapy, into one system: the 3M™ V.A.C.® Ulta Therapy System. With Veraflo Therapy, the user can select topical wound solutions (such as normal saline or wound irrigation solutions and cleansers) to instill into the wound bed, adjust the instillation fill volume and soak time, and customize negative pressure settings and duration of negative pressure therapy between instillation cycles. The system can potentially be used for a variety of indicated wound types such as chronic, acute, traumatic, sub-acute and dehisced wounds. Because these are open wounds, it is not uncommon for them to be colonized, contaminated, or infected. Such wounds may benefit from repetitive, automatic wound cleansing that removes wound exudate and infectious material via the controlled instillation of topical wound solutions or antiseptic solutions.

Background

For more than 25 years, V.A.C.® Therapy has been successfully established in clinical practice for managing acute and chronic wounds and has been increasingly used in complex and difficult-to-treat wounds. NPWT creates a closed, moist wound-healing environment, promotes granulation tissue development, reduces edema, removes exudate and infectious material, and prepares the wound bed for closure. The negative pressure transmitted through the reticulated open cell foam (ROCF) dressing delivers mechanical stress to the tissue, drawing wound edges together, and to the cells, stretching them as tissue is pulled up into the open pores of the ROCF.¹⁻³ Cell stretch triggers mitosis, resulting in proliferation and, ultimately, granulation tissue formation.

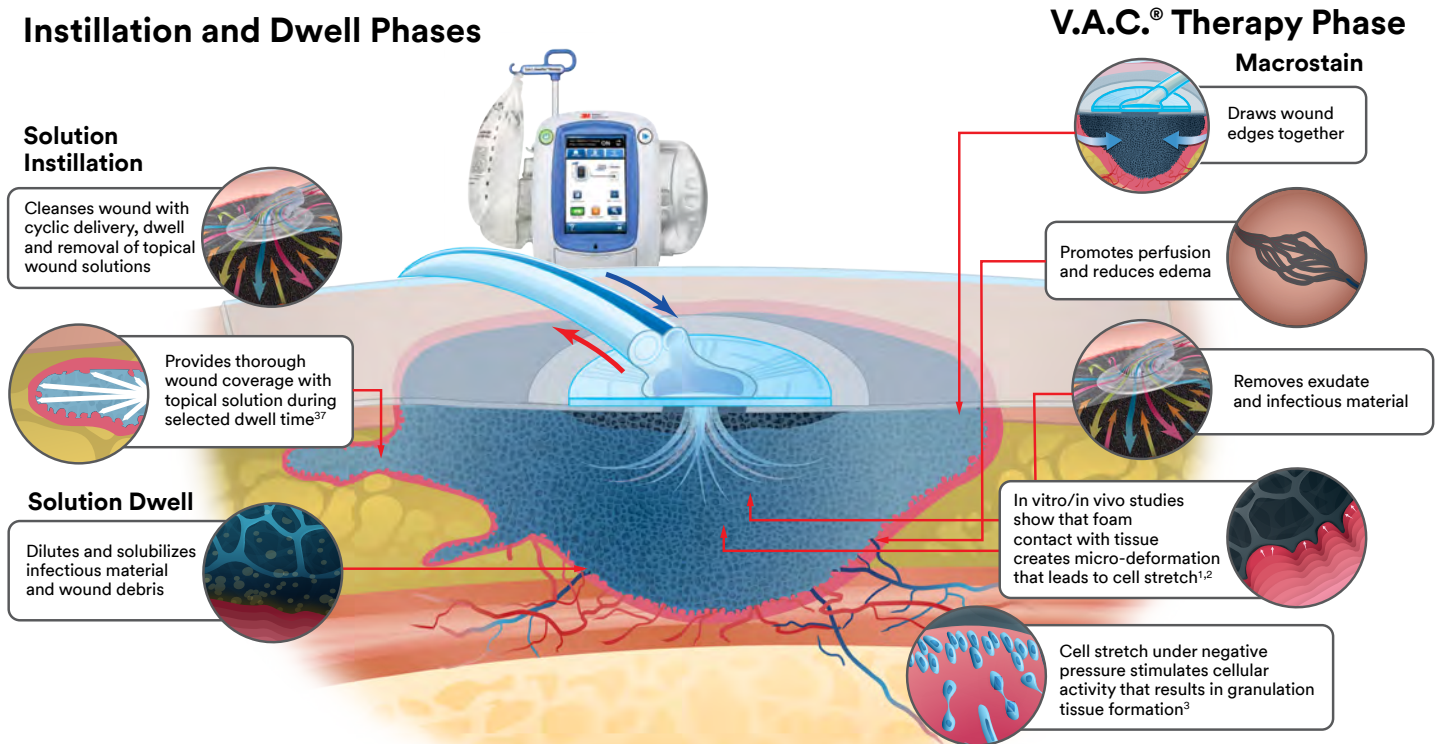
More recently, Veraflo Therapy (negative pressure wound therapy with instillation and dwell time, NPWTi-d) has emerged as an option for patients who would benefit from NPWT and the controlled delivery of topical wound cleansing solutions into the wound bed. Veraflo Therapy differs from wound irrigation (i.e., practice of washing out a wound or body opening with a stream of liquid solution) and lavage (i.e., process of washing out a cavity or organ (e.g., bladder, bowel, or stomach) using a liquid solution for therapeutic purposes). With Veraflo therapy, instilled fluid is slowly introduced into the wound and dwells in the wound bed for a user selected period of time before being removed by applying negative pressure. Automated instillation helps with wound cleansing by loosening soluble contaminants in the wound bed followed by subsequent removal of infectious material and wound exudate during NPWT. As a result, soluble contaminants are removed and the wound cleansed without user interaction.

A study has analyzed the potential cost reduction of Veraflo Therapy versus the standard of care including V.A.C.® Therapy, with economic models resulting in potential savings in therapy time and required OR visits.²²

3M™ Veraflo™ Therapy Mechanism of Action

Veraflo Therapy, delivered with the 3M™ V.A.C.® Ulta Therapy System, starts with the determination of the appropriate amount of topical wound solution to instill into the wound. This can be performed using the 3M™ Smart Instill™ Feature or the Fill Assist Feature on the V.A.C.® Ulta Therapy System. Once the solution fill volume is established, topical wound solution is instilled into the wound where it dwells for a user selected period of time (10 minutes recommended by global panel of experts⁴) to thoroughly saturate and cleanse the wound. This dwell phase dilutes and solubilizes infectious material and wound debris.

After the dwell phase has been completed, negative pressure wound therapy is applied during the V.A.C.® Therapy phase (recommended V.A.C.® Therapy time of 2-3 hours⁴) to help remove the exudate and infectious material while drawing the wound edges together. During negative pressure wound therapy the foam in contact with the tissue creates micro-deformations that lead to cell stretch, which stimulate cellular activity that results in granulation tissue formation.¹⁻³ In addition, V.A.C.® Therapy also reduces edema and promotes perfusion.



When using the 3M™ V.A.C.® Veraflo Cleanse Choice™ Dressing or 3M™ Veraflo™ Cleanse Choice Complete™ Dressings, the unique pattern of holes on the wound contact layer facilitates the removal of thick wound exudate, such as thick fibrin (wet slough), and other infectious materials. These dressings provide an alternative wound cleansing tool when surgical debridement must be delayed or is not possible or appropriate.⁵

Veraflo Therapy with either V.A.C.® Veraflo Cleanse Choice Dressing or Veraflo Cleanse Choice Complete Dressing are the first and only NPWT dressings to be cleared by FDA to hydromechanically remove nonviable tissue and wound debris which reduces the number of surgical debridements required, while promoting granulation tissue formation, creating an environment that promotes wound healing.

Instillation Effect on Granulation Tissue Formation

In an animal study, several possible mechanisms of action of 3M™ Veraflo™ Therapy were demonstrated in porcine excisional wounds when instilling normal saline.⁶ In evaluating the effects of different negative pressure wound therapy modes, Veraflo Therapy demonstrated several advantages over conventional V.A.C.® Therapy. Analysis of 3-D images of full-thickness dorsal excisional wound in swine demonstrated a greater reduction in wound area and perimeter in the cohort treated with NPWTi-d using saline relative to those excisional wounds treated with conventional NPWT. Additionally, mean granulation tissue thickness of wounds treated with NPWTi-d using saline was 4.75 ± 0.54 mm, which was statistically greater ($p < 0.05$) than wounds treated with conventional NPWT by 44% (continuous NPWT), 57% (intermittent NPWT) and 40% (pressure-controlled NPWT). Wounds treated with NPWTi-d using saline also demonstrated, on average, a more rapid wound fill rate than continuous (40% wound fill rate; $p < 0.05$), intermittent (25% wound fill rate; $p < 0.05$) and Dynamic Pressure Control (DPC) (65% wound fill rate; $p < 0.05$) modes of NPWT.

Initially used in wounds that did not respond to traditional NPWT or as a last-resort therapy, NPWTi-d has gained traction as an integral part of wound management. Recent consensus guidelines recommend the use of NPWTi-d as an adjunct therapy, along with debridement and systemic antibiotics, for a wide variety of acute, chronic, and/or infected wounds, including traumatic, surgical, dehisced, and diabetic wounds as well as venous leg ulcers, pressure ulcers, and full-thickness burns among other wound types.⁴

Clinical Evidence

Published literature has been available for Veraflo Therapy since 2011, the year the 3M™ V.A.C.® Ulta Therapy Unit received FDA clearance. More than 139 peer-reviewed articles have been published, including 3 RCTs and 2 meta-analyses (Table 1).

Table 1. Key peer-reviewed literature available for 3M™ Veraflo™ Therapy

Type of Study	Number of Studies Published
Randomized Control Trial	3
Meta-analysis	3
Prospective Cohort	16
Comparative Retrospective Study	9
Case Series	30
Retrospective Study	22
Basic Science	12
Case Study	59
Economic Study	2
Literature Review	9
Therapy Description	1
Other	2
Total	168

Consensus/Evidence Review; Pre-Clinical Studies; Data as of 5/2022

Comparison of 3M™ V.A.C.® Therapy vs. 3M™ Veraflo™ Therapy

The use of Veraflo Therapy has increased in recent years based on a growing body of evidence, and the technology has expanded into many countries around the world. It is often deemed helpful for automatic cleansing of the wound surface and solubilizing devitalized tissue for removal. As wound healing progresses, clinicians may close the wound by secondary intention or step down to NPWT or advanced dressings. The latest consensus⁴ panel identified that NPWTi-d may be discontinued when (a) clinical goals are met, (b) wound is deemed ready for surgical closure or coverage, (c) wound is clinically stable for standard NPWT or other advanced therapy to be applied, or (d) wound has decompensated. While initial studies focused on the benefits of NPWTi-d compared to standard of care, more recent evidence is emerging comparing the benefits of NPWTi-d to NPWT alone.

A 2014 study retrospectively compared results between patients treated with adjunctive NPWT or with NPWTi-d at a single institution.⁷ A total of 142 patients with acutely infected wounds were included in the analysis: 74 NPWT patients versus 34 NPWTi-d with 6-minute dwell time patients and 34 NPWTi-d with 20-minute dwell time patients. All patients in the NPWTi-d group underwent instillation with betaine/polyhexanide (PHMB). All groups had continuous pressure settings of -125 mmHg. The NPWTi group with a 6-minute dwell was followed by 3.5 hours of NPWT versus 2 hours of NPWT for the 20-minute dwell group. Patients in both NPWTi-d groups had a significantly fewer operative visits compared to those treated with standard NPWT ($p=0.043$; 95% CI, 0.014 to 0.75). Overall, the 20-minute dwell time group had significantly lower length of hospital stay compared to the NPWT group (11.4 ± 5.1 vs. 14.92 ± 9.2 , respectively; $p=0.034$). Both NPWTi-d groups also displayed significantly fewer days to final surgical procedure compared to the NPWT group ($p=0.043$; 95% CI, 0.0651 to 4.04; $p=0.0019$; 95% CI, 0.39 to 4.36, respectively). Compared to those in NPWT group, patients treated with NPWTi-d in the 6-minute dwell group had significantly higher percent wounds that closed prior to discharge (94% vs. 62%; $p \leq 0.001$) and showed culture improvement for gram-positive bacteria (90% vs. 63%; $p \leq 0.001$).

In 2020, a multi-center prospective pilot RCT compared the effects of NPWTi-d with instillation of polyhexamethylene biguanide (PHMB) solution vs. NPWT.⁸ The trial reported a statistically significant ($p=0.02$) reduction in bacterial bioburden (the number of bacteria in the wound bed measured in colony forming units) compared with negative pressure wound therapy. This was measured at the time of initial surgical debridement and at the first dressing change with Veraflo Therapy. Bioburden reduction was also supported by data from a smaller randomized controlled trial⁹ ($n=20$) and a comparative observational study¹⁰, which also reported a reduction in bioburden with Veraflo Therapy after 7 days of therapy. However, the 2020 study found no significant difference between the groups in the primary endpoint of the operating room debridements after initial debridement, which was in contrast to the 2014 retrospective single-site study on wounds treated with Veraflo Therapy with PHMB solution.⁷ The 2020 pilot study also found no statistically significant difference between NPWTi-d and NPWT for the following secondary endpoints: time to readiness for wound closure/coverage, proportion of wounds closed, incidence of wound complications. While this pilot study did not meet the primary endpoint and some secondary endpoints, there were many lessons learned regarding why statistical significance was not reached.⁸ Results varied between sites because of differences in site-specific debridement protocols, criteria for readiness for closure, and discharge criteria. However, in this study, NPWT subjects had a lower risk of re-hospitalization compared with NPWTi-d.⁸

In 2021, an analysis was performed using two previously published independent studies from a single investigator and hospital to compare patient characteristics and clinical outcomes of infected wounds from 74 V.A.C.® Therapy patients with 42 Veraflo Therapy with saline-treated patients. Patients from each study underwent debridement and received antibiotics. In the clinical outcomes, Veraflo Therapy-treated patients had significantly lower quantity of surgical procedures ($p=0.0048$), reduced time until final surgery ($p=0.0001$), reduced hospital length of stay ($p=0.0443$), higher percentage of wound closure ($p=0.0004$), and higher percentage of closed wounds intact at one month ($p=0.0001$).¹¹

The choice of instillation fluid for the treatment arms plays a key role in study findings. For the Kim, Lavery, et al. multi-center pilot RCT,⁸ the choice of PHMB was chosen based upon earlier published studies on bacterial colonized wounds treated with NPWTi-d.¹²⁻¹⁶ It was assumed that most of the wounds in the study would have a history of acute or chronic infection and that PHMB would be an appropriate topical cleanser. However, the combination of PHMB with NPWTi-d has subsequently been shown to significantly slow granulation tissue formation in wounds compared to NPWT alone

in two porcine preclinical studies of healthy wounds.^{17,18} Based on these studies, the lead author now utilizes normal saline routinely for the majority of patients requiring NPWTi-d and PHMB for specific wound conditions, such as cases involving orthopedic fixation hardware. In recently published international consensus guidelines, 100% of participants agreed that saline is an appropriate solution for instillation therapy.²⁰

In 2021 a systematic literature review and meta-analysis was published synthesizing existing data across multiple studies to provide a more precise estimate of the clinical effects of NPWTi-d versus control therapy, including 3M™ V.A.C.® Therapy, in the adjunctive management of complex wounds.²⁰ Weighted standardized mean difference or odds ratios and 95% confidence intervals were calculated to pool study and control group results for analysis. Thirteen studies comprising 720 patients were included in the analysis. Significantly fewer surgical debridements were performed in NPWTi-d patients versus control patients ($p=0.01$). Wounds in NPWTi-d group were 2.39 times more likely to close than control group wounds ($p=0.01$) and wounds in the NPWTi-d group were ready for closure faster than control wounds ($p=0.03$).²⁰ The odds of reducing bacterial count from baseline in the NPWTi-d group was 4.4 times greater than control group wounds ($p=0.003$), and percent reduction of bacterial count in NPWTi-d wounds was evident in all studies that captured that endpoint. There was a significantly shorter length of therapy in NPWTi-d patients versus control patients ($p=0.03$). Length of hospital stay was not significantly reduced for NPWTi-d patients compared with that for control patients ($p=0.06$).²⁰

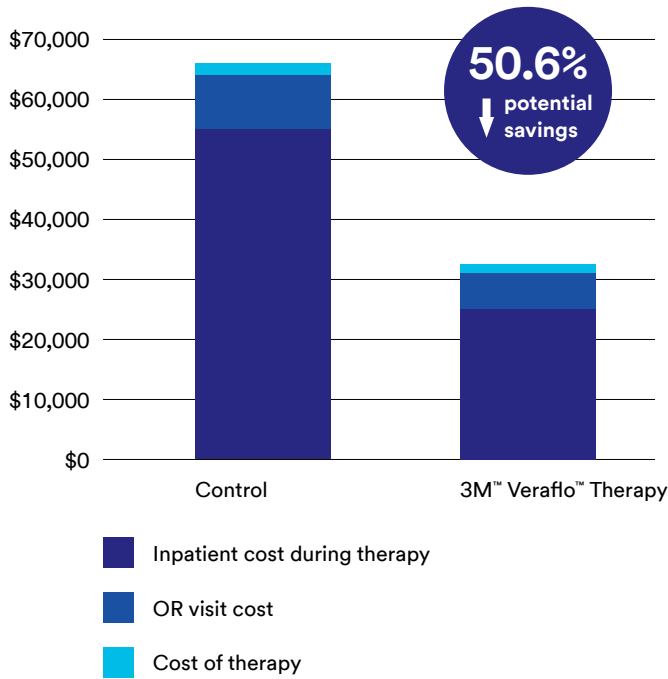
In a second meta-analysis by Kanapathy et al., thirteen articles were included with a total of 624 wounds in 542 patients involving wounds of various etiology.²¹ The pooled proportion of wounds that achieved complete healing was 93.65% (95%CI: 84.02-99.04). Wounds treated with NPWTi-d achieved complete closure via several different techniques, with most common being split-thickness skin graft ($n=126$) followed by local/free flap ($n=99$), primary closure ($n=45$), and secondary intention ($n=32$). The pooled mean time for wound closure for all wounds was 8.49 days (95% confidence interval: 5.09-11.90).²¹

Health Economics

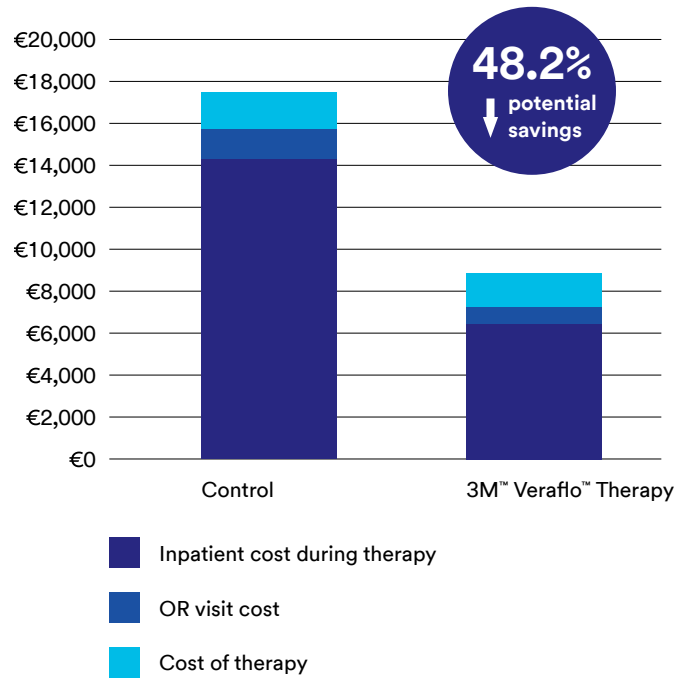
One of the early publications to estimate cost-differences between NPWTi-d and NPWT based on clinical outcomes was conducted by Gabriel et al.²² In this retrospective study, data were extracted from records of patients with extremity or trunk wounds treated with NPWT ($n=34$) or NPWTi-d using saline or polyhexanide ($n=48$). On the basis of outcomes data, a hypothetical economic model using cost assumptions was created to calculate cost savings for NPWTi-d related to the number of debridements and length of therapy. The economic model incorporated the costs of the therapy unit, canisters, and dressings for both treatment modalities. Daily therapy cost for each modality was \$194.80 (NPWTi-d) and \$106.08 (NPWT) based on internal company information. Throughout the length of treatment, NPWTi-d was reported to be more cost-effective by \$1,418 because of the reduced duration of hospital stay in the NPWTi-d groups (NPWTi-d: 8.1 day versus NPWT: 27.4 days).²² Further, there was an estimated per-patient savings of \$8,143 by using NPWTi-d because of the fewer surgical debridements needed in this group (mean of two debridements in the NPWTi-d group versus 4.4 debridements in the NPWT group).²² In this study, NPWTi-d appeared to assist in wound cleansing and exudate removal, which may have allowed for earlier wound closure compared to NPWT.

In 2021, Kim et al. published an economic analysis using means derived from the Gabriel et al. systematic review and meta-analysis to determine the potential cost savings of NPWTi-d versus control therapies.²³ Means across studies (comprising complex acute and chronic wounds) for NPWTi-d versus control (standard NPWT, gauze, or gentamicin polymethylmethacrylate beads) were 1.77 versus 2.69 operating room visits ($p=0.008$), and 9.88 versus 21.80 therapy days ($p=0.02$), respectively.²³ These inputs plus country-specific hospital cost data were used to model a budget impact analysis for patients receiving NPWTi-d versus control therapy within the United States, Germany, or the United Kingdom. Overall costs were estimated as the sum of three main components: cost of hospital stay for duration of therapy, acquisition cost of therapy (device, dressings, canisters and/or instilled solutions), and cost of operating room associated with excisional debridement. Total potential per patient savings for patients receiving NPWTi-d versus control therapies were an estimated \$33,388, €8,467, and £5,626 in the United States, Germany, and the United Kingdom respectively.²³ These cost savings were the result of shorter inpatient LOS (length of stay), shorter duration of NPWT therapy and fewer OR trips for surgical debridements.²³

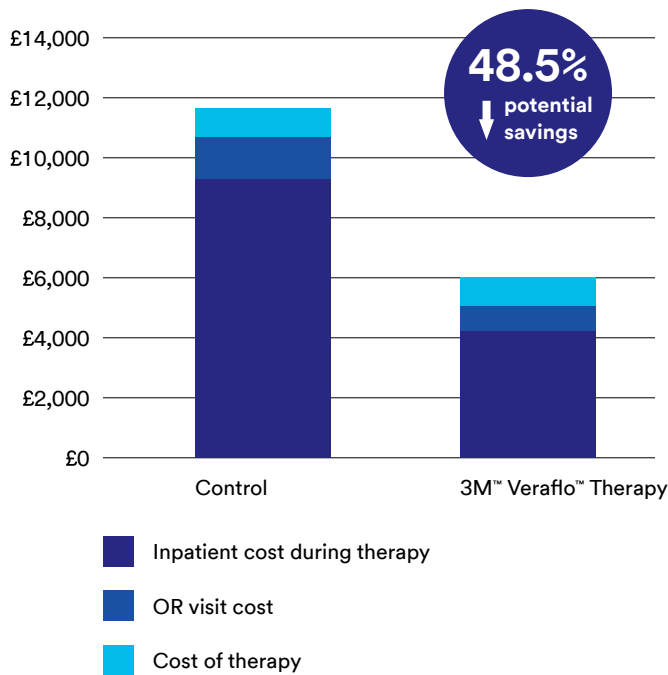
United States per patient cost savings²³



Germany per patient cost savings²³



United Kingdom per patient cost savings²³



Early vs. Late

Several studies have found that early initiation of NPWT resulted in a significant reduction in LOS, treatment days, intensive care unit days, and treatment costs compared to late initiation.²⁴⁻²⁶ Given that NPWTi-d provides wound cleansing that helps manage bioburden, initiating instillation therapy in a timely fashion may further help promote wound healing.²⁷

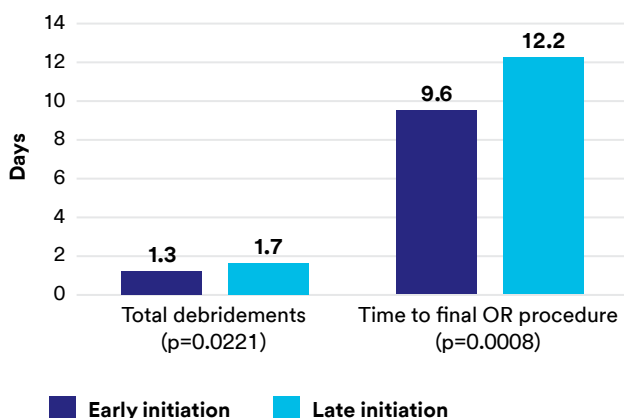
In 2022, a retrospective analysis was done using data from Premier, a large, national all-payer hospital database covering 25% of US hospital days.²⁸ The study population included patients with an inpatient visit in 2019 that received NPWTi-d as indicated by hospital billing data. Clinical outcomes and costs were compared for patients with diverse wound types receiving early (within 1 day of NPWT application) and late (within 2-7 days following NPWT application) NPWTi-d initiation. A matched cohort of 514 patients (257 per group) based on demographics, comorbidities, and wound characteristics was created using propensity scoring.

On average, patients with early NPWTi-d initiation had a statistically significant shorter NPWT duration (7.0 vs. 11.4 days, $p < .0001$) and inpatient stay (13.4 vs. 16.3, $p < .0001$) compared to patients with late NPWTi-d initiation. Early NPWTi-d initiation was also associated with fewer debridements ($p = .0221$), operating room visits during hospitalization ($p = 0.0002$), operating room visits while receiving NPWT ($p < .0001$), days until final operating room procedure ($p = .0008$), and 30-day ($p = .0130$) and 60-day ($p = .0293$) wound-related readmissions. Additionally, patients with early NPWTi-d initiation had a \$10,877 lower (\$34,161 vs. \$45,038, $p < .0001$) mean cost of index admission, which also included lower NPWT costs (\$1,020 vs. \$1,955, $p = .0001$).

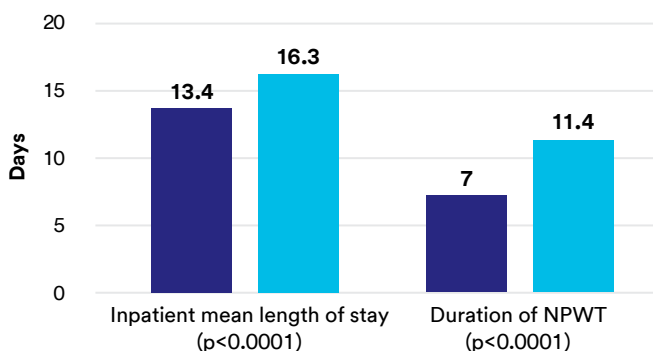
Conclusion

NPWTi-d is intended to manage acute or chronic wounds that would benefit from cyclical instillation, dwell, and removal of topical wound solutions. The benefits of wound cleansing and removal of exudates, wound debris, and infectious materials combined with the known benefits of NPWT help promote wound healing in complex wounds as part of a comprehensive treatment strategy. Clinical evidence has shown the benefits of NPWTi-d, including promotion of granulation tissue formation and preparation of wounds for closure. Clinical and health economic evidence support that early initiation of NPWTi-d has shown reduced time of therapy, fewer debridements and operating room visits, reduced time to wound closure, and reduced length of stay compared to late initiation. Recent innovations have led to ROCF dressings with through holes that provide hydromechanical removal of non-viable tissue and wound debris, which reduces the number of surgical debridements required while promoting granulation tissue formation, creating an environment that promotes wound healing. As the patient population is complex and broad and clinical practice varies, generalization of study results is difficult. Additional studies exploring NPWTi-d as a component of a multi-disciplinary treatment approach will continue to benefit the healthcare community.

Total debridements and time to final OR procedure²⁸



Length of stay and duration of NPWT²⁸



References

1. Saxena V, Hwang CW, Huang S, Eichbaum Q, Ingber D, Orgill DP. Vacuum-assisted closure: microdeformations of wounds and cell proliferation. *Plast Reconstr Surg*. 2004;114(5):1086-1096. doi:10.1097/01.prs.0000135330.51408.97.
2. McNulty AK, Schmidt M, Feeley T, Kieswetter K. Effects of negative pressure wound therapy on fibroblast viability, chemotactic signaling, and proliferation in a provisional wound (fibrin) matrix. *Wound Repair Regen*. 2007;15(6):838-846.
3. McNulty AK, Schmidt M, Feeley T, Villanueva P, Kieswetter K. Effects of negative pressure wound therapy on cellular energetics in fibroblasts grown in a provisional wound (fibrin) matrix. *Wound Repair Regen*. 2009;17(2):192-199.
4. Kim PJ, Attinger CE, Constantine T, et al. Negative pressure wound therapy with instillation: International consensus guidelines update. *International Wound Journal*. 2020;17(1):174-186.
5. Téot L, Boissiere F, Fluieraru S. Novel foam dressing using negative pressure wound therapy with instillation to remove thick exudate. *International Wound Journal*. 2017;14(5):842-848.
6. Lessing C, Slack P, Hong KZ, Kilpadi D, McNulty A. Negative pressure wound therapy with controlled saline instillation (NPWTi): dressing properties and granulation response in vivo. *Wounds*. 2011;23(10):309-19.
7. Kim PJ, Attinger CE, Steinberg JS, et al. The impact of negative-pressure wound therapy with instillation compared with standard negative-pressure wound therapy: a retrospective, historical, cohort, controlled study. *Plastic and Reconstructive Surgery*. 2014;133(3):709-16.
8. Kim PJ, Lavery LA, Galiano RD, et al. The impact of negative-pressure wound therapy with instillation on wounds requiring operative debridement: Pilot randomised, controlled trial. *International Wound Journal*. 2020;17(5):1194-1208.
9. Yang C, Goss SG, Alcantara S, Schultz G, Lantis JC 2nd. Effect of negative pressure wound therapy with instillation on bioburden in chronically infected wounds. *Wounds*. 2017 Aug;29(8):240-246.
10. Goss SG, Schwartz JA, Facchin F, Avdagic E, Gendics C, Lantis II JC. Negative Pressure Wound Therapy with Instillation (NPWTi) Better Reduces Post-debridement Bioburden in Chronically Infected Lower Extremity Wounds than NWPT Alone. *Journal of the American Collage of Clinical Wound Specialists*. 2014; 4(4):74-80.
11. Kim PJ, Silverman R, Attinger CE, et al. Comparison of Negative Pressure Wound Therapy With and Without Instillation of Saline in the Management of Infected Wounds. *Cureus*. 2020;12(7):e9047.
12. Back DA, Scheuermann-Poley C, Willy C. Recommendations on negative pressure wound therapy with instillation and antimicrobial solutions - when, where and how to use: what does the evidence show? *International Wound Journal*. 2013;10(Suppl 1):32-42.
13. Bernstein BH, Tam H. Combination of subatmospheric pressure dressing and gravity feed antibiotic instillation in the treatment of post-surgical diabetic foot wounds: A case series. *Wounds*. 2005;17(2):37-48.
14. Gabriel A, Shores J, Heinrich C, et al. Negative pressure wound therapy with instillation: a pilot study describing a new method for treating infected wounds. *Int Wound J*. 2008;5(3):399-413.
15. Raad W, Lantis JC, II, Tyrie L, Gendics C, Todd G. Vacuum-assisted closure instill as a method of sterilizing massive venous stasis wounds prior to split thickness skin graft placement. *Int Wound J*. 2010;7(2):81-85.
16. Schintler MV, Prandl EC, Kreuzwirt G, Grohmann MR, Spendel S, Scharnagl E. The impact of V.A.C.® Instill in severe soft tissue infections and necrotizing fasciitis. *Infection*. 2009;37(Suppl 1):31-32.
17. Carroll CA, Ingram S. Comparison of topical wound solutions for negative pressure wound therapy with instillation: Effect on granulation in an excisional non-infected acute porcine wound model. Conference Poster presented at: *Proceedings for the Symposium on Advanced Wound Care (Oct 20-22, 2017 Las Vegas NV); Oct 20, 2017 2017*.
18. Carroll CA, Lessing C, Ingram S. Topical Solutions for Negative Pressure Wound Therapy with Instillation: Comparison to Saline Instillation and NPWT in a Non-Infected Acute Wound Porcine Model. Conference Poster. *Proceedings of the Symposium on Advanced Wound Care (October 20-22, 2017, Las Vegas, NV)*.
19. Kim PJ, et al. Negative Pressure Wound Therapy with Instillation: Consensus Guidelines. *Plastic and Reconstructive Surgery*. 2013;132(6):1569-79.
20. Gabriel A, Camardo M, O'Rourke E, Gold R, Kim PJ. Effects of Negative-Pressure Wound Therapy With Instillation versus Standard of Care in Multiple Wound Types: Systematic Literature Review and Meta-Analysis. *Plastic and Reconstructive Surgery*. 2021;147(1S-1): 68S-76S.
21. Kanapathy M, Mantelakis A, Khan N, Younis I, Mosahebi A. Clinical application and efficacy of negative pressure wound therapy with instillation and dwell time (NPWTi-d): A systematic review and meta-analysis. *International Wound Journal*. 2020;17(6):1948-1959.
22. Gabriel A, Kahn K, Karmy-Jones R. Use of negative pressure wound therapy with automated, volumetric instillation for the treatment of extremity and trunk wounds: clinical outcomes and potential cost-effectiveness. *Eplasty*. 2014;14:e41.
23. Kim PJ, Lookess S, Bongards C, Griffin LP, Gabriel A. Economic model to estimate cost of negative pressure wound therapy with instillation vs control therapies for hospitalised patients in the United States, Germany, and United Kingdom. *International Wound Journal*. 2021;19(4):888-894.
24. Baharestani MM, Houliston-Otto DB, Barnes S. Early versus late initiation of negative pressure wound therapy: examining the impact on home care length of stay. *Ostomy Wound Manage*. 2008;54(11):48-53.
25. Kaplan M, Daly D, Stemkowski S. Early intervention of negative pressure wound therapy using Vacuum-Assisted Closure in trauma patients: impact on hospital length of stay and cost. *Advances in Skin and Wound Care*. 2009;22(3):128-132.
26. Gupta S. The impact of evolving V.A.C Therapy technology on outcomes in wound care. *Int Wound J*. 2012;9(Suppl 1):iii-47.

27. Gupta S, Gabriel A, Lantis J, Téot L. Clinical recommendations and practical guide for negative pressure wound therapy with instillation. *Int Wound J*. 2016;13(2):159-74.
28. Collinworth AW, Griffin LP. The effect of timing of instillation therapy on outcomes and costs for patients receiving negative pressure wound therapy. *Wounds*. 2022;34(11):269-275.
29. Kim PJ, Attinger CE, Oliver N, Garwood C, Evans KK, Steinberg JS, Lavery LA. Comparison of Outcomes for Normal Saline and an Antiseptic Solution for Negative-Pressure Wound Therapy with Instillation. *Plastic and Reconstructive Surgery*. 2015;136(5):657e-664e.
30. Deleyto E, Garcia-Ruano A, Gonzalez-Lopez JR. Negative pressure wound therapy with instillation, a cost-effective treatment for abdominal mesh exposure. *Hernia*. 2018 Apr;22(2):311-318.
31. Blome-Eberwein S, Lozano D, Amani H. Utility of Negative Pressure Wound Therapy with Instillation in a Burn Center. *Burns Open*. 2018;2(4):208-212.
32. Garcia-Ruano A, Deleyto E, Garcia-Fernandez S. VAC-instillation therapy in abdominal mesh exposure: a novel indication. *J Surg Res*. 2016;206(2):292-297.
33. Nishii Y. Clinical experience of negative pressure wound therapy with instillation. *Journal of Wound Management and Research*. 2019;15(1):3-4.
34. Omar M, Gathen M, Liodakis E, et al. A comparative study of negative pressure wound therapy with and without instillation of saline on wound healing. *Journal of Wound Care*. 2016;25(8):475-8
35. Timmers MS, Graafland N, Bernards AT, Nelissen RG, van Dissel JT, Jukema GN. Negative pressure wound treatment with polyvinyl alcohol foam and polyhexanide antiseptic solution instillation in posttraumatic osteomyelitis. *Wound Repair Regen*. 2009;17(2):278-286.
36. Chowdhry SA, Wilhelmi BJ. Comparing Negative Pressure Wound Therapy with Instillation and Conventional Dressings for Sternal Wound Reconstructions. *Plastic and Reconstructive Surgery Global Open*. 2019 Jan 4;7(1):e2087.
37. Rycerz AM, Slack P, McNulty AK. Distribution assessment comparing continuous and periodic wound instillation in conjunction with negative pressure wound therapy using an agar-based model. *Int Wound J*. 2013;214-20. DOI:10.1111/j.1742-481X.2012.00968.x
38. Miller-Mikolajczyk C, James R. Real world use: comparing early versus late initiation of negative pressure wound therapy on wound surface area reduction in patients at wound care clinics. Poster presented at The Wound Ostomy and Continence Nurses Society Annual Conference (June 22-26, 2013, Seattle WA)

Appendix A: Evidence Summary of Key Publications

Citation	Wound Type	Treatment Groups	Outcomes
Kim, et al. 2020 ⁸	Wounds requiring surgical debridement	<ul style="list-style-type: none"> NPWTi-d: n=69 Control (NPWT): n=63 	<ul style="list-style-type: none"> Significant mean decrease in total bacterial counts in NPWTi-d group from debridement to dressing change No differences in number of surgical debridements, time to readiness to wound closure, proportion of wounds closed, or incidence of wound complications
Kim, et al. 2015 ²⁹	Infected wounds requiring surgical debridement	<ul style="list-style-type: none"> NPWTi-d with normal saline: n=42 NPWTi-d with PHMB: n=41 	<ul style="list-style-type: none"> Time to final surgical procedure was shorter in the normal saline group (p=0.035) No significant difference in number of operations (p=0.19) The length of hospital stay trended shorter in saline-treated (11.7 days) vs. polyhexanide-treated groups (14.2), though not statistically significant (p=0.08) NPWTi-d with saline had a significantly decreased time to final surgical procedure (5.6 vs. 7.5 days, p=0.04) No difference in wound closure at discharge (p=0.99) or at 1-month follow-up (p=0.90)
Deleyto et al. 2017 ³⁰	Postoperative abdominal wall wound dehiscence with exposed mesh	<ul style="list-style-type: none"> NPWTi-d: n=11 Control (saline-soaked gauze dressings): n=34 	<ul style="list-style-type: none"> Reduced treatment costs in NPWTi-d group Reduced length of stay and number of surgeries required to achieve wound closure, though not statistically significant
Eberwein et al. 2018 ³¹	Burns	<ul style="list-style-type: none"> Burn wounds: n=15, wounds resulting from necrotizing fasciitis: n=6 	<ul style="list-style-type: none"> Mean percent total body surface area was 11.6% for the burn wounds Mean duration of NPWTi-d was 10 days A majority of wounds were closed using split-thickness skin grafts All wounds were successfully closed without complications
Gabriel et al. 2008 ¹⁴	Infected wounds	<ul style="list-style-type: none"> NPWTi-d: n=15 Control (moist wound dressings, retrospective cohort): n=15 	<ul style="list-style-type: none"> Reduced length of treatment, time to infection clearance, time to wound closure, and length of stay in the NPWTi-d group (p<0.001)
Garcia-Ruano et al. 2016 ³²	Postoperative abdominal wall wound dehiscence with exposed mesh	<ul style="list-style-type: none"> NPWTi-d: n=11 Control (saline-soaked gauze dressings): n=34 	<ul style="list-style-type: none"> Reduced number of surgeries to achieve wound closure, length of treatment, and incidence of complications in the NPWTi-d group, though not significant Slightly increased rate of hernia recurrence in NPWTi-d group, though not significant
Goss et al. 2014 ¹⁰	Chronic lower extremity wounds	<ul style="list-style-type: none"> NPWTi-d: n=8 Control (NPWT): n=8 	<ul style="list-style-type: none"> A significant reduction in absolute bioburden observed in NPWTi-d group (p=0.016)
Kim et al. 2014 ⁷	Infected wounds requiring hospital admission	<ul style="list-style-type: none"> NPWTi-d 6-minute dwell: n=34 NPWTi-d 20-minute dwell: n=34 NPWT: n=74 	<ul style="list-style-type: none"> Reduced number of operative visits in NPWTi-d groups (p<0.05) Shorter hospital stay in NPWTi-d 20-minute group (p<0.05) Reduced time to final surgical procedure in NPWTi-d groups (p<0.05) Increased number of wound closures in NPWTi-d 6-minute group (p<0.05)
Nishii. 2019 ³³	Severe wounds	<ul style="list-style-type: none"> NPWTi-d: n=31 Control (NPWT): n=33 	<ul style="list-style-type: none"> Treatment was discontinued due to infection in 7/33 NPWT patients compared to 3/31 NPWTi-d patients Shorter wound healing time in the NPWTi-d group

Citation	Wound Type	Treatment Groups	Outcomes
Omar et al. 2016³⁴	Acute lower extremity wounds	<ul style="list-style-type: none"> NPWTi-d: n=10 Control (NPWT, retrospective cohort): n=10 	<ul style="list-style-type: none"> Significant mean decrease in total bacterial counts in NPWTi-d group from debridement to dressing change No differences in number of surgical debridements, time to readiness to wound closure, proportion of wounds closed, or incidence of wound complications
Timmers et al. 2009³⁵	Posttraumatic osteomyelitis	<ul style="list-style-type: none"> NPWTi-d: n=30 Control (standard dressings): n=94 	<ul style="list-style-type: none"> Reduced rate of recurrence in the NPWTi-d group (p<0.0001) Reduced length of stay and number of surgical procedures in the NPWTi-d group (p<0.0001)
Yang C et al. 2017⁹	Chronically infected wounds	<ul style="list-style-type: none"> NPWTi-d: n=10 Control (NPWT): n=10 	<ul style="list-style-type: none"> A 48% mean reduction in bioburden was observed in the NPWTi-d group (p<0.05) Changes in biofilm-protected bacteria: <ul style="list-style-type: none"> NPWT group mean increase (+14%, p=0.46) NPWTi-d group significant decrease (-48%, p<0.05)
Gabriel et al. 2014²²	Lower extremity or trunk wounds	<ul style="list-style-type: none"> NPWTi-d: n=48 Control (NPWT): n=34 	<ul style="list-style-type: none"> Results showed significant differences (p<0.001) between NPWTi-d and NPWT patients, respectively, for: <ul style="list-style-type: none"> mean OR debridements (2.0 vs. 4.4) mean hospital stay (8.1 vs. 27.4 days) mean LOT (4.1 vs. 20.9 days) mean time to wound closure (4.1 vs. 20.9 days)
Chowdhry and Wilhelmi 2019³⁶	Retrospective single center study on patients with nonhealing sternotomy wounds who underwent surgical debridement	<ul style="list-style-type: none"> NPWTi-d and 20-minute Dakin's solution instillation using Veraflo Therapy: n=15 Standard wound dressings: n=15 	<ul style="list-style-type: none"> There was a significantly shorter time to closure (p<0.0001) for group 1 when compared with group 2 In addition, there were fewer therapy days (p=0.0041), fewer debridements/dressing changes (p=0.0011), and shorter drain duration (p=0.0001) for group 1 when compared with group 2

NPWT = negative pressure wound therapy, 3M™ V.A.C.® Therapy

NPWTi-d = negative pressure wound therapy with instillation and dwell time, 3M™ Veraflo™ Therapy

PHMB = 0.1% polyhexanide plus 0.1% betaine

Note: Specific indications, contraindications, warnings, precautions and safety information exist for these products and therapies. Please consult a clinician and product instructions for use prior to application. Rx only.



3M Company
2510 Conway Ave
St. Paul, MN 55144 USA

Phone 1-800-275-4524 (NPWT products)
1-800-228-3957
Web 3M.com/medical

© 2023 3M. All rights reserved. 3M and the other marks shown are marks and/or registered marks. Unauthorized use prohibited.
70-2013-1108-4