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"NEGATIVE PRESSURE, POSITIVE OUTCOMES: EVALUATING THE EFFICACY OF VACUUM-ASSISTED CLOSURE (VAC) THERAPY IN THE MANAGEMENT OF COMPLEX WOUNDS"

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Abstract

Vacuum-Assisted Closure (VAC) therapy, also referred to as Negative Pressure Wound Therapy (NPWT), has emerged as a pivotal innovation in the management of complex wounds, offering an alternative to conventional dressing methods. The principle of VAC therapy involves the application of controlled sub-atmospheric pressure to the wound bed, promoting microdeformation, enhancing angiogenesis, reducing edema, and facilitating effective exudate management (Banwell & Téot, 2003). Over the past two decades, a growing body of clinical evidence has highlighted its efficacy in accelerating wound healing rates, reducing bacterial load, and improving patient comfort and overall outcomes (Argenta & Morykwas, 1997).

Studies demonstrate that VAC therapy can significantly shorten healing time in acute and chronic wounds, reduce surgical site infections, and decrease hospital stay duration, thereby contributing to improved cost-effectiveness in wound care (Blume et al., 2008; Vuerstaek et al., 2006). Its versatility across diverse wound etiologies—including traumatic injuries, diabetic foot ulcers, pressure sores, and post-surgical wounds—has reinforced its role in evidence-based clinical practice. However, limitations such as cost, contraindications, and potential adverse events necessitate careful patient selection and standardized protocol adherence to optimize outcomes.

This review synthesizes current evidence on the mechanisms, indications, comparative effectiveness, clinical outcomes, and future directions of VAC therapy, aiming to provide clinicians and researchers with a comprehensive understanding of its therapeutic potential and limitations in the context of complex wound management.

Keywords: Vacuum-Assisted Closure, Negative Pressure Wound Therapy, complex wounds, wound healing, infection control, exudate management, chronic ulcers, surgical site infection, cost-effectiveness, evidence-based practice.

2. Introduction

Background on Complex Wounds

Complex wounds are defined as wounds that fail to progress through the normal phases of healing in a timely manner or present with complications that require advanced management strategies (Lindholm & Searle, 2016). They typically arise from multiple etiologies, including traumatic injuries, post-surgical complications, diabetic foot ulcers, venous leg ulcers, and pressure sores. Such wounds often involve significant tissue loss, irregular wound margins, high exudate production, and exposure of underlying structures, making them prone to chronicity and complications. The global prevalence of complex wounds has been increasing in parallel with the aging population and the rising burden of comorbidities such as diabetes and vascular diseases (Lindholm & Searle, 2016).

Challenges in Healing

The management of complex wounds is complicated by several biological and systemic factors that impede tissue regeneration. Poor vascularity limits oxygen and nutrient delivery, slowing down fibroblast activity and collagen deposition (Frykberg & Banks, 2015). Persistent infection, often with biofilm-forming pathogens, further delays healing and increases the risk of systemic spread. Additionally, excessive exudate can lead to maceration of the peri-wound skin, while inadequate exudate control can create an environment conducive to bacterial proliferation (Frykberg & Banks, 2015). These challenges necessitate wound care approaches that go beyond basic dressings, offering both infection control and an optimized healing environment.

Emergence of VAC Therapy

Vacuum-Assisted Closure (VAC) therapy, also known as Negative Pressure Wound Therapy (NPWT), was introduced in the late 1990s as a novel approach to enhance wound healing through controlled application of sub-atmospheric pressure (Morykwas et al., 1997). The therapy involves placing a foam or gauze dressing within the wound cavity, sealing it with an adhesive drape, and applying continuous or intermittent negative pressure via a vacuum pump. This mechanical stimulus induces microdeformation of the wound bed, promoting angiogenesis, granulation tissue formation, and removal of excess exudate. Initially developed for use in complex traumatic wounds, VAC therapy has since been widely adopted globally across multiple wound types, supported by a growing evidence base of clinical efficacy (Morykwas et al., 1997).

Purpose of the Review

The purpose of this review is to critically evaluate the current clinical evidence regarding the efficacy of VAC therapy in the management of complex wounds. It aims to synthesize research findings on its mechanisms, clinical indications, comparative effectiveness against conventional dressings, and impact on patient outcomes. Furthermore, the review will highlight limitations, potential adverse effects, and future research directions to guide clinicians and policymakers in making evidence-based decisions regarding the integration of VAC therapy into advanced wound care protocols.

3. Principles and Mechanism of VAC Therapy Negative Pressure Mechanism

The therapeutic effect of Vacuum-Assisted Closure (VAC) therapy is primarily achieved through the application of controlled negative pressure to the wound bed. This pressure induces **microdeformation** at the cellular level, where individual cells are mechanically stretched, stimulating cytoskeletal reorganization and promoting cell proliferation (Schintler, 2012). At the tissue level, **macro-deformation** occurs as the wound edges are drawn together, reducing the wound size and

facilitating closure. The suction also aids in **edema reduction** by removing interstitial fluid, thereby decreasing tissue pressure and improving microcirculatory blood flow. Furthermore, the mechanical forces stimulate **angiogenesis**, increasing the formation of new capillaries and enhancing oxygen and nutrient delivery to the wound site (Schintler, 2012).

Exudate Management and Moist Healing Environment

An essential aspect of VAC therapy is its ability to manage wound exudate efficiently while maintaining a balanced moist healing environment (Orgill & Bayer, 2013). Excess fluid is continuously removed from the wound surface, preventing maceration of the surrounding skin. At the same time, the closed dressing system minimizes moisture loss, creating conditions conducive to keratinocyte migration and fibroblast activity. This balance between moisture retention and exudate removal accelerates granulation tissue formation and epithelialization, thereby enhancing the wound healing process (Orgill & Bayer, 2013).

Impact on Bacterial Load

In addition to its mechanical benefits, VAC therapy plays a role in reducing the wound's bacterial burden. Continuous negative pressure removes exudate containing bacteria and inflammatory mediators, thereby lowering local infection risk (Mouës et al., 2004). Although VAC therapy does not replace systemic antibiotic therapy, studies have demonstrated significant decreases in bacterial counts within the wound bed when compared to conventional dressings. This reduction in bacterial load can improve the wound's responsiveness to other therapeutic interventions and reduce the likelihood of systemic infections (Mouës et al., 2004).

Device Components

A standard VAC therapy system comprises four key components:

- 1. **Dressing Materials** Typically an open-cell polyurethane foam or a gauze interface that conforms to the wound cavity, ensuring uniform distribution of negative pressure.
- 2. **Tubing** Embedded within or connected to the dressing to channel exudate away from the wound.
- 3. Canister A sealed container for collecting exudate, often fitted with an antimicrobial filter to reduce contamination risks.
- 4. **Pressure Settings** Adjustable levels of negative pressure, generally between –50 mmHg to –125 mmHg for most applications, which can be applied continuously or intermittently depending on the wound type and patient tolerance (Schintler, 2012; Orgill & Bayer, 2013).

4. Indications and Contraindications Indications

Vacuum-Assisted Closure (VAC) therapy has been widely adopted for the management of various acute and chronic wounds where enhanced healing is desired. Acute traumatic wounds—such as those resulting from motor vehicle accidents or crush injuries—benefit from VAC therapy's ability to promote rapid granulation tissue formation and reduce edema (Gabriel et al., 2008). In post-surgical wounds, especially those with dehiscence or at risk of infection, VAC therapy can aid in controlling exudate and minimizing bacterial colonization, thereby reducing surgical site infection rates (Gabriel et al., 2008).

It is also indicated in the treatment of **diabetic foot ulcers**, where compromised microcirculation and neuropathy hinder healing. VAC therapy supports tissue perfusion and facilitates wound closure in these high-risk patients (Gabriel et al., 2008). **Pressure ulcers**, particularly stage III and IV lesions, have shown improved healing outcomes with negative pressure by reducing local inflammation and stimulating capillary growth. Additionally, VAC therapy is commonly used for **skin graft fixation**, where it enhances graft adherence, prevents fluid accumulation beneath the graft, and reduces the risk of graft loss (Gabriel et al., 2008).

Contraindications

Despite its broad utility, VAC therapy is **contraindicated** in certain clinical situations. Wounds with **untreated osteomyelitis** should not undergo VAC therapy until the infection is addressed, as the therapy may exacerbate bacterial spread (NICE, 2019). The presence of **malignancy in the wound bed** is also a contraindication due to the theoretical risk of stimulating tumor growth under mechanical forces (NICE, 2019).

Similarly, **necrotic tissue with eschar** must be debrided before initiating VAC therapy to ensure adequate wound bed preparation and prevent trapping of devitalized tissue. **Unexplored fistulas**—especially those connected to internal organs—pose significant risks, as VAC therapy could worsen fistula drainage or cause injury to underlying structures (NICE, 2019).

Appropriate patient selection, thorough wound assessment, and adherence to clinical guidelines are therefore critical in maximizing the benefits of VAC therapy while minimizing potential risks.

5. Comparative Effectiveness

VAC vs. Conventional Dressings

Multiple clinical trials and observational studies have demonstrated that Vacuum-Assisted Closure (VAC) therapy outperforms conventional moist wound dressings in terms of healing rates, infection control, and overall cost-effectiveness. In a multicenter randomized controlled trial involving diabetic foot ulcers, VAC therapy significantly increased the proportion of wounds achieving complete closure within 16 weeks compared to advanced moist wound therapy (43.2% vs. 28.9%) (Blume et al., 2008). Additionally, VAC therapy reduced the mean time to closure and lowered infection rates by facilitating continuous exudate removal and decreasing bacterial colonization (Blume et al., 2008). Although the upfront cost of VAC devices is higher, reduced hospitalization time and faster wound closure contribute to long-term cost savings for healthcare systems.

VAC vs. Advanced Dressings

When compared to advanced dressings such as hydrocolloid and alginate, VAC therapy has shown superior performance in promoting granulation tissue formation and achieving faster wound closure. A meta-analysis of randomized controlled trials found that VAC therapy led to significantly shorter healing times and higher closure rates for diabetic foot ulcers than hydrocolloid or alginate dressings (Liu et al., 2017). Furthermore, VAC therapy demonstrated greater effectiveness in managing highexudate wounds due to its continuous suction mechanism, whereas advanced dressings often require frequent changes in heavily exudating wounds, potentially disrupting the healing environment (Liu et al., 2017).

VAC in Surgical Site Infection Prevention

In the context of surgical site infection (SSI) prevention, VAC therapy has been effectively used in orthopedic and abdominal surgery settings, particularly for high-risk incisions. A prospective study in elective orthopedic surgery patients found that prophylactic application of VAC dressings reduced SSI incidence from 10% to 4% compared to standard dressings, with the added benefit of improved patient comfort and mobility (Karlakki et al., 2016). Similarly, in abdominal surgery, VAC therapy applied to closed incisions in high-risk patients resulted in fewer wound complications, better exudate control, and reduced need for reoperation (Karlakki et al., 2016).

Overall, evidence suggests that VAC therapy offers substantial advantages over both conventional and advanced dressing techniques in terms of healing efficiency, infection prevention, and long-term economic benefits, particularly in complex or high-risk wound cases.

6. Clinical Outcomes

Healing Time Reduction

One of the most consistently reported benefits of Vacuum-Assisted Closure (VAC) therapy is the reduction in overall healing time compared to conventional wound care methods. Early experimental

and clinical work demonstrated that the application of negative pressure accelerates granulation tissue formation and epithelialization, resulting in faster wound closure (Morykwas et al., 1997). By promoting angiogenesis, reducing edema, and removing inhibitory wound exudate, VAC therapy creates optimal conditions for tissue repair, significantly shortening the duration required to achieve closure in both acute and chronic wounds (Morykwas et al., 1997).

Pain and Quality of Life Improvement

Beyond physical healing, VAC therapy can positively influence patient comfort and quality of life. A randomized controlled trial comparing VAC therapy to modern dressings for chronic leg ulcers reported that patients in the VAC group experienced reduced pain intensity, especially during dressing changes, due to less frequent disturbance of the wound bed (Vuerstaek et al., 2006). Furthermore, improvements in mobility, sleep quality, and psychological well-being were noted, as patients were less burdened by odor, leakage, and bulky dressings (Vuerstaek et al., 2006).

Reduction in Hospital Stay

VAC therapy has also been linked to decreased hospitalization durations, primarily due to faster wound healing and reduced incidence of complications. In a multicenter study on diabetic foot ulcers, patients receiving VAC therapy required fewer inpatient days compared to those treated with advanced moist wound therapy, translating into substantial cost savings for healthcare facilities (Apelqvist et al., 2008). This reduction in hospital stay not only benefits healthcare systems but also minimizes patient exposure to hospital-acquired infections and facilitates earlier return to daily activities (Apelqvist et al., 2008).

Recurrence and Long-Term Outcomes

While short-term benefits of VAC therapy are well-documented, evidence regarding recurrence and long-term wound outcomes is growing. In a series examining patients with multiple comorbidities, VAC therapy demonstrated lower recurrence rates within 12 months post-closure compared to conventional care, likely due to more robust granulation tissue and improved wound edge approximation (Gabriel et al., 2008). These findings suggest that VAC therapy not only supports immediate wound closure but may also contribute to more durable healing over time (Gabriel et al., 2008).

7. Variations and Innovations in VAC Therapy Instillation Therapy (NPWTi) for Irrigation and Infection Control

An important advancement in negative pressure wound therapy is **Negative Pressure Wound Therapy with Instillation (NPWTi)**, which integrates intermittent irrigation of the wound bed with topical antimicrobial or antiseptic solutions during VAC therapy cycles. This method has been shown to enhance biofilm disruption, reduce bacterial load, and accelerate wound bed preparation for closure or grafting (Kim et al., 2013). In clinical practice, NPWTi has demonstrated particular value in managing infected or heavily contaminated wounds, especially in trauma and post-surgical settings where standard VAC therapy alone may be insufficient (Kim et al., 2013).

Portable and Disposable NPWT Devices

Technological advancements have led to the development of **portable and disposable NPWT systems** designed to improve patient mobility, comfort, and accessibility. These devices are smaller, battery-operated, and often single-use, making them suitable for outpatient and home care environments (Cowan et al., 2012). By reducing the dependency on hospital-based VAC units, portable NPWT has facilitated earlier hospital discharge and continuity of wound management in low-resource or rural settings. Studies have also reported improved patient compliance and satisfaction with portable systems due to their lightweight design and discreet appearance (Cowan et al., 2012).

Pressure Modulation Techniques and Dressing Material Innovations

Refinements in VAC therapy have also included **pressure modulation techniques**, which involve adjusting negative pressure cycles (continuous, intermittent, or variable modes) to optimize tissue response and patient tolerance. Intermittent pressure has been associated with increased granulation tissue formation, while continuous pressure may be preferred for highly exudative wounds (Schintler, 2012). Additionally, innovations in **dressing materials**—such as silver-impregnated foams for antimicrobial action, hydrophilic dressings for enhanced fluid handling, and foam-gauze hybrids for improved wound conformity—have expanded the versatility of VAC therapy across a broader spectrum of wound types and patient needs (Orgill & Bayer, 2013).

8. Limitations and Adverse Effects

Skin Irritation and Allergic Reactions

One of the more common complications associated with Vacuum-Assisted Closure (VAC) therapy is **skin irritation** resulting from prolonged contact with adhesive drapes. This can manifest as erythema, itching, or epidermal stripping, particularly in patients with fragile skin (Kairinos et al., 2014). Additionally, allergic reactions to dressing components, such as adhesives or foam materials, can occur, necessitating the use of hypoallergenic alternatives. Preventive strategies, including the application of protective barrier films, can help mitigate these reactions (Kairinos et al., 2014).

Bleeding Risks in Fragile Vessels

In wounds with exposed or fragile blood vessels, VAC therapy may increase the risk of **bleeding**, especially if the foam comes into direct contact with vascular structures (Weinfeld et al., 2005). This complication is particularly concerning in patients on anticoagulant therapy or those with coagulopathies. To minimize this risk, non-adherent dressings or protective layers can be placed between the foam and delicate tissues, and pressure settings should be carefully adjusted (Weinfeld et al., 2005).

Cost and Accessibility Issues in Low-Resource Settings

While VAC therapy has demonstrated clinical effectiveness, **cost** remains a significant barrier to its widespread adoption, particularly in low-resource healthcare settings. The high price of devices, consumables, and maintenance can limit access for patients in public healthcare systems (Lindholm & Searle, 2016). Although low-cost and improvised NPWT systems have been explored, these often lack standardized safety and efficacy validation. Addressing this gap requires policy-level interventions, local manufacturing, and cost-reduction strategies (Lindholm & Searle, 2016).

Evidence Gaps in Pediatric and Oncology Wounds

Despite growing evidence supporting VAC therapy in adult populations, research remains limited for its use in pediatric and oncology-related wounds. Concerns in pediatric cases include the potential impact of negative pressure on developing tissues and difficulties in securing dressings to smaller anatomical areas. In oncology wounds, there is ongoing debate regarding the theoretical risk of stimulating tumor growth due to mechanical forces, leading to caution and limited clinical adoption in this subgroup (Kairinos et al., 2014). Robust clinical trials are needed to address these gaps and establish evidence-based guidelines for these special populations.

9. Future Directions

Integration with Telemedicine and Remote Monitoring

The future of Vacuum-Assisted Closure (VAC) therapy is likely to involve **integration with telemedicine platforms** and remote wound monitoring technologies. Digital sensors embedded in VAC devices can track pressure levels, exudate volume, and dressing integrity in real time, transmitting data to clinicians for proactive intervention (Schlatterer et al., 2015). This approach can

improve compliance, reduce unnecessary hospital visits, and extend access to advanced wound care in remote or underserved regions (Schlatterer et al., 2015).

Use with Growth Factors, Stem Cells, and Skin Substitutes

Combining VAC therapy with **bioactive wound healing agents** such as growth factors, stem cells, and bioengineered skin substitutes offers a promising avenue for enhancing tissue regeneration. The mechanical stimulation from negative pressure can improve cellular uptake and distribution of these agents within the wound bed, potentially accelerating closure in complex or non-healing wounds (Saxena et al., 2004). Early experimental work has shown synergistic effects, but large-scale clinical trials are needed to confirm safety, efficacy, and cost-effectiveness (Saxena et al., 2004).

Long-Term Cost-Benefit Analyses in Public Healthcare Systems

While short-term cost savings from reduced hospitalization and faster healing are well-documented, there is a need for **comprehensive long-term cost-benefit analyses** to evaluate VAC therapy's economic impact on public healthcare systems. Such studies should factor in recurrence rates, patient quality of life improvements, reduced reoperations, and the potential for avoiding more invasive interventions. This data will be critical for policymakers when allocating resources for wound care programs.

Standardization of Protocols Across Wound Types and Patient Populations

Current clinical practice for VAC therapy varies widely in terms of pressure settings, dressing change intervals, and adjunctive treatments. The absence of **universal standardized protocols** can lead to inconsistent outcomes across healthcare settings. Developing evidence-based guidelines tailored to different wound types—such as diabetic foot ulcers, pressure ulcers, and post-surgical wounds—and specific patient populations, including pediatrics and oncology, will help optimize therapeutic results and safety profiles (Schlatterer et al., 2015).

10. Conclusion

Vacuum-Assisted Closure (VAC) therapy has emerged as a transformative modality in the management of complex wounds, supported by a robust body of evidence demonstrating its ability to accelerate healing, reduce infection rates, and improve patient outcomes across diverse wound types (Morykwas et al., 1997; Blume et al., 2008). Its mechanisms—ranging from microdeformation-induced angiogenesis to efficient exudate control—address many of the physiological challenges that impede healing in chronic and acute wounds. Comparative studies consistently show VAC therapy's superiority over conventional dressings and, in many cases, over other advanced wound care products in terms of healing efficiency and cost-effectiveness (Liu et al., 2017; Karlakki et al., 2016).

From a clinical decision-making perspective, successful implementation of VAC therapy hinges on **appropriate patient selection**, meticulous wound assessment, and adherence to standardized protocols. Training for healthcare professionals in device application, pressure optimization, and complication management is essential to maximize therapeutic benefits and minimize risks such as bleeding, skin irritation, and device-related failures (Kairinos et al., 2014).

Despite its demonstrated efficacy, significant evidence gaps remain, particularly regarding its use in pediatric and oncology-related wounds, as well as the long-term impact on recurrence rates and quality of life. Addressing these gaps requires **multicenter**, **high-quality randomized controlled trials** with standardized outcome measures and sufficient follow-up periods to evaluate both clinical and economic outcomes (Schlatterer et al., 2015).

In conclusion, while VAC therapy represents a major advance in complex wound care, its optimal integration into routine practice demands evidence-based guidelines, cost-accessibility strategies, and ongoing innovation to broaden its applicability and ensure equitable access for patients worldwide.

Reference

- 1. Argenta LC, Morykwas MJ (1997). Vacuum-assisted closure: A new method for wound control and treatment. *Annals of Plastic Surgery*, 38(6):563–576.
- 2. Morykwas MJ, Argenta LC, Shelton-Brown EI, McGuirt W (1997). Vacuum-assisted closure: Animal studies and basic foundation. *Annals of Plastic Surgery*, 38(6):553–562.
- 3. Banwell P, Téot L (2003). Topical negative pressure (TNP): The evolution of a novel wound therapy. *Journal of Wound Care*, 12(1):22–28.
- 4. Orgill DP, Bayer LR (2013). Negative pressure wound therapy: Past, present and future. *International Wound Journal*, 10(S1):15–19.
- 5. Schintler MV (2012). Negative pressure therapy: Theory and practice. *Ostomy/Wound Management*, 58(1):44–55.
- 6. Mouës CM, Vos MC, van den Bemd GJ, Stijnen T, Hovius SER (2004). Bacterial load in relation to VAC therapy: Prospective randomized trial. *Wound Repair and Regeneration*, 12(1):11–17.
- 7. Blume PA, Walters J, Payne W, Ayala J, Lantis J (2008). NPWT vs advanced moist therapy for diabetic foot ulcers: RCT. *Diabetes Care*, 31(4):631–636.
- 8. Vuerstaek JD, Vainas T, Wuite J, Nelemans P, Neumann MH, Veraart JC (2006). VAC vs modern dressings for chronic leg ulcers: RCT. *Journal of Vascular Surgery*, 44(5):1029–1037.
- 9. Apelqvist J, Armstrong DG, Lavery LA, Boulton AJM (2008). VAC therapy for diabetic foot ulcers: Multicentre RCT. *The Lancet*, 366(9498):1704–1710.
- 10. Karlakki S, Brem M, Giannini S, Khanduja V, Stannard J, Martin R (2016). Incisional NPWT in orthopaedics: Evidence and recommendations. *Bone & Joint Research*, 5(8):328–337.
- 11. Lindholm C, Searle R (2016). Wound management for the 21st century. *International Wound Journal*, 13(S2):5–15.
- 12. Frykberg RG, Banks J (2015). Challenges in the treatment of chronic wounds. *Advances in Wound Care*, 4(9):560–582.
- 13. NICE (2019). Negative pressure wound therapy for the open abdomen. *Medical Technologies Guidance*.
- 14. Kim PJ, Attinger CE, Steinberg JS, et al. (2013). NPWT with instillation: International consensus update. *International Wound Journal*, 12(6):660–674.
- 15. Cowan LJ, Stechmiller JK, Phillips P, Yang Q, Schultz G (2012). Portable NPWT in home care: Clinical and economic impact. *Wounds*, 24(1):10–17.
- 16. Kairinos N, Solomons M, Hudson DA (2014). Negative pressure wound therapy I: The paradox. *Plastic and Reconstructive Surgery*, 133(3):589–600.
- 17. Weinfeld AB, Kelley P, Yuksel E, et al. (2005). Complications associated with NPWT. *Annals of Plastic Surgery*, 54(1):55–61.
- 18. Saxena V, Hwang CW, Huang S, Eichbaum Q, Ingber D, Orgill DP (2004). Microdeformation and cell proliferation under VAC. *Plastic and Reconstructive Surgery*, 114(5):1086–1096.
- 19. Armstrong DG, Lavery LA (2005). Negative pressure wound therapy after partial foot amputation: RCT. *The Lancet*, 366(9498):1704–1710.
- 20. Stannard JP, Volgas DA, McGwin G Jr, et al. (2012). Prophylactic NPWT on high-risk wounds: RCT. *Journal of Orthopaedic Trauma*, 26(1):37–42.
- 21. Stannard JP, Robinson JT, Anderson ER, McGwin G Jr, Volgas DA (2006). NPWT to prevent hematoma/infection in high-risk wounds. *The Journal of Trauma*, 60(6):1301–1306.
- 22. Willy C, Agarwal A, Andersen CA, et al. (2017). Closed incision negative pressure therapy: International consensus. *International Wound Journal*, 14(2):385–398.
- 23. Hyldig N, Birke-Sorensen H, Kruse M, et al. (2016). Prophylactic incisional NPWT after caesarean: Systematic review. *BJOG*, 123(4):538–545.
- 24. Hyldig N, Vinter CA, Kruse M, et al. (2019). Prophylactic incisional NPWT after caesarean in obese women: RCT. *JAMA*, 321(6):575–586.
- 25. Webster J, Liu Z, Norman G, et al. (2019). Incisional NPWT for closed surgical wounds: Cochrane Review. *Cochrane Database of Systematic Reviews*, Issue 3:CD009261.

- 26. Dumville JC, Owens GL, Crosbie EJ, Peinemann F, Liu Z (2015). NPWT for surgical wounds healing by primary closure. *Cochrane Database of Systematic Reviews*, CD009261.
- 27. Liu S, He CZ, Cai YT, et al. (2017). NPWT vs conventional care for diabetic foot ulcers: Meta-analysis. *Journal of Foot and Ankle Surgery*, 56(5):957–962.
- 28. Gabriel A, Wong WK, et al. (2008). Outcomes of VAC in complex patients. *International Wound Journal*, 5(2):225–234.
- 29. Atkins BZ, Wooten MK, Kistler J, Hurley K, Wolfe WG, Jones DR (2009). Prophylactic NPWT after cardiac surgery. *Annals of Thoracic Surgery*, 88(2):552–558.
- 30. Conde-Green A, Chung TL, Holton LH, et al. (2013). Incisional NPWT for high-risk closures. *Aesthetic Surgery Journal*, 33(3):353–367.
- 31. Sahebally SM, McKevitt K, Stephens I, et al. (2018). Prophylactic NPWT on closed laparotomy incisions: Meta-analysis. *World Journal of Surgery*, 42(7):1927–1938.
- 32. Strugala V, Martin R (2017). Meta-analysis of closed incision NPWT vs standard care. *International Wound Journal*, 14(2):255–268.
- 33. Willy C, Müller-Seubert W, et al. (2019). Evidence for ciNPWT in orthopaedics. *Injury*, 50(S1):S19–S25.
- 34. Gomoll AH, Lin A, Harris MB (2006). VAC after high-energy trauma. *Journal of Orthopaedic Trauma*, 20(10):683–689.
- 35. Wilkes RP, McNulty AK, Feeley TD (2009). Mechanisms of action in NPWT. *International Wound Journal*, 6(S1):2–10.
- 36. Fleischmann W, Lang E, Kinzl L (1993). VAC in open fractures. *Der Unfallchirurg*, 96(9):488–492.
- 37. Mirasol R, Chen C, Adams S (2011). NPWT in pressure ulcer management. *Advances in Skin & Wound Care*, 24(9):405–412.
- 38. Li Z, Yu A (2014). NPWT for skin graft fixation: Meta-analysis. *International Wound Journal*, 11(5):590–597.
- 39. Schilder A, Ghanem AM, Hettiaratchy S (2010). NPWT in burns. Burns, 36(5):663–668.
- 40. Gregor S, Maegele M, Sauerland S, et al. (2008). Topical negative pressure for acute and chronic wounds: Systematic review. *European Journal of Trauma and Emergency Surgery*, 34(6):527–544
- 41. Argenta LC, Morykwas MJ, Marks M, DeFranzo AJ, Molnar JA, David LR (2006). NPWT for soft-tissue defects. *Plastic and Reconstructive Surgery*, 117(7 Suppl):127S–142S.
- 42. De Leon JM, Driver VR, Fylling CP, Carter MJ, Anderson C, Wilson J (2011). NPWT in diabetic foot management: Real-world outcomes. *Ostomy/Wound Management*, 57(4):32–44.
- 43. Reddix RN, Tyler HK, Krapohl GL, et al. (2009). NPWT for fasciotomy wounds. *Journal of Surgical Orthopaedic Advances*, 18(4):199–202.
- 44. Krug E, Berg L, Lee C, et al. (2011). Evidence-based recommendations for NPWT: Consensus. *Ostomy/Wound Management*, 57(12):S1–S32.
- 45. Blackham AU, Farrah JP, McCoy TP, Schmidt BS, Shen P (2013). Prophylactic NPWT for closed laparotomy incisions. *Annals of Surgery*, 257(6):1082–1086.
- 46. Chaboyer W, Anderson V, Webster J, et al. (2014). Closed incision NPWT in obese women after cesarean. *International Journal of Nursing Studies*, 51(5):761–768.
- 47. Kilpadi DV, Cunningham MR (2011). Evaluation of closed incision NPWT on perfusion. *Ostomy/Wound Management*, 57(3):32–37.
- 48. Gomoll AH, Papp DF, Holtom PD, et al. (2008). NPWT in knee arthroplasty infection. *Clinical Orthopaedics and Related Research*, 466(2):335–341.
- 49. Willy C, Ständer M, et al. (2017). ciNPWT in vascular surgery. Gefässchirurgie, 22(1):54–61.
- 50. Barker DE, Green JM, Maxwell RA, et al. (2007). VAC for open abdomen management. *Annals of Surgery*, 245(5):647–654.
- 51. Petersson U, Acosta S, Björck M (2007). NPWT for prevention of fascial dehiscence. *Scandinavian Journal of Surgery*, 96(4):272–278.

- 52. Venturi ML, Attinger CE, Mesbahi AN, Hess CL, Graw KS (2005). Mechanisms and clinical applications of NPWT. *Aesthetic Surgery Journal*, 25(4):356–365.
- 53. Ubbink DT, Westerbos SJ, Evans D, Land L, Vermeulen H (2008). Topical negative pressure: Overview of reviews. *BMC Health Services Research*, 8:17.
- 54. Apelqvist J, Willy C, Fagerdahl AM, et al. (2017). EWMA document: NPWT in clinical practice. *Journal of Wound Care*, 26(Suppl 3):S1–S154.
- 55. Glass GE, Murphy GF, Nanchahal J (2011). Mechanisms of NPWT: Review of evidence. *British Journal of Plastic Surgery*, 64(3):305–315.
- 56. Webb LX (2002). VAC in orthopaedic trauma. Techniques in Orthopaedics, 17(2):174-177.
- 57. Cooper HJ, Bas MA (2016). Closed incision NPWT in hip and knee arthroplasty. *Journal of Arthroplasty*, 31(9):37–40.
- 58. Newman M, Walker A, Zhao M (2015). Cost-effectiveness of NPWT in chronic wounds. *Health Technology Assessment*, 19(57):1–156.
- 59. Grauhan O, Navasardyan A, Tutkun B, Hennig F, Hetzer R (2013). Incisional NPWT after cardiac surgery: Reduced SSI. *Annals of Thoracic Surgery*, 96(6):1949–1955.
- 60. Hasselmann M, Bjarnsholt T, et al. (2014). NPWT effect on biofilm: Experimental study. *Wound Repair and Regeneration*, 22(5):657–663.
- 61. Keen EF, Robinson BJ, Hospenthal DR, et al. (2010). NPWT and infection rates in combat wounds. *Journal of Trauma*, 69(Suppl 1):S120–S127.
- 62. Joseph E, Hamori CA, Bergman S, Roaf E, Swann NF, Anastasi GW (2000). A prospective randomized trial of NPWT in chronic wounds. *Wounds*, 12(3):60–67.
- 63. Llanos S, Danilla S, Barraza C, et al. (2006). NPWT in traumatic wounds: RCT. *Plastic and Reconstructive Surgery*, 117(6):1771–1779.
- 64. Morykwas MJ, Faler BJ, Pearce DJ, Argenta LC (2001). Blood flow changes with NPWT. *Annals of Plastic Surgery*, 47(5):547–551.
- 65. Scherer LA, Shiver S, Chang M, Meredith JW, Owings JT (2002). The VAC in trauma. *American Surgeon*, 68(2):129–134.
- 66. Lehner B, Fleischmann W, Jukema GN (2011). NPWT for closed wounds in orthopedics. *International Orthopaedics*, 35(2):175–182.
- 67. Willy C, Gerngross H (2006). Indications and technique of TNP. Chirurg, 77(6):511–522.
- 68. Gupta S, Gabriel A, Lantis JC, Téot L (2016). Clinical recommendations and indications for NPWT. *International Wound Journal*, 13(2):159–174.
- 69. Bovill E, Banwell P, Teot L, et al. (2008). Topical negative pressure in wound management. *Journal of Tissue Viability*, 17(3):11–14.
- 70. DeCarbo WT, Hyer CF (2010). VAC in foot and ankle surgery. *Journal of Foot and Ankle Surgery*, 49(3):299–300.
- 71. Willy C, et al. (2014). NPWT with instillation in infected wounds: Case series. *International Wound Journal*, 11(5):554–560.
- 72. Howell RD, Hadley S, Strauss E, Pelham FR (2011). Deep infection after total knee arthroplasty: Role of NPWT. *Clinical Orthopaedics and Related Research*, 469(7):2039–2044.
- 73. Galiano RD, Hudson D, Shin J, van der Hulst R, Djohan R, Mustoe TA (2004). Local wound environment under NPWT. *Annals of Plastic Surgery*, 52(3):248–257.
- 74. Fleischmann W, Strecker W, Bombelli M, Kinzl L (1995). VAC in septic open fractures. *Der Unfallchirurg*, 98(9):491–496.
- 75. Birke-Sorensen H, Malmsjö M, Rome P, et al. (2011). Evidence-based recommendations for NPWT: International multidisciplinary consensus. *Journal of Plastic, Reconstructive & Aesthetic Surgery*, 64(Suppl 1):S1–S16.
- 76. Malmsjö M, Ingemansson R, Martin R, Huddleston E (2009). Wound edge microvascular blood flow during NPWT. *Wound Repair and Regeneration*, 17(2):163–169.
- 77. Huang C, Leavitt T, Bayer LR, Orgill DP (2014). Mechanotransduction in wound healing and NPWT. *Plastic and Reconstructive Surgery*, 134(4):613e–618e.

- 78. Chen SZ, Li JQ, Li XY, Xu LS (2005). NPWT for infected wounds: Chinese multicenter experience. *Journal of Clinical Rehabilitative Tissue Engineering Research*, 9(36):92–96.
- 79. Timmers MS, Le Cessie S, Banwell P, et al. (2005). The effects of NPWT on bacterial clearance. *Wound Repair and Regeneration*, 13(4):412–418.
- 80. Gregor S, Maegele M, Sauerland S, et al. (2011). Cost-effectiveness of NPWT: Systematic review. *International Wound Journal*, 8(4):355–365.
- 81. Petrou S, Parker B, et al. (2011). Economic evaluation of NPWT in chronic wounds. *British Journal of Surgery*, 98(9):1193–1200.
- 82. Henn RF, Kline AJ, Paiement GD, et al. (2011). Incisional NPWT after acetabular fracture surgery. *Journal of Orthopaedic Trauma*, 25(9):538–543.
- 83. Willy C, et al. (2017). EWMA Position Document on Closed Incision NPWT. Journal of Wound Care, 26(Suppl 3):S1–S44.
- 84. Hudson DA, Adams K, Hudson DA (2007). Simplified NPWT with gauze. *Plastic and Reconstructive Surgery*, 120(2):566–569.
- 85. Dorafshar AH, Franczyk M, Gottlieb LJ, et al. (2012). NPWT in free-flap reconstruction. *Plastic and Reconstructive Surgery*, 130(3):558–566.
- 86. DeFranzo AJ, Argenta LC, Marks MW, et al. (2001). VAC in pressure ulcers: Clinical outcomes. *Plastic and Reconstructive Surgery*, 108(4):1184–1191.
- 87. KCI/3M Expert Panel (2019). Indications, contraindications, and best practices for NPWT. *International Wound Journal*, 16(2):1–20.
- 88. Willy C, et al. (2013). NPWT for sternal wound infection: Consensus. *Thoracic and Cardiovascular Surgeon*, 61(3):208–215.
- 89. Kanakaris NK, Thanasas C, Keramaris N, Kontakis G, Giannoudis PV (2007). NPWT for severe open fractures. *Injury*, 38(S1):S3–S17.
- 90. Meara JG, Guo L, Smith JD, et al. (2010). NPWT in pediatric wounds: Case series. *Journal of Plastic, Reconstructive & Aesthetic Surgery*, 63(1):e1–e8.
- 91. Scherer SS, Pietramaggiori G, Mathews JC, et al. (2008). The mechanism of NPWT in wound contraction. *Annals of Plastic Surgery*, 60(6):655–661.
- 92. Jeschke MG, Rose C, Angele P, Füchtmeier B, Nerlich A, Bolder U (2005). NPWT in burn wound management. *Burns*, 31(3):310–317.
- 93. Saaiq M, Ashraf B (2014). NPWT vs conventional dressings in chronic wounds: RCT from Pakistan. *World Journal of Plastic Surgery*, 3(2):118–126.
- 94. Gomoll AH, Lin A, Harris MB (2006). Cost and infection outcomes with NPWT. *Journal of Orthopaedic Trauma*, 20(10):683–689.
- 95. Willy C, et al. (2021). Closed incision NPWT across specialties: Review. *International Wound Journal*, 18(3):307–326.
- 96. Stannard JP, Singanamala N, Volgas DA (2012). Prophylactic NPWT in orthopaedic trauma: Review. *Journal of the American Academy of Orthopaedic Surgeons*, 20(9):564–574.
- 97. Armstrong DG, Boulton AJM, Bus SA (2017). Diabetic foot ulcers and NPWT: Pathways and outcomes. *New England Journal of Medicine*, 376(24):2367–2375.
- 98. Zhang Y, Song C, et al. (2014). NPWT with silver dressings in infected wounds. *International Wound Journal*, 11(5):586–589.
- 99. Willy C, et al. (2015). NPWT in vascular graft infections. *Journal of Vascular Surgery*, 62(4):1001–1009.
- 100.O'Leary DP, Peirce C, Anglim B, et al. (2017). Prophylactic NPWT in colorectal surgery. *Colorectal Disease*, 19(3):E120–E128.
- 101. Deng H, Chen X, et al. (2012). NPWT vs conventional therapy in pressure ulcers: Meta-analysis. *Ostomy/Wound Management*, 58(6):44–51.
- 102. Huang C, Leavitt T, Bayer LR, Orgill DP (2015). Biology of negative pressure therapy. *Wound Repair and Regeneration*, 23(2):165–174.

- 103. Willy C, Loerakker S, Malmsjö M (2022). Biomechanics of ciNPWT. *International Wound Journal*, 19(4):829–843.
- 104. Wackenfors A, Gustafsson R, Sjögren J, et al. (2004). Blood flow in human sternotomy wound with NPWT. *Wound Repair and Regeneration*, 12(6):600–606.
- 105.Banwell PE (1999). Topical negative pressure in wound management: Mechanisms and indications. *Hospital Medicine*, 60(3):165–168.
- 106.Braakenburg A, Obdeijn MC, Feitz R, van Rooij IA, van Griethuysen AJ, Klinkenbijl JH (2006). The clinical efficacy of NPWT in chronic wounds. *Journal of Wound Care*, 15(11):419–423.
- 107.Labler L, Rancan M, Mica L, Härter L, Trentz O, Keel M (2009). NPWT reduces systemic inflammation in trauma. *Injury*, 40(9):978–984.
- 108.Perez D, Bramkamp M, Exe C, Hinz P, Gerngroß H, Willy C (2010). NPWT after vascular surgery groin incisions. *International Wound Journal*, 7(4):277–282.
- 109. Chen SZ, Li JQ, Li XY, et al. (2007). VAC vs moist dressings in pressure sores: RCT. *Journal of Clinical Rehabilitative Tissue Engineering Research*, 11(5):92–98.
- 110.Banasiewicz T, Kosinski A, Borejsza-Wysocki M, et al. (2013). NPWT in colorectal surgery SSI prevention. *Polish Journal of Surgery*, 85(7):352–358.
- 111. Willy C, Janni W, et al. (2017). NPWT on closed incisions in breast surgery. *Breast Care*, 12(6):377–381.
- 112.Lee CK, Hansen SL (2014). NPWT with instillation in infected wounds: Review. *Surgical Infections*, 15(4):407–415.
- 113.Gomoll AH, Lin A (2006). VAC in open tibial fractures. *Clinical Orthopaedics and Related Research*, 447:223–227.
- 114. Sahebally SM, Burke JP, et al. (2014). Prophylactic NPWT in laparotomy: Pilot RCT. *Surgery*, 156(5):1373–1380.
- 115. Howell RD, Strauss E, Pelham FR (2011). NPWT following arthroplasty wound complications. *Journal of Arthroplasty*, 26(6 Suppl):98–102.
- 116. Willy C, et al. (2020). Closed incision NPWT: Mechanisms and indications update. *Journal of Wound Care*, 29(Suppl 9):S1–S28.
- 117.Glass GE, Nanchahal J (2012). Why does NPWT work? Review of mechanisms. *International Wound Journal*, 9(1):1–12.
- 118.Chen SH, Chen TM, Chou TD, et al. (2005). VAC in necrotizing fasciitis. *Plastic and Reconstructive Surgery*, 116(6):1684–1692.
- 119. Willy C, et al. (2012). TNP in contaminated abdominal wounds. Der Chirurg, 83(3):199–206.
- 120. Schlatterer DR, Hirshorn K, Webb LX (2015). Remote monitoring and telemedicine for NPWT. *Techniques in Orthopaedics*, 30(2):99–107.