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Medical technology consultation: VAC Veraflo Therapy system for acute infected or chronic wounds that are failing to heal

Supporting documentation – Committee papers

The enclosed documents were considered by the NICE medical technologies advisory committee (MTAC) when making their draft recommendations:

1. **EAC assessment report** – an independent report produced by an external assessment centre who have reviewed and critiqued the available evidence.
2. **Assessment report overview** – an overview produced by the NICE technical lead which highlights the key issues and uncertainties in the company's submission and assessment report.
3. **Scope of evaluation** – the framework for assessing the technology, taking into account how it works, its comparator(s), the relevant patient population(s), and its effect on clinical and system outcomes. The scope is based on the sponsor's case for adoption.
4. **Adoption scoping report** – produced by the adoption team at NICE to provide a summary of levers and barriers to adoption of the technology within the NHS in England.
5. **Sponsor submission of evidence** – the evidence submitted to NICE by the notifying company.
6. **Expert questionnaires** – expert commentary gathered by the NICE team on the technology.
7. **EAC correspondence log** – a log of all correspondence between the external assessment centre (EAC) and the company and/or experts during the course of the development of the assessment report.
8. **Company fact check comments** – the manufacturer's response following a factual accuracy check of the assessment report.

Please use the above links and bookmarks included in this PDF file to navigate to each of the above documents.

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Medical technologies guidance

V.A.C. VERAFLO Therapy System for acute infected or chronic wounds that are failing to heal

External Assessment Centre report

Produced by: Newcastle External Assessment Centre

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Purpose of the assessment report

The purpose of this External Assessment Centre (EAC) report is to review and critically evaluate the company's clinical and economic evidence presented in the submission to support their case for adoption in the NHS. The report may also include additional analysis of the submitted evidence or new clinical and/or economic evidence. NICE has commissioned this work and provided the template for the report. The report forms part of the papers considered by the Medical Technologies Advisory Committee when it is making decisions about the guidance.

Declared interests of the authors

Description of any declared interests with related companies, and the matter under consideration. See NICE's Policy on managing interests for board members and employees.

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Responsibility for report

The views expressed in this report are those of the authors and not those of NICE. Any errors are the responsibility of the authors.

Contents

Abbreviations

Term	Definition
AWC	Advanced wound care
CASP	Critical Appraisal Skills Programme
CFU	Colony forming unit
CI	Confidence interval
DRG	Diagnosis-related group
DSA	Deterministic sensitivity analysis
EAC	External Assessment Centre
HES	Hospital episode statistics
HRG	Healthcare resource group
IPG	Interventional procedures guidance
IQR	Interquartile range
ITT	Intention to treat
KoL	Key opinion leader
LoS	Length of [hospital] stay
LoT	Length of treatment
MAUDE	Manufacturer and User Facility Device Experience
MeSH	Medical subject headings
MHRA	Medicines & Healthcare products Regulatory Agency
MTEP	Medical Technologies Evaluation Programme
MTG	Medical technologies guidance
MIB	Medtech innovation briefing
NHS	National Health Service
NICE	National Institute for Health and Care Excellence
NPWT	Negative pressure wound therapy
NPWTi	Negative pressure wound therapy with instillation
PP	Per protocol
PRESS	Peer Review of Electronic Search Strategies
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PSA	Probabilistic sensitivity analysis
RCT	Randomised controlled trial
SD	Standard deviation
STSG	Split-thickness skin graft
VAS	Visual analogue scale
Vs	Versus

Executive summary

V.A.C. VERAFLO is an automated system that combines negative pressure wound therapy (NPWT) and wound instillation with topical solutions (NPWTi). Following a systematic literature search, 19 studies were identified that were considered by the EAC to be in scope of the assessment. These included 9 comparative studies, of which 2 were RCTs of limited relevance (Kim *et al.*, 2015, Yang *et al.*, 2017), and 6 were observational studies (Chowdhry and Wilhelmi, 2019, Deleyto *et al.*, 2018, Gabriel *et al.*, 2014, Goss *et al.*, 2012, Kim *et al.*, 2014, Omar *et al.*, 2016). One unpublished, directly relevant RCT was also identified, and has since been published (Kim *et al.*, 2020). Ten single-armed observational studies identified were of limited utility.

The EAC considered evidence from the recently published RCT was the most robust (Kim *et al.*, 2020). It compared NPWTi with NPWT in patients with acute and chronic wounds (n = 181) and reported no significant difference in its primary endpoint, the number of follow-on surgical debridements: 1.1 (95% confidence interval [CI] 0.93 to 1.30) for NPWTi compared with 1.1 (95% CI 0.85 to 1.18) for NPWT (p = 0.68). The RCT reported that NPWTi was associated with a significant reduction in bacterial bioburden (p = 0.02), but other secondary outcomes were found to have no significant differences.

The observational comparative studies were generally retrospective and of limited methodological quality. Common issues included poor reporting of patient selection; small sample sizes; use of historical control groups without adequate description of how these were selected; lack of statistical matching; and a lack of confidence in how endpoints were measured, recorded and reported. The EAC considered that these limitations, taken together, meant that causal associations between NPWTi and clinical outcomes had not been established. Additionally, the heterogeneity of the study populations and variance in patient pathways meant the data could not be generalised to the UK NHS. Thus the evidence that NPWTi improves healing or reduces hospital length of stay (LoS) compared with NPWT was equivocal. There was not enough data published to make a meaningful comparison with advanced wound care (AWC).

No useful published economic studies were identified. The company reported a *de novo* economic model that compared NPWTi, NPWT and AWC. This was a cost calculator of cost consequences. Three variables in the model determined overall costs; these were LoS; length of treatment (LoT, direct costs associated with each technology); and repeat surgical debridement costs. The model was informed from selected comparative observational studies identified in the clinical literature. Four scenarios were reported (“lower limb”, “mixed wound”, “prosthetic implant” and “surgical infection”), and these were combined into a base case scenario, based on aggregated data from the

informing studies. Deterministic and probabilistic sensitivity analyses (DSA and PSA) were reported.

The company reported that in the base case, NPWTi was cost saving by £3,251 compared with NPWT, and by £8,312 compared with AWC. The principal driver of the cost savings was the reduction in LoS, as shown by DSA. The company reported that NPWTi was cost-saving in all 4 scenarios and in 3 of these, PSA indicated that the probability of NPWTi being cost saving was ≥ 94%.

The EAC had concerns with the *de novo* model. Firstly, the company's study selection was subject to potential bias. Secondly, the EAC considered the causality between the intervention and the reported outcomes had not been established with enough certainty. Thirdly, some parameter inputs had been derived using data transformation from two unrelated studies. Fourthly, the informing studies were based on heterogeneous case mixes of patients that could not be generalised to NHS population, and there were further issues with the generalisability of patient pathways. Fifthly, the method of reporting the base case results was not directly based on appropriate empirical data and was not accordingly weighted to reflect this. Finally, the EAC considered that the scale of the structural and parameter uncertainty in the model meant that the sensitivity analyses used were not meaningful.

The EAC replicated the company's *de novo* model and changed some assumptions and inputs in an attempt to improve the model's accuracy and internal consistency. The main change was to use data from the Kim *et al*. (2020) RCT to inform the base case. The best EAC estimate using PSA was that NPWTi was cost neutral with respect to NPWT, with a point estimate of £471 cost incurring (95% credibility interval [CrI] -£1085 to £2015). However, this estimate was also subject to several assumptions which were not directly evidenced. Thus, the EAC considers the cost-saving potential of NPWTi cannot currently be confirmed. An important caveat to these findings is that an absence of clinical benefit is not evidence of absent benefit. NICE clinical experts were unanimous the technology is clinically beneficial, and potentially cost-saving, in appropriately selected patients. Further clinical research would be required to confirm and quantify this benefit, and which patients will benefit most.

1 Decision problem

Changes to the decision problem made by the company, with EAC comments, are reported in Table 1.1.

Table 1.1. *Description of decision problem.*

Decision problem	Scope	Proposed variation in company submission	EAC comment
Outcomes	• Length of stay in hospital • Rates of partial and complete wound closure (which may vary depending on wound type, location, depth and size) • Mean time to partial or complete wound closure • Mean time to healing • Number of dressing changes • Number of follow on treatments and visits to hospital • Number of surgical debridements • Number of amputations or skin grafts • Staff time and use of other consumables • Colonisation with antimicrobial resistant pathogens • Antibiotic use	<u>Remove mean time to healing</u> Only 3 studies collected mean time to healing data and whilst 1 showed very high statistical significance p=0.0000 the majority of studies focussed upon wound closure rates and the associated timescales. NPWTi is used to prepare a wound bed for closure, it is not designed to heal wounds and we suggest it is not an appropriate outcome. This may explain why this data was not collected. <u>Remove number of amputations</u> Only 4 studies collected amputation data, 3 of which had no comparator. <u>Modify colonisation with antimicrobial resistant pathogens to colonisation with pathogens</u> Whilst many of the studies record the presence of pathogens, whether or not they were microbially resistant was not usually documented. <u>Remove antibiotic use</u> The majority of studies documenting antibiotic use prescribed them systemically for all patients or for all those who	The EAC considered there was no reason not to report this outcome, in studies that report it. NICE clinical experts confirmed the technology has several use cases, including use as a bridging procedure to surgical repair and as a standalone procedure (EAC External correspondence log, 2020). The EAC considered there was no reason not to report this outcome, in studies that report it. The EAC concurs that colonisation with any pathogens is the relevant measure. The implications for microbial resistance can be inferred from this. The EAC considers that this is potentially a relevant outcome where it is reported.

	• Health-related quality of life • Patient satisfaction and acceptability • Patient-related outcomes such as pain scores	had an infected wound. Data collection in studies more often focussed on pathogen types and colonisation levels. <u>Remove HRQOL</u> None of the studies selected in the systematic review presented any data related to patient's QOL.	The lack of HRQoL data reported is relevant and will be documented in the Assessment Report.

The EAC has made the following clarifications on other aspects of the scope.

1.1. Population

The population described in the scope is "Patients with acute infected or chronic wounds that are failing to heal" (NICE, 2020). This is a very broad population that signifies the versatility of the V.A.C. VERAFLO system in treating wounds of varying aetiologies and anatomical locations, as well as reflecting the heterogeneous nature of study population described in the literature. The company has commented that the population is appropriate because the mechanism of action of the technology is applicable to most wounds, regardless of the aetiology (EAC External correspondence log, 2020). Nevertheless, the breadth of the population makes generalisation of results challenging (see Section 8).

1.2. Intervention

The intervention is the V.A.C. VERAFLO system, in its entirety. This system features the following components:

- Negative Pressure Wound Therapy device with instillation option, namely the V.A.C. ULTA™ with VERAFLO Therapy (launched 2011) OR the V.A.C.ULTA™ 4 Therapy System (launched 2019).

- Specific, bespoke dressings for use with the system, namely the V.A.C. VERAFLO™ Dressing (2011), V.A.C. VERAFLO CLEANSE Dressing (2011), OR the V.A.C. VERAFLO CLEANSE CHOICE Dressing (2016).

- An approved instillation fluid (including Dakin's solution, Prontosan, and normal saline).

The V.A.C. VERAFLO also has other additional features that are bespoke to the system (canisters, cassettes, and drapes). However, these are rarely

reported in published studies, and will not directly affect the technology's efficacy, so have not been considered further. The predecessor technology to the V.A.C. VERAFLO system was V.A.C. Instill™ system, which differs from V.A.C. VERAFLO in some potentially important ways, such as the use of gravity assisted instillation rather than active instillation of controlled volumes of fluid through pumps and software control.

Following discussion with the company (EAC External correspondence log, 2020), the EAC accepts that the V.A.C. VERAFLO system is likely to represent an incremental improvement over the predecessor system (VAC Instill). It is noted that V.A.C. VERAFLO was licenced in the United States under the 510k pathway via its predicate system and will likely result in at least equivalent, if not better, outcomes. This is mainly due to expected system benefits accrued collectively from the components of the technology. However, because many of the innovative aspects of the technology are specific to the V.A.C. VERAFLO system (discussed in Section 2 of the company's clinical submission), the EAC maintains studies of predecessor systems, or technologies from other companies, would not fully capture the operational effectiveness of the V.A.C. VERAFLO system. Therefore the studies reporting on the predecessor system, or other systems, were excluded from clinical assessment. However, some excluded studies were included in the company's economic assessment, to inform model inputs. These have been necessarily included, but limitations have been noted (Section 9.2.3).

For simplicity, the V.A.C. VERAFLO system in this report is referred to as negative wound pressure therapy with instillation (NPWTi).

1.3 Comparator

Two comparators are listed in the scope (NICE, 2020). These are standard advanced wound dressings and negative pressure wound therapy without instillation (NPWT). The company has illustrated the possible position of NPWTi in the patient pathway in Section 3 of the clinical submission (using diabetic foot ulcer as an example). The EAC considers that, because the population is patients with "wounds that are failing to heal", this is indicative that usually NPWTi would be used as second-line treatment to standard care dressings, and as such, NPWT is the most appropriate comparator. This was confirmed by clinical experts (EAC External correspondence log, 2020). However, the company has suggested that earlier use of NPWTi, for instance at the stage in wound care where dressings are used, could lead to better outcomes in the longer-term (EAC External correspondence log, 2020).

1.4 Outcomes

The EAC notes that the clinical management outcomes listed in the scope were generally proxy measurements of healthcare resource use rather than actual clinical outcomes. The EAC notes that there is an absence of standard wound healing endpoints (Driver *et al.*, 2019), such as percentage area reduction in 4 to 8 weeks, reflecting the fact that NPWTi is an intervention that may reduce the time until wound closure, rather than the longer-term outcome of wound healing. See Section 9.2.3.

The EAC noted that outcome assessment is problematic in this medical field, due to population and setting heterogeneity; use of non-standardised definitions and measurement; and use of observational data that is often retrospective. These issues have been confirmed by NICE clinical experts (EAC External correspondence log, 2020) as well as the principal author of an important RCT on the technology. In particular, there are difficulties measuring and interpreting hospital length of stay (Section 5.3.1).

2 Overview of the technology

The V.A.C. VERAFLO Therapy system (3M + KCI) is an automated system that combines negative pressure wound therapy (NPWT) and wound instillation with topical solutions for wound healing. The therapy system delivers automated cycles of wound cleansing (instillation), dissolution and removal of infectious material and exudate (dwell time), and NPWT (completing the cycle). Collectively, this process is known as negative pressure wound therapy with instillation (NPWTi).

During NPWTi, a VeraFlo dressing foam is applied to the wound bed, available in a variety of sizes. A VAC Advance drape is then placed over the wound with a 3 cm margin to make sure there is full adhesion, with a small hole cut into the drape surface. The VAC VERATRAC Pad can then be attached to the drape, using a stabilisation layer to ensure complete contact. The pad is then connected to the VeraFlo Therapy system. This collects fluid and substances produced by the body in response to tissue damage from the wound into a single-use 500 ml or 1000 ml canister. The VAC system fill assist tool is used to determine and ensure an appropriate instillation volume has been applied and the SEAL CHECK leak detector is designed to minimise potential leaks.

The VeraFlo Therapy system is primarily used for patients with open, infected wounds or chronic wounds which are failing to heal. The company has described the technology in Section 2 of the clinical submission. In 2019, international consensus guidelines were published which advised on appropriate settings for the technology (Table 2.1).

Table 2.1 *Recommended settings for NPWTi with V.A.C. VERAFLO system.*

Parameter	**Recommended by consensus (≥80% positive response)**
Instillation fluid*	Hypochlorous acid solution (examples: Vashe, Puracyn, NeutroPhase)
	Sodium hypochlorite solution (Dakin's solution 0.125%)
	Acetic acid solution (0.25% to 1.0%)
	Polyhexamethylene biguanide (0.1%) + betaine (0.1%) (Prontosan)
NPWT cycle time	2.0 to 3.0 hours
NPWT pressure	-125 mmHg
Dwell time	10 minutes
Abbreviations: NPWT, negative pressure wound therapy * Normal saline recommended as first-line treatment. Solutions with antiseptic or anti-microbial actions recommended in some instances (e.g. highly infected wounds). Data from (Kim *et al.*, 2019)	

3 Clinical context

3.1 Clinical guidelines

The company describes the clinical context in which NPWTi is intended to be used in Section 3 of the clinical submission. Because the scope of the population is very broad (Section 1.1), it is not possible to place the technology in a specific part of the patient pathway. In general, however, it may be considered as an alternative or adjunct to NPWT (Section 1.3).

The EAC identified two relevant NICE clinical guidelines which are applicable to this technology (as they make recommendations on NPWT). These were:

- *Pressure ulcers: prevention and management* (CG179) (NICE, 2014b). Recommendation 1.4.13 states "Do not routinely offer adults negative pressure wound therapy to treat a pressure ulcer, unless it is necessary to reduce the number of dressing changes (for example, in a wound with a large amount of exudate)".

- *Diabetic foot problems: prevention and management* (NG19) (NICE, 2015). Recommendation 1.5.9 states "Consider negative pressure wound therapy after surgical debridement for diabetic foot ulcers, on the advice of the multidisciplinary foot care service". The evidence base for NPWT itself is generally poor, with no firm conclusions on the effectiveness of the procedure being able to be drawn. Table 3.1 summarises the conclusions from Cochrane systematic reviews.

Several NICE Interventional Procedures Guidance (IPG). Medical Technology Guidance (MTGs), and Medtech Innovation Briefings (MIBs) have been published which are concerned with the management of wounds that are difficult to heal or chronic infected wounds. The most relevant of these are

- Negative pressure wound therapy for the open abdomen (IPG467) (NICE, 2013).

- *PICO negative pressure wound dressings for closed surgical incisions* (MTG43) (NICE, 2019a).

- *The MIST Therapy system for the promotion of wound healing* (MTG5) (NICE, 2011)

- *The Debrisoft monofilament debridement pad for use in acute or chronic wounds* (MTG17).(NICE, 2014a)

- *Prevena incision management system for closed surgical incisions* (MIB173) (NICE, 2019b)

- *The Versajet II hydrosurgery system for surgical debridement of acute and chronic wounds and burns* (MIB1) (NICE, 2014c).

The two former technologies (subject of MTG43 and MTG5) listed may be regarded as comparators in some patient populations; whereas the latter two (MTG17 and MIB173) technologies may be used in conjunction with NPWTi. In all instances, these technologies might impact on the economics of wound healing (Section 9).

3.2 Use of debridement in wound healing

Debridement is the removal of devitalised, contaminated or foreign material from the surface of an acutely infected or chronic wound. The purpose of debridement is to promote wound healing and as such it is a fundamental component of the management of poorly healing wounds. There are several methods of debriding wounds, each mechanistically distinct, and each with their own advantages and disadvantages. These are (Wounds UK, 2013):

- Autolytic debridement. This is a naturally occurring process in which the body's own enzymes and moisture rehydrate, soften and liquify hard eschar and slough. This can be aided by use of appropriate dressings and can be undertaken in community, generalist or specialist settings.

- Mechanical debridement. This is removal of non-viable material using a specialised monofilament such as Debrisoft (NICE, 2014a). It can be used in a generalist or specialist setting.

- Larval therapy (biosurgical) debridement. The larvae of green bottle fly (*Lucilia sericata*) are used to remove moist devitalised tissue from the wound. It can be used in a generalist or specialist setting.

- Ultrasonic debridement. Use of direct ultrasound or atomised solution to debride tissue. An example of this is MIST therapy (NICE, 2011). Used in specialist settings only (not routinely available).

- Hydrosurgical debridement. Removal of devitalised tissue using a high energy fluid beam as a cutting implement, for example Versajet (NICE, 2014c).

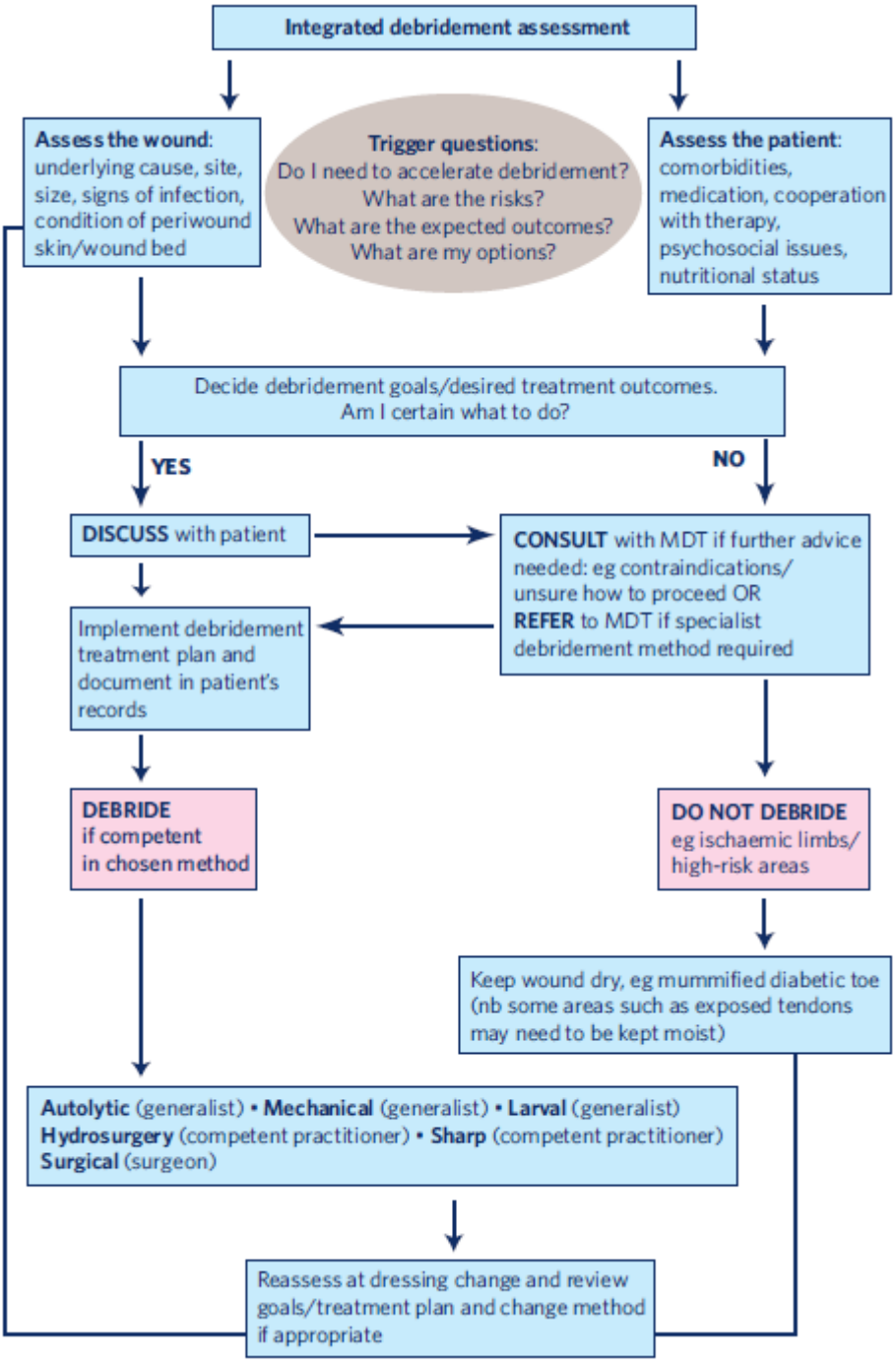
- Sharp debridement. This is removal of dead or devitalised tissue using a scalpel, scissors and/or forceps to just above the viable tissue level. It is undertaken in conjunction with other therapies (e.g. autolytic

debridement). Analgesia is not normally required and it can be done at the bedside. However, complete removal of devitalised tissue is not always possible and it is not without risk. This is a specialist competency undertaken by specialist nurses or podiatrists.

- Surgical debridement. This is excision or wider resection of non-viable tissue, including the removal of healthy tissue from the wound margins, until a healthy bleeding wound bed is achieved. It is suitable for use on large wounds and requires anaesthesia and theatre time. It is a specialist procedure.

There are consensus guidelines published on debridement (Wounds UK, 2013). Patient pathways from initial assessment are published in Figure 3.1.

Figure 3.1. *Flow chart illustrating debridement pathways. Taken from (Wounds UK, 2013)*



3.3. Negative pressure wound therapy.

As discussed in Section 1.3, NPWT might be considered as the main comparator to NPWTi, with the introduction of instillation being considered an adjunctive treatment to this (with advanced dressings having been used

earlier in the pathway, and/or subsequent to either type of NPWT, to progress towards complete healing) (EAC External correspondence log, 2020). However, the evidence base for NPWT itself is generally poor, with no firm conclusions on the effectiveness of the procedure being able to be drawn. Limitations in the evidence base included a general lack of robust, vigorous RCTs, and issues with generalisability. Table 3.1 summarises the conclusions from Cochrane systematic reviews (citations given in the table).

Table 3.1 *Summary of the conclusions of Cochrane systematic reviews reporting on NPWT as the intervention.*

Population of interest	Reference	Number of studies identified	Comparator	Outcomes reported	Summary of conclusion
Partial thickness burns	(Dumville *et al.*, 2014)	1 RCT (interim report on n=23 patients) in patients with bilateral thermal hand burns.	Silver sulphadiazine	Primary outcomes: • Time to complete healing • Rate of change in wound area • Proportion of wound completely healed within the trial period Secondary outcomes: • Incidence of wound infection • Adverse events • Measures of satisfaction or patient preference • Quality of life	"There was not enough evidence available to permit any conclusions to be drawn regarding the use of NPWT for treatment of partial-thickness burn wounds".
Open traumatic wound	(Iheozor-Ejiofor *et al.*, 2018)	7 RCTs (n=1388) 4 studies including open fracture wounds and 2 studies (one with three arms) including open traumatic wounds (not involving a broken bone)	Standard care Different NPWT pressure settings	Primary outcomes: • Complete wound healing (time to complete wound healing, the proportion of wounds healed). • Wound infection • Adverse events Secondary outcomes: • Proportion of wounds closed or covered with surgery • Time to closure or coverage surgery	"There is moderate-certainty evidence for no clear difference between NPWT and standard care on the proportion of wounds healed at six weeks for open fracture wounds."

Population of interest	Reference	Number of studies identified	Comparator	Outcomes reported	Summary of conclusion
				• Participant health-related quality of life/health status • Wound recurrence • Mean pain scores • Within-trial cost effectiveness analysis comparing mean differences in effects with mean cost differences between two arms	
Surgical wounds healing by secondary intention	(Dumville *et al.*, 2015b)	2 RCTs (n=69); one study in open infected groin wounds, one study of excised pilonidal sinus.	Alginate dressing Silicone dressing	<u>Primary outcomes:</u> • Complete wound healing (time to complete wound healing, proportion of wounds healed) • Adverse events <u>Secondary outcomes:</u> • Participant health-related quality of life/health status • Wound infection • Mean pain scores • Resource use • Costs • Complete fascia closure • Proportion of wounds closed or time to wound closure	"There is currently no rigorous RCT evidence available regarding the clinical effectiveness of NPWT in the treatment of surgical wounds healing by secondary intention as defined in this review".
Surgical wounds healing by	(Webster *et al.*, 2019)	30 Intervention trials (n=2957) and two	Standard surgical dressings varied amongst studies	<u>Primary outcomes:</u> • Morality	"Despite the addition of 25 trials, results are consistent with our earlier review, with the evidence judged to be of low or very low

Population of interest	Reference	Number of studies identified	Comparator	Outcomes reported	Summary of conclusion
primary closure		economic studies nested in trials; surgeries included abdominal and colorectal (5 studies), caesarean section (5 studies), knee or hip arthroplasty (5 studies), groin surgery (5 studies), fractures (5 studies), laparotomy (1 study), vascular surgery (1 study), sternotomy (1 study), breast reduction mammoplasty (1 study), mixed (1 study).	(including standard gauze, sterile gauze secured with perforated stretchable cloth tape, non-adhesive silicone layer, bacteriostatic single silver layer, absorbent adhesive dressing, Steri-strips and sterile gauze and Tegaderm transparent film dressing)	• Surgical site infection (SSI) • Dehiscence <u>Secondary outcomes:</u> • Reoperation • Readmission to hospital within 30 days for a wound-related complication • Seroma • Haematoma • Skin blisters • Pain • Quality of life • Dressing-related costs (including the cost of the dressing and healthcare professional time) • Resource use • Quality-adjusted life year gained • Incremental cost-effectiveness ratio	certainty for all outcomes. Consequently, uncertainty remains about whether NPWT compared with a standard dressing reduces or increases the incidence of important outcomes such as mortality, dehiscence, seroma, or if it increases costs".

Population of interest	Reference	Number of studies identified	Comparator	Outcomes reported	Summary of conclusion
Leg ulcers	(Dumville *et al.*, 2015a)	1 RCT (n=60) in patients with recalcitrant ulcers (venous arteriolosclerotic and venous/arterial in origin) that had not healed after treatment over a six-month period.	Standard care with dressings and compression until 100% granulation. Participants also received a punch skin-graft transplant and then further treatment with standard care as in-patients until healing occurred.	Primary outcome: • Complete wound healing (time to complete wound healing, the proportion of ulcers healed) • Adverse events Secondary outcomes: • Participant health-related quality of life/health status • Resource use • Costs • Wound recurrence • Wound infection • Mean pain scores • Proportion of wounds closed with surgery of time to preparation for surgery	"There is limited rigorous RCT evidence available concerning the clinical effectiveness of NPWT in the treatment of leg ulcers. There is some evidence that the treatment may reduce time to healing as part of a treatment that includes a punch skin graft transplant, however, the applicability of this finding may be limited by the very specific context in which NPWT was evaluated. There is no RCT evidence on the effectiveness of NPWT as a primary treatment for leg ulcers".
Pressure ulcers	(Dumville *et al.*, 2015c)	4 RCTs (n=149)	Two studies compared with dressings, one study compared with a series of gel treatments and one study with moist wound healing.	Primary outcomes: • Complete wound healing (time to complete wound healing, the proportion of ulcers healed) • Adverse events Secondary outcomes: • Change (and rate of change) in wound size with adjustment for baseline size	"There is currently no rigorous RCT evidence available regarding the effects of NPWT compared with alternatives for the treatment of pressure ulcers. High uncertainty remains about the potential benefits or harms, or both, of using this treatment for pressure ulcer management".

Population of interest	Reference	Number of studies identified	Comparator	Outcomes reported	Summary of conclusion
				• Participant health-related quality of life/health status • Wound infection • Mean pain scores • Resource use • Costs • Wound recurrence	
Foot wounds in diabetics	(Liu *et al.*, 2018)	11 RCTs (n=972); two studies included post-amputation wounds, the other studies included foot ulcers in people with diabetes mellitus (DM).	Ten studies compared NPWT with dressings, one study compared NPWT delivered at 75 mmHg with NPWT delivered at 125 mmHg.	<u>Primary outcomes:</u> • Complete wound healing (time to wound healing, number of wounds completely healed during follow-up) • Amputation (major amputation, minor amputation) <u>Secondary outcomes:</u> • Proportion of wounds closed or covered with surgery • Time to closure or coverage surgery • Participant health-related quality of life/health status • Other adverse events • Within-trial cost-effectiveness analysis comparing mean differences in effects with mean cost differences between two arms	"There is low-certainty evidence to suggest that NPWT, when compared with wound dressings, may increase the proportion of wounds healed and reduce the time to healing for postoperative foot wounds and ulcers of the foot in people with diabetes mellitus……The limitations in current RCT evidence suggest that further trials are required to reduce uncertainty around decision-making regarding the use of NPWT to treat foot wounds in people with diabetes mellitus".

Population of interest	Reference	Number of studies identified	Comparator	Outcomes reported	Summary of conclusion
				• Wound recurrence	
Abbreviations: NPWT, negative wound therapy; RCT, randomised controlled trial.					

3.4 Special considerations, including issues related to equality

In section 1 of the clinical submission, the company identified older or physically disabled people as being more likely to suffer chronic and complex wounds. Additionally, diabetes is a known risk factor for poor wound healing, and this condition is associated with people of some ethnicities.

No specific equality issues were identified by the EAC for this technology.

4 Clinical evidence selection

4.1 *Evidence search strategy and study selection*

The company search strategy was critiqued using the PRESS tool. The strategy did not utilise any database subject headings, so MeSH headings and their equivalent were added to the updated search. The company had used a limited selection of databases; particularly no nursing databases had been used, which was considered important for wound care, so CINAHL was added to the updated search. Access to QUOSA was not available to EAC information specialists so this was not included in the update search. The search strategy is described in detail in Appendix A.

Following the literature search, studies were sifted according to the final published scope (NICE, 2020) on the basis of title and abstract alone by one reviewer (KK). At this stage, sensitivity was maximised to minimise exclusion of relevant papers. Studies identified as potentially relevant were retrieved and selected during a second sift by a second reviewer (IW). At this stage, specificity was maximised so studies considered out of scope were excluded. In particular, studies were excluded if they did not feature the V.A.C. VERAFLO system as the intervention (Section 1.2). The study selection process is illustrated as a PRISMA diagram in Figure A1.

4.2 *Included and excluded studies*

The company identified 30 fully published studies from their literature search. Additionally, the company reported on 1 abstract and 1 ongoing study as relevant to the evidence base. This study has since been fully published in a peer reviewed journal. The fully published studies are listed in Table 1 of the submission, stratified by anatomical location of the wound or wound type (aetiology).

The EAC performed its own literature search (Section 4.1). All the studies identified by the company were identified with the exception of those excluded on the basis of publication date. Sixty six papers were identified as potentially relevant to the decision problem from the title and abstract alone, and full papers associated with these were retrieved. Studies were excluded if they did not fit the scope, including the specific intervention (Section 1.2); if they were published in abstract form only; if they were not published in English; or if they were a case series with n < 10. Following further consideration on these criteria, 48 papers were rejected, mainly because the intervention did not match the scope (see Figure A1). The EAC identified 19 studies it considered to be relevant. Of these studies, 17 had been identified and included by the company, and 2 additional studies were identified by the EAC (one of which, published in April 2020, was identified during the search for

economic papers, see Section 9.1.1). The EAC excluded 15 of the studies included by the company from the clinical evidence review (see Table 4.1).

Table 4.1. *Studies included by the company and the EAC.*

Study	Company inclusion?	EAC inclusion?
Lower limb		
(Kim *et al.*, 2015)	☑	☑
(Kim *et al.*, 2014)	☑	☑
(Yang *et al.*, 2017a)	☑	☑
(Yang *et al.*, 2015)	☑	☒*
(Goss *et al.*, 2008)	☑	☑
(Omar *et al.*, 2016)	☑	☑
(Brinkert *et al.*, 2013)	☑	☑
(Milcheski *et al.*, 2017)	☑	☑
(Blalock, 2019)	☑	☑
(Gabriel *et al.*, 2008)	☑	☒
(Davis *et al.*, 2019)	☑	☒
(Zelen *et al.*, 2011)	☑	☒
Mixed wounds		
(Latouche and Devillers, 2020)	☒	☑*†
(Fluieraru *et al.*, 2013)	☒	☑
(Gabriel *et al.*, 2014)	☑	☑*
(Ludolph *et al.*, 2018)	☑	☑
(McElroy, 2019)	☑	☑
(Timmers *et al.*, 2009)	☑	☒
Prosthetic implants		
(Garcia-Ruano *et al.*, 2016)	☑	☒
(Deleyto *et al.*, 2018)	☑	☑
(Eckstein *et al.*, 2019)	☑	☑
(Lehner *et al.*, 2011)	☑	☒
(Hehr *et al.*, 2020)	☑	☑
(Morinaga *et al.*, 2013)	☑	☒
(Chen *et al.*, 2018)	☑	☒
(Huang *et al.*, 2020)	☑	☒
(Qiu *et al.*, 2019)	☑	☒
(Ikeno *et al.*, 2019)	☑	☒
Surgical site infections		
(Jurkovic *et al.*, 2019)	☑	☒
(Chowdhry and Wilhelmi, 2019)	☑	☑
(Jain *et al.*, 2018)	☑	☒
(Téot *et al.*, 2017)	☑	☑

Unpublished studies		
(Powers *et al.*, 2013) [Abstract]	☑	☒
(Kim *et al.*, 2020)‡	☑	☑
* Economic studies that are discussed in Section 9.1.2. † Identified through economic literature search. ‡ One study was unpublished and academic in confidence at the time of the company's clinical submission and earlier drafts of this assessment report. However, it has since been published in full (Kim *et al.*, 2020).		

The reasons the EAC excluded the company studies are reported in Table 4.2. The principal reason was that the intervention did not match the scope; that is the NPWT device was not a VAC Ulta device; V.A.C. VERAFLO dressings were not used (VERAFLO, VERAFLO CLEANSE, or VERAFLO CLEANSE CHOICE); or the study did not explicitly state that V.A.C. VERAFLO therapy or system was used, and this could not be confirmed by the company (EAC External correspondence log, 2020). The use of compatible instillation fluids, cycle lengths, and dwell times, were not considered for the purposes of including or excluding studies. Nine of the studies were comparative, or nominally comparative (Table 4.3), and ten were single-armed studies (Table 4.4).

Table 4.2. *Reasons for excluding company studies (N = 15).*

Study name and location	Design	Population	Intervention (and comparator)	EAC comments
	Key: ☑ aspect of study in scope; ☑☒ aspect of study partially in scope, or elements of this are not in scope; ☒ aspect of study not in scope.			
(Huang *et al.*, 2020) China	Retrospective single-armed observational study. ☑	Patients with implant infection/exposure in titanium mesh cranioplasty. n = 21 patients ☒	NPWTi system was not specified, but the company confirmed it was not the V.A.C. VERAFLO system. The instillation fluid used was chemotrypsin, which is not an approved solution for V.A.C. VERAFLO. ☒	The intervention is out of scope (not V.A.C. VERAFLO). It is a complex intervention combining a specific surgical treatment with NPWTi, thus the population is highly specific and not generalisable.
(Davis *et al.*, 2019) United States	RCT (3 armed) ☑	Patients with a chronic or traumatic wound, subacute or dehisced wound, partial-thickness burn, ulcer (such as a diabetic or pressure ulcer), flap or graft of the foot. n = 90 patients ☑	None of the three arms of the RCT utilised V.A.C. VERAFLO. This has been confirmed by the company. ☒	The aim of the study was to compare the use of NPWT with NPWTi with saline, but is excluded because the V.A.C. VERAFLO system was not used.

Study name and location	Design	Population	Intervention (and comparator)	EAC comments
(Ikeno *et al.*, 2019) Japan	Retrospective single-armed observational study ☑	Patients undergoing aortic surgery via a median sternotomy, who developed a deep sternal wound infection. n = 18 ☒	The system used was not V.A.C. VERAFLO, and included use of Mepilex dressings. This has been confirmed by the company. ☒	This study was focused on a complex surgical intervention and did not use V.A.C. VERAFLO. It is not generalisable to a broader population.
(Qiu *et al.*, 2019) China	Retrospective single-armed observational study ☑	Patients with severe oral, maxillofacial, and cervical infections. n = 73 ☑	The device and dressings used were not the V.A.C. VERAFLO system. ☒	Excluded because the intervention was not V.A.C. VERAFLO. Additionally, the technique and patients operated on were highly selected and not generalisable.
(Chen *et al.*, 2018) China	Retrospective single-armed observational study ☑	Patients with post-operative infection following spinal surgery. n = 18 ☑	NPWTi system used was not V.A.C. VERAFLO. This was confirmed by the company. ☒	Exclusion on basis of out-of-scope intervention.
(Jain *et al.*, 2018) United States	Retrospective single-armed observational study ☑	Patients receiving girdlestone orthopaedic operations. n = 10 ☑☒	The study used the V.A.C. VERAFLO system, but combined with an orthopaedic intervention. ☑☒	Excluded because the intervention formed part of a more complex surgical procedure. Data not generalisable.

Study name and location	Design	Population	Intervention (and comparator)	EAC comments
(Garcia-Ruano *et al.*, 2016) Spain	Retrospective comparative cohort study. ☑	Patients who suffered abdominal wall wound dehiscence with mesh exposure. ☑	Intervention: NPWTi using "VAC-instillation therapy". Including use of GranuFoam dressings. ☒ Comparator (historical control): Conventional treatment comprised saline-soaked gauze dressings, antiseptic solutions and open lavage, determined by the judgment, experience, and training. ☑	This study reported on the same patients as an economic study included by the company (Deleyto *et al.*, 2018). As it did not report on additional clinical outcomes, this study was excluded on the basis of duplication.
(Yang *et al.*, 2015) United States	Retrospective economic analysis	Patients with massive venous leg ulcer n = 7 patients ☑☒	Intervention V.A.C. VERAFLO system prior to STSG Instillation fluid: Dakin's solution. 10 minutes dwell time 1 hour cycle time	Excluded on basis of intervention (includes STSG) and patient numbers (n < 10).
(Morinaga *et al.*, 2013) Japan	Retrospective single-armed observational study ☑	Patients with mediastinitis. n = 46 ☒	The device used was Mera Sakume MS-008, not the VAC Ulta. This was confirmed by the company ☒	Excluded because the intervention was not V.A.C. VERAFLO. Additionally, the patient population had mediastinitis arising from open heart surgery, which

Study name and location	Design	Population	Intervention (and comparator)	EAC comments
				may be an off-label use of the technology.
(Lehner *et al.*, 2011) Germany	Prospective observational study ☑	Patients with infected implants (knee, hip, other osteosynthesis material) ☑	VAC Instill wound therapy ☒	Excluded because the intervention was not V.A.C. VERAFLO.
(Zelen *et al.*, 2011) United States	Prospective observational study ☑	Diabetic patients with chronic non-healing foot ulcers. n = 20 ☑	The NPWT system used was the instructions Svedman Wound Treatment System; the company has confirmed the V.A.C. VERAFLO system. ☒	Excluded because the intervention was not V.A.C. VERAFLO.

Abbreviations: NPWT, negative pressure wound therapy; NPWTi, negative wound therapy with instillation; RCT, randomized controlled trial; STSG, split thickness skin graft.

Note. Two studies were excluded because they were published before the search date of the EAC's literature search (Timmers *et al.*, 2009, Gabriel *et al.*, 2008). This indicates they were not reporting on the V.A.C. VERAFLO system (Section 1.2). One study was excluded because it was it was not published in English (Jurkovic *et al.*, 2019). The study by Powers *et al.* (2013) was excluded on the basis it was available as an abstract only.
* The study by Yang *et al.* (2015) reported economic outcomes briefly discussed in Section 9.1.2.

Table 4.3. *Characteristics of comparative studies (N = 9)*.

Study name, design, and location	Participants and setting	Intervention	Comparator	Outcomes
Key: ☑ aspect of study in scope; ☑☒ aspect of study partially in scope, or elements of this are not in scope; ☒ aspect of study not in scope.				
(Chowdhry and Wilhelmi, 2019) Retrospective comparative observational study. USA ☑	Patients undergoing reconstructive surgery by a single surgeon for sternal wound complications. Recruitment June 2015 to October 2017. n = 30 ☑	NPWTi with V.A.C. VERAFLO using VeraFlo Cleanse Choice dressings. Instillation fluid: 1/8th strength Dakin's solution*. Dwell time: 20 minutes NPWT (-125 mm Hg). Dressings changed every 72 hours. n = 15 ☑	Treatment with wet-to-moist dressings soaked in 1/8th strength Dakin's* solution. Dressings changed every 6 hours. n = 15 ☑	• Time to wound closure. • Number of therapy days. • Number of excisional debridements. • Drainage duration. • Complications. ☑
(Deleyto *et al.*, 2018) Retrospective observational study with economic analysis Spain ☑	Patients diagnosed with abdominal wall wound dehiscence and presenting with abdominal mesh exposure. Recruitment January 2010 to December 2013. n = 45	NPWTi with V.A.C. VERAFLO Instillation fluid: hypertonic saline Dressings changed every 3 days n = 11 ☑	Conventional dressings n = 34 ☑	• Number of hospitalization episodes • Number of additional surgeries • Length of hospital stay • Cost analysis ☑

Study name, design, and location	Participants and setting	Intervention	Comparator	Outcomes
	☑			
(Yang *et al.*, 2017b) RCT United States, single-centre ☑	Patients with a leg or foot ulcer > 40 cm^2 that would usually be treated with NPWT and the patient would be hospitalized. Recruitment January 2014 to November 2014. n = 20 ☑	NPWTi using the VAC Ulta device (assumed V.A.C. VERAFLO mode). Instillation fluid: ¼ strength Dakin's solution*. Volume of 0.2 mL per cm^2 wound area. Dwell time: 10 minutes. Cycle length: 60 minutes NPWT (-125 mm Hg). Sharp debridement and wound irrigation repeated at day 7. n = 10	NPWT using the VAC Ulta device. Negative pressure of -125 mm Hg. Sharp debridement and wound irrigation repeated at day 7. n = 10 ☑	• Bacterial bioburden. ☑
(Omar *et al.*, 2016) Prospective observational study with historical cohorts Germany, single centre ☑	Patients with acute wounds of the lower limb (infected or traumatic). Prospective consecutive recruitment between January and July 2014. n = 20 ☑	NPWTi with V.A.C. VERAFLO system. Instillation fluid: saline Dwell time: 15 minutes Cycle length: 4 hours n=10 ☑	NPWT using VAC Ulta without instillation n = 10 ☑	• Surgeries required • Time to wound closure (days) • Length of hospital stay • Wound size (cm^2) ☑

Study name, design, and location	Participants and setting	Intervention	Comparator	Outcomes
(Gabriel *et al.*, 2014) Retrospective observational study with historical controls. Economic analysis. United States ☑	Patients with infected or critically colonized extremity and trunk wounds. Recruitment January 2010 to May 2013. n = 82 ☑	NPWTi with V.A.C. VERAFLO Therapy. V.A.C. VERAFLO dressing. Instillation fluid: Prontosan** or saline. Dwell time: 1 to 60 seconds. Cycle length: 1-2 hours NPWT (-125 mm Hg). Dressing changes occurred every 2 to 3 days. n = 48 ☑	NPWT with VAC. GranuFoam Dressing or VAC. GranuFoam Silver Dressing -125 mm Hg Dressing changes occurred every 2 to 3 days n = 34 ☑	• Number of surgical debridements • Length of hospital stay • Length of therapy • Time to wound closure • Cost analysis ☑
Kim *et al.* (2015) RCT*** United States, single centre NCT01939145 ☑	Patients admitted to a tertiary wound referral academic hospital with an infected wound requiring surgical debridement in an operating room. n = 100 ☑	NPWTi using Prontosan** as the instillation fluid. Received NPWTi with VAC ULTA NPWT system with VeraFlo. Dwell time: 20 minutes. Cycle length: 2 hours NPWT	NPWTi using 0.9% saline as the instillation fluid. Received NPWTi with VAC ULTA NPWT system with VeraFlo. n = 49 ☒	Primary • Number of operating room visits (primary) Secondary • Length of hospital stay in days • Time to final surgical procedure during the admission in days.

Study name, design, and location	Participants and setting	Intervention	Comparator	Outcomes
		n = 51 ☒		• Proportion (percentage) of wounds closed/covered during the admission • Proportion (percentage) of wounds that remained closed or covered approximately30 days after hospital discharge ☑
(Kim *et al.*, 2014) Retrospective cohort study United States, single centre ☑	Patients with infected wounds requiring admission with at least 2 operative debridements and who have received either NPWT or NPWTi application at the time of the initial operation. n = 142 ☑	NPWTi with V.A.C. VERAFLO system. Instillation fluid: Prontosan**. Dwell time: 6 minutes (n=34) Cycle length: 3.5 hours NPWT (-125 mm Hg) Dwell time: 20 minutes (n=34)	NPWT using Info VAC Therapy System (historical controls for the same 6 month period separated by exactly 1 year). −125 mm Hg continuous negative pressure n = 74 ☑	• Number of operating room visits • Length of hospital stay • Time to final surgical procedure • Wound closure • Wound closed at 1 month • Culture improvement with Gram-negative, Corynebacterium, and yeast excluded ☑

Study name, design, and location	Participants and setting	Intervention	Comparator	Outcomes
		Cycle length: 2 hours NPWT (-125 mm Hg) ☑		
(Goss *et al.*, 2012) Prospective comparative cohort study Italy ☑	Patients with chronic lower extremity wounds demonstrating significant bioburden. Recruitment October 2012 to October 2013. n = 13 (16 wounds) ☑	NPWTi (confirmed as V.A.C. VERAFLO by company). Instillation fluid: Dakins solution (1/4 strength)*. Dwell time: 10 minutes. Cycle length: 60 minutes NPWT (-125 mmHg). n = 7 (1 patient received both NPWTi and NPWT) ☑	NPWT 125 mmHg n = 7 ☑	• Bacterial load ☑
(Kim *et al.*, 2020) RCT United States NCT01867580	Inpatients with open wounds (>4 cm) requiring debridement and appropriate for conventional NPWT. Most wounds were chronic (71.8%), with 43.1% being diabetic ulcers.	NPWTi with the V.A.C. VERAFLO system (VAC Ulta with V.A.C. VERAFLO dressings. Instillation fluid: Prontosan**	Continuous NPWT using the VAC Ulta device with GranuFoam dressings. Dressings changed every 3 days. n = 88 (ITT)	Primary • Number of inpatient operating room debridements Secondary • Difference in Total Bacterial Counts Measured in Colony

Study name, design, and location	Participants and setting	Intervention	Comparator	Outcomes
☑	Recruitment December 2012 to November 2015. n = 183 (randomised) ☑	Dwell time: 20 minutes, Cycle length: 3.5 hours continuous NPWT. Dressings changed every 3 days. n = 93 (ITT) ☑	☑	Forming Units (CFU) as Determined by Quantitative PCR Analysis • Time until wound closure/coverage • Proportion of wounds closed • Wound complications ☑

Abbreviations: ITT, intention to treat (group); NPWT, negative pressure wound therapy; NPWTi, negative wound therapy with instillation; RCT, randomized controlled trial.

* Dakin's solution is sodium hypochlorite solution. Full strength is around 0.5%. It is an approved solution for use with the the V.A.C. VERAFLO system.
** Prontosan is a proprietary wound irrigation solution consisting of polyhexamethylene biguanide (0.1% an antimicrobial compound) and betaine (0.1%, a surfactant). It is an approved instillation agent for the V.A.C. VERAFLO system.
*** This study was an RCT that used the V.A.C. VERAFLO system; however, because the comparison being made in the RCT was not relevant to the decision problem, data reported from the study must be considered as a single-armed study. Results which are comparisons are not applicable.

Table 4.4. *Characteristics of single-armed studies (N = 10).*

Study name, design, and location	Participants and setting	Intervention	Outcomes
Key: ☑ aspect of study in scope; ☑☒ aspect of study partially in scope, or elements of this are not in scope; ☒ aspect of study not in scope.			
(Latouche and Devillers, 2020) Retrospective case series France ☑	Patients with pressure ulcers (PUs), postoperative wounds or trauma wounds. Recruitment between October 2015 and March 2018. n = 15 ☑	NPWTi with the V.A.C. VERAFLO system using V.A.C VERAFLO dressings. Instillation fluid: norma saline (0.9%) Dwell time: 10 minutes Pressure: -75 to -125 mmHg Cycle time: 2 to 3 hours Dressing changes: 2 to 3 days ☑	• Patient characteristics. • Duration of treatment • Number of dressing changes • Mean costs of treatment ☑☒
(Blalock, 2019) Retrospective case series United States ☑	Patients with complex wounds. Mixed aetiologies (surgical, trauma, ulcers (pressure and non-pressure). Recruitment between January 2017 and November 2017. n = 19 ☑	NPWTi with the V.A.C. VERAFLO system, using V.A.C. VERAFLO CLEANSE dressings. Instillation fluid: saline or 0.025% Dakin's solution. Dwell time: 1-10 minutes. Cycle length: 2-3.5 hours NPWT (-125 mm Hg). Dressings changed every 2-3 days. ☑	• Patient characteristics. • Duration of therapy ☒
(Eckstein *et al.*, 2019) Retrospective case series	Patients with septic wounds of the head and neck area.	V.A.C. VERAFLO system.	• Procedural success • Leukocyte concentration • CRP

Study name, design, and location	Participants and setting	Intervention	Outcomes
Germany ☑	Recruitment between September 2015 and September 2016. n = 15 ☑	Instillation fluid: polyhexanide 0.04%. Dwell time: 10 minutes. Cycle length: 3 hours NPWT (-125 mm Hg). ☑	• Bacterial loads • Wound size (cm^2) • Pain ☑
(Hehr *et al.*, 2020) Retrospective case series. United States ☑	Patients with open wounds revealing exposed hardware. Recruitment between April 2016 and October 2018. n = 28 ☑	V.A.C. VERAFLO system with VeraFlo or Cleanse Choice dressings. Instillation fluid: Dakin's solution* or Prontosan**. ☑	• Patient characteristics • Initial debridement bacterial culture. • Time to wound closure ☒
(McElroy, 2019) Retrospective case series. United States ☑	Patients with at least one complex wound (including pressure injuries, necrotising fasciitis, diabetic foot ulcers, surgical wounds). Recruitment between September 2016 and October 2017. n = 14 ☑	V.A.C. VERAFLO system with Cleanse Choice dressings. Instillation fluid: normal saline, acetic acid or hypchlorous solution Dwell time: 10 minutes. Cycle length: 0.5-4 hours NPWT (-125 mm Hg). Dressing changes every 2-3 days.	• Patient characteristics • Number of debridements • Return to operating room • Duration of therapy • Improved granulation ☒

Study name, design, and location	Participants and setting	Intervention	Outcomes
		☑	
(Ludolph *et al.*, 2018) Prospective single-armed observational study Germany ☑	Patients with "with wounds of different origins at various body sites" (including different types of ulcers, chronic, acute and trauma-related). Recruited between January 2013 and November 2017. n = 111 ☑	NPWTi, the company has confirmed this was V.A.C. VERAFLO therapy. Instillation fluid: 0.4% polyhexanide solution (Lavasept, not an approved solution) Dwell time: 20 minutes Cycle length: 2 hours NPWT (-125 mm Hg) ☑☒	• Patient characteristics • Microbial colonization. ☑☒
(Milcheski *et al.*, 2017) Prospective observational study Brazil ☑	Patients with infected or contaminated complex wounds. Recruitment between March 2016 and August 2016. n = 10 ☑	V.A.C. VERAFLO system. Instillation fluid: normal saline. 2 hour cycle NPWT (-125 mm Hg), 20 minutes dwell time. ☑	• Patient characteristics • Time to wound closure • Qualitative cultures in each surgical procedure • Number of surgical procedures performed • Length of hospital stay ☒
(Téot *et al.*, 2017) Retrospective case series France	Patients with large complex chronic wounds with viscous wound exudate that contained substantial areas of devitalized tissue (including pressure ulcers,	V.A.C. VERAFLO system. Dressing VeraFlo Cleanse Choice. Instillation fluid: normal saline. Dwell time: 10 minutes	• Patient characteristics • Pain • Number of dressing changes • Surgical debridement (type and frequency) • Wound granulation.

Study name, design, and location	Participants and setting	Intervention	Outcomes
☑	burns, necrosis after skin excision). Recruitment between January 2016 and July 2016. n = 21 ☑	Cycle length: 3.5 hours NPWT (-125 mm Hg). Dressing changes every 3 days. ☑	☑☒
(Brinkert *et al.*, 2013) Prospective observational case series France ☑	Patients with infected wound or wound at risk of infection (including open fracture, infected haematoma, pressure ulcer, non-healing postoperative dehiscence, diabetic foot ulcer, necrotizing fasciitis, limited exposure to osteosynthetic hardware, leg ulcer. Recruited between January 2012 and December 2012. n = 131 ☑	NPWTi with V.A.C. VERAFLO therapy. Dressing: V.A.C. VERAFLO (reticulated open cell). Instillation fluid: normal saline. Dwell time 20 or 30 seconds, soak time 10 minutes. Cycle length: 4 to 12 hours NPWT (-125 mmHg) Average dressing change every 3 days. ☑	• Patient characteristics (including previous treatment) • Length of therapy • Need for NPWT after NPWTi • Surgical closure ☑☒
(Fluieraru *et al.*, 2013) Retrospective case series	Patients receiving NPWTi recruited between January to December 2012. Patients had	NPWTi using V.A.C. VERAFLO dressings (unclear if Ulta sysem was used).	• Patient characteristics (including previous treatment) • Adverse events

Study name, design, and location	Participants and setting	Intervention	Outcomes
France ☑	infected wounds or poor granulation. Recruitment between January 2012 and December 2012. n = 24 ☑	Instillation fluid: normal saline Dwell time 30 seconds, soak time 10 minutes. Cycle length: 4 hours NPWT (-125 mm Hg)Dressings changed every 3 days. ☑☒	• Number of cycles per day • Closing technique ☒

Abbreviations: CRP, C-reactive protein; NPWTi, negative wound therapy with instillation; RCT, randomized controlled trial.

* Dakin's solution is sodium hypochlorite solution. Full strength is around 0.5%. It is an approved solution for use with the the V.A.C. VERAFLO system.
** Prontosan is a proprietary wound irrigation solution consisting of polyhexamethylene biguanide (0.1% an antimicrobial compound) and betaine (0.1%, a surfactant). It is an approved instillation agent for the V.A.C. VERAFLO system.

5 Clinical evidence review

5.1 *Overview of methodologies of all included studies*

Three of the comparative studies (Table 4.3) were randomised controlled trials (RCTs). However, although it used the V.A.C. VERAFLO NPWTi system, one of the RCTs (Kim *et al.*, 2015) compared two instillation fluids (Prontosan compared with 0.9% saline), which did not inform the decision problem. Data derived from this study was considered as a single-armed analysis. One study was reported as a small RCT (n = 19) which compared NPWTi with NPWT (Yang *et al.*, 2017a). The remaining RCT (Kim *et al.*, 2020) also compared NPWTi with NPWT. This study had not been peer-reviewed or published at the time of the company's clinical submission or final drafts of this Assessment Report prepared prior to the covid-19 pandemic. However, it has subsequently been published in *International Wound Journal*. Because of its relative quality and relevance to the scope, the EAC considered this the most informative study overall.

The other comparative studies were described as retrospective (Chowdhry and Wilhelmi, 2019, Gabriel *et al.*, 2014, Kim *et al.*, 2014) or prospective (Goss *et al.*, 2012, Omar *et al.*, 2016). All the studies compared the use of NPWTi with NPWT, with the exception of Chowdry and Wilhelmi (2019) and Deleyto *et al.* (2017), which reported comparison with wet wrap dressings or conventional dressings, respectively. The comparative studies were set in a broad-range of populations overall, with some studies describing a relatively specific wound type as inclusion criteria, and other covering a wide spectrum of wound aetiology. One study was primarily an economic analysis, but was also considered in the clinical evidence review as it reported relevant clinical outcomes (Deleyto *et al.*, 2018).

The single-armed studies were mainly retrospective, with three studies being described as prospective (Brinkert *et al.*, 2013, Ludolph *et al.*, 2018, Milcheski *et al.*, 2017). Most of the studies were descriptive, sometimes on an individual level (case series), and meaningful aggregated data were often not reported. A wide-range of wound type and patient groups were reported on, including acute infected bio-hardware prostheses, surgical infections, pressure ulcers. and chronic diabetic foot ulcers.

In total, there were 636 patients enrolled into comparative studies (of any methodology), of which 365 received NPWTi, 222 received NPWT, and 49 received dressings. In the single-armed studies, 373 patients were enrolled. Thus there was very little data on patients receiving dressings in particular. None of the included studies were set in the NHS or reported on UK populations. Some clinical experts expressed concern that NHS treatment pathways might vary substantially from those used in other countries; for

instance the use of culture to guide requirement for debridement is not practised in the UK (EAC External correspondence log, 2020).

5.2 *Critical appraisal of studies and review of company's critical appraisal*

5.2.1 RCTs

The included RCTs were critically appraised using the *Cochrane Collaboration's tool for assessing risk of bias in randomised trials* (Higgins *et al.*, 2011). These appraisals are reported fully Appendix B (Tables B1 to B3), and summarised in Table 5.1.

The EAC considered the most informative study was the RCT by Kim (2020). This was because it was within scope, made a relevant comparison, had a relatively large sample size (n = 183 randomised), and had relatively high methodological quality. This study enrolled patients with acute or chronic wounds of varying aetiology, with the most common causes being diabetic ulcers, pressure ulcers, and infected surgical wounds (dehisced or non-dehisced). Patients were randomised to receive NPWTi with Prontosan anti-septic fluid or NPWT. Randomisation and allocation concealment were reported, and selection bias was likely to be minimal. However, the study was not blinded, leading to potential performance and detection bias, and had a high attrition rate, with inadequate description of which results reflected *intention to treat* (ITT) or *per protocol* (PP) analysis. The study was powered to detect a reduction in the number of operative debridements (primary outcome: 3.6 in control and 1.6 in treatment, requiring 164 patients, 82 in each arm), which was appropriate. Reporting of secondary outcomes was limited and could have been selective, although there is no evidence of this. However, correction for multiple testing was not applied. There was no information on financial disclosures. In terms of generalisability, the heterogeneous nature of the study population, with relatively small patient numbers for each type of wound, makes interpretation to specific patient groups difficult.

The RCT by Yang *et al.* (2017) also compared NPWTi with NPWT. However, this study was small (n = 19) and of low methodological quality, with potential bias in all domains. In particular, although it was described as an RCT, it is likely randomisation was not employed; instead a consecutive alternating method was used to select the study arms. Only one outcome, bacterial burden, was reported. The generalisability of this study is low because of the very small sample size and mixed aetiologies of the wounds in the study. The RCT by Kim *et al.* (2015) was also of low methodological quality, and had the potential for bias in most domains. Its comparative results were not relevant to the decision problem.

Table 5.1. *Summary of critical appraisal of RCTs.*

Study	Potential source of bias						
	Random allocation sequence	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective reporting	Other bias
(Kim *et al.*, 2020)	☺	☺	☹	☹	☹	☹	?
(Yang *et al.*, 2017a)	☹	☹	☹	☹	☹	☹	?
(Kim *et al.*, 2015)†	☺	☹	☹	☹	☺	☹	☹
Key: ☺ Low risk of bias; ☹ High risk of bias; ? Unclear risk of bias (poor reporting or not ascertainable). * This RCT was provided in draft (academic in confidence), but has since been published. † The comparison the RCT was making was not in scope.							

5.2.2 Comparative observational studies

The comparative observational studies were appraised using the Critical Appraisal Skills Programmes (CASP, 2020) cohort study checklist. These are reported in Appendix B (Tables B4 to B9). All the studies were of poor methodological quality in most domains. In general, there was little reporting about how the control groups, which were usually historical, were selected. Historical control groups are inherently confounded by the passage of time (and improvements in overall healthcare management), whereas in groups where prospective selection is employed, a major confounding factor is that the underlying reason for the patient to be managed with the intervention or comparator is not usually known or controlled. Descriptions of wound characteristics were usually absent, and the patient populations consisted of heterogeneous case mixes. This meant there was high degree of potential for selection bias. None of the studies attempted to identify or control for confounding variables, and the retrospective nature of the outcomes cast some doubt on their robustness. Statistical adjustment for multiple comparisons was not undertaken in any study and in some cases statistical comparative analysis was incorrectly applied (see Table C2). In summary, it was not possible to attribute causality of the intervention to the reported outcomes with confidence.

5.2.3 Single-armed observational studies

The single-armed studies could not be formally appraised, and did not report results that could be meaningfully interpreted. This was because the nature of the intervention did not allow for analysis of a longitudinal effect size (i.e. “before and after” effect). Thus effectiveness results could not be contextualised. Furthermore, several of the studies were restricted to purely descriptive “outcomes” (e.g. description of patient characteristics), or did not

report aggregated data at all (i.e. were case series). These issues were compounded by the heterogeneous case mix of the populations under investigation, which were not generalisable to broader populations. In short, the EAC did not consider any of the single-armed studies provided data that could reliably inform treatment pathways in the NHS.

5.3 *Results from the evidence base*

The company reported results by study in Section 4 (Table 4), and in a narrative format in Section 8. In general, data from the studies were not extracted in a quantitative manner, with sections cut and pasted from the relevant papers without specific context to the outcomes listed in the scope. The EAC has therefore independently reported the results directly from the primary studies. Results are presented on an outcome by outcome basis as listed in the scope. A summary of these are provided in Table 5.2.

5.3.1 Clinical outcome measurements

Several of the comparative studies reported on clinical outcome measures. In general, very little data of this nature was reported by the single-armed studies.

Length of stay in hospital

Length of hospital stay associated with NPWTi compared with NPWT was reported by several comparative observational studies (Gabriel *et al.*, 2014, Kim *et al.*, 2014, Omar *et al.*, 2016). Kim *et al.* (2014) reported a mean length of hospital stay of 14.92 ± 9.2 days in the NPWT group. This was significantly longer than the length of stay (LoS) associated with NPWTi with a 20 minute dwell time (11.4 ± 5.1 days, p = 0.03) and longer than NPWTi with a 6 minute dwell time (11.9 ± 7.8 days), although the latter value was not significant (p = 0.10). Gabriel *et al.* (2014) reported a mean length of hospital stay of 8.1 days in the NPWTi group, compared with 27.4 days in the NPWT group (p < 0.0001). Omar *et al.* reported the median length of hospital stay associated with NPWTi was 21.5 days (interquartile range [IQR] 15.5 to 32.0 days). This was not significantly different from those treated with NPWT (26.5 days, IQR 18.5 to 33.3 days, p = 0.43).

The RCT by Kim *et al.* (2015) reported mean length of hospital stay was 13.6 days and 14.5 days in patients receiving saline and Prontosan respectively (no significant difference between groups, p = 0.68). Although it was measured, the RCT by Kim *et al.* (2020) did not report differences of LoS overall [redacted]. However, the LoS was reported as an outcome in *post hoc* subgroup analysis in patients with surgical dehisced wounds (n = 23). Length of stay was reported as being significantly shorter in patients receiving NPWTi compared with NPWT (9.3 days compared with 21.8 days, p = 0.05).

The economic study by Deleyto *et al.* (2017) reported a mean length of hospital stay of 69.1 ± 33.6 days for patients receiving NPWTi, compared with 88.2 ± 77.1 days for those receiving conventional dressings; this difference was not significant (p = 0.745).

None of the single-armed studies included this outcome.

Note: there are inherent problems in assessing and interpreting LoS data in wound care studies due to study heterogeneity. This is an important consideration because LoS informed the economic model (see Section 9.2.3).

Wound healing

This is a summary of the three outcomes listed in the scope: rates of partial and complete wound closure; mean time to partial or complete wound closure; and mean time to healing.

The most robust evidence for these outcomes was reported in the RCT comparing NPWTi with NPWT (Kim *et al.*, 2020). This study reported the mean time until the wound was deemed ready for closure/coverage was 6.8 days for NPWTi compared with 6.3 days for NPWT. This difference was not significant (p = 0.71). There was also no statistical difference in the proportion of wound closure/coverage by day 56 (± 8 days) between patients receiving NPWTi (68/71, 95.8%) compared with those receiving NPWT (64/66, 97.0%, p = 1.00). No significant differences in healing outcomes were observed for subgroups of patients with high bacteria counts or who had at least one debridement.

The retrospective comparative study by Kim *et al.* (2014) reported 62% of wounds were successfully closed. The closure rate in patients receiving NPWTi with 6 minutes dwell time was significantly improved at 94% (p = 0.0004). For 20 minutes dwell time, the improvement was not significantly different (80%, p = 0.08). The proportion of wounds that remained closed at 1 month was not different between the groups. Gabriel *et al.* (2014) reported a mean time to wound closure of 4.1 days in patients receiving NPWTi compared with 20.9 days in those receiving NPWT (p <0.0001). Omar *et al.* (2016) reported patients receiving NPWTi had a median time to wound closure of 9.0 (IQR 7.0 to 19.3) days compared with12.5 (IQR 7.8 to 23.3) days in those receiving NPWT. This difference was not significant (p = 0.36). The RCT by Kim *et al.* (2015) reported that 85.7% of wounds treated with NPWTi with saline achieved complete closure. This compared with 92.2% in those receiving the Prontosan fluid instillation (p = 0.35).

One study comparing NPWTi with wet wrap dressings reported that the mean time to primary wound closure was 7.9 ± 2.3 days (median 8 days) in the NPWTi group compared with 13.9 ± 3.2 days (median 15 days) (Chowdhry and Wilhelmi, 2019). This difference was significant (p < 0.0001). The population enrolled in this study was specific to sternal wounds that were difficult to heal. Deleyto *et al.* (2018) reported a significantly reduced time to recovery in patients treated with NPWTi compared with those receiving

conventional dressings (mean time of 2.4 months compared with 31.3 months, p < 0.001).

None of the single-armed studies reported on these outcomes.

Number of dressing changes

One single-armed study reported that the mean number of dressing changes in patients receiving NPWTi (with V.A.C. VERAFLO Cleanse Choice dressings) was 2.9, over the course of 8.7 days (Téot *et al.*, 2017). Patients in this study (n = 21) featured a heterogeneous case mix of wounds and comorbidities.

Number of follow on treatments and number of surgical debridements

This section combines the outcomes of number of follow on treatments and visits to hospital, and number of surgical debridements.

The most robust evidence for these outcomes is reported in the RCT comparing NPWTi with NPWT (Kim *et al.* 2020), which had "number of inpatient Operating Room debridements required during the initial inpatient stay after the initial debridement until the wound was deemed ready for closure or coverage by the Investigator" as the primary outcome (and the study was powered to show superiority in this outcome). In patients receiving NPWTi, there was a mean of 1.1 debridements required (95% confidence interval [CI] 0.93 to 1.30). The corresponding number in the NPWT group was also 1.1 (95% CI 0.85 to 1.18) with no significant difference observed between the groups (p = 0.68).

The primary outcome of the observational comparative study by Kim *et al.* (2014) was the number of visits to the operating room following commencement of treatment. In the NPWT this was 3.0 ± 0.9 (SD). There were significantly fewer return visits in patients treated with NPWTi with 6 minute dwell time (2.4 ± 0.9, p = 0.04) or 20 minute dwell time (2.6 ± 0.9, p = 0.003). In the study by Gabriel *et al.* (2014), the mean number of surgical debridements in the NPWTi group was 2.0 compared with 4.4 in the NPWT group (p < 0.0001). Omar *et al.* (2016) reported that patients receiving NPWTi required a median of 3.0 surgical interventions following treatment with NPWTi (IQR 2.0 to 4.3). This was the same as for those receiving NPWT (3.0, IQR 2.8 to 5.3, p = 0.65).

The RCT comparing NPWTi instillation fluids (Kim *et al.*, 2015) reported a mean number of operations of 2.5 ± 0.9 (SD) in patients receiving normal saline and 2.8 ± 0.9 in those receiving Prontosan (p = 0.19).

One study reported data comparing the use of NPWTi with wet dressings (Chowdhry and Wilhelmi, 2019). This study reported the mean number of

surgical debridements was 1.8 ± 0.7 (SD) in patients receiving NPWTi compared with 3.1 ± 1.0 in patients receiving dressings only. This difference was statistically significant (p = 0.0011). One study that compared NPWTi with conventional dressings reported an average of 0.82 ± 0.75 (SD) additional surgeries in the NPWTi group compared with 2.29 ± 2.11 in the control group (p = 0.009) (Deleyto *et al.*, 2018). The same study reported reduced hospitalisation episodes with NPWTi (mean 1.64 vs. 3.59, p = 0.003).

None of the single-armed studies reported on these outcomes.

Number of amputations or skin grafts

The single-armed study of Brinkert *et al.* (2013) reported 58% of patients had closure delivered by skin graft. A flap was used in 17% of patients and 25% achieved closure through primary suturing.

Staff time and use of other consumables

Two single-armed studies reported on the number of dressing changes associated with NPWTi. One study reported a mean of 6.6 ± 6.8 (SD) changes over 19.4 ± 20.8 days treatment (Latouche and Devillers, 2020). This compared with a mean number of 2.9 dressing changes over a mean duration of NPWTi therapy of 9.7 days in another study (Téot *et al.*, 2017).

Colonisation with antimicrobial resistant pathogens

The company requested that this outcome was broadened to include all bacterial pathogens, not just ones which were resistant to antimicrobial drugs. The EAC concurred that this was logical. Several studies reported on the broader outcome, and inferences can be drawn from this data on antimicrobial resistant pathogens.

The best evidence for the potential of NPWTi to reduce bacterial burden is reported in the comparative RCT by Kim *et al.* (2020). Microbiological evaluation of results showed a significant decrease in mean total bacterial counts between time of initial surgical debridement and first dressing change in NPWTi treated patients (n=69, PP analysis) subjects compared with NPWT treated patients (n=63). The values were -0.18 Log_{10} CFU/g [colony forming units per gram tissue] for NPWTi compared with 0.6 Log_{10} CFU/g for NPWT (p = 0.02).

Another RCT, with a small sample size (n = 19) and of low methodological quality (Yang *et al.*, 2017a), reported on the concentration of planktonic and biofilm bacteria following treatment as its only endpoint. In the patients receiving NPWTi (using ¼ strength Dakin's solution as the instillate), there were 10.5 x 10^5 CFU/g ± 15.1 x 10^5 CFU/g planktonic bacteria. This compared with 12.3 x 10^5 CFU/g ± 28.6 x 10^5 CFU/g in patients receiving NPWT alone. There was no statistical difference between groups (p = 0.86).

There was also no initial difference in biofilm-protected bacteria concentrations (8.6 x 10^3 CFU/g ± 8.8 x 10^3 CFU/g compared with 12.9 x 10^3 CFU/g ± 12.5 x 10^3 CFU/g, p = 0.48). The authors reported that following 7 days treatment with NPWTi there was a significant reduction in bacteria (43%, p < 0.05), whereas in the NPWT there was non-significant increase (14%, p = 0.46). However, there was no difference between the groups (p = 0.11).

One comparative observational study reported on bacterial bioburden as its sole outcome (Goss *et al.*, 2012). The authors reported that there was a mean of 3 ± 1 (SD) types if bacteria in the wounds, with most common being *Staphylococcus aureus*, Corynebacterium, and *Pseudomonas aeruginosa.* After 7 days treatment with NPWTi (with Dakin's solution as the instillate) or NPWT alone, the mean absolute reduction in bacteria in the NPWTi was 10.6 x 10^6 per gram of tissue compared with a mean absolute *increase* of 28.7 x 10^6 bacteria per gram of tissue in the NPWT group. This was a significant decrease in bioburden associated with NPWTi (p = 0.016).

The observational study by Kim *et al.* (2014) reported "an overall culture improvement" of 38% in the NPWT group, compared with 59% in patients receiving NPWTi with 6 minutes dwell time, and 50% in patients receiving NPWTi with 20 minutes dwell time. These differences were not significant. However, patients in the 6 minute dwell time group did have significant culture improvement when Gram-negative bacteria, Corynebacterium, and yeast were excluded.

One single-armed observational study reported bacterial loads did not significant decrease over the course of NPWTi therapy (Eckstein *et al.*, 2019).

Antibiotic use

No studies reported on antibiotic use.

5.3.2. Patient outcomes (including adverse events)

The patient outcomes listed in the scope were "Health-related quality of life"; "Patient satisfaction and acceptability"; and "Patient-related outcomes such as pain scores". Only one single-armed study reported on any Patient Related Outcome Measure (PROM). This was the single-armed study by Eckstein *et al.*, (2018), whose authors stated "The course of the pain value determined via the NRS [Numeric rating scale] was highly variable but at the end of the therapy all but 1 patient obtained pain relief". Without quantitative data, it is not possible to qualify or interpret this statement.

The RCT by Kim *et al.* (2020) reported significantly lower pain scores in patients with dehisced surgical wound receiving NPWTi compared with NPWT. In the NPWTi group, the maximum visual analogue score [VAS] pain

score was 52.0, compared with 79.0 in the NPWT group (p = 0.03). However, overall pain scores for the whole cohort were not reported. Additionally, no statistical adjustments for multiple comparisons were made.

The RCT by Kim *et al.* (2020) reported on potential device-related adverse events. More patients experienced at least one treatment-related adverse event in the NPWTi group (20/93, 21.5%) compared with the control group (11/88, 12.5%). The statistical significance of this difference was not reported. The most common adverse event were skin and subcutaneous tissue disorders (skin macerations, rash, dermatitis), which occurred in 18/93 (19.4%) of the NPWTi group compared with 9/88 (10.2%) in the NPWT group. There were 3 deaths in the NPWTi group compared with 1 death in the NPWT group, but none of these were considered to be treatment-related. It was noted the company did not report these adverse events in the submission.

In one observational study comparing NPWTi with wet wrap dressings (Chowdhry and Wilhelmi, 2019), no complications were reported in the NPWTi. Three patients had seromas in the dressings group. This difference was not significant (p = 0.22).

Further discussion of adverse events is in Section 6.

Table 5.2. *Summary of outcomes reported by the included studies.*

	Outcome	Comparative evidence from experimental studies (RCTs, NPWTi vs. NPWT)	Evidence from observational studies (comparative and single-armed)	EAC comment on validity of the evidence*
Clinical Management Outcomes	Length of stay in hospital	One RCT reported significantly reduced LoS associated with NPWTi in a subgroup of patients with surgically dehisced wounds (Kim *et al.*, 2020).	Two comparative observational studies reported NPWTi was associated with reduced length of hospital stay (Gabriel *et al.*, 2014, Kim *et al.*, 2014). One study reported no difference compared with NPWT (Omar *et al.*, 2016). One study reported no difference compared with conventional dressings (Deleyto *et al.*, 2018)	Weak evidence that NPWTi is associated with reduced length of hospital stay compared with in certain patient populations.
	Wound healing	One RCT reported no significant difference in the time until wound healing associated with NPWTi (Kim *et al.*, 2020).	Two studies reported improved wound healing associated with NPWTi (Gabriel *et al.*, 2014, Kim *et al.*, 2014). One study reported no difference (Omar *et al.*, 2016). One study reported improved healing associated with NPWTi compared with wet wrap dressings (Chowdhry and Wilhelmi, 2019).	There is equivocal evidence that NPWTi is associated with improved wound healing parameters. The strongest evidence, from an RCT, did not identify this effect. Non-randomised evidence was largely of poor methodological, particularly regarding patient selection, and might not be generalisable.
	Number of dressing changes	No evidence reported on this outcome.	No comparative evidence reported on this outcome.	No conclusions can be drawn

	Outcome	Comparative evidence from experimental studies (RCTs, NPWTi vs. NPWT)	Evidence from observational studies (comparative and single-armed)	EAC comment on validity of the evidence*
	Number of follow on treatments and number of surgical debridements	One RCT reported there was no difference in the number of operating room debridement between patients receiving NPWTi or NPWT (Kim *et al.*, 2020).	Two studies reported a reduced rate of debridements associated with NPWTi compared with NPWT (Gabriel *et al.*, 2014, Kim *et al.*, 2014). One study reported no significant difference (Omar *et al.*, 2016). One study reported the use of NPWTi was associated with a significantly reduced rate of surgical debridement compared with wet wrap dressings (Chowdhry and Wilhelmi, 2019). One study reported significantly reduced additional surgeries and hospitalisation episodes with NPWTi compared with conventional dressings.	The evidence that NPWTi is associated with reduced requirement for debridement or other follow on treatments compared with NPWT is equivocal, with the most robust evidence not identifying any difference.
	Number of amputations or skin grafts	No evidence reported on this outcome.	No comparative evidence reported on this outcome.	No conclusions can be drawn
	Staff time and use of other consumables	No evidence reported on this outcome.	No comparative evidence reported on this outcome.	No conclusions can be drawn
	Colonisation with antimicrobial resistant pathogens	One RCT reported that NPWTi was associated with significantly reduced bacterial counts compared with NPWT (Kim *et al.*, 2020).	One study reported NPWTi was associated with a decrease in bacterial load compared with NPWT alone (Goss *et al.*, 2012).	The available evidence suggests that NPWTi reduces bacterial bioburden compared with NPWT alone. However, the significance of this on clinical outcomes is

	Outcome	Comparative evidence from experimental studies (RCTs, NPWTi vs. NPWT)	Evidence from observational studies (comparative and single-armed)	EAC comment on validity of the evidence*
		One small RCT identified a trend for decreased bacterial counts in patients receiving NPWTi compared with NPWT (Yang *et al.*, 2017a).		unclear. Additionally, this effect may be dependent on the type of instillation fluid used.
Patient Outcomes	Health-related quality of life	No evidence reported on this outcome.	No comparative evidence reported on this outcome.	No conclusions can be drawn
	Patient satisfaction and acceptability	No evidence reported on this outcome.	No comparative evidence reported on this outcome.	No conclusions can be drawn
	Patient-related outcomes such as pain scores	One RCT reported NPWTi was associated with significant reductions in pain compared with NPWT in a subgroup of patients with surgical dehiscence (Kim *et al.*, 2020).	One study narratively reported that NPWTi reduces pain (Eckstein *et al.*, 2019).	No conclusions can be drawn There is insufficient evidence reported to assess the pain-relieving potential of NPWTi.
	Adverse events	One RCT reported an adverse event rate of 21.5% for NPWTi compared with 12.5% for NPWT (Kim *et al.*, 2020).	One study reported three patients treated with wet wrap dressings had seroma, compared with none who received NPWTi (Chowdhry and Wilhelmi, 2019).	No conclusions can be drawn It is possible that NPWTi is associated with an increased risk of adverse events compared with NPWT, but statistical evidence has not been reported.

Abbreviations: NPWT, negative wound therapy; NPWTi, negative wound therapy with instillation (V.A.C. VERAFLO).

* This is the EAC's subjective judgement on the quality of evidence available to inform conclusions. Objective grading of this level of evidence was not possible, as, for instance, it was not compatible with GRADE methodology (Guyatt *et al.*, 2008).

5.3.3. Subgroups

Five subgroups for special consideration were considered in the scope (NICE, 2020). These were diabetic ulcers, pressure ulcers, surgical site infections, venous leg ulcers, and wounds containing prosthetic implants.

Diabetic ulcers

The company did not report separately on this subgroup, nor were studies any identified which reported specifically on diabetic foot ulcers. However, many studies included patients with diabetic ulcers in their study populations. In the RCT by Kim *et al.* (2020), diabetic ulcers made up 78/181 (43.1%) of the population. However, results were not reported by subgroup, with the exception of surgical dehisced wounds.

Pressure ulcers

The company identified one study included by the EAC that reported mainly on pressure ulcers (Téot *et al.*, 2017). In this study, 18/21 (85.7%) had pressure ulcers, with the remainder having burns or tissue necrosis. In the RCT by Kim *et al.* (2020), pressure ulcers made up 31/181 (17.1%) of the population, the second largest grouping by wound aetiology. However disaggregated data on these patients was not reported.

Surgical site infections

The company identified 2 studies that were specifically on surgical site infections. The study by Jurkovic (2019) was excluded by the EAC on the basis it was published in a foreign language and reliable translation was not available. Additionally, this study was based on a predecessor device (VAC Instill). The study by Chowdry and Willhelmi (2019) was in people with sternal wound complications following reconstruction. It compared NPWTi with wet dress wrappings.

Venous leg ulcers

This subgroup was not specifically addressed by the company. No studies were identified that specifically reported on this condition. The RCT by Kim *et al.* (2020) included 5/181 (2.8%) of people with venous leg ulcers.

Prosthetic implants

Wounds associated with prosthetic implants were the subject of several studies included by the company. Several of these were excluded by the EAC (see Table 4.1). The studies included by the EAC were in patients presenting with abdominal mesh exposure (Deleyto *et al.*, 2018) and patients with open wounds revealing exposed hardware (Hehr *et al.*, 2020). The study by Eckstein *et al.* (2019) was in patients with head and neck reconstructive surgery, but did not report these patients had prosthetic implants.

6 Adverse events

The company summarised adverse events (AEs) from their literature searches in Section 6 of their evidence submission as follows:

- "Garcia-Ruarno. 12 patients who had presented with abdominal mesh exposure developed hernias, 7, reappearance of mesh and 3 an enterocutaneous fistula. No outcomes were given.

- Kim *et al.* (2020). 1 patient developed an infection and another an undefined problem. No outcomes were given".

The EAC considered that the adverse events reported in Garcia-Ruarno (2016) did not appear to be device related. The study by Kim (2020) reported a higher number of skin reactions in the NPWTi group (with Prontosan instillation fluid) compared with the NPWT group, but the clinical significance of this was not stated.

The company also searched the FDA Manufacturer and User Facility Device Experience (MAUDE) database for the terms "V.A.C. VERAFLO DRESSING", "V.A.C. VERAFLO THERAPY", "VERAFLO"," VERAFLOW", "VERAFLO CLEANSE CHOICE" and "ODP", for reports dated from 01/01/2005 to 31/02/2020 (sic). Eight MAUDE reports were summarised by the company as 2 cases of device malfunction, 5 relating to the treatment of patients and 1 with insufficient information to determine reason for the report.

The EAC repeated the company search of the MAUDE database on 16/04/2020 for reports dated from 01/01/2000 to 31/03/2020. Some additional searches were undertaken, to check for any relevant reports registered under the "VAC ULTA" brand name, referring to the relevant pump used in VeraFlo therapy, rather than the dressing terms. Obvious variant spellings were also checked, including "V.A.C.", "V.A.C", and "ULTRA". In total, the EAC MAUDE searches found 29 records. The EAC reviewed each of the narrative reports and removed 17 which did not state that the event report related to a VeraFlo therapy procedure. The remaining 12 reports related to 9 unique MAUDE report numbers with event dates ranging from 03/09/2013 to 18/12/2019. The 9 unique events were categorised as 7 injuries and 2 malfunctions. The EAC review of each narrative report found that 4 of the 9 were events of VeraFlo dressings crumbling or adhering to the wound with either haemorrhage or wound deterioration and malodour being reported as a consequence by the user. In each of these cases, the manufacturer response in MAUDE attributed cause as possible user error, with aspects of the treatment going against the device instructions for use (IFU). Two more reports were of a Cleanse Choice and a VeraFlo dressing being left in the wound, both of which were attributed as possible user error by the manufacturer, as regular monitoring of the

dressing is required in the device IFU. One further report of wound deterioration and malodour was not attributed to the VeraFlo therapy by the manufacturer, after tests on the ULTA system found it met expected specifications. The final 2 of the 9 reports were a fire in the power pack plugged into the wall and an event where the power cord came apart. Neither of these had a manufacturer response in MAUDE.

It is important to note that the FDA states that their medical device report data alone "cannot be used to establish rates of events, evaluate a change in event rates over time or compare event rates between devices. The number of reports cannot be interpreted or used in isolation to reach conclusions about the existence, severity, or frequency of problems associated with devices." The fact that there is no denominator figure of total procedures undertaken means these MAUDE reports cannot be set in context of all patients treated with V.A.C. VERAFLO therapy in the USA.

The EAC agrees with the company in their submission that there are no VeraFlo adverse event reports in the MHRA database.

The NICE Expert Advisors did not raise any specific safety concerns; although one emphasised the skills required and therefore potential for human error. This expert would encourage more research to produce evidence-based data on the correct amount of fluid for soaks/washes, rather than relying upon trial and error to get this right.

The EAC considers that the few injury reports in the FDA MAUDE database, which were predominantly attributed to possible human error, tend to align with the NICE Expert Advisor's opinion on the skills required for administering VeraFlo therapy. Evidence from one RCT suggested that NPWTi using antiseptic instillation fluid may be associated with increased risk of skin reactions, although the importance of this was not clear. In summary, the EAC did not identify any significant safety concerns for the technology.

7 Evidence synthesis and meta-analysis

No evidence synthesis was reported by the company. This was appropriate because of the heterogeneous nature of the studies in terms of methodology, study populations, and outcomes reported.

8 Interpretation of the clinical evidence

The evidence base for NPWTi is dominated in number by observational studies and there are few well-designed and conducted studies of the comparative effectiveness with NPWT. Thus, the quantity and quality of evidence is lacking.

The most robust evidence was from an RCT, which enrolled patients with mixed wound aetiologies which were either acute (30.1%) or chronic in nature (69.9%) (Kim *et al.*, 2020). Although this was also the largest study (n = 181), the heterogeneity of the study population meant that the sample size of individual wound types were small, and did not allow for extensive subgroup analysis. In this study, NPWTi was *not* shown to be superior to NPWT. Outcomes included wound healing and requirement for debridement, which are important economic parameters.

The results of the Kim *et al.* (2020) RCT were contradicted by some, but not all, the observational studies, such as the relatively large (n = 142) retrospective cohort study by Kim et al. (2014). This study also had broad inclusion criteria in common with the later RCT. In contrast, many of the other observational studies had highly selected populations, but these invariably had small sample sizes and the selection of control groups was poorly reported, with statistical matching not performed, and often patient and wound characteristics were under-reported. This made interpretation and contextualisation of results difficult. It was not possible to meaningfully interpret the single-armed studies, which reported few relevant outcomes. There was also not enough data to make any judgement of NPWTi compared with conventional dressings, but this might not be the most relevant comparator (Section 1.3).

It was noted that no study has published HRQoL or PROM outcomes, and this is a substantial omission in the evidence base. Additionally, the evidence for the superiority of NPWT itself over standard care is equivocal in most conditions (Table 3.1), and NICE clinical guidelines have made only limited recommendations for this intervention (Section 3.1).

It should be stressed that a lack of overall evidence is not evidence of no effect. The technology is plausible in its mechanism, and likely represents an incremental improvement over its predecessor, offering clear system benefits through programming and automation. NICE clinical experts who used the technology or were aware of it, were unanimous that judicious use of NPWTi was likely to be effective in selected patients (EAC External correspondence log, 2020). Generally, the patients thought most likely to benefit had complex wounds that were not responding to conventional therapies. The issue is to date are there have been few high-quality experimental studies that have clearly demonstrated this benefit. The recently published RCT by Kim *et al.* (2020) was likely to be underpowered, as were all the other studies, and there were issues with outcome assessment due to the multicentre nature of the study and the heterogeneity of patients included. Furthermore, given these issues with complexity and the heterogeneity of the population the technology is indicated in, future research is likely to be challenging (Section 12).

Nevertheless, in the opinion of the EAC, the claimed benefits of NPWTi were not unequivocally supported by the current evidence base. These claims are summarised in Table 5.3.

Table 5.3. *EAC interpretation of the evidence for the claimed benefits of NPWTi. The first 3 columns are taken directly from the claimed benefits made by the company (page 9 of the clinical submission). The fourth column reflects the EAC's opinion on whether these claims have been adequately substantiated.*

	Claimed benefit	Supporting evidence*	Company Rationale	EAC opinion
Patient benefits	Reduced Hospital Length of Stay	Kim 2014, Gabriel 2014~~, Gabriel 2008, Timmers.~~ Kim 2015, Omar, Deleyto~~, Garcia-Ruano~~ , ~~Powers and Davis~~.	The first four of these studies showed statistically significant reductions in patient's length of hospital stay when NPWTi use was compared to either NPWT or conventional wound care. The remaining studies showed shorter, but non-statistically significant reductions. Patients benefit from reduced LoS as it allows them an earlier return to their home and families and activities of daily living. It also removes them from a hospital environment where they may be vulnerable to hospital acquired infection. Please note the Davis study used an alternative company's product.	**<u>Claim not unequivocally proven</u>** The included studies which reported reduced LoS were observational studies incorporating retrospective patient selection. It is not possible to interpret results from these studies with confidence. One RCT reported NPWTi reduced length of stay in a subgroup analysis (of patients with surgically dehisced wounds). However, results for the cohort as a whole were not reported (Kim *et al.*, 2020).
	Reduced number of surgical debridements	Kim 2014, Gabriel 2014, ~~Garcia-Ruano~~, Choudhry, ~~Timmers, Powers~~	The first 6 of these studies showed statistically significant reductions in the number of surgical debridements required when NPWTi use was compared to either NPWT or conventional wound care. This means that patients have to undergo fewer	**<u>Claim not unequivocally proven</u>** The observational studies reporting this outcome were of limited methodological quality and it was not possible to interpret results with confidence. In particular, there were issues with the generalisbility of this outcome with NHS pathways (Section

	Claimed benefit	Supporting evidence*	Company Rationale	EAC opinion
		~~Jurkovic~~, Kim 2015, Omar, Goss, Kim 2020)	painful procedures and the risk of an anaesthetic.	This was listed as the primary outcome in the study by Kim *et al.* (2020). There was no significant difference reported between NPWTi and NPWT (1.0 vs 1.1, respectively; p = 0.68).
	Higher rates of surgical implant retention	Lehner, ~~Garcia-Ruano~~. Deleyto, Ikeno, Eckstein, ~~Morinaga~~, ~~Huang~~	The first 2 of these studies showed statistically significant retention of surgical implants. The remaining studies recorded either high rates of retention when compared with conventional wound dressings, but without documenting significance, or they reported ranges of retention from 90-100%. Implants documented included life-saving cardiovascular grafts or orthopaedic implants that are essential to allowing patients to maintain their independence. Please note the Ikeno, Morinaga and Huang studies used an alternative company's products.	**Claim not unequivocally proven** This claim was not made in the final scope (NICE, 2020). The studies reporting these outcomes were generally of limited methodological quality and it was not possible to interpret their results into NHS pathways with confidence. Several studies did not report on the V.A.C. VERAFLO device.
	Reduced time to wound closure	Gabriel 2014, ~~Gabriel 2008~~, ~~Qui~~, ~~Garcia-Ruano~~, Choudhry ~~Jurkovic~~, Omar, ~~Morinaga~~, ~~Davis~~ and Kim 2020	The first 5 of these studies showed statistically significant reductions in mean time to complete or partial wound closure when NPWTi was compared with NPWT or conventional wound care.	**Claim not unequivocally proven** The listed studies that were included by the EAC were regarded as being of limited quality and interpretation of results could not be made with confidence, due to the heterogeneous nature of the populations

	Claimed benefit	Supporting evidence*	Company Rationale	EAC opinion
			The remaining studies showed shorter mean times to wound closure but these were not found to be significant. Patients living with open wounds are subject to increased pain and risk of infection. Please note the Qui, Morinaga and Davis studies used an alternative company's products.	studied and lack of generalisability with NHS clinical pathways. One RCT reported no significant difference between NPWTi and NPWT in terms of the proportion of successful wound closure or time until wound closure (Kim *et al.*, 2020).
	Reduced Pain	Eckstein, Kim 2020 Teot, Milcheski, ~~Qui~~, Gabriel 2014, ~~Chen~~	A number of papers referenced reduced pain levels for patients using NPWTi. The first 2 reported statistical significance in pain reduction post treatment with NPWTi The remaining stated pain reduction during and following NPWTi but did not publish statistical analysis. Please note the Qui and Chen studies used an alternative company's products. Nurses using NPWTi in the NHS completed a short survey with 13 patients in February and March 2020. Removal No pain or discomfort = 8 Some pain or discomfort = 5 A lot of pain or discomfort = 0	**Claim not proven** This claim was not made in the final scope (NICE, 2020). The RCT by Kim (2020) only presented analysis of pain outcomes as a *post hoc* subgroup analysis. It was not possible to interpret the results from Eckstein *et al.* with confidence. The survey results provided was not formally part of the submission.

	Claimed benefit	Supporting evidence*	Company Rationale	EAC opinion
			Application No pain or discomfort = 9 Some pain or discomfort = 4 A lot of pain or discomfort = 0	
	Patients discharged more quickly	Kim 2014, Gabriel 2014, ~~Gabriel 2008~~, ~~Timmers~~. Kim 2015, Omar 2016, Deleyto 2017, Garcia-Ruano , ~~Powers~~ and ~~Davis~~.	The papers supporting reductions in LoS have been documented in the Patient Benefit Section of this table. When patients are discharged from hospital more quickly, they release capacity to the NHS for additional patients to receive care. This may include admitting patients who have been subject to long waits in A&E departments. Please note the Davis study used an alternative company's product.	**Claim not proven** The EAC considers the claims for reduced length of stay were equivocal. Thus, so are claims of earlier discharge.
	Higher rates of wound closure	Kim 2014, ~~Garcia-Ruano~~ and ~~Powers~~. Kim 2015, Brinkert, ~~Zelen~~, Yang, ~~Gabriel 2008~~,Eckstein, Hehr~~,~~ ~~Jain~~, ~~Morinaga~~, ~~Davis~~	The first 3 of these studies showed statistically significant higher rates of complete wound closure when NPWTi was compared with NPWT or conventional wound care. The remaining papers showed non-significant differences between NPWTi and comparative care or recorded only closure rates for NPWTi. These ranged from 64 to 100%.	**Claim not unequivocally proven** The evidence for higher rates of wound closure is equivocal. The most robust study, the RCT by Kim *et al.* (2020) did not identify improvements in the rate of wound closure.

	Claimed benefit	Supporting evidence*	Company Rationale	EAC opinion
			Higher wound closure rates are a contributory factor to early hospital discharge, reductions in the number of debridements, dressing changes and skin grafts required as well as reducing the numbers of consumables used and staff time caring for patients.	
System benefits	Reduced follow on treatments	Deleyto, ~~Garcia-Ruano~~, ~~Chen~~, ~~Davis~~	Deleyto was the only paper to document a statistical significance for patients requiring fewer follow on treatments. Patients requiring follow on treatments, in the remaining 3 papers that recorded this data, ranged from 16% to 54% although this higher % was matched with 94% of control patients in this study requiring further treatment. Avoidance of follow on treatments release both physical and clinical capacity to the NHS to offer care to other patients. As fewer consumables will be required too, these factors are likely to reduce overall costs of care for these patients. Please note the Chen and Davis studies used an alternative company's products.	**Claim not unequivocally proven** This claim was not made in the final scope (NICE, 2020). The claim is not proven because the study by Deleyto was a retrospective cohort study that did not match patients or describe adequately how outcomes were reported. Note this study was conducted in a specific population (45 people, selected from 202, with an abdominal mesh) and is not generalisable to other conditions. There therefore remains considerable uncertainty in the interpretation of this paper. The study by Garcia-Ruano reported on the same patients as Deleyto and had the same limitations (as well as double counting patients).
	Reduced colonisation with pathogens	~~Jurkovic~~, Goss, Yang 2017, ~~Garcia-Ruano~~, ~~Timmers~~, Ludolph Kim 2020	The first 7 of these studies showed statistically significant higher rates of reduction in pathogen colonisation when	**Claim proven** This claim was not made in the final scope (NICE, 2020).

	Claimed benefit	Supporting evidence*	Company Rationale	EAC opinion
		Kim 2014, Powers,	NPWTi was compared with NPWT, or conventional wound care. The remaining 2 papers recorded higher rates of reduction by a % although, statistical significance was not reported. Patients with significant pathogenic colonisation are more likely to require additional treatment to achieve wound closure. This may involve longer hospitalisation periods, repeated surgical intervention, removal of implants and long term antibiotic therapy all of which will place demands on clinical time and consume other resources.	Data from the RCTs Yang *et al.* (2017) and Kim *et al.* (2020) substantiate claims that V.A.C. VERAFLO reduces colonisation rates with pathogens. This is also mechanistically plausible. However, the association between this outcome and clinical outcomes has not been proven.
	Overall reduction in staff and resource use	~~Chen~~ Gabriel 2014, Kim 2014, ~~Garcia-Ruano Qui~~, Choudhry, ~~Timmers~~, ~~Powers~~, Kim 2015, ~~Gabriel 2008~~	Chen was the only paper to directly report a significant reduction in clinical and nurse time although this was not quantified. Other papers referenced here relate to reductions in dressing changes, treatment duration, fewer days to final surgical procedure, fewer debridements, length of therapy and shorter mean times to wound closure. For each of these statistically significant differences were reported between cohorts of patients who had access to NPWTi and control groups	**Claim not proven** The study by Chen *et al.* (2018) was excluded on the basis it was not on the V.A.C. VERAFLO device. The other studies did not report on this outcome.

	Claimed benefit	Supporting evidence*	Company Rationale	EAC opinion
			Please note the Chen and Davis studies used an alternative company's products.	
Cost benefits	Reduction of costs	Gabriel 2014, Jurkovic, Deleyto	Each of these papers considered the cost of NPWTi therapy alongside total hospitalisation costs. As a result 2 suggested that that whilst the costs of using NPWTi were significantly higher the total hospitalisation costs did not differ significantly. Deleyto reported that when NPWTi was used as an alternative to conventional wound dressing the mean costs of NPWTi were €2,000 lower. Detailed costs will be modelled in part 2 of this submission.	**Claims considered in Section 9.1.2**
Sustainability	Reduction of consumables	Lehner, ~~Garcia-Ruano~~. Deleyto, Ikeno, Eckstein, ~~Morinaga~~, ~~Huang~~ Gabriel 2014, ~~Jurkovic~~,	Each of these papers referenced high rates of surgical implant retention or fewer dressing changes. Both of these factors would contribute to sustainability. Please note the Ikeno, Morinaga and Huang studies used an alternative company's products.	**Claim not proven** A reduction in consumables, overall, has not been evidenced by these studies.

Abbreviations: NPWT, negative pressure wound therapy; NPWTi, negative wound therapy with instillation; RCT, randomized controlled trial.

* Studies with strike through annotation were not included by the EAC (see Table 4.2).

8.1 *Integration into the NHS*

None of the included studies were undertaken in the UK. The available evidence may not be generalisable to well-defined populations within the NHS. A further issue is the optimal use of the technology in individual wound types is not fully known, concerning the selection of instillation fluids, dwell times, and cycle times, although there is some consensus guidelines on this (Kim *et al.*, 2019).

There are no significant barriers to adoption. NHS providers already providing NPWT with the VAC Ulta or Ulta 4 pump could adopt NPWTi without any substantive change to procedures. Additionally, NPWTi potentially offers system benefits such as improving reproducibility of treatment through automation, and having a user-friendly interface. The company has stated they offer free training, with successful completion of training is signed off using a competency assessment framework.

8.2 *Ongoing studies*

The company did not identify any ongoing studies in their clinical submission (Table 3 of Section 4 was left unpopulated).

The EAC searched the following databases for ongoing studies: Clinicaltrials.gov, and ISRCTN registry (International Standard Randomised Controlled Trial Number, now expanded to include observational studies). The EAC identified one ongoing study (NCT04026334). One completed study was also identified but peer-reviewed publication of results relating to this study were not found (NCT02266771). Additionally one terminated study (due to difficulty enrolling) was identified (NCT02621073) which aimed to compare V.A.C. VERAFLO with Prontosan with NPWT without instillation (using the VAC Ulta Therapy System) in patients with infected lower extremity status-post open reduction and internal fixation. This has not been included. The identified studies (one ongoing, one completed) are reported in Table 8.1. The EAC considered neither of the studies would be likely to significantly add to the evidence base if published. This is due to their small sample sizes and lack of overall generalisability.

Table 8.1. *List of relevant ongoing studies identified by the EAC*.

Study title, reference	Status, estimated completion	Population (n)	Primary outcome measure(s)	Secondary outcome measure(s)
Evaluation of V.A.C. VERAFLO CLEANSE CHOICE dressing using normal saline to promote increased healthy wound bed tissue (NCT04026334)	Recruiting Study Completion : June 2020	Single-arm (n=15) in patients aged 22 years and older, with full thickness wound (such as chronic, acute, traumatic, sub-acute, and dehisced wounds and/or ulcers) measuring ≥ 4 cm in length and ≥ 4 cm in width (before removal of eschar at the bedside) excluding undermining/tunnelling, has no more than 2/3 of the visible wound bed surface area considered to be clean, healthy and viable.	Percentage change in wound bed surface area (cm^2) of clean, healthy, viable tissue [baseline to day -9]	Percent change in total wound volume (cm^3) [Baseline to day 6-9]; Percent change in total wound area (cm^2) [Baseline to day 6-9]; Physician assessment of the need for surgical debridement [day 6-9]
Impact of V.A.C. VERAFLO Therapy in wounds requiring debridement within orthopaedic practice (NCT02266771)	Completed * Study completion: Dec 2017	Randomised (n=20) in patients aged 18 years and older, requiring surgical debridement for wounds with exposed hardware and/or bone, traumatic wounds, dehisced wounds, post-surgical wounds, and pressure ulcers/sores requiring debridement.	Number of days between the initial and final surgical procedure [6 months]	Length of hospital stay [6 months]; Number of days until wound closure [6 months]; Number of operative debridements [6 months]; Recurrence of wound post discharge [30 days]; Wound related readmission [30 days]

9 Economic evidence

9.1 *Published economic evidence*

9.1.1 Search strategy and selection

The company did not perform a dedicated literature search to identify economic studies. The company did not list any economic study as being relevant in their own right, and instead stated “Due to no economic studies reviewing NPWTi vs the comparator within the scope, we have included below the evidence studies used in our cost consequence model”. These studies were used to inform the parameters of the *de novo* model, rather than reported as economic studies in their own right.

9.1.2 Published economic evidence review

The EAC performed dedicated literatures searches on HTA/NHS, EED/DARE, and IDEAS/RePEc databases (Appendix D), with 51 studies being identified. These were sifted and combined with results from the clinical literature search. Four study protocols were identified. Three were studies that reported economic outcomes already identified from the clinical literature search (see Section 4). An additional study was identified through the economic search. These were of border-line relevance and were not considered by the EAC to be of adequate quality to undergo formal critical appraisal, but are briefly described for completeness.

The study by Deleyto *et al.* (2017) was included by the company in both the clinical and economic sections. This was a retrospective observational study comparing patients with abdominal wall dehiscence following mesh implantation, receiving either NPWTi (n = 11) or conventional wound dressings (n = 34). Cost was calculated using diagnosis-resource groups (DRGs) combined with hospital stay (days). Costs in both groups were compared using the Mann-Whitney U test.

The study by Gabriel *et al.* (2014) was a retrospective comparative observational study that reported economic outcomes. It was included by the company in both the clinical and economic sections. It compared patients with infected or critically colonized wound receiving NPWTi (n = 48) with patients receiving NPWT (n = 34). Costs were calculated by calculating the daily cost of treatment and multiplying this by the length of hospital stay. Groups were compared using the 2-sided Wilcoxon ranked sum test.

One study that reported cost outcomes was included by the company, but excluded by the EAC on the grounds it only reported on 7 patients, who received both NPWTi and split-thickness skin grafts (STSG) (Yang *et al.*, 2015). This was a retrospective observational study that enrolled patients with massive venous leg ulcers (> 100 cm^2). This was compared with the

estimated costs associated with use of compression bandages, although the methodologies behind these estimates were not clearly reported.

The study identified in the economic search was a retrospective case series (Latouche and Devillers, 2020). It reported data on 15 patients with hard-to-heal wounds with or without infection who were treated with NPWTi using the V.A.C. VERAFLO system.

9.1.3 Results from the economic evidence

The study by Deleyto *et al.* reported that in the NPWTi group, the mean average total costs (n = 11) were €15,093 (95% CI €11,170 to €19,017). Most of these costs were associated with hospital stay (€13,504) rather than treatment costs (€1589). The mean total costs were substantially higher in the conventional wound therapy group (n = 34, €29,614; 95% CI €20,422 to €38,805). For the NPWTi group, total costs were €15,093 (95% CI €11,170 to €19,017). The difference in total overall costs were €14,520 (95% CI €4459 to €24,581)

In the study by Gabriel *et al.* (2014), total therapy costs were less with NPWTi compared with NPWT ($799 compared with $2217, difference $1418). This was mainly because of a reduction in the number of debridement required (2.0 for NPWTi compared with 4.0 for NPWT). Daily cost of therapy was marginally higher for NPWTi ($195 compared with $106, difference $89), due to increased costs associated with dressings and canisters.

The study by Yang *et al.* (2015) reported total costs of $27,792 for compression therapy compared with $27,152 for NPWTi combined with STSG, a difference of $640 favouring the intervention. It is not clear how these results were calculated.

The study by Latouche and Devillers (2020) reported that the mean cost of treatment with NPWTi was €1643 ± €1709 (SD). The range was €747 to €7470. No information was reported on how these data were calculated. No comparative data was reported.

The results from all these studies should be treated with caution. Clinical parameters were mainly derived from small retrospective cohort studies or studies with historical controls, with questionable selection of patients and measurement of outcomes. Analysis was performed using simple costing calculations with no statistical matching or sensitivity analysis. Costs were derived from foreign healthcare services, not the NHS, and were reported in euros or US dollars. Overall the reporting quality of these studies was lacking and they do not provide robust economic data.

9.2 *Company de novo cost analysis*

The company reported developed an economic model using a cost consequence analysis (CCA) framework, which was appropriate and consistent with the Medical Technologies Evaluation Programme (MTEP) methodology (NICE, 2017). The model did not include any clinical outcomes, clinical states, PROMs, or HRQoL outputs. The model is described and critiqued in the following sections.

9.2.1 Economic model structure

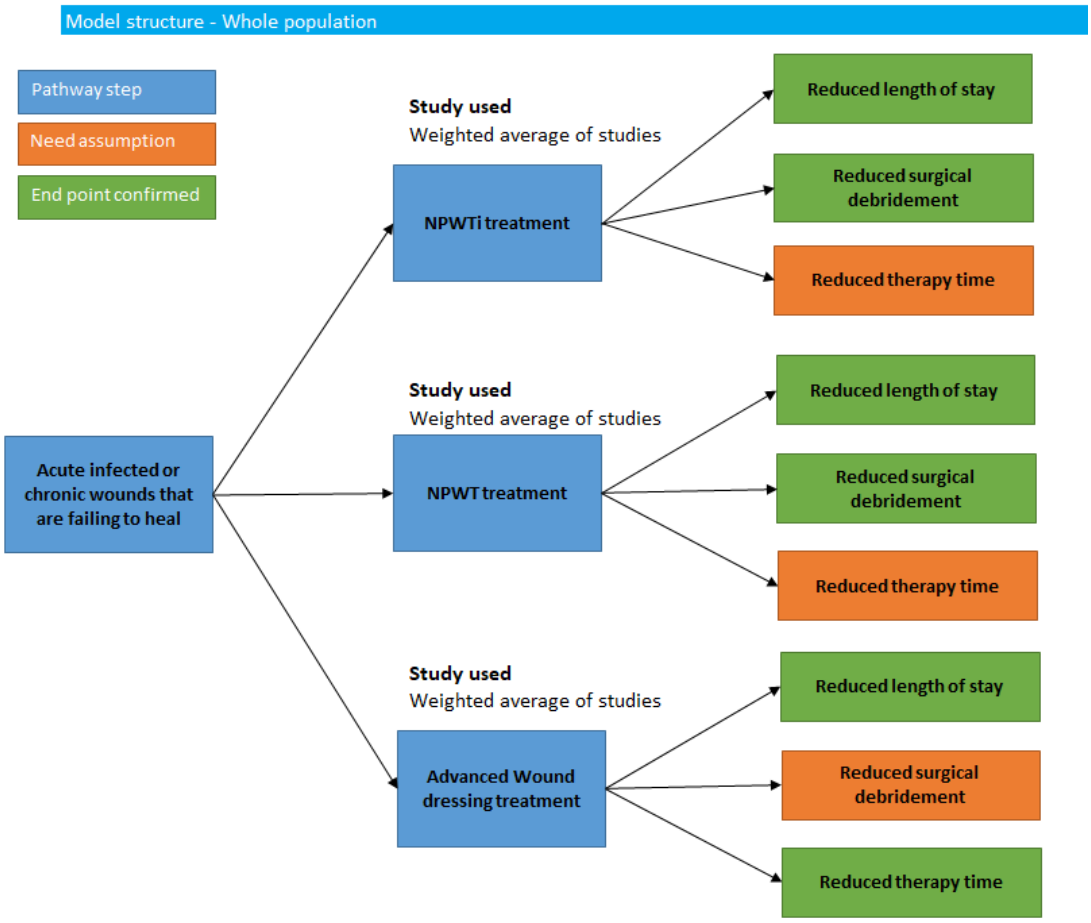
The model was a cost calculator, provided in an executable Excel spread sheet across 23 worksheets. The layout of the spread sheet was generally clear, although the spread sheet was not entirely transparent. For example, some input cells did not contribute to calculations or outputs, and the rationale behind some calculations was not always evident. A series of embedded Macros in the model were used to generate Tornado diagrams (univariate deterministic sensitivity analysis [DSA]) and run probabilistic sensitivity analysis (PSA).

The model incorporated four scenarios, namely that of lower limb; mixed wounds; prosthetic implant; and surgical site infections. Results from these scenarios were aggregated to give an overall cost estimate, which might be regarded as a *de facto* "base case" representing the whole population (this is an unusual method of establishing a base case, see Section 9.2.3).

The model estimated the costs associated with NPWTi compared with NPWT and advanced wound care (AWC). Three costs were accounted for in the model: therapy costs, the length of hospital stay, and the number of surgical debridements required during that stay. The model structure for the base case is reported in Figure 9.1.

The EAC questioned NICE clinical advisors regarding the structure of the model (EAC External correspondence log, 2020). In general, the advisors did not believe the pathways were representative of NHS practice for many patient groups. For instance, the model assumes that there is a requirement for surgical debridement following treatment, but this is often not the case, with patients being discharged and being treated using less intensive nurse-led forms of debridement in clinics.

Figure 9.1. *Structure of the de novo model. Note: The outcomes listed are not all "reduced". Reductions between treatment modalities are relative to each other.*



The company listed the assumptions in the model in Table 2 of the submission. The EAC has critiqued this in Table C1. In the opinion of the EAC, several of the assumptions made by the company could not be justified. The EAC considered there were two principal concerns with the model. These were issues with:

- Structural uncertainty, relating to the scope used in the model and how well this reflected clinical reality, in particular in terms of the population and patient pathways. These issues are further discussed in this section.

- Parameter uncertainty, relating to the clinical effectiveness data that were used to inform the model. This is further discussed in Section 9.2.3.

Population

The population was not clearly defined in the company's economic submission, so the population is assumed to be the same as the scope, namely "patients with acute infected or chronic wounds that are failing to heal" (NICE, 2020). The usual approach to economic analysis would be to use the broader population that is in scope as the base case, and perform scenario analysis to estimate costs in different subgroups. Instead, the company used a different approach, by developing separate scenarios for different subgroups of patients, and combining the data from these to estimate an aggregated total of costs, that it claimed reflected the whole population.

The EAC considered this approach was counter-intuitive and fundamentally unsound, for the following reasons:

- The scenario populations described in the model were lower limb; mixed wounds; prosthetic implant; and surgical site infections. These described mixed concepts and were not clearly defined. For instance, "lower limb" wound is an anatomical description, whereas "mixed wounds" implies it is based on aetiology (both acute and chronic) but this was not explained. Thus, the populations were not mutually exclusive and likely to overlap in an undefined way. Furthermore, these populations did not match the subgroups described in the scope, which were diabetic ulcers; pressure ulcers; surgical site infections; venous leg ulcers; and wounds containing prosthetic implants (NICE, 2020).

- Even though the scenario populations were envisioned to represent more clearly defined cohorts of patients, they still represented broad, heterogeneous cohorts of patients. For instance, there are many possible types of lower limb wounds. Mixed wounds by definition are a heterogeneous concept, and similarly prosthetic implants and surgical site infections include many types of wound and patient groups.

- The populations enrolled in the clinical studies that informed the scenarios did not reflect those of the scenario. Issues with study identification, extraction and extrapolation of key parameters, and the representativeness of key populations are discussed in Section 9.2.3.

- The company claimed that the data informing the whole population ("base case") was weighted. However, this was not the case. Instead the parameters were calculated using simple averages without weighting by study sample size or underlying population prevalence. Thus, even allowing for the limitations of the informing data, the EAC had additional concerns over the aggregated costs.

The EAC notes that one study reflected the population of the scope well. This was the RCT by Kim *et al.* (2020) which enrolled people with both acute (30%) and chronic (70%) wounds. However, this study was not included in the economic analysis. This omission is discussed further in Section 9.2.3. The EAC also notes the contention from the company that the mechanism of action of NPWTi is common to all indicated conditions, and therefore results from these populations may be reasonably aggregated (EAC External correspondence log, 2020). However, the EAC considered that a common mechanism of action would not necessarily mean the benefits would be equivalent in different populations; in fact, this would be highly unlikely. Therefore the EAC did not adopt this approach in its own analysis (see Section 9.2.7).

Intervention

As discussed in Section 1.2, the EAC excluded studies that did not specifically include NPWTi with the V.A.C. VERAFLO device. However, three of the seven studies that the company used to inform the economic model used the predecessor device (VAC Instill). For the purpose of economic modelling, the EAC accepted these studies. However, inclusion of these studies added an extra source of uncertainty into the model, and therefore the results reported (see Section 9.2.3).

Comparator

The EAC accepted clinical data for NPWT from any technology, although the costing used in the economic modelling was restricted to the VAC Ulta device. There was very little evidence on which to base analysis of AWC dressings, and the use of dressings is likely to be very variable depending on the underlying condition as well as on local practice within the NHS. Additionally, AWC may not be an appropriate comparator as NPWT and NPWTi may be used second-line to this in some scenarios (Section 1.3). This meant there was particular uncertainty regarding economic data comparing NPWTi with AWC. This was verified by NICE clinical experts, some of whom considered AWC would be used before or after NPWTi, but was not an appropriate direct comparator (EAC External correspondence log, 2020).

Outcomes

Three outcomes informed the relative costs of the technologies (NPWTi, NPWT, and AWC). These were the frequency of surgical debridement, length of hospital stay (LoS) and length of treatment (LoT).

Surgical debridement.

It was assumed that *post-treatment* surgical debridement would be required in all the scenarios. Reduced requirement for surgical debridement would result in reduced costs relative to the comparator technology. However, the model assumed that all repeat debridement procedures would be surgical, when in fact this is the most invasive option and may be regarded as a third-line option in many patients (see Section 3.2), with less invasive forms of debridement being carried out in community or day clinic settings. One NICE clinical expert stated "the NHS is not set-up to support repeated surgical debridement every 48hrs to negative microbiology, as has been used in trials described in this briefing. Therefore a trial comparing use to standard care within the NHS, including health economic evaluation, would be useful" (EAC External correspondence log, 2020).

Length of hospital stay

The major driver of cost savings in the model was reduction in length of hospital stay, in which it was assumed that there was a causal association between the wound treatment technology and length of hospital stay. However, there are several other factors that could be associated with LoS, such as the underlying condition, and the availability of the necessary social care to allow for discharge. The studies that reported on LoS were not experimental and thus could only infer, rather than prove, causal reductions in this outcome. Furthermore, the studies were all conducted in non-UK settings, and management and discharge pathways might not reflect those of the NHS.

The EAC explored the potential for NPWTi to reduce LoS with the NICE clinical experts (EAC External correspondence log, 2020). There was unanimous agreement that in certain patients and settings, NPWTi had the potential to reduce LoS and consequently reduce healthcare resource use and costs. However, there remained key uncertainties regarding this. One issue was that in the NHS, NPWTi must be performed as an inpatient procedure, meaning it could lead to paradoxical increases in LoS by preventing earlier discharge to community care. Additionally, LoS is frequently not solely related to wound care, but may also be dependent on the underlying condition, comorbidities, and the availability of suitable social care allowing for discharge. In all cases, this outcome is difficult to quantify due to the diverse nature of wounds, even in similarly indicated patients in the same setting. These issues were supported following dialogue with the principal investigator of the RCT (Kim *et al.*, 2020), who, referring to the non-significant difference in LoS between arms of the RCT, stated "[redacted]".

Length of treatment

Length of treatment with the technology was multiplied with the daily cost of that therapy (Section 9.2.4), to establish the overall cost of treatment. Clinical management costs outside this window and upon discharge were not considered. There were concerns about the generalisability of the data reported in the literature when applied to NHS settings.

Time horizon

The model was a cost calculation rather than decision tree, and as such did not have a set time horizon. Instead, costs were calculated based on the length of treatment and length of hospital stay; this was usually measured over the course of days or weeks, depending on the informing study (and therefore scenario). It was thus appropriate not to included discounting.

9.2.2 Validation of the economic model

Company validation

The company described its model validation procedure in the economic submission (page 62). Two modellers were employed to build the model, and the model parameters were reviewed externally by two sources:

- Two tissue viability nurses were used to "gather their view of the resource, the clinical and cost assumptions included [in the model". The names and details of the tissue viability nurses were not reported.

- Two company clinical experts, or Key opinion leaders (KoLs), consisting of a consultant plastic surgeon and a consultant vascular surgeon, were used to allow for the "opportunity to feedback on all elements of the model including resource, pathway, subgroup population levels and the current outputs". This included review of the cost data used as well as review of the informing studies. No formal elicitation process was used.

Given the nature of the uncertainty relating to the model, which related to both the model structure and inputs, the EAC considers the validation process was probably inadequate. Preferably, more KoLs should have been enrolled covering more specialities, particularly considering the broad nature of the intended population. Ideally, formal expert opinion for qualitative evidence (e.g. model structure) and expert elicitation techniques for quantitative (for estimation of model parameters) could have been used to improve the robustness of the model (Peel *et al.*, 2018). However, the EAC appreciates these approaches are difficult to undertake within the timeframe of MTEP assessment, and especially so in the case of this submission (March 2020, during covid 19 pandemic). Nevertheless, there remains a lack of confidence in the validity of the model (Section 9.2.1 and 9.2.3).

EAC validation

The EAC validated the company's base-case and scenario analysis by independently reproducing it in Excel. This highlighted errors in therapy cost associated with NPWTi and NPWT arms in Table 9 of the company's written economic submission where therapy costs of scenario analysis were included instead of base-case therapy cost (these errors were confirmed by the company) (EAC External correspondence log, 2020). Due to the small impact on results (the company submission stated therapy costs for the whole population as £914 and £662 for NPWTi and NPWT respectively, however these should have been £919 and £716), the company was not asked to update the narrative or table 9 of their report. The EAC also validated the

company's PSA by independently reproducing using programming language R (R Core team, 2020).

Due to concerns over the validity and generalisability of the model's inputs, the EAC asked specific questions from the NICE expert advisors regarding these. A full record of questions and responses can be found in the EAC communication log.

9.2.3 Economic model parameters

The key economic model parameters related to measurement of LoS, LoT, and number of surgical debridements for each technology. These were multiplied by unit costs estimated through micro-costing; these values are discussed in Section 9.2.4.

Study selection

The clinical parameters that informed the outcomes were derived from seven comparative studies identified in the clinical evidence section of the submission (Table 4.3). Four studies identified were not included to inform the economic analysis. The EAC noted the small RCT by Yang *et al.* (2017) did not report relevant clinical outcomes, and the larger RCT by Kim *et al.* (2015) did not report on a relevant comparison, and so could not contribute to the economic model. However, it was noted that the RCT by Kim *et al.* (2020) and the prospective observational study by Omar *et al.* (2016) did publish outcomes that were relevant to the model. The company did not report a rationale for the exclusion of these studies in the submission, but in dialogue with the EAC clarified that the study by Kim *et al.* (2020) was excluded because at the time it was not a published peer-reviewed paper (at that time), and additionally that LoS and duration of therapy were not reported for the whole cohort (EAC External correspondence log, 2020).

The key economic results for the omitted studies are reported in Table 9.1. Both studies reported that there was no statistical difference in the key results that could inform the economic model. As with all the studies identified for NPWTi, these studies had considerable limitations. Kim *et al.* (2020) had incomplete reporting of outcomes. Omar *et al.* (2016) was small (10 patients in each cohort) and was not an experimental study. However, both studies were in scope and were relatively well reported, and used appropriate statistical analysis, so in the opinion of the EAC should have been included. Their omission suggests that a degree of selective reporting of studies may have occurred. Both these studies have been included by the EAC in scenario analysis (Section 9.3.4).

Table 9.1. *Relevant economic outcomes reported in omitted studies.*

Outcome	Study	
	(Kim, 2020)	(Omar *et al.*, 2016)
Type	RCT, unpublished (NWTi vs. NPWT)	Prospective observational study with historical controls (NWTi vs. NPWT)
Population	Patients with chronic and acute wounds, mainly of the lower limb (n = 181)	Patients with acute wounds of the lower limb (infected or traumatic). (n = 20)
Length of hospital stay	Not reported *.	Median with (IQR) (days) NPWTi: 21.5 (15.5 to 32.0) NPWT: 26.5 (18.5 to 33.3) Wilcoxon rank-sum test (p = 0.43)
Length of treatment**	Mean (days) NPWTi: 6.8 NPWT: 6.3 Log-rank test (p = 0.71)	Median with (IQR) (days) NPWTi: 9.0 (7.0 to 19.3) NPWT: 12.5 (7.8 to 23.3) Wilcoxon rank-sum test (p = 0.36)
Number of debridements (or "surgeries)	Mean (95% CI) NPWTi: 1.1 (0.93 to 1.30) NPWT: 1.0 (0.85 to 1.1*) Wilcoxon rank-sum test (p = 0.68)	Median with (IQR) (days) NPWTi: 3.0 (2.0 to 4.3) NPWT: 3.0 (2.8 to 5.3) Wilcoxon rank-sum test (p = 0.65)

Abbreviations: IQR, inter-quartile range; NPWT, negative pressure wound therapy; NPWTi, negative pressure wound therapy with instillation; SD, statistical deviation.

*The EAC clarified with the lead author of the RCT that this outcome was measured, but not reported, and that the differences between arms (full cohorts) were non-significant. Subgroup analysis of patients with dehisced wounds (n = 23) reported mean LoS was 9.3 days in the NPWTi arm vs. 21.8 days in NPWT arm (p = 0.05).

** Data derived from "Proportion of patients with closed wounds and time to readiness for closure/coverage" (Kim *et al.*, 2020) and "Time to wound closure" (Omar et al, 2016).

Data extraction and parameter calculation (from included studies)

A description of the included studies that informed the economic parameters is reported in Table C2. The EAC had several concerns about these studies and how they were used to inform economic parameters. These were:

- The studies were retrospective observational studies with inherent methodological limitations, for instance concerning patient selection, small sample sizes, and low generalisability. There were particular issues with the selection of control groups and, in some studies, inappropriate statistical analysis. In summary, the EAC considered these studies did not demonstrate a causal association between the interventions and their reported outcomes with any certainty (Section 5.2.2).

- Some of the studies were considered to be out of scope by the EAC because they reported on the predecessor technology (Gabriel *et al.*, 2008, Jurkovic *et al.*, 2019, Timmers *et al.*, 2009). These have not been fully appraised by the EAC.

- Some studies did not enrol patients that were entirely consistent with the scenario described. For instance, the studies by Kim *et al.* (2014) and Gabriel *et al.* (2008), used to inform the "lower limb" scenario, enrolled patients trunk and arm wounds. In the case of other studies, there was insufficient information to determine whether the population was reflective of the described scenario, for instance Gabriel *et al.* (2014) in the "mixed wound" scenario. This scenario also utilised data from Timmers *et al.* (2009) which only enrolled patients with osteomyelitis and related tissue infections. In other instances, such as in the prosthetic implants scenario (Deleyto *et al.*, 2018) and the surgical site infection scenario (Jurkovic *et al.*, 2019, Chowdhry and Wilhelmi, 2019), the population enrolled in the studies was highly selective and did not necessarily represent the study population as a whole.

- Because not all the studies reported the three outcomes necessary to inform the model, the company combined data from two studies to estimate some model parameters. This was done by calculating the ratio between two parameters of interest (a scaling factor) and then applying this to a second study. The EAC considered this was inappropriate, because the studies were performed in different populations, and sometimes different comparators, and could not be directly compared. This data manipulation added a further layer of uncertainty that could not be adequately addressed using sensitivity analysis.

Summary

The EAC considers that an important weakness of the economic model is that the clinical parameters were not sufficiently robust and were subject to high levels of uncertainty. This was due to a combination of how the studies were selected; the quality of the studies selected; and the way data was extracted and manipulated from these studies.

9.2.4 Resource identification, measurement and valuation

Resource use (costs) in the model was broadly described in the company's economic submission and detailed costs were reported in the model itself. The following costs were included.

- Direct costs associated with the interventions themselves.
- Debridement costs associated with repeated surgical debridement following commencement of treatment.
- Hospital stay costs associated with excess bed stay in hospital before discharge.

Direct costs

The company derived direct costs from the NHS Supply Chain. Costs for NPWTi included average costs for dressings (V.A.C. VERAFLO™, V.A.C. VERAFLO CLEANSE™, and V.A.C. VERAFLO CLEANSE CHOICE™) in various sizes (small, medium, or large), as well as costs of the V.A.C. VERALINK™ Canister and V.A.C. VERALINK™ Cassette. In addition, a £16 daily rental charge associated with the V.A.C. Ulta NPWT device was included. The costs of instillation fluids (including normal saline, Prontosan, or Dakin's solution) were not included. The EAC checked these costs, and concluded that, due to the small cost of these relative to the total costs, it was acceptable to exclude these from the model. The EAC also identified from NHS Supply Chain potential costs associated with additional tubing (ELZ414: Negative Pressure Wound Therapy Accessories Duo tubing set for use with instillation unit), which may be used alongside V.A.C. VERAFLO, but does not appear in the economic model. The company confirmed that this product is used on some large wound dressings and certain types of wounds to support the increased fluid exchange. However it was clarified that it is rarely used in the UK and therefore was considered; the EAC accepted this (EAC External correspondence log, 2020).

Cost associated with NPWT (without instillation) were based on costs of unit rental (the V.A.C. Ulta device), NPWT canisters, and medium foam kit. Costs associated with AWC were based on Aquacel and Alleyvn dressings. All costs were verified by the EAC and, where found to be incorrect, they were updated or changed for the EAC's base case model (see Table C4). However, because these technology costs were low compared with the other costs in the model, further work on micro-costing of comparator technologies was not undertaken.

Debridement costs

All debridement were assumed to be surgical requiring theatre time (the EAC does not agree with this assumption, see Section 9.2.1). Theatre costs were based on Public Health Scotland average theatre costs per hour by speciality This is inclusive of staff, utility, and infrastructure costs (Public Health Scotland, 2019). There is no equivalent data for the NHS of England and Wales. The duration of debridement (17.7 minutes) was estimated using data from an RCT (n = 41) that compared Versajet Hydrosurgery System with conventional surgical debridement (Caputo *et al.*, 2008). This was multiplied by the theatre cost per minute (£13.37) to give a cost of £237 per surgical debridement. This cost was fixed regardless of the intervention.

The EAC revised the theatre costs, using the most up-to-date data averaged across all relevant specialities, which slightly increased the theatre cost to £16.46 per minute (Table C4). The duration of surgery time was not challenged. One NICE clinical expert considered that the surgical debridement cost was likely to be a substantial underestimate (EAC External correspondence log, 2020), and this reflected the general consensus of NICE clinical experts. Therefore, the cost of surgical debridement used in the model is likely to be conservative, but this is based on the premise this outcome is relevant to the NHS in most patient groups which the EAC considered is unlikely to be true (Section 9.2.1).

Length of stay costs

The estimated the unit costs of LoS using excess bed days as reported by NHS Reference Cost (2017/2018) (NHS Improvement, 2018). The company used subchapter healthcare resource groups (HRGs) for mixed wounds and prosthetic implants, whereas the other scenarios (lower limb and surgical site infections) used national average costs. The EAC considered that this approach wasn't justified given the paucity of data, and simplified the model by applying national average costs to all groups (Table C4).

Excess bed days are not an ideal surrogate measure of cost of hospital stay as they only cover bed, food, accommodation, utilities, and management costs. However, even within an HRG the complexity of patient clinical needs vary, as well as the availability of social care on discharge, as sometimes medically fit patients cannot be discharged due to delays in setting up support packages. Nevertheless, the cost applied (£431) was broadly consistent with other NICE MTGs utilising LoS as an economic outcome. It should be noted that because the costs associated with a day of LoS were roughly twice as costly as one surgical debridement procedure, and because LoS was significantly higher in comparator groups compared with NPWTi in most scenarios, this parameter was the main driver of the model.

9.2.6 Sensitivity analysis

Sensitivity analysis was applied by the company in several ways. Firstly, separate scenarios were reported on, which were combined in a bottom up manner to report an aggregated *de facto* base case. Secondly, extensive univariate deterministic sensitivity analysis (DSA) was performed to create Tornado diagrams, from which the key drivers of the model could be identified. And thirdly, probabilistic sensitivity analysis (PSA) was employed in an attempt to quantify the level of uncertainty between the model input and outputs (YHEC, 2016b).

Scenario analysis

The EAC had serious concerns regarding the combination of distinct and separate scenarios to inform the base case. These principal concern was the scenarios were poorly defined and that evidence from the informing studies was not sufficiently robust, and not generalisable, to inform the key parameters. These issues are discussed in Section 9.2.1 and 9.2.3.

Deterministic sensitivity analysis

For univariate sensitivity analysis, the company used the upper and lower bounds of the 95% confidence intervals (CIs) where these data were available, which was appropriate. Where these could not be calculated, the company assumed the standard error was 20%.The EAC considered this value was arbitrary unlikely to cover the feasible range of variability in poorly evidenced parameters, thus it did not usefully inform the degree of uncertainty in the model (Briggs *et al.*, 2012).

Probabilistic sensitivity analysis

One thousand runs of the model were performed by applying random draws to parameter distributions for each scenario and the base case scenario. Most of the model parameters were subject to PSA, using beta or gamma distributions as appropriate (listed in the economic submission, pages 49 to 52). The data from the PSA was used to report median probabilistic estimates of cost savings, as well as the probability NPWTi was cost saving in each scenario.

The EAC considered that whilst PSA can be a valuable tool in understanding second order (parameter) uncertainty, by reflecting the level of precision of point estimate, it does not address issues concerning the validity of the point estimate itself. It does not replace the application of evidence-based best practice, for instance seeking to incorporate all available evidence, rather than selectively picking single sources and using best-practice methods to avoid potential biases (Briggs *et al.*, 2012). Furthermore, PSA is not useful in

understanding the structural uncertainty or heterogeneity present in the model (Briggs *et al.*, 2006).

The EAC retained the PSA, primarily to report credibility intervals in the revised model. However, parameters which the EAC considered should be fixed, such as technology costs, were not included in the PSA (Section 9.2.7).

9.2.7 EAC changes to model

The EAC made two sets of changes to the model. Firstly, as the EAC did not accept the company's method of estimating key clinical parameters (primarily LoS and LoT) through combining data from very heterogeneous studies, the EAC instead only used data reported within a single study. This had two implications:

- The scenarios reported by the EAC are applicable to the population described in that study only. However, because of the observational nature of the informing studies, the generally small sample sizes, and the lack of generalisability to the NHS, these scenarios were still subject to very high levels of uncertainty.

- Not all studies reported all the informing parameters. In the absence of data, crude assumptions were made, namely that LoS was the same as LoT. This assumption disbenefits NPWTi, as the assumption in the model is that, whilst NPWTi is more costly than its comparators, it introduces savings by reducing LoS.

The EAC also included scenarios using data from two studies that were not included by the company. Of these, the study by Kim *et al.* (2020) was regarded the most robust and was the closest that could be considered a "base case". This was because this was a relatively high quality experimental study, it was conducted in a well-defined population (case mix of patients with acute and chronic wounds), and it was the largest study (n = 181). Data from the small observational study by Omar *et al.* (2016), which reported on patients with acute wounds of the lower limb (n = 20) was also included. The revised parameter estimates are list in Table C3a (versus NPWT) and Table C3b (versus AWC).

Secondly, the EAC modified some of the inputs concerning resource use and rounding techniques. This was to improve the accuracy and internal consistency of the model. Additional procedural costs that the company included for "prosthetic implant subgroup" (simple wound closure, debridement and closure, mesh removal, mesh replacement), from data reported in the Deleyto study (2018) were also excluded. This was because, in the opinion of the EAC, the data reported in this study, and the application of costs through HRG codes, were not sufficiently robust to support these assumptions. These changes are reported in Table C4.

9.3 *Results from the economic modelling*

9.3.1 Company's base case results

The company's base case results were reported in Table 9 of the company's submission. The EAC independently reproduced the company base case and cross-referenced results reported in the submission which highlighted errors in the tabulated results of the NPWT comparison included company's written submission (these errors were confirmed by the company). The corrected results are reported in Table 9.2a (NPWTi vs. NPWT) and 9.2b (NPWTi vs. AWC).

Table 9.2a. *Corrected base case results of company's economic analysis for comparison of NPWTi and NPWT.*

	NPWTi	NPWT	Mean cost saving per patient
Length of stay	£5,741	£8,880	-£3139
Therapy	£919	£716	£203
Debridement	£505	£820	-£316
Total	£7,165	£10,416	**-£3,251**

Table 9.2b. *Base case results of company's economic analysis for comparison of NPWTi and AWC.*

	NPWTi	AWC	Mean cost saving per patient
Length of stay	£12,309	£20,623	-£8,314
Therapy	£1,136	£149	£986
Debridement	£534	£1,519	-£984
Total	£13,979	£22,291	**-£8,312**

The key results of the company's base case analysis, based on aggregated data from 3 studies (NPWT) or 4 studies (AWC) indicated that NPWTi incurred additional treatment costs compared with both comparators, but these were outweighed by cost savings associated with reduced LoS and requirement for surgical debridement.

9.3.2 EAC's base case results

The EAC's base case results are reported in Table 9.3. Restricting the analysis to the data reported by Kim (2020), NPWTi was found to be cost-expending compared to NPWT in the three cost domains, with an overall cost of £480. The EAC did not consider there was data of sufficient quality to

inform a base case cost analysis of NPWTi versus AWC. This was also considered to be a less suitable comparator (see Section 1.3).

Table 9.3. *EAC base case results of company's economic analysis for comparison of NPWTi and NPWT.*

	NPWTi	NPWT	Mean cost saving per patient
Length of stay	£2555	£2386	£169
Therapy	£526	£258	£268
Debridement	£260	£237	£23
Total	£3342	£2862	**£480**

9.3.2 Sensitivity analysis results

The company reported results from the individual disaggregated scenarios. These are reported in Table 9.4a (NPWTi vs. NPWT) and 9.4b. (NPWT vs. AWC). As can be seen, NPWTi was found to be cost-saving in all these scenarios, with cost-savings ranging from £300 (Jurkovic *et al.*, 2019) to £13,403 (Timmers *et al.*, 2009).

Table 9.4a. *Results of scenarios comparing NPWTi with NPWT.*

Subgroup (study used for clinical parameters)	**NPWTi**	**NPWT**	**Mean cost saving per patient**
Lower Limb (Kim 2014)	£6,427	£7,657	-£1,230
Mixed Wounds (Gabriel 2014)	£3,890	£12,113	-£8,223
Surgical Site infection (Jurkovic 2019)	£11,179	£11,479	-£300

Table 9.4b. *Results of scenarios comparing NPWTi with AWC.*

Subgroup (study used for clinical parameters)	**NPWTi**	**AWC**	**Mean cost saving per patient**
Lower Limb (Gabriel 2008)	£7,915	£18,934	-£11,018
Mixed Wounds (Timmers 2009)	£15,478	£28,880	-£13,403
Prosthetic Implant (Deleyto 2018)	£29,234	£36,957	-£7,723
Surgical Site infection (Chowdry 2019)	£3,289	£4,394	-£1,105

The company also performed extensive one-way DSA. In general, the model was not sensitive to these analyses (that is, varying individual parameters did not change the direction of results). In all cases, the model was most sensitive to parameter or cost changes in LoS. In the case of the surgical site infection scenario, applying changes to these did change the direction of results (versus NPWT).

The company performed PSA on the base case results and all the scenarios, which the EAC replicates. In the base case, the company reported 100% of simulations found that NPWTi was cost saving compared with NPWT or AWC. Probabilistic sensitivity analysis was also employed in the contributing scenarios, with all reporting ≥ 94% probability of NPWTi being cost saving,

with the exception of the surgical site infection scenario (informed by Jurkovic *et al.*, 2008), where 58% of simulations reported cost savings in favour of NPWTi.

The EAC considered that although the DSA and PSA performed by the company were extensive, it did not address the underlying structural and parameter uncertainties present (Section 9.2.6).

9.3.4 EAC sensitivity analysis

A comparison of the differences in cost savings estimated by the company and the EAC is reported in Table C5a and C5b. The parameter and resource use changes introduced by the EAC did not greatly affect the results of NPWTi compared with NPWT (ranging from -£76 to £225). There were greater differences in the estimates when NPWTi was compared with AWC (range -£25 to £4673). The larger difference in the Deleyto estimate was largely due to stripping several assumptions out of this scenario (Section 9.2.7).

The EAC has reported the economic results from its scenarios, with a breakdown in costs, in Table 9.5. Using scenario analysis, other than the base case analysis (using data from Kim 2020, resulting in a £480 cost expenditure for NPWTi), all the recalculated scenarios reported cost-savings associated with NPWTi. Costs saving were predominantly due to savings in LoS, which accounted for 70% to 95% of the reductions in cost. Conversely, technology costs and costs associated with repeat debridement were relatively low. It is notable in the model that the cost of an overnight stay (average cost £407) was almost double the cost of a surgical debridement (£237), and there were more excess overnight stays than excess debridement procedures.

The EAC performed adjusted PSA on the data at a scenario level (Section 9.2.6). The EAC reported the results as 95% credibility intervals (95% CrI). These are broadly synonymous with confidence intervals, and predict the probability the true cost values will fall within the range (95%) (YHEC, 2016a). These results of this analysis are reported in Table 9.6. The results show that, using the company analysis, 4/7 scenarios reported that NPWTi resulted in significant cost savings; whereas in 3/7 scenarios there was uncertainty because the 95% CrI range crossed zero. In the revised EAC estimate, 3/9 scenarios, based solely on the populations reported by the informing studies, indicated cost saving associated with NPWTi were highly likely, whereas there was considerable uncertainty in 6/9 scenarios.

However, the EAC considered that PSA did not address the fundamental limitation and uncertainties of the economic model (see Section 9.2.6).

Table 9.5: *Breakdown of total costs for intervention and comparator arms for each modelled scenario: length of therapy (LOT), length of stay (LOS) and number of debridements (nOR).*

		Intervention (NPWTi)				Comparator (NPWT/AWC)				
	Study	LoS (%)	LoT (%)	nOR (%)	**Total costs**	LoS (%)	LoT (%)	nOR (%)	**Total costs**	**Δ costs**
NPWT	Kim 2020*	£2555 (76%)	£526 (16%)	£260 (8 %)	**£3342**	£2367 (83%)	£258 (9%)	£237 (8%)	**£2862**	**-£480**
	Kim 2014	£5129 (76%)	£1020 (15%)	£568 (9%)	**£6717**	£6431 (83%)	£581 (8%)	£710 (9%)	**£7722**	**£1,005**
	Gabriel 2014	£3044 (79%)	£356 (9%)	£473 (12%)	**£3873**	£10,297 (85%)	£775 (6%)	£1041 (9%)	**£12,113**	**£8,240**
	Jurkovic 2019	£9051 (82%)	£1578 (14%)	£473 (4%)	**£11,103**	£9913 (86%)	£856 (7%)	£710 (6%)	**£11,479**	**£376**
	Omar 2016	£9267 (87%)	£696 (7%)	£710 (7%)	**£10,673**	£11,422 (90%)	£501 (4%)	£710 (6%)	**£12,632**	**£1,959**
AWC	Gabriel 2008	£6323 (88%)	£850 (12%)	£0 (0%)	**£7173**	£16,895 (99%)	£173 (1%)	£0 (0%)	**£17,068**	**£9,895**
	Timmers 2009	£13,528 (80%)	£2785 (17%)	£544 (3%)	**£16,857**	£27,433 (97%)	£347 (1%)	£568 (2%)	**£28,347**	**£11,490**
	Deleyto 2018	£27,057 (83%)	£5261 (16%)	£106 (0%)	**£32,424**	£34,545 (97%)	£419 (1%)	£510 (1%)	**£35,474**	**£3,050**
	Chowdry 2019	£2327 (71%)	£510 (16%)	£426 (13%)	**£3263**	£3620 (82%)	£40 (1%)	£734 (17%)	**£4394**	**£1,131**

Abbreviations: AWC, advanced wound care; LoS, length of stay; LoT, length of treatment; nOR, number of debridements; NPWT, negative pressure wound therapy; NPWTi, negative pressure wound therapy with instillation.

Table 9.6 *Company and EAC PSA applied to all scenarios.*

	Study	**Company estimate**	**EAC estimate**	**EAC estimate (PSA changes applied)***
		Median cost (NPWTi-comparator) [95% CrI]	**Median cost (NPWTi-comparator) [95% CrI]**	**Median cost (NPWT-comparator) [95% CrI]**
Vs. NPWT	Kim 2020	N/A	£491 [-£1037, £2031]	£471 [-£1085, £2015]
	Kim 2014	-£795 [-£2041, £209]	-£1011 [-£2831, £557]	-£1079 [-£2907, £567]
	Gabriel 2014	-£7968 [-£14,293, -£3966]	-£7759 [-£14,252, -£3775]	-£7960 [-£14,125, -£3887]
	Jurkovic 2019†	-£219 [-£3664, £2631]	-£269 [-£3521, £2644]	-£359 [-£3468, £2809]
	Omar 2016	N/A	-£1905 [-£7793, £3494]	-£1821 [-£8659, £3749]
Vs. AWC	Gabriel 2008†	-£7669 [-£12,527, -£4317]	-£9751 [-£15,497, -£5226]	-£9670 [-£15,501, -£5102]
	Timmers 2009†	-£12,845 [-£23,309, -£6370]	-£10,939 [-£28,000, £1070]	-£10,844 [-£26,046, £176]
	Deleyto 2018	-£8112 [-£17,678, £1838]	-£2918 [-£18,536, £11,407]	-£2731 [-£18,761, £9,431]
	Chowdry 2019	£1103 [-£2178, -£195]	-£1066 [-£2327, -£202]	-£1083 [-£2291, -£310]

Abbreviations: AWC, advanced wound care; CrI, credibility interval; NPWT, negative pressure wound therapy; NPWTi, negative pressure wound therapy with instillation.
Key: Green means costs do not cross zero, NPWTi is cost-saving. Amber means costs cross zero, there is increased uncertainty on whether NPWTi is cost-saving.
* EAC removed PSA in parameters it considered were fixed (dressing and V.A.C. VERAFLO daily rental costs).
† Studies excluded in the EAC clinical assessment.

9.4 *The EAC's interpretation of the economic evidence*

Four published economic studies were identified that were considered to be in scope. However, these were based on data from small retrospective studies of limited methodological quality, and were not considered to be generalisable to the UK NHS.

The company submitted a *de novo* model set in the NHS of England and Wales. This was a costing model that was conceptually simple, comparing NPWTi with NPWT alone or AWC. There were three outcomes in the model that determined overall costs; these were LoS, which reported costs incurred through bed usage; LoT, which reported direct costs associated with each technology; and debridement costs, which was a cost associated with the requirement for assumed repeat surgical debridement. The model was informed from mainly retrospective studies of low methodological quality identified through the clinical literature search, including studies that had been excluded by the EAC, and not including two studies that the EAC considered were relevant. Input from clinical experts was minimal. The company performed extensive sensitivity analysis, which included scenario (or subgroup) analysis, DSA, and PSA. The base case was reported by aggregating data from the informing scenarios ("lower limb", "mixed wound", "prosthetic implant" and "surgical infection").

The company reported that in the base case NPWTi was cost saving by £3,251 compared with NPWT, and by £8,312 compared with AWC. The principal driver of the cost savings was the reduction in LoS, as shown by DSA. The company reported that NPWTi was cost-saving in all scenarios and in most of these PSA indicated the probability of NPWTi being cost saving was ≥ 94%.

The EAC had significant reservations concerning the *de novo* model. Firstly, the company's study selection was unsatisfactory. The selected studies did not match the scenarios described, and two studies that reported equivocal outcomes were not included. Secondly, the EAC considered the quality of the studies was insufficient to establish causality between the intervention and the reported outcomes. This was exacerbated by the company transforming data from one study using data from another unrelated study. Thirdly, the informing studies were based on heterogeneous case mixes of patients that could not be generalised to an NHS population; furthermore the applicability of patient pathways, in particular use of repeated surgical debridement, was unclear. And fourthly, the method of reporting the base case results was unsatisfactory, as it was not directly based on appropriate empirical data and was not accordingly weighted to reflect this. The EAC also considered that the scale of the structural and parameter uncertainty in the model meant that sensitivity analyses were uninformative.

The EAC replicated the company's *de novo* model and made some modifications, in an attempt to improve accuracy and consistency. The main alteration was to use data from the RCT by Kim *et al.* (2020), which the EAC considered was the most robust evidence available. The main limitation to this analysis was that the RCT did not report LoS, so this was assumed to be the same as LoT. Using these assumptions, NPWTi was found to be cost-incurring by £480 using deterministic analysis. However, there was considerable uncertainty in this result, with PSA from the EAC indicating an average cost expenditure of £471 (95% CrI -£1085 to £2015). Thus the cost saving potential of NPWTi was considered to be uncertain.

10 Conclusions

10.1 *Conclusions from the clinical evidence*

The company performed a literature search which identified 32 studies they considered were in scope, including one conference abstract and an unpublished study that was academic in confidence and now fully published (Kim *et al.*, 2020). The EAC repeated the search and identified 19 studies that were considered to be in scope. The principal reason the EAC excluded the company's studies was due to the intervention not being in scope (either the predecessor technology or NPWTi from a different company).

Nine studies were comparative, and of these, 3 were RCTs (combined n = 303), and 6 were observational (combined n = 302). Ten were single-armed (combined n = 373). The EAC considered the RCT by Kim *et al.* (2020) was the most relevant and robust of the identified studies. This study randomised patients with acute or chronic wounds of various aetiologies (n = 181) to receive either NPWTi or NPWT. The authors reported that NPWTi was associated with significant reductions in bacterial bioburden. This is a surrogate outcome not directly related to clinical endpoints. The study did not report significant differences in the primary outcome, the frequency of surgical debridement, or any of the other secondary outcomes. Length of hospital stay for the whole cohort was not reported [redacted].

The other comparative studies were generally retrospective observational studies. Issues common to many of these studies included poorly reported patient selection; small sample sizes; use of historical control groups without adequate description of how these were selected; lack of sufficient matching of cohorts, including a lack of statistical matching techniques; and a lack of confidence in how endpoints were measured, recorded and reported. Taking these issues together, the EAC concluded that a unequivocal association between the intervention and outcomes had not been satisfactorily demonstrated. Uncertainty in the patient pathways and the heterogeneous case mix of patients included in the studies meant it was not possible to generalise data to the NHS (none of the studies were conducted in the UK). None of the studies reported PROMS or HRQoL data necessary to understand the impact of the technology from a patient perspective. Additionally, there is a lack of evidence in general regarding the benefits of NPWT compared with other treatment modalities (Section 3.3). The single-armed studies reported on patient characteristics and some procedural measurements, but otherwise did not inform the decision problem.

Thus the EAC concluded that there was insufficient evidence from the published evidence base on which to inform clinical recommendations on the benefits of NPWTi. However, the caveat to this is that a lack of evidence is not the same as evidence of no effect. The EAC noted the technology had plausible system benefits over precursor technologies. Additionally, it was noted that NICE clinical experts were supportive of the technology, and unanimously believed it had clinical benefits in appropriately selected patients (EAC External correspondence log, 2020). Further research is therefore required to establish the place of VAC VERAFLO in the NHS.

10.2 *Conclusions from the economic evidence*

Current economic evidence in the published literature base was not directly relevant to the decision problem. The company constructed a *de novo* economic model which focussed on the potential for NPWTi to reduce healthcare costs, by reducing LoS, LoT, and reducing the requirement for repeat surgical debridement. It estimated cost savings of around £3,300 (compared NPWT) to £8,300 (compared with AWC) could be made if NPWTi was used in the average, indicated patient.

The EAC did not consider the economic analysis was representative of NHS practice. This was for two fundamental reasons. Firstly, because there was a lack of confidence in the informing clinical data. In the opinion of the EAC the studies selected for use in the model did not demonstrate a causal relationship between the use of NPWTi and improved clinical outcomes. It was noted that the one informative RCT (Kim *et al.*, 2020) did not replicate the benefits reported in the observational studies selected. Secondly, the heterogeneous case mix of the populations used to inform the model, in combination with doubts about the appropriateness of the clinical pathways described, meant that the economic results could not be clearly generalised to the NHS of the UK.

The EAC reran the model using finessed assumptions and parameters, most notably the use of the Kim *et al*. (2020) RCT as the base case scenario. Using PSA, it was found that NPWTi was potentially cost-incurring by £471 (95% CrI -£1085 to £2015); thus there was material uncertainty in the direction of results. However, this analysis was subject to much of the same limitations as the company's analysis. In conclusion, the EAC did not consider there was adequate clinical evidence to inform meaningful economic analysis and the cost-saving potential of NPTWi remains unknown.

11 Summary of the combined clinical and economic sections

The clinical evidence to inform the effectiveness of NPWTi using the VAC VERAFLO system is limited in terms of quality. Nineteen studies were identified by the EAC, nine of which were comparative observational studies or RCTs. Whilst most of these published studies reported positive outcomes, firm conclusions could not be made because they were of low methodological quality. Limitations included the retrospective nature of the research, poor reporting, and lack of generalisability to the NHS. One recently published RCT did not report significant clinical benefits of NPWTi compared with NPWT.

The company developed a *de novo* economic model that reported large cost savings associated with NPWTi, principally through the reduction in hospital LoS, allowing earlier discharge into the community. However, in the opinion of the EAC, the informing clinical evidence was not sufficiently robust to give confidence in these findings. In the future, improved economic analysis will be dependent on data generated from better-quality clinical research.

12 Implications for research

Further clinical research into the safety and effectiveness of NPWTi using VAC VERAFLO would be beneficial in establishing its place in therapy. Ideally, experimental research in the form of an RCT would be most informative. The study population should consist of a definable cohort (for example pressure ulcers or diabetic foot ulcers). Inclusion and exclusion criteria should be clearly stated. It should be adequately powered using a primary outcome which is clinically important, and preferably it should also report PROMs or HRQoL outcomes.

It is recognised that RCTs are difficult, time-consuming and expensive to design and implement. If for these reasons observational research was preferred, this should be undertaken to a high standard of quality. If possible, such research should be publically registered, prospective, have a large sample size, and include statistical matching techniques to minimise the effects of confounding and bias. Once a clinical effect has been established through high-quality research, it may be possible to reasonably extrapolate this to other patient groups, and to validate this with additional observational research.

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14 Appendices

Appendix A - Literature searching methodology

Appendix B – Critical appraisal of clinical studies

Appendix C – Economic assumptions and additional results

Appendix D – Economic literature search

Appendix A: Literature searching methodology

Search strategy

The search strategy was designed to identify evidence related to the V.A.C. Veraflo™ therapy system. A search strategy developed by the company was submitted as below:

The following strategy was used to perform a literature search in PubMed, EMBASE and QUOSA.

("Lavage" OR "instil" OR "instillation" OR "irrigated" OR "irrigation" OR "topical solution" OR "topical wound solution" OR "topic solution" OR "VERAFLO" OR "VERAFLOW" OR "Veraflo dressing" OR "Veraflo cleanse dressing" OR "Veraflo cleanse choice dressing" OR "Ulta") AND ("Negative Pressure Wound Therapy" OR "NPWT" OR "vacuum assisted closure" OR "vacuum sealing" OR "NPWTi" OR "NPWTi-d")

This strategy was critiqued using the PRESS (Peer Review of Electronic Search Strategies) tool as shown below:

Question	Y/N	Notes
Translation of the research question		
Does the search strategy match the research question/PICO?	Query	The strategy focusses on the intervention only, but this may be appropriate as this may retrieve only a small number of results, as it is very specific.
Are the search concepts clear?	Query	The 2 concepts appear to be: Topical interventions AND negative pressure wound therapy
Are there too many or too few PICO elements included?	Query	See above
Are the search concepts too narrow or too broad?	Okay	

Does the search retrieve too many or too few records? (Please show number of hits per line.)	Okay	
Are unconventional or complex strategies explained?	N/A	
Boolean and proximity operators (these vary based on search service)		
Are Boolean or proximity operators used correctly?	Yes	
Is the use of nesting with brackets appropriate and effective for the search?	N/A	
If NOT is used, is this likely to result in any unintended exclusions?	N/A	
Could precision be improved by using proximity operators (e.g., adjacent, near, within) or phrase searching instead of AND?	Query	Possibly, I will test this when I develop the search strategy further
Is the width of proximity operators suitable (e.g., might adj5 pick up more variants than adj2)?	N/A	
Subject headings (database specific)		
Are the subject headings relevant?	Query	It appears that no MeSH headings have been used
Are any relevant subject headings missing; for example, previous index terms?	Query	I will investigate if there are any appropriate MeSH headings
Are any subject headings too broad or too narrow?	N/A	
Are subject headings exploded where necessary and vice versa?	N/A	

Are major headings (“starring” or restrict to focus) used? If so, is there adequate justification?	N/A	
Are subheadings missing?	N/A	
Are subheadings attached to subject headings? (Floating subheadings may be preferred.)	N/A	
Are floating subheadings relevant and used appropriately?	N/A	
Are both subject headings and terms in free text (see the following) used for each concept?	N/A	
Text word searching (free text)		
Does the search include all spelling variants in free text (e.g., UK vs. US spelling)?	N/A	I can’t see any terms that would have an alternative spelling.
Does the search include all synonyms or antonyms (e.g., opposites)?	Query	I will check this when I develop the search strategy
Does the search capture relevant truncation (i.e., is truncation at the correct place)?	Query	No truncation has been used, though this may be appropriate e.g. instil*
Is the truncation too broad or too narrow?	N/A	
Are acronyms or abbreviations used appropriately? Do they capture irrelevant material? Are the full terms also included?	Query	Most acronyms appear appropriate, I’m not sure if “Ulta” is an acronym or a spelling mistake (I think this may be a type of veraflo technology)
Are the keywords specific enough or too broad? Are too many or too few keywords used? Are stop words used?	Query	I will review this using some of the known papers provided

Have the appropriate fields been searched; for example, is the choice of the text word fields (.tw.) or all fields (.af.) appropriate? Are there any other fields to be included or excluded (database specific)?	Query	It is not clear which fields have been searched
Should any long strings be broken into several shorter search statements?	No	
Spelling, syntax, and line numbers		
Are there any spelling errors?	Query	See comment above re “ulta”
Are there any errors in system syntax; for example, the use of a truncation symbol from a different search interface?	No	No syntax has been used
Are there incorrect line combinations or orphan lines (i.e., lines that are not referred to in the final summation that could indicate an error in an AND or OR statement)?	No	
Limits and filters		
Are all limits and filters used appropriately and are they relevant given the research question?	Query	A date restriction of January 2005 has been applied, but no justification is given for this
Are all limits and filters used appropriately and are they relevant for the database?	Query	It is not obvious how the date restriction was applied in each database
Are any potentially helpful limits or filters missing? Are the limits or filters too broad or too narrow? Can any limits or filters be added or taken away?	Query	An animal/human limit could be applied, though preclinical trials are included. Certain publication types could be excluded according to the exclusion criteria.

Are sources cited for the filters used?	N/A	
Further comments:		
Limited databases used – PubMed, Embase and QUOSA (I think this may be an internal database of articles within the company). I would certainly add in CINAHL as this is a wound management device, which is likely to match relevant literature in a nursing database. The inclusion/exclusion criteria are contradictory – conference abstracts are included in both lists A number of the included papers refer to other companies' products, not the VAC Veraflo		

The concepts of the search were identified as:

(Instillation/irrigation AND Negative Pressure Wound therapy) OR (veraflo OR ulta)

Terms relating to the population were not necessary, as the intervention is specific to those with wounds.

The search strategy was developed in MEDLINE and tested using papers that had been previously identified by the company.

The company strategy did not include subject headings so these were identified and added as appropriate. The final strategy comprised a combination of subject headings and free text searching using the title, abstract and keyword fields.

Non-English language publications were excluded from the results, and the search was restricted to publications from 2011 onwards to coincide with the introduction of the V.A.C. Veraflo™ therapy system.

The MEDLINE strategy was translated as appropriate into other relevant databases:

- Embase (OVID) 1996 – 2020 March 19

- CINAHL (EBSCO) 1981 – March 2020
- Cochrane Database of Systematic Reviews (Cochrane Library, Wiley)
- Cochrane Central Register of Controlled Trials (Cochrane Library, Wiley)

The search dates, search strategies and retrieved record numbers for each of the database searches are presented below (A1 to A4).

In total 983 records were retrieved across all databases, following deduplication 606 unique records remained.

A.1: Source: MEDLINE Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Daily and Versions(R) 1946 to February 17, 2020.

Interface/URL: OvidSP
Database coverage dates: 1946 to present
Search date: 20/03/20
Retrieved records: 305
Search strategy:

1 Therapeutic Irrigation/

2 lavage.ti,ab,kw,kf.

3 Instillation, Drug/

4 instillation.ti,ab,kw,kf.

5 irrigation.ti,ab,kw,kf.

6 Administration, Topical/

7 (topic* adj2 solution*).ti,ab,kw,kf.

8 or/1-7

9 veraflo*.ti,ab,kw,kf.

10 ulta*2.ti,ab,kw,kf.

11 9 or 10

12 Negative-Pressure Wound Therapy/

13 "negative pressure wound therapy".ti,ab,kw,kf.

14 NPWT*.ti,ab,kw,kf.

15 "vacuum assisted closure".ti,ab,kw,kf.

16 "vacuum sealing".ti,ab,kw,kf.

17 or/12-16

18 8 and 17

19 11 or 18

20 limit 19 to (english language and yr="2011 -Current")

A.2: Source: Ovid Embase 1974 to 2020 March 19.

Interface/URL: OvidSP
Database coverage dates: 1996 to present
Search date: 20/03/20
Retrieved records: 397
Search strategy:

1 lavage/

2 lavage.ti,ab,kw.

3 drug instillation/

4 instillation.ti,ab,kw.

5 irrigation.ti,ab,kw.

6 topical drug administration/

7 (topic* adj2 solution*).ti,ab,kw.

8 or/1-7

9 veraflo*.ti,ab,kw.

10 ulta*2.ti,ab,kw.

11 9 or 10

12 vacuum assisted closure/

13 "negative pressure wound therapy".ti,ab,kw.

14 NPWT*.ti,ab,kw.

15 "vacuum assisted closure".ti,ab,kw.

16 "vacuum sealing".ti,ab,kw.

17 or/12-16

18 8 and 17

19 11 or 18

20 limit 19 to (english language and yr="2011 -Current")

A.3: Source: CINAHL®

Interface/URL: EBSCOhost Web
Database coverage dates: 1981 to present
Search date: 20/03/20
Retrieved records: 221
Search strategy:

S20 S16 OR S18 Limiters - Published Date: 20110101-20201231; Narrow by Language: - english

S19 S16 OR S18

S18 S8 AND S17

S17 S11 OR S12 OR S13 OR S14 OR S15

S16 S9 OR S10

S15 TI "vacuum sealing" or AB "vacuum sealing"

S14 TI "vacuum assisted closure" or AB "vacuum assisted closure"

S13 TI NPWT* or AB NPWT*

S12 TI "Negative Pressure Wound Therapy" or AB "Negative Pressure Wound Therapy"

S11 (MH "Negative Pressure Wound Therapy")

S10 TI ulta* or AB ulta*

S9 TI veraflo* or AB veraflo*

S8 S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7

S7 TI (topic* N2 solution*) or AB (topic* N2 solution*)

S6 (MH "Administration, Topical")

S5 TI irrigation or AB irrigation

S4 TI instillation or AB instillation

S3 (MH "Instillation, Drug")

S2 TI lavage or AB lavage

S1 (MH "Therapeutic Irrigation")

A.4: Source: Cochrane Database of Systematic Reviews (CDSR) and Cochrane Central Register of Controlled Trials (CENTRAL)

Interface/URL: Cochrane Library, Wiley
Database coverage dates: 1996 to present
Search date: 20/03/20
Retrieved records:
CDSR: 0
CENTRAL: 60
Search strategy:

#1 MeSH descriptor: [Therapeutic Irrigation] this term only

#2 (lavage):ti,ab,kw

#3 MeSH descriptor: [Instillation, Drug] this term only

#4 (instillation):ti,ab,kw

#5 (irrigation):ti,ab,kw

#6 MeSH descriptor: [Administration, Topical] this term only

#7 ((topic* near/2 solution*)):ti,ab,kw

#8 (Mahmoudiasl *et al.*-#7)

#9 (veraflo*):ti,ab,kw

#10 (ulta*):ti,ab,kw

#11 MeSH descriptor: [Negative-Pressure Wound Therapy] this term only

#12 ("negative pressure wound therapy"):ti,ab,kw

#13 (NPWT*):ti,ab,kw

#14 ("vacuum assisted closure"):ti,ab,kw

#15 ("vacuum sealing"):ti,ab,kw

#16 (Mahmoudiasl *et al.*-#15)

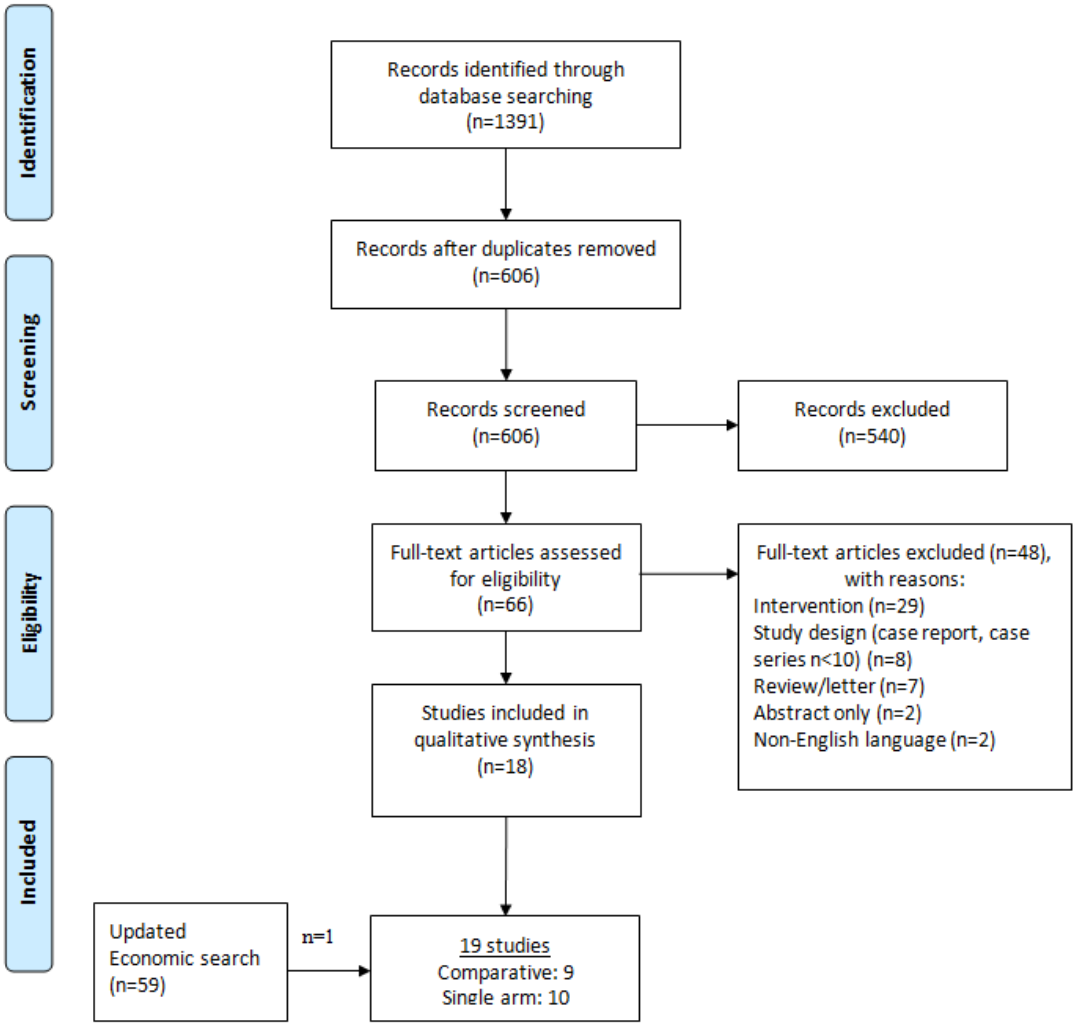
#17 #8 and #16

#18 #17 or #9 or #10

References:

McGowan, J., Sampson, M., Salzwedel, D.M., Cogo, E., Foerster, V. and Lefebvre, C., 2016. PRESS peer review of electronic search strategies: 2015 guideline statement. Journal of clinical epidemiology, 75, pp.40-46.

Figure A1. *PRISMA diagram illustrating literature search.*



Appendix B: Critical appraisal of clinical studies

Table *B1 Critical appraisal of (Kim et al., 2020)*

Bias domain	Source of bias	Support for Judgement	Review authors' judgement (assess as low, unclear, or high risk of bias)
Selection bias	Random sequence generation	Permuted block randomisation. . "Stratified randomization by investigative site was used. For each investigative site (stratum), permuted blocks were used to achieve equal numbers of Subjects assigned to NPWTi-d and NPWT to generate a randomization schedule".	Low risk of bias
	Allocation concealment	Allocation through sealed envelopes: "Envelopes were prepared corresponding to each row in the randomization schedule. Opening of the randomization envelope occurred intraoperatively at the conclusion of the initial surgical debridement of the wound and after confirmation that patient met inclusion and no exclusion criteria"	Low risk of bias
Performance bias	Blinding of participants and personnel*	No blinding of participants or treating personnel attempted.	High risk of bias
Detection bias	Blinding of outcome assessment*	No blinding of assessors or analysts used. Some subjectivity possible in measurement of the outcomes.	High risk of bias
Attrition bias	Incomplete outcome data*	CONSORT statement provided, with reasons for loss to follow up described. Substantial attrition reported (70% in NPWTi arm, 73% in NPWT arm at follow up). Inconsistent reporting of ITT and PP analysis.	High risk of bias
Reporting bias	Selective reporting	Study protocol published (NCT01867580), 1 primary and 1 secondary outcome reported (compared with 5 secondary in draft manuscript). Secondary outcome and subgroup analysis reported without adjustment for multiple analyses.	High risk of bias
Other bias	Anything else, ideally pre-specified.	This paper is an AiC draft and has not been peer-reviewed. No disclosures reported.	Unclear risk of bias

Abbreviations: CONSORT, Consolidated Standards of Reporting Trials; ITT, intention to treat; pp, per protocol.

*Assessments should be made for each main outcome or class of outcomes.

Table B2. *Critical appraisal of (Yang et al., 2017a).*

Bias domain	Source of bias	Support for Judgement	Review authors' judgement (assess as low, unclear, or high risk of bias)
Selection bias	Random sequence generation	No randomisation described. "Patients were sequentially enrolled into either the NPWT group or the NPWTi group in an unblinded fashion".	High risk of bias
	Allocation concealment	No description of allocation concealment.	High risk of bias
Performance bias	Blinding of participants and personnel*	No blinding of participants or treating personnel attempted.	High risk of bias
Detection bias	Blinding of outcome assessment*	No blinding of assessors or analysts used.	High risk of bias
Attrition bias	Incomplete outcome data*	No patient flow chart reported. Sample size was very small (total n = 19) but unclear if there was any withdrawal or ITT or PP were applied.	High risk of bias (ITT)
Reporting bias	Selective reporting	Only one outcome reported (bacterial concentration). No trial protocol published.	High risk of bias
Other bias	Anything else, ideally pre-specified.	Some authors had financial connections to the company: "Dr. Schultz is a paid consultant for Acelity and Smith & Nephew. Dr. Lantis is a paid consultant for Acelity, Smith & Nephew, Kerecis, and Intregra".	Unclear risk of bias

Abbreviations: ITT, intention to treat; pp, per protocol.

*Assessments should be made for each main outcome or class of outcomes.

Table B3. *Critical appraisal of (Kim et al., 2015).*

Bias domain	Source of bias	Support for Judgement	Review authors' judgement (assess as low, unclear, or high risk of bias)
Selection bias	Random sequence generation	A priori randomisation with "1:1 allocation using a random number generator producing a list of 100 discrete spreadsheet cells [Excel], with 1 representing normal saline and 2 representing 0.1% polyhexanide plus 0.1% betaine"	Low risk of bias
	Allocation concealment	No description of allocation concealment.	High risk of bias
Performance bias	Blinding of participants and personnel*	No blinding of participants or treating personnel attempted.	High risk of bias
Detection bias	Blinding of outcome assessment*	No blinding of assessors or analysts used.	High risk of bias
Attrition bias	Incomplete outcome data*	Patient flow chart reported. All patients in ITT included in analysis. Reasons for exclusion reported for PP analysis.	Low risk of bias (ITT)
Reporting bias	Selective reporting	Outcomes were reported in trial protocol (NCT01939145). Only limited outcomes reported, but no evidence of omission (except qualitative bacterial culture).	Low risk of bias
Other bias	Anything else, ideally pre-specified.	Patients may have been inappropriately selected prior to randomisation (see Discussion)	Generalisability issues

Abbreviations: ITT, intention to treat; pp, per protocol.

*Assessments should be made for each main outcome or class of outcomes.

Table B4. *CASP checklist (cohort study) (Chowdhry and Wilhelmi, 2019).*

Question	Yes, No, Can't tell	Comment
1. Did the study address a clearly focused issue?	☑	"In this study, NPWTi-d was retrospectively compared with standard wet-to-moist dressing changes as an adjunctive modality for managing sternal wounds resulting from sternal incision complications."
2. Was the cohort recruited in an acceptable way?	☑	Appears to be consecutive recruitment: "30 most recent patients (15 patients who received NPWTi-d and 15 patients who received wet-tomoist dressings)"
3. Was the exposure accurately measured to minimise bias?	☑	The intervention and comparator are described in some detail.
4. Was the outcome accurately measured to minimise bias?	☒	Probably not possible as the study was retrospective.
5a. Have the authors identified all important confounding factors?	☒	No effort made to identify confounding variables.
5b. Have they taken account of the confounding factors in the design and/or analysis?	☒	No propensity matching or statistical adjustment employed.
6a. Was the follow up of subjects complete enough?	?	Follow up was not defined.
6b. Was the follow up of subjects long enough?	?	
7. What are the results of this study?	☑ (positive results)	"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".
8. How precise are the results?	☑	Graphs with confidence levels reported, hypothesis testing employed.
9. Do you believe the results?	☒	The methodology of the study is not sufficiently high enough to have confidence in the results.

10. Can the results be applied to the local population?	☒	The indication for NPWTi in this study was very specific. Therefore results cannot be generalised to other populations.
11. Do the results of this study fit with other available evidence?	?	No other studies identified for this indication.
12. What are the implications of this study for practice?	☒	No recommendations are possible on the basis of this study.

Table B5. *CASP check list (Cohort study) (Deleyto et al., 2018)*

Question	Yes, No, Can't tell	Comment
1. Did the study address a clearly focused issue?	☑	"[We] have therefore, conducted a study of costs and global efficiency, comparing the use of NPWTi with conventional wound treatment (CWT) options."
2. Was the cohort recruited in an acceptable way?	☑	Retrospective recruitment of consecutive patients with the diagnosis of abdominal wall wound dehiscence with mesh exposure during the period January 2010 to December 2013.
3. Was the exposure accurately measured to minimise bias?	☑	The NPWTi and conventional dressing processes were described in appropriate detail.
4. Was the outcome accurately measured to minimise bias?	☒	Outcome data was retrospective and may not have been accurate. No description on how outcomes were measured.
5a. Have the authors identified all important confounding factors?	☒	No effort made to identify confounding variables.
5b. Have they taken account of the confounding factors in the design and/or analysis?	☒	No propensity matching or other statistical adjustment undertaken.
6a. Was the follow up of subjects complete enough?	?	Follow up was not defined.
6b. Was the follow up of subjects long enough?	?	
7. What are the results of this study?	☑ (positive results)	Reduction in costs associated with NPWTi.
8. How precise are the results?	☑	Mean costs with 95% confidence intervals presented.
9. Do you believe the results?	☒	The reporting of the study was not sufficient to establish the veracity of the results with confidence.
10. Can the results be applied to the local population?	☒	This was primarily a Spanish economic study. The results were not generalisable to the UK.
11. Do the results of this study fit with other available evidence?	☒	Not known.
12. What are the implications of this study for practice?	☒	No recommendations are possible on the basis of this study.

Table B6. *CASP check list (Cohort study) (Omar et al., 2016)*

Question	Yes, No, Can't tell	Comment
1. Did the study address a clearly focused issue?	☑	"The purpose of this study was to compare the outcomes for patients who received negative-pressure wound therapy with instillation versus a historical control cohort of patients who received traditional negative- pressure wound therapy without instillation."
2. Was the cohort recruited in an acceptable way?	☒	NPWTi and NPWT patients were recruited retrospectively from an electtonic medical records system at a hospital. Recruitement dates and methods not reported. There is scope for selection bias.
3. Was the exposure accurately measured to minimise bias?	☑	The NPWTi and NPWT processes were described in appropriate detail.
4. Was the outcome accurately measured to minimise bias?	☒	Outcome data was retrospective and may not have been accurate.
5a. Have the authors identified all important confounding factors?	☒	No effort made to identify confounding variables.
5b. Have they taken account of the confounding factors in the design and/or analysis?	☒	No propensity matching or other statistical adjustment undertaken.
6a. Was the follow up of subjects complete enough?	?	Follow up was not defined.
6b. Was the follow up of subjects long enough?	?	
7. What are the results of this study?	☑ (positive results)	Improvements in debridements, hospital stay, wound closure.
8. How precise are the results?	☒	Standard deviation may have been reported for some outcomes. However, overall precision of results does not appear robust.
9. Do you believe the results?	☒	The study was not methodologically robust enough to interpret the results with confidence. Conclusions appear to be stronger than justified by the results given the limitations.
10. Can the results be applied to the local population?	☒	The results cannot be generalised to other populations (very broad inclusion criteria with low patient numbers in each category).

11. Do the results of this study fit with other available evidence?	☒	The evidence base in general is equivocal. However, these are not consistent with the only RCT (Kim *et al.* 2020, AiC).
12. What are the implications of this study for practice?	☒	No recommendations are possible on the basis of this study.

Table B7. *CASP check list (Cohort study) (Gabriel et al., 2014)*

Question	Yes, No, Can't tell	Comment
1. Did the study address a clearly focused issue?	☑	"To compare the outcomes of patients with extremity and trunk wounds treated with standard NPWT versus NPWTi-d with volumetric fluid instillation and to estimate differences in costs for the 2 treatment arms based on the outcomes"
2. Was the cohort recruited in an acceptable way?	☒	"All patients were treated with a similar protocol by one investigator" No information on cohort selection.
3. Was the exposure accurately measured to minimise bias?	☒	Details of interventions and co-interventions are lacking.
4. Was the outcome accurately measured to minimise bias?	☒	Probably not possible as the study was retrospective.
5a. Have the authors identified all important confounding factors?	☒	No effort made to identify confounding variables.
5b. Have they taken account of the confounding factors in the design and/or analysis?	☒	No propensity matching or statistical adjustment employed.
6a. Was the follow up of subjects complete enough?	?	Follow up was not defined.
6b. Was the follow up of subjects long enough?	?	
7. What are the results of this study?	☑ (positive results)	NPWTi reduced debridements, mean hospital stay, and time to wound closure.
8. How precise are the results?	☒	No confidence levels reported.
9. Do you believe the results?	☒	There is too much uncertainty, in particular regarding patient selection and outcome measurement, to be confident about the results.
10. Can the results be applied to the local population?	☒	The results cannot be generalised to other populations.
11. Do the results of this study fit with other available evidence?	?	The results are not consistent with the only RCT reporting these outcomes (Kim *et al.*; 2020).
12. What are the implications of this study for practice?	☒	No recommendations are possible on the basis of this study.

Table B8. *CASP check list (Cohort study) (Kim et al., 2014).*

Question	Yes, No, Can't tell	Comment
1. Did the study address a clearly focused issue?	☑	"The purpose of this study was to compare the outcomes for patients who received negative-pressure wound therapy with instillation versus a historical control cohort of patients who received traditional negative- pressure wound therapy without instillation."
2. Was the cohort recruited in an acceptable way?	☒	NPWTi and NPWT patients were recruited retrospectively from an electronic medical records system at a hospital. Recruitment dates and methods not reported. There is scope for selection bias.
3. Was the exposure accurately measured to minimise bias?	☑	The NPWTi and NPWT processes were described in appropriate detail.
4. Was the outcome accurately measured to minimise bias?	☒	Outcome data was retrospective and may not have been accurate.
5a. Have the authors identified all important confounding factors?	☒	No effort made to identify confounding variables.
5b. Have they taken account of the confounding factors in the design and/or analysis?	☒	No propensity matching or other statistical adjustment undertaken.
6a. Was the follow up of subjects complete enough?	?	Follow up was not defined.
6b. Was the follow up of subjects long enough?	?	
7. What are the results of this study?	☑ (positive results)	Improvements in debridements, hospital stay, wound closure.
8. How precise are the results?	☒	Standard deviation may have been reported for some outcomes. However, overall precision of results does not appear robust.
9. Do you believe the results?	☒	The study was not methodologically robust enough to interpret the results with confidence. Conclusions appear to be stronger than justified by the results given the limitations.
10. Can the results be applied to the local population?	☒	The results cannot be generalised to other populations (very broad inclusion criteria with low patient numbers in each category).

11. Do the results of this study fit with other available evidence?	☒	The evidence base in general is equivocal. However, these are not consistent with the only RCT (Kim *et al.* 2020, AiC).
12. What are the implications of this study for practice?	☒	No recommendations are possible on the basis of this study.

Table B9. *CASP check list (Cohort study) (Goss et al., 2012).*

Question	Yes, No, Can't tell	Comment
1. Did the study address a clearly focused issue?	☑	"The primary objective of this study was to assess the difference in chronic wound planktonic bioburden after operative debridement and 1 week of treatment with either standard NPWT or NPWT with instillation using a mild concentration of Dakin's solution."
2. Was the cohort recruited in an acceptable way?	☒	The study used prospective recruitment, but the methods of patient selection are not adequately reported. Highly likely to be susceptible to selection bias.
3. Was the exposure accurately measured to minimise bias?	☑	The NPWTi and NPWT processes were described.
4. Was the outcome accurately measured to minimise bias?	?	It is not possible to tell if the outcomes were subject to particular levels of bias.
5a. Have the authors identified all important confounding factors?	☒	No effort made to identify confounding variables.
5b. Have they taken account of the confounding factors in the design and/or analysis?	☒	No propensity matching or other statistical adjustment undertaken.
6a. Was the follow up of subjects complete enough?	?	Follow up was not defined.
6b. Was the follow up of subjects long enough?	?	
7. What are the results of this study?	☑ (positive results)	"there was a statistically significant reduction in the absolute bioburden in those wounds treated with NPWTi (p 5 0.016)".
8. How precise are the results?	☒	Distributional data not reported..
9. Do you believe the results?	☒	The study was not methodologically robust enough to interpret the results with confidence.
10. Can the results be applied to the local population?	☒	The results cannot be generalised to other populations. Sample was heterogeneous and small.
11. Do the results of this study fit with other available evidence?	☒	Not consistent with another "RCT" (Yang *et al.* 2017)
12. What are the implications of this study for practice?	☒	No recommendations are possible on the basis of this study.

Appendix C: Economic assumptions and additional results

Table C1. *EAC's critique of the assumptions made in the model (Table 2 of the Economic Submission).*

Company assumption	Company justification	Evidence source	EAC comment
The model assumes canisters, cassettes and dressing kits needs changing three times per week	In line with instructions for use	NPWTi IFU	The EAC has checked the IFU and accepts this is likely to be accurate. However, it is noted that the size of canister required will depend on patient and wound characteristics.
Number of OR visits / operations were assumed for the purpose of a debridement	KOL opinion indicates it is likely debridements would be performed for such patients even if it is not reported explicitly.	KOL opinion	The EAC considered there may be multiple reasons for OR attendances other than surgical debridement. Furthermore, NICE clinical experts verified UK guidelines (Wounds UK, 2013) that surgical debridement is often not the first-line method of debridement in many patients considered in scope (EAC External correspondence log, 2020). The EAC notes that the company's contact with KoLs was restricted to two individuals who provided confirmation of company assumptions rather than being directly involved in making them (see Section 9.2.2).
Length of therapy in Kim 2014 was assumed to be 8.01 and 13.88 days respectively for NPWTi and NPWT respectively	A ratio was worked between length of therapy and length of stay in Gabriel 2008 and was then multiplied by length of stay reported at Kim 2014	Reference Gabriel 2008 and Kim 2014	The EAC does not accept this is an appropriate method to calculate this parameter. See Section 9.2.3.
Number of debridements in Gabriel 2008 was assumed to be 2.96 and 7.88 days for NPWTi and standard wound care respectively	A ratio was worked between number of OR visits and length of stay in Kim 2014 and was then multiplied by length of stay reported at Gabriel 2008	Reference Gabriel 2008 and Kim 2014	The EAC does not accept this is an appropriate method to calculate this parameter. See Section 9.2.3.
Length of therapy in Timmers 2009 was assumed to be 18.22 and 55.68 days for NPWTi and	A ratio was worked between length of therapy and length of stay in Gabriel 2014 and was	Reference Timmers 2009 and Gabriel 2014	The EAC does not accept this is an appropriate method to calculate this parameter. See Section 9.2.3.

Company assumption	Company justification	Evidence source	EAC comment
standard wound care respectively	then multiplied by length of stay reported at Timmers 2009		
Deleyto 2018 was assumed more appropriate for extracting endpoints for prosthetic implants subgroup compared to Garcia 2016	Both studies were conducted one the same group of patients and reported the same results. Deleyto 2018 was preferred because it reported mean values for all outcomes and to the second decimal place	Reference Deleyto 2018 & Garcia 2016	The EAC accepts that selection of this study rather than the study by Garcia-Ruano *et al.* (2016) was appropriate. However, the EAC did not consider the way the studies were selected in general were acceptable. Section 9.2.3.
Length of therapy in Deleyto 2018 was assumed to be 25.19 days for standard wound care	A ratio was worked between length of therapy and length of stay in Deleyto 2018 for NPWTi and was then multiplied by length of stay for standard wound care reported at Deleyto 2018	Reference Deleyto 2018	The EAC considered this assumption was not justified. Extrapolation of data from one cohort to another does not replace direct empirical evidence. See Section 9.2.3.
Length of stay in the surgical site infections subgroup was assumed equal to length of therapy	None of the relevant studies reported the outcome of interest. Therefore, this conservative assumption was made to complete the model inputs	Reference Jurkovic 2019 and Chowdhry 2019	The EAC considered this assumption was not justified. The methodological and reporting quality of the informing studies was not adequate to estimate this parameter.
Nurse training time on NPWTi was assumed to be negligible	The assumption was made based on 1.5 hours of training needed per nurse with expected high estimations of the workload or capacity in terms of number of treated patients per nurse after training	N/A	The rationale for this assumption is not clear. However, the EAC accepts that opportunity costs forgone through training would be unlikely to have significant cost impacts in the longer term.

Abbreviations: KoL, key opinion leader; IFU, instructions for use; NPWT, negative pressure wound therapy; NPWTi, negative pressure wound therapy with instillation.

Table C2. *Studies included by company to inform economic parameters.*

<table>
<tr><th>Company scenario</th><th>Study reference, type, and setting</th><th>Population</th><th>Intervention and comparator</th><th>Outcome(s) used in economic model</th><th>Critique of statistical analysis</th><th>EAC comments</th></tr>
<tr><td>Lower limb</td><td>(Kim et al., 2014)
Retrospective observational study.
United States</td><td>“All patients with infected wounds requiring admission with at least two operative debridements and that received either negative-pressure wound therapy or negative-pressure wound therapy with instillation application at the time of the initial operation”
(n = 142)

<table><tr><th>Anatomical location</th><th>Aetiological cause</th></tr><tr><td>Forefoot</td><td>Ischaemic</td></tr><tr><td>Midfoot</td><td>Neuropathic</td></tr><tr><td>Hindfoot/heel</td><td>Decubitus wound</td></tr><tr><td>Ankle</td><td>Surgical</td></tr><tr><td>Leg</td><td>Venous</td></tr><tr><td>Thigh</td><td>Traumatic</td></tr><tr><td>Amputation site (metatarsal/below knee)</td><td></td></tr><tr><td>Back/buttock</td><td>Other</td></tr><tr><td>Abdomen</td><td></td></tr><tr><td>Arm</td><td></td></tr></table>
☑☒</td><td>I: NPWTi with VAC VeraFlo
Dwell time with Prontosan:
6 minutes (n = 34)
20 minutes (n = 34)
☑
C: NPWT (InfoVAC therapy system)
☑</td><td>LoS (NPWTi and NPWT)
☑

LoT: derived variable by multiplying LoS by scaling factor calculated from data from (Gabriel et al., 2008).
☒

Number of OR visits (surgical debridements) (NPWTi and NPWT)
☑</td><td>• Correction for multiple testing not applied.
• Test for normality for continuous variables not reported.
• Incorrect test for comparing LoS, time to final surgical procedure and number of operative visits*</td><td>The population enrolled in this study included people with wounds not of the lower leg (11.2% of population). This study was regarded as relatively high quality compared with other informing studies.
Data for NPWTi has been taken from the 6 minutes dwell time arm.
Inappropriate statistical analysis.
Note in the original study there was no evidence of dose response in dwell time.</td></tr>
<tr><td></td><td>(Gabriel et al., 2008)
Small retrospective case series
United States</td><td>Patients with a “diagnosis of complex, open, infected wounds”.
NPWTi group patient data reported only:
<table><tr><th>Type of wound</th></tr><tr><td>Abdominal necrotising fasciitis</td></tr></table></td><td>I: NPWTi with VAC Instill treatment
☒</td><td>Used to calculate ratio between LoS and LoT, and this scaling factor then applied to study</td><td>• Correction for multiple testing not applied.
• Test for normality for continuous variables not</td><td>The population was not specific to lower limb wounds.

The intervention was the</td></tr>
</table>

		Necrotising fasciitis of chest and upper extremity Stage IV sacral pressure ulcer Open knee joint with exposed hardware (n = 2) Surgical wound dehiscence Lower extremity wound Soft tissue loss of lower extremity Open ankle joint with exposed hardware Lower extremity wound with exposed bone Soft tissue loss of the lower extremity Lower extremity wound with exposed bone Abdominal surgical wound dehiscence Stage IV pressure ulcer Necrotising fascitis of the upper extremity n = 15 ☒	C: "Standard moist wound-care therapy" ☑☒	data in (Kim *et al.*, 2014). ☑ LoS (NPWTi and AWC) ☑ LoT (NPWTi and AWC) ☑	explicitly reported (but they do use t-tests and Wilcoxon rank sum meaning that they did treat parametric and non-parametric variables differently).	predecessor device (out of scope). The comparator was not NPWT. The EAC does not agree data from this study can be used to extrapolate data in the study by (Kim *et al.*, 2014).
Mixed wounds	(Gabriel *et al.*, 2014) Retrospective observational study. United States	Patients with "an infected or critically colonized wound". Anatomical position / Proportion Upper extremity: 25/82 (30%) Lower extremity: 18/82 (22%) Trunk: 40/82 (49%) n = 82 ?	I: NPWTi with VAC VeraFlo system. (n = 48) ☑ C: NPWT with VAC Granufoam dressings. (n = 34) ☑	LoS (NPWTi and NPWT) ☑ Number of OR visits (surgical debridements) (NPWTi and NPWT) ☑ Used to calculate ratio between LoS and LoT in "mixed wound" population . This was used as scaling factor to estimate LoT	• Correction for multiple testing not applied – but given the huge differences shown this wouldn't have changed anything. • Test for normality for continuous variables not reported. The authors assumed non-normal distribution (of	The population having "mixed infection" was not clearly defined by the company. This study did not clearly define its population. The EAC does not agree data from this study can be used to extrapolate data in the study by (Timmers *et al.*, 2009).

<table>
<tr><td></td><td></td><td></td><td></td><td>in study by (Timmers et al., 2009).
☒</td><td>LoS, LoT, nOR, time to closure) and applied Wilcoxon rank sum test to compare continuous variables (valid approach).</td><td></td></tr>
<tr><td></td><td>(Timmers et al., 2009)

Retrospective observational study.

Netherlands</td><td>Patients with osteomyelitis [or other tissue infection] of the pelvis or lower leg.

<table><tr><th>Diagnosis</th><th>Proportion</th></tr><tr><td>Osteomyelitis</td><td>33/62 (53%)</td></tr><tr><td>Soft tissue infection</td><td>13/62 (21%)</td></tr><tr><td>Trauma wound</td><td>12/62 (19%)</td></tr><tr><td>Necrotising fasciitis</td><td>3/62 (5%)</td></tr><tr><td>Pilonoidal sinus</td><td>1/62 (2%)</td></tr></table>
n = 156

☒</td><td>I: NPWTi with VAC Insillation therapy. Antispetic instillation fluid (“Lavasept”). Initial debridement.
(n = 59)
☒

C: Standard care, consisting of “surgical debridement, repeated as often as felt necessary by attending physicians, systemic administration of antibiotics with confirmed activity against the aetiologic microbial agent and implantation of gentamicin beads at the site of osteomyelitis”</td><td>LoS multiplied by scaling factor derived from (Gabriel et al., 2014).
☑

LoS (NPWTi and AWC)
☑

Surgical deridements (NPWTi and AWC)
☑</td><td>Correction for multiple testing not applied.
Test for normality for continuous variables not reported.
Incorrect test for comparing number of hospital admissions, LoS *</td><td>This study was excluded by the EAC in the clinical report on the basis the intervention were not in scope.

The population of this study was in patients with osteomyelitis or related soft tissue infections. The EAC considered this was a specific population and did not represent the description of “mixed wounds”.</td></tr>
</table>

			☒ (n = 94)			
Prosthetic implants	(Deleyto *et al.*, 2018) Retrospective observational study Spain	Patients with abdominal wall wound dehiscence with mesh exposure. No patient characteristics data reported. n = 45 ?	I: NPWTi with VAC VeraFlo (n = 11) ☑ C: Conventional dressings (n = 34) ☑	LoS (NPWTi and AWC)) ☑ Surgical debridements (NPWTi and AWC) ☑ Additional mesh surgeries (NPWTi and AWC) ☒	• Correction for multiple testing not applied. • Test for normality for continuous variables not reported – the authors just assumed non-normal distribution and tested using Mann-Whitney to compare these continuous variables (valid approach).	This was a small study (11 patients in NPWTi group) specific to patients with surgical dehiscence following abdominal mesh failure. Patient characteristics were not reported. NPWT was not included in this scenario. Additional parameters are challenged by the EAC.
Surgical site infections	(Jurkovic *et al.*, 2019) Retrospective observational study Slovenia	People with infected laparotomies exhibiting fasciitis. Detailed patient characteristics unknown. n = 41 ?	I: NPWTi with VAC Instill (n = 19) ☒ C: NPWT (technology unknown) (n = 22) ☑	LoS (NPWTi and NPWT) ☒ LoT (NPWTi and NPWT) ☑ Number of surgical debridements (NPWTi and NPWT) ☑	• Published in a foreign language and difficult to interpret. • Results appear to have non-significant p value.	This study was excluded from the clinical assessment because it was published in a foreign language, and the intervention was deemed out of scope. Data from this study has not been verified as it was published in a foreign language.

	(Chowdhry and Wilhelmi, 2019) Retrospective observational study United States	People with infected sternal wounds following reconstructive surgery Wound characteristics not reported n = 30 ☑	I: NPWTi with VAC VeraFlo (n = 15) ☑ C: wet-to-moist wrappings (n = 15) ☑	LoS (NPWTi and AWC) ☑ LoT (NPWTi and AWC) ☑ Number of surgical debridements (NPWTi and AWC) ☑	• Correction for multiple testing not applied. • Test for normality for continuous variables not explicitly reported (but used Wilcoxon rank sum meaning that they did treat parametric and non-parametric variables differently).	The population enrolled in this study was highly specific and unlikely to be generalisable to other forms of surgical infection. Insufficient information was provided on wound characteristics, patient selection, and outcome measurement.

Abbreviations: ANOVA, analysis of variance; AWC, advanced wound care (not specified further, understood to mainly include use of dressings); C, comparator; I, intervention; LoS, length of [hospital] stay; Lot, length of therapy; NPWTi, negative pressure wound therapy; NPWTi, negative pressure wound therapy with instillation.

Key: ☑ aspect of study in scope; ☑☒ aspect of study partially in scope, or elements of this are not in scope; ☒ aspect of study not in scope; ? unknown.

* The authors appear to have used parametric tests, such as ANOVA and Student's t-test) on variables which are highly unlikely to follow normal distribution (e.g.LoS).

Table C3a: *Point estimates of cost differences between NPWTi and NPWT using data from different studies.*

Study	Population	NPWTi			NPWT		
		nOR	LoT	LoS	nOR	LoT	LoS
(Kim *et al.*, 2020)	Patients with Open wound > 4 cm in any plane of measurement excluding tunnels after initial surgical debridement. Acute and chronic wounds. Wound appropriate for NPWT use. (n = 181)	1.1	6.8	6.8*	1.0	6.3	6.3*
(Kim *et al.*, 2014)	Patients with infected wounds requiring admission with for operative debridement. Suitable for NPWT or NPWTi. (n = 142)	2.4	11.9*	11.9	3.0	14.92*	14.92
(Gabriel *et al.*, 2014)	Patients with “an infected or critically colonized wound”.	2	4.1	8.1	4.4	20.9	27.4
(Jurkovic *et al.*, 2019)	People with infected laparotomies exhibiting fasciitis. (n = 82)	2	21*	21	3.0	23*	23
(Omar *et al.*, 2016)	Patients with acute wounds of the lower limb. (n = 20)	3.0 [median]	9.0 [median]	21.5 [median]	3.0 [median]	12.5 [median]	26.5 [median]

Abbreviations: LoS, length of stay; LoT, length of treatment; nOR, number of debridements; NPWT, negative pressure wound therapy; NPWTi, negative pressure wound therapy with instillation.

* No data was available. LoS assumed to be the same as LoT *or vice versa*.

Table C3b: Point estimates of cost differences between NPWTi and AWC using data from different studies.

Study	Population	NPWTi			NPWT		
		nOR	LoT	LoS	nOR	LoT	LoS
(Gabriel *et al.*, 2008)*	Patients with complex, open, infected wounds. (n = 15)	Not reported	9.87	14.67	Not reported	34.47	39.2
(Timmers *et al.*, 2009)*	Patients with osteomyelitis [or other tissue infection] of the pelvis or lower leg. (n = 156)	2.3	36*	36	2.4	73*	73
(Deleyto *et al.*, 2018)	Patients with abdominal wall wound dehiscence with mesh exposure. (n = 45)	0.45	69.09**	69.09	2.15	88.21**	88.21
(Chowdhry and Wilhelmi, 2019)	Patients with infected sternal wounds following reconstructive surgery. (n = 30)	1.8	5.4**	5.4	3.1	8.4**	8.4

Abbreviations: AWC, advanced wound care; LoS, length of stay; LoT, length of treatment; nOR, number of debridements; NPWTi, negative pressure wound therapy with instillation.
* Study not included in EAC clinical assessment.
** LoS assumed to be the same as LoT. Note that in Deleyto *et al.* (2018) LoT was reported in the NPWTi cohort only.

Table C4. *Summary of EAC's modifications to the model (see also Table C3a and C3b).*

Issue	Change	Justification
Aggregation of different subgroups to create a whole population	Removed	Results will be reported for each indication separately.
V.A.C. VERAFLO dressing cost (£77.76)	Average dressing cost increased to £84.36	Using latest costs on NHS Supply Chain (April 2020): [redacted]
VAC VERALINK Cassette cost (£21.52)	Decreased to £19.37	Using latest costs on NHS Supply Chain (April 2020): [redacted]
VAC VERALINK Canister cost (£47.23)	Decreased to £44.51	Using latest costs on NHS Supply Chain (April 2020): [redacted] (1000ml canister advised by company)
NPWT Canister cost [redacted]	Decreased to [redacted]	Using latest costs on NHS Supply Chain (April 2020): [redacted] (using smaller 500ml infoVAC/ULTA canister also manufactured by KCI Medical Ltd – which replicates the NPWT control arm of the studies included in the economic submission)
NPWT Dressing cost [redacted]	Average dressing costs increased to [redacted]	Using latest costs on NHS Supply Chain (April 2020): average of small, medium and large granufoam dressings [redacted] which are compatible with the V.A.C. VERAFLO system
AWC Allevyn gentle border 10 cm x 10 cm [redacted]	Decreased to [redacted]	Using latest costs on NHS Supply Chain (April 2020): [redacted]
AWC Aquacel 10 cm x 10 cm [redacted]	Decreased to [redacted]	Using latest costs on NHS Supply Chain (April 2020): [redacted]
Hourly theatre costs (£802.20)	Increased to £989	Using average theatre costs (ISD 2019) across all specialities
Cost per bed night (£431 for lower limb, £375.79 for mixed wound, £391.62 prosthetic implant, £431 for surgical site infection)	Maintained at £431 for each subgroup/indication	Using average excess bed day costs across all HRGs (NHS Reference costs 2017/18)
Additional procedural costs included for Prosthetic Implant subgroup only (Simple wound closure, Debridement and closure, Mesh	Removed	Costs are derived from HRG codes (which are broad and will include a range of other procedures which are irrelevant to the scope). Additional procedure costs not considered for other arms. Minimal impact on debridement costs.

removal, Mesh replacement)		
Rounding number of dressings to nearest whole number (modelled as “wastage”)	Removed	Rounding to nearest whole number not applied consistently in model by company (was applied to dressings but not length of stay). Mean number of dressings and mean length of stay (not rounded) applied.
Median no. of OR visits/debridement (2.0) in Mixed wound population – NPWTi arm (Timmers 2009)	Changed to mean value, 2.3	Mean value used for other subgroups, changed for consistency.
Median no. of OR visits/debridement (5.0) in Mixed wound population – AWC arm (Timmers 2009)	Changed to mean value, 2.4	Mean value used for other subgroups, changed for consistency.
Mean no. of surgeries (0.8, SD 0.7) in Prosthetic implants – NPWTi arm (Deleyto 2018)	Changed to 0.82 (SD 0.75)	Using significant figures reported in the study.
Standard deviation for no. of operations, and length of stay in Mixed wound – NPWTi and AWC arms (Timmers 2009)	Calculation of standard deviation removed and assumed standard error to be 20% of the mean.	Standard deviation calculated incorrectly.
Standard deviation for length of stay (33.56) in Prosthetic implants - AWC arm (Deleyto 2018)	Changed to 77.05	In line with value reported in study (will only impact PSA).
Calculated values of length of therapy inferred from other studies/other arm	Any study which did not explicitly report length of therapy in both arms, will assume length of therapy matches length of stay.	Broad assumption but applied equally to all scenario/subgroups.
Calculated values of number of surgeries/debridement inferred from other studies/other arm	Any study which did not explicitly report number of surgeries/debridement in both arms, did not incur any debridement costs.	Debridement costs are minimal, low impact on total costs.
RCT Kim 2020 not included in economic submission	Mixed population described in Kim 2020 RCT used as the base-case.	This study represents the only randomised comparative data. Due to missing length of stay data, the author has been contacted, but until that time length of stay will be assumed to match reported length of therapy in each arm.

Abbreviations: AWC, advanced wound care dressings; NPWT, negative pressure wound therapy; NPWTi, negative pressure wound therapy with instillation.

Table C5a: *Comparison of point-estimates of cost saving when compared to the company base-case (NPWTi vs. NPWT).*

	Company base-case			EAC base-case			
Subgroup	NPWTi	NPWT	Difference	NPWTi	NPWT	Difference	Δ (EAC-Company), £
Kim 2020*	N/A	N/A	N/A	£3342	£2862	£479	N/A
Kim 2014 (lower limb)	£6427	£7657	-£1230	£6717	£7722	-£1005	**£225**
Gabriel 2014 (mixed wound)	£3890	£12,113	-£8223	£3873	£12113	-£8240	**-£17**
Jurkovic 2019 (surgical site infection)	£11,179	£11,479	-£300	£11,103	£11,479	-£376	**-£76**
Omar 2016	N/A	N/A	N/A	£10,673	£12,632	-£1960	N/A
Abbreviations: N/A, not applicable; NPWTi, negative pressure wound therapy with instillation; NPWT, negative pressure wound therapy.							

Table C5b: *Comparison of point-estimates of cost saving when compared to the company base-case (NPWTi vs. AWC).*

	Company base-case			EAC base-case			
Subgroup	NPWTi	AWC	Difference	NPWTi	AWC	Difference	Δ (EAC-Company), £
Gabriel 2008 (lower limb)	£7915	£18,934	-£11,018	£7173	£17,068	-£9895	**£1,123**
Timmers 2009 (mixed wound)	£15,478	£28,880	-£13,403	£16,857	£28,347	-£11,490	**£1,913**
Deleyto 2018 (prosthetic implants)	£29,234	£36,957	-£7723	£32,424	£35,474	-£3050	**£4,673**
Chowdry 2019 (surgical site infection)	£3289	£4394	-£1105	£3263	£4394	-£1130	**-£25**
Abbreviations: AWC, advanced wound care; NPWTi, negative pressure wound therapy with instillation.							

Appendix D – Economic literature search

The company's economics submission search strategy is as follows:

("Lavage" OR "instil" OR "instillation" OR "irrigated" OR "irrigation" OR "topical solution" OR "topical

wound solution" OR "topic solution" OR "VERAFLO" OR "VERAFLOW" OR "Veraflo dressing" OR

"Veraflo cleanse dressing" OR "Veraflo cleanse choice dressing" OR "Ulta")

AND

("Negative Pressure Wound Therapy" OR "NPWT" OR "vacuum assisted closure" OR "vacuum sealing" OR "NPWTi" OR "NPWTi-d" or "economic")

This is the same as the search conducted for the initial submission, with the addition of "economic" Or-ed into the second search concept.

This will retrieve articles that include any of the first concept terms e.g. lavage or instillation AND economic, but not necessarily any of the other terms from the second search concept. This will retrieve many unnecessary results.

As the same databases (PubMed, EMBASE AND QUOSA) were used in the company's strategy, it would be appropriate to identify any relevant articles during screening of the searches run for the initial submission. To ensure all relevant articles have been retrieved during this process, the searches were re-run with the addition of a validated filter such as those found at https://www.cadth.ca/resources/finding-evidence/strings-attached-cadths-database-search-filters#eco, https://www.crd.york.ac.uk/CRDWeb/ or https://sites.google.com/a/york.ac.uk/issg-search-filters-resource/filters-to-find-i to specifically identify relevant papers.

As the previous searches were run from 2011 onwards it would be appropriate to use specialised databases including NHSEED, DARE and HTA which were updated up to and including 2014 and are available via the CRD website https://www.crd.york.ac.uk/CRDWeb/ The IDEAS database https://ideas.repec.org/ indexes RePEc (**Re**search **P**apers in **Ec**onomics) and includes publications up to the present date.

Unpublished data from ClinicalTrials.gov should be identified in the initial search so no additional search would be necessary. Additional resources could include the ISRCTN registry (https://www.isrctn.com/), the WHO ICTRP

(https://www.who.int/ictrp/en/) or the EU Clinical Trials Register (https://www.clinicaltrialsregister.eu/ctr-search/search). The WHO ICTRP is currently unavailable due to high demand related to the COVID-19 pandemic, so this will not be searched at this stage.

Additional economics searches:

Additional searches were conducted in the databases identified above, the strategies used and results obtained are shown below. The results were exported to an EndNote database, and following checking for duplicate entries, was sent to the EAC staff.

NHS EED/DARE/HTA via the CRD website (searched 23 April 2020)

1	MeSH DESCRIPTOR Therapeutic Irrigation EXPLODE ALL TREES
2	(lavage)
3	MeSH DESCRIPTOR Instillation, Drug EXPLODE ALL TREES
4	(instillation)
5	(irrigation)
6	MeSH DESCRIPTOR Administration, Topical EXPLODE ALL TREES
7	(topic* ADJ2 solution*)
8	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7
9	(veraflo*)
10	(ulta*)
11	#9 OR #10
12	MeSH DESCRIPTOR Negative-Pressure Wound Therapy EXPLODE ALL TREES
13	(negative pressure wound therapy)
14	(NPWT*)
15	(vacuum assisted closure)
16	(vacuum sealing)
17	#12 OR #13 OR #14 OR #15 OR #16
18	#8 AND #17
19	#11 OR #18

When results were restricted to publications from 2011 onwards 2 records remained.

IDEAS/RePEc (searched 23 April 2020)

The search conducted was:

"negative pressure wound therapy" | NPWT | veraflo | VAC | ulta | "vacuum assisted closure" | "vacuum sealing" in the title only

Where | = OR

Restricting to title only removed many irrelevant hits, one article about Ulta beauty company was excluded before sending to the EAC.

Databases

The initial database searches were re-run on 28 April 2020 with the **"broad economics filter"** from CADTH applied, which is available at https://www.cadth.ca/resources/finding-evidence/strings-attached-cadths-database-search-filters#eco

The number of articles retrieved from these searches are shown below:

Database	**Number of results**
NHS EED/DARE/HTA (CRD website)	2
IDEAS/RePEc	2
MEDLINE Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Daily and Versions(R) 1946 to April 27, 2020.	15
Embase: OvidSP 1996 to present	28
CINAHL: EBSCOhost Web 1981 to present	22
Cochrane Library, Wiley 1996 to present	8 (trials only, no reviews)
Total number retrieved	**77**
Total following deduplication	**59**

The same date (2011 onwards) and language restrictions (English language only) were applied as the original search.

A.1: Source: MEDLINE Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Daily and Versions(R) 1946 to April 27, 2020.

Interface/URL: OvidSP
Database coverage dates: 1946 to present
Search date: 28/04/20
Retrieved records: 15
Search strategy:

1 Therapeutic Irrigation/

2 lavage.ti,ab,kw,kf.

3 Instillation, Drug/

4 instillation.ti,ab,kw,kf.

5 irrigation.ti,ab,kw,kf.

6 Administration, Topical/

7 (topic* adj2 solution*).ti,ab,kw,kf.

8 or/1-7

9 veraflo*.ti,ab,kw,kf.

10 ulta*2.ti,ab,kw,kf.

11 9 or 10

12 Negative-Pressure Wound Therapy/

13 "negative pressure wound therapy".ti,ab,kw,kf.

14 NPWT*.ti,ab,kw,kf.

15 "vacuum assisted closure".ti,ab,kw,kf.

16 "vacuum sealing".ti,ab,kw,kf.

17 or/12-16

18 8 and 17

19 11 or 18

20 limit 19 to (english language and yr="2011 -Current")

21 Economics/

22 exp "Costs and Cost Analysis"/

23 Economics, Nursing/

24 Economics, Medical/

25 Economics, Pharmaceutical/

26 exp Economics, Hospital/

27 Economics, Dental/

28 exp "Fees and Charges"/

29 exp Budgets/

30 budget*.ti,ab,kf.

31 (economic* or cost or costs or costly or costing or price or prices or pricing or pharmacoeconomic* or pharmaco-economic* or expenditure or expenditures or expense or expenses or financial or finance or finances or financed).ti,kf.

32 (economic* or cost or costs or costly or costing or price or prices or pricing or pharmacoeconomic* or pharmaco-economic* or expenditure or expenditures or expense or expenses or financial or finance or finances or financed).ab. /freq=2

33 (cost* adj2 (effective* or utilit* or benefit* or minimi* or analy* or outcome or outcomes)).ab,kf.

34 (value adj2 (money or monetary)).ti,ab,kf.

35 exp models, economic/

36 economic model*.ab,kf.

37 markov chains/

38 markov.ti,ab,kf.

39 monte carlo method/

40 monte carlo.ti,ab,kf.

41 exp Decision Theory/

42 (decision* adj2 (tree* or analy* or model*)).ti,ab,kf.

43 or/21-42

44 20 and 43

A.2: Source: Ovid Embase 1974 to 2020 April 27.

Interface/URL: OvidSP
Database coverage dates: 1974 to present
Search date: 28/04/20
Retrieved records: 28
Search strategy:

1 lavage/

2 lavage.ti,ab,kw.

3 drug instillation/

4 instillation.ti,ab,kw.

5 irrigation.ti,ab,kw.

6 topical drug administration/

7 (topic* adj2 solution*).ti,ab,kw.

8 or/1-7

9 veraflo*.ti,ab,kw.

10 ulta*2.ti,ab,kw.

11 9 or 10

12 vacuum assisted closure/

13 "negative pressure wound therapy".ti,ab,kw.

14 NPWT*.ti,ab,kw.

15 "vacuum assisted closure".ti,ab,kw.

16 "vacuum sealing".ti,ab,kw.

17 or/12-16

18 8 and 17

19 11 or 18

20 limit 19 to (english language and yr="2011 -Current")

21 Economics/

22 Cost/

23 exp Health Economics/

24 Budget/

25 budget*.ti,ab,kw.

26 (economic* or cost or costs or costly or costing or price or prices or pricing or pharmacoeconomic* or pharmaco-economic* or expenditure or expenditures or expense or expenses or financial or finance or finances or financed).ti,kw.

27 (economic* or cost or costs or costly or costing or price or prices or pricing or pharmacoeconomic* or pharmaco-economic* or expenditure or expenditures or expense or expenses or financial or finance or finances or financed).ab. /freq=2

28 (cost* adj2 (effective* or utilit* or benefit* or minimi* or analy* or outcome or outcomes)).ab,kw.

29 (value adj2 (money or monetary)).ti,ab,kw.

30 Statistical Model/

31 economic model*.ab,kw.

32 Probability/

33 markov.ti,ab,kw.

34 monte carlo method/

35 monte carlo.ti,ab,kw.

36 Decision Theory/

37 Decision Tree/

38 (decision* adj2 (tree* or analy* or model*)).ti,ab,kw.

39 or/21-38

40 20 and 39

A.3: Source: CINAHL®

Interface/URL: EBSCOhost Web
Database coverage dates: 1981 to present
Search date: 28/04/20

Retrieved records: 22
Search strategy:

S43 S20 AND S42

S42 S21 OR S22 OR S23 OR S24 OR S25 OR S26 OR S27 OR S28 OR S29 OR S30 OR S31 OR S32 OR S33 OR S34 OR S35 OR S36 OR S37 OR S38 OR S39 OR S40 OR S41

S41 TX (decision* N2 (tree* or analy* or model*))

S40 MH "decision theory+"

S39 TX monte carlo

S38 MH "monte carlo method"

S37 TX markov

S36 MH "markov chains"

S35 AB economic model*

S34 MH "models, economic+"

S33 TX (value N2 (money or monetary))

S32 AB (cost* N2 (effective* or utilit* or benefit* or minimi* or analy* or outcome or outcomes))

S31 AB (economic* or cost or costs or costly or costing or price or prices or pricing or pharmacoeconomic* or pharmaco-economic* or expenditure or expenditures or expense or expenses or financial or finance or finances or financed)

S30 TX (economic* or cost or costs or costly or costing or price or prices or pricing or pharmacoeconomic* or pharmaco-economic* or expenditure or expenditures or expense or expenses or financial or finance or finances or financed)

S29 TX budget*

S28 (MH "Budgets")

S27 (MH "Fees and Charges+")

S26 MH "economics, medical"

S25 MH "economics, hospital+"

S24 MH "economics, nursing"

S23 (MH "Economics, Dental") OR (MH "Economics, Pharmaceutical")

S22 (MH "Costs and Cost Analysis+")

S21 (MH "Economics")

S20 S16 OR S18 Limiters - Published Date: 20110101-20201231

Narrow by Language: - english

S19 S16 OR S18

S18 S8 AND S17

S17 S11 OR S12 OR S13 OR S14 OR S15

S16 S9 OR S10

S15 TI "vacuum sealing" or AB "vacuum sealing"

S14 TI "vacuum assisted closure" or AB "vacuum assisted closure"

S13 TI NPWT* or AB NPWT*

S12 TI "Negative Pressure Wound Therapy" or AB "Negative Pressure Wound Therapy"

S11 (MH "Negative Pressure Wound Therapy")

S10 TI ulta* or AB ulta*

S9 TI veraflo* or AB veraflo*

S8 S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7

S7 TI (topic* N2 solution*) or AB (topic* N2 solution*)

S6 (MH "Administration, Topical")

S5 TI irrigation or AB irrigation

S4 TI instillation or AB instillation

S3 (MH "Instillation, Drug")

S2 TI lavage or AB lavage

S1 (MH "Therapeutic Irrigation")

A.4: Source: Cochrane Database of Systematic Reviews (CDSR) and Cochrane Central Register of Controlled Trials (CENTRAL)

Interface/URL: Cochrane Library, Wiley
Database coverage dates: 1996 to present
Search date: 28/04/20
Retrieved records:
CDSR: 0
CENTRAL: 8
Search strategy:

#1 MeSH descriptor: [Therapeutic Irrigation] this term only

#2 (lavage):ti,ab,kw

#3 MeSH descriptor: [Instillation, Drug] this term only

#4 (instillation):ti,ab,kw

#5 (irrigation):ti,ab,kw

#6 MeSH descriptor: [Administration, Topical] this term only

#7 ((topic* near/2 solution*)):ti,ab,kw

#8 (Mahmoudiasl *et al.*-#7)

#9 (veraflo*):ti,ab,kw

#10 (ulta*):ti,ab,kw

#11 MeSH descriptor: [Negative-Pressure Wound Therapy] this term only

#12 ("negative pressure wound therapy"):ti,ab,kw

#13 (NPWT*):ti,ab,kw

#14 ("vacuum assisted closure"):ti,ab,kw

#15 ("vacuum sealing"):ti,ab,kw

#16 (Mahmoudiasl *et al.*-#15)

#17 #8 and #16

#18 #17 or #9 or #10

#19 MeSH descriptor: [Economics] this term only

#20 MeSH descriptor: [Costs and Cost Analysis] explode all trees

#21 MeSH descriptor: [Economics, Nursing] this term only

#22 MeSH descriptor: [Economics, Medical] this term only

#23 MeSH descriptor: [Economics, Pharmaceutical] this term only

#24 MeSH descriptor: [Economics, Hospital] explode all trees

#25 MeSH descriptor: [Economics, Dental] this term only

#26 MeSH descriptor: [Fees and Charges] explode all trees

#27 MeSH descriptor: [Budgets] explode all trees

#28 (budget*):ti,ab,kw

#29 ((economic* or cost or costs or costly or costing or price or prices or pricing or pharmacoeconomic* or pharmaco-economic* or expenditure or expenditures or expense or expenses or financial or finance or finances or financed)):ti,ab,kw

#30 ((cost* NEAR/2 (effective* or utilit* or benefit* or minimi* or analy* or outcome or outcomes))):ab

#31 (value NEAR/2 (money or monetary))

#32 MeSH descriptor: [Models, Economic] explode all trees

#33 (economic model*):ab

#34 MeSH descriptor: [Markov Chains] this term only

#35 ("Markov"):ti,ab,kw

#36 MeSH descriptor: [Monte Carlo Method] this term only

#37 ("monte carlo"):ti,ab,kw

#38 MeSH descriptor: [Decision Theory] explode all trees

#39 ((decision* NEAR/2 (tree* or analy* or model*))):ti,ab,kw

#40 {OR #19-#39}

#41 #18 and #40

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Medical technology guidance

Assessment report overview

V.A.C. Veraflo Therapy System for acute infected or chronic wounds that are failing to heal

This assessment report overview has been prepared by the Medical Technologies Evaluation Programme team to highlight the significant findings of the External Assessment Centre (EAC) report. It includes **brief** descriptions of the key features of the evidence base and the cost analysis, any additional analysis carried out, and additional information, uncertainties and key issues the Committee may wish to discuss. It should be read along with the company submission of evidence and with the EAC assessment report. The overview forms part of the information received by the Medical Technologies Advisory Committee when it develops its recommendations on the technology.

Key issues for consideration by the Committee are described in section 6, following the brief summaries of the clinical and cost evidence.

This report contains information that has been supplied in confidence and will be redacted before publication. This information is highlighted in yellow (academic in confidence) and in blue (commercial in confidence). This overview also contains:

- Appendix A: Sources of evidence
- Appendix B: Comments from professional bodies
- Appendix C: Comments from patient organisations
- Appendix D: Decision problem and claimed benefits from the scope

1 The technology

V.A.C. Veraflo Therapy system (3M+KCI) uses negative pressure wound therapy and wound instillation with topical solutions to promote wound healing. Wound instillation is a controlled process in which topical solutions are slowly introduced to the wound bed where they remain for a defined period before being removed using negative pressure. Treatment is delivered in automated treatment cycles allowing wounds to be repetitively cleansed without the need for dressing removal.

V.A.C. Veraflo Therapy system consists of the following components:

- V.A.C. Ulta therapy unit – delivers V.A.C. Veraflo Therapy
- Exudate canister – single-patient use, disposable canister (500, or 1000ml) which collects fluid
- V.A.C. Veralink cassette – instillation cassette which connects the topical wound solution container and dressing tubing to the V.A.C. Ulta unit
- V.A.C. Veraflo dressing kit of clinician's choice (V.A.C Veraflo dressing, V.A.C. Veraflo Cleanse dressing or V.A.C. Veraflo Cleanse Choice dressing). The V.A.C. Veraflo dressing kits include the appropriate dressing as well as V.A.C. VeraT.R.A.C. Pad with tubing, V.A.C. Advanced Drape and 3M Cavilon No Sting Barrier Film.
- Topical wound solution of clinician's choice that is indicated for topical wound treatment and is compatible with V.A.C. Veraflo dressings and disposable components (examples include Dakin's solution, Prontosan, and normal saline).

V.A.C. Veraflo Therapy system received a CE mark in March 2017 as a class II medical device. Each component part of the system including sterile foam dressing kits and tube sets, and electrically powered accessories are also individually CE marked.

2 Proposed use of the technology

2.1 Disease or condition

It is estimated that over 2 million patients a year have treatment for a wound. For most people healing is normal and achieved in a timely manner. For some people, healing is prolonged and can be accompanied by symptoms which adversely affect patients' quality of life. Patient age, comorbidities and the cause of the wound all affect the healing process. Wound factors such as wound size and depth, location and the presence of bacteria can also have an impact. There are several clinical situations that may result in acutely infected or chronic non-healing wounds, such as surgical site infections, diabetic foot problems and pressure ulcers. Older patients are more likely to suffer chronic and complex wounds. Diabetes is a known risk factor for poor wound healing and is the most common cause of of non-traumatic limb amputation.

Normal healing progresses through a series of 4 main phases; haemostasis, inflammatory, proliferative and remodelling. Exudate is produced by the wound during the inflammatory phase. As part of the normal healing process, the presence of wound exudate helps promote healing by preventing the wound bed from drying out. It also enables tissue-repairing cells to migrate across the surface of the wound and contains growth factors and nutrients that are necessary for healing. During normal healing, the levels of exudate usually reduce over time. In chronic and non-healing wounds, the production of exudate may continue, which delays healing and can increase the risk of infection. Monitoring of exudate is important throughout the healing process as changes to the quality, colour consistency and odour can indicate a change in wound status and underlying complications. Damaged tissue and excess exudate may also be removed (debridement) as part of wound management to help promote healing.

2.2 Patient group

The V.A.C. Veraflo Therapy system is used to treat acute infected or chronic wounds that do not respond to standard care and need additional therapy to

promote healing and wound closure. A retrospective cohort analysis of 1,000 NHS patients reported that 79% of acute wounds and 43% of chronic wounds heal within 12 months (Guest et al. 2015). Results from this study suggest that approximately 21% of acute wounds and 57% of chronic wounds may not respond to standard care and may need additional therapy.

2.3 Current management

Care of acutely infected or chronic non-healing wounds is targeted towards promoting healing and minimising risk of further complications. If infection of the wound is suspected, a microbiological sample is taken, and an antibiotic is prescribed to treat the infection. The wound is also treated with cleansing and debridement (the removal of damaged tissue or foreign objects from a wound), the frequency of which is dependent on ongoing wound assessment. This is followed by the application of a dressing which is changed weekly to daily or more depending on the level of exudate and dressing used. Hospital staff choose a dressing that will promote healing and manage exudate on a case-by-case basis. Some wounds are treated with negative pressure wound therapy. Chronic non-healing wounds typically need more advanced dressings. Advanced dressings are those that have been designed to actively hydrate the wound or to remove and retain excess fluid in order to promote wound healing. Examples of these dressings include alginate, film, foam, hydrocolloid and hydrogel dressings. Patients may be referred to a specialist for multidisciplinary care and the need for this varies depending on the cause of the wound.

The following publications have been identified as relevant to this care pathway because they make recommendations on negative pressure wound therapy:

- NICE guideline on diabetic foot problems: prevention and management (NG19, last updated 2019) recommends considering negative pressure wound therapy after surgical debridement, on the advice of the multidisciplinary foot care service.

- NICE clinical guideline on pressure ulcers: prevention and management (CG179, 2014) does not recommend routinely offering adults negative pressure wound therapy, unless it is necessary to reduce the number of dressing changes.

- NICE interventional procedures guidance on the use of negative pressure wound therapy for the open abdomen (IPG467, 2013) supports the use of this procedure provided that normal arrangements are in place for consent, audit and clinical governance.

NICE medical technologies guidance has published on the following technologies:

- PICO negative pressure wound dressings for closed surgical incisions (2019) NICE medical technologies guidance MTG43 recommends considering the technology as an option for closed surgical incisions in people who are at high risk of developing surgical site infections.

- The MIST Therapy system for the promotion of wound healing (2011) NICE medical technologies guidance MTG5 was recommended for research due to uncertainties about the outcomes of patients with chronic, 'hard-to-heal', complex wounds treated by the MIST Therapy system compared with those treated by standard methods of wound care.

- The Debrisoft monofilament debridement pad for use in acute or chronic wounds (2014) NICE medical technologies guidance MTG17 recommneds the use of this technology as part of the management of acute or chronic wounds in the community.

2.4 Proposed management with new technology

V.A.C. Veraflo would be considered as an alternative to negative pressure wound therapy in people with acute infected or chronic wounds that do not respond to standard care. The V.A.C. Veraflo Therapy system differs from other negative pressure wound therapy therapies because it is designed to

both apply and wash out a cleansing solution, as well as giving automated cycles of negative pressure wound therapy. The technology allows for repeated cleansing without needing to remove the dressing. The technology is applied by healthcare professionals (including surgeons, podiatrists, and tissue viability nurses) in a hospital setting. Clinical experts state that where surgical debridement is required the technology is applied in theatre by a surgeon. When surgical debridement is not required or where wounds can be managed on the ward, a healthcare professional specialised in the use of the technology applies the system at the bedside. The ward nurses then take over subsequent bedside dressing changes (please refer to the adoption scoping report for further information). Healthcare staff using the technology will need training provided by the company.

3 Company claimed benefits and the decision problem

Details of the company's claimed benefits and the decision problem are described in Appendix D. The company submission proposed some variations to the decision problem, specifically to the clinical management outcomes. The proposed variations to the decision problem are described in table 1.1 of the assessment report (page 8), along with the EAC's views of these variations. The EAC agreed with the company's proposed change to modify the outcome 'colonisation with antimicrobial resistant pathogens' to 'colonisation with pathogens', stating that colonisation with any pathogens is the relevant measure and implications for microbial resistance can be inferred from this. The EAC however did not agree to the company's proposed removal of other clinical management outcomes (mean time to healing, number of amputations, antibiotic use and health-related quality of life). The EAC considered all these outcomes to be relevant and saw no reason not to report on these outcomes when available.

4 The evidence

4.1 Summary of evidence of clinical benefit

The company identified 30 full text published studies from its literature search. The company also included 1 abstract and 1 ongoing study, which has since been published.

The EAC undertook its own literature search and identified 19 relevant clinical studies. This included 17 of the 30 studies submitted by the company, as well as 2 additional full text studies. The rationale for the selection of these studies is in sections 4.1 and 4.2 of the EAC assessment report. Of the included studies, 9 were comparative (3 RCTs and 6 observational studies) and 10 were single-armed (see table 1). One of the RCTs (Kim et al., 2015) compares the use of 2 different instillation solutions administered by V.A.C. Veraflo Therapy system. This comparison was not relevant to the decision problem and so the study was considered a single-arm analysis for the purpose of this assessment.

Table 1 Included studies and excluded studies

Studies included by both EAC and company	
Publication and study design	17 studies included by both: • 3 RCTs (Kim et al. 2015; Yang et al. 2017a; Kim et al. 2020) • 2 prospective comparative observational studies (Goss et al. 2012; Omar et al. 2016) • 3 retrospective comparative observational studies (Chowdhry and Wilhelmi 2019; Gabriel et al. 2014; Kim et al. 2014). • 3 prospective non-comparative studies (Ludolph et al. 2018; Milcheski et al. 2017; Brinkert et al. 2013) • 6 retrospective non-comparative studies (Latouche and Devillers 2020; Blalock 2019; Eckstein et al. 2019; Hehr et al. 2020; McElroy 2019; Fluieraru et al. 2013)
Studies in submission excluded by EAC	
Publication and study design	15 studies were excluded by the EAC: • 2 RCTs (Davis et al. 2019; Jurkovic et al. 2019)

	• 2 prospective observational study (Lehner et al. 2011; Zelen et al. 2011; Gabriel et al. 2008) • 1 retrospective comparative cohort study (Garcia-Ruano et al. 2016; Timmers et al. 2009) • 7 retrospective non-comparative studies (Huang et al. 2020; Ikeno et al. 2019; Qiu et al. 2019; Chen et al. 2018; Chen et al. 2018; Jain et al. 2018; Morinaga et al. 2013) • 1 retrospective economic analysis (Yang et al. 2015) • 1 unpublished study (abstract; Powers et al. 2013) The main reason for exclusion was the intervention not being in scope (i.e. predecessor technology or negative pressure wound therapy with instillation from a different company). Other reasons include: the study being in abstract form only (Powers et al. 2013); not published in English (Jurkovic et al. 2019); or study date before the EAC literature search date (Timmers et al. 2009; Gabriel et al. 2008).
Studies not in company submission included by EAC	
Publication and study design	• 2 retrospective case series (Fluieraru et al. 2013; Latouche and Devillers 2020)

The EAC considered the RCT by Kim et al. (2020) to be the most informative study because it was within scope, made a relevant comparison (V.A.C. Veraflo compared with negative pressure wound therapy), had a relatively large sample size (n = 183), and relatively high methodological quality. This study was unpublished and academic in confidence at the time of the company's clinical submission but has since been published in full. The study included patients with acute (28% of patients) or chronic wounds (72% of patients) of various types; including diabetic ulcers (43%), pressure ulcers (17%) and surgical wounds (13% dehisced and 13% non-dehisced). Results reported that V.A.C. Veraflo was associated with a statistically significant (p=0.02) reduction in bacterial bioburden (the amount of bacteria in the wound bed measured in colony forming units (CFU), although this was a surrogate outcome not directly related to clinical endpoints. There was no statistically significant difference in the primary endpoint, the number of follow-on surgical debridements (1.1 vs.1.1, p=0.68), or other secondary outcomes. Length of

hospital stay for the whole cohort was not reported. The EAC highlighted that there were some issues with outcome assessment because of the heterogeneous patient population and the multicentre nature of the study. The sample sizes of people with individual wound types included in the study were small and so were not suitable for subgroup analysis.

The EAC considered the other RCTs by Yang et al. (2017) and Kim et al. (2015) to be of low methodological quality, with potential bias.

The EAC considered all the comparative observational studies to be of poor methodological quality and concluded that it was not possible to attribute causality of the intervention to the reported outcomes with confidence. The EAC did not consider any of the single-armed studies to provide data that could reliably inform treatment pathways in the NHS. Neither the company or the EAC did a meta-analysis because they considered the evidence to be heterogeneous in terms of study populations, methodology, and outcomes reported.

Results from included studies have been summarised by the EAC on an outcome by outcome basis and are presented in table 5.2 of the EAC assessment report (page 52) along with the EAC interpretation of the validity of the evidence. According to the EAC, there is weak evidence to suggest that V.A.C. Veraflo is associated with reduced length of hospital stay compared with negative pressure wound therapy in some populations (people with acute wounds of the lower limb [Omar et al. 2016] and people with infected extremity and trunk wounds [Gabriel et al. 2014; Kim et al. 2014). The evidence that V.A.C. Veraflo Therapy system reduces the need for debridement or other follow on treatments and improves wound healing parameters compared with negative pressure wound therapy, is uncertain. The available evidence suggests that the technology reduces bacterial bioburden compared with negative pressure wound therapy. However, the EAC note that the significance of this is unclear and could be dependent on the instillation fluid used. No conclusions could be drawn for the following clinical management and patient outcomes: number of dressing changes,

number of amputations or skin grafts, staff time and use of other consumables, health-related quality of life, and patient satisfaction and acceptability. Further discussion on the results from the clinical evidence base can be found in section 5.3 of the EAC assessment report.

Overall, the comparative evidence covered a broad range of populations. Some of the studies were conducted in people with a relatively specific wound type while other studies involved a wide range of wound types. According to the EAC, the heterogeneous nature of the study populations combined with the relatively small patient numbers for each wound type made interpretation to specific patient groups difficult. There was no published evidence on health-related quality of life (HRQoL) or patient-reported outcome measures (PROMs). None of the studies were set in the NHS or reported on UK populations. Most of the evidence base compared the use of V.A.C. Veraflo with negative pressure wound therapy and only 2 studies comparing use of the technology with dressings (Chowdry and Wilhelmi 2019; and Deleyto et al. 2017). The EAC stated there was not enough data to draw conclusions on the clinical benefit of V.A.C. Veraflo compared with conventional dressings but highlighted that dressings may not be the most relevant comparator. In total, there were 636 patients enrolled into comparative studies, of which 365 received V.A.C. Veraflo, 222 received negative pressure wound therapy, and 49 received dressings.

In conclusion, the EAC considered the evidence base for V.A.C. Veraflo to be lacking in quantity and quality. They state that it was mainly dominated by retrospective observational studies and that there were few well-designed and conducted studies. The EAC concluded that the claimed benefits of V.A.C. Veraflo were not fully supported by the current evidence base. The EAC noted however that the technology had plausible system benefits through programming and automation and that clinical experts were supportive of the technology and believed the technology had clinical benefits in appropriately selected patients.

Table 2: Key results from comparative studies

Study name, design and funding	Participants/ population	Intervention & comparator	Outcome measures and follow up	Results (Intervention vs comparator)	EAC Comments
RCT (N=3)					
Kim et al., (2020) RCT Location: USA KCI provided funding for the study.	183 inpatients with open wounds (>4 cm) requiring debridement and appropriate for conventional NPWT.	Intervention V.A.C. Veraflo system using Prontosan as the instillation fluid. Dwell time: 20 minutes, cycle length: 3.5 hours continuous NPWT. n = 93 (ITT) Comparator Continuous NPWT using the VAC Ulta device with GranuFoam dressings. n = 88 (ITT) Dressings changed every 3 days.	Primary • Number of inpatient operating room debridements Secondary • Difference in total bacterial counts (CFU) • Time until wound closure/coverage • Proportion of wounds closed • Wound complications	Number of inpatient operating room debridements 1.1 (95% CI 0.93 to 1.30) vs 1.0 (95% CI 0.85 to 1.18); p=0.68 Difference in Total Bacterial Counts -0.18 Log10 CFU/g vs 0.6 Log10 CFU/g; p = 0.02 Time until wound closure/coverage Intervention comparator 6.8 days vs 6.3 days; p = 0.71 Proportion of wounds closed	Study had a relatively large sample size and high methodological quality. Study enrolled patients with acute or chronic wounds of varying types, with the most common causes being diabetic ulcers, pressure ulcers, and infected surgical wounds (dehisced or non-dehisced). The heterogeneous nature of the study

				95.8% vs 97.0%, p = 1.00. Wound complications 28 (39.4%) patients vs 21 patients (31.8%), p=0.38.	population, with relatively small patient numbers for each type of wound, makes interpretation to specific patient groups difficult.
Yang et al., (2017b) RCT Location: USA	20 patients with a leg or foot ulcer > 40 cm^2 that would usually be treated with NPWT and the patient would be hospitalized.	Intervention V.A.C. Veraflo using ¼ strength Dakin's solution, as the instillation fluid. Dwell time: 10 minutes, cycle length: 60 minutes NPWT (-125 mm Hg). n = 10 Comparator NPWT using the V.A.C. Ulta device. Negative pressure of -125 mm Hg. n = 10 Sharp debridement and wound irrigation	Bacterial bioburden (change in biofilm-protected bacteria concentration following 7 days of treatment)	Bacterial bioburden 43% reduction (p < 0.05) vs 14% increase (p = 0.46), p=0.11	Study was small and of low methodological quality, with potential bias in all domains. Only one outcome was reported. The generalisability of this study is low because of the very small sample size and mixed wound types. Some authors had financial connections to the company.

		repeated at day 7.			
Kim et al. (2015) RCT Location: USA	100 patients admitted to a tertiary wound referral academic hospital with an infected wound requiring surgical debridement in an operating room.	Intervention V.A.C. Veraflo using Prontosan as the instillation fluid. n = 51 Comparator V.A.C. Veraflo using 0.9% saline as the instillation fluid. n = 49 Dwell time: 20 minutes, cycle length: 2 hours NPWT.	Primary • Number of operating room visits Secondary • Length of hospital stay in days • Time to final surgical procedure during the admission in days. • Proportion (percentage) of wounds closed/covered during the admission • Proportion (percentage) of wounds that remained closed or covered approximately 30 days after hospital discharge	Number of operating room visits (primary) 2.5 vs 2.8, p=0.19. Length of hospital stay in days 13.6 vs 14.5, p=0.68. Time to final surgical procedure during the admission in days. 5.7 vs 7.7, p=0.04. Proportion of wounds closed/covered during the admission 86% vs 92%, p=0.35. Proportion of wounds that remained closed or covered approximately 30 days after hospital discharge 69% vs 65%, p=0.83.	The study's comparative results were not relevant to the decision problem (compared the use of two different instillation solutions), data reported from the study must be considered as a single-armed study. Study was of low methodological quality and had the potential for bias in most domains.
Comparative observational studies (N=6)					

Chowdhry and Wilhelmi, (2019) Retrospective comparative observational study Location: USA	30 patients undergoing reconstructive surgery by a single surgeon for sternal wound complications.	Intervention V.A.C. Veraflo using 1/8th strength Dakin's solution as the instillation fluid. Dwell time: 20 minutes NPWT (-125 mm Hg). Dressings changed every 72 hours. n = 15. Comparator Treatment with wet-to-moist dressings soaked in 1/8th strength Dakin's solution. Dressings changed every 6 hours. n = 15.	• Time to wound closure • Number of therapy days • Number of excisional debridements • Drainage duration • Complications	Time to wound closure 7.9 ± 2.3 days (median 8 days) vs 13.9 ± 3.2 days (median 15 days), p < 0.0001. Number of therapy days 5.4 ± 2.1 days (median 6 days) vs 8.4 ± 3.0 days (median 8 days), p= 0.0041 Number of excisional debridements 1.8 ± 0.7 (SD) vs 3.1 ± 1.0, p = 0.0011. Drainage duration 15.0 ± 2.0 days (median 14 days) vs 21.7 ± 3.9 days (median 22 days), p = 0.0001 Complications None reported for intervention. Three patients had	The study was not methodologically robust enough to interpret the results with confidence. The indication for V.A.C. Veraflo in this study was very specific. Results cannot be generalised to other populations.

				seromas in the comparator group, p = 0.22.	
Deleyto et al., (2018) Retrospective observational study with economic analysis Location: Spain	45 patients diagnosed with abdominal wall wound dehiscence and presenting with abdominal mesh exposure.	Intervention V.A.C. Veraflo using hypertonic saline as instillation fluid. Dressings changed every 3 days. n = 11. Comparator: Conventional dressings. n = 34.	• Number of hospitalisation episodes • Number of additional surgeries • Length of hospital stay • Cost analysis	Number of hospitalisation episodes 3.59 ± 3.19 vs 1.64 ± 0.67, p = 0.003 Number of additional surgeries 0.82 ± 0.75 (SD) vs 2.29 ± 2.11, p = 0.009. Length of hospital stay 69.1 ± 33.6 days vs 88.2 ± 77.1 days, p = 0.745. Cost analysis Difference in total overall costs were €14,520 (95% CI €4459 to €24,581) in favour of intervention.	The study was not methodologically robust enough to interpret the results with confidence. This was primarily a Spanish economic study. The results were not generalisable to the UK.

Omar et al., (2016) Prospective observational study with historical cohorts Location: Germany Study obtained support from KCI for the surgical material.	20 patients with acute wounds of the lower limb (infected or traumatic).	Intervention V.A.C. Veraflo using saline as the instillation fluid. Dwell time: 15 minutes, cycle length: 4 hours. n=10. Comparator NPWT using V.A.C. Ulta without instillation. n = 10.	• Surgeries required • Time to wound closure (days) • Length of hospital stay • Wound size (cm^2)	Surgeries required Median with (IQR); 3.0 (2.0 to 4.3) vs 3.0 (2.8 to 5.3) Wilcoxon rank-sum test (p = 0.65) Time to wound closure (days) Median with (IQR) (days); 9.0 (7.0 to 19.3) vs 12.5 (7.8 to 23.3), p = 0.35) Length of hospital stay Median with (IQR) (days); 21.5 (15.5 to 32.0) vs 26.5 (18.5 to 33.3) Wilcoxon rank-sum test (p = 0.43) Wound size (cm^2) Median with (IQR); 144.0 (33.5 to 855.0) vs 240.0 (152.5 to 459.0) Wilcoxon rank-sum test (p = 0.41)	The study was not methodologically robust enough to interpret the results with confidence. The results cannot be generalised to other populations (very broad inclusion criteria with low patient numbers in each category).

Gabriel et al., (2014) Retrospective observational study with historical controls. Economic analysis. Location: USA	82 patients with infected or critically colonised extremity and trunk wounds.	Intervention V.A.C. Veraflo using Prontosan or saline as the instillation fluid. Dwell time: 1 to 60 seconds, cycle length: 1-2 hours NPWT (-125 mm Hg). Dressing changes occurred every 2 to 3 days. n = 48 Comparator NPWT with V.A.C. GranuFoam Dressing or V.A.C. GranuFoam Silver Dressing -125 mm Hg. Dressing changes occurred every 2 to 3 days. n = 34.	• Number of surgical debridements • Length of hospital stay • Length of therapy • Time to wound closure • Cost analysis	Number of surgical debridements 2.0 vs 4.4, p < 0.0001 Length of hospital stay 8.1 days vs 27.4 days, p < 0.0001. Length of therapy 4.1 days vs 20.9 days, p <0.0001. Time to wound closure 4.1 days vs 20.9 days, p <0.0001. Cost analysis Total therapy costs were less with the intervention ($799 vs $2217, difference $1418)	The study was not methodologically robust enough to interpret the results with confidence
Kim et al., (2014) Retrospective cohort study	142 patients with infected wounds requiring admission with at least 2 operative debridements	Intervention V.A.C. Veraflo using Prontosan as the instillation fluid. Dwell time: 6 minutes (n=34),	• Number of operating room visits • Length of hospital stay	Number of operating room visits 6 min dwell time; 2.4 ± 0.9 vs 3.0 ± 0.9 (SD), p = 0.04	The study was not methodologically robust enough to interpret the

Location: USA	and who have received either NPWT or NPWTi application at the time of the initial operation.	cycle length: 3.5 hours NPWT (-125 mm Hg); dwell time: 20 minutes (n=34), cycle length: 2 hours NPWT (-125 mm Hg) <u>Comparator</u> NPWT using Info V.A.C. Therapy System (historical controls for the same 6-month period separated by exactly 1 year). −125 mm Hg continuous negative pressure. n = 74.	• Time to final surgical procedure • Wound closure • Wound closed at 1 month • Culture improvement with Gram-negative, Corynebacterium, and yeast excluded	20 min dwell time; 2.6 ± 0.9 vs 3.0 ± 0.9 (SD), p = 0.003 <u>Length of hospital stay</u> 6 min dwell time; 11.9 ± 7.8 days vs 14.92 ± 9.2 days, p = 0.10 20 min dwell time; 11.4 ± 5.1 days vs 14.92 ± 9.2 days, p = 0.03 <u>Time to final surgical procedure</u> 6 min dwell time; 7.8 ± 5.2 vs 9.23 ± 5.2, p = 0.04 20 min dwell time; 7.5 ± 3.1 vs 9.23 ± 5.2, p = 0.002 <u>Wound closure</u> 6 min dwell time; 94% improvement, p = 0.0004. 20 min dwell time; 80% improvement, p = 0.08.	results with confidence. The results cannot be generalised to other populations (very broad inclusion criteria with low patient numbers in each category).

				Wound closed at 1 month 6 min dwell time; 75% vs 61%, p=0.23 20 min dwell time; 52% vs 61%, p = 0.47 Culture improvement with Gram-negative, Corynebacterium, and yeast excluded 6 min dwell time; 90% vs 63%, p = 0.001 20 min dwell time; 65% vs 63%, p=0.77.	
Goss et al., (2012) Prospective comparative cohort study Location: Italy	13 patients (16 wounds) with chronic lower extremity wounds demonstrating significant bioburden.	Intervention V.A.C. Veraflo using 1/4 strength Dakins solution as the instillation fluid. Dwell time: 10 minutes, cycle length: 60 minutes NPWT (-125 mmHg). n = 7 (1 patient received both NPWTi and NPWT)	• Bacterial load	Bacterial load The mean absolute reduction in bacteria after 7 days of 10.6 x 106 per gram of tissue vs an increase of 28.7 x 106 bacteria per gram of tissue, p = 0.016.	The results cannot be generalised to other populations. Sample was heterogeneous and small. The study was not methodologically robust enough to interpret the

		Comparator NPWT 125 mmHg. n = 7.			results with confidence.
Abbreviations: CFU/g, colony forming units per gram tissue; CI, confidence interval; ITT, intention to treat (group); NPWT, negative pressure wound therapy; NPWTi, negative wound therapy with instillation; PCR; polymerase chain reaction; RCT, randomised controlled trial.					

4.2 Summary of economic evidence

The company provided details of studies used to inform parameters in their de novo cost modelling but did not identify any published studies that were reported as economic studies in their own right. The EAC did their own economic literature search (see appendix D of the EAC assessment report). Overall, 4 studies were identified (Deleyto et al. 2017; Gabriel et al. 2014; Yang et al., 2015; Latouche and Devillers, 2020), 3 of which had already been identified as part of the clinical literature search. The EAC stated that results from these studies should be treated with caution because the reporting quality of these studies was lacking and did not provide robust economic data. According to the EAC, all of these studies were somewhat relevant but were not considered to be of adequate quality to undergo formal critical appraisal (see section 9.1.2 of the EAC assessment report).

De novo analysis

The company presented a cost calculator model using a cost consequence analysis framework that compared V.A.C. Veraflo with either negative pressure wound therapy or advanced wound care. The EAC highlighted some structural uncertainties in the model which were mainly due to the population and patient pathway. The EAC felt that the population as not clearly defined in the company's economic submission. The company base case evaluated 4 clinical scenarios: lower limb, mixed wounds, prosthetic implant (for advanced wound care comparator only), and surgical site infections. The company then combined the data for these scenarios to estimate an aggregated total cost that the it claims is reflective of the whole population. The EAC did not agree with this approach, noting that populations were not mutually exclusive and likely to overlap in an undefined way. They also noted that parameters were calculated by the company using simple averages without weighting by study sample size or underlying population prevalence. The EAC also highlighted that the model includes the requirement for surgical debridement after treatment in every scenario, which clinical experts advise may not be needed for all patients captured by the model. The company's model structure is

shown in figure 1 and is described in section 9.2.1 of the EAC assessment report (page 71).

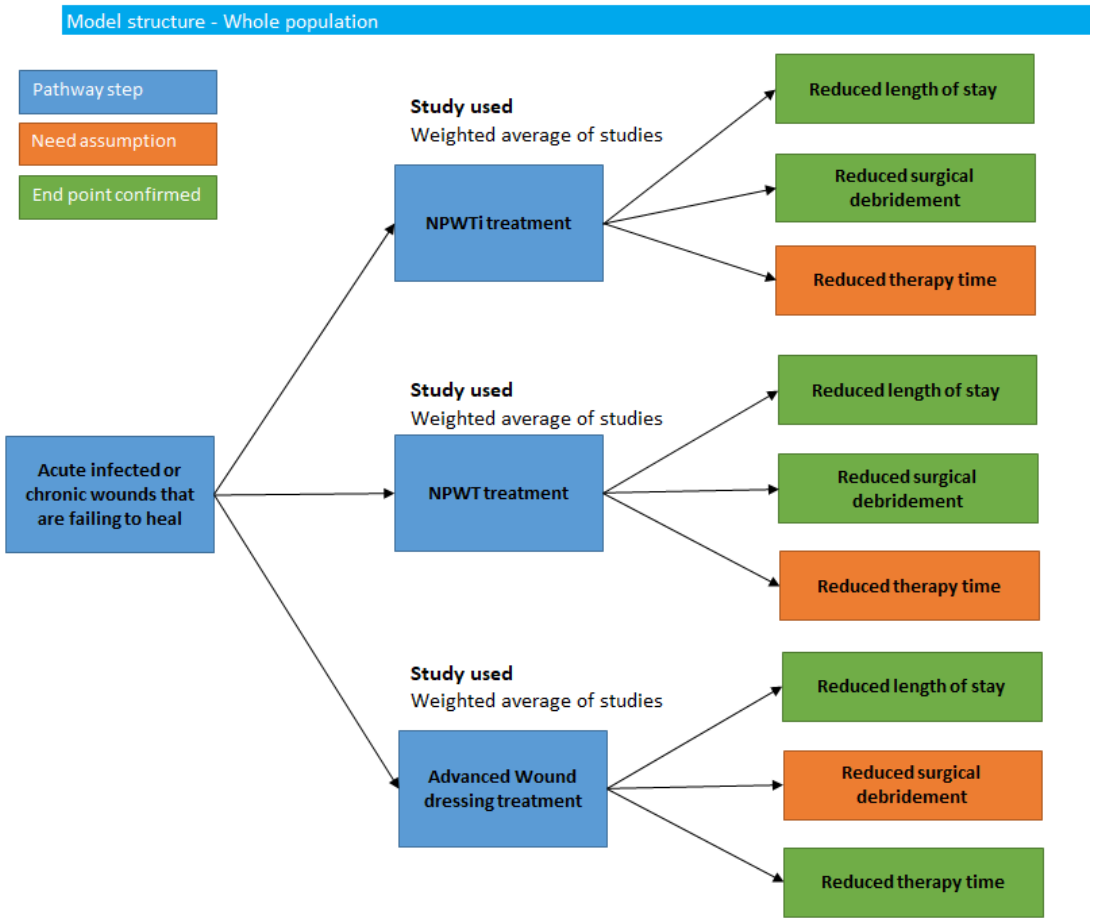
The company's model made several assumptions which can be found in table C1 of the EAC assessment report (page 128) along with the EAC's critique. Many of the assumptions were of clinical parameters that could not be sourced from an individual study (discussed further in 'model clinical parameters' section of this document). Other assumptions included:

- There is a need for surgical debridement following treatment and that the number of operating room visits / operations were for the purpose of a debridement only – the EAC considered there may be multiple reasons for operating room attendances other than surgical debridement. In addition, advice from clinical experts is that surgical debridement is often not the first-line method of debridement in many patients within the scope and that some patients may be discharged and treated using less intensive nurse-led forms of debridement in clinics.

- Canisters, cassettes and dressing kits need changing three times per week – the EAC felt this was likely based on the technology's instructions for use.

- Nurse training time on V.A.C. Veraflo was assumed to be negligible – EAC agreed that training costs are unlikely to have a substantial cost impact in the long term.

Figure 1 Company economic model structure



The EAC considered the company's validation process to be inadequate and felt more key opinion leaders covering more specialties should have been enrolled. The EAC also found an error in the company's written economic submission where therapy costs of scenario analysis were included instead of base-case therapy cost for the V.A.C. Veraflo and negative pressure wound therapy arms. The errors were confirmed by the company and the corrected results are presented in the EAC assessment report.

Model clinical parameters

The main parameters driving the model related to length of stay, length of therapy and number of surgical debridements. The company derived these parameters from 7 comparative studies identified in the clinical evidence section of their submission. Three of these studies were used to inform

parameters for the comparison with negative pressure wound therapy (Kim et al., 2014; Gabriel et al., 2014; Jurkovic et al., 2019) and 4 were used for the comparison with advanced wound care (Gabriel et al., 2008; Timmers et al., 2009; Deleyto et al., 2018; Chowdhry and Wilhelmi, 2019). Details of these studies as well as the EAC's views on the company's study selection and data extraction can be found in section 9.2.3 (page 79) and in table C4 (page 137) of the EAC assessment report.

The EAC noted that the clinical parameters in the company model were mainly from retrospective studies of low methodological quality and felt that these studies did not adequately demonstrate an association between the interventions and the reported outcomes. Also, some of the studies involved people that did not match with the scenario described by the study or there was not enough information reported in the study to determine whether the study population was appropriate. In studies that did not report all 3 clinical parameters, the company combined data from another study to estimate the missing model parameter.

The EAC also noted that the company had used data from 3 studies that were considered to be out of scope by the EAC in the clinical evaluation because they reported on the predecessor technology (Gabriel et al. 2008, Jurkovic et al. 2019, Timmers et al. 2009). The EAC accepted these studies for the purpose of economic modelling but noted that they added an extra source of uncertainty into the model.

The EAC made the following changes to improve accuracy and consistency:

- Only used data reported within a single study. In the absence of data, the EAC made the following assumptions: length of stay was assumed to be the same as length of therapy; and when a study did not explicitly report number of surgeries/debridement in both arms, no debridement costs were incurred.

- Used data from Kim et al. (2010) to inform the base case scenario. This study was regarded by the EAC as the most robust evidence and most representative of a base case because of the mixed study population. Kim et al. (2020) did not report length of stay so this was assumed by the EAC to be equal to length of therapy.

- Included additional scenarios using data from the studies that were not included by the company (Kim et al. [2020] and Omar et al. [2016]). Both studies reported no statistical difference in the key results used to inform the model (see table 9.1 of EAC assessment report, page 80).

Costs and resource use

The cost parameters of the company base case model include the following:

- Direct costs associated with the interventions themselves

- Debridement costs due to repeated surgical debridement after starting treatment

- Hospital stay costs associated with excess bed stay in hospital before discharge

The company derived all direct therapy costs from NHS supply chain. For V.A.C. Veraflo, the direct costs included an average cost for dressings (3 different types of V.A.C. Veraflo dressings in various sizes), costs associated with the V.A.C. Veralink canister and V.A.C. Veralink cassette, and a daily rental charge for the V.A.C. Ulta negative pressure wound therapy device. The cost of instillation fluids was not included. The costs associated with negative pressure wound therapy without instillation were based on the rental costs for the V.A.C. Ulta device, and costs for negative pressure wound therapy canisters and medium foam dressings. The costs associated with advanced wound care were based on Aquacel (ConvaTec Inc.) and Alleyvn (Smith & Nephew plc) dressings.

Theatre costs for surgical debridement were based on average theatre costs per hour by specialty (Public Health Scotland, 2019). The theatre cost per minute (£13.37) was then multiplied by the duration of debridement (17.7 minutes; estimated using data from Caputo *et al.*, [2008] RCT), to give a cost of £237 per surgical debridement. This cost was applied regardless of the intervention.

The costs of length of stay were based on excess bed days as reported by NHS Reference Cost (2017/2018).The company used subchapter healthcare resource groups for mixed wounds and prosthetic implants, whilst national average costs were used for the other 2 scenarios (lower limb and surgical site infections). The EAC noted that this parameter was the main driver of the model. This is because one day of length of stay was around twice as costly as one surgical debridement, and length of stay was significantly higher in the comparator groups compared with V.A.C. Veraflo.

The EAC made the following changes to the model:

- Updated all direct therapy costs to reflect the latest costs on NHS Supply Chain (April 2020).
- Revised the surgical debridement theatre costs using the most up-to-date cost, averaged across all relevant specialties (increased hourly theatre costs from £802 to £989)
- Applied the national average costs for length of stay (using excess bed days) to all subgroups (maintained at £431 for each subgroup)
- Removed the additional procedural costs for the prosthetic implant subgroup that were included by the company

The company base case cost values and sources, as well as the EAC's changes are shown in table C4, and described in detail in section 9.2.4 of the EAC assessment report.

Table 3 Base case costs and EAC changes

Parameter	Company base-case	EAC base-case	Source	Comments
V.A.C. Veraflo dressing cost	£77.76	Average dressing cost increased to £84.36	NHS Supply Chain (April 2020):	Used latest costs on NHS Supply Chain (April 2020)
V.A.C. Veralink cassette cost	£21.52	Decreased to £19.37	NHS Supply Chain (April 2020):	Used latest costs on NHS Supply Chain (April 2020)
V.A.C. Veralink canister cost	£47.23	Decreased to £44.51	NHS Supply Chain (April 2020):	Used latest costs on NHS Supply Chain (April 2020)
Negative pressure wound therapy canister cost	[redacted]	Decreased to [redacted]	NHS Supply Chain (April 2020):	Used latest costs on NHS Supply Chain (April 2020)
Negative pressure wound therapy dressing cost	[redacted]	Average dressing costs increased to [redacted]	NHS Supply Chain (April 2020): average of small, medium and large granufoam dressings	Used latest costs on NHS Supply Chain (April 2020)
Advanced wound care Allevyn gentle border 10 cm x 10 cm	[redacted]	Decreased to [redacted]	NHS Supply Chain (April 2020):	Used latest costs on NHS Supply Chain (April 2020)
Advanced wound care Aquacel 10 cm x 10 cm	[redacted]	Decreased to [redacted]	NHS Supply Chain (April 2020):	Used latest costs on NHS Supply Chain (April 2020)
Hourly theatre costs	£802.20	Increased to £989		Using average theatre costs (ISD 2019) across all specialities

Cost per bed night	£431 for lower limb, £375.79 for mixed wound, £391.62 prosthetic implant, £431 for surgical site infection	Maintained at £431 for each subgroup/indication	NHS Reference costs 2017/18	Using average excess bed day costs across all healthcare resource groups
Additional procedural costs included for prosthetic implant subgroup only (simple wound closure, debridement and closure, mesh removal, mesh replacement)	From data reported in Deleyto et al. (2018)	Removed	N/A	Costs are derived from healthcare resource group codes (which are broad and will include a range of other procedures which are irrelevant to the scope). Additional procedure costs not considered for other arms. Minimal impact on debridement costs.

Results

The company estimated a cost saving from the use of V.A.C. Veraflo of -£3,251 per patient compared with negative pressure wound therapy and £8,312 per patient compared with advanced wound care. In the company's model, the technology had higher therapy costs, but this was outweighed by cost savings associated with reduced length of stay and surgical debridement. The EAC's base case (using data from Kim et al [2020] only) found V.A.C. Veraflo to be more costly than negative pressure wound therapy for all cost domains (LoS, therapy and debridement), with an overall cost difference of +£480 per patient for the technology. The EAC did not report a base case for V.A.C. Veraflo compared with advanced wound care because it considered there was insufficient data to inform this analysis. The company and EAC base case results are presented in tables 4 and 5.

Table 4 ***Company and EAC base case results for comparison of V.A.C. Veraflo and negative pressure wound therapy***

	Company base case (corrected)			EAC base case		
	V.A.C. Veraflo	Negative pressure wound therapy	Mean cost difference per patient	V.A.C. Veraflo	Negative pressure wound therapy	Mean cost difference per patient
Length of stay	£5,741	£8,880	-£3139	£2,555	£2,386	£169
Therapy	£919	£716	£203	£526	£258	£268
Debridement	£505	£820	-£316	£260	£237	£23
Total	£7,165	£10,416	**-£3,251**	£3,342	£2,862	**£480**

Table 5 ***Company base case results for comparison of V.A.C. Veraflo and advanced wound care***

	Company base case (corrected)		
	V.A.C. Veraflo	Advanced wound care	Mean cost saving per patient
Length of stay	£12,309	£20,623	-£8,314
Therapy	£1,136	£149	£986
Debridement	£534	£1,519	-£984
Total	£13,979	£22,291	**-£8,312**

Sensitivity analysis

The company's sensitivity analysis included scenario analyses (reporting results from the individual disaggregated scenarios), one-way deterministic sensitivity analysis, and probabilistic sensitivity analysis on the base case results and all the contributing scenarios. The main driver of the cost savings was the reduction in length of stay, as shown by the deterministic sensitivity analysis. Changes to individual parameters did not change the overall direction of cost saving. The company reported that V.A.C. Veraflo was cost saving in all 4 scenarios (ranging from £300 to £13,403). In 3 scenarios, probabilistic sensitivity analysis showed the probability of the technology being cost saving was ≥ 94% (58% for surgical site wounds).

The EAC conducted additional scenario analyses which included data from two studies that were not included by the company. Table C5a and C5b of the EAC assessment report show the differences in cost savings estimated by the company and the EAC and the impact of the EAC's changes across all scenarios. In the EAC's scenario analyses V.A.C. Veraflo was cost saving in all scenarios except for the EAC base case scenario (£480 cost incurring). Cost savings were mainly due to savings in length of stay (accounting for 70-95% reduction in costs). The EAC performed PSA on the data at a scenario level (excluding fixed costs such as technology costs; please see table 9.6 of the external assessment centre's report). Probabilistic sensitivity analysis results on the EAC base case found that V.A.C. Veraflo was potentially cost incurring by £471 (95% credibility interval -£1085 to £2015). The EAC's probabilistic sensitivity analysis on all scenarios showed that cost savings with V.A.C. Veraflo were highly likely in 3 out of 9 scenarios but there was considerable uncertainty in the other 6 scenarios. The EAC concluded that the cost saving potential of V.A.C. Veraflo is uncertain.

5 Ongoing research

The company did not identify any ongoing studies in their submission. The EAC identified 1 ongoing and a completed study (not peer-reviewed or published). Details of these 2 studies can be found in table 8.1 of the EAC assessment report (page 68). The EAC did not believe these studies would significantly add to the evidence base because they had small sample sizes and lacked overall generalisability.

6 Issues for consideration by the Committee

Clinical evidence

The clinical evidence base consisted of 9 comparative studies (3 RCTs and 6 observational studies) and 10 single arm studies which covered a mix of various wound types and comorbidities. In addition, none of the included clinical studies were done in the UK. Clinical experts have noted that NHS treatment pathways may vary substantially from those used in other countries; for example, the use of laboratory culture to guide requirement for debridement is not practised in the UK (EAC External correspondence log, 2020). The heterogenous mix of patients included in the studies as well as uncertainties around the patient pathways makes it difficult generalise data to the NHS.

Whilst most of the published evidence for V.A.C. Veraflo reported positive outcomes, the evidence mainly consisted of retrospective observational studies which may have been insufficient in methodological quality to confidently draw conclusions on the claimed benefits of the technology. Results from the Kim et al (2020) RCT, which was deemed to be the most robust source of evidence, did not report statistically significant clinical benefits of V.A.C. Veraflo compared with negative pressure wound therapy. Although the study showed statistically significant reductions in bacterial bioburden with the technology, this was considered a surrogate outcome not directly related to clinical endpoints. None of the studies reported patient

reported outcome measures or health-related quality of life so the impact of the technology from a patient perspective is not well understood. There was also not enough data published to make a meaningful comparison with advanced wound care, only 2 of the included studies evaluated this comparison. However, advice from clinical experts was that advanced wound care may not be the most relevant comparator since advanced wound care would have been used earlier in the pathway, and/or subsequent to V.A.C. Veraflo or negative pressure wound therapy.

The main comparator of V.A.C. Veraflo is negative pressure wound therapy. However, the evidence base for negative pressure wound therapy itself is generally poor and there appears to be no firm conclusions on the effectiveness of the procedure. NICE clinical guidelines have made only limited recommendations for negative pressure wound therapy.

Despite a lack of robust evidence for V.A.C. Veraflo, it was noted that the technology does have plausible benefits and that all clinical experts involved in the development of this guidance were supportive of the technology, and unanimously believed it had clinical benefits in appropriately selected patients. Experts stated that the instillation feature of the technology was a substantial advancement to negative pressure wound therapy alone. The ability to washout the wound and instill solution, in their opinion, leads to faster granulation, reductions in contamination and biofilm and improvements in healing times. One of the experts felt that this technology is one of the biggest innovations in wound care for many years and has a positive impact for patients. Another stated that the technology was a “game changer”, adding that it reduces length of stay and is capable of preventing patients from returning to theatre for washout procedures.

Cost evidence

No useful published economic studies were identified. The economic model submitted by the company assumed that surgical debridement was needed following treatment. Clinical experts advised that this pathway may not be fully

representative of NHS practice for some patients in the scope, explaining that a number of patients may be discharged and treated using less intensive nurse-led forms of debridement in clinics.

The company's economic model reported large cost savings associated with the technology, mainly driven by a reduction in hospital LoS. After the EAC changes to the model, V.A.C. Veraflo was shown to be cost incurring by £480. The EAC's PSA analysis however, highlighted that this estimate was associated with considerable uncertainty (average cost expenditure of £471 [95% credibility interval -£1085 to £2015]).

The main change the EAC made to the company model was including data from an RCT (Kim et al. 2020). However, the limitation of this change was that the RCT did not report on the length of stay for the whole cohort, so this was assumed to be the same as length of therapy. This assumption may negatively impact the cost saving estimates for the technology, since the main driver of cost savings in the company model was a reduction in length of hospital stay.

Although the EAC changes were aimed at improving the accuracy and consistency of the model, in the opinion of the EAC, its analysis was subject to much of the same limitations as the company's because there is inadequate clinical evidence to inform meaningful economic analysis. The EAC concluded that the cost-saving potential of V.A.C. Veraflo remains unknown.

7 Authors

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NICE Medical Technologies Evaluation Programme

August 2020

Appendix A: Sources of evidence considered in the preparation of the overview

Details of assessment report:

- Willits I, Keltie K, Richmond C, et al. V.A.C. Veraflo Therapy System for acute infected or chronic wounds that are failing to heal, July 2020.

Submissions from the following sponsors:

- 3M+KCI

Related NICE guidance

Published

- Pressure ulcers: prevention and management (2014) NICE guideline CG179
- Diabetic foot problems: prevention and management (2015) NICE guideline NG19. Last updated: January 2016
- Negative pressure wound therapy for the open abdomen (2013) NICE interventional procedures guidance IPG467.
- PICO negative pressure wound dressings for closed surgical incisions (2019) NICE medical technologies guidance MTG43
- The MIST Therapy system for the promotion of wound healing (2011) NICE medical technologies guidance MTG5
- The Debrisoft monofilament debridement pad for use in acute or chronic wounds (2014) NICE medical technologies guidance MTG17
- Prevena incision management system for closed surgical incisions (2019) NICE advice MIB173
- The Versajet II hydrosurgery system for surgical debridement of acute and chronic wounds and burns (2014) NICE advice MIB1.

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Appendix B: Comments from professional bodies

Expert advice was sought from experts who have been nominated or ratified by their Specialist Society, Royal College or Professional Body. The advice received is their individual opinion and does not represent the view of the society.

Mr David Russell

Consultant Vascular Surgeon and Honorary Clinical Associate Professor, Leeds General Infirmary, [professional society]

Mr Haitham Khalil

Consultant Oncoplasty and Reconstructive Surgeon, Division of Plastic and Reconstructive Surgery, University Hospitals Birmingham,

Dr Fania Pagnamenta,

Clinical Academic Nurse Consultant (Tissue Viability), Newcastle upon Tyne Hospitals NHS Foundation Trust,

Ms Claire Porter,

Advanced Nurse Practitioner; lead nurse burns and plastics, Leicester Hospitals NHS Foundation Trust

Patricia Littlewood,

Lead Tissue Viability Clinical Nurse Specialist, Frimley Health Foundation Trust (Wexham Site),

Vicki Tapley

Advanced Specialist Podiatrist, The Royal Free Hospital Foundation Trust,

Please see responses to the expert advisor questionnaire (EAQ) included in the committee pack for full details.

Appendix C: Comments from patient organisations

The following patient organisations were contacted and no response was received.

- British Skin Foundation
- Leg Ulcer Charity
- Pressure Ulcers UK
- Leonard Cheshire disability
- British Obesity Surgery Patients Association (BOSPA)
- Children's Burn Trust (CBT)
- Colostomy Association
- Crohn’s and Colitis UK (NACC)
- Diabetes UK
- Foot in Diabetes UK
- IA (Ileostomy and Internal Pouch Support Group)

Appendix D: Decision problem and claimed benefits from scope

The benefits to patients claimed by the company are:

- Reduced wound healing time by combining the benefits of negative pressure wound therapy with automatically instilling solutions to remove infectious material
- Reduced number of surgical debridements, resulting in fewer painful procedures and possible general anaesthetics
- More patients leaving hospital with closed wounds allowing them to return to normal daily activities
- Reduced hospital length of stay

The benefits to the healthcare system claimed by the company are:

- Patients discharged more quickly
- Reduction in follow on treatment costs
- Overall reduction in staff and resource use

Population	Patients with acute infected or chronic wounds that are failing to heal
Intervention	The V.A.C. Veraflo Therapy system
Comparator(s)	• Standard advanced wound dressings (e.g. hydrogel dressings, hydrocolloid dressing, capillary-acting dressings, alginate dressings) • Negative pressure wound therapy
Outcomes	The outcome measures to consider include: Clinical management outcomes: • Length of stay in hospital • Rates of partial and complete wound closure (which may vary depending on wound type, location, depth and size) • Mean time to partial or complete wound closure • Mean time to healing • Number of dressing changes

	• Number of follow on treatments and visits to hospital • Number of surgical debridements • Number of amputations or skin grafts • Staff time and use of other consumables • Colonisation with antimicrobial resistant pathogens • Antibiotic use Patient outcomes: • Health-related quality of life • Patient satisfaction and acceptability • Patient-related outcomes such as pain scores • Device-related adverse events.	
Cost analysis	Costs will be considered from an NHS and personal social services perspective. The time horizon for the cost analysis will be long enough to reflect differences in costs and consequences between the technologies being compared. Sensitivity analysis will be undertaken to address uncertainties in the model parameters, which will include scenarios in which different numbers and combinations of devices are needed.	
Subgroups to be considered	• Diabetic ulcers • Pressure ulcers • Surgical site infections • Venous leg ulcers • Wounds containing prosthetic implants	
Special considerations, including those related to equality	People who are older or physically disabled are more likely to suffer chronic and complex wounds. People with certain family origins are more prone to poor wound healing due to increased risk of diabetes. Age, disability, and race are protected characteristics.	
Special considerations, specifically related to equality	Are there any people with a protected characteristic for whom this device has a particularly disadvantageous impact or for whom this device will have a disproportionate impact on daily living, compared with people without that protected characteristic?	No
	Are there any changes that need to be considered in the scope to eliminate unlawful discrimination and to promote equality?	No
	Is there anything specific that needs to be done now to ensure the Medical Technologies Advisory Committee will have relevant information to consider equality issues when developing guidance?	No
Any other special considerations	Not applicable	

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Medical technology guidance scope

V.A.C. VERAFLO Therapy System for acute infected or chronic wounds that are failing to heal

1 Technology

1.1 Description of the technology

V.A.C. VERAFLO Therapy System (3M+KCI) combines negative pressure wound therapy (NPWT) and wound instillation with topical solutions, with the aim of promoting wound healing. Wound instillation is a controlled process in which topical solutions are slowly introduced to the wound bed where they remain for a defined period of time before being removed using negative pressure. Treatment is delivered in automated treatment cycles allowing wounds to be repetitively cleansed without the need for dressing removal.

V.A.C. VERAFLO therapy system consists of the following components:

- V.A.C. ULTA therapy unit – delivers V.A.C. VERAFLO therapy (NPWTi-d; Negative Pressure Wound Therapy with instillation and a dwell time)
- Exudate canister – single-patient use, disposable canister (500, or 1000ml) which collects exudate/fluid
- V.A.C. VERALINK Cassette – instillation cassette which connects the solution bag/bottle and dressing tubing to the V.A.C.ULTA unit
- V.A.C. VERAFLO Dressing Kit of clinician's choice (V.A.C VERAFLO dressing, V.A.C. VERAFLO CLEANSE dressing or V.A.C. VERAFLO CLEANSE CHOICE dressing). The V.A.C. VERAFLO Dressing Kits includes the appropriate dressing as well as V.A.C. VERAT.R.A.C. Pad

with tubin, V.A.C. Advanced Drape and 3M Cavilon No Sting Barrier Film.

- Manufacturer's approved topical wound solution of clinician's choice

The V.A.C. VERAFLO system can be used with a number of topical wound solutions and suspensions. Suitable solutions and suspensions should be those indicated for topical wound treatment in their instructions for use. They should also be compatible with V.A.C VERAFLO dressings and disposable components.

Before using the V.A.C. VERAFLO Therapy system, the V.A.C. VERAFLO dressing foam of the appropriate size is applied to the wound bed. A V.A.C. Advance Drape is then placed over the wound with a 3-cm margin to make sure there is full adhesion, with a small hole cut into the drape surface. The V.A.C. VERAT.R.A.C. Pad can then be attached to the drape, using a stabilisation layer to ensure complete contact. The pad is then connected to the V.A.C. ULTA therapy unit. This collects fluid and substances produced by the body in response to tissue damage in the wound into a single-use 500-ml or 1,000-ml canister. The V.A.C. ULTA therapy unit fill assist tool is used to determine and ensure an appropriate instillation volume has been applied and the SEAL CHECK leak detector feature allows the user to observe the dressing for leaks.

The V.A.C. VERAFLO Therapy system is applied by healthcare professionals in a hospital setting. Healthcare staff using the technology will need training provided by the company. The company provides online resources to reinforce the training

1.2 Relevant diseases and conditions

The V.A.C. VERAFLO Therapy system is used to treat acute infected or chronic wounds that do not respond to standard care and need additional therapy to promote healing and wound closure. The population who could potentially benefit from this technology is significant. It is estimated that over 2 million patients a year have treatment for a wound, 48% of which are

considered chronic. Guest et al. (2015) reported that 79% of acute wounds and 43% of chronic wounds heal within 12 months. Results from this study suggest that approximately 21% of acute wounds and 57% of chronic wounds may not respond to standard care and may need additional therapy.

1.3 Current management

There are a number of clinical situations that may result in acutely infected or chronic non-healing wounds, such as surgical site infections, diabetic foot problems and pressure ulcers, for which NICE has published recommendations and advice.

Care of acutely infected or chronic non-healing wounds is targeted towards promoting healing and minimising risk of further complications. If infection of the wound is suspected, a microbiological sample is taken and an antibiotic prescribed to treat the causative organisms. The wound is treated with regular cleansing and debridement followed by the application of a dressing. Hospital staff choose a dressing that will promote healing and manage exudate on a case-by-case basis. Some wounds are treated with negative pressure wound therapy. Chronic non-healing wounds typically need more advanced dressings. Patients may be referred to a specialist for multidisciplinary care and the need for this varies depending on the cause of the wound.

NICE has also issued guidance on the use of negative pressure wound therapy for the open abdomen, which recommends the use of NPWT in patients at risk of developing surgical site infections.

1.4 Regulatory status

V.A.C. VERAFLO Therapy system received a CE mark in March 2017 as a class II medical device. Each component part of the system including sterile foam dressing kits and tube sets, and electrically powered accessories are also individually CE marked.

1.5 Claimed benefits

The benefits to patients claimed by the company are:

- Reduced wound healing time by combining the benefits of NPWT with automatically instilling solutions to remove infectious material
- Reduced number of surgical debridements, resulting in fewer painful procedures and possible general anaesthetics
- More patients leaving hospital with closed wounds allowing them to return to normal daily activities
- Reduced hospital length of stay

The benefits to the healthcare system claimed by the company are:

- Patients discharged more quickly
- Reduction in follow on treatment costs
- Overall reduction in staff and resource use

2 Decision problem

Population	Patients with acute infected or chronic wounds that are failing to heal
Intervention	The V.A.C. VERAFLO Therapy system
Comparator(s)	• Standard advanced wound dressings (e.g. hydrogel dressings, hydrocolloid dressing, capillary-acting dressings, alginate dressings) • Negative pressure wound therapy
Outcomes	The outcome measures to consider include: Clinical management outcomes: • Length of stay in hospital • Rates of partial and complete wound closure (which may vary depending on wound type, location, depth and size) • Mean time to partial or complete wound closure • Mean time to healing • Number of dressing changes • Number of follow on treatments and visits to hospital • Number of surgical debridements • Number of amputations or skin grafts • Staff time and use of other consumables • Colonisation with antimicrobial resistant pathogens • Antibiotic use

	Patient outcomes: • Health-related quality of life • Patient satisfaction and acceptability • Patient-related outcomes such as pain scores • Device-related adverse events.	
Cost analysis	Costs will be considered from an NHS and personal social services perspective. The time horizon for the cost analysis will be long enough to reflect differences in costs and consequences between the technologies being compared. Sensitivity analysis will be undertaken to address uncertainties in the model parameters, which will include scenarios in which different numbers and combinations of devices are needed.	
Subgroups to be considered	• Diabetic ulcers • Pressure ulcers • Surgical site infections • Venous leg ulcers • Wounds containing prosthetic implants	
Special considerations, including those related to equality	People who are older or physically disabled are more likely to suffer chronic and complex wounds. People with certain family origins are more prone to poor wound healing due to increased risk of diabetes. Age, disability, and race are protected characteristics.	
Special considerations, specifically related to equality	Are there any people with a protected characteristic for whom this device has a particularly disadvantageous impact or for whom this device will have a disproportionate impact on daily living, compared with people without that protected characteristic?	No
	Are there any changes that need to be considered in the scope to eliminate unlawful discrimination and to promote equality?	No
	Is there anything specific that needs to be done now to ensure the Medical Technologies Advisory Committee will have relevant information to consider equality issues when developing guidance?	No
Any other special considerations	Not applicable	

3 Related NICE guidance

Published

Pathways:

- Pressure ulcers overview (2019) NICE Pathway
- Prevention and control of healthcare-associated infections overview (2019) NICE Pathway
- Foot care for people with diabetes overview (2019) NICE Pathway
- Skin conditions overview (2019) NICE Pathway

Guidelines:

- Surgical site infections: prevention and treatment (2019) NICE guideline NG125
- Pressure ulcers: prevention and management (2014) NICE guideline CG179
- Diabetic foot problems: prevention and management (2015) NICE guideline NG19. Last updated: January 2016

Guidance:

- UrgoStart for treating diabetic foot ulcers and leg ulcers (2019) NICE medical technologies guidance 42
- PICO negative pressure wound dressings for closed surgical incisions (2019) NICE medical technologies guidance 43
- Mepilex Border Heel and Sacrum dressings for preventing pressure ulcers (2019) NICE medical technologies guidance 40
- The Debrisoft monofilament debridement pad for use in acute or chronic wounds (2014) NICE medical technologies guidance 17. Last updated: March 2019
- moorLDI2-BI: a laser doppler blood flow imager for burn wound assessment (2011) NICE medical technologies guidance 2. Last updated: August 2017
- Parafricta Bootees and Undergarments to reduce skin breakdown in people with or at risk of pressure ulcers (2014) NICE medical technologies guidance 20

- The ReCell Spray-On Skin system for treating skin loss, scarring and depigmentation after burn injury (2014) NICE medical technologies guidance 21
- The MIST Therapy system for the promotion of wound healing (2011) NICE medical technologies guidance 5
- Negative pressure wound therapy for the open abdomen (2013) NICE interventional procedures guidance 467

Advice:

- Prevena incision management system for closed surgical incisions (2019) NICE medtech innovation briefing 173
- SEM Scanner for pressure ulcer prevention (2019) NICE medtech innovation briefing 182
- EpiFix for chronic wounds (2018) NICE medtech innovation briefing 139
- TopClosure Tension Relief System for wound closure (2017) NICE medtech innovation briefing 97
- Woundchek Protease Status for assessing elevated protease status in chronic wounds (2016) NICE medtech innovation briefing 83
- Mersey Burns for calculating fluid resuscitation volume when managing burns (2016) NICE medtech innovation briefing 58
- The Juxta CURES adjustable compression system for treating venous leg ulcers (2015) NICE medtech innovation briefing 25
- Oxyzyme and Iodozyme 2-layer hydrogel wound dressings with iodine for treating chronic wounds (2014) NICE medtech innovation briefing 11
- The Versajet II hydrosurgery system for surgical debridement of acute and chronic wounds and burns (2014) NICE medtech innovation briefing 1

Quality standards:

- Pressure ulcers (2015) NICE quality standard 89

In development

NICE is developing the following guidance:

- Diabetic foot infection: antimicrobial prescribing. NICE guideline. Publication expected October 2019
- Leg ulcer infection: antimicrobial prescribing. NICE guideline. Publication expected February 2020
- Diabetic foot ulcers - new treatments. NICE guideline. Publication date TBC

4 External organisations

4.1 Professional

The following organisations have been asked to comment on the draft scope:

- Association of Breast Surgery
- Association of Surgeons of Great Britain and Ireland
- British Association for Surgery of the Knee
- British Association of Paediatric Surgeons
- British Association of Plastic Reconstructive and Aesthetic Surgeons
- British Obesity and Metabolic Surgery Society
- British Obesity Surgery Society
- Royal College of Obstetricians and Gynaecologists
- Royal College of Surgeons
- Society of Vascular Nurses
- Surgical Dressing Manufacturers Association
- Society for Cardiothoracic Surgery in GB and Ireland
- British Association of Aesthetic Plastic Surgeons
- Primary Care Diabetes Society

4.2 Patient

NICE's Public Involvement Programme contacted the following organisations for patient commentary and asked them to comment on the draft scope:

- British Skin Foundation
- Leg Ulcer Charity
- Pressure Ulcers UK

- Leonard Cheshire disability
- British Obesity Surgery Patients Association (BOSPA)
- Children's Burn Trust (CBT)
- Colostomy Association
- Crohn’s and Colitis UK (NACC)
- Diabetes UK
- Foot in Diabetes UK
- IA (Ileostomy and Internal Pouch Support Group)

NICE National Institute for Health and Care Excellence

Adoption report: MTG 471 The V.A.C. Veraflo Therapy system for infected wounds

Summary

Adoption levers

- May encourage faster healing
- May reduce the need for surgical debridement in theatre
- May need less dressing changes compared to a standard dressing
- Manages large amounts of exudate

Adoption barriers

- Cost of the system
- Perceived poor quality of evidence to support its use by clinicians
- Staff training required prior to use
- Lack of awareness of the system by some clinicians

1. Introduction

This adoption report includes some of the benefits and difficulties that may be faced by organisations when planning to adopt the V.A.C. Veraflo therapy system into routine NHS use.

The technology described in this report is the V.A.C. Veraflo therapy system which includes:

- the device (reusable, hired on contract, manages the negative pressure system and alarms if there is a problem)
- dressings (choice of 3 types available in variable sizes, dressing packs include advanced drapes, pad and tubing set, barrier film and a disposable ruler)
- canister (for drainage)
- cassette (for solution delivery)

Issue date: April 2020

2. Contributors

Adoption information was gathered from the company and 8 NHS clinicians specialising in wound care (4 with direct experience of using the system). The table below provides more detail about the contributors and how the system has been adopted in their trust.

Site	Job title	Experience
1	Tissue viability clinical nurse specialist	Used on 62 patients in 2019 on general surgical and orthopaedic ward where wounds were infected, dehisced or released large amounts of exudate. Has been using for 6 years.
2	Vascular podiatrist	Used in 25 – 30 patients in 2019 on a vascular surgical ward on patients not fit for anaesthesia for surgical debridement in theatre. Has been using for 3 years.
3	Consultant colorectal and general surgeon	Used on 5 patients in 2019. All patients had necrotising fasciitis and system was applied after surgical debridement in theatre. Has been using for 2 years.
4	Lead tissue viability specialist nurse	Used on 3 patients in 2019 where patients were not fit for anaesthesia for surgical debridement in theatre and wounds developed an infection or dehisced. Has been using for 3 years.
5	Diabetes specialist podiatrist	No experience using the system but familiar with its use in plastic and vascular surgery in the trust.
6	Consultant oncoplastic surgeon (breast)	No experience using the system.
7	Professor of orthopaedic surgery - consultant knee surgeon	No experience using the system.
8	Consultant trauma orthopaedic surgeon	No experience using the system.

3. Standard practice in managing infected wounds without V.A.C Veraflo

Standard therapy without V.A.C. Veraflo for large (greater than 10cm^2) infected wounds includes irrigation with saline and surgical debridement. This is done in theatre by a surgeon, frequency will depend on ongoing wound assessment. The wound may be treated with antibiotic loaded cement beads or larval therapy. If the patient is having surgical debridement in theatre this would involve a general, local or spinal anaesthetic, depending on location of the wound, and the patient's condition. For smaller wounds bedside irrigation and debridement is common.

Most sites then use other negative pressure wound therapy (NPWT) for infected wounds with once or twice weekly dressing changes. Some sites use standard or honey dressings for infected wounds. The number of dressing changes depend on the amount of exudate from a wound (every 2 hours to 4 times a week).

4. Use of the V.A.C Veraflo in practice

Prior to using the system, a specialist trained in the use of V.A.C. Veraflo (surgeon, tissue viability nurse [TVN] or podiatrist) needs to assess the wound and decide on which dressing and device setting to use.

Sites report that where surgical debridement is required the V.A.C. Veraflo is applied in theatre by a surgeon. Where this degree of debridement is not required or where wounds can be managed on the ward, the trust's dedicated V.A.C. Veraflo specialist applies the system at the bedside. The ward nurses then take over subsequent bedside dressing changes.

Users can either use the default system setting or have the option of altering the soak time, cycle time and negative pressure setting. Setting preference varied between users, for example one user preferred a shorter soak and cycle time as they report this as a more effective setting for wound healing.

All users change the dressings twice weekly. The dressings and drape need cutting to size, and this is reported to be time consuming to get the right fit. The type of dressing and size is selected based on a wound assessment.

The average length of treatment is 2-3 weeks. If the wound is healing well, the patient would continue with standard NPWT.

Sites report that patients with V.A.C. Veraflo are generally kept in hospital. Open infected or chronic wounds require ongoing intensive nursing and medical support which community services may not be equipped to provide.

Most users have 2 devices in stock and the company is informed when one is used to issue a replacement in accordance to their contract.

Genuine leaks are uncommon. Only 2 users reported having a problem with a leak and this was either due to wound location (non-flat area such as the groin) or the cassette cap not being sealed sufficiently.

Users have a choice of which wound irrigation solution to use, this includes saline, Octenilin and Prontosan depending upon an assessment, for example whether the wound is infected. No issues have been reported with the solutions or container compatibility with the system.

If the patient requires mobilisation the integral rechargeable battery which can provide up to 6 hours power is used. A drip stand or wheelchair is used to hold the device as it is heavy and bulky. No users reported any incidents with the battery.

The company report that 73 NHS trusts had a V.A.C. Veraflo account with the company within the UK at January 2020.

5. Reported benefits

The potential benefits of adopting the V.A.C. Veraflo, as reported to the adoption team by the healthcare professionals using the system or with expertise in this area are that it:

- may encourage faster healing

- may reduce the need for surgical debridement in theatre
- may need less dressing changes compared to a standard dressing
- manages large amounts of exudate

6. Insights from the NHS

Patient selection

No sites have a specific patient selection criterion but used the system in the following circumstances:

- patients previously requiring surgical debridement in theatre
- patients unfit for anaesthesia for surgical debridement in theatre
- infected wounds
- dehisced wounds
- necrotising fasciitis
- highly exudating wounds

The decision to use the system is made by a multidisciplinary team (MDT), at a ward round, by the trust's dedicated V.A.C. Veraflo specialist or a surgeon.

There was uncertainty about the number of patients who would be suitable for V.A.C. Veraflo therapy. Some were concerned that ward nurses may not remain competent in using the system if usage is low and that it may be best placed in a specialist or tertiary care service.

Clinician confidence

All contributors agreed the benefit of having V.A.C. Veraflo available for appropriate patients and all recognised the advantages of NPWT. Most agreed the evidence for the system to be of limited quality but that the potential for cost savings if surgical debridement in theatre can be avoided was a potential benefit.

Users reported that in most cases, nurses spend the same length of time with the V.A.C. Veraflo system compared to standard NPWT. There was agreement that the system generally used less nursing time than standard wound dressings.

There was no agreement on whether the system reduced length of stay. Patients are generally kept in hospital with V.A.C. Veraflo but can be discharged with a standard NPWT. Some users reported faster healing with the system enabling patients to be discharged earlier, but no site have data to support this.

One user explained that the lack of awareness of the system and how it works was an initial barrier at their trust. This user reported resistance from some surgeons who were reluctant to consider treatment with the system preferring to debride large infected wounds in theatre, despite potential cost savings.

Staff training and demonstrations are reported to have helped overcome staff reservations about the system appearing complicated.

Procurement

Most contributors agreed the initial financial outlay to stock V.A.C. Veraflo is a barrier to adoption, especially if usage is low. Three users have existing contracts with the company for standard V.A.C. NPWT. Training and the 24-hour 7 day per week helpline support are included for free as part of the contract .

Maintenance

The company state the rental contract model includes 6 or 12 monthly device servicing and repairs. Under some contracts the company decontaminate and quality control the device between patients if this is not available at the trust.

Training

The company offer tailored training. This includes off-site, webinars, virtual and onsite training for hospital staff.

Most users spent time with a company representative for a product overview and demonstration of the device and settings. The company representative then shadowed the user when applying their first 1-5 dressings.

Most sites receive weekly visits from a company representative to support ward staff with V.A.C. products in accordance with their contract.

Patient experience

Users report that patients feel secure with V.A.C. Veraflo as it manages large amounts of exudate and reduces the number of dressing changes compared to a standard dressing.

Patient safety

The company state the device has a Seal Check Leak Detector that provides visual and audio assistance in identifying leaks. Air leaks can be identified by listening with a stethoscope or moving a hand around the edges of the dressing while applying light pressure. Once the leak source is identified the wound can be patched with additional drape to ensure seal integrity. If there is no negative pressure applied (for example if the device is switched off) the company recommends changing the dressing within 2 hours.

At one site the hospital protocol for an alarm sounding over a weekend or overnight instructs seeking advice from the company's 24-hour helpline. If the issue remains unresolved within 2 hours, the V.A.C. dressing is replaced with a standard dressing until a specialist is available to review.

Two users report the device has been turned off after the alarm sounded overnight or over a weekend as ward staff did not know what to do. These patients kept the same V.A.C Veraflo dressing on with the device turned off. Neither users report any negative consequences as a result of this.

A user found power cords and tubing may present as a trip hazard as most of their patient wounds are below the waist. No users have reported any incidents.

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Medical technologies guidance

GID-MT 543 and V.A.C VERAFLO™ Therapy System for acute infected or chronic wounds that are failing to heal

Company evidence submission

Part 1: Decision problem and clinical evidence

Company name	3M+KCI
Submission date	11th March 2020
Regulatory documents attached	417670a_IFU VeraFlo Application - BSI – WEB.PDF 417282a_mnl VACUlta 1_5 user – WEB.PDF 417659a_SIS VAC VeraFlo Therapy - OUS – WEB.PDF CE 661656 KCI USA EC Cert (exp 240526).PDF
Contains confidential information	Yes

Contents

1 Decision problem

	Scope issued by NICE	Variation from scope (if applicable)	Rationale for variation
Population	Patients with acute infected or chronic wounds that are failing to heal		
Intervention	The V.A.C. VERAFLO™ Therapy system		
Comparator(s)	• Standard advanced wound dressings (e.g. hydrogel dressings, hydrocolloid dressing, capillary-acting dressings, alginate dressings) • Negative pressure wound therapy		
Outcomes	• Length of stay in hospital • Rates of partial and complete wound closure (which may vary depending on wound type, location, depth and size) • Mean time to partial or complete wound closure • Mean time to healing • Number of dressing changes • Number of follow on treatments and visits to hospital • Number of surgical debridements • Number of amputations or skin grafts	Remove mean time to healing. Remove number of amputations.	<u>Mean time to healing</u> Only 3 studies collected mean time to healing data and whilst 1 showed very high statistical significance p=0.0000 the majority of studies focussed upon wound closure rates and the associated timescales. NPWTi is used to prepare a wound bed for closure, it is not designed to heal wounds and we suggest it is not an appropriate outcome. This may explain why this data was not collected.

	• Staff time and use of other consumables • Colonisation with antimicrobial resistant pathogens • Antibiotic use • Health-related quality of life • Patient satisfaction and acceptability • Patient-related outcomes such as pain scores • Device-related adverse events.	Modify colonisation with antimicrobial resistant pathogens to colonisation with pathogens Remove antibiotic use Remove HRQOL	<u>Amputations</u>. Only 4 studies collected amputation data, 3 of which had no comparator. <u>Pathogen Colonisation</u> Whilst many of the studies record the presence of pathogens, whether or not they were microbially resistant was not usually documented. <u>Antibiotic Use</u> The majority of studies documenting antibiotic use prescribed them systemically for all patients or for all those who had an infected wound. Data collection in studies more often focussed on pathogen types and colonisation levels. <u>HR QOL</u> None of the studies selected in the systematic review presented any data related to patient's QOL. .
Cost analysis	Costs will be considered from an NHS and personal social services perspective. The time horizon for the cost		

	analysis will be long enough to reflect differences in costs and consequences between the technologies being compared. Sensitivity analysis will be undertaken to address uncertainties in the model parameters, which will include scenarios in which different numbers and combinations of devices are needed.		
Subgroups to be considered	• Diabetic ulcers • Pressure ulcers • Surgical site infections • Venous leg ulcers Wounds containing prosthetic implants		
Special considerations, including issues related to equality	People who are older or physically disabled are more likely to suffer chronic and complex wounds. People with certain family origins are more prone to poor wound healing due to increased risk of diabetes. Age, disability, and race are protected characteristics.		

2 The technology

Give the brand name, approved name and details of any different versions of the same device (including future versions in development and due to launch). Please

also provide links to (or send copies of) the instructions for use for each version of the device.

Brand name	The V.A.C. VERAFLO™ Therapy System
Approved name	The V.A.C. VERAFLO™ Therapy System
CE mark class and date of authorisation	CE 661656 V.A.C. ULTA™ System with V.A.C. VERAFLO™ Therapy – Class IIa 03.03.20 V.A.C. ULTA 4™ Therapy – Class IIa 03.03.20 V.A.C. VERAFLO™ Dressings – Class IIb 03.03.20

Version(s)	Launched	Features
Device		
V.A.C. Instill™*	2003	Controlled topical solution treatment in conjunction with V.A.C.® Therapy
V.A.C. ULTA™ with VERAFLO Therapy	2011	The V.A.C.ULTA™ System is an integrated wound management system that provides Negative Pressure Wound Therapy (V.A.C.® Therapy) with an instillation option (V.A.C. VERAFLO™ Therapy). Combines the benefits of V.A.C.® Therapy with automated solution distribution and removal: • Volumetric delivery: Automated pump delivers topical wound solutions • Fill assist: Monitor the correct instil volume and saves data for future use • Dressing soak: Instils topical wound solution into the wound for easier dressing removal and increased patient comfort
V.A.C. ULTA™ 4 Therapy	2019	The V.A.C.ULTA™ 4 Therapy System is an integrated wound management system that provides Negative Pressure Wound Therapy (V.A.C.® Therapy) with an instillation option (V.A.C. VERAFLO™ Therapy). V.A.C.® Therapy in the absence of instillation 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 oedema, promoting granulation tissue formation and perfusion, and by removing exudate and infectious material • V.A.C. VERAFLO™ Therapy is indicated for patients who would benefit from vacuum assisted drainage and controlled delivery of

		topical wound treatment solutions and suspensions over the wound bed The V.A.C.ULTA™ 4 Therapy System with and without instillation is indicated for patients with chronic, acute, traumatic, sub-acute and dehisced wounds, partial-thickness burns, ulcers (such as diabetic, pressure and venous insufficiency), flaps and grafts V.A.C.® Therapy in the absence of instillation may also be used for: • The temporary bridging of abdominal wall openings where primary closure is not possible and/ or repeat abdominal entries are necessary and for open abdominal wounds with exposed viscera including, but not limited to, abdominal compartment syndrome. The intended care setting is a closely monitored area within the acute care hospital, such as the ICU. The abdominal dressing will most often be applied in the operating theatre. • The management of the environment of surgical incisions that continue to drain following sutured or stapled closure by maintaining a closed environment, and removing exudate via the application of negative pressure wound therapy.
Dressings		
V.A.C. VERAFLO™ Dressing	2011	Open wounds, including wounds with shallow undermining or tunnel areas where the distal aspect is visible When used in conjunction with V.A.C. VERAFLO™ Therapy, to help facilitate the removal of infectious material and other wound bioburden. • Generation of robust granulation tissue
V.A.C. VERAFLO CLEANSE Dressing	2011	Cavity wounds or wounds with complex geometries When used in conjunction with V.A.C. VERAFLO™ Therapy, to initiate therapy and to help facilitate the removal of infectious material and other wound bioburden. • Easy application into tunnelling and undermining
V.A.C. VERAFLO CLEANSE CHOICE Dressing	2016	Cavity wounds or wounds with complex geometries When used in conjunction with V.A.C. VERAFLO™ Therapy, to initiate therapy and to help facilitate the removal of infectious material and other wound bioburden. • Easy application into tunnelling and undermining

* The acronym NPWTi is used to describe this technology throughout the remainder of this document.

Glossary

Acronym	Definition
HRQOL	Health Related Quality Of Life
NHS	National Health Service
ICU	Intensive Care Unit
NPWT	Negative Would Pressure Therapy
A&E	Accident & Emergency
NICE	National Institute for Health & Care Excellence
RCT	Randomized Control Trial
SD	Standard Deviation
NDB	Number Different Bacteria
AB	Amount of Bacteria
CRP	C-reactive protein
ESR	Erythrocyte sedimentation rate
MRP	Mandibular Reconstruction Plate
DSWI	Deep Sternal Wound Infection
LVAD	Left ventricle Assistive Device
VAD	Ventricular Assisted Device
CABG	Coronary artery bypass grafting
AEs	Adverse events
MRSA	Methicillin-resistant Staphylococcus aureus
TTME	Total titanium mesh explantation
PTME	Partial titanium mesh explantation
CKD	Chronic kidney disease
HTN	Hypertension
DVT	Deep vein thrombosis
NS	No Statistic
STSG	Split thickness skin graft
FDA	Food & drug Administration
MHRA	Medicines & Healthcare Regulatory Agency
MAUDE	Manufacturer and User Facility Device Experience
WUWHS	World Union of Wound Healing Societies
DFU	Diabetic Foot ulcer
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
DM	Diabetes mellitus
NPWTi	Negative Pressure Wound Therapy with instillation

What are the claimed benefits of using the technology for patients and the NHS?

Claimed benefit	Supporting evidence	Rationale
Patient benefits		
Reduced Hospital Length of Stay	Kim 2014, Gabriel 2014, Gabriel 2008, Timmers. Kim 2015, Omar, Deleyto, Garcia-Ruano , Powers and Davis.	The first four of these studies showed statistically significant reductions in patient's length of hospital stay when NPWTi use was compared to either NPWT or conventional wound care. The remaining studies showed shorter, but non statistically significant reductions. Patients benefit from reduced length of stay as it allows them an earlier return to their home and families and activities of daily living. It also removes them from a hospital environment where they may be vulnerable to hospital acquired infection. Please note the Davis study used an alternative company's product.
Reduced number of surgical debridements	Kim 2014, Gabriel 2014, Garcia-Ruano, Choudhry, Timmers, Powers Jurkovic, Kim 2015, Omar, Goss, Kim 2020)	The first of these 6 studies showed statistically significant reductions in the number of surgical debridements required when NPWTi use was compared to either NPWT or conventional wound care. This means that patients have to undergo fewer painful procedures and the risk of an anaesthetic.
Higher rates of surgical implant retention	Lehner, Garcia-Ruano. Deleyto, Ikeno, Eckstein, Morinaga, Huang	The first 2 of these studies showed statistically significant retention of surgical implants. The remaining studies recorded either high rates of retention when compared with conventional wound dressings, but without documenting

		significance, or they reported ranges of retention from 90-100%. Implants documented included life-saving cardiovascular grafts or orthopaedic implants that are essential to allowing patients to maintain their independence. Please note the Ikeno, Morinaga and Huang studies used an alternative company's products.
Reduced time to wound closure	Gabriel 2014, Gabriel 2008, Qui, Garcia-Ruano, Choudhry Jurkovic, Omar, Morinaga, Davis and Kim 2020	The first 5 of these studies showed statistically significant reductions in mean time to complete or partial wound closure when NPWTi was compared with NPWT or conventional wound care. The remaining studies showed shorter mean times to wound closure but these were not found to be significant. Patients living with open wounds are subject to increased pain and risk of infection. Please note the Qui, Morinaga and Davis studies used an alternative company's products.
Reduced Pain	Eckstein, Kim 2020 Teot, Milcheski, Qui, Gabriel 2014, Chen	A number of papers referenced reduced pain levels for patients using NPWTi. The first 2 reported statistical significance in pain reduction post treatment with NPWTi The remaining stated pain reduction during and following NPWTi but did not publish statistical analysis. Please note the Qui and Chen studies used an alternative company's products. Nurses using NPWTi in the NHS completed a short survey with 13 patients in February and March 2020.

		Patient's views were sought at dressing removal and application. Removal No pain or discomfort = 8 Some pain or discomfort = 5 A lot of pain or discomfort = 0 Application No pain or discomfort = 9 Some pain or discomfort = 4 A lot of pain or discomfort = 0
System benefits		
Patients discharged more quickly	Kim 2014, Gabriel 2014, Gabriel 2008, Timmers. Kim 2015, Omar 2016, Deleyto 2017, Garcia-Ruano , Powers and Davis.	The papers supporting reductions in length of stay have been documented in the Patient Benefit Section of this table. When patients are discharged from hospital more quickly, they release capacity to the NHS for additional patients to receive care. This may include admitting patients who have been subject to long waits in A&E departments. Please note the Davis study used an alternative company's product.
Higher rates of wound closure	Kim 2014, Garcia-Ruano and Powers. Kim 2015, Brinkert, Zelen, Yang, Gabriel 2008,Eckstein, Hehr, Jain, Morinaga, Davis	The first 3 of these studies showed statistically significant higher rates of complete wound closure when NPWTi was compared with NPWT or conventional wound care. The remaining papers showed non-significant differences between NPWTi and comparative care or recorded only closure rates for NPWTi. These ranged from 64 to 100%. Higher wound closure rates are a contributory factor to early hospital discharge, reductions in the number of debridements, dressing changes and skin grafts required as well as reducing the numbers of consumables used and staff time caring for patients.

		Please note the Zelen, Morinaga and Davis studies used an alternative company's products.
Reduced follow on treatments	Deleyto, Garcia-Ruano, Chen, Davis.	Deleyto was the only paper to document a statistical significance for patients requiring fewer follow on treatments. Patients requiring follow on treatments, in the remaining 3 papers that recorded this data, ranged from 16% to 54% although this higher % was matched with 94% of control patients in this study requiring further treatment. Avoidance of follow on treatments release both physical and clinical capacity to the NHS to offer care to other patients. As fewer consumables will be required too these factors are likely to reduce overall costs of care for these patients. Please note the Chen and Davis studies used an alternative company's products.
Reduced colonisation with pathogens	Jurkovic, Goss, Yang 2017, Garcia-Ruano, Timmers, Ludolph Kim 2020 Kim 2014, Powers,	The first 7 of these studies showed statistically significant higher rates of reduction in pathogen colonisation when NPWTi was compared with NPWT, or conventional wound care. The remaining 2 papers recorded higher rates of reduction by a % although, statistical significance was not reported. Patients with significant pathogenic colonisation are more likely to require additional treatment to achieve wound closure. This may involve longer hospitalisation periods, repeated surgical intervention, removal of implants and long term antibiotic therapy all of which will place demands on clinical time and consume other resources.

Overall reduction in staff and resource use	Chen Gabriel 2014, Kim 2014, Garcia-Ruano Qui, Choudhry, Timmers, Powers, Kim 2015, Gabriel 2008	Chen was the only paper to directly report a significant reduction in clinical and nurse time although this was not quantified. Other papers referenced here relate to reductions in dressing changes, treatment duration, fewer days to final surgical procedure, fewer debridements, length of therapy and shorter mean times to wound closure. For each of these statistically significant differences were reported between cohorts of patients who had access to NPWTi and control groups Please note the Chen and Davis studies used an alternative company's products.
Cost benefits		
Reduction of costs	Gabriel 2014, Jurkovic, Deleyto	Each of these papers considered the cost of NPWTi therapy alongside total hospitalisation costs. As a result 2 suggested that that whilst the costs of using NPWTi were significantly higher the total hospitalisation costs did not differ significantly. Deleyto reported that when NPWTi was used as an alternative to conventional wound dressing the mean costs of NPWTi were €2,000 lower. Detailed costs will be modelled in part 2 of this submission.
Sustainability benefits		
Reduction of consumables	Lehner, Garcia-Ruano. Deleyto, Ikeno, Eckstein, Morinaga, Huang Gabriel 2014, Jurkovic,	Each of these papers referenced high rates of surgical implant retention or fewer dressing changes. Both of these factors would contribute to sustainability. Please note the Ikeno, Morinaga and Huang studies used an alternative company's products.

Briefly describe the technology (no more than 1,000 words). Include details on how the technology works, any innovative features, and if the technology must be used alongside another treatment or technology.

The V.A.C VERAFLO™ Therapy system combines the use of Negative Pressure Wound Therapy (NPWT) and wound irrigation with topical solutions.

The V.A.C VERAFLO™ Therapy system helps to promote healing in 2 distinct phases:

Instillation and Dwell

- Topical wound solutions are delivered to the wound and allowed to dwell across the whole wound surface for a predetermined length of time.
- During this phase infectious material and wound debris are diluted and solubilised.
  NPWT Phase
- Wound exudate and infectious material is removed
- Contact with the hydrophobic foam under pressure stimulates the formation of granulation tissue
- Tissue perfusion is stimulated and tissue oedema reduced
- Wound edges are drawn together to support closure

The V.A.C. VERAFLO™ Therapy system consists of a number of elements that can be tailored to individual patient needs so that the benefits of NPWT and automated solution distribution and removal can be achieved.

Once the wound bed has been prepared the clinician applies a V.A.C. VERAFLO™ dressing foam so that it is in contact with the whole wound. These are available in a number of sizes and shapes to provide the flexibility required for treating complex wounds and meeting individual patient need.

Once the wound has been filled with foam a barrier film (3M Cavilon™ No Sting Barrier Cream) is applied to clean skin around the wound and allowed to dry.

A V.A.C®. Advanced drape is then placed and sealed over the wound leaving a 3cm margin to ensure full adhesion and reduction of air or fluid leaks (a ruler is included in the dressing pack to assist with accurate measurement). A small hole is then cut in the drape surface over the wound without damaging the foam.

Finally, the V.A.C. VERAT.R.A.C ™ Pad that delivers the instillation solution and applies NPWT, applying pressure and removing wound exudate through separate channels, is attached to the drape. A stabilisation layer is used to ensure that the pad is fully in contact with the drape.

The V.A.C. VERAT.R.A.C™ Pad is then connected to the V.A.C. VERAFLO™ Therapy Unit and the automated cycle of wound cleansing and NPWT is begun. Fluids and wound exudate are removed from the wound and are retained in a single-use disposable 500ml or 1000ml canister.

When initiating instillation, a VAC Fill Assist tool is used to help the operator to set the correct level of fluid instillation and prevent leakage of fluids. In addition to this the system uses a SEAL CHECK™ leak detector to assist the user in finding negative pressure leaks in the system through the use of audible tones and on-screen visual aids.

The V.A.C. VERAFLO™ Therapy unit is innovative due to its mode of action and the automation of its use that can be modified to meet the needs of individual patients. The features offering the highest level of innovation are:

1. The automation of the treatment cycle means that wounds can be repetitively cleansed without the need for dressing removal. This means that the usual practice of manual wound cleansing is avoided, thereby saving nursing time and reducing contamination.
2. The Therapy unit has a function to allow the dressing and wound to be soaked prior to a dressing change so that it is softened and moistened to assist with easier removal and reduced pain for patients.
3. The combination of a determined instillation time and solution dwell time not only ensures that the wound bed receives fluids reliably and uniformly but also supports making sure that the fluids are in contact with the wound for sufficient time to solubilise infectious materials and wound debris.
4. As therapy begins the VERAFLO™ Therapy Unit deploys a “fill assist” function that allows the operator to determine the appropriate instil volume for fluid. This volume is then set for the duration of the therapy ensuring optimal therapy and reducing the risk of dressing leaks caused by wound over filling.
5. The specialised VERAFLO CLEANSE CHOICE™ dressings are composed of an innovative block foam, which has been felted using heat and compression so that it is able to more effectively manage wounds with thick exudate, slough, infectious material and other wound bioburden.
6. The foam that accompanies the V.A.C. VERAFLO™ dressings is available in a number of different sizes and shapes. It can also be cut to ensure the entirety of the wound bed is covered allowing even instillation and application of NPWT.
7. V.A.C. VERAFLO™ dressings are less hydrophobic than the current V.A.C.® Therapy dressings and provide improved fluid distribution within the wound bed.
8. The instillation therapy allows for better solution distribution
across the wound surface, including into tunnels and undermined areas from which exudate can be removed.

Briefly describe the environmental impact of the technology and any sustainability considerations (no more than 1,000 words).

KCI/3M takes our responsibility to preserve the natural resources of the communities in which we live and work seriously. We carefully consider the impact of our manufacturing and related materials to reduce the environmental footprint of our products and their packaging. When a product reaches the end of its usable life, we reclaim materials for reuse whenever possible, and aim to utilize renewable resources in the design and manufacturing of our products and in our daily business practices. Our major manufacturing and distribution sites follow ISO 14001, a globally recognized standard for environmental management systems (EMS) designed to manage and improve environmental performance across industries.

Our 2025 Sustainability Goals reflect our commitment to continually strive to incorporate measures within the development, manufacture and delivery of our therapies that reduce the overall environmental impact of our processes and our products. As a global leader in our markets, we are committed to global environmental leadership to help ensure sustainable development and the improved health of our planet.

Energy and Climate

- Improve energy efficiency indexed to net sales by 30%
- Increase renewable energy to 25% of total electricity use
- Ensure CHG emission at least 50% below our 2002 baseline, while growing our business
- Help our customers reduce their GHGs by 250 million tons of CO2 equivalent emissions through use of 3M products

Raw Materials

- Invest to develop more sustainable materials and products to help our customers reach their environmental goals
- Reduce manufacturing waste by an additional 10%, indexed to sales
- Achieve “zero landfill” status at more than 30% of manufacturing sites
- Drive supply chain sustainability through targeted raw material traceability and supplier performance assurance

Water

- Reduce global water use by an additional 10%, indexed to sales
- Engage 100% of water-stressed/water-scarce communities where 3M manufactures on community-wide approaches to water management

Additionally, we manage our daily business operations in a manner that is regulatory compliant, energy efficient and environmentally responsible. We ensure the selection and deployment of fuel-efficient vehicles within our service fleet and use ecologically friendly cleaning materials in our global services centres. In all global facilities we implement recycling programs for paper, metals and glass and we have introduced initiatives to minimize the use of printed materials in our communications and record keeping. We are fully committed to educating our employees, health care professionals, and the end-users of our products on proper waste disposal methods and how to be good environmental stewards.

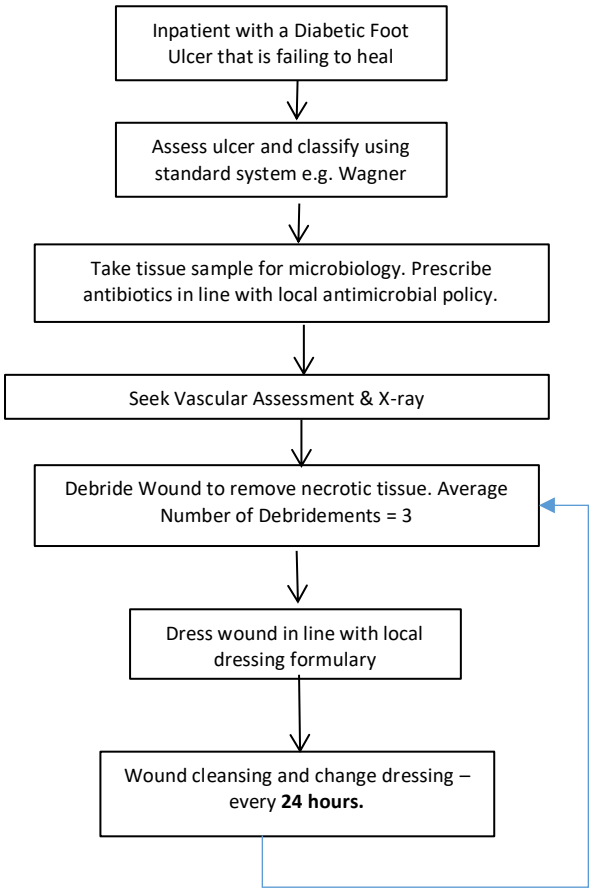
V.A.C. VERAFLO™ therapy helps to reduce the number of dressings and shorten time to final wound closure. By healing more wounds more quickly, the environmental impact is reduced, as well as the costly consequences of complications and infections.

3 Clinical context

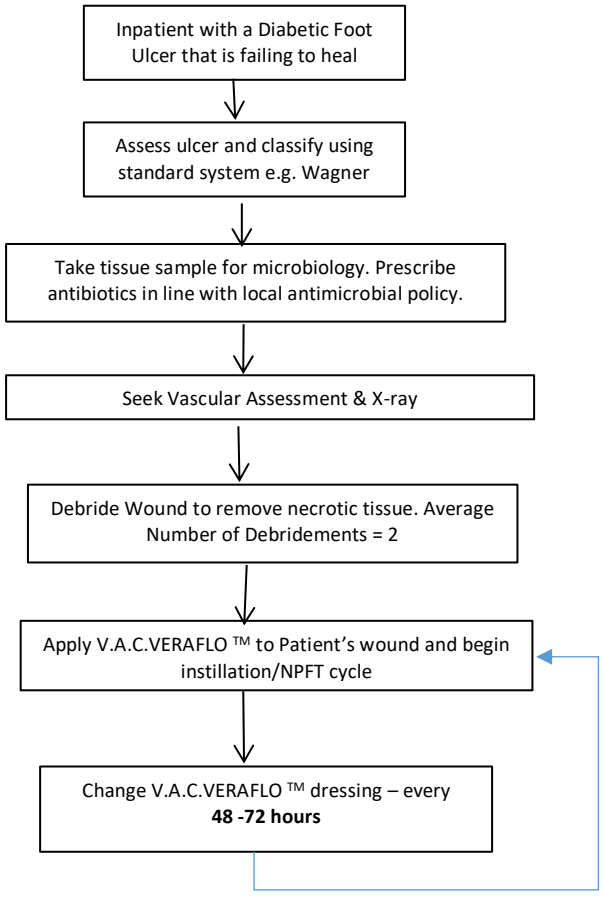
Describe the clinical care pathway(s) that includes the proposed use of the technology, ideally using a diagram or flowchart. Provide source(s) for any relevant pathways.

This submission includes patient cohorts with a wide range of different wound types and who will follow very different care pathways. The following illustrative care pathway for diabetic foot ulcer is based upon NICE's evidence based care pathway and shows how V.A.C. VERAFLO™ Therapy can be used to support healing of complex wounds by replacing conventional care. It also helps to show the impact V.A.C. VERAFLO™ Therapy can have on reducing resource use and the clinical time needed to care for patients.

Illustrative Pathway Current Care.



V.A.C. VERAFLO™ Therapy



Describe any training (for healthcare professionals and patients) and system changes that would be needed if the NHS were to adopt the technology.

3M+KCI have a competency-based training programme available to healthcare professionals. This includes:-

- eLearning sessions
- practical hands-on training
- machine instructions including alarm handling and specialist support for very complex wounds.

3M+KCI provide their training programme free of charge.

Standard training consists of a 2-hour lecture and/or web based elearning sessions with practical hands-on training. The programme includes mechanisms of action, safe and effective use, patient selection, instillation solution selection, dressing application and machine settings as well as troubleshooting.

Successful completion of training is signed off using a competency assessment framework.

One day Bio skills labs are also offered to health care professionals. These courses consist of lectures and attendees carry out practical hands-on techniques within wet labs. An independent faculty of surgeons or nurses who are experts in the technology help lead the course content and delivery.

Supporting educational literature is provided for clinicians to include patient pathway examples, operating room guides, troubleshooting guides and consensus guidelines advising on patient selection, treatment goals, dwell times and recommended instillation solutions.

Training and support is provided in hospitals by the 3m+KCI specialist team. As well as new user training they provide face-to-face bedside and theatre assistance for complex cases and to help new users. Staff are also instructed how to access the 24- hour helpline for out-of-hours assistance. There is a clinical and medical support service additionally provided by the company for advice with very complex cases. Simple instructions may be given to patients, but patients would not normally be responsible for operating the device.

4 Published and unpublished clinical evidence

Identification and selection of studies

Complete the following information about the number of studies identified.

Please provide a detailed description of the search strategy used, and a detailed list of any excluded studies, in appendix A.

Number of studies identified in a systematic search.		Text
Number of studies identified as being relevant to the decision problem.		32
Of the relevant studies identified:	Number of published studies (included in table 1).	30
	Number of abstracts (included in table 2).	1
	Number of ongoing studies (included in table 3).	1

List of relevant studies

In the following tables, give brief details of all studies identified as being relevant to the decision problem.

- Summarise details of published studies in table 1.
- Summarise details of abstracts in table 2.
- Summarise details of ongoing and unpublished studies in table 3.
- List the results of all studies (from tables 1, 2 and 3) in table 4.

For any unpublished studies, please provide a structured abstract in appendix A. If a structured abstract is not available, you must provide a statement from the authors to verify the data.

Any data that is submitted in confidence must be correctly highlighted. Please see section 1 of the user guide for how to highlight confidential information. Include any confidential information in appendix C.

Table 1 Summary of all relevant published studies

Data source	Author, year and location	Study design	Patient population, setting, and withdrawals/lost to follow up	Intervention	Comparator(s)	Main outcomes
Lower limb						
Plast. Reconstr.surg	Kim et al, 2015, USA	RCT	83 patients with infected wounds that required hospital admission and operative debridement, 17 patients excluded from an initially randomised cohort of 100 patients due to deviations from protocol inclusion criteria. 9 of these were lost to follow up.	NPWTi with 0.9% normal saline solution	NPWTi with 0.1% polyhexadine + 0.1% betadine solution	Number of operating room visits, length of hospital stay, time to final surgical procedure during admission, percentage of wounds closed/covered during admission, proportion of wounds that remained closed or covered 30 days after hospital discharge
Plast. Reconstr.surg	Kim et al 2014,USA	Comparative Retrospective	142 patients with infected wounds who required admission with at least 2 operative debridements, no withdrawals or losses.	NPWTi with 6 or 20 minute dwell time following debridement in the operating room	NPWT following debridement in the operating room	Number of operating room visits, length of hospital stay, time to final surgical procedure during admission, percentage of wounds closed/covered during admission, percentage of wounds that remained closed or covered 30 days after hospital discharge, reduction in microorganisms
Wounds	Yang, 2017, USA	RCT	19 patients with chronically infected lower extremity ulcers, hospital setting, no withdrawals or losses.	Sharp surgical debridement, wound biopsy and irrigation followed by NPWTi,	Sharp surgical debridement , wound biopsy and irrigation followed by	Bioburden in chronic wounds, bacterial types and concentration

				debridement at biopsy on day 7	NPWT, debridement at biopsy on day 7	
Society for Vascular Surgery	Yang, 2015, USA	Prospective Cohort	7 patients (10 ulcers) with massive chronic Venous Leg Ulcers, hospital setting and outpatients, no withdrawals or losses.	Surgical debridement, followed by NPWTi, STSG on day 7 followed by NPWT for 4 days and 6 months standard compression therapy	None	Wound size, wound age, hospital length of stay, skin graft take at 30 days skin graft take at 180 days
Journal of the American College of Wound Specialists	Goss et al, 2008, USA and Italy	Prospective	13 patients with chronically Infected lower leg wounds, hospital setting, no withdrawals or losses.	Operative debridement followed by one week of NPWTi	Operative debridement followed by one week of NPWT	Wound chronicity, wound surface area, wound characteristics, wound tissue cultures
Journal of Woundcare	Omar et al, 2016, Germany	Prospective	20 patients with acute lower limb wounds, hospital setting , no withdrawals or losses.	Surgical debridement followed by NPWTi	Surgical debridement followed by NPWT	Revision surgeries, length of hospital stay, wound microbiological status, duration of treatment to final healing, type of wound closure
International Wound Journal	Brinkert et al, 2013, France	Prospective clinical study	131 patients with complex wounds or wound at risk of infection, hospital setting, no withdrawals or losses.	35% of patients were previously treated with NPWT, remaining 65% had radical surgical bone and soft tissue debridement	None	Number of days with NPWTi, wound closure rates, time to wound closure, numbers of skin grafts

				prior to starting NPWTi		
Rev.Col.Cras Cir	Milcheski et al, 2017, Brazil	Prospective Cohort	10 patients with infected contaminated lower leg wounds, hospital setting, no withdrawals or losses.	Clinical evaluation, surgical debridement, NPET-I, graft and patch coverage	None	Time between admission and wound closure, qualitative cultures in each surgical procedure, number of surgical procedures, wound preparation time, length of hospital stay
Wounds	Blalock, 2019, USA	Retrospective Case Series	19 patients with complex wounds, hospital setting, no withdrawals or losses.	Sharp debridement if appropriate followed by NPWTi		Duration of NPWTi, wound odour, improved granulation tissue
International Wound Journal	Gabriel 2008, USA	Prospective	30 patients with open Infected Wounds – venous, diabetic, mixed, hospital setting, no withdrawals or losses.	NPWTi	Standard moist wound care therapy	Number of days of wound treatment, number of days to wound closure, number of days to discharge, type of infection present
Wound Repair and Regeneration	Davis et al, 2019, USA	RCT	Complex Foot Infections DFU, hospital setting, no withdrawals or losses.	NPWTi	NPWT	Primary – proportion of wounds with complete healing at 12 weeks Secondary – number of surgeries, length of hospital stay, proportion of wounds surgically, proportion of wounds left open prior to discharge, time to heal, number of postoperative re admissions, need for readmission, need for further surgery or amputation
Journal of Plastic Surgery	Zelen et al, 2011, USA	Prospective Cohort	19 patients with diabetic foot ulcers, hospital setting, no withdrawals or losses.	Wound debridement and	None	Primary – Wound closure rates over a 6 week period

				measurement, NPWTi		Secondary – Proportion of healing at 6 weeks, device safety
Mixed wounds						
eplasty	Gabriel et al, 2014, USA	Comparative Retrospective	82 patients with infected or critically colonised extremity or trunk wounds treated with NPWT or NPWTi, hospital setting, no withdrawals or losses.	Wound debridement and systemic antibiotics administered prior to instillation NPWTi	Wound debridement and systemic antibiotics administered prior to NPWT	Number of surgical debridements, hospital stay, length of therapy, time to wound closure. Hypothetical economic model developed using outcome data
International Wound Journal	Ludolph et al, 2018, Germany	Open prospective study	111 patients who required a minimum of 4 operative procedures to facilitate wound closure, hospital setting, no withdrawals or losses.	Surgical debridement, application of NPWTi, further debridement if necessary and definitive reconstruction	None	Number of different bacterial species, amount of bacteria
International Wound Journal	McElroy, 2019, USA	Retrospective Case Series	14 patients with multiple morbidities and complex wounds which were inappropriate for surgical debridement, hospital, no withdrawals or losses	NPWTi	None	Number of debridements, Duration of treatments, dwell time, Number of NPWT cycles, Granulation, returns to operating room
Wound Repair and Regeneration	Timmers et al, 2008, The Netherlands	Comparative Retrospective	124 patients with osteomyelitis of the pelvis or lower extremity, hospital setting, 1 patient died due to cardiac	Operative debridement followed by NPWTi	Surgical debridement, systemic antibiotics, gentamicin	Duration of hospitalisation, number and duration of hospital stays, number of surgical procedures, number of clinical and microbiological recurrences

			condition 5 patients died during the follow-up period due to unrelated causes.		beads at site of osteomyelitis.	
Prosthetic implants						
Journal of Surgical Research	Garcia-Ruano et al, 2016, Spain	Comparative Retrospective	46 patients with abdominal mesh exposure due to dehiscence, hospital setting, no withdrawals or losses.	NPWTi	Saline soaked gauze, antiseptic solutions and open lavage	Number and type of surgical procedures to achieve stable wound closure, length of hospital stay, time of treatment, final result and complication occurrence.
Hernia	Deleyto et al, 2017, Spain	Comparative Retrospective	45 patients with abdominal mesh exposure due to dehiscence, hospital setting, no withdrawals or losses.	NPWTi	Conventional wound therapy	Number of hospitalisation episodes, number of additional surgeries, total time for hospitalisation
Journal of Cranio-Maxillo-Facial Surgery	Eckstein et al, 2018, Germany	Retrospective Case Series	15 patients with infected osteoradionecrosis and osteomyelitis of the jaw who were diagnosed with impaired wound healing, hospital setting, 1 withdrawal due to an exposed mandibular reconstruction plate	Operative debridement followed by NPWTi	None	Wound surface reduction, pain values, bacterial load, inpatient treatment time, number of dressing changes
International Orthopaedics	Lehner et al, 2011, Germany and Switzerland	Prospective Cohort	32 patients with infected orthopaedic implants, hospital	NPWTi	None	Primary -Percentage of implant retention without infection at 4-6

			setting, 1 patient died due to age prior to follow-up			month follow-up from start of treatment Secondary – Percentage of retained implants for patients with chronic infection, incidence of treatment related adverse events, incidence of infection recurrence. Duration of NPWTi duration of infection, length of hospital stay
International Wound Journal	Hehr et al, 2019, USA	Retrospective Case Series	28 patients with infected hardware, (spinal, extremity & sternal), hospital setting, no withdrawals or losses.	Operative debridement followed by NPWTi	None	Wound location, culture data, instillation solution, time to definitive closure, ultimate status of hardware
Journal of Plastic Surgery and Hand Surgery	Morinaga et al, 2012, Japan	Retrospective Case Series	46 patients with mediastinitis following open chest surgery, hospital setting, 2 patients died (sepsis and organ failure).	Operative debridement followed by NPWTi	None	Treatment duration, time to skin graft, period required for healing
Journal of Orthopaedic Surgery and Research	Chen et al, 2018, China	Retrospective Case Series	18 patients with wound infections after posterior spinal surgery, hospital, no withdrawals or losses	Debridement followed by NPWTi	None	Wound healing time, wound size, colonising bacteria type, laboratory examinations, hospital stay
Journal of Craniofacial Surgery	Huang et al, 2020,China	Prospective Cohort	21 patients with exposed/infected titanium mesh implants in Cranioplasty, hospital setting, no withdrawals or losses.	Debridement, NPWTi	None	Bacterial culture results, operation time, incision treatment, duration of hospital stay

Journal of Cranio-Maxillo-Facial Surgery	Qui al, 2019, China	Retrospective Case Series	73 patients with severe multiple space infections (oral, maxiofacial and cervical), hospital setting, no withdrawals or losses	Incision and abscess drainage followed by NPWTi	Incision and abscess drainage, irrigation of infected spaces, semi-latex drainage tubes inserted	Cure duration, incision length, physician workload (dressing changes), treatment costs
European Journal of Cardio Thoracic Surgery	Ikeno et al, 2019, Japan	Retrospective Case Series	18 patients who had deep sternal wound infection following aortic grafting, hospital setting, 3 in hospital deaths due to GI bleeding, pneumonia and false aneurysm. 5 late deaths due to secondary causes.	Debridement followed by NPWTi	None	Duration from initial surgery to resternotomy, Pathogens identified, open wound duration, reconstruction procedures
Surgical site infections						
Perspectives V surgery	Jurkovic et al, 2019, Czech Republic	RCT	41 patients with infected laparotomy wounds and fasciitis, hospital setting, no withdrawals or losses	NPWTi with instillation & 4% povodine iodine solution	NPWT	Primary – Length of therapy, number of surgical debridements, evaluation of financial costs. Secondary – Observed changes in biological load and bacterial spectrum
American Society of Plastic Surgeons	Chowdhry et al, 2019, USA	Retrospective Case Series	30 patients with sternal wound complications, hospital setting, no withdrawals or losses.	Operative debridement followed by NPWTi. Following muscle flap reconstruction NPWT was applied	Benzoin and wound closure strips applied over closed incisions and were evaluated	Days to wound closure, total therapy days, number of debridements, number of dressing changes, drain duration, complications

					after 1&2 weeks. Dressings discontinued after 2 weeks.	
Pressure ulcers						
Cureus	Jain et al, 2018, USA	Retrospective Case Series	10 patients with invasive Osteomyelitis of the Proximal Femur, hospital setting, 1 patient refused surgical intervention and died.	Girdlestone procedure followed by NPWTi and delayed primary closure	None	Length of stay, wound closure rates, time to wound closure, cultures
International Wound Journal	Teot et al, 2017, France	Retrospective Case Series	21 patients with thick wound exudate and infectious materials, hospital setting, no withdrawals or losses.	NPWTi with surgical debridement and bone biopsy where necrosis found to confirm presence of bacteria and sensitivities. MRI to confirm presence of bone infection where suspected, use of reticulated open cell foam instillation dressing	None	Percent increase in granulation tissue, decrease in devitalised tissue

Table 2 Summary of all relevant abstracts

Data source	Author, year and location	Study design	Patient population, setting, and withdrawals/lost to follow up	Intervention	Comparator(s)	Main outcomes
Presented at Symposium of Advanced Wound Care May 2013	Powers et al, 2013. USA.	Comparative Retrospective	52 patients with infected wounds requiring hospital admission and serial surgical debridement	NPWTi with 6 or 20 minute dwell time.	NPWT	Number of OR visits, Length of hospital stay, Time to final surgical closure (in hospital), % closed prior to discharge, % wounds with no growth or a decrease in all bacteria or excluding gram negative and other pathogens

Table 3 Summary of all relevant ongoing or unpublished studies

Data source	Author, year (expected completion) and location	Study design	Patient population, setting, and withdrawals/lost to follow up	Intervention	Comparator(s)	Outcomes
ClinicalTrials.gov	Text	Text	Text	Text	Text	Text
Text	Text	Text	Text	Text	Text	Text
Text	Text	Text	Text	Text	Text	Text
Text	Text	Text	Text	Text	Text	Text
Text	Text	Text	Text	Text	Text	Text
Text	Text	Text	Text	Text	Text	Text
Text	Text	Text	Text	Text	Text	Text
Text	Text	Text	Text	Text	Text	Text
Text	Text	Text	Text	Text	Text	Text

Table 4 Results of all relevant studies (from tables 1, 2 and 3)

Study	Results	Company comments
Lower limb		
Kim, 2015	A total of 123 patients were assessed for eligibility. Twenty-three patients were excluded, with five patients not meeting the eligibility criteria and 18 refusing to participate. A total of 100 patients were randomized and enrolled in this study. For the intention-to-treat analysis, there were 49 patients in the normal saline cohort and 51 patients in the 0.1% polyhexanide plus 0.1% betaine cohort. For the per-protocol analysis, there were 42 patients in the normal saline cohort and 41 patients in the 0.1% polyhexanide plus 0.1% betaine cohort (total attrition rate, 17 per-cent). Seven patients were removed in the normal saline cohort and 10 patients were removed from the 0.1% polyhexanide plus 0.1% betaine cohort for one of the following reasons: (1) greater than 30-day length of stay (normal saline, n = 2; 0.1% polyhexanide plus 0.1% betaine, n = 3), (2) lost to follow-up after discharge (normal saline, n = 4; 0.1% polyhexanide plus 0.1% betaine, n = 5), or (3) had less than two visits to the operating room (normal saline, n = 1; 0.1% polyhexanide plus 0.1% betaine, n = 2) (Demographics were similar in each cohort for both the intention-to-treat and per-protocol analyses, with the only statistically significant difference being more male and fewer female patients in the 0.1% polyhexanide plus 0.1% betaine cohort compared with the normal saline cohort (p = 0.004). There was also no statistically significant difference in comorbidities including smoking history between the two cohorts for both the intention-to-treat and per-protocol analyses. There was no statistically significant difference in the wound location or wound cause for both the intention-to-treat and per-protocol analyses between the two cohorts. The outcome data reveal no statistically significant difference between the normal saline and 0.1% polyhexanide plus 0.1% betaine cohorts for the number of operating room visits, length of hospital stay, proportion of wounds closed/covered, and proportion of wounds that remained closed at the 30-day follow-up for both the intention-to-treat and per-protocol analyses (Table4). There was a statistically significant difference between the normal saline and the 0.1% polyhexanide plus 0.1% betaine cohorts for the time to final surgical procedure [intention-to-treat, 5.73 (SD, 3.75) and 7.73 (SD, 5.49), respectively, p = 0.038; per-proto-col, 5.57 (SD, 3.61) and 7.46 (SD, 4.42), respectively, p = 0.035].	This randomised controlled trial contributed useful data concerning two types of instillation fluid that can be used as part of V.A.C, VERAFLO™ Therapy. This study suggests that normal saline, an inexpensive and readily available irrigation solution, may be as effective as a wound cleanser containing polyhexanide plus 0.1% betaine. Data collected during the trial showed ○ Shorter lengths of stay ○ Increased wound closure rates ○ Fewer surgical debridements ○ Statistically significant shorter time to final surgical procedure

Kim 2014	A total of 142 patients, 74 subjects in the negative-pressure wound therapy group, 34 subjects in the 6-minute dwell time negative-pressure wound therapy with instillation group, and 34 subjects in the 20-minute dwell time negative-pressure wound therapy with instillation group were included in the analysis. Age, sex, body mass index, current smoking status, and medical comorbidities were not statistically different between the negative-pressure wound therapy group and the 6- or 20-minute dwell time negative-pressure wound therapy with instillation groups. The only difference was a statistically higher percentage of African Ameri-cans in the 6-minute dwell time negative-pressure wound therapy with instillation group compared with the negative-pressure wound therapy group (p=0.03). There was no difference between the negative-pressure wound therapy group and the 6- or 20-minute dwell time negative-pressure wound therapy with instillation group in the primary wound cause. There was a statistically significant difference between the anatomical location of the wound in negative-pressure wound therapy group and the 20-minute dwell time negative-pressure wound therapy with instillation group for the forefoot and hindfoot/heel (p=0.04 and p=0.03, respectively). There was a higher percentage of forefoot wounds and a lower percentage of hind-foot/heel wounds for the 20-minute dwell time negative-pressure wound therapy with instillation group compared with the negative-pressure wound therapy group. There is a statistically significant difference in the following outcomes: (1) length of hospital stay between the negative-pressure wound therapy group and the 20-minute dwell time negative-pressure wound therapy with instillation group (p=0.034; 95 percent CI, 0.27 to 6.86), (2) number of operative visits between the negative-pressure wound therapy group and the 6-minute dwell time negative-pressure wound therapy with instillation group (p=0.043; 95 percent CI, 0.014 to 0.75) and between the negative-pressure wound therapy group and the 20-minute dwell time negative-pressure wound therapy with instillation group (p=0.003; 95 percent CI, 0.19 to 0.93), (3) time to final surgical procedure between the negative-pressure wound therapy group and the 6-minute dwell time negative-pressure wound therapy group (p=0.043; 95 percent CI, 0.065 to 4.04) and between the negative-pressure wound therapy group and the 20-minute dwell time negative-pressure wound therapy with instillation group (p=0.0019; 95 percent CI, 0.39 to 4.36). The percentage of wounds closed before dis-charge was significantly higher in the 6-minute dwell	This comparative retrospective study provides highly valuable data due to the fact that NPWT was compared to NPWTi, contributing to the evidence base about the relative benefits of instillation towards wound closure. There were some differences between the control groups and intervention groups with 20 minute dwell time related to anatomical location of the wound. It is not clear whether this impacted upon outcomes. This study demonstrated clear statistical significance for important patient outcomes between the control and NPWTi groups. Authors concluded that the results suggest NPWTi is superior to NPWT for the patient cohort in this trial whilst recognising that further research is required.

	time negative-pressure wound therapy with instillation group compared with the negative-pressure wound therapy group (p=0.0004). The overall wound culture improvement was not different between the negative-pressure wound therapy group and the 6- or 20-minute dwell time negative-pressure wound therapy with instillation groups; however, when Gram-negative bacteria, Coryne-bacterium, and yeast were excluded from analysis, there was a significantly greater improvement in the 6-minute dwell time negative-pressure wound therapy with instillation group than in the negative-pressure wound therapy group (p=0.0001)	

Yang, 2017	A total of 19 patients with 20 chronic leg ulcers were included in this study. No statistical differences were found between the NPWT and NPWTi groups. There was no statistical difference in the initial plank-tonic bacteria concentration between the 2 groups (P = .86), which was 12.3 x 105 CFU/g ± 28.6 x 105CFU/g and 10.5 x 105 CFU/g ± 15.1 x 105 CFU/g for the NPWT and NPWTi groups, respectively. Following initial debridement, there was no significant decrease in planktonic bacteria concentration for the NPWT (83.4%; P = .16) and NPWTi (72.5%; P = .32) groups, respectively. For planktonic bacteria no statistical difference between the 2 groups was seen at any time in the study. Initial biofilm-protected bacteria concentrations did not differ (P = .48) between the NPWT and NPWTi groups, 8.6 x 103 CFU/g ± 8.8 x 103 CFU/g and 12.9 x 103 CFU/g ± 12.5 x 103 CFU/g, respectively. Sharp debridement did not produce a significant change in either of the groups. Analyzing the change in biofilm-protected bacteria concentration following 7 days of NPWT or NPWTi shows a significant reduction (43%; P < .05) in the NPWTi group and a nonsignificant increase (14%; P = .46) in the NPWT group. However, between-group analysis did not find a significant difference (P = .11) in biofilm-protected bacteria concentration. Interestingly, pseudomonal biofilms were eradicated easily in both groups, as were methicillin-resistant Staphylococcus aureus (MRSA) biofilms. However, streptococcal and fastidious organisms showed the most resilience independent of the therapeutic group. There were no observable differences between the 2 therapies that were specific to bacterial species .	This randomised controlled trial of 19 with chronically infected leg ulcers has extended the evidence that NPWTi therapy provides an effective means of reducing bioburden to assist with creating conditions that support wound closure. This paper offers additional valuable data as it states that despite the fact that initial bio-film protected bacteria concentrations did not differ between the NPWTi and control groups. Following 7 days of NPWTi usage there was a statistically significant reduction in these bacteria whereas in the control group bacterial concentrations increased. It is notable that authors commented that sharp debridement did not appear to make a significant change to bacterial levels in either group, which perhaps challenges the frequent reliance upon this as a sole treatment option.

Yang, 2015	We identified 18 wounds in 16 patients. Six wounds did not meet size criteria, and two did not have ultrasound-documented venous insufficiency; therefore, we analysed 10 ulcers in seven patients that were treated with NPWTi and STSG. Mean initial ulcer area was 251 cm2(range, 112-325 cm2), and mean ulcer age was 38 months(range, 3-120 months). Inpatient hospitalization averaged13.4 days (range, 11-19 days). At 6 months, eight of 10patients had complete closure of VLUs. In the two wounds that remained open, the percentage of STSG take was 70% and 80%. The estimated cost of the NPWTi and STSG protocol as $27,000, which included a 13.4-day hospital stay and monthly follow-up visits. The cost for standard compression therapy was estimated to be $28,000.	This prospective cohort study of 7 patients with 10 chronic massive >100cm^2 venous leg ulcers provides a range of valuable evidence about the care provided. These patients went split thickness skin grafts and the paper documents the levels of take of 91% at 30 days and 95% at 180 days. Despite the significant size of these chronic wounds (3-120 months) 8 out of 10 were closed at 6 months follow up after skin grafting Importantly authors were able to demonstrate that use of NPWTi, hospitalisation and monthly follow up outpatient visits remained more cost effective than care using standard compression therapy.

Goss	There were a total of 13 patients, with 7 patients in the NPWTi group, corresponding to 8 wounds, and 7 patients in the standard NPWT group, corresponding to 8 wounds. The NPWTi group was composed of 2 female and 5 male patients. The mean age was 57. The mean age was 61. The majority of patients in both arms had significant comorbidities: diabetes mellitus (DM), chronic kidney disease (CKD), and hypertension (HTN). Two patients corresponding to 3 wounds in the NPWTi group had a history of deep vein thrombosis (DVT), while 1 patient with 1 wound in the NPWT group had a history of DVT. There were no sta-tistical differences between groups (NS). Patients in the standard NPWT group had a mean wound chronicity of 30 months while in the NPWTi group had a mean wound chronicity of 23 months (p=0.31) .The mean wound surface area was 63 cm^2 prior to debridement in the NPWTi group and 123 cm^2 prior to debride-ment in the NPWT group (p=0.94). After operative debridement (post-operative day 0) there was a mean of 3 (+- 1) types of bacteria per wound. The most common types of bacteria for both groups were Staphylococcus aureus, Corynebacterium, and Pseudomonas aer-uginosa. The mean CFU/gram tissue culture was 3.7x 10^6 in the NPWTi group, while in the NPWTgroup the mean was 1.8x 10^6 CFU/gram tissue culture .There was a statistically greater number of bacteria in the NPWTi cohort than the NPWT group at baseline (p=0.016), however, at the end of therapy there was a non-statistically significant difference be-tween the two groups (p=0.44). At 7 days, the mean number of bacterial species per wound was 2 (+-1) in the NPWTi group, with a decreased number demonstrating S. aureusas compared to the NPWTgroup. Wounds treated with NPWTi had a mean of 2.6 x10^5 CFU/gram of tissue culture while wounds treated with NPWT had a mean of 2.79 x 10^6 CFU/gram of tissue culture (p=0.43). The mean absolute reduction in bacteria for the NPWTi group was 10.6 x10^6 bacteria per gram of tissue while there was a mean absolute increase in bacteria for the NPWT group of 28.7 x 10^6 bacteria per gram of tissue, therefore there was a statistically significant reduction in the absolute bioburden in those wounds treated with NPWTi (p=0.016). However this significance was not as great when examined as a percent in change from the wound bioburden at baseline, with each wound acting as its own control.	This prospective trial of 13 patients with chronically infected lower leg wounds has further strengthened the evidence that NPWTi therapy provides an effective means of reducing bioburden to assist with creating conditions that support wound closure. The co-morbidities experienced by patients in the trial were likely to create significant challenges in achieving closure for both the NPWTi group and NPWT control group. Although there was a non-statistically significant difference in bacterial load between the two groups after the end of therapy this finding is important because at the outset patients in the NPWTi group had a statistically significant higher count. Mean absolute reductions in bacteria for the NPWTi group in comparison to the NPWT one were also statistically significant. The 16% increase in bacteria from baseline for the NPWT group when compared to an 87% reduction in the NPWTi group, which demonstrated a statistically significant difference between the group, is further evidence of NPWTi's effectiveness at reducing bacterial load.

	The percentage change in the planktonic bacteria after debridement was 90% (84%–100%) (absolute bacterial count mean reduction $2.62x10^7$to $2.51x10^6$) for the NPWTi group versus 88% (68%–100%) (absolute bacterial count mean reduction 2.14!$10^6$to $4.76x10^5$) for the NPWT group (p =0.87). The ability to maintain the post-debridement reduced bioburden was a 16% increase in quantitative bacterial count in one week (81% increase to 2% reduction) (absolute mean increase from $4.76x10^5$to $5.74x10^6$) for the NPWT group; when the wound was treated with NPWTi there was only a 4.6% increase in bacterial count from post debridement levels (53% increase to 15% further reduction) (absolute mean increase from $2.51x10^6$to $3.15x10^6$)(p=0.078). From baseline the NPWT group had a 16% increase in bacteria (8200% increase to 100% reduction) over the course of therapy while the NPWTi group had an 87%reduction (45%–100% reductions) (p=0.078).	

Omar	We recruited 10 consecutive patients with acute wounds of the lower limb. No patient had to be excluded. Regarding the demographic data and patient-related risk factors, there was no statistically significant difference between the NPWT and NPWTi group. 10 matched patients received NPWT and were examined retrospectively. The wound size and type of wounds were similar in both cohorts. Comparing NPWTi and NPWT, there was a tendency towards decreased time of hospitalisation (21.5 versus. 26.5 days), and accelerated wound healing (9.0 versus 12.5 days) in patients undergoing NPWTi with saline, however without reaching statistical significance.	This prospective trial of 20 patients compared the use of NPWTi with NPWT. Whilst patients who received NPWTi were found to have shorter lengths of hospital stay and accelerated healing in this study these were not shown to be significant. Nevertheless the authors commented that they believe these factors would reduce the costs of care.

Brinkert	A total of 131 patients were treated with V.A.C. VeraFlo Therapy; of these 41·9% patients were female and 58·1% patients were male. On an average, the patients were aged 59·2 years(range: 21 – 101 years). Comorbidities (e.g. diabetes, arteriopathy, renal failure and blood hypertension) were present in a high percentage of the studied population .Wound aetiologies are listed below. 1. Open fracture (n=46; 35%) 2. Infected haematoma (leg, thorax, abdomen and perineal area) (n=31; 24%) 3. Pressure ulcer (perineal area and heel) (n=27; 21%) 4. Non-healing postoperative dehiscence (n=25; 19%) 5. Diabetic foot ulcer (n=17; 13%) 6. Necrotising fasciitis (n=13; 10%) 7. Limited exposure to osteo synthetic hardware (n=7;5%) 8. Leg ulcer (n=3; 2%) In 46 of 131 (35%) cases, the patients had already been receiving conventional NPWT, which had been unsuccessful in promoting productive granulation tissue formation owing to comorbidities, residual infection and poor debridement. NPWTi was initiated for a mean period of 12·19 days. In 48·8% of the cases, conventional NPWT was reinitiated after this period of NPWTi until secondary closure occurred or a surgical closing technique was indicated. Wound closure was achieved in 128 of 131 wounds. Closure was performed surgically via skin graft, flap or primary suture in 74 (57·76%), 22 (17·33%) and 32 (24·83%)patients, respectively. There was no incidence of wound recurrence or dehiscence at the operated site. Incomplete wound closure was observed in 3 of 131 cases(2·2%) – one due to limb ischaemia and two due to death unrelated to the therapy. Investigators from all three test sites observed a common positive effect of the saline instillation after a few days with respect to increased granulation tissue formation and reduced wound volume. The newly formed granulation tissue after NPWTi was more beefy red and moist. Granulation tissue production was enhanced compared to conventional NPWT, in terms of filling the dead space more rapidly and completely. Undermined cavities and exposed bones were also more rapidly covered during NPWTi. The effects of instillation were likely more striking owing to systematic surgical debridement prior to initiating NPWTi and at each dressing change as appropriate.	This prospective study showed that in 98% of cases the wounds could be closed after debridement and the use of NPWTi. This study is important because of the wide range of different wound types that were included in this trial. In addition 35% of the patients had wounds that were previously non-responsive to conventional NPWT but began to develop productive granulation tissue when NPWTi was applied. Authors reinforced 3M/KCl's assertion that the use of NPWTi does not preclude the need for treating the biofilm appropriately with more active antibacterial products when biofilm has been documented Wound closure was achieved in 128 of 131 wounds via skin graft, flap or primary suture and only 3 patients had incomplete closure one related to limb ischaemia and 2 to unrelated death. Clinicians delivering care to these patients observed enhanced granulation tissue and rapid covering of exposed bones and cavities, which they attributed to the instillation. Nurses also reported the ease of use of the system.

Milcheski	We operated on ten patients. All had contaminated or infected wounds and were treated according to the protocols of the institution's Wound Group, consisting of global clinical evaluation, surgical debridement, NPT use and graft and patch coverage. The only change in conduct was the replacement of traditional NPT by NPT with instillation (NPWTi). The mean time of outpatient follow-up was six months (ranging from three to nine). We observed no relevant clinical or surgical complications. Only one case had a partial dehiscence of the flap suture (case 9). There was no partial or total loss of graft or flap.	This Prospective cohort of 10 patients with complex contaminated wounds of the lower limb or trunk elected to use previously published studies as their method of comparison. As a result authors concluded that their initial impression of negative pressure therapy with instillation showed both reductions in treatment times and length of hospitalisation when compared with historical controls. This is a helpful study because patient follow-up data was collected at an average of 6, but up to 9 months, after hospital discharge. This is unusual for these patient groups and demonstrated that of the 9 patients, only one had had a partial dehiscence of a flap structure

Blalock	Nineteen patients with a mean age of 57.1 ± 18.1 years were treated. Comorbidities included diabetes (N = 8), obesity (N = 7), current tobacco use (N = 6), and hypertension (N = 5). Treated wound types included surgical (N = 8),trauma (N = 4), ulcers/ injuries (pressure and non-pressure, N = 7). The average duration of NPWTi-d with ROCF-CC use was 9.0 ± 6.9 days. All wounds displayed less malodour, reduced devitalized tissue, and improved granulation tissue formation following NPWTi-d with ROCF-CC dressings. Once the wound bed was clean and free of debris, fibrinous material and slough, and/or thick exudate, NPWTi-d with ROCF-CC was discontinued. Following discontinuation, patients were discharged to a skilled nursing facility, long-term acute care facility, home health, or home with encouragement to follow up at a wound care centre. In 2 patients at risk of lower extremity amputations due to their complex wounds, amputation was no longer suggested after the use of NPWTi-d with ROCF-CC dressings.	This retrospective case series offers notable information about the role of NPWTi in both supporting preparation of a wound bed for closure and limb salvage. Authors report their conclusion that NPWTi therapy is a safe and efficient adjunctive treatment. Authors reported similar positive outcomes to those reported in literature including the work of Kim, Gabriel, Fluierara, and Fernandez. In addition they report NPWTi's contribution to achieving hospital discharge for all patients either following a wound closure procedure or with advanced wound dressings. This paper proposed that 2 patients avoided amputation following use of NPWTi, this demonstrates potential cost savings for the NHS.

Gabriel 2008	There were no statistically significant differences between the control and NPWT instillation groups with regard to age, wound area, pre-albumin levels, diabetes history, smoking history and incidence of infection. Patients in the NPWT instillation group did differ significantly from the control group with respect to treatment outcome endpoints. Compared with controls, patients in the NPWT instillation group required significant fewer hospital days of wound treatment (36.5 +- 13.1 versus 9.9 +- 4.3days,P,0001). The NPWT instillation-treated wounds cleared of clinical infection (based on qualitative cultures) earlier (25.4 +- 6.6 versus 6.0 +- 1.5 days,P,0001), were closed earlier (29.6 +- 6.5 versus13.2 +- 6.8 days,P,0001) and were discharged earlier (39.2 +- 12.1 versus14.7 +- 9.2 days,P,0001). The Kaplan–Meier survival analysis confirmed highly significant (P,0001) shorter duration of treatment for the NPWT instillation group compared with the control group for wound clearance of clinical infection, wound closure, treatment and discharge. In the NPWT instillation group, all 15 wounds cleared the bacteria bioburden, versus 10 of 15 for the control group. The reason these five control wounds remained colonised throughout care is unknown and the patients have since been lost to follow-up. Eleven of the 15 NPWT instillation-treated wounds progressed to the point where they could be surgically closed. Four wounds were left open to be closed by secondary intention. In the control group, 9 of the 15 wounds progressed to the point of surgical closure and 6 were left to be closed by secondary intention.	This comparative retrospective study of 82 patients with infected or critically colonised extremity and trunk wounds is unusual because it identified a number of statistically significant improved outcomes for patients who received NPWTi when compared to NPWT. Published in 2008 it made an early contribution to demonstrating the benefits that NPWTi can offer including reduced lengths of stay, shorter treatment durations, shorter average times to wound closure, a reduction in surgical debridements, shorter clearance of infection and fewer dressing changes. These findings have been confirmed in further work by Gabriel et al and other publications included in this submission.

Davis	A total of 93 subjects were screened and consented in the study between April 2016 and January 2018 after the enrolment goal was met. Two patients were excluded because they failed screening, and one withdrew consent before the initiation of therapy. A total of 90 subjects were randomised; 30 were randomized to each of the three treatment groups, NPWTi, NPWT-C, or NPWT-K. The study was conducted at Parkland Hospital. There were no differences in demographics, wound characteristics or comorbidities in the three treatment groups with the exception of race, CKD, and wound aetiology. There were no differences in outcomes among NPWTi, NPWT-C, and NPWT-K groups in the proportion of healed wounds (63.3%, 50.0%, 46.7%p= 0.39), surgical wound closure (83.3%, 80.0%, 63.3%,p= 0.15), number of surgeries(2.00.49, 2.40.77, 2.40.68,p= 0.06), length of stay(16.315.7, 14.77.4, 15.310.5 days, p=0.87),time to wound healing (46.222.8, 40.918.8, 45.928.3 days,p= 0.78) and the duration of NPWT (118.288.4,109.9101.0, 134.196.9 hours, p= 0.61). Finally, a Kaplan–Meier analysis was performed to evaluate the time to heal. Th ere was no significant difference between the treatment groups (Figure 2). The median standard error(95% confidence interval) days to heal for NPWTi, NPWT-C, or NPWT-K was 43.09.4 (24.5–61.5), 41.06.3(28.6–53.4), 42.013.1 (15.3–51.2). The log Rank comparison is p=0.69.	This study was a randomised controlled trial of 90 patients with complex foot infections. The comparator was NPWT. Whilst a number of improved outcomes were demonstrated including shorter lengths of stay, higher wound closure rates and shorter use of antibiotics post discharge, none of the outcomes in this study achieved statistical significance.

Zelen	A total of 20 patients were enrolled at a single diabetic foot clinic in the United States. Enrolment was concluded after 20 patients. A total of 11 women and 8 men were enrolled, 89% white (n= 17) and 11%African American (n= 2). The median patient age was 64 years, ranging from 43 to 81.Approximately, half of the wounds occurred on the right lower limb and half on the left lower limb. The most frequently reported wound locations were right plantar in 4 of /19(21%) cases, followed by the right heel and left heel with 3 of /19 (16%) cases each. Wound sizes at the initial visit ranged from 1.0 cm×1.0cm to 5.0cm×7.0 cm, with a mean wound size of 2.4 cm×2.2 cm. The median baseline necrosis was 50% (range, 15-100). A total of 14 of /19 (74%) patients healed completely using NPWT, with a median time to healing of 34 days (range, 9-124). Eleven of 19 patients (58%) healed within the 6-week evaluation period. Of those patients healing within 6 weeks, the median baseline wound size was 2.52 cm2(range, 1.0-13.72 cm2) and the median baseline amount of necrosis was 40% (range, 15%-80%). Three of the 5 remaining patients required additional interventions. Patient 5 required a skin graft on day 88 to complete healing and was healed on day 113. Patient 6 underwent a muscle flap and skin graft on day 61, completely healing on day 124. Patient 17 had the largest wound (5.0 cm×7.0 cm) in the study with 100% necrosis at baseline. This patient underwent 2 split-thickness wound grafts after initial NPWT therapy with 60% successful raft take to the wound but still had not healed as of day 135 and was referred to an outside specialist for treatment. One serious adverse event was reported with patient 12 who experienced cellulites and infection after 12 days in the study. She was admitted to the hospital and although she was given ample options for limb salvage, having a long history of diabetic ulcers and infections with her foot, the patient opted for limb amputation. The serious adverse event was unrelated to the negative pressure therapy device.	This Prospective cohort of 19 patients with diabetic foot ulcers used an another company's device. Despite some sizeable wounds and high levels of necrosis, 74% of patients healed their wounds completely in a mean time of 34 days. Other patients required skin grafts to achieve healing.

Kim 2020	There was no statistically significant demographic difference between the NPWTi and NPWT Subjects at baseline. Most of the wounds were classified as chronic, and most chronic wounds were diabetic ulcers. Effectiveness Results There was no statistically significant difference in the primary endpoint: mean number of inpatient OR debridements required during the inpatient stay after the initial debridement until the wound was deemed ready for closure/coverage between NPWTi and NPWT Subjects (1.0 vs 1.1, respectively; p=0.68). Microbiological evaluation of results showed a mathematically significant decrease in mean total bacterial counts between time of initial surgical debridement and first dressing change in NPWTi-d (n=69) Subjects compared with NPWT (n=63) Subjects (-0.18 Log10 CFU/g vs 0.6 Log10 CFU/g, respectively; p = 0.02). Subjects with high bacterial count after initial OR debridement, the NPWTi-d group had a bacterial count decrease while the NPWT group had a bacterial count increase at the first dressing change (-1.5*106 vs 3.1*105 p = 0.09). Similarly, of Subjects who had a high bacterial count after the initial OR debridement, a lower percentage of the NPWTi-d group vs the NPWT group had an increase in bacterial count at the first dressing change (0/7 vs 8/12, p = 0.25), but the difference was not significant (Table 8). There were no statistically significant differences in the mean time until wound was deemed ready for closure/coverage between NPWTi-d (n=71) and NPWT (n=66) subjects (mean 6.8 vs 6.3 days, p = 0.71). Time to readiness for closure was shorter in the NPWTi-d group vs NPWT group for patients with higher bacteria counts among all Subjects and Subjects who received at least one debridement, but this was not significant (5.3 days vs. 7.9 days, p=0.18; 4.8 days vs. 6.5 days, p=0.16). There was no statistical difference in proportion of wound closure/coverage by Day 56 (± 8 days) between the two groups (68/71 [95.8%] vs 64/66 [97.0%], p = 1.00). There was no significant difference in incidence rate of Subjects experiencing wound complications between NPWTi-d (n=71) and NPWT (n=66) Subjects (28 vs 21, respectively;	This prospective, randomised, multi-centre study of 132 patients with wounds that required operative debridement examined a number of outcomes within the scope of this submission. The comparator used was NPWT. The strongest findings were a significantly greater decrease in mean total bacterial counts between the time of initial surgical debridement and the first dressing change in negative pressure wound therapy plus instillation (n=69) . This echoes findings found in earlier research. Unexpectedly there were no differences in required inpatient operating room (OR) debridements, time to readiness for wound closure/coverage, proportion of wounds closed, or incidence of wound Complications. However, this was not the case for a subgroup of patients with dehisced wounds where decreases in bacterial load were maintained. Statistically significant reductions in debridements, hospital length of stay and lower pain scores were also reported. Whilst in total this study reported that 18 patients had skin maceration, rash or dermatitis, these are common occurrences with therapy for this cohort of patients. It is generally believed this can be mitigated by high quality staff training. 1 patient developed an infection and another an undefined problem. This number is consistent with the control group.

	p=0.38) in the PP Population. Fewer patients were re-hospitalized in the NPWTi-d group vs NPWT group for the ITT population after initial hospital discharge, but the difference wasn't statistically significant (3 vs 9, p=0.07). However, an ad-hoc analysis to determine relative risk based on original categorial parameters did show that NPWT Subjects had 3.1 times the risk of re-hospitalization compared to NPWTi-d Subjects. Safety There were 4 deaths (3 NPWTi-d Subjects and 1 NPWT Subject), none of which were treatment related. A total of 20/93 (21.5%) of the NPWTi-d Subjects and 11/88 (12.5%) of the NPWT Subjects experienced at least one treatment-related adverse event. Surgical Dehisced Wounds Subgroup Analysis Further subgroup analysis of wounds classified by aetiology showed that for surgical dehisced wounds (n=23), there was a significant decrease in mean bacterial count (Log10 CFU/g) in the NPWTi-d versus NPWT group at first dressing change (-0.6 vs +0.5, $p < 0.01$) as well as at the point the wound was deemed ready for closure (-0.8 vs +0.6, $p < 0.01$). There was also a significantly lower mean number of debridements in the NPWTi-d group vs. NPWT group (0.7 vs 1.8, $p = 0.01$). Hospital length of stay was marginally significantly shorter (9.3 days vs 21.8 days, $p = 0.05$), and a significantly lower pain score (52.0 vs 79.0, $p = 0.03$) was recorded in the NPWTi-d group.	

Mixed wounds		
Gabriel, 2014	Forty-eight patients received NPWTi-d and were compared to a historical control group of 34 patients who received standard NPWT. Patient demographic variables were similar between the 2 groups. Comorbidities for both groups included obesity and diabetes. Clinical results showed patients who received NPWTi-d required fewer surgical OR debridements (2.0 vs 4.4) and experienced a shorter average length of hospital stay (8.1vs 27.4 days), LOT (4.1 vs 20.9 days), and time to wound closure (4.1 vs 20.9 days) (P<0.0001), compared to patients treated with NPWT. The hypothetical model showed an average reduction of $8143 for OR debridement costs with NPWTi-d versus NPWT patients ($6786 vs $14,929, respectively), based on average actual frequency of OR debridements (2.0 vs 4.4) received by the NPWTi-d versus NPWT groups. When average hospital stay was multiplied by the daily cost of NPWTi-d therapy, average therapy cost was $1418 lower for the NPWTi-d group ($799 for NPWTi-d vs $2,217 for NPWT).	This comparative retrospective study provided strong statistical evidence of positive clinical benefits and potential cost savings gained by the use of NPWTi instead of standard NPWT without instillation. Wounds were evenly divided between the intervention and control groups and were a mixture of upper and lower extremity and trunk wounds. Patients with infected or critically colonised wounds were included in the trial. The inclusion of the financial model developed by the authors is a very useful contribution to demonstrating potential cost savings of NPWTi in comparison to NPWT.

Ludolph	In the period from January 2013 to November 2017, we investigated a total of 267 patients who were treated with NPWTi. Of these, 148 patients (55.4%) had 4 or more surgical interventions, and 111 patients (41.6%) met the inclusion criteria for this study; 45 female (40.5%) and 66 male(59.5%) patients were included. The average age was58.6 years (range 20-86 years). Average duration of NPWTi was 11.5 days (SD 3.9 days), with a range of 7 up to31 days. Mean hospital stay was 22.6 days (SD 8.6 days),ranging from 10 to 54 days. Wounds were localised in 17.1% at upper extremities, 52.3% at lower extremities, and 30.6% at the trunk. Wounds treated with NPWTi were:- postoperative infections 10.8%(n= 12 patients), osteomyelitis 11.7% (n= 13 patients), chronic ulcers 10.8% (n= 12 patients), chronic wounds at different locations 12.6% (n= 14 patients), necrosis 4.5%(n= 5 patients), wounds after trauma 8.1% (n= 9 patients), abscesses 20.7% (n= 23 patients, defined as invasive infections), and pressure ulcers 9.0% (n= 10 patients), wounds after tumour excision 1.8% (n= 2 patients)(Further indications (9.9%,n= 11 patients) for NPWTi were any wounds with higher potential of infectivity, such as local excisions of hidradenitis suppurativa. Final wound reconstruction, including local or free flaps 49.5% (n= 55 patients), skin grafts 28.8% (n= 32 patients),or secondary wound closure 18.0% (n= 20 patients), was performed in 96.4% of all cases. In the other cases, secondary healing was intended in 3.6% (n= 4 patients). The average of the number of different bacterial species (NDB) of all 111 patients was 1.7 NDB at the first operation, with a range of 0 up to 6 different bacteria. In 41.5% (n= 46), 2 or more different bacteria were found, and in 43.2% (n= 48) and in 15.3% (n= 17),1 and no bacteria were found at all, respectively. At the fourth operation, a decrease of the mean number of 48% to 0.9 was observed (P< .001). In 22.5% (n= 25), 2 or more different bacteria were found, 1 in 28.8% (n= 32), and no verifiable bacteria in 48.7% (n= 54) at this time.	This Prospective study is important because it was designed to evaluate whether the NPWTi supports a decrease in bacterial load and facilitates wound closure. Despite patients with a range of complex wounds being recruited to the trial it showed that with the application of NPWTi the average numbers of different bacterial species (NDB) reduced from 1.7 at the first surgical operation to 0.9 by the fourth. This was highly statistically significant. Similarly the mean amount of bacteria (AB fell from 4.2 to 1.5 over the same time scale and was also highly statistically significant. As a result 96.4% of patients had wounds closed by skin grafts, skin flaps or secondary wound closure. This study is also valuable as it recorded the reduction in NDB and AB between the first and fourth operation by the different types of patient's wounds therefore helping to demonstrate the value of NPWTi in reducing bacterial load and preparing the wound bed for closure. A small number of patients (5) with pressure ulcers close to their anus did not see reduction in NDB and AB as the other 100 participating in the study.

	The amount of bacteria (AB) of each swab was documented as described above. The mean AB was 4.2 AB at the first operation, with a maximum of13. At the fourth operation, the mean AB showed a significant (P< .001) decrease of 65% to 1.5 AB. The distribution of microbial colonisation depending on diagnosis showed a maximum of bacterial load for pressure ulcers, chronic wounds at different locations, and chronic ulcers. During NPWTi, a reduction of the mean bacterial number to 46% for pressure ulcers, 22% for chronic wounds at different locations, and 56% for chronic ulcers was observed. Of 111 patients, 51 were eligible for a repeated bacteria load follow up over at least 4 cycles of NPWTi. In this sub-group, we treated 15.7% (n= 8 patients) with I infections; 21.6% (n= 11 patients) with osteomyelitis;13.7% (n= 7 patients) with chronic ulcers; 7.8% (n=4patients) with necrosis, wounds after trauma, and abscesses;9.8% (n= 5 patients) with pressure ulcers; and 3.9% (n=2patients) with wounds after tumour excision. The results show a continuous reduction of the mean bacterial number as well as of the mean AB in nearly all groups. In the groups with initially purulent infections and in wounds after tumour excision, no more bacteria could be found in the swab at the fourth operation. For patients with wounds because of osteomyelitis, the reduction of NDB was 40% and 61% for AB. An effective reduction for NDB and AB was also found in chronic ulcers showing a decrease of61% and 69%, respectively. In patients suffering from pressure ulcers, NDB and AB presented minimally higher at the fourth operation, with an increase of 16% and 3%, respectively. All pressure ulcers were located sacral in proximity to the patient's anus. Only one patient in this small group(n= 5) demonstrated an increase of NDB and AB. This patient was admitted to the hospital in poor condition and developed a sepsis during the course. Of the group, 2 patients showed an unchanged NDB and 2 patients a decrease of NDB, whereas AB dropped in 3 of the patients and presented unchanged in 1 patient. During all operations, the analysis of average NDB and AB of all 51 patients demonstrated a decrease of both parameters at every single operation. Bacterial number showed 1.7 NDB at the first operation, 1.2 NDB at the sec-ond, 1.0 NDB at the third, and 0.9 at the fourth. A similar course was observed for the AB, with 3.8 AB at the first operation, 2.4 AB at the second, 2.0 AB at the third, and 1.7AB at the fourth (Figure 6). A shift of bacteria from Gram-positive to Gram-negative or vice versa was not observed	

McElroy	NPWTi-d with ROCF-CC was used in adjunctive treatment of 14 complex wounds of seven men and seven women, with an average age of 63.6 years. Wound types included pressure injuries, necrotising fasciitis, diabetic foot ulcers, and surgical wounds. Culture results showed presence of fungal and/or bacterial infection in 10 (71.4%) wounds. For all wounds, NPWTi-d with ROCF-CC was used as part of an adaptive, individualised treatment plan, with reassessments performed at each dressing change. NPWTi-d with ROCF-CC was the only negative pressure wound therapy system used in four (28.6%) patients. In three cases (21.4%), the wounds were initially managed with conventional NPWT or NPWTi-d with standard ROCF-V dressings. Treatment with NPWTi-d with ROCF-CC was subsequently transitioned to NPWTi-d with ROCF-V and/or conventional NPWT in five (35.7%) cases. A pre- and post-treatment combination of either NPWT or NPWTi-d with ROCF-V was used in two (14.3%) patients. Complete surgical or sharp bedside debridement was performed on eight (57.1%) of wounds, and one patient received an incomplete debridement in the operating room (OR). Normal saline was instilled in all cases. However, in one case, the solution was switched to acetic acid during NPWTi-d with ROCF-V dressing, and in two separate cases, a hypochlorous solution was used during the first 2 days of NPWTi-d with ROCF-CC dressing. Duration of treatment with NPWTi-d with ROCF-CC ranged between 1 and 15 days, with an average of 6.1 days. Dressings were changed every 2 to 3 days, with a mean number of 2.6 ROCFCC dressing changes. Based on wound photos and the health care practitioner's assessment, all wounds showed improved granulation tissue formation and a decrease in devitalised tissue, with improved colour, less malodour, less surrounding erythema, and demarcation of healthy skin from devitalised tissue. In some cases, this enabled excisional debridement to be undertaken successfully after NPWTi-d. Twelve (85.7%) of the patients did not require a return to the OR for further debridements.	This retrospective case series provides useful data about the benefits individualised application of NPWTi delivers by combining different system components to meet patient's needs. Authors identified 3 common clinical situations that prompted use of NPWTi, these are consistent with its use as an adjunctive therapy and included inability to go to the operating room, patients having a palliative treatment goal or recalcitrant none viable tissue. Despite a mixed aetiology of wounds and evidence of bacterial and fungal colonisation in over 70% of cases health care practitioners considered that all wounds showed improvement within an average of 6 days treatment. As a result 85.7% of patients were not required to undergo further surgical debridement as had previously been anticipated. Authors concluded that NPWTi appeared to provide added benefit of wound cleansing when thick exudate and other devitalised tissue remained in the wound.

Powers	In 2012 when NPWTi was applied, 16 of the 28 subjects (57%) improved as opposed to 12 of the 28 subjects (43%) worsened. In 2011, with use of NPWT alone, 11 of our 24 subjects (46%) improved leaving 13 out of 24 subjects (54%) who worsened. The mean number of OR visits decreased from 2.7 with NPWT to 2.4 with the use of NPWTi. The mean duration of hospital stay decreased from 13.4 days with use of NPWT to 12.9 days when NPWTi was applied. The median values also reflect a decrease showing a median duration of hospital stay being 11.0 days with NPWT and dropping 1 full hospital day to 10.0 days when NPWT was administered.	This abstract from a retrospective historical cohort controlled study of 52 patients with infected wounds evaluated NPWTi and NPWT, including the use of different dwell times. Presented at the Symposium in Advanced wound care results showed patient benefits in the reduction of debridements, wound closure rates and time to wound closure.

Timmers	In 4 years, we treated 59 patients (30 males; mean age 53 [range, 2–94] years) with NPIT. Thirty-three patients were treated for osteomyelitis. We matched the osteomyelitis patients with 94 controls (58 males; median age 46.6 [range, 9–85] years). In these cases the cause of osteomyelitis was posttraumatic because of various types of injuries or trauma in the past. In controls the principal cause of osteomyelitis was posttraumatic (84.0%), tumour surgery (8.5%), hematogenous (4.3%), or other (3.2%), with areas affected: lower leg (68.1%), femur/pelvis (29.8%), and other (2.1%). In the total NPIT group, a total of 72 bacterial species (13 patients had two bacterial species isolated from the wound) were identified, including S. aureus (40.3%), Enterobacter cloacae (12.5%), and Pseudomonas aeruginosa (9.7%), the latter two being common microorganisms colonizing chronic wounds, whereas S. aureus and streptococci are common isolates in osteomyelitis. Therefore, a different distribution of microorganisms in the NPIT group for treatment of osteomyelitis was observed, with 38 bacterial species identified with more S. aureus species (50%) and more non-common isolates (39.3%) than in the total group, most likely related to the facts that S. aureus is often isolated in case of osteomyelitis and many noncommon isolates could be observed as many patients had an extensive history of antibiotic treatments, before admission to our hospital. Scope of this study was primarily focused on treatment of osteomyelitis, therefore, from this point microbiologic considerations are only used for patients treated for osteomyelitis. In all controls, an etiologic agent was cultured from the initial culture. Microbiological examination revealed 108 bacterial specimens (83 patients with one bacterial specimen causing infection, eight patients with two, and three patients with three bacterial infestations). Principal bacterial specimens as cause of osteomyelitis were S. aureus (67.6%), P. aeruginosa (5.6%), Streptococcus sp. (4.6%), Gram-negative stains, and other bacterial species (22.2%). Although there are methodological limitations to this study (a prospective treatment group compared with a historical control group), in our opinion new information about treatment of posttraumatic osteomyelitis is provided and. First of all, no statistically significant difference in appearance of the two most important cultured bacterial specimens over the time could be detected (S. aureus and P. aeruginosa) between the groups could be observed (p = 0.153). In the period January 1999–February 2003 (4 years) patients suffering osteomyelitis who were admitted to the trauma department were treated with TNIP, while their counterparts treated in the orthopaedic department were treated with	This comparative retrospective trial included 59 patients focussed upon clinical outcomes for patients with osteomyelitis. It provides important new information about the treatment of osteomyelitis with NPWTi. The NPWTi group and controls (94 patients) were matched. There was no statistical significance between the treatment and control groups in the appearance of the most important cultured bacteria over time however those patients who had been treated with NPWTi had a recurrence rate for their osteomyelitis of 10% vs >50% for control patients. This finding was highly statistically significant and adds important weight to the evidence of NPWTi's clinical effectiveness. 88% of patients had successful infection removal wound (shown by sterile swabs being taken) by one NPWTi cycle. Whilst 12% of wounds failed to become sterile, authors report that sufficient granulation tissue was formed to enable surgical wound closure. 52% of patients had delayed primary surgical wound closure, and 40% split thickness skin grafting. The remainder closed by secondary intention and showed NPWTi's positive impact on achieving high closure rates. Finally this paper documents a high number of rehospitalisations in the control group resulting in a highly statistically significant difference in cumulative hospital stay and surgical reinterventions.

	standard therapy. The recurrence rate of osteomyelitis in the TNIP group was 10%, but the recurrence rate in the prospective control group was still > 50%. Sterile wound swabs were obtained in 35 (59.3%) of 59 treatment courses, whereas, in another 17 (28.8%) patients in whom clinical signs of infection of the wound had vanished, bacteria known to colonize the skin (e.g., coagulase-negative staphylococci) were repeatedly cultured but no longer the pathogens held responsible for the infection. Thus, the wound infection had been treated successfully in the first treatment episode in 52 (88.1%) of the 59 patients. The average time until an infected wound had become sterile or yielded skin bacteria only amounted to 12 (range,3–38) days. Also, in the three patients with fresh traumatic injuries at high-risk sites such as the pelvis, no infection occurred after start of NPIT. A small percentage of wounds failed to become sterile (n57; 11.9%), yet enough new granulation tissue was formed to permit surgical closure of the wound. Principal surgical closure techniques were delayed primary closure (n532; 51.6%) and split-thickness skin grafting (n525; 40.3%). In five patients (8.1%), spontaneous secondary wound healing occurred. During a 43–89 month follow-up period of patients treated with NPIT, three patients had a recurrence of the infection, caused by the identical bacterial species cultured in the first episode. All these patients suffered of osteomyelitis. The recurrence rate of clinical infection in the group of patients with osteomyelitis was three in 30 (10%). The average time to recurrence was 8 months. None of the patients treated for indications other than osteomyelitis suffered a relapse of infection. After surgical closure of the wound, one patient, aged 78years, died due to underlying condition unrelated to the wound (i.e., a cardiac insufficiency). Furthermore, five patients died during follow-up, after apparent successful treatment of the wound. None of the deaths were related to the primary indication for which NPIT had been ap-plied: e.g., one patient died as result of an accident, one patient died of an underlying haematological disorder, whereas three patients died due to myocardial infarction in combination with severe diabetes. To determine whether NPIT had shortened hospital stay and reduced the risk of recurrent exacerbations of infection in osteomyelitis cases, a comparison was made be-tween the NPIT and a historical control group. Controls were identified as described before from the	

	electronic hospital information system including the bacterial specimens causing the osteomyelitis. Patients and controls did not differ with respect to age, sex, or underlying medical conditions. In the osteomyelitis control group (n594), the median duration of hospital stay was 27.3 (range, 3–196) days. Fifty-five patients (58.5%) had to be rehospitalized at least once because of a recurrence of the osteomyelitis. The median number of hospitalizations amounted to 2.0 (range,1–25) per patient. When taken together, the median cumulative duration of hospital stay in this group was 73 (range,6–419) days. Related to these recurrences, many patients underwent multiple surgical interventions (median, 5.0 per patient; range, 2–42), varying from the removal of osteo-synthesis material to extensive debridement of the wound and the local application of gentamycin polymethylmeth-acrylate (PMMA) polymer chains. The cases and controls did not differ in the duration of the first hospital stay (p50.624); however, due to the high number of rehospitalizations because of recurrences in the control group, the cumulative duration of hospital stay 419) days vs. 36 (range, 15–75) days in the NPIT group which was statistically significant different (p<0.0001). Also, by consequence, the number of surgical interventions was significantly higher in the control group (five vs. two in the NPIT group [p<0.0001]). Overall, three recurrences (10%) occurred in the NPIT group while 55 recurrences (58.5%) were observed in the control group(p<0.0001). Furthermore, the time to a first recurrence differed significantly between the groups, as illustrated in the Kaplan–Meier curve for recurrence-free survival.	

Garcia-Ruano	Of the initial cohort of 202 patients with postoperative abdominal wall wound dehiscence, 45 presented with mesh exposure and were included in the study. Out of these 45, 34 were treated with conventional dressings and 11 with VAC instillation therapy. For each patient, demographics, existing risk factors, indication for abdominal surgery, and operative reports were reviewed. Median patient follow-up was 18.6 m (minimum 0.7 m and maximum 158.6 m). Patient ages ranged from 34 to 81 y, with a mean age of 59.1 +- 14.6 y (range, 54.6-63.5), with no differences between groups (P = 0.124). Similarly, there was no difference in sex distribution (68.9% male versus 31.1% female, P = 0.124). Of the existing risk factors, smoking was the most common overall (46.7%), followed by chronic obstructive pulmonary disease (42.2%) and obesity (40%), with a mean body mass index of 32.4 +- 12.3 kg/m2 (range, 28.2-36.5). According to Kanter's classification of risk of development of complications after an abdominal wall surgery, 64.4% of the patients included in our study were considered high risk and only 8.9% low risk, with no significant differences between the groups (P > 0.05); 93.3% of the patients had undergone previous abdominal surgeries, increasing their risk for complications. Patients' initial diagnosis, understood as the disease that led to the abdominal surgery immediately preceding the dehiscence, was most commonly an oncological process (44.4%), followed by intestinal disease (17.8%), morbid obesity (8.9%), and isolated disorders of the abdominal wall (11.1%). This initial surgery, in which an abdominal mesh was placed, was performed as an emergency procedure in 28.9%, and in 35.6%, the procedure included surgery on the bowel as well as the abdominal wall, which, according to Kanters, are factors that increase the risk of complications. Wound dehiscence occurred at a mean of 13.1 +- 8.6 d (CI95 10.1-15.5 d) following laparotomy (14.8 +- 10.3, CI95 7.5-22.2 d in the conventional treatment group and 12.4 +- 8.1, CI95 9.1- 15.6 d in the VAC-instillation group). Initial assessment of the wound included measurements and photographs as well as microbiological samples. All cases presented with clinical signs of infection at the start of the episode with purulent discharge and bad odour, with positive cultures in 82.2% of the cases. Infection was generally polymicrobial, with a variety of microorganisms including Grampositive (Estreptococcus beta-hemolitic, Staphylococcus aureus), Gram-negative (Pseudomonas spp., Enterobacteriaceae: Escherichia coli, Proteus sp, Klebsiella sp, Enterobacter sp, Serratia marcescens), anaerobia (Clostridium sp), fungi (Candida albicans), and antibiotic-resistant bacteria (Acinetobacter sp).	This comparative retrospective study of 46 patients with abdominal mesh exposure due to dehiscence further supports the evidence for use of NPWTi in comparison to conventional wound care. As has been seen with similar studies for those patients who received adjuvant treatment with NPWTi implant preservation was significantly higher, numbers of surgical procedures were significantly lower, fewer patients continued to have positive microbiological cultures. Whilst patients in the NPWTi therapy group had higher rates of definitive wound closure, than those receiving traditional dressings, this was not statistically significant. Nevertheless it is important to note that once again the duration of treatment was statistically significantly shorter than for patients receiving conventional care. In this study the NPWTi group had a non-significant longer length of stay. No explanation is offered for this, or the small numbers of patients who developed hernia recurrence, reappearance of mesh exposure, enterocutaneous fistula.

	In all cases, remission of all clinical signs of infection was a necessary condition for the episode to be considered concluded. However, in the conventional treatment group, of the 76.5% initially positive cultures, 50% remained positive at the end of the episode, whereas out of the 100% of patients with positive cultures in the VAC-instillation group, only 36.4% remained positive at the end of treatment. These differences were statistically significant (P = 0.04). In the group treated with VAC-instillation, no patient required a new implant, and in one patient (9.1%), the original implant was partially removed during VAC dressing changes without requiring an extra surgical procedure. The implant preservation rate in the conventional group was 20.6%, with a statistical significance (90.9% versus 20.6%, P < 0.001). The majority of patients in the conventional treatment group (94.1%) required additional surgeries to obtain a definite wound closure, as opposed to only 54.5% from the VAC instillation group. Furthermore, the procedure required in most cases to achieve wound closure in the VAC-instillation group was simple closure (45.5%), whereas in the conventional treatment group, removal of the original mesh (41.1%) and mesh replacement (32.3%) were the most frequent . Overall, the number of additional surgeries ranged between 0 and 9, with a median of two interventions in the conventional treatment group (mean 2.3 +- 2.1) and one intervention in the VAC-instillation group (mean 0.8 +- 0.7) (P = 0.009) . A definite wound closure was achieved in 53.3% of cases with no differences between groups (P > 0.05) with 63.6% of patients in the VAC-instillation group and 50% in the conventional treatment group achieving a definite wound closure. Overall, there was a 24.4% incidence of hernia recurrence, 15.6% of reappearance of mesh exposure, and 6.7% of enterocutaneous fistula. Despite the slightly lower incidence of complications in the VAC-instillation group, recurrence of abdominal hernia was more frequently observed in this group, although with no statistical significance (P =0.637). Total duration of treatment, defined as the period of time from the occurrence of abdominal mesh exposure to the achievement of a stable wound closure with patient discharge, varied from 0.2 to 158.6 m, with 31.3 +- 37.2 m the mean duration (median 15.63 m) in the conventional treatment group and 2.4 +- 1.6 m (median 1.88 m) in the VAC instillation	

	group (P < 0.001). Patients who received VAC-instillation treatment, however, had a longer hospital stay (median 66 d) than the conventional treatment group (median 60 d), but with no statistical significance (P = 0.745).	

Deleyto	Both groups were comparable regarding clinical characteristics. The analysis of the sample showed that the number of hospitalization episodes was higher in the CWT group (0–19, median 3) than in the NPWTi group (1–3, median 2). In addition, total hospitalization stay was measured in 88.21 days (SD 77.05) for the CWT group and 69.09 (SD 33.56) for the NPWTi group. Finally, 94.1% of patients in the CWT group required one or more additional surgeries to obtain a definite wound closure (5 simple closures, 2 debridements, 14 mesh removals, 11 mesh substitutions), as opposed to only 54.5% in the NPWTi group (5 simple closures, 1 debridement, 0 mesh removals or substitutions). Based on this data, the cost analysis was performed as explained above. In the NPWTi group, therapy was applied for a period ranging from 7 to 36 days (mean 19.73 ± 9.5 days). Taking also into account the prices of the consumables, mean cost of VAC Veraflo® therapy (NPWTi) was in our sample 76.07€ per patient day. According to the previously described equation, mean cost of the therapy was 1588.45€ (DT 723.25; IC95: 1102.17–2074.74).	This comparative retrospective study of 45 patients with abdominal mesh exposure due to wound dehiscence provides significant clinical and financial information about the effectiveness of Veraflo when compared with conventional wound therapy. Not only did patients whose wounds were dressed with conventional dressings spend longer in hospital ,and have a higher number of operative debridements, they also had a higher number of hospital admissions. All of these factors impact upon the levels of resources consumed. Authors calculated the cost of a hospital stay by including expenses related to surgery. As a result they concluded that the mean cost of care when NPWTi was used as an alternative to conventional wound dressing was over €2,000 lower. This finding is important because NPWTi is often perceived to be an expensive option in comparison to standard care.

Eckstein	NPIT was performed successfully in 14 out of 15 cases. The application lasted for a mean of 13.3±4.6 days. Over the course of the treatment 4.1±1.6 dressing changes were performed, whereas in one case only 2 were needed. The longest treatment lasted for 26days and a total of 8 dressing changes had to be performed until clinically sufficient results were obtained. Before the first application of the NPIT the mean leukocyte concentration was 8.55103/mL±2.23103/mL. After ending of therapy leukocyte concentrations showed a significant decrease to 6.76103/mL±2.26103/mL(p<leukocyte concentrations and 0.012). CRP was calculated by absolute values as well as by percentage. For the first day of treatment CRP values ranged from 55.7±68.0 mg/L. These values decreased to 12.3±10.9 mg/mL and thereby dropped highly significantly (p<0.001) when compared to the initial value. When normalized to percent, a highly significant reduction of the CRP could be observed (p<0.001). Regarding bacterial loads no significant decrease was found over the course of the therapy. In one case an increase in the bacterial load could be observed to the end of therapy. The course of the pain value determined via the NRS was highly variable but at the end of the therapy all but 1 patient obtained pain relief. The mean WS before NPIT was18.48±12.83 cm2 which was highly significantly reduced to 7.6±7.4 cm2(p<0.001) . A complete wound closure was obtained by secondary intention in all but one case. Before the therapy, oro-cutaneous fistulae could be observed in 9 of 15 cases. By therapy-ending no fistulae were present. MRP not covered by soft tissue could be found in 12 out of 15 cases. In 11 cases this did not cause any interference with the NPIT and a complete coverage of the osteosynthesis materials by newly formed granulation tissue could be observed. The NPIT had to be discontinued due to progression of soft tissue loss and skin ulceration in one case with an exposed MRP. In that case the therapy regimen was switched to open wound therapy after MRP removal.	This retrospective case series investigated the use of NPWTi for patients with complex facial septic wound healing defects to consider whether it might replace the current standard of care, which is prolonged open wound treatment. This is a valuable paper because unlike all other papers included in this submission it used serum inflammatory parameters as markers of success. These showed statistically significant reductions in leukocyte concentrations and CRP values. Likewise wound sizes were highly significantly reduced. Importantly pain levels were measured with a numerical rating scale and all but 1 patient reported less pain by the end of therapy. Whilst bacterial loads were not found to reduce significantly in this trial it may be important to take the complexity of these patient's wounds into account. It is encouraging that the mean length of stay was 13.33 days and the longest treatment lasted for 26 days as an alternative to prolonged open wound care. Authors described these results as astonishing.

Lehner	Forty-two patients from eight centres in Germany, The Netherlands and the UK were enrolled in the study. Four patients did not meet the inclusion criteria (OI explanted prior to NPWTi) and were excluded from the analysis because retention of the OI at follow-up could not be analysed. One patient was lost to follow-up, one patient was discontinued by the investigator and four patients received off-label treatment and were omitted from the analysis. This left 32 patients from which data were analysed. Of 32 patients, 20 (62.5%) had an infected hip implant, 10 (31.3%) an infected knee implant and 2 (6.2%) infected osteosynthesis material (acetabulum fixation device, metal plate upper arm). Of 32 patients, 22 (68.7%) had an acute infection and 10 (31.3%) a chronic infection. Treatment consisted of surgical debridement of the wound in combination with lavage, systemic antibiotic therapy and NPWTi. In 25 of 32 (78.1%) cases, debridement of the wound was documented, and in all cases (100%) lavage was performed (jet lavage (4/32, 12.5%) with polyhexamethylene biguanide 0.04% solution (polyhexanide or PHMB, B. Braun Melsungen AG, Melsungen, Germany) (16/32, 50.0%), Ringer's solution (1/32, 3.1%), povidone-iodine (9/32, 28.1%) or octenidine dihydrochloride (Octenisept, Schülke & Mayr, Norderstedt, Germany) (2/32, 6.2%). Prior to NPWTi, all wounds (39/39, 100%) were clinically infected. Infection was defined as: presence of at least one of the following: positive culture, abnormally elevated C-reactive protein/white blood cell count and in addition clinical signs, such as exudating wound, redness, swelling or pain. Positive cultures were obtained from 28 of 32 patients (87.5%) . Typical microorganisms were present prior to NPWTi, and 8 of 32 cases had more than one type of microorganism present. No multi-resistant microorganisms were discovered. Systemic antibiotic treatment depended on the microorganism(s) present in the wound and was administered per institutional standards. Generally, antibiotic treatment was given for 6 weeks after termination of NPWTi. Thirty-two patients had a mean of 11.8 days (median 6.0 days, range 1.0–109.0 days) between diagnosis of infection and start of NPWTi. The results showed that the time interval had no influence on implant retention (p=0.382). The mean time of follow-up was 176 days (median 164 days, range 57–490 days). Overall findings showed that 27 of 32 patients (84.4%) retained their implant: 19 of 22 patients (86.4%) with an acute infection (< 8 weeks) and 8 of 10 patients (80%) with a chronic infection (>8 weeks and 0.05). For acutely infected Ois, assuming an average retention rate of 65% based on published data , there was a significant difference between patients who retained their implant versus those patients who did not retain their implant (i.e. 86.4 and 13.6%, respectively, p=0.036). Likewise, for chronically infected Ois,	This prospective cohort of 32 patients with infected orthopaedic implants published not only overall outcomes for patients but also for some findings was able to differentiate between patients with chronic and acute infections. One of the first findings was that whilst there was a significant range between diagnosis of infection and the start of NPWTi (median 6.0 days, range 1.0–109.0 days) this time interval had no influence on implant retention. This is important as it reinforces the potential contribution that NPWTi can make to outcomes in both acute and chronic scenarios. This was also supported by the data showing that implant retention was significantly higher for patients in the NPWTi cohort than the average figures based on published data for both acute and chronic infections, as well as overall. 4 of the 32 patients had a recurrence of their infection and were required to reattend hospital. 3 of these were given a further cycle of NPWTi therapy after which their infection resolved. The therapy unit was replaced on two occasions due to a faulty alarm. No adverse events were attributed to the technology.

	assuming an average retention rate of 30% , there was a significant difference between patients who retained their implant versus those patients who did not retain their implant (i.e. 80 vs 20%, respectively, p=0.001). When considering overall implant retention (acutely and chronically infected Ois), and assuming an average retention rate of 50% , a significant difference was detected between patients who retained their implant versus patients who did not retain their implant (84.4 vs 15.6%, respectively, with p<0.001). The mean duration of NPWTi was 16.3 days (median 15.0 days, range 9–46, p=0.486). Reasons to discontinue treatment were local negative bacterial culture (25/32, 78.1%) as per institutional procedure and clinical judgment of the surgeon (6/32, 18.7%). One case was not documented. PHMB was used in 31 of 32 (96.9%) cases (concentrations 0.04–0.2%); in 1 case (3.1%), saline was used. The mean NPWTi negative pressure setting was 138.3 mmHg (median 125 mmHg, range 125–200 mmHg). Instillation time was in all cases < 1 min. The mean hold time was 19 min (median 20.0, range 5–30 min), and the mean vacuum time was 70.3 min (median 60.0, range: 30–270 min). A mean of 16.5 cycles (instillation+hold+vacuum) per day were applied (median 18.0 cycles, range 5–40 cycles per day). Recurrence of infection was monitored by the investigator or general practitioner through regular wound checks as per institutional standard. In cases of wound problems such as pain, swelling, redness, discharge or systemic signs of infection patients were required to return to the hospital for clinical control to confirm recurrence of infection. Infection eradication was reported in 24 of 32 patients (75%). In 6 of 32 patients (18.8%) recurrence of infection was reported and 2 of 32 patients (6.2%) had an ongoing infection. In 3 of 32 patients (9.4%), where recurrence of infection was diagnosed, the surgeons decided to perform a second treatment with NPWTi and were thereafter able to eradicate the infection and retain the implant. Thirty patients (93.8%) had a mean duration of clinical signs of infection of 27.3 days (median 20.5 days, range 10–125 days). Duration of clinical signs of infection was defined as the date that the infection was diagnosed until surgical closure. For all 32 patients evaluated, the mean number of dressing changes was 3.5 (median 4.0 dressing changes, range 1–8 dressing changes). The mean hospital stay was 39.5 days (median 35 days, range 12–97 days). The influence of known major risk factors was not significant. Four of six patients with diabetes were able to retain their implant (p=0.228), as did all eight patients who were smokers or had a history of smoking (p=1.0). Safety analyses were	

	described by the secondary endpoints: incidence of treatment-related complications and device complaints. Of 32 patients, 12 (37.5%) experienced a total of 17 Aes; however, none of the Aes were treatment or device related. One patient (3.1%) died prior to follow-up due to age and condition. In two instances, device problems were reported (not able to reset alarm), and the systems had to be replaced	

Hehr	A total of 28 patients were included in this review. Three cohorts were identified, including patients with exposed or infected spinal, extremity, or sternal hardware. Overall, 25 of 28 (89%) patients had successful retention or replacement of hardware, with clearance of infection and healed wounds. Specifically, 17 of 28 (61%)patients maintained their original hardware, having successful salvage. In 11 patients, original hardware was removed, with subsequent replacement in 8 (73%) of those patients after a clean wound was achieved. To date, all hardware has been maintained without sign of infection or wound complication at last follow-up. Patients with exposed or infected spinal hardware(n = 11) represent patients with original clinical indications for spinal internal fixation ranging from chordoma(n = 4), metastatic cancer (n = 4), trauma (n = 1), scoliosis (n = 1), and spinal stenosis (n = 1). Average age was 52.3 years (range 20-73 years) and five patients had prior radiation. Initial post-debridement cultures were poly-microbial in 8 of 11 patients. Seven patients were treated with Dakin's instillation, while the remaining four received Prontosan. Only the patient previously treated for scoliosis underwent hardware removal, as hardware was prominent, contributing to soft tissue defect, and deemed not necessary for bony stability. All 10 other patients had salvage of their hardware(90%) and eventual closure of their wounds at an average of 12.2 days from initial debridement. All patients had healed wounds, without signs of recurrent infection at last follow-up appointment (average 174 days, range41-650 days). Those patients with extremity hardware (n = 12) had prior internal fixation for pathology affecting 10 lower extremities and 2 upper extremities. Upper extremity indications were traumatic in nature. Lower extremity fixation had been previously completed for traumatic fractures in nine patients, and tumour resection in one patient. Average age of patients was 55.5 years (range17-86 years). Initial post-debridement cultures were poly-microbial in the majority of patients and the vast major-ity (n = 10) received Dakin's instillation. Original hardware was salvaged in 33% of these patients. All patients who had hardware removed at time of initial debridement (n = 8) went on to have additional hard-ware successfully placed on the same admission after negative cultures were achieved, except in two patients. Internal fixation was not re-attempted because of patient's non-compliance in one upper extremity patient. A second patient with tibial/fibular non-union in the set-ting of chronic osteomyelitis ultimately decided to proceed	This retrospective case series of 28 patients with infected or exposed spinal, extremity or sternal hardware has notably demonstrated that following use of NPWTi 89% of patients were able to retain hardware, have it replaced following infection clearance and go on to achieve wound healing. Furthermore at last follow up 100% of these patients have been maintained without infection or wound complication. This is an important finding as significant number of patients were found to have poly-microbial infections following initial debridement which increased the challenge of removing infection. This paper adds to the evidence base that use of NPWTi supports retention of hardware across a range of different clinical scenarios.

	with below-knee amputation. All other hardware remains intact and without signs of infection at time of last follow-up (average 180 days, range 21-502 days).Average time until definitive closure was 7.6 days (range3-14 days) in those patients having hardware salvaged or successfully re-implanted. There were five patients who presented to the Plastic Surgery service with infected sternal hardware. Three patients had exposed LVAD components, while two had exposed wiring/plating from prior sternotomies. All VAD devices were maintained through reconstruction; however, one patient required delayed device removal and replacement 4 weeks later because of a mechanical pump failure. One patient had removal of sternotomy wiring at initial debridement, with placement of sternal plating at definitive closure. Regrettably, this patient passed away from reasons unrelated to her sternal wound shortly after closure. The average age of these patients was 66.2 years (range 51-75). Unfortunately, initial post-debridement cultures were not obtained for the sternotomy patients. The three patients with exposed LVAD components grew Coagulase negative Staphylococcus and Serratia marcescens, Coagulase-negative Staphylococcus, and Methicillin-sensitive Staphylococcus aureus, respectively. All patients in the sternal wound cohort were given Dakin's as their instillation fluid. Average day to definitive closure was 19.2 days (range 3-72). Including the patient who went on to LVAD replacement due to mechanical pump failure, all patients have retained hard-ware/LVAD, without signs of active infection at time of last evaluation (average 63.75 days, range 37-80 days).	

Morinaga	The described treatment was used as the treatment of choice after open chest surgery in 46 cases with mediastinitis, who were referred to our department from December 2005 until May 2012 . The breakdown of these patients was: 30 men and 16 women, who ranged in age from 16–88 years (mean age 67 years). The primary diseases for which open chest surgery were performed included: acute myocardial infarction in 26 cases, thoracic aortic aneurysm in seven cases, valvular disease in six cases, myocardial infarction + valvular disease in three cases, and other diseases, including thyroid tumour, thymic tumour, and oesophageal tumour, in four cases. CABG was performed in 29 cases, valve replacement in nine cases, graft replacement in seven cases, and tumourectomy in four cases. It should be noted that, in three cases of aneurysm, the replacement graft was observed to be exposed. In addition, there were 30 cases that showed acute conditions within 2 months after the operation and 16 cases with chronic conditions. Of these 46 cases, there were two deaths, yielding a mortality rate of 4.3%. In the 44 surviving cases (95.7%), after undergoing this treatment, the mediastinal sinus infection subsided and benign granulation tissue grew over the wound. The transplantation of muscle flaps (pectoralis major muscle in 15 cases, latissimus dorsi muscle in three cases, and pectoralis major muscle + rectus abdominis in three cases) and split thickness grafting were performed in 21 cases, split thickness grafting alone was performed in 10 cases, and conservative management alone was carried out in 13 cases. As a result, full recovery was achieved in all of these cases of mediastinitis. The duration of this treatment varied between 13–115 days (average 38 days). In terms of additional treatment performed after this treatment, the duration was: 13–44 days (average 27 days) for 21 patients in whom the transplantation of muscle flaps and epidermisation were performed, 13–51 days (average 26 days) for 10 patients in whom split thickness grafting alone was performed, and 14–125 days (average 65 days) for 13 patients in whom conservative management alone was performed for some reason (e.g. a deterioration in the general patient condition in patients or patient refusal). It should be noted that, as in many other patients in whom surgery was actually performed, for the 13 patients in whom conservative management alone was carried out, the wounds healed sufficiently so that surgery could thus be performed within ~ 1 month. The period required for healing for all patients ranged from 23–125 days (average 50 days).	This retrospective case series of 46 patients with severe mediastinitis did not use NPWTi. Authors captured data showing higher rates of wound closure, wound closure and retention of surgical implants when compared against conservative management. No statistical significance was reported

	In terms of the additional treatment performed following this treatment, the period was: 23–61 days (average 37 days) for 21 patients in whom the transplantation of muscle flaps and epidermisation were performed, 31–61 days (average 41 days) for 10 patients in whom only skin grafts were performed, and 31–142 days (average 78 days) for 13 patients in whom conservative management alone was carried out. In other words, many of these patients could be cured within either 1 month or 1.5 months with additional surgery.	

Chen	Eighteen patients with a wound infection after posterior spinal surgery were included in the study; A laboratory examination revealed increased C-reactive protein (CRP) in 16(88.9%) patients, an increase in the erythrocyte sedimentation rate (ESR) in 12 (66.6%) patients, and leucocytosis in six (33.3%) patients. All patients received treatment until wound healing was achieved. One of the patients developed a back rash during the VAC treatment, which was alleviated after taking antiallergic drugs. No other complications were observed during the modified VAC treatment. Another patient developed liver dysfunction after taking vancomycin, which was thus replaced by levofloxacin during subsequent treatment. All patients were treated with prophylactic antibiotics before starting treatment; two were treated with clindamycin because of allergies. After the wound infection diagnosis, the antibiotics were changed according to the drug sensitivity test results. We obtained the wound change parameters from the medical records after 1 week of VAC treatment. The results show that the size of the wound after treatment with modified VAC was significantly smaller than that after debridement ($p<0.05$). After 1week of treatment, the length of the wound did not change significantly, but the width decreased from an average of 3.2 cm to 1.6 cm ($p<0.05$).The average wound size was reduced from 23.5 to 13.2 cm2.T The diagnosis of a surgical site infection was made 10.2 days after internal fixation. The average cost of a full course of VAC wound treatment was $1558.80. The total cost of the VAC dress-ing was significantly higher than that of a traditional dressing, but the time cost for clinicians and nursing staff was significantly lower for the VAC treatment than for the traditional dressing treatment. An excellent wound bed was achieved in all patients after an average of 8 days of VAC treatment. The patients were sent to the operating room to close the wound under anaesthesia. Three patients were treated with VAC three times and one patient received VAC treatment four times, while the remainder received two VAC treatments. The average wound healing time and hospital stay of patients treated with modified VAC was 17 and 33 days, respectively. Wound secretions from 18 patients were cultured after debridement: there were six patients with Staphylococcus aureus,4withStaphylococcus epidermi-dis,3withEnterobacter faecalis,1with Pseudomonas aeruginosa, and 1withEnterobacter aerogenes;3patients had	This retrospective case series of 18 patients with an SSI following spinal surgery used an another company's device. Whilst the paper gives an overview of costs for the whole of a patient's treatment the most important findings documented in this paper are that the time needed by clinicians and nursing staff to deliver care was significantly lower than traditional dressing treatment.

	no bacteria in the wound (There were seven cases with multidrug-resistant organisms, including three cases of . Aureus, three of S. Epidermidis, and one of P . Aeruginosa. The postoperative levels of leucocyte count were 6.03 ± 1.50 × 109cells/ml, and the erythrocyte sedimentation rate amounted to 15.72 ± 6.60 mm/h. The C-reactive protein level decreased to 6.88 ± 5.12 mg/L. All patients were followed-up for at least 1 year, and none of the patients developed a recurrent infection.	

Huang	There were 32 post-cranioplasty patients who underwent surgical treatment due to implant-related scalp infection from May 2010 to March 2016 in our hospital. Of these 32 patients, 11 patients were excluded for the following reasons: cranioplasties were non-titanium mesh, including bone cement (n = 1), cerebrospinal fistula (n = 3), autologous bone flap (n= 4), frontal sinus-related infection (n =2), and autologous skin flap (n = 1). Thus, 21 of 32 patients were assessed in the study. According to our procedure mentioned in the method, 4 of the 21 patients underwent TTME, and all 4 patients recovered after treatment. Fourteen patients received a U-shape debridement, and 13 of the 14 patients recovered, except 1 patient with infection who required an extra TTME surgery, the other 3 patients who received PTME surgery and then recovered. No patient had implant-related systemic infection.	This retrospective cohort of 21 patients with exposed/infected mesh following cranioplasty used another company's device. The principle outcome relevant to this systematic review was that treatment success, in the form of implant retention, was achieved in 95.2% of cases. There was no comparator.
Qui	There were no statistically significant differences in sex, age, disease location, and underlying disease between the two groups. The patients in both groups were cured after treatment . The cure duration was compared between the two groups; the indicator improvement period of the negative-pressure group was significantly shorter than that of the traditional group ($p<0.05$). The incision length was also compared between the two groups; the incision length in the negative-pressure group was significantly shorter than that in the traditional group ($p<0.05$). We evaluated the physician's workload based on the frequency of the change of dressing. The mean frequency of the dressing-change of the negative-pressure group was significantly less than that of the traditional group ($p<0.05$). While the expenses for the materials of the VSD kit in the negative-pressure group were higher, the fee for dressing-change in the traditional group was higher because of the longer period of dressing-change; hence, there was no significant difference in cost of treatment between the two groups ($p>0.05$)	This retrospective case series of 73 patients with severe multiple-space infections in the oral, maxillofacial and cervical regions used another company's device. It was compared with conventional incision, drainage and dressing techniques. The paper confirms some of the outcomes seen with NPWTi use including statistically significant shorter mean wound closure times and numbers of dressing changes. Reduced pain levels were also reported in comparison to standard care.

Ikeno	The mean patient age was 71.9 ± 15.3 years with 12 male patients and 6 female patients. Seven patients underwent emergent surgery including 6 patients who were diagnosed with acute type A aortic dissection. Aortic operation under circulatory arrest was performed for 16 patients including 10 patients who underwent partial or total arch replacement. Three patients underwent aortic root replacement, 2 of those patients with valve-sparing reimplantation. Four patients underwent coronary artery bypass grafting, with the internal mammary artery being used in 2 patients. The mean operating time was 408.4 ± 139.1 min and the mean cardiopulmonary bypass time was 196.9 ± 38.2 min. The duration from initial aortic surgery to resternotomy and debridement was 23.7 ± 15.9 days. The mean time from the suspicion of DSWI to resternotomy was 3.4 ± 1.9 days. Organisms were identified from the mediastinal tissue cultures in all patients. The most common pathogen was methicillin-resistant Staphylococcus aureus (MRSA), which was found in 8 patients, followed by Serratia marcescens, Klebsiella aerogenes (formerly Enterobacter aerogenes) and S. aureus in 2 patients. Other identified pathogens include Pseudomonas aeruginosa, coagulase-negative staphylococci, Citrobacter freundii and Corynebacterium.	This retrospective case series of 18 patients with deep sternal wound infections ,following prosthetic grafting, used another company's device. Despite all patients having organisms identified in their wound, including MRSA for 8 of them, 100% of patients went on to retain their implants and 17 (one patient died) had skin grafts following their resternotomy. Authors stated that they believed NPWTi had improved both early and late patient survival.
Surgical site infection		

Jurkovic, 2019	A total of 41 patients were enrolled in the study between November 2016 and September 2018 (trial Group – 19 patients, control Group – 22 Patients) with a finding of deep fascional infection after Surgical Performance. Both patient groups were comparable in basic demographic and clinical parameters. Although there were higher number of patients after onco-Surgical care and a greater volume of defects in the trial Group this did not reach the statistical significance. The average duration of treatment in the NPWTi trial group was two days shorter, but this difference was not statistically significant. The figures were not differed by the number of debridements, but in the experimental group was the apparent trend to a shorter time to clean the defect (13 vs. 19 days). The secondary suture was achieved with the same relative frequency in both groups (NPWTi 84% vs. NPWT 73%). The rest of the defects were treated with the help of the wet therapy method. The suppression of secondary sutures with a necessity to heal with wet therapy was significantly higher in the control Group compared to the trial Group (37% vs. 25%). Eventeration was observed in the trial Group in two patients with advanced findings of a deep Fascial infection. In the control group, there was no need for the surgery during therapy. The financial cost of the treatment was significantly higher in patients with the instillation system used (13 769 kč vs. 7892 CZK). However, the total cost of hospitalization was not statistically differentiated (177 469 CZK vs. 119 467 CZK)	This randomised controlled trial has made a useful contribution to the evidence base for NPWTi as it demonstrated, that in line with its purpose the combination of NPWT with instillation is an effective method of accelerating the wound cleaning phase of wound closure. Data collected during the trial showed ○ Shorter average treatment duration ○ Shorter mean times to wound closure ○ Fewer surgical debridements ○ Statistically significant difference in reduction of pathogens p=0.035 Whilst the cost of using NPWTi were significantly higher than NPWT alone the total hospitalisation costs did not differ significantly. When considered against the improved patient outcomes gained this study is helpful in demonstrating NPWTi's clinical and cost effectiveness.

Chowdhury	During the study period, a total of 30 patients under-went muscle flap reconstruction for pre-existing sternal wounds that had failed to close following a previous cardiac procedure. Each group comprised 15 patients, all of which had undergone a previous CABG procedure. In addition, all patients in both groups had the left internal mammary artery harvested. Overall, the mean age of the patients in this study was 70.0±7.4 years, and the mean application of body mass index (BMI) was 31.5±4.7kg/m2. There were no significant differences in patient age, BMI, or sex when comparing the 2 groups . There was also no statistical difference between groups in the duration of the sternal wounds before reconstruction, with the overall du-ration of the wound being 7.9±4.5 weeks, and all wounds from both groups were positive for bacterial cultures. Lastly, patients in both groups displayed various comorbidities, including hypertension, coronary artery disease, hyper lipidemia, and diabetes mellitus; however, there were no significant differences in either the number of overall comorbidities or the number of specific comorbidities when comparing the groups. When comparing the 2 groups, there was a significantly shorter time to primary wound closure for group 1 when compared with group 2 (P < 0.0001). The mean time to primary wound closure for the group 1 was 7.9±2.3 days with a median of 8 days, whereas patients in group 2 required 13.9±3.2 days to primary wound closure with a median of 15 days. Furthermore, 75% of the patients in group 1 could be closed within 9 days, and the remaining NPWTi-d-treated patients were closed within 12 days. In contrast, at least 16 days were required until primary closure of 75% of patients in group 2, and 20 days were required until all patients in group 2 under-went primary closure. In addition to time to primary closure, the number of therapy days was also compared between groups. There were significantly fewer therapy days for patients in group 1 when compared with patients in group 2 (P = 0.0041). The mean number of therapy days for group 1 was 5.4±2.1 with a median of 6 days, whereas group 2 required 8.4±2.9 days of therapy with a median of 8 days. The total number of excisional debridements and dressing changes were also compared between the 2 groups—dressing changes were performed at the time of surgical debridements. There were significantly fewer surgical debridements and dressing changes for patients in group 1 when compared with patients in group 2 (P = 0.0011). The mean number of debridements for patients in group 1 was 1.8±0.7 with a median of 2, where-as patients in group 2 required 3.1±1.0 debridements with a median of 3.	This retrospective comparative case series evaluated the use of NPWTi, in comparison to traditional moist wound dressings, as an adjuvant treatment to muscle flap reconstruction, which is viewed as the mainstay approach following treatment of sternal wound complications. Success is dependent upon the removal of wound exudate and infectious material before reconstruction and wound closure. This paper clearly shows the significant contribution NPWTi made towards the improved outcomes for this patient cohort. It is significant because improved outcomes were demonstrated across a number of important measures relevant to this submission. These included significant differences in time to primary wound closure, fewer therapy days, fewer surgical debridements and dressing changes. When use of NPWTi for the treatment cohort of patients was compared to use of wound closure strips then statistically significant shorter durations of drain use were observed. Whilst this paper recorded 3 occurrences of seroma in the control group this was not a statistically significant difference

	Furthermore, most patients in group 2 required 3–4 debridements, whereas only 2 patients in group 1 received 3 surgical debridements and none received more than 3. Lastly, drain duration was compared between group 1, which received ciNPT over the closed incision, and group 2, which had wound closure strips placed over the closed incision. There was a significantly shorter drain duration for patients in group 1 when compared with patients in group 2 (P = 0.0001). The mean drain duration for group 1 was 15.0±2.0 days with a median of 14 days, whereas the mean drain duration for group 2 was 21.7±3.9 days with a median of 22 days (Fig.5A). In group 1, 75% of patients underwent drain removal by day 16, and the remaining patients in group 1 had drains removed by day 21 (Fig.5B). In group 2, 75% of patients underwent drain removal by day 24 and all patients had drains removed by day 28 (Fig.5B). There were 3 patients with complications (ie, seromas) in group 2 and no complications in the group 1 patients; however, the difference in complications between groups was not statistically significant (P = 0.2241). For patients in both groups, all incisions remained healed at the 90-day follow-up visit.	

Pressure ulcers		
Jain	Our review of the case log resulted in 10 patients with 11 Girdlestone procedures (nine unilateral, one bilateral) within our two-year study period. Patients were predominantly male (90%). The average age was 40 years. Operative cultures were polymicrobial in 10/11 cases. Methicillin-resistant Staphylococcus aureus (MRSA) was the most common pathogen, present in six of 11 cases. Delayed partial and primary closure occurred an average of 4.5 days (median day three) after the initial debridement. In the four patients without preoperative greater trochanter ulcers who underwent primary closure over a drain with topical negative pressure therapy after closure for five to seven days, there were no local wound complications. In the remaining five patients with pre-existing ulcers, two underwent complete primary closure while the rest underwent partial closure. After final closure, there were no surgical site infections nor post-operative 75instillation. Complications included wound dehiscence in one patient and further dislocation of the femur in another. Two patients developed new pressure ulcers of the ischium and greater trochanter on the contralateral side from their procedure. Three other patients had a progression of a pre-existing ulcer on the contralateral side, with one undergoing a Girdlestone procedure for that ulcer and the other being evaluated for such a surgery. No patients were re-admitted within 30 days.	This retrospective case series examined the outcomes for 10 patients who underwent a Girdlestone Pseudo-arthroscopy and NPWTi for invasive osteo myelitis of the proximal femur. 1 patient had 2 procedures. This procedure is traditionally used to manage invasive and resistant infection of the acetabular cavity and proximal femur. Despite 10 of the 11 wounds being polymicrobial and 6 colonised with MRSA delayed partial and primary closure was completed on an average of 4.5 days after initial debridement. Authors concluded that the Girdelstone procedure and NPWTi resulted in control of osteomyelitis in 100% of patients. Perhaps one of the most significant findings of this study was that despite significant preoperative infection with over 50% colonised with MRSA no patients were readmitted within 30 days of discharge.

Teot	NPWTi-d with ROCF-CC was applied on 21 wounds from 21patients. Wounds consisted of pressure ulcers from patients with and without neurological disorders, burns and necrosis after skin excision. A total of 16 patients were male, and the mean age of patients was 55·4 years. Comorbidities included diabetes, vascular insufficiency, renal insufficiency, Parkinson's disease and cardiac insufficiency. A total of 11 patients were paraplegic or quadriplegic. Most of the patients had poor nutritional status. The mean number of dressing changes using the NPWTi-d with ROCF-CC cleansing technique was 2·9(8·7 days). Seven(33%) of the patients received conventional NPWT prior to NPWTi-d with ROCF-CC. Surgical debridement was performed on 11/21 (52·4%) wounds prior to application of NPWTi-d with ROCF-CC. In the remaining 10/21 (47·6%)wounds, a superficial layer of non-viable tissue or at least 60% fibrin cover was present when NPWTi-d with ROCF-CC was applied for the first time. None of these 10 patients received surgical operating room (OR) debridement; they either received autolytic debridement, incomplete excisional debridement using a scalpel or curette or no debridement following the application of the NPWTi-d with ROCF-CC cleansing technique. Bone infection was confirmed and treated in 15 cases. Of the 21 wounds, 20 (95·2%) wounds displayed rapid granulation tissue formation under the portion of the foam directly in contact with the wound bed. We observed that the holes of the dressing were filled with a deep layer of granulation tissue covered with fibrin. For patient 2 (pressure ulcer with necrosis), no wound-healing progress was observed because of the amount of non-viable tissue present. NPWTi-d with ROCF-CC was discontinued because of a deep tissue infection unrelated to the therapy. Most of the non-viable tissue was removed at the first dressing change after 3 days of therapy. In 18/21 (85·7%) cases, the wound bed contained≤10% black devitalised tissue at the third dressing change after 9 days of therapy. In the subgroup of non-surgically debrided wounds with a necrosis/fibrin cover, a rapid decrease of the necrotic/fibrinous tissue was observed at each dressing change. In cases where NPWTi-d with ROCF-CC was used over bone infection that was being treated, a difference in colour was observed between the beefy red appearance of the soft tissues surrounding the bone and the granulation tissue covering the bone itself. The granulation tissue covering the bone remained pale and yellow until the systemic antibiotic therapy took effect. Enhanced granulation tissue was observed in the wound bed directly adjacent to the wound contact layer of the dressing versus the cover layer. This increased production was more pronounced over areas of the wound largely exposed to the wound	This retrospective case series of 21 patients primarily focussed upon the use of NPWTi to remove thick exudate, dry fibrin, wet slough and other infectious materials from wounds by loosening, solubilising, detaching and removing them. 85.7% of the patients (18) had pressure ulcers wounds and the other 3 for burns or necrosis. As previously noted, NPWTi is used to create an environment that promotes wound healing by preparing the wound for closure, including the promotion of granulation tissue. This study reviewed patients with large complex wounds that contained substantial areas of devitalised tissue (up to 80%) and/or yellow slough. This study provides important data because debridement of wounds prior to application of NPWT is standard practice, however 48% of patients in this study were, due to the condition of their wound, unable to have operative debridement. Despite this the percentage surface area of black non-viable tissue was reduced to 10% or less after an average of 1-3 applications of NPWTi and yellow slough by 57.1% in the same time scale. 95.2% of the wounds developed rapid granulation tissue suggesting that there is evidence that NPWTi may help to clean large complex wounds when complete surgical debridement is not possible, or appropriate and slough/non-viable tissue remains on the surface.

	contact layer, compared to cavities or deep undermined areas where the cover layer was placed.	Authors reported that patients did not appear to experience pain at dressing changes up to day 9 of therapy.

5 Details of relevant studies

Please give details of all relevant studies (all studies in table 4). Copy and paste a new table into the document for each study. Please use 1 table per study.

Lower limb

Kim et al, 2015. Comparison of Outcomes for Normal Saline and an Antiseptic Solution for Negative Pressure Wound Therapy with Instillation	
How are the findings relevant to the decision problem?	Patients in this trial had infected wounds that require hospital admission and operative debridement. The majority of wounds were on the lower limb and were neuropathic , surgical or ischaemic in nature.
Does this evidence support any of the claimed benefits for the technology? If so, which?	Evidence supports:- o Reduced hospital lengths of stay o Increased wound closure rates o Fewer surgical debridements o Statistically significant shorter time to final surgical procedure
Will any information from this study be used in the economic model?	Not currently planned
What are the limitations of this evidence?	Authors acknowledge that their institution applies an aggressive debridement policy which may vary from others practise. There was no control group and there may have been investigator bias due to previous experience with solutions. The study was not blinded and authors commented that its design best defines it as an effectiveness study
How was the study funded?	Not supported by Acelity/KCI although authors have previously received research funding for other studies.

Kim 2014. The Impact of Negative-Pressure Wound Therapy with Instillation compared with standard Negative-Pressure Wound Therapy: A Retrospective, Historical, Cohort, Controlled Study.	
How are the findings relevant to the decision problem?	Patients in this trial had infected wounds that required admission to hospital and at least two operative debridement procedures. NPWTi was compared with standard NPWT
Does this evidence support any of the claimed benefits for the technology? If so, which?	Evidence supports:- o Statistically significant reductions length of stay for patients with a 20 minute dwell time

Kim 2014. The Impact of Negative-Pressure Wound Therapy with Instillation compared with standard Negative-Pressure Wound Therapy: A Retrospective, Historical, Cohort, Controlled Study.	
	○ Statistically significant reductions in the number of debridements for patients receiving both 6 and 20 minute swell times. ○ Statistically significant reductions in patient's time to final surgical procedure for both 6 and 20 minute dwell times ○ Statistically significant reductions in wound closure rates for patients receiving 6 minutes of dwell time ○ A statistically significant improvement in wound cultures when certain bacteria and yeasts were excluded when patients received a 6 minute dwell time.
Will any information from this study be used in the economic model?	This study may be used
What are the limitations of this evidence?	The choice of instillation solution and the volume used, the duration of NPWT and the maximum or minimum duration of therapy may have impacted upon outcomes.
How was the study funded?	Not stated

Yang C, Goss S, Alcantra S, Schultz G, Lantis J. (2017) Effect of Negative Pressure Wound Therapy with Instillation in Chronically Infected Wounds.	
How are the findings relevant to the decision problem?	Patients in this study had colonisation of their chronically infected wounds with pathogens
Does this evidence support any of the claimed benefits for the technology? If so, which?	Evidence supports:- ○ Statistically significant reduced colonisation with pathogens ○
Will any information from this study be used in the economic model?	This study may be used
What are the limitations of this evidence?	Routine use of debridement in the centre was for only a few millimetres, and may not have removed all infected tissue, small sample size, absence of a standardized biopsy schema.
How was the study funded?	Not stated. Drs Schultz and Lantis are paid consultants for Acelity and other companies.

Yang K, Alcantara S, Goss S, Lantis J. (2015) Cost analysis of negative-pressure wound therapy with instillation for wound bed preparation preceding split-thickness skin grafts for massive(>100 cm2) chronic venous leg ulcers.	
How are the findings relevant to the decision problem?	Patients in this study had massive chronic venous leg ulcers requiring slit-thickness skin grafts
Does this evidence support any of the claimed benefits for the technology? If so, which?	Evidence supports:- o Overall reduction in staff and resource use o Cost reduction
Will any information from this study be used in the economic model?	Not currently planned
What are the limitations of this evidence?	There was no matched comparison group
How was the study funded?	There were no funding conflicts of interest

Goss SG, Schwartz JA, Facchin F, Avdagic E, Gendics C, Lantis JCII. (2014) Negative pressure wound therapy with instillation (NPWTi) better reduces post debridement bioburden in chronically infected lower extremity wounds than NPWT alone	
How are the findings relevant to the decision problem?	Patients in this trial had chronically infected lower extremity wounds
Does this evidence support any of the claimed benefits for the technology? If so, which?	Evidence supports:- o Reduced colonisation with pathogens
Will any information from this study be used in the economic model?	This study may be used
What are the limitations of this evidence?	The study was small and non-randomised. Only one type of instillation fluid was used.
How was the study funded?	Not stated

Omar M, Gathen M, Liodakis E, Suero EM, Krettek C, Zeckey C, Petri M. (2016) A comparative study of negative pressure wound therapy with and without instillation of saline on wound healing.	
How are the findings relevant to the decision problem?	Patients in this trial had acute lower limb wounds

Omar M, Gathen M, Liodakis E, Suero EM, Krettek C, Zeckey C, Petri M. (2016) A comparative study of negative pressure wound therapy with and without instillation of saline on wound healing.	
Does this evidence support any of the claimed benefits for the technology? If so, which?	Evidence supports:- o Reduced Hospital Length of Stay o Reduced time to wound closure o Reduction of costs
Will any information from this study be used in the economic model?	This study may be used
What are the limitations of this evidence?	This study had a small sample size. The prospective arm evaluated NPWTi and retrospective NPWT. Bias was possible due to mixed wound and patient characteristics
How was the study funded?	Not stated

Brinkert et al 2013. Negative pressure wound therapy with saline instillation: 131 patient case series.	
How are the findings relevant to the decision problem?	Patients in this trial had complex infected wounds or wounds at risk of infection. These included Pressure Ulcers (21%), non-healing post-operative dehiscence (19%)Diabetic foot ulcer (13%), exposure to osteo synthetic hardware (7.5%) and leg ulcers (2%) The study also minimised the length of the instillation period as their first aim was to condition the wound for closure at the earliest opportunity. The reduction in instillation additionally helped to reduce the cost of therapy.
Does this evidence support any of the claimed benefits for the technology? If so, which?	Evidence supports:- o High rates of wound closure o Reduced time to wound closure o Successful use of skin grafting techniques o Reduction of resource use
Will any information from this study be used in the economic model?	Not currently planned
What are the limitations of this evidence?	This study was largely observational and cannot be generalised to larger populations
How was the study funded?	Not stated. Dr Teot has previously received educational grants from KCI

Micheski et al. (2017) Initial experience with negative-pressure wound therapy with instillation in complex wounds	
How are the findings relevant to the decision problem?	Patients in this trial had contaminated or infected lower extremity and trunk wounds
Does this evidence support any of the claimed benefits for the technology? If so, which?	Evidence supports:- o Reduced hospital length of stay o Reductions in treatment times
Will any information from this study be used in the economic model?	Not currently planned
What are the limitations of this evidence?	This is a small study that relied upon other published studies for comparators
How was the study funded?	Not stated.

Blalock L. (2019) Use of Negative Pressure Wound Therapy With Instillation and a Novel Reticulated Open-cell Foam Dressing With Through Holes at a Level 2 Trauma Centre	
How are the findings relevant to the decision problem?	Patients in this trial had complex difficult to treat wounds that can pose a significant burden on health care systems
Does this evidence support any of the claimed benefits for the technology? If so, which?	Evidence supports:- o High rates of complete and partial wound closure o Reduced hospital lengths of stay o Cost benefits
Will any information from this study be used in the economic model?	Not currently planned
What are the limitations of this evidence?	Small patient numbers with a retrospective non comparative design.
How was the study funded?	Not stated. Author is a consultant for KCI

Gabriel A, Shores J, Heinrich C, et al. (2008) Negative pressure wound therapy with instillation: a pilot study describing a new method for treating infected wounds	
How are the findings relevant to the decision problem?	Patients in this trial had infected or critically colonised extremity and trunk wounds

Gabriel A, Shores J, Heinrich C, et al. (2008) Negative pressure wound therapy with instillation: a pilot study describing a new method for treating infected wounds	
Does this evidence support any of the claimed benefits for the technology? If so, which?	Evidence supports:- o Statistically significant reduced hospital length of stay o Statistically significant reduced time to wound closure o Statistically significant reduced number of surgical debridements o Statistically significant overall reduction in resource use o Reduction in costs
Will any information from this study be used in the economic model?	This study may be used
What are the limitations of this evidence?	There was a risk of potential selection bias, incomplete data
How was the study funded?	Not stated

Davis et al. (2020) Randomized clinical study to compare negative pressure wound therapy with simultaneous saline irrigation and traditional negative pressure wound therapy for complex foot infections	
How are the findings relevant to the decision problem?	Patients in this trial had complex foot infections. This trial did not use NPWTi as the NPWTi in this study
Does this evidence support any of the claimed benefits for the technology? If so, which?	Evidence supports:- o LOS shorter with NPWTi 16.3 to 14.7 days. o 63.3% wound closure vs 46.7%. o Shorter use of antibiotics post discharge for NPWTi.
Will any information from this study be used in the economic model?	Not currently planned
What are the limitations of this evidence?	This study had a small sample size, being in a single specialist medical centre may have influenced high limb salvage rates selection bias
How was the study funded?	Cardinal Health funded this study

Zelen C, Stover B, Neilseon D Cunningham M. (2011) A Prospective Study of Negative Pressure Wound Therapy With Integrated Irrigation for the Treatment of Diabetic Foot Ulcers	
How are the findings relevant to the decision problem?	Patients in this trial had diabetic foot ulcers. This study used another company's device.
Does this evidence support any of the claimed benefits for the technology? If so, which?	Evidence supports:- o Reduced time to wound closure
Will any information from this study be used in the economic model?	Not currently planned
What are the limitations of this evidence?	There was a small sample, with small wound sizes and no comparator
How was the study funded?	Not stated.

Kim 2020. The impact of negative pressure wound therapy with instillation on wounds requiring operative debridement: pilot randomised, controlled trial. In Press	
How are the findings relevant to the decision problem?	Patients in this trial had wounds that required debridement.
Does this evidence support any of the claimed benefits for the technology? If so, which?	Evidence supports:- Statistically significant reduced colonisation with pathogens Statistically significant reductions in the number of debridements Significantly significant reductions in hospital length of stay
Will any information from this study be used in the economic model?	Not currently planned
What are the limitations of this evidence?	High wound type heterogeneity and potential for inconsistent documentation and wound type classification, institutional variation in lengths of stay
How was the study funded?	In draft not stated.

Mixed wounds

Gabriel A, Kahn K, Karmy-Jones R. 2014 Use of negative pressure wound therapy with automated, volumetric instillation for the treatment of extremity and trunk wounds: clinical outcomes and potential cost-effectiveness	
How are the findings relevant to the decision problem?	Patients in this trial had infected or critically colonised extremity or trunk wounds. NPWTi was compared with standard NPWT.
Does this evidence support any of the claimed benefits for the technology? If so, which?	Evidence supports:- o Statistically significant reduced hospital lengths of stay o Statistically significant reduced number of surgical debridements o Statistically significant reduced times to wound closure. o Statistically significant shorter average treatment durations o Statistically significant reduction in dressing changes resulting in a reduction in staff and resource use o Cost benefits o Patients reported less pain
Will any information from this study be used in the economic model?	This study may be used
What are the limitations of this evidence?	Potential selection bias and some lost data
How was the study funded?	Not stated. Staff at KCI offered practical support with statistical analysis, economic modelling and editing the paper

Ludolph, 2018. Negative Pressure wound treatment with computer controlled irrigation/instillation decreases in bacterial load in contaminated wounds and facilitates wound closure.	
How are the findings relevant to the decision problem?	Patients in this trial had infected or chronic complex wounds that required a minimum of 4 operative procedures to facilitate wound closure. These wounds included postoperative infections (10.8%), chronic ulcers (10.8%), pressure ulcers (9%)
Does this evidence support any of the claimed benefits for the technology? If so, which?	Evidence supports:- o Highly statistically significant reductions in the numbers of pathogens o High rates of wound closure o Successful use of skin grafting techniques

Ludolph, 2018. Negative Pressure wound treatment with computer controlled irrigation/instillation decreases in bacterial load in contaminated wounds and facilitates wound closure.	
Will any information from this study be used in the economic model?	Not currently planned
What are the limitations of this evidence?	None given
How was the study funded?	Not stated

McElroy E. (2019) Use of Negative Pressure Wound Therapy With Instillation and a Reticulated Open Cell Foam Dressing With Through Holes in the Acute Care Setting.	
How are the findings relevant to the decision problem?	Patients in this trial had multiple morbidities and complex wounds of different aetiology which were inappropriate for surgical debridement.
Does this evidence support any of the claimed benefits for the technology? If so, which?	Evidence supports:- o Reduced number of hospital debridements o Reduction in resource use
Will any information from this study be used in the economic model?	Not currently planned
What are the limitations of this evidence?	Small number of patients, lack of a control group selection bias
How was the study funded?	Not stated. Author is a consultant for KCl

Powers K, Kim P, Attinger C, Steinberg J, Evans K, Rocha Z, Smith J, Hung R. (2013) Early experience with negative pressure wound therapy with instillation in acutely infected wounds. Presented to the Symposium on Advanced Wound Care Denver Co.	
How are the findings relevant to the decision problem?	Patients in this trial had acutely infected wounds
Does this evidence support any of the claimed benefits for the technology? If so, which?	Evidence supports:- o Statistically significant reductions in the number of surgical debridements o Statistically significant reduced time to wound closure o Statistically significant higher rates of wound closure.

Powers K, Kim P, Attinger C, Steinberg J, Evans K, Rocha Z, Smith J, Hung R. (2013) Early experience with negative pressure wound therapy with instillation in acutely infected wounds. Presented to the Symposium on Advanced Wound Care Denver Co.	
Will any information from this study be used in the economic model?	Not currently planned
What are the limitations of this evidence?	This has not been published in a peer reviewed journal
How was the study funded?	Not stated

Timmers MS, Graafland N, Bernards AT, Nelissen RG, van Dissel JT, Jukema GN. (2017) Negative pressure wound treatment with polyvinyl alcohol foam and polyhexanide antiseptic solution instillation in posttraumatic osteomyelitis	
How are the findings relevant to the decision problem?	Patients in this trial had osteomyelitis of the pelvis or lower extremity requiring surgical debridement.
Does this evidence support any of the claimed benefits for the technology? If so, which?	Evidence supports:- o Highly statistically significant reduction in hospital length of stay o Highly statistically significant reduction in surgical debridements o Highly statistically significant reduction in the number of visits to hospital and follow on treatments o Highly significant reductions in colonisation with pathogens o High rates of wound closure
Will any information from this study be used in the economic model?	This study may be used
What are the limitations of this evidence?	Selection of control patients may not have identified all those eligible to join this group
How was the study funded?	No funding was received from KCI

Prosthetic implants

Garcia-Ruano A, Deleyto E, Garcia-Fernandez S VAC-instillation therapy in abdominal mesh exposure: a novel indication. . Journal of surgical research.2016 (206) 292-297	
How are the findings relevant to the decision problem?	Patients in this trial had abdominal mesh exposure due to wound dehiscence
Does this evidence support any of the claimed benefits for the technology? If so, which?	Evidence supports:- o Statistically significant reduced time to wound closure o Statistically significant higher rates of implant reduction o Statistically significant reduction of colonisation with pathogens o Statistically significant reductions in surgical procedures o Statistically significant reduction in staff and resource use. o
Will any information from this study be used in the economic model?	This study may be used
What are the limitations of this evidence?	Observational and retrospective design, reduced sample size.
How was the study funded?	Not stated but authors stated no proprietary interests in the product

Deleyto E, García-Ruano A, González-López J. ((2017) Negative Pressure Wound Therapy With Instillation, a Cost-Effective Treatment for Abdominal Mesh Exposure.	
How are the findings relevant to the decision problem?	Patients in this trial had abdominal mesh exposure due to wound dehiscence.
Does this evidence support any of the claimed benefits for the technology? If so, which?	Evidence supports:- o Reductions in hospital length of stay in comparison to convention wound treatment o Reductions in staff and resource use due to fewer hospital admissions o Statistically significant reduced time to wound closure o Statistically significant reduction in surgical debridements o Cost benefits due to smaller mean cost of a hospital stay for patients who received care with NPWTi rather than conventional wound dressings

Deleyto E, García-Ruano A, González-López J. ((2017) Negative Pressure Wound Therapy With Instillation, a Cost-Effective Treatment for Abdominal Mesh Exposure.	
Will any information from this study be used in the economic model?	This study may be used
What are the limitations of this evidence?	The sampling method used means generalisation of data is likely to be imprecise.
How was the study funded?	Not stated but authors stated no proprietary interests in the product

Eckstein FM et al (2019) Antiseptic negative pressure instillation therapy for the treatment of septic wound healing deficits in oral and maxillofacial surgery	
How are the findings relevant to the decision problem?	Patients in this trial had infected osteoradionecrosis and osteomyelitis of the jaw and had been diagnosed with impaired wound healing
Does this evidence support any of the claimed benefits for the technology? If so, which?	Evidence supports:- o High rates of complete and partial wound closure o Reduced times to wound closure o Shorter lengths of stay
Will any information from this study be used in the economic model?	Not currently planned
What are the limitations of this evidence?	A retrospective study and lack of an RCT
How was the study funded?	No internal or external funding

Lehner B, Fleischmann W, Becker R, Jukema GN. (2011) First experiences with negative pressure wound therapy and instillation in the treatment of infected orthopaedic implants: a clinical observational study	
How are the findings relevant to the decision problem?	Patients in this trial had infected orthopaedic implants
Does this evidence support any of the claimed benefits for the technology? If so, which?	Evidence supports:- o Statistically higher rates of implant retention o
Will any information from this study be used in the economic model?	Not currently planned

Lehner B, Fleischmann W, Becker R, Jukema GN. (2011) First experiences with negative pressure wound therapy and instillation in the treatment of infected orthopaedic implants: a clinical observational study	
What are the limitations of this evidence?	This was a single armed prospective nonrandomised observational study with no control arm. The follow up period was short at 6 months after treatment.
How was the study funded?	Not stated. 2 authors were appointed as consultants to the trial. One holds the patent for V.A.C Instil.

Hehr J, Hodson T, West J, Schulz S, Poteet S, Chandawarkar R, Valerio I. (2019) Instillation Negative Pressure Wound Therapy: An Effective Approach for Hardware Salvage.	
How are the findings relevant to the decision problem?	Patients in this trial had infected or exposed spinal, extremity or sternal hardware
Does this evidence support any of the claimed benefits for the technology? If so, which?	Evidence supports:- o Higher rates of surgical implant retention o Reduced colonisation with pathogens o Cost benefits due to 100% of patients maintain closed wounds with no infection or complications at a range of 41-650 days.
Will any information from this study be used in the economic model?	Not currently planned
What are the limitations of this evidence?	The study was observational and retrospective. Patients were not randomised and there were no controls. Results were limited to a single centre and may not be generalisable.
How was the study funded?	KCI did not fund this study. Some authors have previously received un-restricted research grants from KCI

Morinaga K, Kiyokawa K, Rikimaru H, Aoyagi S, Tayama K, Akashi H. (2013) Results of intra-wound continuous negative pressure irrigation treatment for mediastinitis	
How are the findings relevant to the decision problem?	Patients in this trial had diabetic foot ulcers. This study used another company's device.
Does this evidence support any of the claimed benefits for the technology? If so, which?	Evidence supports:- o Higher rates of wound closure o Reduced time to wound closure o Higher rates of surgical implant retention
Will any information from this study be used in the economic model?	Not currently planned

Morinaga K, Kiyokawa K, Rikimaru H, Aoyagi S, Tayama K, Akashi H. (2013) Results of intra-wound continuous negative pressure irrigation treatment for mediastinitis	
What are the limitations of this evidence?	None given
How was the study funded?	None stated

Chen K, Lin J, Sun S, Lin J, Kong J, Tian N. (2018) Vacuum assisted closure combined with a closed suction irrigation system for treating postoperative wound infections following posterior spinal internal fixation.	
How are the findings relevant to the decision problem?	Patients in this trial had post-operative wound infections following posterior spinal fixation. This study used another company's device.
Does this evidence support any of the claimed benefits for the technology? If so, which?	Evidence supports:- o Overall reduction in staff use
Will any information from this study be used in the economic model?	Not currently planned
What are the limitations of this evidence?	This study had a small sample size, and was conducted in a single medical centre
How was the study funded?	There was no specific funding

Huang Z, Lei C, Zhang L, Zue H, Shen J, Wu S, Wang B, Chen J. (2017) Negative Pressure Wound Therapy with Chymotrypsin Irrigation.: A maximal implant retention procedure treating the exposure/infection of titanium mesh in cranioplasty.	
How are the findings relevant to the decision problem?	Patients in this trial had exposed or infected titanium mesh implants following cranioplasty. This study used another company's device.
Does this evidence support any of the claimed benefits for the technology? If so, which?	Evidence supports:- o High rates of surgical implant
Will any information from this study be used in the economic model?	Not currently planned
What are the limitations of this evidence?	Contraindication criteria were not clear or evidence based.

Huang Z, Lei C, Zhang L, Zue H, Shen J, Wu S, Wang B, Chen J. (2017) Negative Pressure Wound Therapy with Chymotrypsin Irrigation.: A maximal implant retention procedure treating the exposure/infection of titanium mesh in cranioplasty.	
How was the study funded?	The study was supported by the Natura Science Foundation of China. Authors report no conflict of interest.

Qui K Li Y, Gai B, Li J, Pan L, Ye Z, Lin Y. (2019) Therapeutic efficacy of vacuum sealing drainage assisted irrigation in patients with severe multiple space infections in the oral, maxillofacial and cervical regions.	
How are the findings relevant to the decision problem?	Patients in this trial had severe multiple-space infections in the oral, maxillofacial and cervical regions. This study used another company's device.
Does this evidence support any of the claimed benefits for the technology? If so, which?	Evidence supports:- o Statistically significant reduced time to wound closure o Overall reduction in staff and resource use
Will any information from this study be used in the economic model?	Not currently planned
What are the limitations of this evidence?	This study was in a single centre with a small sample size, clinical practice may have impacted on results
How was the study funded?	Not stated. No declared conflicts of interest

Ikeno Y, Sakakibara S, Yokawa K, Kitani K, Nakai H, Yamanaka Ket al. (2019) Post-sternotomy deep wound infection following aortic surgery: wound care strategies to prevent prosthetic graft replacement	
How are the findings relevant to the decision problem?	Patients in this trial had deep sternal wound infections. This study used another company's device.
Does this evidence support any of the claimed benefits for the technology? If so, which?	Evidence supports:- o Statistically significant higher rates of surgical implant retention o Reduced colonisation with pathogens.
Will any information from this study be used in the economic model?	Not currently planned
What are the limitations of this evidence?	The study was retrospective. With only 18 patients it was too small to allow for an analysis of the risk factors, patient characteristics and conditions were strongly influenced by aortic diseases and the outcomes of primary aortic surgery.

Ikeno Y, Sakakibara S, Yokawa K, Kitani K, Nakai H, Yamanaka Ket al. (2019) Post-sternotomy deep wound infection following aortic surgery: wound care strategies to prevent prosthetic graft replacement	
How was the study funded?	Not stated.

Surgical site infection

Jurkovic et al, 2019. The instilating sub pressure Ultravac in the therapy of infected laparotomy with fascitits- continuous results of a prospective randomised study.	
How are the findings relevant to the decision problem?	Patients in this trial had an acute and serious surgical site infection. Data were collected for a number of clinical outcomes in the decision problem as well as resource use. NPWTi was compared with standard NPWT
Does this evidence support any of the claimed benefits for the technology? If so, which?	Evidence supports:- Reduced number of surgical debridements Reduced time to wound closure Reduced colonisation with pathogens
Will any information from this study be used in the economic model?	This study may be used.
What are the limitations of this evidence?	This trial's limitations were stated as the non homogeneity of the patients within the groups, the absence of blinding for patients and clinicians and the small number of patients included in the study overall.
How was the study funded?	Not declared but authors stated they had no conflict of interest.

Chowdhry S, Wilhelmi B. (2019) Comparing Negative Pressure Wound Therapy With Instillation and Conventional Dressings for Sternal Wound Reconstructions.	
How are the findings relevant to the decision problem?	Patients in this trial underwent reconstructive surgery for pre-existing sternal wounds that had failed to close following previous surgery.
Does this evidence support any of the claimed benefits for the technology? If so, which?	Evidence supports:- o Statistically significant reduced time to wound closure o Overall reduction in staff and resource use o Statistically significant reduction in surgical debridements

Chowdhry S, Wilhelmi B. (2019) Comparing Negative Pressure Wound Therapy With Instillation and Conventional Dressings for Sternal Wound Reconstructions.	
	○ Cost benefits due to 100% of patients maintain closed wounds with no infection or complications at a range of 41-650 days.
Will any information from this study be used in the economic model?	This study may be used
What are the limitations of this evidence?	Non given
How was the study funded?	Non stated

Pressure ulcers

Jain N, Horn C B, Andrade E G, et al. (2018) Combination of Girdlestone Pseudoarthroplasty and Negative Pressure Wound Therapy with Instillation and Dwell in the Treatment of Invasive	
How are the findings relevant to the decision problem?	Patients in this trial had invasive osteomyelitis of the proximal femur.
Does this evidence support any of the claimed benefits for the technology? If so, which?	Evidence supports:- ○ Reduced colonisation with pathogens
Will any information from this study be used in the economic model?	Not currently planned
What are the limitations of this evidence?	This study had a small number of patients who had a wide range of co-morbidities and poor nutritional status . Follow up was only for one month,
How was the study funded?	No financial support was given for the study. One author provides consultation to the company.

Teot 2017. Novel foam dressing using negative pressure wound therapy with instillation to remove thick exudate.	
How are the findings relevant to the decision problem?	Patients in this trial had large complex chronic wounds with viscous wound exudate that contained substantial areas of devitalised necrotic tissue. Operational debridement was not possible or appropriate for 48% of the 21 patients.

Teot 2017. Novel foam dressing using negative pressure wound therapy with instillation to remove thick exudate.	
Does this evidence support any of the claimed benefits for the technology? If so, which?	Evidence supports:- o Rapid generation of granulated tissue (95.2% of patients) and decreases in necrotic tissue supported reduced times to wound closure. o Patients did not report pain during the first 9 days of treatment
Will any information from this study be used in the economic model?	Not currently planned
What are the limitations of this evidence?	This study is an uncontrolled case series and so has large selection biases and does not consider confounding variables.
How was the study funded?	Not stated. Staff at Acelity provided editorial assistance.

6 Adverse events

Describe any adverse events and outcomes associated with the technology in national regulatory databases such as those maintained by the MHRA and FDA (Maude). Please provide links and references.

During preparation of this submission a search was performed of the **MHRA** database, as per our search criteria listed in Appendix B. No adverse events have been reported to MHRA.

A search was also performed of the **MAUDE** database, as per our search criteria listed in Appendix B. There were 8 reports of adverse events as follows.

One report was submitted with very limited information, it was not possible therefore to ascertain the reason for the submission.

There were 2 reports of device malfunction.

- The first of these was due to the cord that connects to the wall causing the machine to come apart in the middle, little other information about this occurrence is available.
- The other was due to an electrical malfunction with the suggestion that this led to some smoke in the patient's room. . Due lack of detailed information it could not be determined as to whether the smoke related to the malfunction

Five further adverse were reported in relation to the treatment of the patients. After further investigation the evidence supplied was categorised as "Adverse Event Without Identified Device" or "Use Problem; Insufficient Information"

Describe any adverse events and outcomes associated with the technology in the clinical evidence.

A small number of adverse events were reported in the papers selected during the systematic review.

Garcia-Ruarno. 12 patients who had presented with abdominal mesh exposure developed hernias, 7 , reappearance of mesh and 3 an enterocutaneous fistula. No outcomes were given.

Kim 2020. 1 patient developed an infection and another an undefined problem. No outcomes were given.

7 Evidence synthesis and meta-analysis

Although evidence synthesis and meta-analyses are not necessary for a submission, they are encouraged if data are available to support such an approach.

If an evidence synthesis is not considered appropriate, please instead complete the section on qualitative review.

If a quantitative evidence synthesis is appropriate, describe the methods used. Include a rationale for the studies selected.

Enter text.

Report all relevant results, including diagrams if appropriate.

Enter text.

Explain the main findings and conclusions drawn from the evidence synthesis.

Enter text.

Qualitative review

Please only complete this section if a quantitative evidence synthesis is not appropriate.

Explain why a quantitative review is not appropriate and instead provide a qualitative review. This review should summarise the overall results of the individual studies with reference to their critical appraisal.

Enter text.

8 Summary and interpretation of clinical evidence

Summarise the main clinical evidence, highlighting the clinical benefit and any risks relating to adverse events from the technology.

Evidence suggests that NPWTi's mode of action, working as an adjutant therapy to other wound care interventions including debridement and appropriate use of anti-microbial medicines, supports preparation for closure of acute infected or chronic wounds that are failing to heal.

NPWTi supports this through the combination of NPWT and the application and dwell time of instillation fluids that loosen and remove wound exudate and infectious material in the wound bed.

Kim et al confirm this approach in the update of International consensus guidelines for NPWTi, developed by an international multi-disciplinary expert panel of clinicians and published in 2019. This stated that:-

> In conjunction with appropriate wound care, such as debridement and systemic antibiotics, NPWTi may be used as an adjunct therapy in the following acute, chronic, and/or infected wound types:
>
> - traumatic wounds
> - surgical, including dehisced, wounds
> - diabetic wounds
> - venous leg ulcers
> - pressure injuries/ulcers
> - wounds with exposed intact bone
> - wounds with treated, underlying osteomyelitis
> - infected or contaminated wounds in the presence of orthopaedic fixation hardware
> - full thickness burns after excision
> - wounds resulting from evacuation of a haematoma and when haemostasis is achieved and wounds that are a bridge between staged/delayed amputation.

Some of these conditions are outside of the scope of this evaluation however this submission contains evidence of clinical benefit for those in scope.

In 2018 the Health Service Executive in Ireland published National Guidelines for Wound Management. The role of NPWTi was considered during their development. The guidelines state there is evidence that when NPWTi is used as the standard of care in properly selected cases it provides better overall clinical outcomes than NPWT alone.

In 2016 the World Union of Wound Healing Societies published a consensus document in which they stated that "Wound bed preparation to include removal of slough and necrotic tissue combined with cleansing with an appropriate cleansing agent on a regular/timely basis is fundamental.

This statement is further reinforced by Gupta et al's clinical recommendations for NPWTi which stated that automated instillation creates a controlled, protected environment for flushing and cleansing wounds by the proposed mechanism of loosening soluble contaminants in the wound bed followed by subsequent removal during NPWT.

Evidence within this submission has clearly shown that NPWTi has demonstrated its ability to support the reduction of bioburden, an essential aspect of preparing for wound closure, when compared to either conventional wound dressings, or NPWT. Papers published by Jurkovic, Yang 2017,Goss, Gabriel 2008, Garcia-Ruano, Timmers and Kim 2020 showed statistically significant reductions in wound's bacterial load following application of NPWTi.

In addition in those cohorts of patients, where a reduction in bioburden has been demonstrated, they underwent fewer surgical debridements, reduced mean times to wound closure, increased wound closure rates and reductions in length of stay (Jurkovic, Kim 2014, Garcia-Ruano, Timmers, and Powers). Each of these contribute towards a reduction in the use of staff time and other resources.

Evidence considered during the systematic review also demonstrated that in wounds treated with conventional care, or NPWT, the number of bacteria, which can prevent or stall wound closure, either

increased or decreased by a smaller amount than those patients treated with NPWTi. (Jurkovic, Kim 2014, Yang, Goss, Garcia-Ruano, Timmers, Powers and Kim 2020).

This evidence also showed that, where recorded, complete wound closure rates range from 63% to 100%. Approximately 1 third of studies included in this submission documented times to wound closure with a comparator. 50% of these studies showed statistically significant closure with NPWTi. (Gabriel 2008, 2014, Chowdhary and Qui) These studies also showed shorter average treatment durations.

The systematic review also recorded evidence of successful implant retention in patients who have undergone cardiac, orthopaedic and mesh insertion procedures where the initial clinical expectation was that they were unlikely to be salvaged. (Moringa, Huang, Lehner, Ekstein, Ikeno, Deleyto, Garciia-Ruano) Importantly in those studies where a comparator was included in the study design statistical significance of retention was achieved (Lehner, Garcia-Ruano).

The evidence presented has shown a number of key outcome benefits for patients following use of NPWTi as part of their care. A number of papers also captured or modelled the reduction in use of resources and associated cost reductions (). One important finding in some of the studies was that despite the additional costs of NPWTi when compared to alternatives when the over costs of hospitalisation were calculated NPWTi was either cost equivalent or cost reducing.

Very few adverse events were captured by studies included in this review. A small number reported skin maceration and one alarm malfunctioning. No patient deaths were attributed to the product.

References for clinical recommendations, guidelines and consensus statements referred to in this section:-

Kim et al. Negative pressure wound therapy with instillation: International consensus guidelines update. Int Wound J 2019; 1-132019.

Health Service Executive National Wound Guidelines 2018 www.hse.ie/eng/about/who/onmsd/practicedevelopment/WoundManagement/

World Union of Wound Healing Societies (WUWHS). (2016). Biofilm Management in Practice. Position Document: Management of Biofilm. Florence: World Union of Wound Healing Societies

Gupta et al Clinical recommendations and practical guide for negative pressure wound therapy with instillation. Int Wound J 2016; 13:159–174

Briefly discuss the relevance of the evidence base to the scope. This should focus on the claimed benefits described in the scope and the quality and quantity of the included studies.

The benefits listed below were all listed in the Scope document published by NICE. The associated evidence relevant to the scope are drawn from the systematic review and discussed below. * denotes statistical significance

Reduced Hospital Length of Stay
10 studies measured length of stay for patients receiving NPWTi with either standard NWPT or conventional dressings. 4 showed statistically significant reductions in length of stay. One was a level 2 prospective trial of 30 patients with mixed venous and diabetic wounds, and the remainder mixed infected wounds with 142, 82 and 124 patients in comparative retrospective trials at level 3 and 4. Whilst not achieving statistical significance the remaining studies all showed shorter lengths of stay than their

comparators demonstrating a reduction in staff and resource use. One study (Davies) used an alternative NPWTi product and did not show statistical significance.
(Kim 2014*, Gabriel 2014*, Gabriel 2008*, Timmers*, Kim 2015, Omar 2016, Deleyto 2017, Garcia-Ruano , Powers, Davis)

Reduced Number of Surgical Debridements
10 studies measured the number of surgical debridements for patients receiving NPWTi with either standard NWPT or conventional dressings. 6 showed statistically significant reductions in the number of debridements. 5 were comparative retrospective studies related to surgical site infections, extremity and trunk wounds and infected implants. These studies included 124, 142, 82, 46 and 52 patients. One study was a level 2 trial, 3 were level 3 and 1 level 4. The final trial was a level 3 retrospective case series with 30 patients experiencing surgical wound complications.
(Kim 2014*, Gabriel 2014*, Garcia-Ruano*, Choudhry*, Timmers*, Powers*, Jurkovic, Kim 2015, Omar, Goss, Kim 2020)

High rates of surgical implant retention
7 studies measured rates of surgical implant retention for patients receiving NPWTi and compared with either standard NWPT or conventional dressings. 2 showed statistically significant higher retention rates. 2 were comparative retrospective studies both of which related to abdominal wound dehiscence and mesh exposure, 2 were prospective cohorts related to orthopaedic and cranial implants and 3 retrospective case series for wounds failing to heal. These studies included 45, 46, 32, 31, 18,15 and 46 patients. 2 were level 2 trials, 2 level 3 and 3 level 4.
(Lehner*, Garcia-Ruano*,Deleyto, Ikeno, Eckstein, Morinaga, Huang

Reduced Pain
7 studies reported patient's pain levels at dressing change. 1 recorded a statistically significant difference in pain levels following application of NPWTi. 1 was a randomised controlled trial relating to wounds requiring debridement, 1 was a prospective cohort study of complex lower limb wounds, 1 was a comparative retrospective study of infected extremity and trunk wounds and 4 were retrospective case series related to severe complex and chronic wounds and one SSI. These studies included 132, 82, 21, 18, 73, 15, and 10 patients. 1 was a level 1 trial, 1 a level 2 and 4 level 4.
(Eckstein, Kim 2020 Teot, Milcheski, Qui, Gabriel 2014, Chen)

Reduced time to wound closure
10 studies recorded reduced time for wound closure for patients receiving NPWTi and compared with either standard NWPT or conventional dressings. 5 showed statistically significant shorter times to wound closure. 3 were RCTs relating to abdominal, DFU and wounds requiring operative debridement, 2 were comparative retrospective studies related to critically colonised wounds and dehisced wounds, 2 were prospective related to wound complications related to lower limb wounds, and 3 retrospective case series related to wound complications. These studies included 82, 46, 91, 40, 181,20 and 30, 78, 46, and 30 patients. Three were level 1 trials, 3 level 2 and 3 level 3 and 1 level 4.
(Gabriel 2014*, Gabriel 2008*, Qui*, Garcia-Ruano*, Choudhry* Jurkovic, Omar, Morinaga, Davis, Kim 2020)

Patients discharged more quickly
The 10 studies that measured length of stay for patients receiving NPWTi with either standard NWPT or conventional dressings have been listed in the patient benefit section of this table.
Additional outcome data collected in the papers included in the systematic review, that are likely to support earlier patient discharge relate to time to final surgical procedure and average treatment duration. These are listed here:-

> 3 studies recorded time to final hospital procedure for patients receiving NPWTi and compared with either standard NWPT, saline or polyhexadine fluid. Each of these showed statistically shorter times to final hospital procedure. 1 study was an RCT for patients with infected wounds that required debridement, the remaining 2 were comparative retrospective studies also for

infected wounds that required debridement. These studies included 83, 142 and 52 patients. 1 was a level 1b trial and 2 were level 3.
(Kim 2014, Kim 2014 & Powers)

4 studies recorded average treatment durations for patients receiving NPWTi and compared with either standard NWPT or conventional wound dressings. 3 of these showed statistically shorter average treatment durations. 1 was a prospective study of open infected / mixed wounds, 1 was a comparative retrospective study of patients with infected or critically colonised extremity or trunk wounds and 1 a retrospective studies of patients with sternal wound complications. These studies included 82,30 and 30 patients. 1 was a level 2 trial, 1 was a level 3 trial and 1 was a level 4 trial.
(Gabriel 2014*, Gabriel 2008*, Choudhry*, and Jurkovic.

Higher rates of wound closure
5 studies recorded higher wound closure rates for patients receiving NPWTi and compared with either standard NWPT or conventional dressings. 3 showed statistically significant shorter times to wound closure. 2 were RCTs relating to abdominal, DFU and wounds requiring operative debridement, 3 were comparative retrospective studies related to open infected and dehisced wounds with exposed mesh. These studies included 90, 83, 142, 46 and 52 patients. 2 were level 1 trials, 3 were level 3.
(Kim 2014*, Garcia-Ruano*, Powers*, Davis, Kim 2015)

Reduced follow on treatments
4 studies recorded data about follow on treatments for patients who had received NPWTi and were compared with standard NWPT or conventional dressings. 1 showed statistical significance for fewer follow on treatments. 1 was an RCT about DFU care, 2 were comparative retrospective studies related dehisced wounds with exposed mesh and 1 was a retrospective case series. These studies included 19, 18, 45 and 46. 1 was a level 1 trial, 2 were level 3 and 1 was level 4.
(Deleyto*, Garcia-Ruano, Chen, Davis)

Reduced Colonisation with pathogens
9 studies recorded reduced colonisation with pathogens for patients receiving NPWTi and compared with either standard NWPT or conventional dressings. 8 showed statistically significant reduced colonisation. 3 were RCTs relating to infected acute and chronic wounds, 1 was a prospective study of patients with infected orthopaedic implants, 1 was a prospective cohorts of patients with lower leg wounds and ulcers, 4 were comparative retrospective studies related to open infected, dehisced wounds with exposed mesh and osteomyelitis. These studies included 41, 13, 19, 142, 32, 7, 46, 30, 52 and 181 patients. 3 were level 1 trials, 3 were level 2 and 3 were level 3.
(Jurkovic*, Goss*, Yang 2017*, Garcia-Ruano*, Timmers*, Ludolph* Kim 2020*, Kim 2014, Powers.)

Overall reduction in staff and resource use
1 study directly commented on findings of a significant reduction of clinical and nurse time. This level 4 paper examined the care of 18 patients with surgical site infections

Cost Savings
3 studies recorded data about reduced or equivalent costs for patients receiving NPWTi compared with either standard NWPT or conventional dressings. 2 were related to infected abdominal wounds and 1 infected and extremity and trunk wounds. 1 was a randomised controlled trial and 2 were comparative retrospective studies. These studies included 41, 82, 7 and 45 patients. 1 was a level 1 trial, 1 a level 3 and 1 a level 4. Costs benefits will be detailed further in part 2 of this submission.

Sustainability
No studies referenced sustainability. 3M-KCI have laid out their approach to supporting sustainability in section

Identify any factors which might be different between the patients in the submitted studies and patients having routine care in the UK NHS.

None expected.

Describe any criteria that would be used in clinical practice to select patients for whom the technology would be most appropriate.

In line with the scope patients who have acute infected or chronic wounds that are failing to heal would be most appropriate to benefit from NPWTi. This is because rapid preparation of wound beds to create the conditions for wound closure, including use of skin grafts, flaps or primary sutures is critically important to patient wellbeing and improved outcomes.

NPWTi has been shown to improve wound closure rates for patients who, despite treatment with conventional NPWT, have not achieved this. NPWTi is therefore most likely to be appropriate for those patients who despite treatment with more conventional therapies have not achieved wound closure.

Data in this submission has also demonstrated the impact that NPWTi can have when utilised as an adjuvant to treatment for infected implants, particularly due to the high retention rates achieved. This data suggests that NPWTi may also be appropriate for these patients.

Briefly summarise the strengths and limitations of the clinical evidence for the technology.

The systematic review undertaken during preparation of this submission identified over 600 publications related to wound care and NPWT. Whilst the majority were excluded due to their being outside of scope, having small patient numbers, or lacking data for the required outcomes, over 30 were selected for detailed analysis. This suggests that the clinical community has identified NPWTi as a technology likely to deliver benefit to both patients and health systems and that it therefore warrants careful evaluation.

The V.A.C. NPWTi Therapy System is composed of equipment to instil fluids and apply NPWT, instillation fluids and a range of dressings that are selected depending upon a patient's wound status. As a result many studies typically focus upon different aspects of the system including the most appropriate instillation solution to use, the volume and dwell time for instillation fluids as well as the time frame and pressure levels of the NPWT. Whilst there is good evidence for outcomes in the scope for this submission the numbers of papers dealing with patient sub-groups and individual outcomes can be small.

There are now 4 published RCTs, and one in press, that have considered the use of NPWTi, These studies add to NPWTi's evidence base with three of the five demonstrating statistical significance for reductions in bacterial colonisation as well as potential shortening of treatment times and acceleration of wound healing. The limitations of the RCTs included in this submission related to small sample sizes, lack of blinding, different practices within institutions and the different clinical conditions being researched across the studies.

4 of the 11 prospective trials included comparator data and 3 of these were for NPWT. Once again studies concluded that NPWTi demonstrated statistical significance related to bioburden and the time to achieve their reduction through the removal of infectious materials. Reductions in length of stay, wound closure rates from 74% to 100% and shortened time to wound closure were associated with views that costs and care requirements for patients can be reduced. Limitations included small sample sizes, potential bias due to mixed wound and patient characteristics, short follow up times and, in 7 studies, lack of a comparator.

Half of the studies selected following the systematic review were retrospective and once again included studies across all wound types included in the scope. All comparative studies showed reductions in length of stay, 3 of these with statistical significance. 80% of these studies demonstrated statistical significance in fewer surgical debridements and 40% also recorded statistically fewer hospital visits.

Reductions in pathogen levels reflected figures seen in RCTS and prospective trials. Authors stated that studies demonstrated the superiority of NPWTi to NPWT. As a result of improved wound beds frequent dressing changes were avoided and reduced times to wound closure supported a reduction in costs. A number of studies had evaluated NPWTi's role in treating infected implants with the majority being retained. These studies also concluded that there is evidence on NPWTi reducing mortality levels. Limitations of these studies included small sample sizes of patients who had different levels of wellbeing, studies being undertaken in single medical centres, the fact that studies were retrospective and that some did not have a control group.

Across the 33 studies selected in the systematic review evidence is strongest for NPWTi's impact upon reduction of bioburden, shortened treatment and wound closure times, fewer debridements, higher rates of wound closure, reductions in lengths of stay and retention of implants.

Common limitations include small sample sizes, few RCT studies or controls, potential bias due to patient factors and research being conducted in single centres where clinical practices may have impacted upon outcomes.

9 References

Please include all references below using NICE's standard referencing style.

Blalock L. (2019) Use of Negative Pressure Wound Therapy With Instillation and a Novel Reticulated Open-cell Foam Dressing With Through Holes at a Level 2 Trauma Centre. Wounds 31(2):5558

Brinkert D, Ali M, Naud M, Maire N, Trial C, Teot L.(2013) Negative pressure wound therapy with saline instillation: 131 patient case series. International Wound Journal. 10(Suppl 1):56-60

Chen K, Lin J, Sun S, Lin J, Kong J, Tian N. (2018) Vacuum assisted closure combined with a closed suction irrigation system for treating post-operative wound infections following posterior spinal internal fixation. Journal of Orthopaedic Surgery and Research. 13:321

Chowdhry S, Wilhelmi B. (2019) Comparing Negative Pressure Wound Therapy With Instillation and Conventional Dressings for Sternal Wound Reconstructions. Plast Reconstr Surg Glob Open. 7 (1), e208

Davis et al. (2020) Randomized clinical study to compare negative pressure wound therapy with simultaneous saline irrigation and traditional negative pressure wound therapy for complex foot infections. Wound repair and Regeneration. 28(1);97-104

Deleyto E, , García-Ruano A, González-López J. (2017) Negative Pressure Wound Therapy With Instillation, a Cost-Effective Treatment for Abdominal Mesh Exposure. Hernia: (2), 311-318

Eckstein FM et al. (2019) Antiseptic negative pressure instillation therapy for the treatment of septic wound healing deficits in oral and maxillofacial surgery, Journal of Cranio-Maxillo-Facial Surgery. 47(3): 389-39

Gabriel A, Kahn K, Karmy-Jones R. (2014) 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 14:328-338

Gabriel A, Shores J, Heinrich C, et al. (2008)Negative pressure wound therapy with instillation: a pilot study describing a new method for treating infected wounds. Int Wound J. 5(3):399–413

Garcia-Ruano A, Deleyto E, Garcia-Fernandez.(2016) VAC-instillation therapy in abdominal mesh exposure: a novel indication. Journal of Surgical Research. (206):292-297

Goss SG, Schwartz JA, Facchin F, Avdagic E, Gendics C, Lantis JCII. (2008) Negative pressure wound therapy with instillation (NPWTi) better reduces post debridement bioburden in chronically infected lower extremity wounds than NPWT alone. J Am Coll Clin Wound Spec. 4:74–80

Hehr J, Hodson T, West J, Schulz S, Poteet S, Chandawarkar R, Valerio I. (2019) Instillation Negative Pressure Wound Therapy: An Effective Approach for Hardware Salvage. Int Wound J. 17 (2), 387-393

Huang Z, Lei C, Zhang L, Zue H, Shen J, Wu S, Wang B, Chen J. (2020) Negative Pressure Wound Therapy with Chymotrypsin Irrigation.: A maximal implant retention procedure treating the exposure/infection of titanium mesh in cranioplasty. The Journal of Craniofacial Surgery. [Online ahead of print]

Ikeno Y, Sakakibara S, Yokawa K, Kitani K, Nakai H, Yamanaka Ket al.(2019) Post-sternotomy deep wound infection following aortic surgery: wound carestrategies to prevent prosthetic graft replacement. Eur J Cardiothorac Surg 55:975–82

Jain N, Horn C B, Andrade E G, et al. (2018) Combination of Girdlestone Pseudoarthroplasty and Negative Pressure Wound Therapy with Instillation and Dwell in the Treatment of Invasive Osteomyelitis of the Proximal Femur. Cureus 10(11): e3552

Jurkovic A, Bartos J, Bencurik V, Martinek L, Throttle M. (2019) Negative pressure therapy with the ULTRAVAC instillation in the therapy of infected laparotomies with fasciitis -continuous results of a prospective randomised study. Perspectives V Surgery. Vol 98 (4) 152-159

Kim 2020. The impact of negative pressure wound therapy with instillation on wounds requiring operative debridement: pilot randomised, controlled trial. In Press

Kim PJ, Attinger CE, Oliver N, et al. (2015) Comparison of outcomes for normal saline and an antiseptic solution for negative-pressure wound therapy with instillation. Plast Reconstr Surg. 136:657-664

Kim PJ, Attinger CE, Steinberg JS, et al. (2014) The impact of negative-pressure wound therapy with instillation compared with standard negative-pressure wound therapy: a retrospective, historical, cohort, controlled study.PlastReconstr Surg.133709-716

Lehner B, Fleischmann W, Becker R, Jukema GN. (2011) First experiences with negative pressure wound therapy and instillation in the treatment of infected orthopaedic implants: a clinical observational study. International Orthopaedics. 35(9):1415-20

Ludolph I, Fried FW, Kneppe K, Arkudas A, Schmitz M, Horch RE. (2018) Negative pressure wound treatment with computer-controlled irrigation/instillation decreases bacterial load in contaminated wounds and facilitates wound closure. International Wound Journal. 15:978-984

McElroy E. ((2019) Use of Negative Pressure Wound Therapy With Instillation and a Reticulated Open Cell Foam Dressing With Through Holes in the Acute Care Setting. Int Wound J, 16 (3), 781-787
Micheski et al. (2017) Initial experience with negative-pressure wound therapy with instillation in complex wounds Rev. Col. Bras. Cir. 44(4): 348-353

Morinaga K, Kiyokawa K, Rikimaru H, Aoyagi S, Tayama K, Akashi H. (2013) Results of intra-wound continuous negative pressure irrigation treatment for mediastinitis. J Plast Surg Hand Surg, Volume 47, 297- 302

Omar M, Gathen M, Liodakis E, Suero EM, Krettek C, Zeckey C, Petri M. (2016) A comparative study of negative pressure wound therapy with and without instillation of saline on wound healing. Journal of Wound Care. (8):475-8

Powers K, Kim P, Attinger C, Steinberg J, Evans K, Rocha Z, Smith J, Hung R. (2013) Early experience with negative pressure wound therapy with instillation in acutely infected wounds. Presented to the Symposium on Advanced Wound Care Denver Co

Qui K Li Y, Gai B, Li J, Pan L, Ye Z, Lin Y. (2019) Therapeutic efficacy of vacuum sealing drainage assisted irrigation in patients with severe multiple space infections in the oral, maxillofacial and cervical regions. Journal of Craniomaxillo Facial Surgery. 47 837-841

Teot L, Boissiere F, Fluieraru S. (2017) Novel foam dressing using negative pres-sure wound therapy with instillation to remove thick exudate.Int Wound J. 14:842-848

Timmers MS, Graafland N, Bernards AT, Nelissen RG, van Dissel JT, Jukema GN. (2009) Negative pressure wound treatment with polyvinyl alcohol foam and polyhexanide antiseptic solution instillation in posttraumatic osteomyelitis. Wound Repair Regeneration. (2):278-86

Yang C, Goss S, Alcantra S, Schultz G, Lantis J. (2015) Effect of Negative Pressure Wound Therapy with Instillation in Chronically Infected Wounds. Wounds 29(8):240–246

Yang K, Alcantara S, Goss S, Lantis J. (2017) Cost analysis of negative-pressure wound therapy with instillation for wound bed preparation preceding split-thickness skin grafts for massive(>100 cm2) chronic venous leg ulcers. J Vasc Surg: 61: 995-9

Zelen C, Stover B, Neilseon D Cunningham M. (2011) A Prospective Study of Negative Pressure Wound Therapy With Integrated Irrigation for the Treatment of Diabetic Foot Ulcers. Eplasty. 11: e5

10 Appendices

Appendix A: Search strategy for clinical evidence

Describe the process and methods used to identify and select the studies relevant to the technology. Include searches for published studies, abstracts and ongoing studies in separate tables as appropriate. See section 2 of the user guide for full details of how to complete this section.

Date search conducted:	February 3 2020
Date span of search:	January 1 2005 to January 31 2020
List the complete search strategies used, including all the search terms: text words (free text), subject index headings (for example, MeSH) and the relationship between the search terms (for example, Boolean). List the databases that were searched.	
The following strategy was used to perform a literature search in PubMed, EMBASE and QUOSA. ("Lavage" OR "instil" OR "instillation" OR "irrigated" OR "irrigation" OR "topical solution" OR "topical wound solution" OR "topic solution" OR "VERAFLO" OR "VERAFLOW" OR "Veraflo dressing" OR "Veraflo cleanse dressing" OR "Veraflo cleanse choice dressing" OR "Ulta") AND ("Negative Pressure Wound Therapy" OR "NPWT" OR "vacuum assisted closure" OR "vacuum sealing" OR "NPWTi" OR "NPWTi-d") **Unpublished Data** Registered studies at ClinicalTrials.gov, was reviewed using the same search criteria for completed and terminated studies to determine publication bias. References from identified publications and abstracts will also be reviewed. Unpublished data including complete trials that have not yet been published and specific outcomes not reported have been reviewed and referenced in the relevant section of this document.	
Brief details of any additional searches, such as searches of company or professional organisation databases (include a description of each database):	
Enter text.	
Inclusion and exclusion criteria:	
EXCLUSION CRITERIA Conference abstracts Expert opinion Reviews Meta-analyses Protocols Case reports Studies with < 10 patients	

Languages other than English
Veterinary studies
Preclinical (in vitro, in vivo, in silico) studies
Non-clinical reports

INCLUSION CRITERIA
Conference abstracts
Published manuscripts
Preclinical (in vitro, in vivo, in silico) studies
Clinical studies (regardless of patient #)
Discusses subject matter

Data abstraction strategy:

All comparative manuscripts and abstracts evaluating effectiveness and safety that meet all the inclusion criteria and none of the exclusion criteria will be included, regardless of the study design.

Review Process
Titles of manuscripts and abstracts that meet the search criteria were logged and investigated for duplicates. The abstracts and manuscripts were assessed for inclusion and exclusion criteria by two independent reviewers. When discordance is identified, the two reviewers discuss until consensus is reached. For abstracts and manuscripts that meet all the inclusion criteria and none of the exclusion criteria, they will be read critically

i) to assess whether they contain reference of any other articles that meet the inclusion criteria and scope, and
ii) extract study characteristics by at least two independent reviewers.

Initial Search

Articles and abstracts that met the search criteria or identified in the references of a selected manuscript or abstract will have the following collected:
• Article reference
• Inclusion or exclusion status
• If excluded from the study, reason for exclusion

Quality Assessment
Each study was reviewed and assessed for quality. All data collected in the excel tracker was reviewed by two independent reviewers to ensure consensus is met with regards to overall assessment.

Excluded studies

List any excluded studies below. These are studies that were initially considered for inclusion at the level of full text review, but were later excluded for specific reasons.

Excluded study	Design and intervention(s)	Rationale for exclusion	Company comments
Text	Text	Text	Text
Text	Text	Text	Text
Text	Text	Text	Text
Text	Text	Text	Text

Report the numbers of published studies included and excluded at each stage in an appropriate format (e.g. PRISMA flow diagram).

Enter text.

Structured abstracts for unpublished studies

Study title and authors The Impact of Negative Pressure Wound Therapy with Instillation on Wounds Requiring Operative Debridement: Pilot Randomised Control Trial. Kim 2020.
Introduction Presence of bacteria in wounds can delay healing. Addition of a regularly instilled topical solution over the wound during negative pressure wound therapy may reduce bioburden levels compared to standard negative pressure wound therapy alone.
Objectives To compare the effects of NPWTi with instillation of polyhexamethylene biguancide with standard NPWT.
Methods We performed a prospective, randomized, multi-centre, postmarket trial to compare effects of negative pressure wound therapy with instillation and dwell of polyhexamethylene biguanide solution versus negative pressure wound therapy without instillation therapy in wounds requiring operative debridement.
Results Results showed a significantly greater decrease in mean total bacterial counts between time of initial surgical debridement and first dressing change in negative pressure wound therapy plus instillation (n=69) Subjects compared with standard negative pressure wound therapy (n=63) Subjects (-0.18 vs 0.6 Log10 CFU/g, respectively). There was no significant difference between the groups in the primary

endpoint of required inpatient operating room debridements. Time to readiness for wound closure/coverage, proportion of wounds closed, and incidence of wound complications were similar. Negative pressure wound therapy Subjects had 3.1 times the risk of re-hospitalization compared to negative pressure wound therapy plus instillation Subjects.
Conclusion This study provides a basis for exploring research options to understand the impact of negative pressure wound therapy with instillation on wound healing.
Article status and expected publication: International Wound Journal. Autumn 2020

Appendix B: Search strategy for adverse events

Date search conducted:	31/01/2020
Date span of search:	01/01/2005 to 31/02/2020
List the complete search strategies used, including all the search terms: text words (free text), subject index headings (for example, MeSH) and the relationship between the search terms (for example, Boolean). List the databases that were searched.	
MAUDE – (Manufacturer and User Facility Device Experience) "V.A.C. VERAFLO DRESSING", "V.A.C. VERAFLO THERAPY", "VERAFLO"," VERAFLOW" "VERAFLO CLEANSE CHOICE","ODP" **MHRA – (Medicines and Healthcare products Regulatory Agency)** **Section - Alerts and recalls for drugs and medical devices** "V.A.C. VERAFLO DRESSING", "V.A.C. VERAFLO THERAPY", "VERAFLO"," VERAFLOW" "VERAFLO CLEANSE CHOICE"	
Brief details of any additional searches, such as searches of company or professional organisation databases (include a description of each database):	
Enter text.	
Inclusion and exclusion criteria:	
Enter text.	
Data abstraction strategy:	
Enter text.	

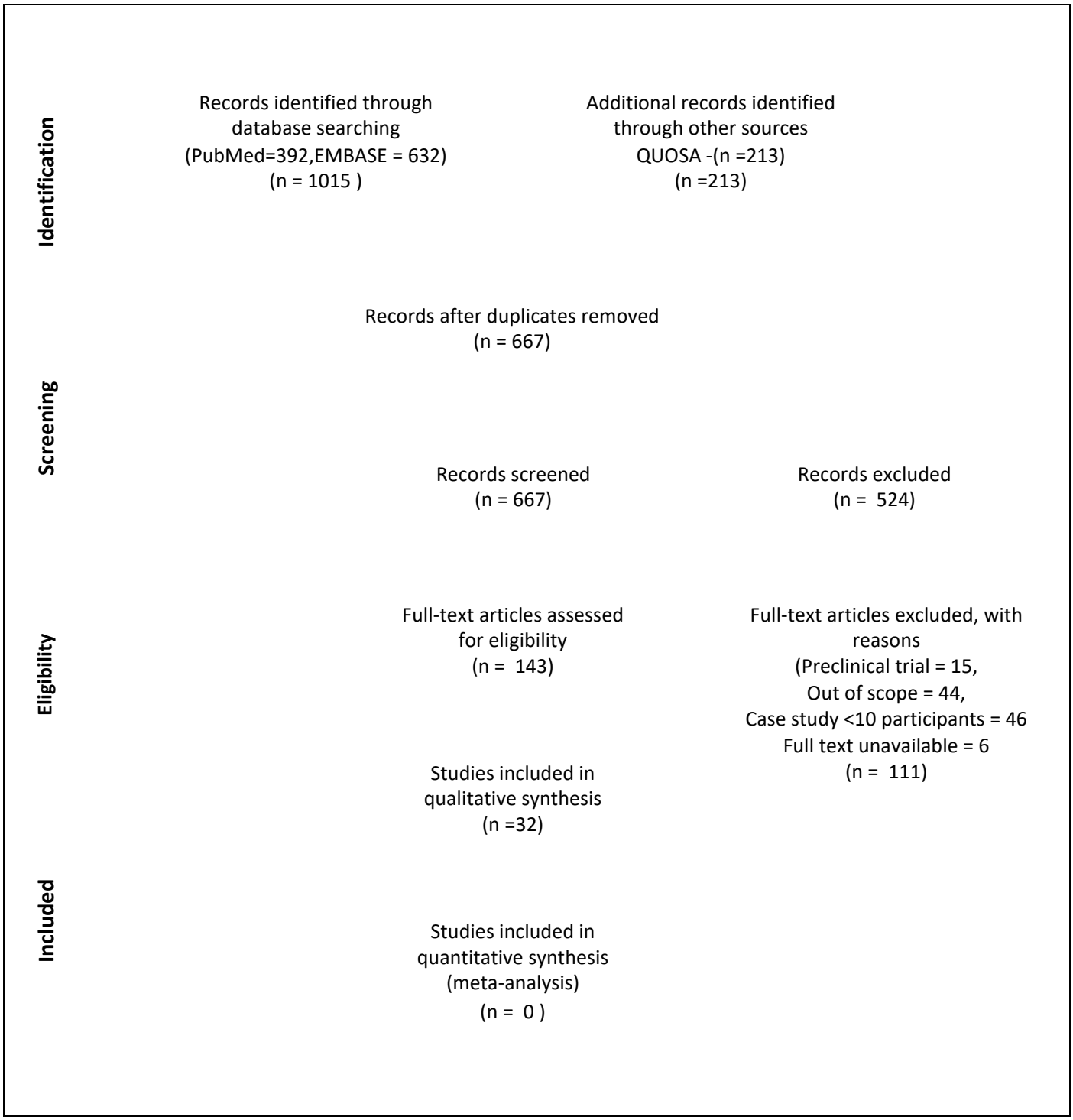
Adverse events evidence

List any relevant studies below. If appropriate, further details on relevant evidence can be added to the adverse events section.

Study	Design and intervention(s)	Details of adverse events	Company comments
Text	Text	Text	Text
Text	Text	Text	Text
Text	Text	Text	Text
Text	Text	Text	Text
Text	Text	Text	Text

Text	Text	Text	Text
Text	Text	Text	Text

Report the numbers of published studies included and excluded at each stage in an appropriate format (e.g. PRISMA flow diagram).



Appendix C: Checklist of confidential information

Please see section 1 of the user guide for instructions on how to complete this section.

Does your submission of evidence contain any confidential information? (please check appropriate box):

No ☐ If no, please proceed to declaration (below)

Yes ☒ If yes, please complete the table below (insert or delete rows as necessary). Ensure that all relevant sections of your submission of evidence are clearly highlighted and underlined in your submission document, and match the information in the table. Please add the referenced confidential content (text, graphs, figures, illustrations, etc.) to which this applies.

Page	Nature of confidential information	Rationale for confidential status	Timeframe of confidentiality restriction
9, 10, 12, 46, 47, 84, 96, 98, 99, 100, 101, 105, 109,110.	☐ Commercial in confidence ☒ Academic in confidence	Unpublished RCT study	Anticipated publication Q3 or 4 2020.

Details	Enter text.		
#	☐ Commercial in confidence ☐ Academic in confidence	Enter text.	Enter text.
Details	Enter text.		

Confidential information declaration

I confirm that:

- all relevant data pertinent to the development of medical technology guidance (MTG) has been disclosed to NICE
- all confidential sections in the submission have been marked correctly
- if I have attached any publication or other information in support of this notification, I have obtained the appropriate permission or paid the appropriate copyright fee to enable my organisation to share this publication or information with NICE.

Please note that NICE does not accept any responsibility for the disclosure of confidential information through publication of documentation on our website that has not been correctly marked. If a completed checklist is not included then NICE will consider all information contained in your submission of evidence as not confidential.

Signed*:

** Must be Medical Director or equivalent*

Date: 11th March 2020

Print: Dr Ron Silverman

Role / organisation: Medical Director

Contact email: rsilverman@mmm.com

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Medical technologies guidance

[GID-MT 543 and V.A.C VERAFLO™ Therapy System for acute infected or chronic wounds that are failing to heal]

Company evidence submission

Part 2: Economic evidence

Company name	3M+KCl
Submission date	2nd April 2020
Contains confidential information	YES

Company evidence submission (part 2) for [**GID-MT 543 and V.A.C VERAFLO™ Therapy System for acute infected or chronic wounds that are failing to heal**

Contents

1 Published and unpublished economic evidence

Identification and selection of studies

Complete the following information about the number of studies identified.

Please provide a detailed description of the search strategy used, and a detailed list of any excluded studies, in appendix A.

Number of studies identified in a systematic search.		0
Number of studies identified as being relevant to the decision problem.		0
Of the relevant studies identified:	Number of published studies.	0
	Number of abstracts.	0
	Number of ongoing studies.	0

List of relevant studies

In table 1, provide brief details of any published or unpublished economic studies or abstracts identified as being relevant to the decision problem.

For any unpublished studies, please provide a structured abstract in appendix A. If a structured abstract is not available, you must provide a statement from the authors to verify the data provided.

Any data that is submitted in confidence must be correctly highlighted. Please see section 1 of the user guide for how to highlight confidential information. Include any confidential information in appendix C.

Table 1 Summary of all relevant studies (published and unpublished)

Due to no economic studies reviewing NPWTi vs the comparator within the scope, we have included below the evidence studies used in our cost consequence model. We have followed the EMB process in our allocation of these studies to each subgroup.

Data source	Author, year and location	Patient population and setting	Intervention and comparator	Unit costs	Outcomes and results	Sensitivity analysis and conclusion
Lower limb						
Plast. Reconstr.surg	Kim et al. 2014,USA	142 patients with infected wounds who required admission with at least 2 operative debridements, no withdrawals or losses.	Intervention - NPWTi with 6 or 20 minute dwell time, following debridement in the operating room - - Comparator - NPWT following debridement in the operating room.	NA	Number of operating room visits, length of hospital stay, time to final surgical procedure during admission, percentage of wounds closed/covered during admission, percentage of wounds that remained closed or covered 30 days after hospital discharge, reduction in microorganisms.	No sensitivity analysis completed in study.
International Wound Journal	Gabriel et al. 2008, USA	30 patients with open Infected Wounds – venous, diabetic, mixed, hospital setting, no withdrawals or losses.	Intervention – NPWTi	NA	Number of days of wound treatment, number of days to wound closure, number of days to	No sensitivity analysis completed in study.

			Comparator – Advanced wound care		discharge, type of infection present.	
Mixed wounds						
eplasty	Gabriel et al. 2014, USA	82 patients with infected or critically colonised extremity or trunk wounds treated with NPWT or NPWTi, hospital setting, no withdrawals or losses.	Intervention – NPWTi Comparator - NPWT	NA	Number of surgical debridements, hospital stay, length of therapy, time to wound closure. Hypothetical economic model developed using outcome data.	No sensitivity analysis completed in study.
Wound Repair and Regeneration	Timmers et al. 2008, The Netherlands	124 patients with osteomyelitis of the pelvis or lower extremity, hospital setting, 1 patient died due to cardiac condition, 5 patients died during the follow-up period due to unrelated causes.	Intervention – NPWTi Comparator – Advanced wound care	NA	Duration of hospitalisation, number and duration of hospital stays, number of surgical procedures, number of clinical and microbiological recurrences.	No sensitivity analysis completed in study.
Prosthetic implants						

Hernia	Deleyto et al. 2017, Spain	45 patients with abdominal mesh exposure due to dehiscence, hospital setting, no withdrawals or losses.	Intervention – NPWTi Comparator – Advanced wound care	NA	Number of hospitalisation episodes, number of additional surgeries, total time for hospitalisation.	No sensitivity analysis completed in study.
Surgical site infection						
Perspectives V surgery	Jurkovic et al. 2019, Czech Republic	41 patients with infected laparotomy wounds and fasciitis, hospital setting, no withdrawals or losses.	Intervention – NPWTi Comparator - NPWT	NA	Primary – Length of therapy, number of surgical debridements, evaluation of financial costs. Secondary – Observed changes in biological load and bacterial spectrum.	No sensitivity analysis completed in study.
American Society of Plastic Surgeons	Chowdhry et al. 2019, USA	30 patients with sternal wound complications, hospital setting, no withdrawals or losses.	Intervention – NPWTi Comparator – Advanced wound care	NA	Days to wound closure, total therapy days, number of debridements, number of dressing changes, drain	No sensitivity analysis completed in study

					duration, complications.	

2 Details of relevant studies

Please give details of all relevant studies (all studies in table 1). Copy and paste a new table into the document for each study. Please use 1 table per study.

Lower limb

Kim et al. 2014. The Impact of Negative-Pressure Wound Therapy with Instillation compared with standard Negative-Pressure Wound Therapy: A Retrospective, Historical, Cohort, Controlled Study.	
What are main differences in resource use and clinical outcomes between the technologies?	The use of NPWTi was associated with reduced use of resources and improved clinical outcomes due to shorter LOS, LOT and reductions in theatre time due to fewer debridements when compared to NPWT.
How are the findings relevant to the decision problem?	Patients in this trial had infected wounds that required admission to hospital and at least two operative debridement procedures. NPWTi was compared with standard NPWT.
Does this evidence support any of the claimed benefits for the technology? If so, which?	Evidence supports:- o Statistically significant reductions length of stay for patients; o Statistically significant reductions in the number of debridements for patients; o Statistically significant reductions in patient's time to final surgical procedure; o Statistically significant reductions in wound closure rates; o A statistically significant improvement in wound cultures when certain bacteria and yeasts were excluded.
Will any information from this study be used in the economic model?	Yes
What cost analysis was done in the study? Please explain the results.	No cost analysis – clinical results used in the parameter section in relation to the outcomes reported.
What are the limitations of this evidence?	The choice of instillation solution and the volume used, the duration of NPWT and the maximum or minimum duration of therapy may have impacted upon outcomes.

Kim et al. 2014. The Impact of Negative-Pressure Wound Therapy with Instillation compared with standard Negative-Pressure Wound Therapy: A Retrospective, Historical, Cohort, Controlled Study.	
How was the study funded?	Not stated.

Gabriel A, et al. (2008) Negative pressure wound therapy with instillation: a pilot study describing a new method for treating infected wounds.	
What are main differences in resource use and clinical outcomes between the technologies?	The use of NPWTi was associated with reduced use of resources and improved clinical outcomes due to shorter LOS, LOT and reductions in theatre time due to fewer debridements when compared to AWC.
How are the findings relevant to the decision problem?	Patients in this trial had infected or critically colonised extremity and trunk wounds.
Does this evidence support any of the claimed benefits for the technology? If so, which?	Evidence supports:- ○ Statistically significant reduced hospital length of stay; ○ Statistically significant reduced time to wound closure; ○ Statistically significant reduced number of surgical debridements; ○ Statistically significant overall reduction in resource use. ○ Reduction in costs
Will any information from this study be used in the economic model?	Yes
What cost analysis was done in the study? Please explain the results.	No cost analysis – clinical results used in the parameter section in relation to the outcomes reported.
What are the limitations of this evidence?	There was a risk of potential selection bias, incomplete data.
How was the study funded?	Not stated.

Mixed wounds

Gabriel A, et al. 2014 Use of negative pressure wound therapy with automated, volumetric instillation for the treatment of extremity and trunk wounds: clinical outcomes and potential cost-effectiveness	
What are main differences in resource use and clinical outcomes between the technologies?	The use of NPWTi was associated with reduced use of resources and improved clinical outcomes due to shorter LOS, LOT and reductions in theatre time due to fewer debridements when compared to NPWT.
How are the findings relevant to the decision problem?	Patients in this trial had infected or critically colonised extremity or trunk wounds. NPWTi was compared with standard NPWT.
Does this evidence support any of the claimed benefits for the technology? If so, which?	Evidence supports:- o Statistically significant reduced hospital lengths of stay; o Statistically significant reduced number of surgical debridements; o Statistically significant reduced times to wound closure; o Statistically significant shorter average treatment durations; o Statistically significant reduction in dressing changes resulting in a reduction in staff and resource use; o Reduction in Costs. o Patients reported less pain
Will any information from this study be used in the economic model?	Yes
What cost analysis was done in the study? Please explain the results.	No cost analysis – clinical results used in the parameter section in relation to the outcomes reported.
What are the limitations of this evidence?	Potential selection bias and some lost data.
How was the study funded?	Not stated. Staff at KCI offered practical support with statistical analysis, economic modelling and editing the paper.

Timmers MS et al.. (2017) Negative pressure wound treatment with polyvinyl alcohol foam and polyhexanide antiseptic solution instillation in posttraumatic osteomyelitis.	
What are main differences in resource use and clinical outcomes between the technologies?	The use of NPWTi was associated with reduced use of resources and improved clinical outcomes due to shorter LOS, LOT and reductions in theatre time due to fewer debridements when compared to AWC.
How are the findings relevant to the decision problem?	Patients in this trial had osteomyelitis of the pelvis or lower extremity requiring surgical debridement.
Does this evidence support any of the claimed benefits for the technology? If so, which?	Evidence supports:- o Highly statistically significant reduction in hospital length of stay; o Highly statistically significant reduction in surgical debridements; o Highly statistically significant reduction in the number of visits to hospital and follow on treatments; o Highly significant reductions in colonisation with pathogens. o High rates of wound closure. o
Will any information from this study be used in the economic model?	Yes
What cost analysis was done in the study? Please explain the results.	No cost analysis – clinical results used in the parameter section in relation to the outcomes reported.
What are the limitations of this evidence?	Selection of control patients may not have identified all those eligible to join this group.
How was the study funded?	No funding was received from KCI.

Prosthetic implants

Deleyto E, et al.. ((2017) Negative Pressure Wound Therapy With Instillation, a Cost-Effective Treatment for Abdominal Mesh Exposure.	
What are main differences in resource use and clinical outcomes between the technologies?	The use of NPWTi was associated with reduced use of resources and improved clinical outcomes due to shorter LOS, LOT and reductions in theatre time due to fewer debridements when compared to AWC.
How are the findings relevant to the decision problem?	Patients in this trial had abdominal mesh exposure due to wound dehiscence.
Does this evidence support any of the claimed benefits for the technology? If so, which?	Evidence supports:- o Reductions in hospital length of stay in comparison to convention wound treatment; o Reductions in staff and resource use due to fewer hospital admissions; o Statistically significant reduced time to wound closure; o Statistically significant reduction in surgical debridements. o Cost benefits due to smaller mean cost of a hospital stay for patients who received care with NPWTi rather than conventional wound dressings.
Will any information from this study be used in the economic model?	Yes
What cost analysis was done in the study? Please explain the results.	No cost analysis – clinical results used in the parameter section in relation to the outcomes reported.
What are the limitations of this evidence?	The sampling method used means generalisation of data is likely to be imprecise.
How was the study funded?	Not stated but authors stated no proprietary interests in the product.

Surgical site infection

Jurkovic et al, 2019. The instilating sub pressure Ultravac in the therapy of infected laparotomy with fascitits- continuous results of a prospective randomised study.	
What are main differences in resource use and clinical outcomes between the technologies?	The use of NPWTi was associated with reduced use of resources and improved clinical outcomes due to shorter LOS, LOT and reductions in theatre time due to fewer debridements when compared to NPWT.
How are the findings relevant to the decision problem?	Patients in this trial had an acute and serious surgical site infection. Data were collected for a number of clinical outcomes in the decision problem as well as resource use. NPWTi was compared with standard NPWT.
Does this evidence support any of the claimed benefits for the technology? If so, which?	Evidence supports:- • Reduced number of surgical debridements; • Reduced time to wound closure; • Reduced colonisation with pathogens. •
Will any information from this study be used in the economic model?	Yes
What cost analysis was done in the study? Please explain the results.	No cost analysis – clinical results used in the parameter section in relation to the outcomes reported.
What are the limitations of this evidence?	This trial's limitations were stated as the non homogeneity of the patients within the groups, the absence of blinding for patients and clinicians and the small number of patients included in the study overall.
How was the study funded?	Not declared but authors stated they had no conflict of interest.

Chowdhry S et al. (2019) Comparing Negative Pressure Wound Therapy With Instillation and Conventional Dressings for Sternal Wound Reconstructions.	
What are main differences in resource use and clinical outcomes between the technologies?	The use of NPWTi was associated with reduced use of resources and improved clinical outcomes due to shorter LOS, LOT and

Chowdhry S et al. (2019) Comparing Negative Pressure Wound Therapy With Instillation and Conventional Dressings for Sternal Wound Reconstructions.	
	reductions in theatre time due to fewer debridements when compared to AWC.
How are the findings relevant to the decision problem?	Patients in this trial underwent reconstructive surgery for pre-existing sternal wounds that had failed to close following previous surgery.
Does this evidence support any of the claimed benefits for the technology? If so, which?	Evidence supports:- o Statistically significant reduced time to wound closure; o Overall reduction in staff and resource use; o Statistically significant reduction in surgical debridements. o Cost benefits due to 100% of patients maintain closed wounds with no infection or complications at a range of 41-650 days.
Will any information from this study be used in the economic model?	Yes
What cost analysis was done in the study? Please explain the results.	No cost analysis – clinical results used in the parameter section in relation to the outcomes reported.
What are the limitations of this evidence?	Non given
How was the study funded?	Non stated

3 Economic model

This section refers to the de novo economic model that you have submitted.

Description

Patients

Describe which patient groups are included in the model.

The CCA model provided by NICE only allows for 2 subgroups. It was therefore necessary for 3M/ KCI to build their own model to support this submission for NPWTi. The model has been built in the absence of any purely economic focussed papers or CCA analysis published for NPWTi vs comparators of NPWT or AWC. Due to the diversity of wound types in the scope we felt it would be more robust to build an economic model that recognised the lack of commonality between them. This required an approach that focussed on creating the subgroups which are detailed in the model and are aligned with the evidence submission, they are as follows: -

- Lower limb
- Mixed wounds
- Prosthetic implants
- Surgical site infections

This approach has allowed us to demonstrate the benefits of NPWTi using the appropriate evidence for the cohort of patients in the associated subgroup.

The majority of the end points within the model have been focused on Length of Stay, Length of therapy and debridement times in theatres. Once again these are significantly different across the subgroups for both economic and clinical outcomes.

Technology and comparator(s)

State the technology and comparators used in the model. Provide a justification if the comparator used in the model is different to that in the scope.

The V.A.C Veraflo technology (NPWTi) is the main technology used. Therefore throughout this document it will referred to as NPWTi for ease of reading.

The comparator has either been NPWT or Advanced wound care (AWC). This is fully in line with the scope document provided and has been made clear in the model when compared against either technologies.

Model structure

Provide a diagram of the model structure you have chosen in Appendix B.

Justify the chosen structure of the model by referring to the clinical care pathway outlined in part 1, section 3 (Clinical context) of your submission.

The scope of the submission includes a wide range of different wound types, which follow distinctive care pathways. The example mentioned regarding diabetic foot ulcer was to demonstrate how NPWTi could influence the frequency of therapy and number of debridements needed.

Submitted clinical evidence across the different subgroups mostly shared three clinical outcomes; length of stay, duration of treatment, and number of operations/operation room visits/debridements required for the wound to heal. These outcomes were the most consistently reported regardless of either the subgroup of studied patients or the comparator intervention.

The economic model was therefore developed using these endpoints in the consequence analysis.

The model starts with a simple decision node where there is a choice to put a patient on either NPWTi or one of its comparators, either NPWT or advanced wound care (whatever the clinical evidence permits). Costs related to length of hospital stay, therapy and its duration, and number of debridements are calculated, and these summed to a final figure for the average total costs per patient.

This analysis was carried out for each subgroup, and a weighted average was calculated to estimate average total costs per patient from the whole population.

To account for the uncertainty in the means of parameter values, we conducted one-way sensitivity analysis (OWSA) which measures the impact of varying each individual item separately on the cost savings, as well as a probabilistic sensitivity analysis (PSA) to account

for the collective uncertainty in the mean values. Scenario analysis were also conducted in instances where an endpoint was not reported and more than estimation approach was deemed reasonable.

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Table 2 Assumptions in the model

In this table, list the main assumptions in the model and justify why each has been used.

Assumption	Justification	Source
The model assumes canisters, cassettes and dressing kits needs changing three times per week	In line with instructions for use	NPWTi IFU
Number of OR visits / operations were assumed for the purpose of a debridement	KOL opinion indicates it is likely debridements would be performed for such patients even if it is not reported explicitly	KOL opinion
Length of therapy in Kim 2014 was assumed to be 8.01 and 13.88 days respectively for NPWTi and NPWT respectively	A ratio was worked between length of therapy and length of stay in Gabriel 2008 and was then multiplied by length of stay reported at Kim 2014	Reference Gabriel 2008 and Kim 2014
Number of debridements in Gabriel 2008 was assumed to be 2.96 and 7.88 days for NPWTi and standard wound care respectively	A ratio was worked between number of OR visits and length of stay in Kim 2014 and was then multiplied by length of stay reported at Gabriel 2008	Reference Gabriel 2008 and Kim 2014
Length of therapy in Timmers 2009 was assumed to be 18.22 and 55.68 days for NPWTi and standard wound care respectively	A ratio was worked between length of therapy and length of stay in Gabriel 2014 and was then multiplied by length of stay reported at Timmers 2009	Reference Timmers 2009 and Gabriel 2014
Deleyto 2018 was assumed more appropriate for extracting endpoints for prosthetic implants subgroup compared to Garcia 2016	Both studies were conducted one the same group of patients and reported the same results. Deleyto 2018 was preferred because it reported mean	Reference Deleyto 2018 & Garcia 2016

	values for all outcomes and to the second decimal place	
Length of therapy in Deleyto 2018 was assumed to be 25.19 days for standard wound care	A ratio was worked between length of therapy and length of stay in Deleyto 2018 for NPWTi and was then multiplied by length of stay for standard wound care reported at Deleyto 2018	Reference Deleyto 2018
Length of stay in the surgical site infections subgroup was assumed equal to length of therapy	None of the relevant studies reported the outcome of interest. Therefore, this conservative assumption was made to complete the model inputs	Reference Jurkovic 2019 and Chowdhry 2019
Nurse training time on NPWTi was assumed to be negligible	The assumption was made based on 1.5 hours of training needed per nurse with expected high estimations of the workload or capacity in terms of number of treated patients per nurse after training	NA

Table 3 Clinical parameters, patient and carer outcomes and system outcomes used in the model

In this table, describe the clinical parameters, patient and carer outcomes and system outcomes used in the model.

Parameter/outcomes	Source	Relevant results	Range or distribution	How are these values used in the model?
Lower limb				
No of OR visits - NPWTi	Kim 2014 et al.	2.40	Lower 2.11- Upper 2.71	This value is used in the model to support the number of visits to theatre for debridement.

LOS (days) NPWTi	Kim 2014 et al.	11.90	Lower 9.42- Upper 14.66	This value is used in the model to identify the length of stay for technology used
LOT (days) NPWTi	Kim 2014 et al.	8.01	No range	This value is used in the model to identify the length of time the therapy is applied to the patient either for the intervention or comparator
Time to final surgical procedure NPWTi	Kim 2014 et al.	7.80	Lower 6.15- Upper 9.64	This value is used in the model to identify the length of time the therapy is applied to the patient either for the intervention or comparator
No of OR visits NPWT	Kim 2014 et al.	3.00	Lower 2.8- Upper 3.21	This value is used in the model to support the number of visits to theatre for debridement.
LOS (days) NPWT	Kim 2014 et al.	14.92	Lower 12.9- Upper 17.09	This value is used in the model to identify the length of stay for technology used
LOT (days) NPWT	Kim 2014 et al.	13.88	No range	This value is used in the model to identify the length of time the therapy is applied to the patient either for the intervention or comparator
Time to final surgical procedure NPWT	Kim 2014 et al.	9.23	Lower 8.08- Upper 10.45	This value is used in the model to identify the length of time the therapy is applied to the patient either

				for the intervention or comparator
LOT (days) NPWTi	Gabriel 2008 et al.	9.87	Lower 7.81- Upper 12.17	This value is used in the model to identify the length of time the therapy is applied to the patient either for the intervention or comparator
LOS (days) NPWTi	Gabriel 2008 et al.	14.67	Lower 10.4- Upper 19.67	This value is used in the model to identify the length of stay for technology used
Number of debridements NPWTi	Gabriel 2008 et al.	2.96	No range	This value is used in the model to support the number of visits to theatre for debridement.
LOT (days) AWC	Gabriel 2008 et al.	36.47	Lower 30.16- Upper 43.37	This value is used in the model to identify the length of time the therapy is applied to the patient either for the intervention or comparator
LOS (days) AWC	Gabriel 2008 et al.	39.20	Lower 33.33- Upper 45.54	This value is used in the model to identify the length of stay for technology used
Number of debridements AWC	Gabriel 2008 et al.	7.88	No range	This value is used in the model to support the number of visits to theatre for debridement.
Mixed wound subgroup				

No of debridements NPWTi	Gabriel 2014 et al.	2.00	Lower 1.29- Upper 2.86	This value is used in the model to support the number of visits to theatre for debridement.
LOS (days) NPWTi	Gabriel 2014 et al.	8.10	Lower 5.24- Upper 11.57	This value is used in the model to identify the length of stay for technology used
LOT (days) NPWTi	Gabriel 2014 et al.	4.10	Lower 2.65- Upper 5.86	This value is used in the model to identify the length of time the therapy is applied to the patient either for the intervention or comparator
No of debridements NPWT	Gabriel 2014 et al.	4.40	Lower 2.85- Upper 6.28	This value is used in the model to support the number of visits to theatre for debridement.
LOS (days) NPWT	Gabriel 2014 et al.	27.40	Lower 17.73- Upper 39.14	This value is used in the model to identify the length of stay for technology used
LOT (days) NPWT	Gabriel 2014 et al.	20.90	Lower 13.53- Upper 29.85	This value is used in the model to identify the length of time the therapy is applied to the patient either for the intervention or comparator
No of operations NPWTi	Timmers 2009 et al.	2.00	Lower 1.74- Upper 2.28	This value is used in the model to support the number of visits to theatre for debridement.
LOS (days) including rehospitalisations NPWTi	Timmers 2009 et al.	36.00	Lower 30.83- Upper 41.56	This value is used in the model to identify the length of stay for technology used

LOT (days) NPWTi	Timmers 2009 et al.	18.22	No range	This value is used in the model to identify the length of time the therapy is applied to the patient either for the intervention or comparator
No of operations AWC	Timmers 2009 et al.	5.00	Lower 3.74- Upper 6.43	This value is used in the model to support the number of visits to theatre for debridement.
LOS (days) including rehospitalisations AWC	Timmers 2009 et al.	73.00	Lower 59.75- Upper 87.56	This value is used in the model to identify the length of stay for technology used
Recurrence of osteomyelitis (%) AWC	Timmers 2009 et al.	0.59	Lower 0.48- Upper 0.68	
LOT (days) AWC	Timmers 2009 et al.	55.68	No range	This value is used in the model to identify the length of time the therapy is applied to the patient either for the intervention or comparator
Prosthetic implants subgroup				
LOS (days) NPWTi	Deleyto 2018 et al.	69.09	Lower 50.7- Upper 90.29	This value is used in the model to identify the length of stay for technology used
LOT (days) NPWTi	Deleyto 2018 et al.	19.73	Lower 14.52- Upper 25.73	This value is used in the model to identify the length of time the therapy is applied to the patient either for the intervention or comparator

Number of additional surgeries NPWTi	Deleyto 2018 et al.	0.80	Lower 0.44- Upper 1.26	This value is used in the model to support the number of visits to theatre for debridement.
Simple closure % from surgical procedures NPWTi	Deleyto 2018 et al.	0.83	Lower 0.48- Upper 0.99	This value is used to understand the additional end points which are related to the sub group of Prosthetic implants - due to costs incurred
Debridement and closure % from surgical procedures NPWTi	Deleyto 2018 et al.	0.17	Lower 0.01- Upper 0.52	This value is used to understand the additional end points which are related to the sub group of Prosthetic implants - due to costs incurred
Mesh removal % from surgical procedures NPWTi	Deleyto 2018 et al.	0.00	No range	This value is used to understand the additional end points which are related to the sub group of Prosthetic implants - due to costs incurred
Mesh substitution % from surgical procedures NPWTi	Deleyto 2018 et al.	0.00	No range	This value is used to understand the additional end points which are related to the sub group of Prosthetic implants - due to costs incurred
LOS (days) AWC	Deleyto 2018 et al.	88.21	Lower 77.29- Upper 99.84	This value is used in the model to identify the length of stay for technology used

LOT (days) AWC	Deleyto 2018 et al.	25.19	No range	This value is used in the model to identify the length of time the therapy is applied to the patient either for the intervention or comparator
Simple closure % from surgical procedures AWC	Deleyto 2018 et al.	0.16	Lower 0.05- Upper 0.3	This value is used to understand the additional end points which are related to the sub group of Prosthetic implants - due to costs incurred
Debridement and closure % from surgical procedures AWC	Deleyto 2018 et al.	0.06	Lower 0.01- Upper 0.17	This value is used to understand the additional end points which are related to the sub group of Prosthetic implants - due to costs incurred
Mesh removal % from surgical procedures AWC	Deleyto 2018 et al.	0.44	Lower 0.27- Upper 0.61	This value is used to understand the additional end points which are related to the sub group of Prosthetic implants - due to costs incurred
Mesh substitution % from surgical procedures AWC	Deleyto 2018 et al.	0.34	Lower 0.19- Upper 0.51	This value is used to understand the additional end points which are related to the sub group of Prosthetic implants - due to costs incurred
Surgical site infections subgroup				

LOT (days) NPWTi	Jurkovic 2019 et al.	21	Lower 16.75- Upper 25.73	This value is used in the model to identify the length of time the therapy is applied to the patient either for the intervention or comparator
Number of debridements NPWTi	Jurkovic 2019 et al.	2	Lower 1.2- Upper 2.99	This value is used in the model to support the number of visits to theatre for debridement.
LOT (days) NPWT	Jurkovic 2019 et al.	23	Lower 19.01- Upper 27.36	This value is used in the model to identify the length of time the therapy is applied to the patient either for the intervention or comparator
Number of debridements NPWT	Jurkovic 2019 et al.	3	Lower 2.6- Upper 3.43	This value is used in the model to support the number of visits to theatre for debridement.
LOT (days) NPWTi	Chowdhry 2019 et al.	5.4	Lower 4.39- Upper 6.51	This value is used in the model to identify the length of time the therapy is applied to the patient either for the intervention or comparator
Number of debridements NPWTi	Chowdhry 2019 et al.	1.8	Lower 1.46- Upper 2.17	This value is used in the model to support the number of visits to theatre for debridement.

LOT (days) AWC	Chowdhry 2019 et al.	8.4	Lower 6.95- Upper 9.98	This value is used in the model to identify the length of time the therapy is applied to the patient either for the intervention or comparator
Number of debridements AWC	Chowdhry 2019 et al.	3.1	Lower 2.61- Upper 3.63	This value is used in the model to support the number of visits to theatre for debridement.

If any outcomes listed in table 4 are extrapolated beyond the study follow-up periods, explain the assumptions that underpin this extrapolation.

NA

Table 4 Other parameters in the model

Describe any other parameters in the model. Examples are provided in the table. You can adapt the parameters as needed.

Parameter	Description	Justification	Source
Time horizon	From admission to discharge of patient	Studies have been developed to review this period of time and therefore enables clear resources and costs to be allocated in secondary care. Also UK practice of NPWTi is indicated for use only in secondary care.	All relevant studies and IFU for the technology
Discount rate	NA	NA	NA
Perspective (NHS/PSS)	NHS	As per scope	NICE methods guide
Cycle length	NA	NA	NA
Transition probabilities	NA	NA	NA
Health states	NA	NA	NA
Sources of unit costs	Unit costs were sourced from NHS reference costs 2017/18, PSSRU 2018, BNF 2018/19 , Public health 2019	All unit costs were validated with clinical experts during model development	NHS reference costs 2017/18, PSSRU 2018, Public health Scotland 2019

Explain the transition matrix used in the model and the transformation of clinical outcomes, health states or other details.

NA

Resource identification, measurement and valuation

Technology costs

Provide the list price for the technology (excluding VAT).

Product description	Unit pack size	NHS supply chain code	NHSCC Pack price – excluding VAT
V.A.C. VERAFLO™ Dressing Small	5	ELZ410	£ 206.56
V.A.C. VERAFLO™ Dressing Medium	5	ELZ411	£ 182.00
V.A.C. VERAFLO™ Dressing Large	5	ELZ676	£ 330.41
V.A.C. VERAFLO CLEANSE™ Dressing	5	ELZ412	£ 494.73
V.A.C. VERAFLO CLEANSE CHOICE™ Dressing Medium	5	ELZ826	£ 570.93
V.A.C. VERAFLO CLEANSE CHOICE™ Dressing Large	5	ELZ971	£ 861.51

V.A.C.ULTA™ Therapy System is charged at a rental of £16 per day +VAT

If the list price is not used in the model, provide the price used and a justification for the difference.

NA

NHS and unit costs

Describe how the clinical management of the condition is currently costed in the NHS in terms of reference costs, the national tariff and unit costs (from PSSRU and HSCIC). Please provide

relevant codes and values (e.g. OPCS codes and ICD codes) for the operations, procedures and interventions included in the model.

Due to the variation in wound types, their location and severity, it was not feasible to allocate an HRG code to the cost of delivering the care. The main reason for this is that under the HRG code structure other procedures, not related to these patients, as well as the use of consumables would be included and would introduce bias. The main focus therefore has been on deriving the following:-

Reduction in length of stay (LOS)

The model uses the cost of a bed day at the national weighted average level for 2017-18 reference costs. Please note we did not use 2018-19 reference costs, due to their recent exclusion from the publication by NHS Improvement. In order to achieve standardisation across the sub-groups we used the 2017-18 figures for all costings.

Therefore the subgroups were allocated as follows:-

Subgroup	HRG groups	2017-18 reference costs (£)
Lower limb	National average	£431
Mixed wounds	EC & ED*	£375
Prosthetic implants	FF*	£391
Surgical site infections	National average	£431
Whole population	Weighted avg. of all subgroups	£407

*NB – please note these are subchapter HRG codes, which reflect a more appropriate aggregating than just the national average, which is based on the study used in the model against the subgroup. However, where the wound type is varied then the national weighted average was used.

Reduction in debridement

The debridement costs are considered key factors in all studies reviewed and included in the model. As this is performed in an operating room which has considerable costs associated with it. Several studies report the theatre time taken to perform a debridement of this type and we have used the figure of 17.7 minutes which is not only conservative but also reported by Cupto et al. 2008. This was used by another NICE submission for VersaJet technology. The cost taken was from the public health Scotland for 2019 which demonstrates the cost per hour for delivery of theatre. This only covers the resources used for both staff and running the theatre, but excludes any consumables associated.
The figure supplied was £802.20 per hour, which equates to £13.37 per minute. This was then calculated to give a debridement cost in theatre of £236.65.

Resource use

Describe any relevant resource data for the NHS in England reported in published and unpublished studies. Provide sources and rationale if relevant. If a literature search was done to identify evidence for resource use then please provide details in appendix A.

A structured process was followed to gather all relevant clinical parameters from the literature identified and reviewed in preparation of the initial submission under part 1. It was also clear that in some cases assumptions had to be made, to ensure consistency with UK practice, however this is clearly documented in the model and within this part 2 submission.

Where costs were sourced, they were either inflated to current prices using the health component of the consumer price index, or when the NHS reference costs were used they were updated to the most recent year if applicable or if they contained the correct information.

The model contains all Unit Costs, assumptions and resource used for each step of the model.

Also the calculation when reviewing the NPWTi and NPWT, was factored to ensure we included any wastage elements if the frequency of change was in excess of the life of the consumable.

Describe the resources needed to implement the technology in the NHS. Please provide sources and rationale.

The prime resource needed to implement NPWTi in the NHS is the training of staff to apply and change dressings, manage the changing of cassettes and canisters and to use the appropriate instillation and pressure settings for their patients. 3m/KCI provides this training free of charge. In addition, a 24 hour support helpdesk is provided for customer to use.

Whilst the time to train staff is likely to incur a small cost this has not been included in the model. This is because it is a one-off cost for staff and would also be matched for the training of staff using NPWT and the multiple types of AWD in use by tissue viability nurses.

Describe the resources needed to manage the change in patient outcomes after implementing the technology. Please provide sources and rationale.

Resource use to manage the change in patient outcomes will reduce significantly following the implementation of NPWTi by reducing the number of dressing changes that nurses will have to undertake vs advanced wound care.

As NPWTi decreases LOT and reduces the number of debridements required then fewer resources will be consumed in delivering improved outcomes in comparison to both NPWT and AWC.

SoPs within the hospital would be routinely updated by clinical staff on a regular basis and therefore would not incur additional time or costs.

Describe the resources needed to manage the change in system outcomes after implementing the technology. Please provide sources and rationale.

Resource use to manage the change in system outcomes following introduction of NPWTi would be reduced due to faster healing times. These are demonstrated by the reduced LOT captured in the evidence. The impact of this is reduced LOS with an associated reduction in the requirement to undertake wound care and dressing changes in the community. Therefore the improved healing of these wounds and the reduction in LOS, will support the NHS Trust with both capacity issues, performance against the NHS targets of 18 weeks, and help support the domains published by NHS England.

Table 5 Resource use costs

In this table, summarise how the model calculates the results of these changes in resource use. Please adapt the table as necessary.

As we reported in the result section of table 9, we have calculated the NPWTi daily cost and have multiplied it by the LOT from the relevant study. We have rounded up the resources used for canister, cassette & dressing costs to account for wastage.

	Technology costs	Comparator 1 costs	Comparator 2 costs	Difference in resource use costs (technology vs comparator 1)	Difference in resource use costs (technology vs comparator 2)
Cost of resource use to implement technology	As we reported in the result section of table 9, we have calculated the NPWTi daily cost and have multiplied it by the LOT from the relevant study. We have rounded up the resources used for canister, cassette & dressing costs to account for wastage.	As we reported in the result section of table 9, we have calculated the NPWT daily cost and have multiplied it by the LOT from the relevant study. We have rounded up the resources used for canister, cassette & dressing costs to account for wastage. t	As we reported in the result section of table 9, we have calculated the AWC daily cost and have multiplied it by the LOT from the relevant study.	The difference in resource use cost is a attributed to the difference in the therapy daily cost and the LOT as shown in table 9 in the results section.	The difference in resource use cost is a attributed to the difference in the therapy daily cost and the LOT as shown in table 9 in the results section

Cost of resource use associated with patient outcomes	All patient outcomes were measured against the reduction in LOS, LOT and debridement, as shown in table 9 in the results section.	All patient outcomes were measured against the reduction in LOS, LOT and debridement, as shown in table 9 in the results section.	All patient outcomes were measured against the reduction in LOS, LOT and debridement, as shown in table 9 in the results section.	All patient outcomes were measured against the reduction in LOS, LOT and debridement, as shown in table 9 in the results section.	All patient outcomes were measured against the reduction in LOS, LOT and debridement, as shown in table 9 in the results section.
Cost of resource use associated with system outcomes	The resource cost saving, is predicated to the study used, which would result in a reduction in LOS and theatre usage . As shown in table 9 in the results section				

Adverse event costs

If costs of adverse events were included in the analysis, explain how and why the risk of each adverse event was calculated.

NA

Table 6 Adverse events and costs in the model

In this table, summarise the costs associated with each adverse event included in the model. Include all adverse events and complication costs, both during and after long-term use of the technology. Please explain whether costs are provided per patient or per event.

Adverse event	Items	Cost	Source
Adverse event 1	Technology	Text	Text
	Staff	Text	Text
	Hospital costs	Text	Text
	[Other items]	Text	Text
	Total	Text	Text
Adverse event 2	Technology	Text	Text
	Staff	Text	Text
	Hospital costs	Text	Text
	[Other items]	Text	Text
	Total	Text	Text
[Add more rows as needed]			

Miscellaneous costs

Describe any additional costs or resource considerations that have not been included elsewhere (for example, PSS costs, and patient and carer costs). If none, please state.

Enter text.

Are there any other opportunities for resource savings or redirection of resources that have not been possible to quantify?

Primary care

- Reduction in district wound treatment visits (e.g. sharp debridement) when patients are discharged with healed wounds.
- Improved patient wellbeing and mobility.
- Reduction in carer support needed for patient's with unhealed wounds.
- Reduction in consumable costs in primary care.
- Reduction in the frequency of district nurse visits to change dressings.
- Reduction in the risk of infection for open wounds in primary care (NICE guidance has previously stated this as approximately £12,000.

- Reduction in future admissions for patients whose unhealed wounds deteriorate in the community following discharge.

Secondary care

- Additional consumables for debridement in theatre, such a trays, saline, drapes.
- Nurse time in wound dressing changes.
- Increased follow-ups for patients with unhealed wounds which are requiring a further admission to resolve the issue.

Quality of life

- Improved patient mental wellbeing following earlier discharge and wound healing.

Total costs

In the following tables, summarise the total costs:

- Summarise total costs for the technology in table 7.
- Summarise total costs for the comparator in table 8. This can only be completed if the comparator is another technology.

Table 7 Total costs for the technology in the model

NPWTi

Description		Cost	Source
Cost per treatment/patient over lifetime of device		£0	NA
Consumables per year (if applicable) and over lifetime of device	Item / Units per pack / Cost (£) / Total per day V.A.C ULTA™ Rental of unit — 1 — £16.00 — £16.00 V.A.C. VERALINK™ Canister — 1 — £47.23 — £20.24 V.A.C. VERALINK™ Cassette — 1 — £21.52 — £9.22 V.A.C. VERAFLO™ Dressing — 1 — £77.76 — £33.33 *Based on consumable changes of 3 times a week*		CCA Model : GID-MT 543 and V.A.C VERAFLO™ Therapy System for acute infected or chronic wounds that are failing to heal
Maintenance cost per year		£0	NA

and over lifetime of device		
Training cost over lifetime of device	NA	Expected to be negligible
Other costs per year and over lifetime of device	£0	NA
Total cost per treatment/patient over lifetime of device	£78.79 per day *Based on consumable changes of 3 times a week*	CCA Model : GID-MT 543 and V.A.C VERAFLO™ Therapy System for acute infected or chronic wounds that are failing to heal

Table 8 Total costs for the comparator in the model

NPWT

Description	Cost	Source
Cost per treatment/patient over lifetime of device	£0	NA
Consumables per year (if applicable) and over lifetime of device	Item / Units per pack / Cost (£) / Total per day NPWT Rental of unit / 1 / [redacted] / [redacted] NPWT canister multiple sizes / 1 / [redacted] / [redacted] Foam/Gauze kit / 1 / [redacted] / [redacted] *Based on consumable changes of 3 times a week*	CCA Model : GID-MT 543 and V.A.C VERAFLO™ Therapy System for acute infected or chronic wounds that are failing to heal
Maintenance cost per year and over lifetime of device	Text	Text
Training cost over lifetime of device	Text	Text
Other costs per year and over lifetime of device	Text	Text
Total cost per treatment/patient over lifetime of device	£36.90 per day *Based on consumable changes of 3 times a week*	CCA Model : GID-MT 543 and V.A.C VERAFLO™ Therapy System for acute infected or chronic wounds that are failing to heal

AWC

Description	Cost	Source
Cost per treatment/patient over lifetime of device	£0	NA
Consumables per year (if applicable) and over lifetime of device	Text Item / Units per pack / Cost (£) / Total per day Alleyvn gentle border 10 x10cm / 1 / [redacted] / [redacted] Aquacel 10cm x 10cm / 1 / [redacted] *Based on consumable changes every day*	CCA Model : GID-MT 543 and V.A.C VERAFLO™ Therapy System for acute infected or chronic

		wounds that are failing to heal
Maintenance cost per year and over lifetime of device	Text	Text
Training cost over lifetime of device	Text	Text
Other costs per year and over lifetime of device	Text	Text
Total cost per treatment/patient over lifetime of device	£4.75 per day *Based on consumable changes every day*	CCA Model : GID-MT 543 and V.A.C VERAFLO™ Therapy System for acute infected or chronic wounds that are failing to heal

Results

Table 9 Base-case results

In this table, report the results of the base-case analysis. Specify whether costs are provided per treatment or per year. Adapt the table as necessary to suit the cost model. If appropriate, describe costs by health state.

	Mean cost per patient using VERAFLO (£)	Mean cost per patient using NPWT (£)	Mean cost per patient using standard wound care (£)	Difference in mean cost per patient (£): VERAFLO vs NPWT	Difference in mean cost per patient (£): VERAFLO vs standard wound care
Whole population (versus NPWT)					
LOS cost	£5,741	£8,880	N/A	-£3,139	N/A
Therapy cost	£914	£662	N/A	£252	N/A
Debridement costs	£505	£820	N/A	-£316	N/A
Total	£7,160	£10,362	N/A	-£3,202	N/A
Whole population (versus standard wound care)					
LOS cost	£12,309	N/A	£20,623	N/A	-£8,314
Therapy cost	£1,136	N/A	£149	N/A	£986
Debridement costs	£535	N/A	£1,519	N/A	-£984
Total	£13,979	N/A	£22,291	N/A	-£8,312
Lower limb subgroup (versus NPWT)					
LOS cost	£5,129	£6,431	N/A	-£1,302	N/A
Therapy cost	£730	£517	N/A	£213	N/A
Debridement costs	£568	£710	N/A	-£142	N/A
Total	£6,427	£7,657	N/A	-£1,230	N/A
Lower limb subgroup (versus standard wound care)					

LOS cost	£6,323	N/A	£16,895	N/A	-£10,572
Therapy cost	£893	N/A	£173	N/A	£719
Debridement costs	£700	N/A	£1,865	N/A	-£1,165
Total	£7,916	N/A	£18,934	N/A	-£11,018
Mixed wounds subgroup (versus NPWT)					
LOS cost	£3,044	£10,297	N/A	-£7,253	N/A
Therapy cost	£373	£775	N/A	-£402	N/A
Debridement costs	£473	£1,041	N/A	-£568	N/A
Total	£3,890	£12,113	N/A	-£8,223	N/A
Mixed wounds subgroup (versus standard wound care)					
LOS cost	£13,528	N/A	£27,433	N/A	-£13,904
Therapy cost	£1,476	N/A	£264	N/A	£1,212
Debridement costs	£473	N/A	£1,183	N/A	-£710
Total	£15,478	N/A	£28,880	N/A	-£13,403
Prosthetic implants subgroup (versus standard wound care)					
LOS cost	£27,057	N/A	£34,545	N/A	-£7,488
Therapy cost	£1,639	N/A	£120	N/A	£1,519
Debridement costs	£539	N/A	£2,293	N/A	-£1,754
Total	£29,234	N/A	£36,957	N/A	-£7,723
Surgical site infections subgroup (versus NPWT)					
LOS cost	£9,051	£9,913	N/A	-£862	N/A
Therapy cost	£1,655	£856	N/A	£799	N/A
Debridement costs	£473	£710	N/A	-£237	N/A
Total	£11,179	£11,479	N/A	-£300	N/A

Surgical site infections subgroup (versus standard wound care)					
LOS cost	£2,327	N/A	£3,620	N/A	-£1,293
Therapy cost	£536	N/A	£40	N/A	£496
Debridement costs	£426	N/A	£734	N/A	-£308
Total	£3,289	N/A	£4,394	N/A	-£1,105
* Negative values indicate a cost saving. Abbreviations: LOS: length of stay, NPWT: Negative Pressure Wound Therapy.					

Scenario analysis

If relevant, explain how scenario analyses were identified and done. Cross-reference your response to the decision problem in part 1, section 1 of the submission.

In lower limb subgroup, Kim et al. 2014 reported the mean time to final surgical procedure. A scenario was conducted using the mentioned means in place of the assumed length of therapy used in the base case.

Describe the differences between the base case and each scenario analysis.

The base case assumes a length of therapy of 8.01 and 13.88 days for NPWTi and NPWT respectively. In the scenario analysis, time to final surgical procedure was equal to 7.8 and 9.23 days respectively.

Describe how the scenario analyses were included in the cost analysis.

Mean values of time to final surgical procedure were multiplied by the daily frequency usage of each of the technology items to estimate therapy costs.

Describe the evidence that justifies including any scenario analyses.

Time to final surgical procedure could be used as an estimate of length of therapy needed.

Table 10 Scenario analyses results

In this table, describe the results of any scenario analyse that were done. Adapt the table as necessary.

	Mean cost per patient using the technology (£)	Mean cost per patient using the comparator (£)	Difference in cost per patient (£)*
Scenario 1 (total costs)	£6,411	£7,496	-£1,085
* Negative values indicate a cost saving.			

Sensitivity analysis

Describe what kinds of sensitivity analyses were done. If no sensitivity analyses have been done, please explain why.

One-way sensitivity analysis (OWSA) and probabilistic sensitivity analyses (PSA) were used to examine the impact that uncertainty in parameters would have on the base case results. The uncertainty around parameters was determined using standard deviation whenever available. Standard error around the mean value was therefore calculated using standard deviation and sample size. A 95% confidence interval was then created for each parameter, where both lower and upper bounds were tested separately per each parameter in the OWSA. Whenever this was not available, the standard error was assumed to be 20% of the mean value, and a range was constructed accordingly.

For PSA, appropriate probability distributions were selected. For positive values such as costs, lengths of stay and therapy, and number of debridements, gamma distributions were selected. For percentages, a beta distribution was selected. For percentages that need to vary simultaneously to ensure a certain sum is achieved (e.g. 1), a multivariate beta (dirichlet) distribution was assigned.
To conduct PSA, we ran the model 1000 times where different parameter values were selected each time from the respective distributions. Averages were then calculated and probability of NPWTi to be a cost-saving technology was then computed.

Summarise the variables used in the sensitivity analyses and provide a justification for them. This may be easier to present in a table (adapt as necessary).

All variables extracted from clinical studies were varied in accordance with their standard deviation and sample size. Costs were assigned a 20% standard error variation in respect to the mean value. Please see table below for detailed endpoints.

Parameters	Mean Value	N	Standard Deviation	Standard Error	Lower	Upper	Distribution	Alpha	Beta
Lower limb subgroup									
No of OR visits - NPWTi - Kim 2014	2.4	34	0.9	0.154	2.11	2.71	Gamma	242	0
LOS (days) - NPWTi - Kim 2014	11.9	34	7.8	1.338	9.42	14.66	Gamma	79	0
Time to final surgical procedure - NPWTi - Kim 2014	7.80	34	5.2	0.892	6.15	9.64	Gamma	77	0
No of OR visits - NPWT - Kim 2014	3.0	74	0.9	0.105	2.80	3.21	Gamma	822	0
LOS (days) - NPWT - Kim 2014	14.92	74	9.2	1.069	12.90	17.09	Gamma	195	0
Time to final surgical procedure - NPWT - Kim 2014	9.23	74	5.2	0.604	8.08	10.45	Gamma	233	0
LOT (days) - NPWTi - Gabriel 2008	9.87	15	4.31	1.113	7.81	12.17	Gamma	79	0
LOS (days) - NPWTi - Gabriel 2008	14.67	15	9.18	2.370	10.40	19.67	Gamma	38	0
LOT (days) - standard - Gabriel 2008	36.47	15	13.07	3.375	30.16	43.37	Gamma	117	0
LOS (days) - standard - Gabriel 2008	39.2	15	12.07	3.116	33.33	45.54	Gamma	158	0
Mixed wound subgroup									
No of debridements - NPWTi - Gabriel 2014	2	48		0.4	1.29	2.86	Gamma	25	0
LOS (days) - NPWTi - Gabriel 2014	8.1	48		1.6	5.24	11.57	Gamma	25	0
LOT (days) - NPWTi - Gabriel 2014	4.1	48		0.8	2.65	5.86	Gamma	25	0
No of debridements - NPWT - Gabriel 2014	4.4	34		0.9	2.85	6.28	Gamma	25	0

LOS (days) - NPWT - Gabriel 2014	27.4	34		5.5	17.73	39.14	Gamma	25	1
LOT (days) - NPWT - Gabriel 2014	20.9	34		4.2	13.53	29.85	Gamma	25	1
No of operations - NPWTi - Timmers 2009	2	30	0.75	0.137	1.74	2.28	Gamma	213	0
LOS (days) including rehospitalisations - NPWTi - Timmers 2009	36	30	15	2.739	30.83	41.56	Gamma	173	0
No of operations - standard - Timmers 2009	5	94	6.67	0.688	3.74	6.43	Gamma	53	0
LOS (days) including rehospitalisations - standard - Timmers 2009	73	94	68.8	7.100	59.75	87.56	Gamma	106	1
Prosthetic implants subgroup									
LOS (days) - NPWTi - Deleyto 2018	69.09	11	33.56	10.119	50.70	90.29	Gamma	47	1
LOT (days) - NPWTi - Deleyto 2018	19.73	11	9.50	2.864	14.52	25.73	Gamma	47	0
Number of additional surgeries - NPWTi - Deleyto 2018	0.8	11	0.7	0.211	0.44	1.26	Gamma	14	0
Simple closure % from surgical procedures - NPWTi - Deleyto 2018	83%	6			48%	99%	Beta	5	1
Debridement and closure % from surgical procedures - NPWTi - Deleyto 2018	17%	6			1%	52%	Beta	1	5
Mesh removal % from surgical procedures - NPWTi - Deleyto 2018	0%	6			0%	0%	Beta	0	6
Mesh substitution % from surgical procedures - NPWTi - Deleyto 2018	0%	6			0%	0%	Beta	0	6
Patients in need of additional surgeries for wound closure (%) - NPWTi - Deleyto 2018	54.5%	11			26%	81%	Beta	6	5

LOS (days) - standard - Deleyto 2018	88.21	34	33.56	5.755	77.29	99.84	Gamma	235	0
Number of additional surgeries - standard - Deleyto 2018	2.29	34	2.11	0.362	1.64	3.05	Gamma	40	0
Simple closure % from surgical procedures - standard - Deleyto 2018	16%	32			5%	30%	Beta	5	27
Debridement and closure % from surgical procedures - standard - Deleyto 2018	6%	32			1%	17%	Beta	2	30
Mesh removal % from surgical procedures - standard - Deleyto 2018	44%	32			27%	61%	Beta	14	18
Mesh substitution % from surgical procedures - standard - Deleyto 2018	34%	32			19%	51%	Beta	11	21
LOT (days) - NPWTi - Qui 2019	8.7	38	1.1	0.178	8.35	9.05	Gamma	2377	0
LOT (days) - standard - Qui 2019	16.30	35	1.60	0.270	15.77	16.83	Gamma	3632	0
Surgical site infections subgroup									
LOT (days) - NPWTi - Jurkovic 2019	21	19	10.00	2.294	16.75	25.73	Gamma	84	0
Number of applications - NPWTi - Jurkovic 2019	5	19	2	0.459	4.14	5.94	Gamma	119	0
Number of debridements - NPWTi - Jurkovic 2019	2	19	2	0.459	1.20	2.99	Gamma	19	0
LOT (days) - NPWT - Jurkovic 2019	23	22	10.00	2.132	19.01	27.36	Gamma	116	0
Number of applications - NPWT - Jurkovic 2019	4	22	2	0.426	3.21	4.88	Gamma	88	0
Number of debridements - NPWT - Jurkovic 2019	3	22	1	0.213	2.60	3.43	Gamma	198	0
LOT (days) - NPWTi - Chowdhry 2019	5.4	15	2.1	0.542	4.39	6.51	Gamma	99	0
Number of debridements - NPWTi - Chowdhry 2019	1.8	15	0.7	0.181	1.46	2.17	Gamma	99	0

LOT (days) - standard - Chowdhry 2019	8.4	15	3	0.775	6.95	9.98	Gamma	118	0
Number of debridements - standard - Chowdhry 2019	3.1	15	1.0	0.258	2.61	3.63	Gamma	144	0

If any parameters or variables listed in table 3 were omitted from the sensitivity analysis, please explain why.

Wherever parameters were calculated, via assumptions from other uncertain parameter values, the calculated parameters were not varied because uncertainty was not inherent to them. Therefore, it was deemed sufficient to vary the original parameters used in the calculations.

Sensitivity analyses results

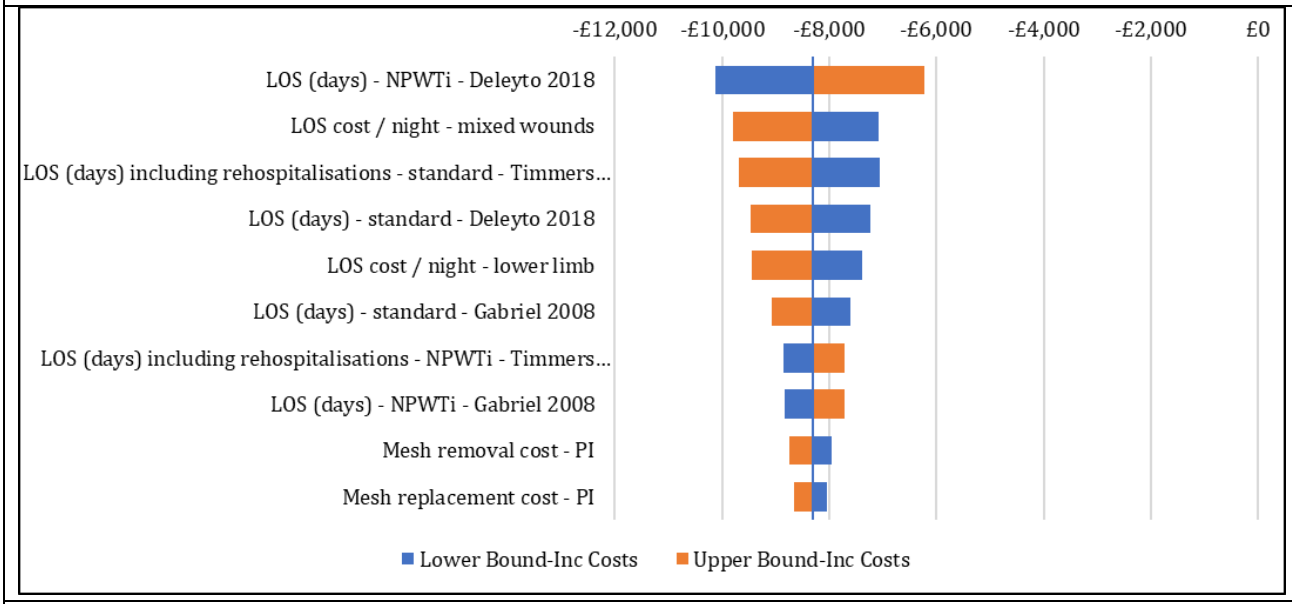
Present the results of any sensitivity analyses using tornado plots when appropriate.

OWSA:-

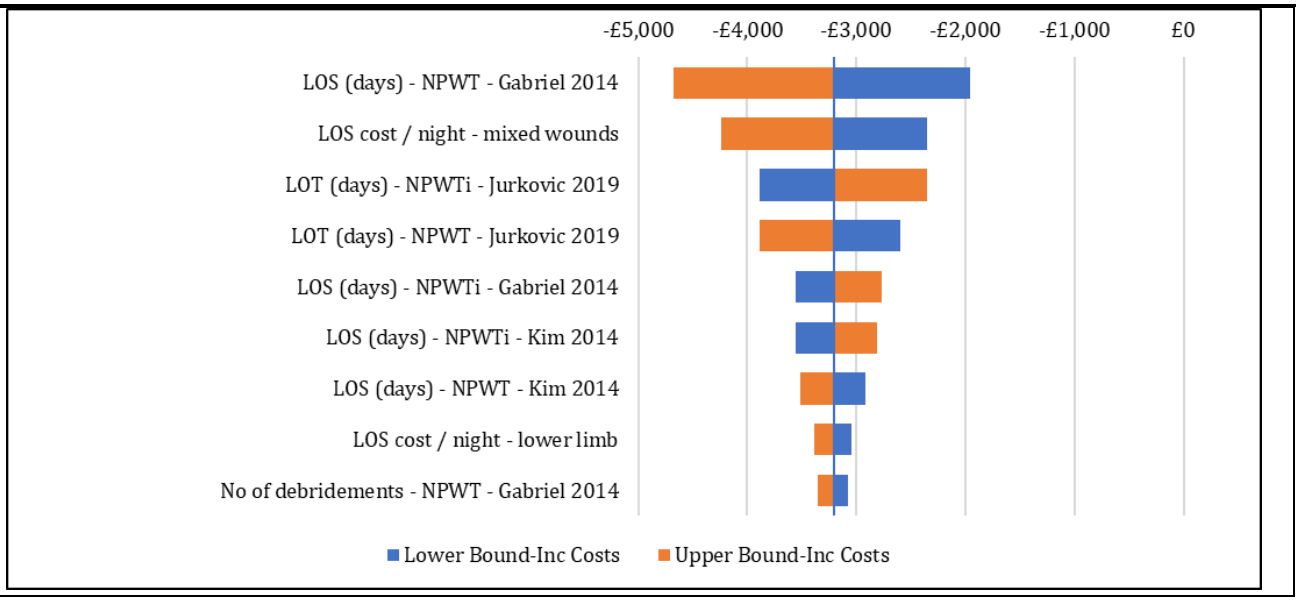
Whole population:

Tornado plots show that results are robust to univariate changes in parameters in the whole population and NPWTI was cost saving against both comparators. Lengths of stay and associated costs across different subgroups are more influential than other parameters.

Versus NPWT



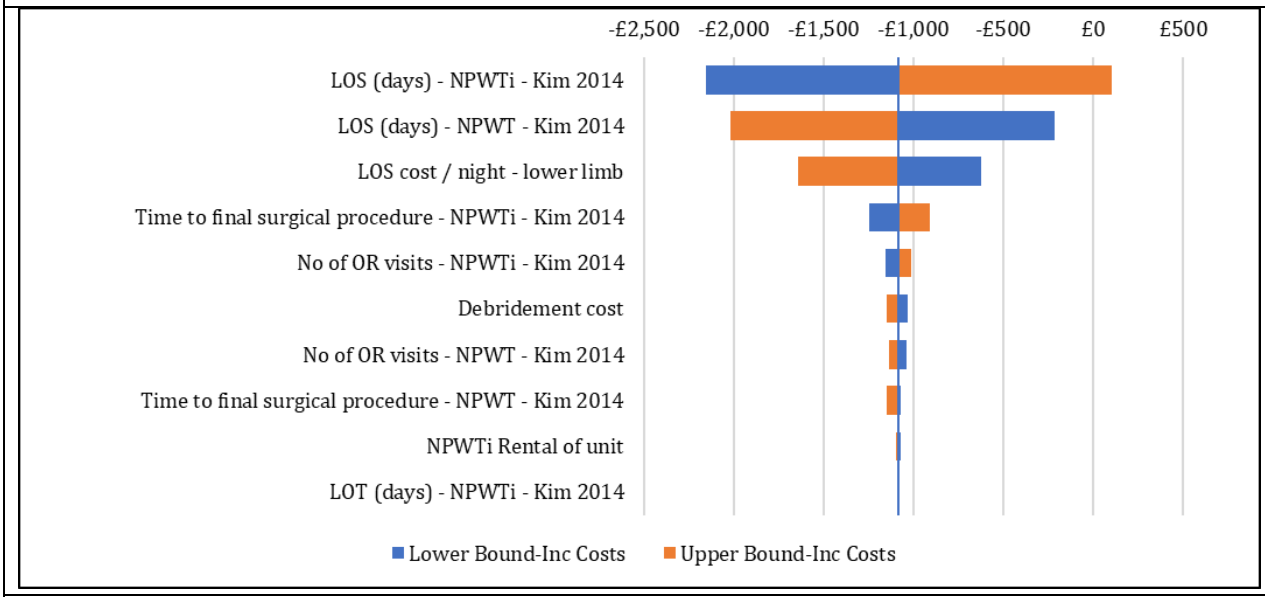
Versus standard wound care



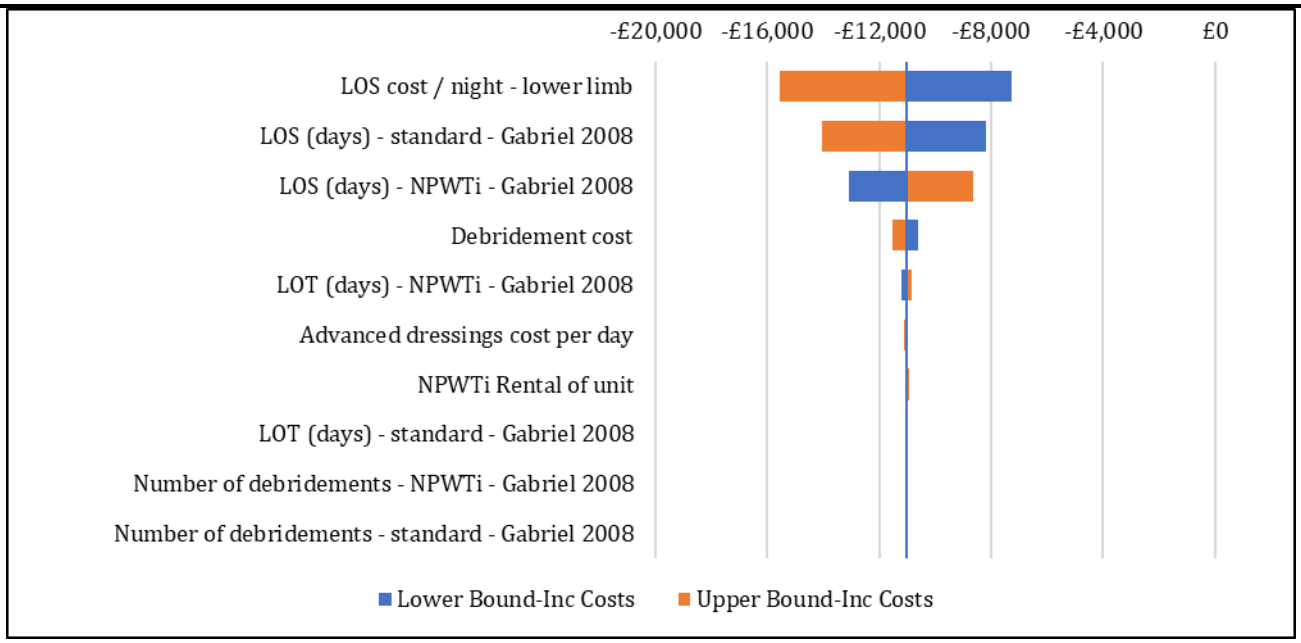
Lower limb subgroup:

Tornado plots show that results are robust to univariate changes in parameters in the lower limb subgroup and NPWTi was cost saving against standard wound care. NPWTi was also cost saving in all scenarios against NPWT except when length of stay on NPWTi is similar to that on NPWT (14.66 versus 14.92 days respectively).

Versus NPWT



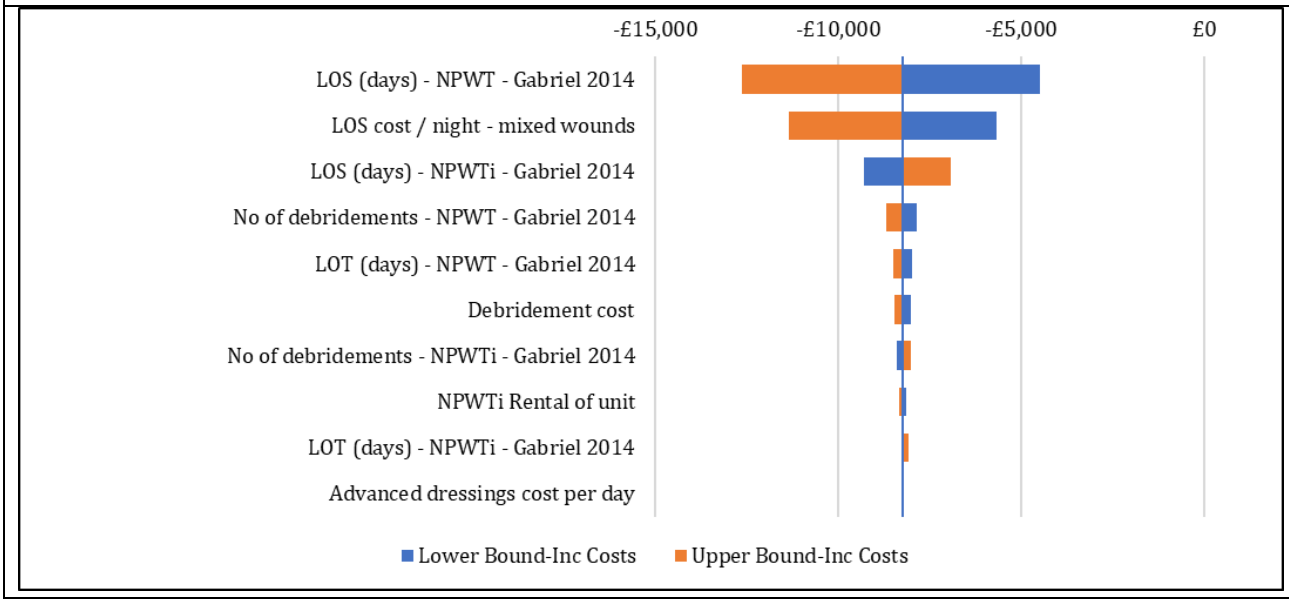
Versus standard wound care



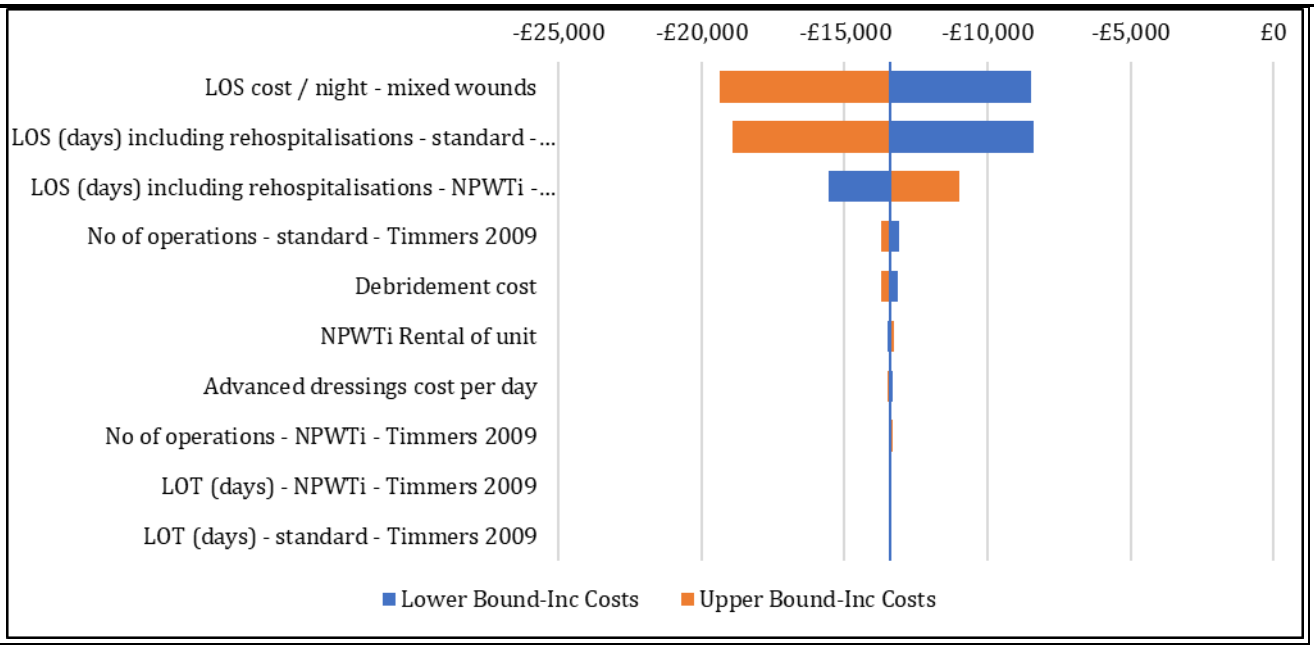
Mixed wounds subgroup:

Tornado plots show that results are robust to univariate changes in parameters in the mixed wound subgroup and NPWTi was cost saving against both comparators. Lengths of stay and associated costs across different subgroups are more influential than other parameters.

Versus NPWT



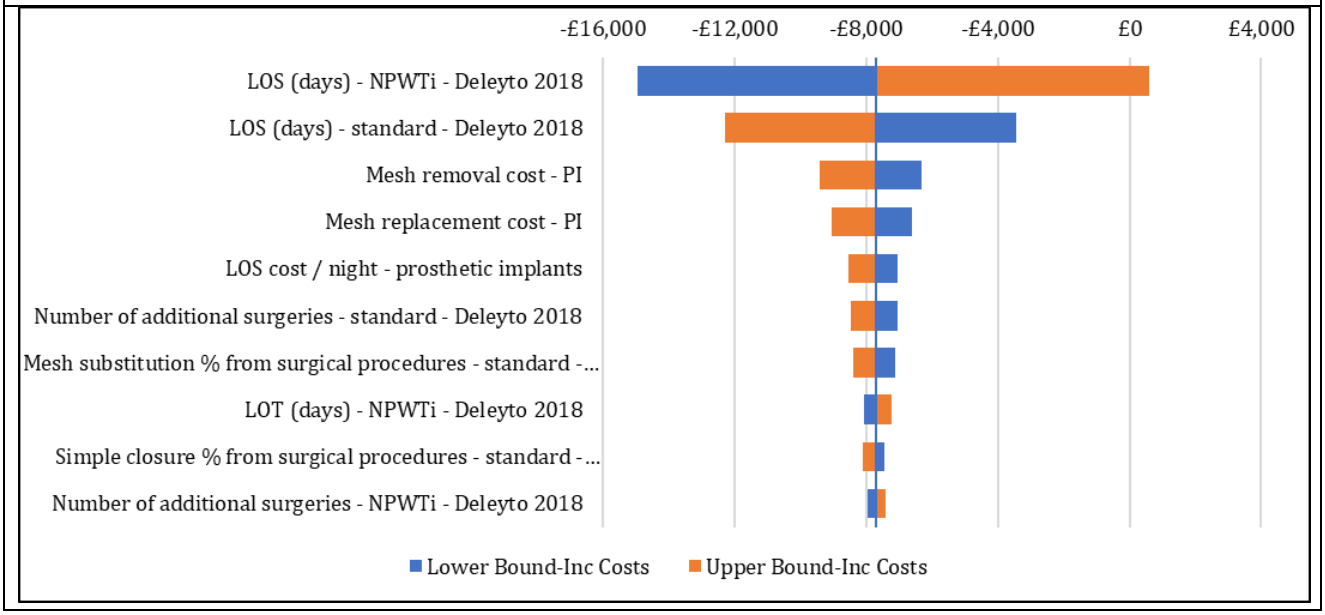
Versus standard wound care



Prosthetic implants subgroup:

The tornado plot shows that results are almost robust to univariate changes in parameters in the prosthetic implants subgroup and NPWTi was cost saving in all scenarios against standard wound care except when length of stay on NPWTi is higher than that on standard wound care (90.29 versus 88.21 days respectively).

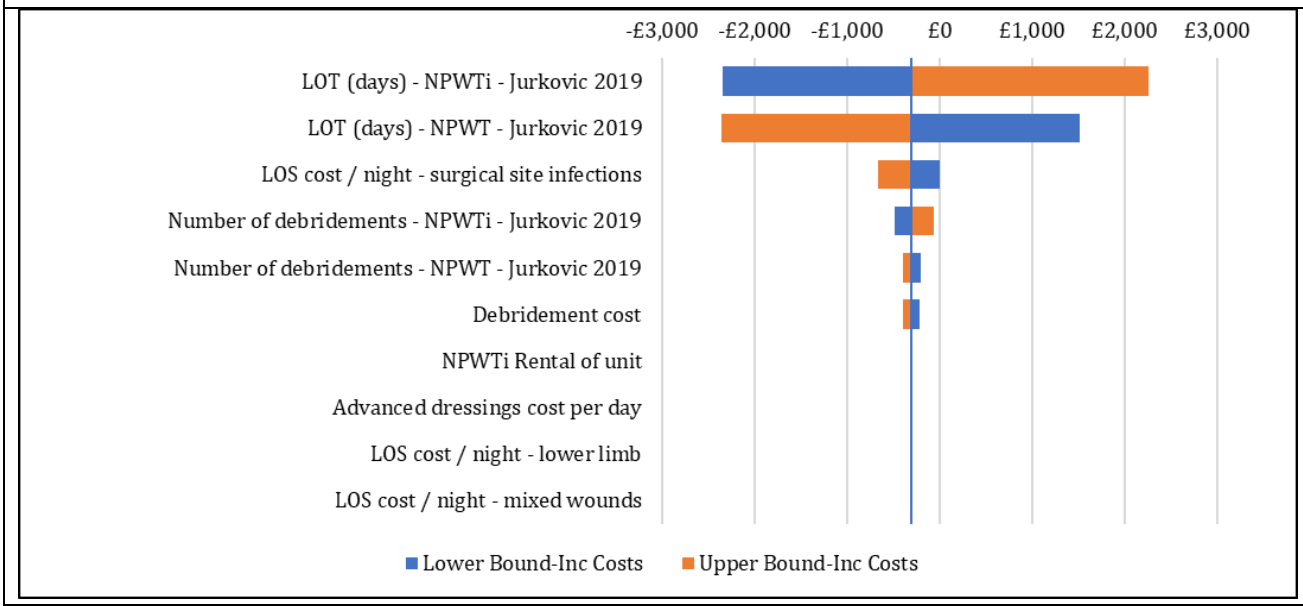
Versus standard wound care



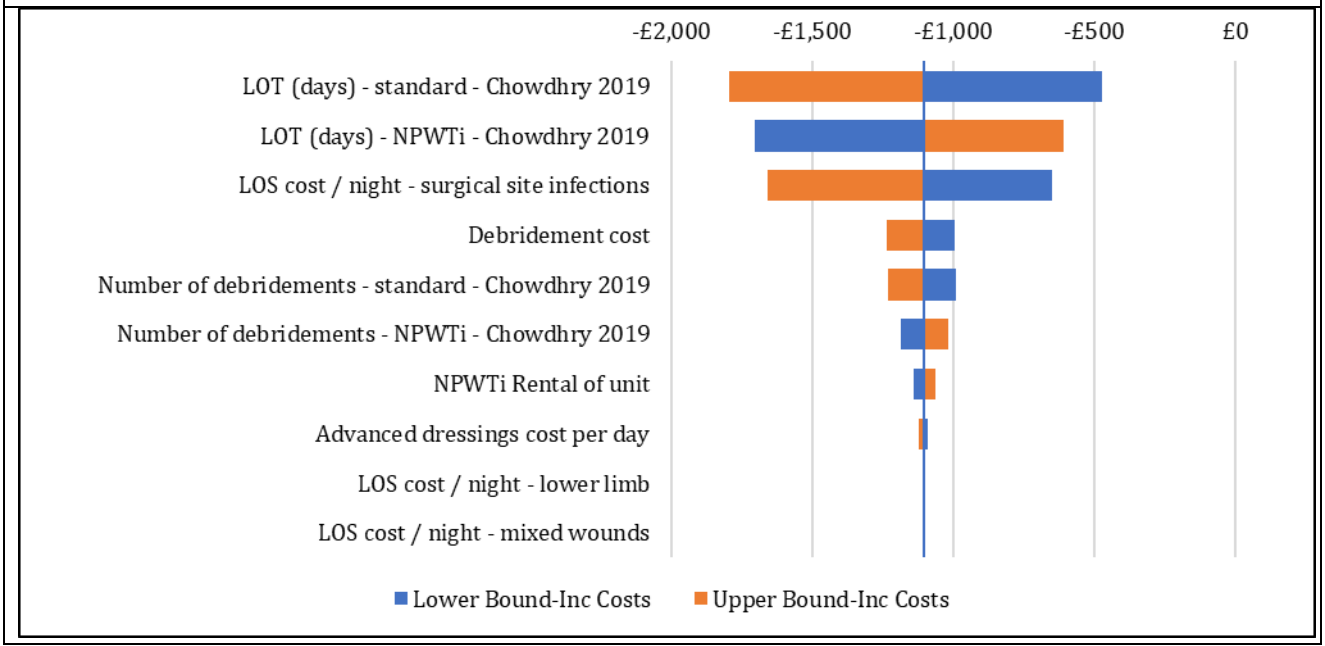
Surgical site infections subgroup:

Tornado plots show that results are robust to univariate changes in parameters in the lower limb subgroup and NPWTi was cost saving against standard wound care. NPWTi was also cost saving in all scenarios against NPWT except when length of therapy on NPWTi is higher than that on NPWT (25.73 versus 23 days respectively) or when length of therapy on NPWT is lower than that on NPWTi (19.01 versus 21 days respectively). Length of stay per night was also influential at its lower bound of £279 per night stay.

Versus NPWT



Versus standard wound care



PSA:-

Whole population:

PSA results demonstrate that NPWTi is cost saving in 100% of the runs although of incurring therapy costs in 95% of runs versus NPWT and 100% of runs versus standard wound care.

	Length of stay costs	Therapy costs	Debridement costs	Total costs
Versus NPWT				
Average difference	-£3,479	£185	-£320	-£3,614

across PSA runs				
% of runs where NPWTi is cost saving	100%	5%	100%	100%
Versus standard wound care				
Average difference across PSA runs	-£9,829	£989	-£948	-£9,788
% of runs where NPWTi is cost saving	100%	0%	100%	100%

Lower limb subgroup:

PSA results demonstrate that NPWTi is cost saving in 94% of the runs versus NPWT and in 100% of the runs versus standard wound care although of incurring therapy costs in 89% of runs versus NPWT and 100% of runs versus standard wound care.

	Length of stay costs	Therapy costs	Debridement costs	Total costs
Versus NPWT				
Average difference across PSA runs	-£1,300	£195	-£141	-£1,246
% of runs where NPWTi is cost saving	97%	11%	100%	94%
Versus standard wound care				
Average difference across PSA runs	-£10,570	£688	-£1,175	-£11,057
% of runs where NPWTi is cost saving	100%	0%	100%	100%

Mixed wounds subgroup:

PSA results demonstrate that NPWTi is cost saving in 100% of the runs versus both comparators. It even shows savings in therapy costs in 99% of runs versus NPWT.

	Length of stay costs	Therapy costs	Debridement costs	Total costs
Versus NPWT				
Average difference across PSA runs	-£7,259	-£382	-£583	-£8,224
% of runs where NPWTi is cost saving	100%	99%	100%	100%
Versus standard wound care				
Average difference across PSA runs	-£13,940	£1,317	-£705	-£13,329
% of runs where NPWTi is cost saving	100%	0%	100%	100%

Prosthetic implants subgroup:

PSA results demonstrate that NPWTi is cost saving in 94% of the runs versus standard wound care. Although it is not cost saving in terms of therapy costs, however in terms of length of stay costs and debridement costs, it is cost saving in 95% and 87% of the runs respectively.

	Length of stay costs	Therapy costs	Debridement costs	Total costs
Versus standard wound care				
Average difference across PSA runs	-£7,589	£1,526	-£1,697	-£7,760
% of runs where NPWTi is cost saving	95%	0%	87%	94%

Surgical site infections subgroup:

PSA results demonstrate that NPWTi is cost saving in 58% of the runs versus NPWT and 99% of the runs versus standard wound care. Cost savings were more certain in debridement costs (96% and 100% respectively).

	Length of stay costs	Therapy costs	Debridement costs	Total costs

Versus NPWT				
Average difference across PSA runs	-£895	£850	-£236	-£281
% of runs where NPWTi is cost saving	75%	0%	96%	58%
Versus standard wound care				
Average difference across PSA runs	-£1,311	£482	-£307	-£1,136
% of runs where NPWTi is cost saving	100%	0%	100%	99%

What were the main findings of each of the sensitivity analyses?

PSA shows that probability of NPWTi being cost saving is greater than 90% in all subgroups against both comparators except versus NPWT in surgical site infections subgroup.

The same subgroup showed more uncertainty in OWSA compared with other subgroups. The most influential parameter was duration of therapy that was used to indicate both length of therapy and length of stay.

What are the main sources of uncertainty about the model's conclusions?

The main source of uncertainty is the structural and parameter assumptions made for the economic model, both of which were decided on based on paucity in evidence.
In terms of structural assumptions, it was assumed the technology impacts only length of stay, duration of therapy and number of debridements. It is highly likely that these does not capture the full impact range of the product. The product is expected to have also beneficial impact on complication rates, re-admittance rates, primary care costs and most importantly quality of life of patients and carers

In terms of parameter assumptions, we had to derive some missing values from other reported parameters values in the same study and similar studies within the studied subgroup. We sometimes relied on strong conservative assumptions like what we did in the

surgical site infections subgroup where length of stay was assumed to equate to duration of therapy.

Miscellaneous results

Include any other relevant results here.

NA

Validation

Describe the methods used to validate, cross-validate (for example with external evidence sources) and quality assure the model. Provide sources and cross-reference to evidence when appropriate.

The validation of the model was performed in several stages to ensure its consistency and quality. This was undertaken using the following steps:-

1. Model concept and design phase
2. Model design and development phases
3. Model assumption and mapping
4. Model data tracking and reference updates including
    - o are up-to-date;
    - o source is documented;
    - o is based on a robust sample;
    - o is consistent with other sources;
    - o meets the requirements it is being used for.

The model was produced by two modellers who focused on two key areas. The first modeller approached the clinical input review using the identified studies. The second modeller focused on the cost data and resource used to support the outcomes. The modellers then each reviewed each other's processes and technical updates.

Once the model was completed it was then further reviewed by 3 3m/KCI internal reviewers to ensure processes and outcomes were consistent. Iterations were completed to ensure format and usability

External review of the model was undertaken by a number of expert groups. .

TVN Tissue viability nurses

The evidence to support the model was discussed with 2 TVNs to gather their view of the resource, the clinical and cost assumptions included.

Clinician review

The model and outputs were shared with two clinicians who had the opportunity to feedback on all elements of the model including resource, pathway, subgroup population levels and the current outputs. This allowed the model to be adapted to ensure the pathway and resource was UK centric.

Cost data review

A full review was completed of the cost data which is included in the model. This process included the review of the latest reference costs, as the latest version of 2018/19 was not fit for purposes due to the lack of inclusion of bed day costs in the publication. Also the relevant data from NHS Scotland was used in the input process for the theatre calculation, to support debridement costs.

Publication references used

Each modeller reviewed the references for all the studies. This supported confirmation that the correct study was associated with the correct end point and subgroup. Other studies were reviewed to establish bench marks in terms of calculation, however they were for assurance.

Give details of any clinical experts who were involved in validating the model, including names and contact details. Highlight any personal information as confidential.

Consultant of plastic surgery -[redacted]
Consultant of Vascular surgery -[redacted]

TVN 1 –

TVN 2-

4 Summary and interpretation of economic evidence

Describe the main findings from the economic evidence and cost model. Explain any potential cost savings and the reasons for them.

The findings of the cost consequence model have demonstrated that the unique elements of NPWTi delivers savings across the different patient subgroups. This will result in significant savings for the NHS as well as improvements in patient outcomes.

Group Savings based on PSA results

Whole population

- Versus NPWT -£3,614
- Versus AWC - -£9,788

Lower Limb

- Versus NPWT -£1,246
- Versus AWC -£11,057

Mixed wounds

- Versus NPWT-£8,224
- Versus AWC -£13,329

Prosthetics

- Versus AWC -£7,760

SSI

- Versus NPWT -£281
- Versus AWC -£1,136

==

The cost savings are focused on three principle end points:-

1. Length of stay
2. Length of therapy
3. Debridement reduction

As the national average bed day cost is £431 these reductions in length of stay offer significant financial savings to the NHS budget. Likewise the reduction in the number of debridements that patients require during a hospital admission, at a cost of £237, not only directly saves financial resources but also releases capacity for other patients needing surgical interventions.

The model includes a PSA analysis which, whilst not essential allowed us to confirm we had considered all aspects of uncertainty. The positive outcomes the PSA demonstrated across the different subgroups has reinforced NPWTi ability to support cost savings for the NHS.

Briefly discuss the relevance of the evidence base to the scope.

The evidence reviewed and included in the model is in line with the final scope which was widened considerably following consultation.

There have been very no papers that considered cost effectiveness of NPWTi as the main outcome to be evaluated. The majority of research to date has focussed upon clinical outcomes, which is perhaps due to NPWTi innovative approach. The principle end points are however tangible and are reflected in the scope.

Due to the variation in the patient populations across the subgroups it was not felt that aggregation of all data into the total population included in the scope was the most effective way to demonstrate cost effectiveness. Whilst for completeness sake a whole population section has been included in the mode the main focus and relevance to the evidence is within the subgroups.

Overall the evidence is supportive of the technology which is being recognised by the increased adoption rates of NPWTi in the NHS.

Briefly discuss if the results are consistent with the published literature. If they are not, explain why and justify why the results in the submission be favoured over those in the published literature.

The results are in line with the published literature which demonstrates a cost saving across the health care sector.

Describe if the cost analysis is relevant to all patient groups and NHS settings in England that could potentially use the technology as identified in the scope.

Despite the broadness of the of the decision problem, our cost analysis was in line with the scope. As discussed above, due to the availability of evidence, most inputs in the base case analysis were taken from studies in a subgroup of the patient population eligible for NPWTi.

Any uncertainty in these data was analysed and tested through our sensitivity and scenario process, using wide ranges of the alternative values.

Briefly summarise the strengths and limitations of the cost analysis, and how these might affect the results.

Strengths:

- A consistent approach was used to modelling across the different subgroups which allowed comparisons and averaging to be made for the whole population.
- There is a high degree of certainty in the results. The PSA predicted a high likelihood that NPWTi would be cost saving across all subgroups.
- Extensive sensitivity and scenario analyses were undertaken to assess the impact of uncertainty and variability on the model results. This resulted in a conclusion that the model is robust to wide variations in the input parameters.
- All of the inputs for resource use have been sourced from a UK NHS viewpoint using an amalgamation of bottom-up procedure pricing and NHS reference costs where appropriate.

Limitations:

- We were unable to model several end points such as QALYs gained, complication rates, readmission rates, primary care costs and staff time. This was due to the limited availability of evidence.
- We were unable to model the total population from a single study as this has not yet been published due to the variability of wounds for which NPWTi can deliver therapy.
- We were unable to quantify the level of care & consumables provided to patients within an NHS secondary setting, prior to the use of NPWTi for those patients with acute infected and chronic hard to heal wounds. It is our understanding that these patients consume a large amount of resource and consumables.

Detail any further analyses that could be done to improve the reliability of the results.

Publication of an economic study for the use of V.A.C. Veraflo in comparison to NPWT and AWC would further strengthen the current body of evidence. Studies that collected data about the associated wound care costs in primary care for both comparators would demonstrate the total cost of care.

5 References

Please include all references below using NICE's standard referencing style.

Deleyto E, , García-Ruano A, González-López J. (2017) Negative Pressure Wound Therapy With Instillation, a Cost-Effective Treatment for Abdominal Mesh Exposure. Hernia: (2), 311-318

Gabriel A, Kahn K, Karmy-Jones R. (2014) 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 14:328-338

Gabriel A, Shores J, Heinrich C, et al. (2008)Negative pressure wound therapy with instillation: a pilot study describing a new method for treating infected wounds. Int Wound J. 5(3):399–413

Garcia-Ruano A, Deleyto E, Garcia-Fernandez.(2016) VAC-instillation therapy in abdominal mesh exposure: a novel indication. Journal of Surgical Research. (206):292-297

Jurkovic A, Bartos J, Bencurik V, Martinek L, Throttle M. (2019) Negative pressure therapy with the ULTRAVAC instillation in the therapy of infected laparotomies with fasciitis -continuous results of a prospective randomised study. Perspectives V Surgery. Vol 98 (4) 152-159

Kim PJ, Attinger CE, Oliver N, et al. (2015) Comparison of outcomes for normal saline and an antiseptic solution for negative-pressure wound therapy with instillation. Plast Reconstr Surg. 136:657-664

Kim PJ, Attinger CE, Steinberg JS, et al. (2014) The impact of negative-pressure wound therapy with instillation compared with standard negative-pressure wound therapy: a retrospective, historical, cohort, controlled study.PlastReconstr Surg.133709-716

Timmers MS, Graafland N, Bernards AT, Nelissen RG, van Dissel JT, Jukema GN. (2009) Negative pressure wound treatment with polyvinyl alcohol foam and polyhexanide antiseptic solution instillation in posttraumatic osteomyelitis. Wound Repair Regeneration. (2):278-86

Cupto et el 2008 A prospective randomised controlled clinical trial comparing hydrosurgery debridement with conventional surgical debridement in lower extremity ulcers.

6 Appendices

Appendix A: Search strategy for economic evidence

Describe the process and methods used to identify and select the studies relevant to the technology being evaluated. See section 2 of the user guide for full details of how to complete this section.

Please note that due to there being no economic studies returned for the inclusion of this submission, the EBM process was followed in line with NICE methods and process regarding inclusion.

Date search conducted:	February 3 2020
Date span of search:	January 1 2005 to January 31 2020
List the complete search strategies used, including all the search terms: text words (free text), subject index headings (for example, MeSH) and the relationship between the search terms (for example, Boolean). List the databases that were searched.	
The following strategy was used to perform a literature search in PubMed, EMBASE and QUOSA. ("Lavage" OR "instil" OR "instillation" OR "irrigated" OR "irrigation" OR "topical solution" OR "topical wound solution" OR "topic solution" OR "VERAFLO" OR "VERAFLOW" OR "Veraflo dressing" OR "Veraflo cleanse dressing" OR "Veraflo cleanse choice dressing" OR "Ulta") AND ("Negative Pressure Wound Therapy" OR "NPWT" OR "vacuum assisted closure" OR "vacuum sealing" OR "NPWTi" OR "NPWTi-d" or "economic") **Unpublished Data** Registered studies at ClinicalTrials.gov, was reviewed using the same search criteria for completed and terminated studies to determine publication bias. References from identified publications and abstracts will also be reviewed. Unpublished data including complete trials that have not yet been published and specific outcomes not reported have been reviewed and referenced in the relevant section of this document.	
Brief details of any additional searches, such as searches of company or professional organisation databases (include a description of each database):	
Enter text.	
Inclusion and exclusion criteria:	
EXCLUSION CRITERIA Conference abstracts Expert opinion Reviews	

Meta-analyses
Protocols
Case reports
Studies with < 10 patients
Languages other than English
Veterinary studies
Preclinical (in vitro, in vivo, in silico) studies
Non-clinical reports

INCLUSION CRITERIA
Conference abstracts
Published manuscripts
Preclinical (in vitro, in vivo, in silico) studies
Clinical studies (regardless of patient #)
Discusses subject matter

Data abstraction strategy:

All comparative manuscripts and abstracts evaluating effectiveness and safety that meet all the inclusion criteria and none of the exclusion criteria will be included, regardless of the study design.

Review Process
Titles of manuscripts and abstracts that meet the search criteria were logged and investigated for duplicates. The abstracts and manuscripts were assessed for inclusion and exclusion criteria by two independent reviewers. When discordance is identified, the two reviewers discuss until consensus is reached. For abstracts and manuscripts that meet all the inclusion criteria and none of the exclusion criteria, they will be read critically

i) to assess whether they contain reference of any other articles that meet the inclusion criteria and scope, and
ii) extract study characteristics by at least two independent reviewers.

Initial Search

Articles and abstracts that met the search criteria or identified in the references of a selected manuscript or abstract will have the following collected:
• Article reference
• Inclusion or exclusion status
• If excluded from the study, reason for exclusion

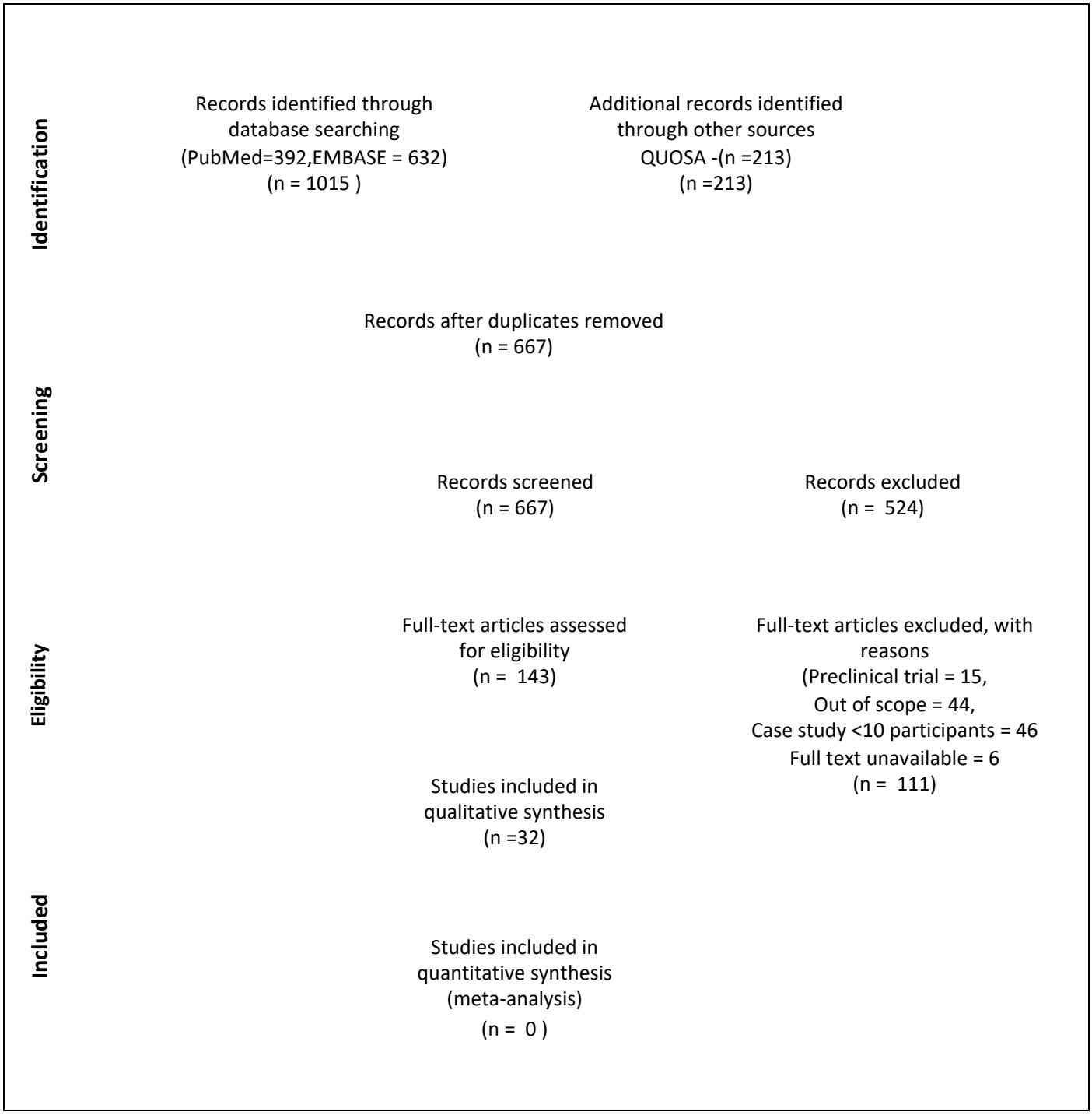
Quality Assessment
Each study was reviewed and assessed for quality. All data collected in the excel tracker was reviewed by two independent reviewers to ensure consensus is met with regards to overall assessment.

Excluded studies

List any excluded studies below. These are studies that were initially considered for inclusion at the level of full text review, but were later excluded for specific reasons.

Excluded study	Design and intervention(s)	Rationale for exclusion	Company comments
Text	Text	Text	Text
Text	Text	Text	Text
Text	Text	Text	Text
Text	Text	Text	Text
Text	Text	Text	Text
Text	Text	Text	Text
Text	Text	Text	Text

Report the numbers of published studies included and excluded at each stage in an appropriate format (e.g. PRISMA flow diagram).



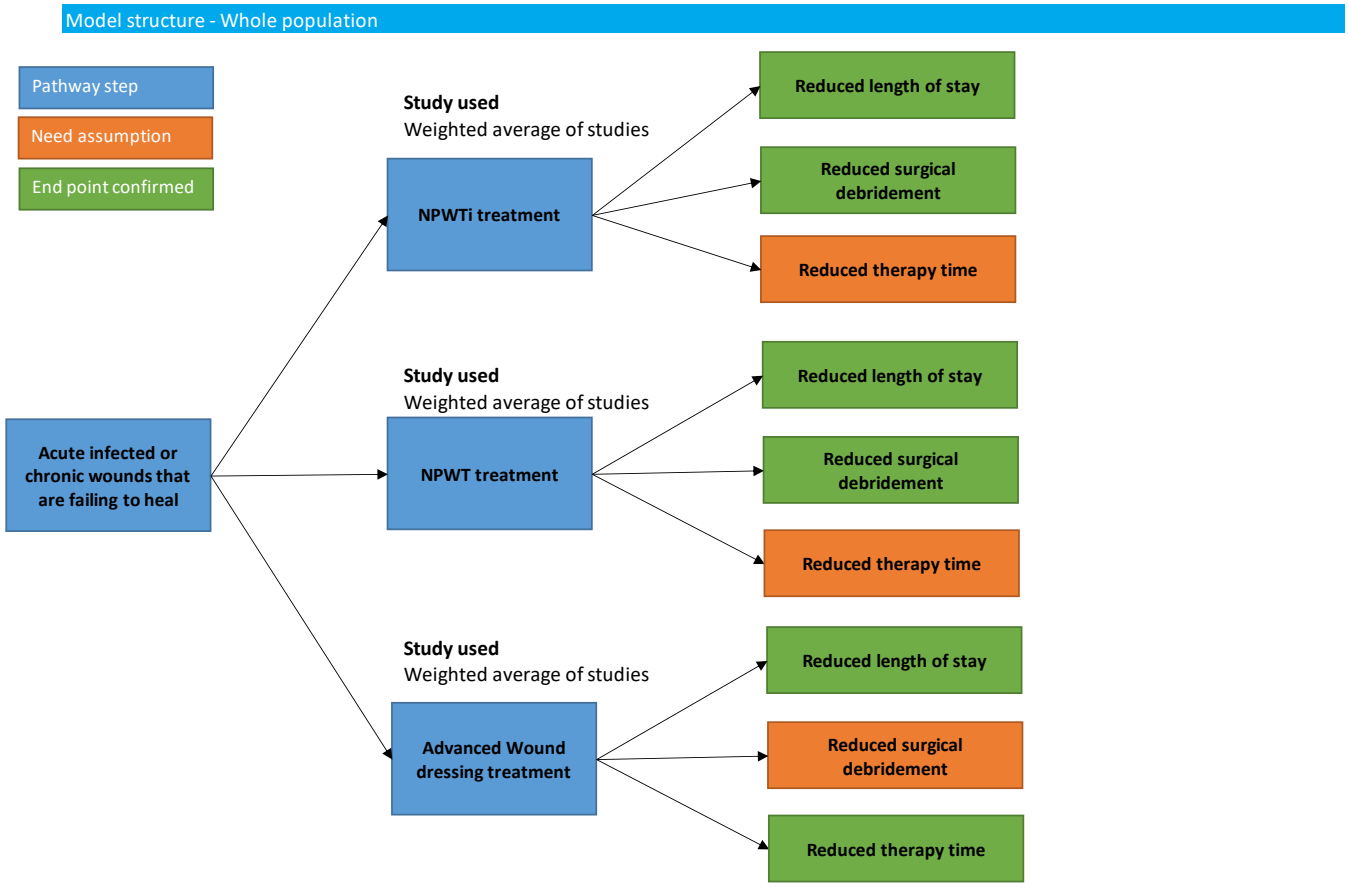
Structured abstracts for unpublished studies

Study title and authors
Introduction
Objectives
Methods
Results
Conclusion
Article status and expected publication: Provide details of journal and anticipated publication date

Appendix B: Model structure

Please provide a diagram of the structure of your economic model.

This structure was replicated for all subgroups, please see accompanying CCA model



Appendix C: Checklist of confidential information

Please see section 1 of the user guide for instructions on how to complete this section.

Does your submission of evidence contain any confidential information? (please check appropriate box):

No ☐ If no, please proceed to declaration (below)

Yes ☒ If yes, please complete the table below (insert or delete rows as necessary). Ensure that all relevant sections of your submission of evidence are clearly highlighted and underlined in your submission document, and match the information provided in the table. Please add the referenced confidential content (text, graphs, figures, illustrations, etc.) to which this applies.

Page	Nature of confidential information	Rationale for confidential status	Timeframe of confidentiality restriction
62	☒ Commercial in confidence ☐ Academic in confidence	Personal details of expert advisors	Enter text.
Details	Personal details of expert advisors under section of Validation within the submission. These are highlighted yellow and underlined		
#	☐ Commercial in confidence ☐ Academic in confidence	Enter text.	Enter text.
Details	Enter text.		

Confidential information declaration

I confirm that:

- all relevant data pertinent to the development of medical technology guidance (MTG) has been disclosed to NICE
- all confidential sections in the submission have been marked correctly
- if I have attached any publication or other information in support of this notification, I have obtained the appropriate permission or paid the appropriate copyright fee to enable my organisation to share this publication or information with NICE.

Please note that NICE does not accept any responsibility for the disclosure of confidential information through publication of documentation on our website that has not been correctly marked. If a completed checklist is not included then NICE will consider all information contained in your submission of evidence as not confidential.

Signed*: ** Must be Medical Director or equivalent*		**Date:**	Click or tap here to enter text.
Print:	Click or tap here to enter text.	**Role / organisation:**	Click or tap here to enter text.
Contact email:	Click or tap here to enter text.		

NICE National Institute for Health and Care Excellence

Medical technologies guidance

Collated expert questionnaires

Technology name & indication: V.A.C. VERAFLO Therapy System for acute infected or chronic wounds that are failing to heal

Experts & declarations of interest (DOI)

Expert #1	Mr David Russell, Consultant Vascular Surgeon and Honorary Clinical Associate Professor, Leeds General Infirmary
	DOI: Non-financial interest: chief Investigator for NIHR HTA funded MIDFUT trial comparing hydrosurgical debridement +/- NPWT +/- decellularized cadaveric dermis graft for chronic diabetic foot ulcers (interest arose April 2017); financial interest: consultancy fee received to Leeds vascular research fund from URGO medical as advisory board member (fee not received personally) for advice on chronic wound healing (interest arose June 2017), consultancy fee received to Leeds vascular research fund from Integra Lifesciences as advisory board member (fee not received personally) for advice on chronic wound healing (interest arose June 2018).
Expert #2	Mr Haitham Khalil, Consultant Oncoplasty & Reconstructive Surgeon, Division of Plastic and Reconstructive Surgery (University Hospitals Birmingham)
	DOI: Yes – invited as a speaker at the Verflow Innovation Council Frankfurt 2018 and verflow meeting Cambridge 2019 in NPWTi. An honorarium has been paid for these tutorial as an invited speaker
Expert #3	Dr Fania Pagnamenta, Clinical Academic Nurse Consultant (Tissue Viability), Newcastle upon Tyne Hospitals NHS Foundation Trust
	DOI: NONE
Expert #4	Ms Claire Porter, Advanced Nurse Practitioner; lead nurse burns and plastics, Leicester Hospitals NHS Foundation Trust
	DOI: NONE
Expert #5	Patricia Littlewood, Lead Tissue Viability Clinical Nurse Specialist, Frimley Health Foundation Trust (Wexham Site)
	DOI: NONE

Expert #6	Vicki Tapley, Advanced Specialist Podiatrist , The Royal Free Hospital Foundation Trust, NHS
	DOI: NONE

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1. **Please describe your level of experience with the technology, for example: Are you familiar with the technology? Have you used it? Are you currently using it? Have you been involved in any research or development on this technology? Do you know how widely used this technology is in the NHS?**

Expert #1	I am familiar with, and am a regular user of the technology, mainly after surgical debridement of acutely diabetic foot infection in line with the published evidence. I have not been involved in any research or development of the technology. The technology is used in a large number of acute trusts in the UK, and use in diabetic foot and trauma management is becoming increasingly common place.
Expert #2	Yes, I am familiar with this technology and have being using it for nearly 3 years. Mainly as a bridge for preparation of complex infected wounds/pathology for reconstructive procedures or as the sole treatment pathway in certain cases. Myself and my team have successfully published the first reported use of Verflow in chronic intrathoracic infection in Plastic and Reconstructive Global Journal (PRS Global) which is currently in press. We are currently working on submission of our experience in using verflow in management of complex perineal wounds especially necrotizing fasciitis. Having been involved in the wounds UK expert meeting on negative pressure wound therapy instillation (NPWTi) we have been briefed that according to their statistics it is used around 5-10% only in management of grade III and IV infected wounds.
Expert #3	Yes, I am very familiar with the technology We have use it in a number of wounds, mainly in orthopaedics but also in surgical abdominal wounds, vascular surgery & plastic surgery. Yes we are currently using it and will continue to do so. No, we have not been involved in the development of this technology.

	This is used in Acute Trusts where quality wound care is offered.
Expert #4	I have been an advocator of the Veraflo system for approx. 7 years. I am familiar with all its functions and have used all the different dressing applications within the range available. I would confidently say that I am an expert user of this system. It is in current and frequent use within our Plastic Surgery department. I am not currently involved in a research I am aware of other units across the UK that use this
Expert #5	I have been using this technology since 2014, and we are still using it with increasing regularity. I have not been involved in any research or development other than feeding back to the company if we had any difficulties or problems. I do not know how widely used the item is.
Expert #6	I have a large amount of experience with the application of the VeraFlo therapy system in regards to application of the dressings to infected (controlled infection) and semi necrotic diabetic, renal and vascular foot ulcerations/post-surgical amputations. This involves fitting and application of the dressing to multiple different sized ulcerations, amputations and on a variety of complex patients (physical and mental health wise) and places on the foot. This has always included setting up the machine, settings and saline bags. I'm very familiar with the technology and often called to help set up, show the application of use and educate on the settings for our own podiatrists, nursing staff and junior doctors. I have on average, applied a Veraflo therapy system at least twice a week since we started using them at the RFH to varying patients described above. It can then vary from once a day doing a veraflo dressing change to maximum 3 dressing changes on the veraflo a day. We are currently using the VeraFlo system on multiple patients, mainly based as inpatients and on vascular, diabetic and renal foot ulcerations.

	I cannot comment on how widely used this technology is used within the NHS, but within the RFH trust it is widely used, specifically with the vascular team.

2. Has the technology been superseded or replaced?

Expert #1	No
Expert #2	No
Expert #3	No, but the very first VAC had a 'VAC instill', but this is now 15-18 years old. The VeraFlow is the (much) newer version of that product.
Expert #4	No.
Expert #5	Not that I am aware
Expert #6	The technology has not been replaced, it is still in use. Due to multiple options of VAC systems, it isn't the main option to use. We assess the ulceration/amputation site and symptoms of the ulceration to whether we use a VeraFlo or other form of VAC system/dressing.

Current management

3. How innovative is this technology, compared to the current standard of care? Is it a minor variation or a novel concept/design?

Expert #1	This is a variation of the standard negative pressure wound therapy systems. However, the ability to washout a wound on an automated cycle, or instil antimicrobial or antiseptic solutions significantly improves the prospects of source control in acute infection following a surgical debridement, and in the lower limb and foot therefore increases the chance if functional limb salvage.

Expert #2	The NPWTi is novel design which is an instinctive upgrade from the previous VAC therapy due to the introduction of the instillation technique to promote more granulation tissue formation, reduce contamination load/ biofilm efficiently and more quicker, hence promotes wound healing or prepare wound for primary closure or reconstruction
Expert #3	TNP has now been accepted as standard care. This is taking it a step forward. Wound bed preparation with stronger granulation tissue that develop faster. VeraFlow is an intensive method of wound healing – once it has done its job (1-2 weeks), it can be stepped down to TNP and then to conventional dressings until fully healed.
Expert #4	This is a technological advance within wound care. As a Plastic Surgery ANP Nurse I feel that this is one of the biggest innovations in wound care that I have seen for many years, having a positive impact for patients. I have been using the VAC system for over 20 years, but with Veraflo adding fluid into a wound to I have seen the impact on faster granulation, improved healing times and it has been used positively in pre-operative preparation to close a wound.
Expert #5	It is my belief that this technology is a game changer – it reduces bed stay length and is capable of preventing patients from returning to theatre for washout procedures
Expert #6	This technology is unique in that it's a NPWT, application and treatment is 24/7 and the successful outcomes out-weight basic dressings and debridement. The outcomes of good debridement, good granulation growth and to be able to see an obvious improvement shows the technology is innovative. I wouldn't say it was innovative in regards to the machinery; its large, requires a lot of time to set up and application. It's not easy for a patient to carry around unlike the Acti-VAC that can be placed into a shoulder bag. When comparing to normal VAC i.e No saline/washes/soaks, this is innovative compared to current practice but it is only helpful on the right wound bed and if application is correct. I don't feel the technology is innovative enough or the AI of automatically being able to define the fluid needed for the wound bed is good enough. I feel it needs personal touches to really ensure treatment is successful; i.e. manually adding in the fluid/ forcing through the fluid to non-gravity areas myself – all these points could be improved with the innovative idea of soaks/VAC NWPT.

	With the soaks and washes – I feel less is more in our patients. The soaks can often damage surrounding sink if not careful as the technology of the dressing isn't good enough to stop some fluid going form the ulcer bed to the surrounding edges and over, which causes maceration and wound edge deterioration.

4. Are you aware of any other competing or alternative technologies available to the NHS which have a similar function/mode of action to the notified technology? If so, how do these products differ from the technology described in the briefing?

Expert #1	No
Expert #2	I am aware of other companies who provide negative pressure wound therapy but not sure if they comprise the instillation mode of action.
Expert #3	VeraFlow is unique.
Expert #4	No, not aware of any other companies that can provide this technology.
Expert #5	No
Expert #6	In regards to (in my opinion) Veraflo unique selling point – Soaks, saline wash to aid debridement and the different style of foams, in a less painful setting as well as a quicker granulation formation – No, there are not any other competing alternatives. However, our ulcerations were previously treated with acti-VAC, SNAP, PICO, Smith and newphew VAC and they had the same outcome of granulation of a wound bed. So they would be the alternatives to me. The benefit of the Veraflo is areas of difficult debridement on the foot in the ward setting or if a patient isn't neuropathic and is in pain , so the Veraflo helps with pain and better debridement management of these wounds. The other options of acti-VAC/NWPT used would be too painful for some levels of pain, ischemia and would take longer to debride an ulcerated area on the ward setting. The technology difference is just that there is no soak or wash of saline and the foams used are different.

Potential patient benefits

5. What do you consider to be the potential benefits to patients from using this technology?

Expert #1	Reduced dressing changes; reduced need for further surgical debridements; earlier definitive wound reconstructive/closure surgery; reduced hospital stay; reduced risk of recurrent infection.	
Expert #2	Better wound healing through promotion of more healthy granulation tissue, significant reduction of contamination and bacterial count in a shorter period hence more quicker treatment and possibly more cost effective on the longer run	
Expert #3	Faster healing times, less infection (especially anaerobic growth, which can occur in deep wounds and under long term TNP use); exudate management	
Expert #4	Quicker rates of healing. Reducing infection in a chronic wound. Faster granulation. Reduced the size of the wound which has resulted in our department reducing the severity of the surgical procedure.	
Expert #5	Reduced bed stay, and preventing multiple washout procedures in theatre	
Expert #6	1. Pain management The benefit of the Veraflo is areas of difficult debridement on the foot in the ward setting or if a patint isn't neuropathic and is in pain , so the Veraflo helps with pain and better debridement management of these wounds 2. Better and cleaner debridement of the ulceration bed I feel the Veraflow helps to debride the wound bed quicker and with a quicker growth rate of granulation tissue. However the first couple of sessions of the VeraFlo can actually make it look like its deteriorating. 3. Faster granulation tissue growth The Veraflo cleans up the wound bed faster and granulation growth appears quicker, therefore aiding earlier discharge, less time non-weight bearing and quicker healing rates.	

	Negatives 1. Not great on patients with poor renal and diabetic health. Often the fluid has caused deterioration to the foot and resulted in further debridement. 2. Needs skilled and experience use/monitoring of the fluid entering the wash/soak and effect on the wound bed as too much fluid can cause deterioration to surrounding skin if not managed correctly. 3. Time: it can be a lengthily first assessment and application of the system, especially if there are a large, difficult areas or multiple foot ulcerations.	

6. Are there any groups of people who would particularly benefit from this technology?

Expert #1	Any acute soft tissue infections requiring surgical debridement. Largest single group is probably diabetic foot infections. There is also potential benefit for patients with a wound infection involving a prosthetic implant
Expert #2	Complex infected wounds especially in septic patients
Expert #3	Patients with challenging, non-healing wounds
Expert #4	Pressure Ulcer Wound breakdown following surgery Pre-operative wound bed preparation
Expert #5	General surgeons, Orthopaedic surgeons, Plastic surgeons
Expert #6	1. Diabetic foot amputations: Normally beneficial on diabetic foot amputation sites especially if blood flow is good. This helps debride and granulate quickly. 2. Large amputation sites : Trans-metatarsal Amputation sites – Any area bigger than 5-6cm by 5-6cm, I feel a Veraflo has a significant input in helping the ulcer site improve compared with basic dressings, especially if its difficult to debride.

	3. Patients who struggle with pain ; Painful Neuropathy, ischemia (but use of the veraflo should be on patients with a blood flow that will aid healing, often applied post angio/bypass) I would be very careful with use on patients with poor small vessel disease (renal, vascular and diabetic patients) as it can often macerate the wound bed too much (even on low soaks – but again, that needs editing with human skill – its not AI based – the machine isn't able to tell that less fluid is required)

7. Does this technology have the potential to change the current pathway or clinical outcomes? Could it lead, for example, to improved outcomes, fewer hospital visits or less invasive treatment?

Expert #1	It could lead to: shortened hospital stays; reduced number of surgical interventions, fewer hospital visits if wound can be closed (e.g. by split skin graft, dermal matrix, plastic surgery flaps).
Expert #2	Yes, this instillation technology provides an additional dimension to negative pressure wound therapy with the ability to deliver a solution to the wound in a programmed manner. From our observational practice we have witnessed enhancement in the management of complex infected wound with subsequent improvement of patient care and outcomes with decrease length of hospital stay.
Expert #3	Yes. Current thinking amongst wound clinicians is to treat wounds aggressively at the right beginning, to prevent wounds from becoming chronic.
Expert #4	Yes improved length of stay if used appropriately Potential use in pressure ulcer patients with careful consideration In our department we have found that we have changed our operative plan due to the quicker and improved outcome of healing such as going from a free flap to a local flap. Patients wounds may heal quicker which will also reduce the number of long term dressing changes
Expert #5	Without a doubt
Expert #6	Current Pathway: As each patient is very different, each patient needs an assessment and often MDT input and this is where the Veraflo is often agreed or implemented as treatment.

	It would be a complex algorithm/pathway to set to decide who/when to use the VeraFlo, but it could be done. Currently it is based on experience, ability to use it and within a MDT agreement. I do feel if a pathway was made to incorporate set use of this, then it must include the assessment from a Podiatrist/MDT setting as the complexity of some renal patients do not fare well with Veraflo and some hidden underlying infections would only be picked up by podiatrists as they are assessing the wounds and are more invasive in the assessment that other MDT medical members. Clinical Outcomes; Yes, again on the right patients this would improve clinical outcomes ; better healing rates, quicker granulation and therefore earlier discharge, earlier healing so less returns to Outpatients and less risk of infection if it heals quicker. VeraFlo normally follows quite invasive treatment, large debridement of heel ulcerations, transmet amputations or at least 2 toe amputations. It is rarely used on one toe amputation sites unless it included a metatarsal or large opening down the foot. So I don't feel it would stop less invasive treatment per se, but could limit risk of further amputation/ leg amputation – If used correctly and managed correctly.

Potential system impact

8. What do you consider to be the potential benefits to the health or care system from using this technology?

Expert #1	Has potential to: shorten hospital stay; reduce risk of complex wounds being discharged for management in the community; reduced risk of recurrent infection. However it is currently only available as an inpatient treatment (certainly in our trust) and therefore conversely may increase inpatient stay compared to discharge home with standard negative pressure wound therapy.
Expert #2	Overall enhancement and Improvement management of complex infected wounds with more predictable outcomes,
Expert #3	Reduced healing times; reduction of SSI; reduction in antibiotic prescribing; reducing staff time spent on wound care. Higher patient satisfaction
Expert #4	Speed up the rate of healing

	Speed up the time a patients wound in preparation for surgery e.g at times patients can be on long term wound regimes and often patients may not go back to theatre until the 'wound is ready' This can often delay a patients recovery as traditional wound care options are not as aggressive in cleaning and improving granulation. Reduced length of stay due to quicker healing, less rates of infections therefore a reduction in use of antibiotics.
Expert #5	Faster healing times, reduced bed stay in hospital and reduced visits to theatre
Expert #6	1. Faster healing rates; Less risk of new infection, less risk of further surgical debridement required – therefore cost saving to not requiring surgical time/consultant time. 2. Faster healing rates: Quicker healing rates for the patient, so has a positive effect on their mental and physical health. 3. Dressing change is 2 x week – This is 24/7, so less dressing changes in the long term for ward staff (in comparison to people who require daily/alternate day redressing's).

9. Considering the care pathway as a whole, including initial capital and possible future costs avoided, is the technology likely to cost more or less than current standard care, or about the same?

Expert #1	There is potential for savings if wound closure and healing occurs more quickly, both form nursing care time for dressings, but also reduced risk of recurrent wound infections with associated antibiotic costs, and potentially readmission costs. I don't feel the evidence is currently available to confidently answer this question either way.
Expert #2	On the longer run yes
Expert #3	It depends on the TNP system in place in acute organisation. For us: we invested heavily in VAC technology, bought a number of pumps over the years. The pumps can be used for simple TNP therapy or Veraflow. The only difference is in the consumables (the main dressing)
Expert #4	The system does cost more on paper, but anecdotally in my experience I have found that the number of trips back to theatre are less and the time in theatre is reduced so the cost does balance out in the long run. It currently is only available within an acute setting which I feel needs to be re-evaluated as I feel this is also a therapy that could be managed in a community setting. I am aware that there are some community areas that have started to use it.

Expert #5	The dressings are more costly than the conventional dressings but the costs are outweighed by the benefits. Because it has a two fold benefit, it is capable of cleansing a wound bed and stimulates healing approx. 40% faster than other forms of negative wound healing products.
Expert #6	Cost less (in my opinion)

10. What do you consider to be the resource impact from adopting this technology? Could it, for example, change the number or type of staff needed, the need for other equipment, or effect a shift in the care setting such as from inpatient to outpatient, or secondary to primary care?

Expert #1	It would allow earlier transition of patients from inpatient to outpatient care, and potentially reduce the outpatient wound care burden if healing occurs more quickly.
Expert #2	The technology requires training for staff to be familiar with dressing application and the use of the V.A.C. ULTA machine. Currently it is mainly used as inpatient setting which could have an impact on patient discharge. Therefore more efforts are required to establish community and outpatient care for patients having their treatment to facilitate wider use and also provide more cost effective service (e.g initial treatment in tertiary or secondary setting then shifting to primary or community care once deemed possible)
Expert #3	This product is for acute care only (initially). It is for wounds that are significant and required added technology. The pump is not very portable and would be probably unsuitable for community use (heavy to carry from one room to the other – in acute care, it is placed on a drip stand with wheels on); risk of trips and falls. Also if the dressing leaks, it relies on staff being trained and at hand 24/7 to patch or redress.
Expert #4	There may be an clinical work load impact within current wound care services if the therapy is advocated more frequently. I feel that some patients could be transferred into a community setting for this treatment to free acute beds
Expert #5	It reduces nursing time on multiple dressing applications for infected wound, reduces hours spent in theatres and gets patient home faster.
Expert #6	1. Time : The time it takes to apply a Veraflo is longer that normal VAC/dressings but in the long term its less work in the week.

	2. Skill level : Assessment of the wound bed in changes would need to be highly skilled to assess it hadn't deteriorated or was increasing infection risk. 3. Verflo is mainly used in inpatients, so if more machines were used for inpatients, more podiatrists would be needed on the ward. It wouldn't shift care from outpatients to inpatients due to how we are paid for our care in both settings. 4. If the technology was to spread to an OP setting it would still need to be within a high risk foot clinic, tier 4 hospital setting as appointment time would need to be longer 5. Equipment/Dressings resource – These would be an issue, in regards to ordering them in from GPS. We do not offer this level of treatment in OP setting due to cost / budgets. The community have to pay for the treatment and we can apply/treat. It is very difficult to also order the dressings in the community/Outpatient setting as they come from a GP budget.

11. Are any changes to facilities or infrastructure, or any specific training needed in order to use the technology?

Expert #1	Health care professionals require training in application and troubleshooting the device. No changes in infrastructure would be required.
Expert #2	Not really, just the provision of the machines, regular training of staff, regular audits on outcomes Provision of local guidelines/helpline for troubleshooting
Expert #3	Not if TNP is currently used; however it may cause additional costs to those Trust who do not currently use VAC (KCI brand of TNP).
Expert #4	Staff within wound care are often trained to use traditional VAC dressings. This therapy would require staff to be trained prior to its use and be signed off as competent. Our training was only a few hours.
Expert #5	The application of the dressings are the same, but the clinician only needs to be shown how to set up the initial fluid mechanism
Expert #6	Specific training would be required on the machinery, dressing types, uses, contra-indicators

12. Are you aware of any safety concerns or regulatory issues surrounding this technology?

Expert #1	No.
Expert #2	Not that I am aware of, however all devices should be up to the required standard and they are all usually checked by the local hospital authority
Expert #3	none
Expert #4	no
Expert #5	None other than the normal protocol for application of negative wound closure
Expert #6	Safety concern – human error but also human skill needed to ensure correct fluid amount is in the dressing for soaks/washes. Trial and error to get it right and maybe there should be more research – evidence based data to support this.

General advice

13. Please add any further comments on your particular experiences or knowledge of the technology, or experiences within your organisation.

Expert #1	We have observed good results in healing and/or earlier surgical closure of complex infected diabetic foot wounds post-surgical debridement, including at least one limb that was likely to require amputation using standard care pathways. However, I do not have any audit data to hand to be more specific.
Expert #2	From my prospective It has been a game changer in management of septic patients with complex infected wound (e.g necrotizing fasciitis perineum and trunk, chronic intrathoracic empyema and infected breast implants). Notably has been a valuable addition in the armamentarium of management of these patients.
Expert #3	See above.

Expert #4	Our experience has been positive. We are experienced using this therapy for many different types of wounds such as pressure ulcers, pre-op preparation, surgical wound breakdown and joint ortho-plastics cases.
Expert #5	Our main stumbling block is reluctance of clinical staff to use it because it looks more complicated than the “traditional” machine.
Expert #6	Helpful to do a 30 second soak on first application to ensure enough fluid goes in and cover s the sponge – check that it all goes dark when it drains, as this is an indicator that fluid is everywhere. Helpful to soak the sponge prior to application if possible with sterile technique, otherwise ensure once fluid level is good, do a 5 min soak to check all seals work. On heal areas – ensure significant amount of drape is all over the dressing area and surrounding the sponge/wound bed by at least 2 inches. In situations where there are toes – cut semi-circle half-moon shaped crescents into drape to place around toes to stop crease in the drape and use tegaderm or something that it can bind to when close to a toe, as there’s no chance you’ll get a 2 inch spread around the ulcer in those places. Painful wounds / large areas use the foam with holes in first. Layer this if the ulcer/wound bed is deep (even if not – don’t forget to place full foam over the hole foam) . Normally 3 changes of the hole foam is fine and then onto the normal grey foam.

Other considerations

14. Approximately how many people each year would be eligible for intervention with this technology, either as an estimated number, or a proportion of the target population?

Expert #1	This would vary according to indication and current institutional pathways. In our institution approximately 10-15% of diabetic foot wounds requiring debridement would be considered for this technology.
Expert #2	Despite it is difficult to quantify the usage however I believe that in a tertiary referral hospital it can vary between 50- 100 cases covering necrotizing fasciitis in general, colorectal, gynaecology and urology surgery, orthopaedic, thoracic, trauma patients.

Expert #3	We use traditional TNP delivered via VAC (KCl) on over 500 patients per year. At a very rough estimate 10% would be suitable for VeraFlow.
Expert #4	Difficult to assess for each sub-speciality. I believe standardised care pathways should be developed locally for each trust, otherwise there may be a risk of unnecessary over use which would have a cost implication. I am un happy to estimate
Expert #5	Year on year we are using it more and more as the consultants become aware of the benfits. Out of 240 patients using vacuum assisted closure last year 62 were on the Veraflo
Expert #6	80% of our diabetic foot ulcers/amputaions 50-60% of our renal diabetic foot ulcerations/amputations. This could be higher if there was more skilled staff / podiatrists to review. This % woiuld drop to 30 -40 if they were ischemic + diabetic/renal and with small vessel disease it would also be around 30-40% (again could be higher depending on the reviews and skill level assessing / reviewing this)

15. Would this technology replace or be an addition to the current standard of care?

Expert #1	An addition to standard care
Expert #2	It would be considered the next generation of standard VAC therapy and potentially a reasonable percent of these patients would have their treatment shifted to instillation negative wound therapy.
Expert #3	Addition to current technology
Expert #4	It would be an adjunct to care, and sit with the negative pressure family of products. At times it has replaced the need for surgical input but this is on an individual patient assessment basis.
Expert #5	An addition to current
Expert #6	Addition to current standard but could become best practice to use it first if research and support was available

16. Are there any issues with the usability or practical aspects of the technology?

Expert #1	No, in suitably trained health care professionals. Currently used as an inpatient treatment as the pump with instillation solution pump has limited portability and changing of the solution in the community would be labour intensive.
Expert #2	The provision of outpatient and community run pathways to facilitate patient early patient discharge. This will have a great impact of the feasibility of offering this technology to the majority of patients as it is superior to the standard VAC therapy
Expert #3	Only that the wounds suitable for this therapy need to be selected carefully, namely, a seal needs to be obtained, otherwise the machine leaks.
Expert #4	No
Expert #5	The pump is larger and therefore has to be on a drip stand.
Expert #6	Usability : difficult for patients to carry around. Difficult for some staff who aren't used to technology to use the screens and settings. Practical : Quite big and heavy. Fine for resting on the end of the bed, but if the patient is mobile or needs to be mobile – it can hinder this factor.

17. Are you aware of any issues which would prevent (or have prevented) this technology being adopted in your organisation or across the wider NHS?

Expert #1	Please see answer to question 16.
Expert #2	Not that I am aware off
Expert #3	Costs if Trusts are not using TNP via VAC (KCI) and knowledge if staff are not familiar with VAC (KCI)
Expert #4	Attitudes of staff to change practice. Initial anxiety about learning to use an new piece of equipment. It costs more than traditional VAC so cost may be an issue for some trusts, however our procurement have been involved .

Expert #5	Fear of new things!
Expert #6	Cost, training, need for the use of it.

18. Are you aware of any further evidence for the technology that is not included in this briefing?

Expert #1	No.
Expert #2	No
Expert #3	No
Expert #4	No
Expert #5	No
Expert #6	No

19. Are you aware of any further ongoing research or locally collected data (e.g. audit) on this technology? Please indicate if you would be able/willing to share this data with NICE. Any information you provide will be considered in confidence within the NICE process and will not be shared or published.

Expert #1	No. NIHR HTA have funded a trial of standard NPWT vs standard care for surgical wounds left to heal by secondary intention (SWISHI2, CI Professor Ian Chetter, Hull), but I am not aware of any planned trials on instillation NPWT..
Expert #2	We are auditing the outcomes of the use of negative pressure wound therapy instillation on management of infected breast implants and its effect on salvage rates in this cohort of patients There is a publication which will be available in the press next month ***(Negative Pressure Wound Therapy Instillation for management of intrathoracic chronic infection)***, I am willing to send a draft of this article ahead of publication in the PRS Global open Journal if that would be helpful
Expert #3	No – only our experience, which I have shared.

	n/a
Expert #4	No
Expert #5	Nothing that I am aware of
Expert #6	No

20. Is there any research that you feel would be needed to address uncertainties in the evidence base?

Expert #1	The NHS is not set-up to support repeated surgical debridment every 48hrs to negative microbiology, as has been used in trials described in this briefing. Therefore a trial comparing use to standard care within the NHS, including health economic evaluation, would be useful. Use in non-surgically debrided wound (either chronic wounds or infected wounds as an adjunct to antibiotics) also needs exploration
Expert #2	Possibly outcome differences between using different antimicrobial agents when compared with standard saline instillation.
Expert #3	Standard care is not defined clearly enough in your first draft. Standard VAC need to be included.
Expert #4	Maybe further research into it's role of pressure ulcers.
Expert #5	None that I know about
Expert #6	More research in the fluid soaks / 'washing' of the ulcerations – audit times/amount of sessions with size of ulcerations, along with healing rates. This verse the normal VAC.

External Assessment Centre correspondence log

MT471 VAC Veraflo

The purpose of this log is to show where the External Assessment Centre relied in their assessment of the topic on information or evidence not included in the company's original submission. This is normally where the External Assessment Centre:

a) become aware of additional relevant evidence not submitted by the company;
b) needs to check "real world" assumptions with NICE's expert advisers, or;
c) needs to ask the company for additional information or data not included in the original submission, or;
d) needs to correspond with an organisation or individual outside of NICE

These events are recorded in the table to ensure that all information relevant to the assessment of the topic is captured. The table is shared with the NICE medical technologies advisory committee (MTAC) as part of the committee documentation, and is published on the NICE website at public consultation.

#	Date	Who / Purpose	Question/request	Response received
1.	18/03/2020	Questions sent to Company in advance of planned call on 19/03/2020. Call was subsequently cancelled and queries addressed via email		Appendix 2 – Questions and responses from Company Also, file attachments listed in Appendix 1
2.	07/04/2020	Additional questions sent in advance of post-submission call with Company on 08/04/2020	Appendix 3 – additional questions to company sent 07/04/2020	Appendix 4 – response from Company received 14/04/2020. Also, file attachments listed in Appendix 1
3.	08/04/2020	NICE EAC Company call	Appendix 5 – Notes from NICE EAC Company call 08/04/2020	

4.	15/04/2020	Additional questions on economic model sent to Company		Appendix 6 – additional questions to company and responses received 17/04/2020
5.	22/04/2020	Questions sent to 6 expert advisers	Appendix 7	2 of the expert advisers responded, 4 were unable to do so due to COVID 19 pandemic. Questions were re-sent to these 4 on 01/07/2020. Collated responses to EAQs and additional EAC questions Appendix 8
6.	08/07/2020	Email to Paul Kim, author of newly published RCT *The impact of negative-pressure wound therapy with instillation on wounds requiring operative debridement: Pilot randomised, controlled trial* (Kim et al., 2020) to request LoS data	Dear Dr Kim Allow me to introduce myself. My name is Iain Willits and I am currently working on a Health Technology Assessment (HTA) on the VAC VeraFlo technology, for the National Institute for Health and Care Excellence (NICE) here in the UK. We note with interest the recent publication of your study, The impact of negative-pressure wound therapy with instillation on wounds requiring operative debridement: Pilot randomised, controlled trial. In our opinion, this probably represents the most robust evidence of the technology to date, and its publication has been timely and helpful. Part of the HTA concerns an economic evaluation and a key input into the model we are using is the length of stay (LoS) in hospital, which we have struggled to get reliable data for. We notice in the RCT that LoS was reported in subgroup analysis for dehisced wounds, and therefore we assume it is likely that data was collected for the cohort overall? If so, and if you could share these data, that would be greatly appreciated. It would be necessary to present these data in front of a committee (MTAC), but otherwise we could redact it so it was not available publically, if this helps.	Dr. Willits Thank you for your email. Yes, the subanalysis of the surgically dehisced wound category group was reported be significantly less in length of hospitalization for the veraflo group versus the standard NPWT group. The analysis of the entire ITT group did not show a significant difference in the length of hospitalization between the veraflo and the traditional NPWT group. I think this reflects wholly on the nonstandarized method of determining hospitalization length. In other words, due to the multi center nature of this study, individual practice patterns dictated length of hospitalization rather than any effect of Veraflo. This is also the case for the number of operations which is also impacted by access to the OR at each investigative site as well as the differing surgical techniques and aggressiveness of the surgeons on excisions debridement. As an aside the surgical dehisced cohort also showed decrease number of operations in favor of veraflo. I think this reflects a more straightforward treatment pathway for these patients, unlike those in other wound categories (e.g. diabetic ulcers).

			Please let me know if you can help us on this matter. Kind regards Iain	I have attached 3 papers published out of Georgetown University Hospital, my former employer, which all consistently report a decrease in length of hospitalization for Veraflo vs standard NPWT. This data reflects a very regimented assessment and treatment algorythm at this institution. Therefore, the confounders reported in the multi center RCT had minimal impact. Further, the service is led by Christopher E Attinger, MD (Plastic Surgeon, Division chief) who also trained all the surgeons that participated in the Georgetown studies. Thus technique was very similar. I hope that helps, please let me know if you require any further information. Paul J Kim, DPM, MS Professor Dept of Plastic Surgery Dept of Orthopedic Surgery University of Texas Southwestern Medical Director Wound Program University of Texas Southwestern Medical Center 1801 Inwood Rd Dallas, TX 75390-9132 File attachments listed in Appendix 1
7.				

8.				

Insert more rows as necessary

Appendix 1

During correspondence with the company and experts, additional information is sometimes included as file attachments, graphics and tables. Any questions that included additional information of this kind is added below in relation to the relevant question/answer:

External Assessment Centre correspondence log

MT471 VAC Veraflo

The purpose of this log is to show where the External Assessment Centre relied in their assessment of the topic on information or evidence not included in the company's original submission. This is normally where the External Assessment Centre:

a) become aware of additional relevant evidence not submitted by the company;
b) needs to check "real world" assumptions with NICE's expert advisers, or;
c) needs to ask the company for additional information or data not included in the original submission, or;
d) needs to correspond with an organisation or individual outside of NICE

These events are recorded in the table to ensure that all information relevant to the assessment of the topic is captured. The table is shared with the NICE medical technologies advisory committee (MTAC) as part of the committee documentation, and is published on the NICE website at public consultation.

#	Date	Who / Purpose	Question/request	Response received
1.	18/03/2020	Questions sent to Company in advance of planned call on 19/03/2020. Call was subsequently cancelled and queries addressed via email		Appendix 2 – Questions and responses from Company Also, file attachments listed in Appendix 1
2.	07/04/2020	Additional questions sent in advance of post-submission call with Company on 08/04/2020	Appendix 3 – additional questions to company sent 07/04/2020	Appendix 4 – response from Company received 14/04/2020. Also, file attachments listed in Appendix 1
3.	08/04/2020	NICE EAC Company call	Appendix 5 – Notes from NICE EAC Company call 08/04/2020	

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Insert more rows as necessary

Appendix 1

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Acelity™

V.A.C.ULTA™ NEGATIVE PRESSURE WOUND THERAPY SYSTEM (V.A.C.ULTA™ THERAPY SYSTEM)

SAFETY INFORMATION

ONLY FOR USE WITH THE KCI V.A.C.ULTA™ THERAPY SYSTEM

Rx Only

TABLE OF CONTENTS

IMPORTANT INFORMATION FOR USERS

The V.A.C.ULTA™ Negative Pressure Wound Therapy System (V.A.C.ULTA™ Therapy System) is an integrated wound therapy system that can be used for:

- **V.A.C. VERAFLO™ Therapy** (Instillation), which consists of negative pressure wound therapy (**V.A.C.® Therapy**) coupled with controlled delivery and drainage of topical wound irrigation treatment solutions and suspensions over the wound bed.

OR

- **V.A.C.® Therapy,** which consists of negative pressure wound therapy alone.

When using V.A.C. VERAFLO™ Therapy (Instillation), there are important **Contraindications**, **Warnings**, and **Precautions** that should be considered in addition to the **Contraindications**, **Warnings** and **Precautions** for V.A.C.® Therapy. **Contraindications**, **Warnings** and **Precautions** specific to V.A.C. VERAFLO™ Therapy are highlighted in grey throughout the document and are identified by the V.A.C. VERAFLO™ Therapy symbol to the left of the text. When using V.A.C.® Therapy alone, the V.A.C. VERAFLO™ Therapy **Contraindications**, **Warnings** and **Precautions** are not applicable.

IMPORTANT: As with any prescription medical device, failure to consult a physician and carefully read and follow all safety information and application instructions provided with the therapy unit and dressing cartons prior to use may lead to improper product performance and the potential for serious or fatal injury. Do not adjust therapy unit settings or perform therapy application without directions from / or supervision by the clinical caregiver.

DRESSING SYSTEMS FOR USE WITH V.A.C.ULTA™ THERAPY UNIT

V.A.C.® Therapy can be used with any of the following dressings:

- V.A.C.® GRANUFOAM™ Dressings
- V.A.C.® GRANUFOAM SILVER™ Dressings
- V.A.C. WHITEFOAM™ Dressings
- PREVENA™ Incision Management Dressings
- ABTHERA™ SENSAT.R.A.C.™ Open Abdomen Dressings
- KCI™ Negative Pressure Wound Therapy Gauze Dressing

V.A.C. VERAFLO™ Therapy should be delivered with V.A.C. VERAFLO™ or V.A.C. VERAFLO CLEANSE™ Dressings.

PRODUCTS NOT INTENDED FOR USE WITH V.A.C. VERAFLO™ THERAPY (INSTILLATION)

- Cellular or accellular bioengineered tissues.
- V.A.C.® GRANUFOAM SILVER™ Dressings
- PREVENA™ Incision Management Dressings
- The ABTHERA™ SENSAT.R.A.C.™ Open Abdomen Dressing
- KCI™ Negative Pressure Wound Therapy Gauze Dressing

Refer to the additional warnings and precautions for V.A.C. VERAFLO™ Therapy.

INDICATIONS FOR USE

The V.A.C.ULTA™ Negative Pressure Wound Therapy System is an integrated wound management system that provides Negative Pressure Wound Therapy with an instillation option.

- Negative Pressure Wound Therapy in the absence of instillation 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 instillation option is indicated for patients who would benefit from vacuum assisted drainage and controlled delivery of topical wound treatment solutions and suspensions over the wound bed.

The V.A.C.ULTA™ Negative Pressure Wound Therapy System with and without instillation is indicated for patients with chronic, acute, traumatic, sub-acute and dehisced wounds, partial-thickness burns, ulcers (such as diabetic, pressure and venous insufficiency), flaps and grafts.

- Negative Pressure Wound Therapy in the absence of instillation may also be used for:
  - The temporary bridging of abdominal wall openings where primary closure is not possible and/or repeat abdominal entries are necessary and for open abdominal wounds with exposed viscera including, but not limited to, abdominal compartment syndrome. The intended care setting is a closely monitored area within the acute care hospital, such as the ICU. The abdominal dressing will most often be applied in the operating theater.
- The management of the environment of closed surgical incisions and surrounding intact skin in patients at risk for developing post-operative complications, such as infection, by maintaining a closed environment via the application of a negative pressure wound therapy system to the incision. The PREVENA™ Incision Dressing skin interface layer with silver reduces microbial colonization in the fabric.

TRANSITIONING V.A.C.® THERAPY INTO HOME CARE

- **The V.A.C.ULTA™ Therapy System is not intended for home use*.**
- **If there is a need to continue V.A.C.® Therapy when a patient transitions home, consider using one of the KCI Therapy Systems approved for the post-acute environment, such as:**
  - **PREVENA™ 125 Therapy Unit**
  - **PREVENA PLUS™ 125 Therapy Unit**
  - **ACTIV.A.C.™ Therapy Unit**
  - **V.A.C. FREEDOM™ Therapy Unit**
  - **V.A.C. SIMPLICITY™ Unit**
  - **V.A.C.VIA™ Therapy System**

Refer to the safety information included with those devices for important information.

V.A.C.ULTA™ THERAPY SYSTEM CONTRAINDICATIONS

- Do not place foam dressings of the V.A.C.ULTA™ Therapy System (including both V.A.C.® Therapy and V.A.C. VERAFLO™ Therapy Dressings) directly in contact with exposed blood vessels, anastomotic sites, organs or nerves.

  NOTE: *Refer to **Warnings** section for additional information concerning Bleeding.*

- V.A.C.® Therapy and V.A.C. VERAFLO™ Therapy are contraindicated for patients with:
  - Malignancy in the wound
  - Untreated osteomyelitis

    NOTE: *Refer to **Warnings** section for Osteomyelitis information.*
  - Non-enteric and unexplored fistulas
  - Necrotic tissue with eschar present

    NOTE: *After debridement of necrotic tissue and complete removal of eschar, V.A.C.® Therapy may be used.*
  - Sensitivity to silver (V.A.C.® GRANUFOAM SILVER™ Dressing and PREVENA™ Incision Management Dressings only)

* In France, the V.A.C.ULTA™ Therapy System (P/N HCULTDEV01/FR) may be used in the HAD Healthcare System.

ADDITIONAL CONTRAINDICATIONS SPECIFIC TO V.A.C. VERAFLO™ THERAPY

- Do not use V.A.C.® Dressings with Octenisept®*, hydrogen peroxide or solutions that are alcohol-based or contain alcohol.
- Do not deliver fluids to the thoracic or abdominal cavity due to the potential risk to alter core body temperature and the potential for fluid retention within the cavity.
- Do not use V.A.C. VERAFLO™ Therapy unless the wound has been thoroughly explored due to the potential for inadvertent instillation of topical wound solutions to adjacent body cavities.

*Not available in the United States. Brand name referenced is not a trademark of KCI, its affiliates and / or licensors.

V.A.C.ULTA™ THERAPY SYSTEM WARNINGS

Bleeding: With or without using V.A.C.® Therapy or V.A.C. VERAFLO™ Therapy, certain patients are at high risk of bleeding complications. The following types of patients are at increased risk of bleeding, which, if uncontrolled, could be potentially fatal.

- Patients who have weakened or friable blood vessels or organs in or around the wound as a result of, but not limited to:
  - Suturing of the blood vessel (native anastamoses or grafts) / organ
  - Infection
  - Trauma
  - Radiation
- Patients without adequate wound hemostasis
- Patients who have been administered anticoagulants or platelet aggregation inhibitors
- Patients who do not have adequate tissue coverage over vascular structures.

If V.A.C.® Therapy or V.A.C. VERAFLO™ Therapy is prescribed for patients who have an increased risk of bleeding complications, they should be treated and monitored in a care setting deemed appropriate by the treating physician.

If active bleeding develops suddenly or in large amounts during V.A.C.® Therapy or V.A.C. VERAFLO™ Therapy, or if frank (bright red) blood is seen in the tubing or in the canister, immediately stop therapy, leave dressing in place, take measures to stop the bleeding, and seek immediate medical assistance. The V.A.C.ULTA™ Therapy Unit and dressings (both V.A.C.® Therapy and V.A.C. VERAFLO™ Therapy) should not be used to prevent, minimize or stop vascular bleeding.

- **Protect Vessels and Organs:** All exposed or superficial vessels and organs in or around the wound must be completely covered and protected prior to the administration of V.A.C.® Therapy or V.A.C. VERAFLO™ Therapy.

  Always ensure that V.A.C.® Foam Dressings and V.A.C. VERAFLO™ Foam Dressings do not come in direct contact with vessels or organs. Use of a thick layer of natural tissue should provide the most effective protection. If a thick layer of natural tissue is not available or is not surgically possible, multiple layers of fine-meshed, non-adherent material may be considered as an alternative, if deemed by the treating physician to provide a complete protective barrier. If using non-adherent materials, ensure that they are secured in a manner as to maintain their protective position throughout therapy.

  Consideration should also be given to the negative pressure setting and therapy mode used when initiating therapy.

  Caution should be taken when treating large wounds that may contain hidden vessels, which may not be readily apparent. The patient should be closely monitored for bleeding in a care setting deemed appropriate by the treating physician.

- **Infected Blood Vessels:** Infection may erode blood vessels and weaken the vascular wall which may increase susceptibility to vessel damage through abrasion or manipulation. **Infected blood vessels are at risk of complications, including bleeding, which, if uncontrolled, could be potentially fatal. Extreme caution should be used when V.A.C.® Therapy or V.A.C. VERAFLO™ Therapy is applied in close proximity to infected or potentially infected blood vessels.** (Refer to **Protect Vessels and Organs** section.)

- **Hemostasis, Anticoagulants and Platelet Aggregation Inhibitors:** Patients without adequate wound hemostasis have an increased risk of bleeding, which, if uncontrolled, could be potentially fatal. These patients should be treated and monitored in a care setting deemed appropriate by the treating physician.

  Caution should be used in treating patients on doses of anticoagulants or platelet aggregation inhibitors thought to increase their risk for bleeding (relative to the type and complexity of the wound). Consideration should be given to the negative pressure setting and therapy mode used when initiating therapy.

- **Hemostatic Agents Applied at the Wound Site:** Non-sutured hemostatic agents (for example, bone wax, absorbable gelatin sponge or spray wound sealant) may, if disrupted, increase the risk of bleeding, which, if uncontrolled, could be potentially fatal. Protect against dislodging such agents. Consideration should be given to the negative pressure setting and therapy mode used when initiating therapy. (Refer to **Additional Warnings for V.A.C. VERAFLO™ Therapy** section).

- **Sharp Edges:** Bone fragments or sharp edges could puncture protective barriers, vessels or organs causing injury. Any injury could cause bleeding, which, if uncontrolled, could be potentially fatal. Beware of possible shifting in the relative position of tissues, vessels or organs within the wound that might increase the possibility of contact with sharp edges. Sharp edges or bone fragments must be eliminated from the wound area or covered to prevent them from puncturing blood vessels or organs before the application of V.A.C.® Therapy or V.A.C. VERAFLO™ Therapy. Where possible, completely smooth and cover any residual edges to decrease the risk of serious or fatal injury, should shifting of structures occur. Use caution when removing dressing components from the wound so that wound tissue is not damaged by unprotected sharp edges.

1000 mL Canister: DO NOT USE the 1000 mL canister on patients with a high risk of bleeding or on patients unable to tolerate a large loss of fluid volume, including children and the elderly. Consider the size and weight of the patient, patient condition, wound type, monitoring capability and care setting when using this canister. This canister is recommended for acute care (hospital) use only.

Infected Wounds: Infected wounds should be monitored closely and may require more frequent dressing changes than non-infected wounds, dependent upon factors such as wound conditions, treatment goals and V.A.C. VERAFLO™ Therapy parameters (for the V.A.C.ULTA™ Therapy System). Refer to dressing application instructions (found in V.A.C.® Dressing and V.A.C. VERAFLO™ Dressing cartons) for details regarding dressing change frequency. As with any wound treatment, clinicians and patients / caregivers should frequently monitor the patient's wound, periwound tissue and exudate for signs of infection, worsening infection or other complications. Some signs of infection are fever, tenderness, redness, swelling, itching, rash, increased warmth in the wound or periwound area, purulent discharge or strong odor. Infection can be serious, and can lead to complications such as pain, discomfort, fever, gangrene, toxic shock, septic shock and / or fatal injury. Some signs or complications of systemic infection are nausea, vomiting, diarrhea, headache, dizziness, fainting, sore throat with swelling of the mucus membranes, disorientation, high fever, refractory and / or orthostatic hypotension, or erythroderma (a sunburn-like rash). **If there are any signs of the onset of systemic infection or advancing infection at the wound site, contact a physician immediately to determine if V.A.C.® Therapy or V.A.C. VERAFLO™ Therapy should be discontinued.** For wound infections relating to blood vessels, please also refer to the section titled **Infected Blood Vessels.**

Infected Wounds with V.A.C.® GRANUFOAM SILVER™ Dressing: In the event of clinical infection, V.A.C.® GRANUFOAM SILVER™ Dressing is not intended to replace the use of systemic therapy or other infection treatment regimens. V.A.C.® GRANUFOAM SILVER™ Dressing may be used to provide a barrier to bacterial penetration. Refer to the section titled **Additional Precautions for V.A.C.® GRANUFOAM SILVER™ Dressing**.

Osteomyelitis: V.A.C.® Therapy and V.A.C. VERAFLO™ Therapy should NOT be initiated on a wound with untreated osteomyelitis. Consideration should be given to thorough debridement of all necrotic, non-viable tissue, including infected bone (if necessary), and appropriate antibiotic therapy.

Protect Tendons, Ligaments and Nerves: Tendons, ligaments and nerves should be protected to avoid direct contact with V.A.C.® Foam Dressings or V.A.C. VERAFLO™ Therapy Foam Dressings. These structures may be covered with natural tissue or meshed non-adherent material to help minimize risk of desiccation or injury.

Foam Placement: Always use V.A.C.® Dressings or V.A.C. VERAFLO™ Therapy Dressings from sterile packages that have not been opened or damaged. Do not place any foam dressing into blind / unexplored tunnels. The V.A.C. WHITEFOAM™ Dressing may be more appropriate for use with explored tunnels. The V.A.C. VERAFLO CLEANSE™ Dressing System may be more appropriate for use with explored tunnels when using V.A.C. VERAFLO™ Therapy where robust granulation tissue formation is not desired. Do not force foam dressings into any area of the wound, as this may damage tissue, alter the delivery of negative pressure, or hinder exudate and foam removal. Always count the total number of pieces of foam used in the wound and the dressing change date and document that number on the drape, in the patient's chart and on the foam quantity label attached to the pad tubing (if provided).

Foam Removal: V.A.C.® Foam Dressings and V.A.C. VERAFLO™ Therapy Foam Dressings are not bioabsorbable. **Always count the total number of pieces of foam removed from the wound and ensure the same number of foam pieces was removed as placed.** Foam left in the wound for greater than the recommended time period may foster ingrowth of tissue into the foam, create difficulty in removing foam from the wound, or lead to infection or other adverse events. **If significant bleeding develops, immediately discontinue the use of the V.A.C.ULTA™ Therapy System, take measures to stop the bleeding, and do not remove the foam dressing until the treating physician or surgeon is consulted. Do not resume the use of the V.A.C.® Therapy or V.A.C. VERAFLO™ Therapy until adequate hemostasis has been achieved and the patient is not at risk for continued bleeding.**

Keep V.A.C.® Therapy and V.A.C. VERAFLO™ Therapy On: Never leave a V.A.C.® Dressing or V.A.C. VERAFLO™ Therapy Dressing in place without active V.A.C.® Therapy or V.A.C. VERAFLO™ Therapy for more than two hours. If therapy is off for more than two hours, remove the old dressing and irrigate the wound. Either apply a new V.A.C.® Dressing or V.A.C. VERAFLO™ Therapy Dressing from an unopened sterile package and restart therapy; or apply an alternative dressing at the direction of the treating clinician.

Acrylic Adhesive: The V.A.C.® Drape (supplied with V.A.C.® Dressings) and the V.A.C.® Advanced Drape (supplied with V.A.C. VERAFLO™ Therapy Dressings) have an acrylic adhesive coating, which may present a risk of an adverse reaction in patients who are allergic or hypersensitive to acrylic adhesives. If a patient has a known allergy or hypersensitivity to such adhesives, do not use the V.A.C.ULTA™ Therapy System. If any signs of allergic reaction or hypersensitivity develop, such as redness, swelling, rash, urticaria or significant pruritus, discontinue use and consult a physician immediately. If bronchospasm or more serious signs of allergic reaction appear, seek immediate medical assistance.

Defibrillation: Remove the V.A.C.® Dressing or V.A.C. VERAFLO™ Therapy Dressing if defibrillation is required in the area of dressing placement. Failure to remove the dressing may inhibit transmission of electrical energy and / or patient resuscitation.

Flammable Environment: Equipment not suitable for use in the presence of a flammable anesthetic mixture of air, oxygen, or nitrous oxide, or in an oxygen enriched environment.

Magnetic Resonance Imaging (MRI) – Therapy Unit: The V.A.C.ULTA™ Therapy Unit is **MR Unsafe.** Do not take the V.A.C.ULTA™ Therapy Unit into the MR environment.

Magnetic Resonance Imaging (MRI) – V.A.C.® Dressings: V.A.C.® Dressings and V.A.C. VERAFLO™ Therapy Dressings can typically remain on the patient with minimal risk in an MR environment, assuming that use of the V.A.C.ULTA™ Therapy System is not interrupted for more than two hours (refer to **Keep V.A.C.® Therapy and V.A.C. VERAFLO™ Therapy On** above).

NOTE: *If using V.A.C. VERAFLO™ Therapy ensure that irrigation fluid or treatment solutions are fully removed from the dressing prior to stopping negative pressure wound therapy.*

The V.A.C.® GRANUFOAM SILVER™ Dressing has been shown to pose no known hazards in an MR environment with the following conditions of use:

- Static magnetic field of 3 Tesla or less,
- Spatial gradient field of 720 Gauss / cm or less, and
- Maximum whole-body-averaged specific absorption rate (SAR) of 3 W / kg for 15 minutes of scanning

Non-clinical testing under these same conditions produced a temperature rise of <0.4°C.
MR image quality may be compromised if the area of interest is in the same area or relatively close to the position of the V.A.C.® GRANUFOAM SILVER™ Dressing.

Hyperbaric Oxygen Therapy (HBO): Do not take the V.A.C.ULTA™ Therapy Unit into a hyperbaric oxygen chamber. The V.A.C.ULTA™ Therapy Unit is not designed for this environment and should be considered a fire hazard. After disconnecting the V.A.C.ULTA™ Therapy Unit, either (i) replace the V.A.C.® Dressing or V.A.C. VERAFLO™ Therapy Dressing with another HBO compatible material during the hyperbaric treatment, or (ii) cover the unclamped end of the V.A.C.® Tubing with dry gauze. For HBO therapy, the V.A.C.® Tubing or V.A.C. VERAFLO™ Therapy Tubing must not be clamped. Never leave a V.A.C.® Dressing in place without active V.A.C.® Therapy for more than two hours; please refer to the **Keep V.A.C.® Therapy On** section.

NOTE: *If using V.A.C. VERAFLO™ Therapy ensure that irrigation fluid or treatment solutions are fully removed from the dressing prior to stopping negative pressure wound therapy.*

ADDITIONAL WARNINGS FOR V.A.C. VERAFLO™ THERAPY

Topical Wound Solutions: Topical wound solutions or suspensions may enter internal body cavities if the wound is open to such cavities. They should not be infused into wounds with unexplored tunnels or unexplored undermining as they may enter into unintended cavities.

Pauses in Negative Pressure: Application of V.A.C. VERAFLO™ Therapy will result in pauses of negative pressure wound therapy, which is not recommended on wounds requiring continuous V.A.C.® Therapy. Do not use V.A.C. VERAFLO™ Therapy over unstable structures, such as unstable chest wall or non-intact fascia, on patients at increased risk of bleeding, on flaps, grafts or wounds with acute enteric fistulae.

Bioengineered Tissue: V.A.C. VERAFLO™ Therapy is not intended for use with cellular or accellular bioengineered tissues.

Hemostasis: Patients with difficult or fragile wound hemostasis are at increased risk of bleeding associated with V.A.C. VERAFLO™ Therapy due to the potential for disruption of clots or dilution of clotting factors. Do not use V.A.C. VERAFLO™ Therapy where hemostatic agents have been used in the wound bed.

Closed Surgical Incisions: DO NOT use V.A.C. VERAFLO™ Therapy with PREVENA™ Dressings over closed surgical incisions. Instillation may result in pooling of fluid which may result in maceration.

Open Abdomen: DO NOT use V.A.C. VERAFLO™ Therapy with the ABTHERA™ SENSAT.R.A.C.™ Open Abdomen Dressing over an open abdomen. Potential risks of instillation into the open abdomen include:

- Instillation of fluid in the abdomen without sufficient fluid recovery may lead to abdominal compartment syndrome.
- Instillation of fluids in the abdomen that are untested for safety and efficacy with this application could lead to severe hollow viscus and solid organ damage.
- Instillation of unwarmed fluid in large quantities may lead to hypothermia.

V.A.C.ULTA™ THERAPY SYSTEM PRECAUTIONS

Standard Precautions: To reduce the risk of transmission of bloodborne pathogens, apply standard precautions for infection control with all patients, per institutional protocol, regardless of their diagnosis or presumed infection status. In addition to gloves, use gown and goggles if exposure to body fluids is likely.

Continuous Versus DPC (Dynamic Pressure Control) V.A.C.® Therapy: Continuous V.A.C.® Therapy is recommended over unstable structures, such as an unstable chest wall or non-intact fascia, in order to help minimize movement and stabilize the wound bed. Continuous therapy is also generally recommended for patients at increased risk of bleeding, fresh flaps and grafts, and wounds with acute enteric fistulae.

NOTE: *V.A.C. VERAFLO™ Therapy, due to the controlled delivery of wound irrigation and treatment solutions, provides intermittent V.A.C.® Therapy and is not recommended in the above wound types or conditions.*

Patient Size and Weight: The size and weight of the patient should be considered when prescribing V.A.C.® Therapy or V.A.C. VERAFLO™ Therapy. Infants, children, certain small adults and elderly patients should be closely monitored for fluid loss and dehydration. Also, patients with highly exudating wounds or large wounds in relation to the patient size and weight should be closely monitored, as they have a risk of excessive fluid loss and dehydration. When monitoring fluid output, consider the volume of fluid in both the tubing and canister.

Spinal Cord Injury (SCI): In the event an SCI patient experiences autonomic dysreflexia (sudden changes in blood pressure or heart rate in response to stimulation of the sympathetic nervous system), discontinue V.A.C.® Therapy or V.A.C. VERAFLO™ Therapy to help minimize sensory stimulation and seek immediate medical assistance.

Bradycardia: To minimize the risk of bradycardia, V.A.C.® Therapy and V.A.C. VERAFLO™ Therapy must not be placed in proximity to the vagus nerve.

Enteric Fistulas: Wounds with enteric fistulas require special precautions to optimize V.A.C.® Therapy. Refer to V.A.C.® Therapy Clinical Guidelines for more detail. V.A.C.® Therapy is not recommended if enteric fistula effluent management or containment is the sole goal of therapy.

NOTE: *V.A.C. VERAFLO™ Therapy should not be used in the presence of enteric fistula to prevent wound contamination.*

Protect Periwound Skin: Consider use of a skin preparation product to protect periwound skin. Do not allow foam to overlap onto intact skin. Protect fragile / friable periwound skin with additional V.A.C.® Advanced Drape, skin protectant, hydrocolloid or other transparent film. Multiple layers of the V.A.C.® Advanced Drape may decrease the moisture vapor transmission rate, which may increase the risk of maceration. If any signs of irritation or sensitivity to the drape, foam or tubing assembly appear, discontinue use and consult treating physician. To avoid trauma to the periwound skin, do not pull or stretch the drape over the foam dressing during drape application. Extra caution should be used for patients with neuropathic etiologies or circulatory compromise.

Circumferential Dressing Application: Avoid use of circumferential dressings except in the presence of anasarca or excessively weeping extremities, where a circumferential drape technique may be necessary to establish and maintain a seal. Consider using multiple small pieces of V.A.C.® Advanced Drape rather than one continuous piece to minimize the risk of decreased distal circulation. Extreme care should be taken not to stretch or pull the drape when securing it, but let it attach loosely and stabilize the edges with an elastic wrap, if necessary. When using circumferential drape applications, it is crucial to systematically and recurrently palpate distal pulses, and assess distal circulatory status. If circulatory compromise is suspected, discontinue therapy, remove dressing and contact treating physician.

Pressure Points: Periodically assess and monitor the location of tubing connectors, caps, clamps or other rigid components to ensure they do not create inadvertent pressure points in relation to patient position.

V.A.C.ULTA™ Therapy Unit Pressure Excursions: In rare instances, tubing blockages with the V.A.C.ULTA™ Therapy Unit may result in brief vacuum excursions to more than 250 mmHg negative pressure. Resolve alarm conditions immediately. Refer to the V.A.C.ULTA™ Therapy System User Manual or contact your KCI representative for additional information.

ADDITIONAL PRECAUTIONS FOR V.A.C. VERAFLO™ THERAPY

Suitable Solutions: V.A.C. VERAFLO™ Therapy is intended for use with V.A.C. VERAFLO™ Therapy disposables and topical wound treatment solutions and suspensions. Only use solutions or suspensions that are:

- Indicated for topical wound treatment according to solution manufacturer's instructions for use. Some topical agents may not be intended for extended tissue contact. If in doubt about the appropriateness of using a particular solution for V.A.C. VERAFLO™ Therapy, contact the solution's manufacturer about its suitability for saturated topical wound exposure.
- Compatible with V.A.C.® Dressings and disposable components. Contact your KCI representative for a list of solutions shown to be compatible with V.A.C.® Dressings and disposable components.

  NOTE: *Hypochlorous acid solutions applied frequently at high concentrations can lead to significant material degradation. Consider utilizing concentrations and exposure durations as low as clinically relevant.*

  NOTE: *The V.A.C.® GRANUFOAM SILVER™ Dressing is not intended to be used with V.A.C. VERAFLO™ Therapy because instillation solutions may negatively impact the benefits of the V.A.C.® GRANUFOAM SILVER™ Dressing.*

KCI™ Negative Pressure Wound Therapy Gauze Dressing: The KCI™ Negative Pressure Wound Therapy Gauze Dressing is not intended for use with V.A.C. VERAFLO™ Therapy.

Canister Changes: Monitor fluid level in canisters frequently during use of the V.A.C. VERAFLO™ Therapy. Frequent canister changes may be necessary depending on volume of fluid instilled and wound exudates. At a minimum the canister should be changed weekly and disposed of according to institutional protocol.

ADDITIONAL PRECAUTIONS FOR THE PREVENA™ INCISION MANAGEMENT DRESSING

PREVENA™ Incision Management Dressing: When using the V.A.C.ULTA™ Therapy Unit as the negative pressure source for the PREVENA™ Incision Management Dressings, **refer to the Instructions for Use provided with PREVENA™ Incision Management Dressing for complete safety information, dressing application instructions and the procedure for connection to the V.A.C.ULTA™ Therapy Unit**.

The PREVENA™ Incision Management System is intended to manage the environment of closed surgical incisions and surroundig intact skin in patients at risk for developing post-operative complications such as infection, by maintaining a closed environment via the application of a negative pressure wound therapy system to the incision. The PREVENA™ Incision Dressing skin interface layer with silver reduces microbial colonization in the fabric.

Before transitioning the patient to home care, the V.A.C.ULTA™ Therapy Unit must be replaced with one indicated for home care (refer to **Transitioning V.A.C.® Therapy Into Home Care**).

ADDITIONAL PRECAUTIONS FOR THE ABTHERA™ SENSAT.R.A.C.™ OPEN ABDOMEN DRESSING

ABTHERA™ SENSAT.R.A.C.™ Open Abdomen Dressing: When using the V.A.C.ULTA™ Therapy Unit as the negative pressure source for the ABTHERA™ SENSAT.R.A.C.™ Open Abdomen Dressing, **refer to the Instructions for Use provided with the ABTHERA™ SENSAT.R.A.C.™ Open Abdomen Dressing for complete safety information, dressing application instructions and the procedure for connection to the V.A.C.ULTA™ Therapy Unit**.

The ABTHERA™ SENSAT.R.A.C.™ Open Abdomen Dressing is indicated for temporary bridging of abdominal wall openings where primary closure is not possible and/or repeat abdominal entries are necessary. The intended use of this dressing is in open abdominal wounds with exposed viscera including, but not limited to, abdominal compartment syndrome. The intended care setting is a closely monitored area within the acute care hospital, such as the ICU. The abdominal dressing will most often be applied in the operating theater.

ADDITIONAL PRECAUTIONS FOR V.A.C.® GRANUFOAM SILVER™ DRESSING

When using the V.A.C.ULTA™ Therapy Unit as the negative pressure source for the V.A.C.® GRANUFOAM SILVER™ Dressing, **refer to the Instructions for Use provided with the V.A.C.® GRANUFOAM SILVER™ Dressing for complete safety information and dressing application instructions**.

V.A.C.® GRANUFOAM SILVER™ Dressing may be used in the acute care as well as home settings with a therapy unit indicated for home care (refer to **Transitioning V.A.C.® Therapy Into Home Care**).

ADDITIONAL PRECAUTIONS FOR THE KCI™ NEGATIVE PRESSURE WOUND THERAPY GAUZE DRESSING

When using the V.A.C.ULTA™ Therapy Unit as the negative pressure source for the KCI™ NPWT Gauze Dressing, refer to the Instructions for Use provided with the KCI™ NPWT Gauze Dressing for complete safety information and dressing application instructions.

The KCI™ NPWT Gauze Dressing is not intended for use with V.A.C. VERAFLO™ Therapy.

Before transitioning the patient to home care, the V.A.C.ULTA™ Therapy Unit must be replaced with one indicated for home care (refer to **Transitioning V.A.C.® Therapy Into Home Care**).

Additional warnings and precautions apply to certain V.A.C.® specialty dressings and V.A.C.® Therapy Units. Please refer to the specific product instructions for use prior to use.

If there are any questions regarding the proper placement or usage of V.A.C.® Therapy, please refer to the V.A.C.® Therapy Clinical Guidelines for more detailed instructions or contact your local KCI representative. For additional and most current information, please see KCI's website at www.acelity.com (US) or www.kci-medical.com (OUS).

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CE 0086

KCI USA, Inc.
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San Antonio, TX 78249 USA
1-800-275-4524
www.acelity.com

KCI™
An Acelity Company

V.A.C.ULTA™ THERAPY SYSTEM

USER MANUAL

For Clinicians

Do not discard. Please retain this user manual for future reference. For additional copies, in the US, visit www.acelity.com, www.veraflo.com and www.vaculta.com or contact KCI at 1-800-275-4524. Outside the US, visit www.kci-medical.com.

Acelity™

Rx Only

Important Safety Information Accompanies This Device

Indications, Contraindications, Warnings, Precautions and other Safety Information are contained in the V.A.C.ULTA™ Negative Pressure Wound Therapy System (V.A.C.ULTA™ Therapy System) Safety Information. This safety information booklet is provided with the therapy unit and also included in V.A.C. VERAFLO™ Dressing cartons. Please consult this V.A.C.ULTA™ Therapy System User Manual and the safety information before applying **V.A.C.® Therapy** or **V.A.C. VERAFLO™ Therapy**. Before applying **PREVENA™ Therapy** or **ABTHERA™ Therapy**, consult the safety information and instructions for use provided in **PREVENA™** and **ABTHERA™** Dressing cartons. If there are questions, or if the safety information is missing, immediately contact your local KCI representative.

Additional product information can be found at www.acelity.com, www.veraflo.com or www.vaculta.com (US), www.kci-medical.com (OUS).

As with all prescription medical devices, failure to follow product instructions or adjusting settings and performing therapy applications without the express direction and/or supervision of your trained clinical caregiver may lead to improper product performance and the potential for serious or fatal injury. For medical questions, please consult a physician. In case of medical emergency, immediately contact your local emergency services provider.

CAUTION: Federal law (US) restricts this device to sale or rental by or on the order of a physician.

DISCLAIMER OF WARRANTY AND LIMITATION OF REMEDY

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Descriptions or specifications in KCI printed matter, including this publication, are meant solely to generally describe the product at the time of manufacture and do not constitute any express warranties except as set forth in the written limited warranty included with this product. Information in this publication may be subject to change at any time. Contact KCI for updates.

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Warnings: Important Information For Users

In order for KCI products to perform properly, KCI recommends the following conditions. Failure to comply with these conditions will void any applicable warranties.

- Use this product only in accordance with this manual and applicable product labeling.
- Assembly, operations, extensions, re-adjustments, modifications, technical maintenance or repairs must be performed by qualified personnel authorized by KCI. For these authorized personnel, KCI will make available upon request circuit diagrams, component parts lists, etc. as required for repairs.
- Ensure the electrical installation of the room complies with the appropriate national electrical wiring standards. To avoid the risk of electrical shock, this product must be connected to a grounded power receptacle.
- Do not operate this product if it has a damaged power cord, power supply or plug. If these components are worn or damaged, contact KCI.
- Do not drop or insert any object into any opening or tubing of this product.
- Do not connect this product or its components to devices not recommended by KCI.
- Use only V.A.C.® Dressings (**V.A.C.® GRANUFOAM™ Dressings**, **V.A.C.® GRANUFOAM SILVER™ Dressings**, **V.A.C. WHITEFOAM™ Dressings**, **V.A.C. VERAFLO™ Dressings)**, **PREVENA™ Dressings** or **ABTHERA™ SENSAT.R.A.C.™ Open Abdomen Dressings** and associated disposables with this product.
- Keep this product away from heated surfaces.
- Although this product conforms to the intent of the standard IEC 60601-1-2 in relation to Electromagnetic Compatibility, electrical equipment may produce interference. If interference is suspected, separate the equipment and contact KCI.
- Avoid spilling fluids on any part of this product.

  Fluids remaining on the electronic controls can cause corrosion that may cause the electronic components to fail. Component failures may cause the unit to operate erratically, possibly producing potential hazards to patient and staff. If spills do occur, unplug the unit immediately and clean with an absorbent cloth. Ensure there is no moisture in or near the power connection and power supply components before reconnecting power. If the product does not work properly, contact KCI.
- Do not use this product while bathing / showering or where it can fall or be pulled into a tub, shower or sink.
- Do not reach for a product that has fallen into water. Unplug the unit immediately if plugged into electrical source. Disconnect the unit from dressing and contact KCI.
- Do not use this product in the presence of a flammable anesthetic mixture with air, oxygen, or nitrous oxide, or an oxygen enriched environment.
- Do not take this product into an MR environment. This product is **MR Unsafe**.

Notice - This product has been configured from the manufacturer to meet specific voltage requirements. Refer to the product information label for specific voltage.

Colors Used in this Manual

Screen Button / *Screen name* - *Screen names* and **Screen Buttons**.

ABTHERA™ Therapy - Items and information that relate specifically to **ABTHERA™ Therapy**.

V.A.C.® Therapy - Items and information that relate specifically to **V.A.C.® Therapy**.

PREVENA™ Therapy - Items and information that relate specifically to **PREVENA™ Therapy**.

V.A.C. VERAFLO™ Therapy - Items and information that relate specifically to **V.A.C. VERAFLO™ Therapy**.

System - Items and information that relate specifically to the **V.A.C.ULTA™ Therapy Unit**.

Introduction

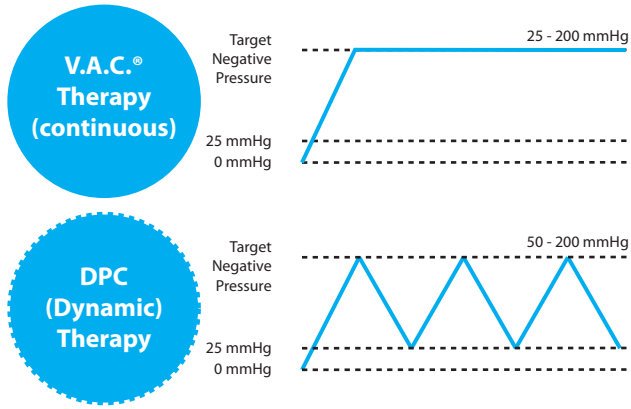
The V.A.C.ULTA™ Negative Pressure Wound Therapy System is an integrated wound management system that provides:

- **V.A.C.® Negative Pressure Wound Therapy** (**1**)
- **V.A.C. VERAFLO™ Instillation Therapy** (**2**)
- **PREVENA™ Incision Management Therapy** (**3**)
- **ABTHERA™ SENSAT.R.A.C.™ Open Abdomen Therapy** (**4**).

Refer to the V.A.C.ULTA™ Negative Pressure Wound Therapy System (V.A.C.ULTA™ Therapy System) Safety Information that accompanies the V.A.C.ULTA™ Therapy Unit for complete Indications for Use for each of these therapies and safety and use information.

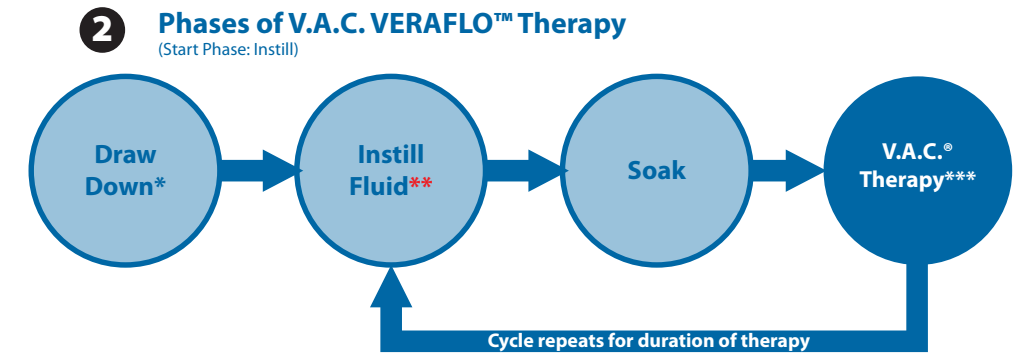
V.A.C.® Negative Pressure Wound Therapy (with two negative pressure modes):

1



The **V.A.C.® GRANUFOAM™**, **V.A.C.® GRANUFOAM SILVER™** and, **V.A.C. WHITEFOAM™ Dressings** are available for use with the **V.A.C.® Therapy** option by the V.A.C.ULTA™ Therapy System. Additional dressings specific to **V.A.C. VERAFLO™ Therapy** are also available.

V.A.C. VERAFLO™ Instillation Therapy:



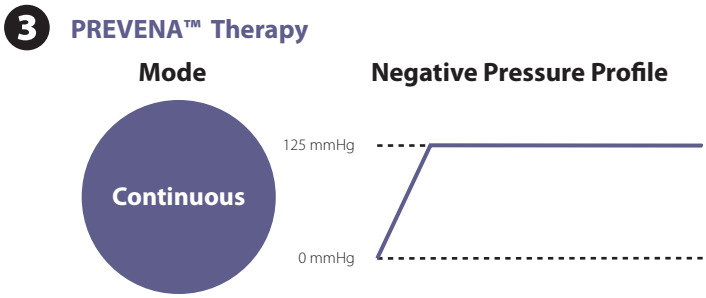
* SEAL CHECK™ Leak Detector

** Fill Assist allows the user to monitor initial wound fill by manually starting and stopping instillation to determine correct instill volume after dressing is applied. Once determined, this volume will be the set point for each subsequent instill phase of V.A.C. VERAFLO™ Therapy.

*** Continuous and DPC Therapy negative pressure modes are available with V.A.C. VERAFLO™ Therapy.

The **V.A.C. VERAFLO™**, **V.A.C. VERAFLO CLEANSE™** and **V.A.C. VERAFLO CLEANSE CHOICE™ Dressings** are available for use with the **V.A.C. VERAFLO™ Therapy** option provided by the V.A.C.ULTA™ Therapy System.

PREVENA™ Incision Management Therapy:



The **PREVENA™ PEEL & PLACE™** and **PREVENA™ CUSTOMIZABLE™ Dressings** are available for use with the **PREVENA™ Therapy** option provided by the V.A.C.ULTA™ Therapy System.

ABTHERA™ SENSAT.R.A.C.™ Open Abdomen Therapy:

4 ABTHERA™ Therapy

Mode

Continuous

Negative Pressure Profile

The ABTHERA™ SENSAT.R.A.C.™ Open Abdomen Dressing is available for use with the **ABTHERA™ Therapy** option provided by the V.A.C.ULTA™ Therapy System.

The V.A.C.ULTA™ Negative Pressure Wound Therapy System is intended to be operated by qualified clinical caregivers in the acute care setting. In-service and training programs for use of **V.A.C.® Therapy**, **V.A.C. VERAFLO™ Therapy**, **PREVENA™ Therapy** and **ABTHERA™ Therapy** are available. Therapy unit information signals should be monitored by the clinical caregiver. Patients are not expected to apply or change dressings or adjust therapy unit settings.

Therapy Selection - Allows user to select **V.A.C. VERAFLO™**, **V.A.C.®**, **PREVENA™** or **ABTHERA™** Therapies.

Fill Assist (**V.A.C. VERAFLO™ Therapy**)- Allows the user to monitor the initial wound fill by manually starting and stopping instillation to determine the appropriate instill volume after the dressing is applied. Once determined, this volume will be the set point for each future instill phase of **V.A.C. VERAFLO™ Therapy**.

Benefits:

- Removes the guesswork related to volume setting
- Helps reduce leaks caused by wound overfilling

Volumetric Delivery with Solution Dwell Time (**V.A.C. VERAFLO™ Therapy**) - The V.A.C.ULTA™ Therapy Unit provides unique and patented volumetric fluid delivery utilizing a pump.

Benefits:

- Delivers fluid reliably and uniformly across wound bed.
- Allows time for solubilizing infectious materials and wound debris.

Automated and Cyclic Wound Cleansing (**V.A.C. VERAFLO™ Therapy**) - **V.A.C. VERAFLO™ Therapy** is 100% automated after set-up, providing hands-free, repeating wound cleansing cycles through instillation of topical wound solutions.

Benefits:

- Delivers automatic and repetitive topical wound cleansing without dressing removal.
- Eliminates need for manual wound cleansing between dressing changes.

V.A.C. VERALINK™ Cassette (**V.A.C. VERAFLO™ Therapy**) - This disposable component connects the V.A.C.ULTA™ Therapy Unit to the solution bag / bottle and dressing tubing.

Benefits:

- It provides convenient solution storage and delivery.

Dressing Soak (**V.A.C.® Therapy** and **V.A.C. VERAFLO™ Therapy**)- This tool allows the clinician to soak the dressing and the wound with instillation solution in preparation for a dressing change.

Benefits:

- Provides ability to help "float" the dressing by increasing instillation volume and soak time.
- Moistens and softens the dressing for easier removal and patient comfort.

Additional Features

Touch Screen User Interface: The touch screen user interface allows for easy navigation through operational and help menus. A screen guard is available to help prevent unintentional changes. A settings lock is available to prevent patient access to therapy settings.

Adjustable Negative Pressure Settings and Therapy Modes: Settings can be selected from a range of 25 mmHg to 200 mmHg in increments of 25 mmHg depending on settings available for selected therapy. In addition, **V.A.C.® Therapy** and **V.A.C. VERAFLO™ Therapy** can be set for continuous negative pressure or Dynamic Pressure Control™ (DPC) Therapy.

SEAL CHECK ™ Leak Detector: This tool assists the user in finding negative pressure leaks in the system through the use of audible tones and on-screen visual aids during the troubleshooting process.

History Reports: The V.A.C.ULTA™ Therapy System provides three possible reports: 1. Alarm History, 2. Therapy History, and 3. Patient History. These chronologically logged reports include the date and times for therapy starts / stops, therapy settings, alarm occurrences, and disposable component changes. They can be reviewed on-screen or transferred electronically from the V.A.C.ULTA™ Therapy Unit via a non-powered USB flash memory stick or SD memory card.

SENSAT.R.A.C.™ System: The SENSAT.R.A.C.™ System (also incorporated in the **V.A.C. VERAT.R.A.C.™ Pad**, **V.A.C. VERAT.R.A.C. DUO™ Tube Set**, **PREVENA PLUS™ Incision Management System**, and **ABTHERA™ SENSAT.R.A.C.™ Open Abdomen Dressing System**) monitors and maintains target pressure at the wound site, helping to deliver consistent therapy. This system includes therapy unit hardware and software, wound exudate collection canister, canister detection method, multi-lumen tubing, connector and SENSAT.R.A.C.™ Pad.

Not available with the PREVENA™ Dressing without SENSAT.RA.C.™ Pad.

In-Line Tubing Connectors: The system incorporates an in-line dressing connector and tubing clamps to conveniently allow the wound dressing to be temporarily disconnected from the therapy unit.

Canisters: The V.A.C.ULTA™ Therapy Unit is optimized for use with 300 mL, 500 mL or 1000 mL canisters. These are the same canisters used with INFOV.A.C.™ Therapy Unit. Canisters are single use, manufactured without natural rubber latex, sterile components.

Canister Release Button: The canister release button is illuminated and will flash when the canister is full.

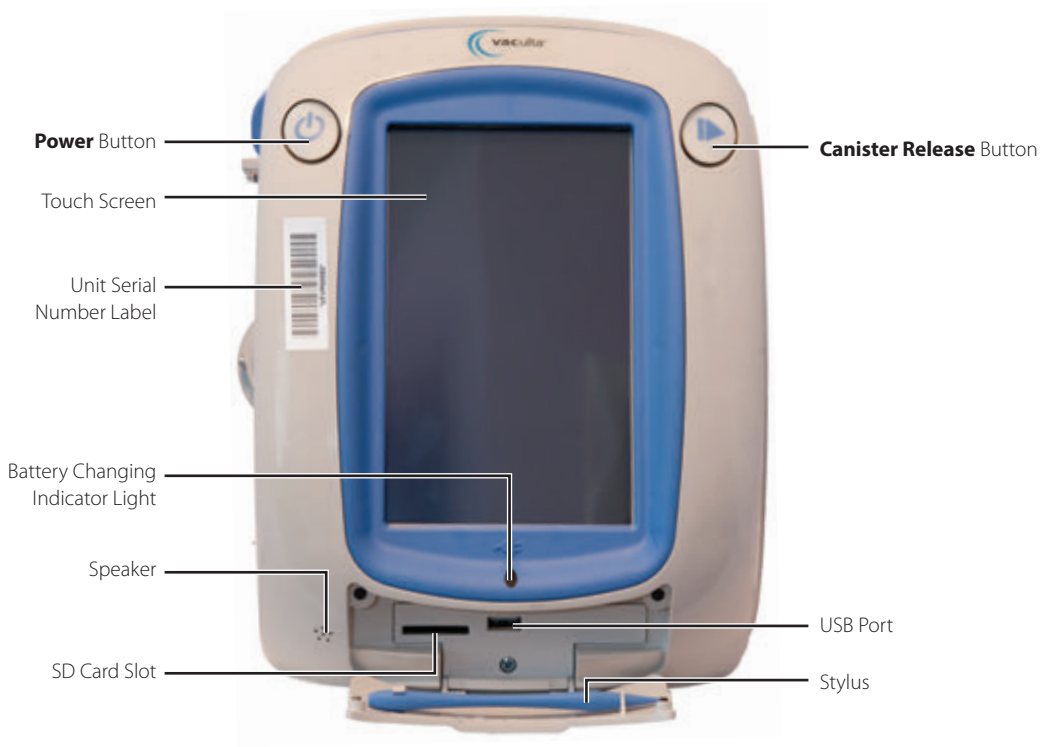
Intensity Setting: Intensity is related to the time it takes to reach the target negative pressure therapy level after the initiation of therapy. The lower the intensity setting, the longer it will take to reach the target negative pressure.

Wound Image Analysis: Digital wound images can be uploaded from a digital camera into the V.A.C.ULTA™ Therapy Unit. When the wound perimeter is traced on-screen with the provided stylus, wound image surface area and volume can be calculated and trended by the therapy unit. A chronological graphical history of the wound (with wound image area trend chart) can be viewed on-screen or this information can be transferred from the V.A.C.ULTA™ Therapy Unit electronically. This information is intended to be used by the treating clinician as a mechanism for providing a record of wound healing progress; it is not intended for use in the diagnosis and treatment of wounds.

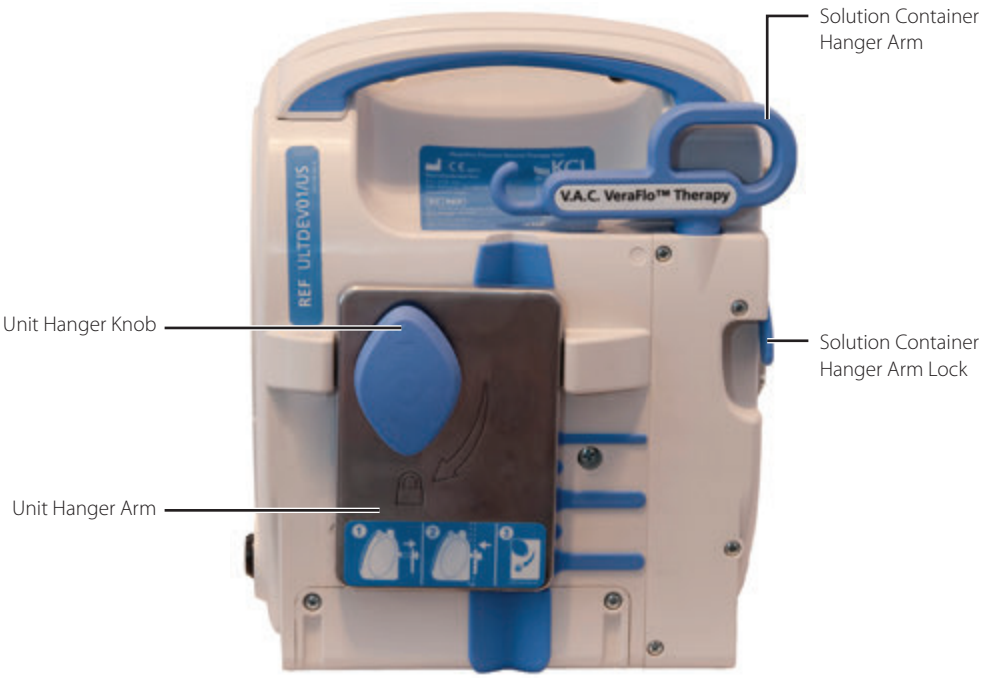
Hanger Mechanism: The therapy unit can be securely mounted to an I.V. pole, a bed footboard or a wheelchair.

Battery Operation: In order to facilitate patient transfer, battery operation is available with the V.A.C.ULTA™ Therapy Unit. During typical usage, the battery may provide up to six hours of operation before needing to be recharged.

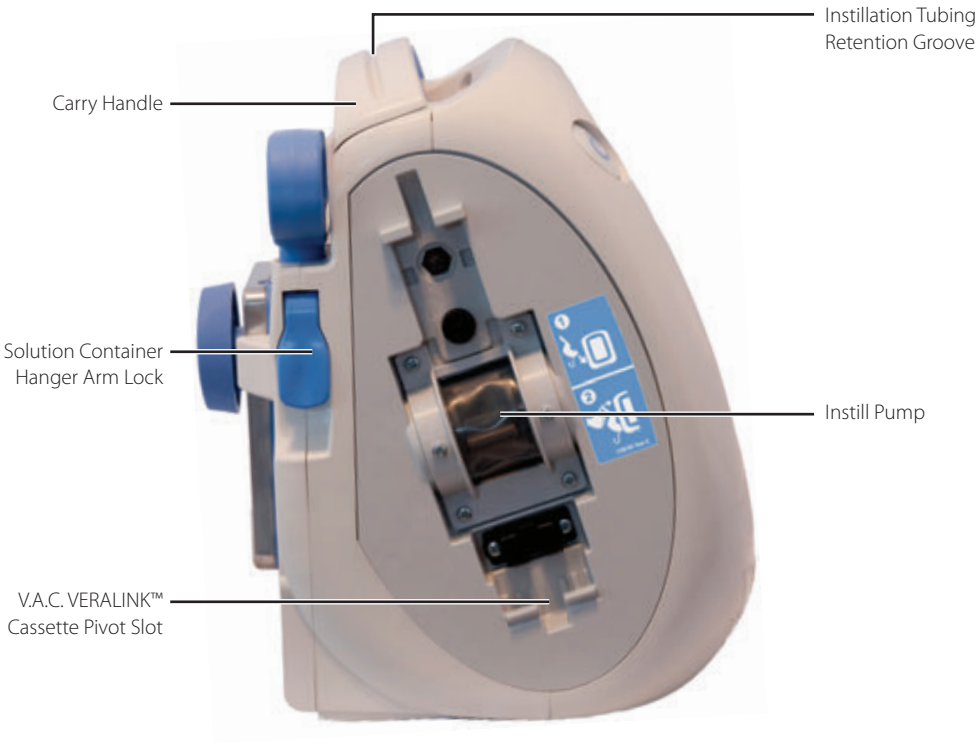
V.A.C.ULTA™ Therapy Unit Component Identification



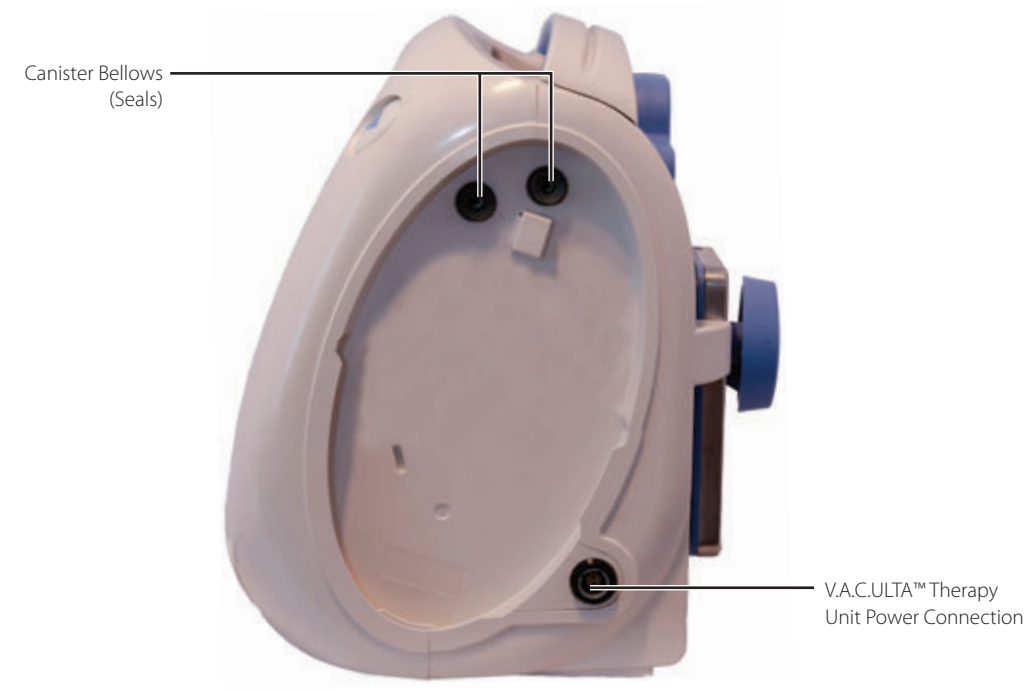
V.A.C.ULTA™ Therapy Unit - Front



V.A.C.ULTA™ Therapy Unit - Back



V.A.C.ULTA™ Therapy Unit - Left



V.A.C.ULTA™ Therapy Unit - Right

Alert / Alarm	V.A.C. VERAFLO™ Therapy	V.A.C.® Therapy	PREVENA™ Therapy	ABTHERA™ Therapy
Blockage 	ALERT	ALERT	ALERT	ALERT
Blockage (Therapy Interrupted) 	ALARM	ALARM	ALERT	ALERT
Canister Full 	ALARM	ALARM	ALERT	ALERT
Canister Not Engaged 	ALARM	ALARM	ALERT	ALERT
Therapy Inactive 	ALARM	ALARM	ALERT	ALERT
Leak 	ALARM	ALARM	ALERT	ALERT
Leak (Therapy Interrupted) 	ALARM	ALARM		
Low Pressure 	ALARM	ALARM		
V.A.C. VERALINK™ Not Engaged 	ALERT	ALERT		
Solution Bag / Bottle Empty 	ALERT	ALERT		
V.A.C. VERAFLO™ Fill Assist Inactive 	ALERT			
V.A.C. VERAFLO™ Pressure Deviation 	ALARM	ALARM		
V.A.C. VERAFLO™ Instill Tube Blockage (Therapy Interrupted) 	ALERT	ALERT		

Alert / Alarm Symbol	V.A.C. VERAFLO™ Therapy	V.A.C.® Therapy	PREVENA™ Therapy	ABTHERA™ Therapy
Battery Low 	ALERT	ALERT	ALERT	ALERT
Battery Critical 	ALARM	ALARM	ALERT	ALERT
Battery Exhausted 	ALARM	ALARM	ALERT	ALERT
Internal Temperature 	ALERT	ALERT	ALERT	ALERT
System Error 	ALARM	ALARM	ALERT	ALERT

Charge Battery

The V.A.C.ULTA™ Therapy Unit comes with its own power supply and a rechargeable battery. The battery is not user accessible or serviceable. The power supply has a two-part cord, one that plugs into an AC wall outlet and one that plugs into the V.A.C.ULTA™ Therapy Unit.

Use only the power supply provided with the V.A.C.ULTA™ Therapy Unit (part number: 4103730). Using any other power supply may damage the V.A.C.ULTA™ Therapy Unit.

If environmental conditions (specifically, low humidity) pose a risk of static electricity, take care when handling the V.A.C.ULTA™ Therapy Unit while it is plugged into an AC wall outlet. In rare instances, discharge of static electricity when in contact with the therapy unit may cause the touch screen to darken, or the therapy unit to reset or turn off. If therapy does not restart by powering the unit off and then on, immediately contact KCI.

To isolate the therapy unit from supply mains, unplug the AC power cord from the wall outlet. Do not block access to the plug or wall outlet.

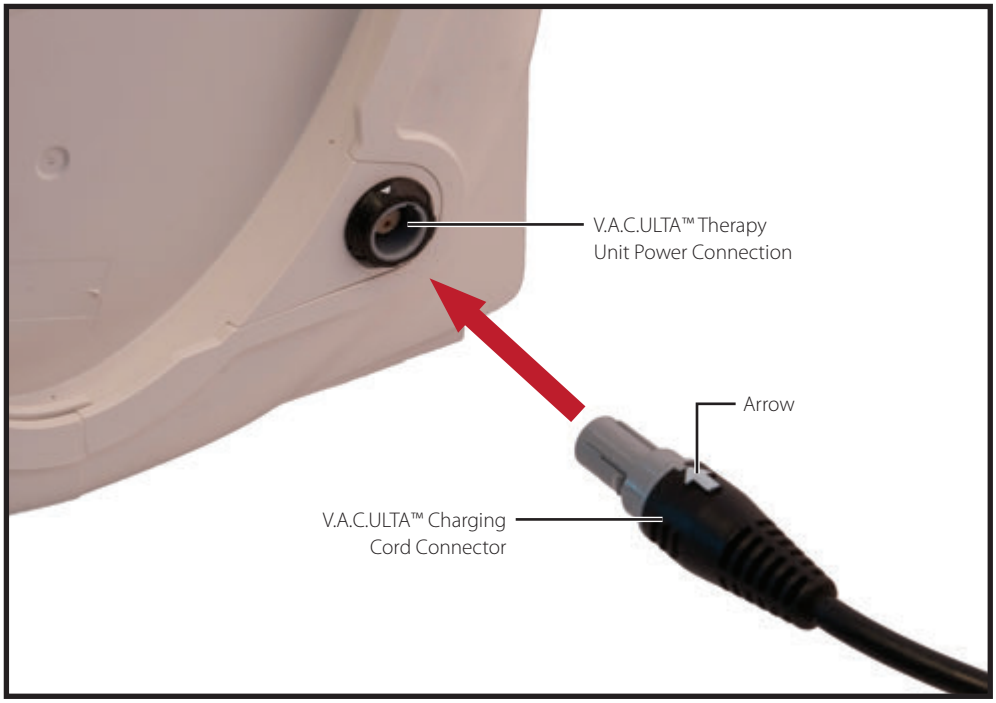
Power cords may present a tripping hazard. Ensure that all cords are out of areas where people may walk.

1. Plug the AC power cord into the DC power supply.

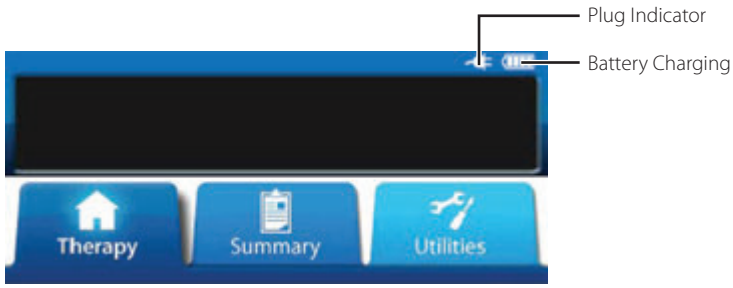
2. Plug the AC wall plug into an AC wall outlet.

DC power supply must remain accessible at all times to allow for immediate disconnect from power source, if necessary.

3. Locate the arrow on the charging cord connector. The arrow should face up as the connector is plugged into the power connection on the V.A.C.ULTA™ Therapy Unit.



4. A plug indicator appears on screen while the unit is plugged into a wall outlet.



It should take approximately four hours to fully recharge the battery. To maximize battery life, keep the unit plugged in whenever possible.

When the V.A.C.ULTA™ Therapy Unit is correctly plugged into the V.A.C.ULTA™ Power Supply, the battery charging indicator light on the front of the unit (page 18) will glow amber while the battery is charging. When the battery has reached full charge the battery charging indicator light will glow green.

Therapy Unit Placement

The V.A.C.ULTA™ Therapy Unit can be attached to an I.V. pole or the footboard of a hospital bed. If required, it can be placed on a solid, level surface where it does not cause an obstruction. The V.A.C.ULTA™ Therapy Unit should be placed where cables and tubes cannot be caught on passing objects.

Power cords and tubing may present a tripping hazard. Ensure that all cords and tubing are out of areas where people may walk.

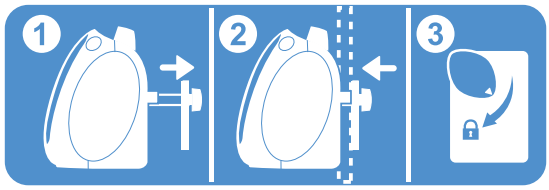
The V.A.C.ULTA™ Therapy Unit is not to be carried or worn by an ambulatory patient. Consult your physician and contact KCI for V.A.C.® Therapy Units designed for ambulatory patient use. The V.A.C.ULTA™ Therapy Unit can be placed on an I.V. pole, bed frame or wheelchair during patient transport.

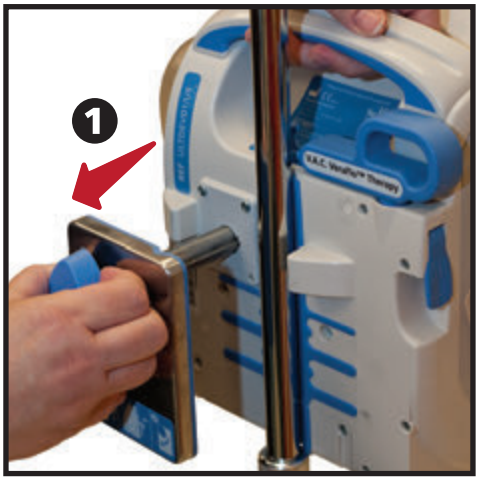
Attaching the Therapy Unit to an I.V. Pole

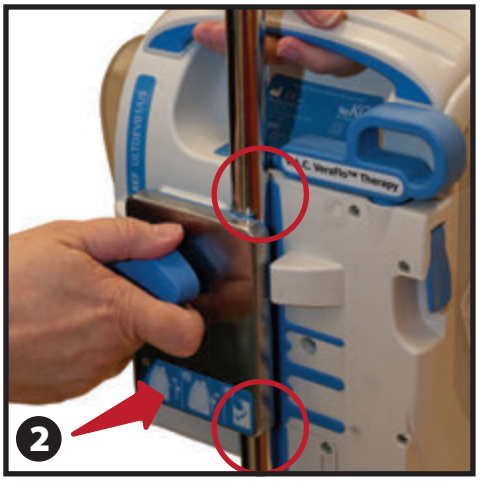
1. Hold the V.A.C.ULTA™ Therapy Unit by the carry handle, grip the hanger knob and pull the hanger arm out (**1**).

2. Place the hanger around the I.V. pole and allow the hanger to close, pulling the unit onto the I.V. pole (**2**). Ensure that the pole is in the vertical rubber groove (at both top and bottom) on the rear of the V.A.C.ULTA™ Therapy Unit.

3. Turn the hanger knob to lock the hanger arm in place (**3**). When the arrow symbol on the hanger knob aligns with the lock symbol, the hanger arm is locked.



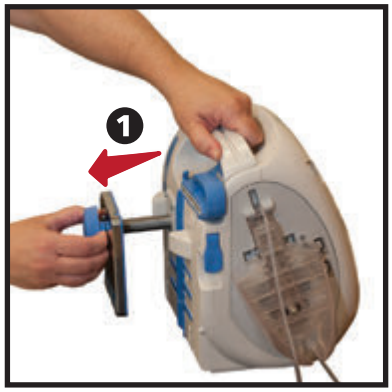


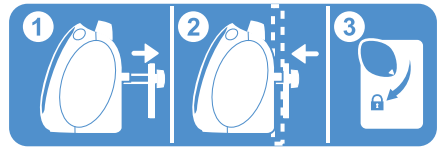


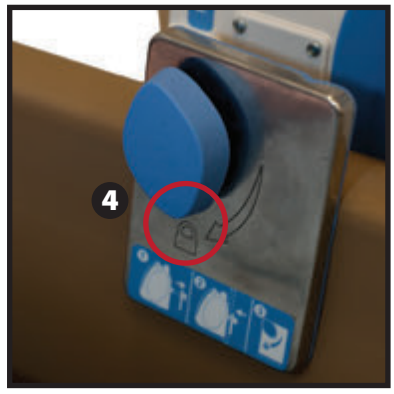
4. Reverse procedure to remove therapy unit.

Attaching the Therapy Unit to a Bed Footboard

1. Hold the V.A.C.ULTA™ Therapy Unit by the carry handle, grip the hanger knob and pull the hanger arm out (**1**).
2. Place the hanger over the footboard. Allow the hanger to close, pulling the unit onto the footboard (**2**).
3. Turn the hanger knob to lock the hanger arm in place (**3**). When the arrow symbol on the hanger knob aligns with the lock symbol, the hanger arm is locked (**4**).



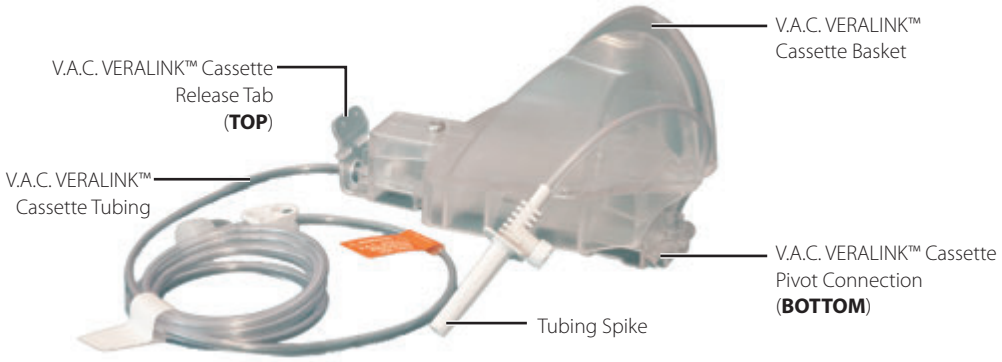




4. Reverse procedure to remove therapy unit.

Attaching the V.A.C. VERALINK™ Cassette

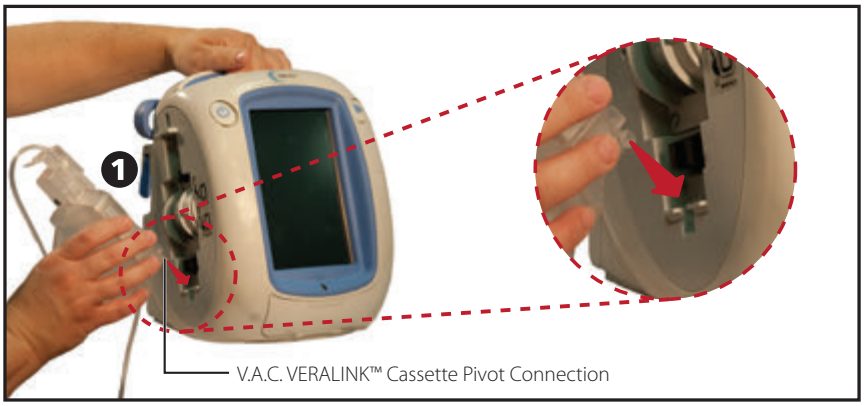
For use only with the V.A.C.® Therapy when using the Dressing Soak Feature or V.A.C. VERAFLO™ Therapy.

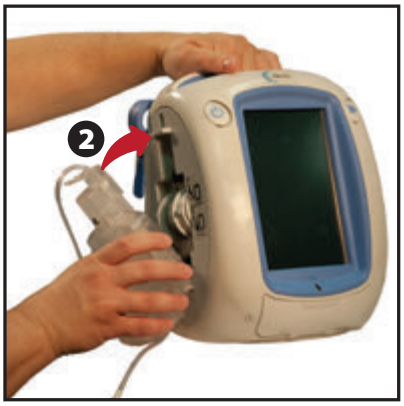


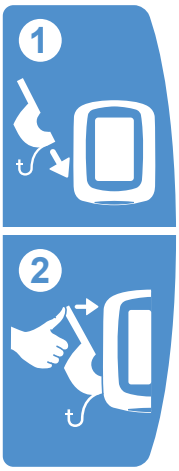
1. Remove the V.A.C. VERALINK™ Cassette from packaging and insert the pivot connection of the V.A.C. VERALINK™ Cassette (**1**) into the pivot slot on the V.A.C.ULTA™ Therapy Unit.

2. Pivot the V.A.C. VERALINK™ Cassette Release Tab toward the unit (**2**) and press firmly until it clicks into place (**3**).

The V.A.C. VERALINK™ Cassette is designed to fit tight to the therapy unit. Apply very firm pressure to ensure the cassette is properly installed.





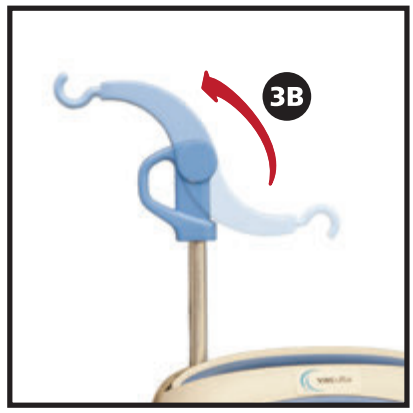


Attaching Solution Bag / Bottle

For use only with the V.A.C.® Therapy when using the Dressing Soak Feature or V.A.C. VERAFLO™ Therapy

Extend Solution Container Hanger Arm:

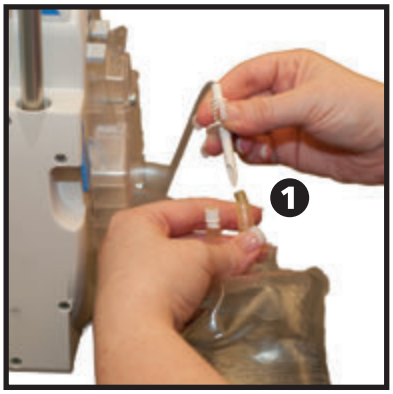
1. Fully lift the solution container hanger arm lock (**1**).
2. Raise solution container hanger arm (**2**). Depending on unit, either rotate the handle 180 degrees (**3A**) or flip the handle up (**3B**).
3. Fully push the solution container hanger arm lock down (**4**) to lock solution container hanger arm in place.

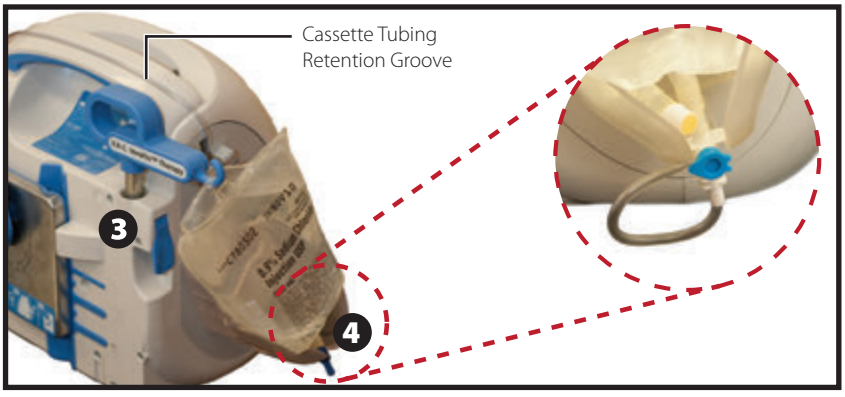


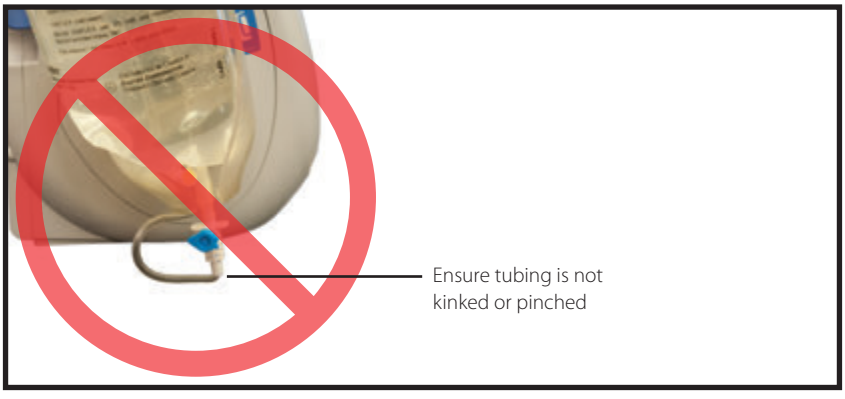
Hang Solution Bag / Bottle

For use only with the V.A.C.® Therapy Dressing Soak Feature or V.A.C. VERAFLO™ Therapy.

1. Ensure cassette tubing is routed in the retention groove on the unit handle by applying pressure to push tubing into the groove.
2. Spike solution bag / bottle according to manufacturer's instructions using the V.A.C. VERALINK™ Cassette's tubing spike (**1**).
3. Hang the solution bag / bottle from the therapy unit's solution container hanger arm (**2**).
4. Adjust the solution container hanger arm (**3**) while manipulating the bag / bottle to ensure that the spike is held inside the slot in the V.A.C. VERALINK™ Cassette Basket (**4**).





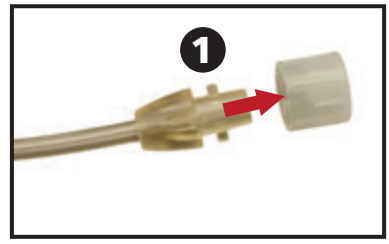


Connect Instillation Line

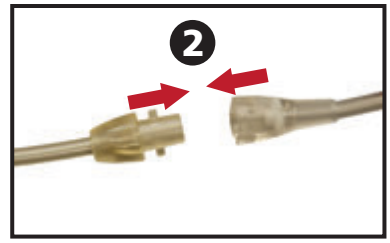
For use only with the V.A.C.® Therapy Dressing Soak Feature or V.A.C. VERAFLO™ Therapy.

Refer to the appropriate dressing Instructions for Use for safety information and procedures to apply and change the dressing.

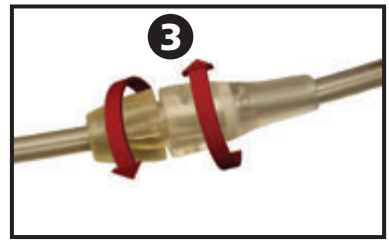
1. Remove the cap from the end of the V.A.C. VERALINK™ Cassette tubing (**1**).



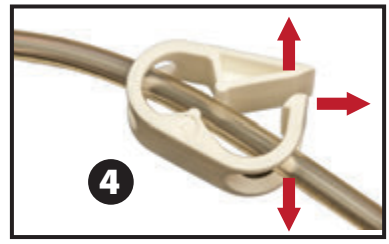
2. Connect the V.A.C. VERALINK™ Cassette tubing to the instillation line of the V.A.C. VERAT.R.A.C.™ Pad / V.A.C. VERAT.R.A.C. DUO™ Tube Set by pushing the connectors together (**2**).



3. Twist connectors until the locking tabs are fully engaged (**3**).



4. Open all tubing clamps (**4**).



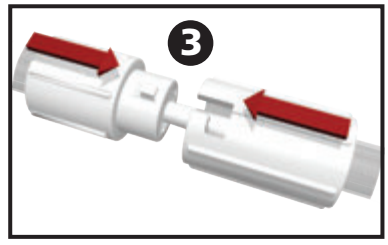
When selecting canister size (300 mL, 500 mL, 1000 mL), consider the amount of wound exudate and selected therapy. If delivering V.A.C. VERAFLO™ Therapy, also consider the amount of wound instillation fluid and frequency of instillation.

If delivering PREVENA™ Therapy, consider using the smallest available canister for the V.A.C.ULTA™ Therapy Unit.

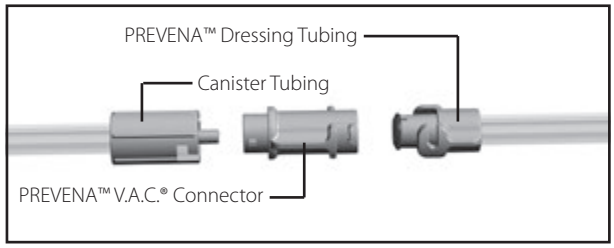
1. Slide the canister into the side of the V.A.C.ULTA™ Therapy Unit (**1**)

2. Push the canister (500 mL shown) firmly into place on the V.A.C.ULTA™ Therapy Unit (**2**). An audible click indicates the canister is fully seated. Ensure the canister is installed directly onto the therapy unit. Do not twist or turn the canister as it is being installed.

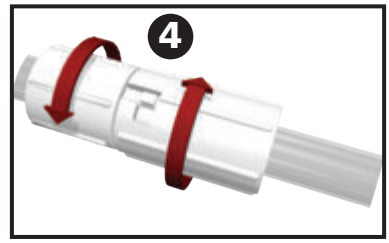
3. Connect the canister tubing to the dressing tubing by pushing the connectors together (**3**).



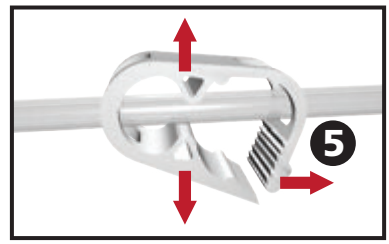
A PREVENA™ V.A.C.® Connector will be needed to connect the PREVENA™ Dressing to the V.A.C.ULTA™ Therapy Unit Canister. This connector, which is available in the PREVENA™ Dressing package, must be used for negative pressure wound therapy to work effectively and accurately.



4. Twist connectors until the locking tabs are fully engaged (**4**).



5. Open all tubing clamps (**5**).



Changing the Canister

A canister may be changed under routine conditions or under alarm conditions. Under routine conditions the canister release button will NOT be flashing. When changing the canister **DO NOT** power off the V.A.C.ULTA™ Therapy Unit.

Under Canister Full Alarm conditions, the canister release button (page 18) will be flashing, an alert / alarm screen (pages 56, 90, 116 and 134) will be displayed and therapy will be off (unit power remains on).

When delivering PREVENA™ Therapy, a canister change should not be required. Contact the treating physician immediately if a Canister Full Alarm occurs during PREVENA™ Therapy.

The canister used for V.A.C.® Therapy, V.A.C. VERAFLO™Therapy and ABTHERA™ Therapy should be changed when full (the alarm will sound), or at least once a week to control odor.

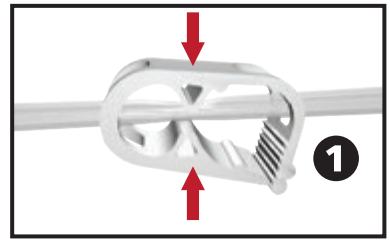
If a Canister Full Alarm has occurred, pump will be OFF. Proceed to Step 2.

1. **V.A.C.® Therapy**, **PREVENA™ Therapy**, **ABTHERA™ Therapy** - Stop therapy by selecting **Start / Stop** on the touch screen. Do not turn power off to the V.A.C.ULTA™ Therapy Unit.

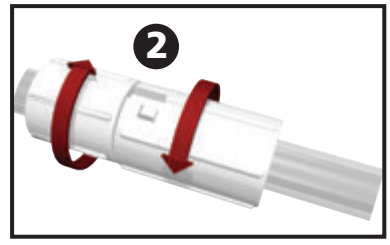
V.A.C. VERAFLO™ Therapy - Stop therapy by selecting **Pause / Resume** on the touch screen. Do not turn power off to the V.A.C.ULTA™ Therapy Unit.

2. Slide both tubing clamps toward the tubing connector.

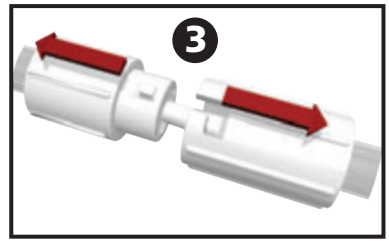
3. Tightly close both tubing clamps (**1**) to prevent spillage of contents in tubing. Several clicks should be heard.



4. Twist the tubing connectors until the locking tabs are disengaged (**2**).



5. Pull the connector apart (**3**) to disconnect the dressing tubing from the canister tubing.



6. Press the **Canister Release** Button.

If the 300 mL ACTIV.A.C.™ Canister is used, it is NOT held in place by the cradle of the V.A.C.ULTA™ Therapy Unit. When removing the 300 mL ACTIV.A.C.™ Canister from the V.A.C.ULTA™ Therapy Unit, hold the canister FIRMLY before pressing the canister release button.

7. Remove the canister from the therapy unit by lifting and pulling the canister away from the unit (**4**).

Dispose of the used canister according to institution and / or local environmental regulations.

8. Install the new canister and reconnect tubing as described in the **Canister Installation** section (page 32) of this user manual.

9. **V.A.C.® Therapy**, **PREVENA™ Therapy**, **ABTHERA™ Therapy** - Select **Start / Stop** on the touch screen to restart therapy.

V.A.C. VERAFLO™ Therapy - Select **Pause / Resume** on the touch screen to restart therapy.

Operation

This chapter contains instructions for setting and adjusting functions of the V.A.C.ULTA™ Therapy Unit.

Review all sections of this manual prior to product use. Carefully read the Indications, Contraindications, Warnings, and Precautions included with the unit prior to operating the V.A.C.ULTA™ Therapy Unit.

Touch Screen

The display on the front of the unit is touch sensitive. The user interface screens will be shown on this display. These screens will display information on current system operations and settings based on the tab selected (**Therapy**, **History** or **Utilities**).

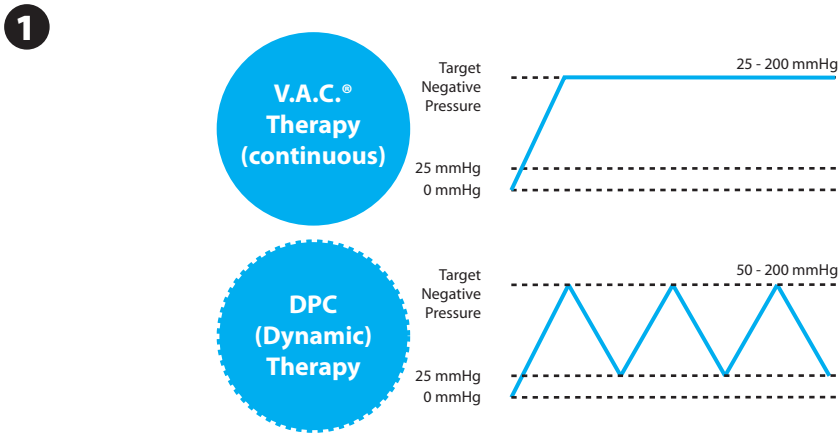
The operation of the touch screen is detailed in the following pages.

The touch screen should only be operated by finger or the supplied stylus. Using pens or other pointing devices will damage the screen.

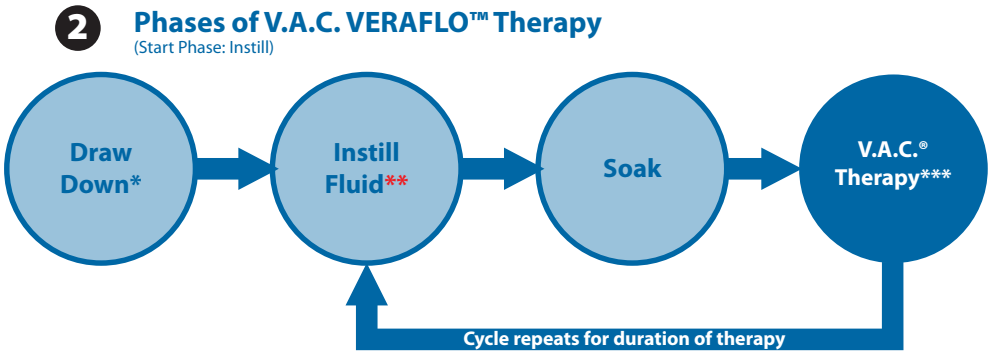
V.A.C.ULTA™ Therapy System - Therapy Options

The V.A.C.ULTA™ Therapy System can be used with four different therapies depending on physician orders:

V.A.C.® Negative Pressure Wound Therapy (**1**):



V.A.C. VERAFLO™ Instillation Therapy (**2**):

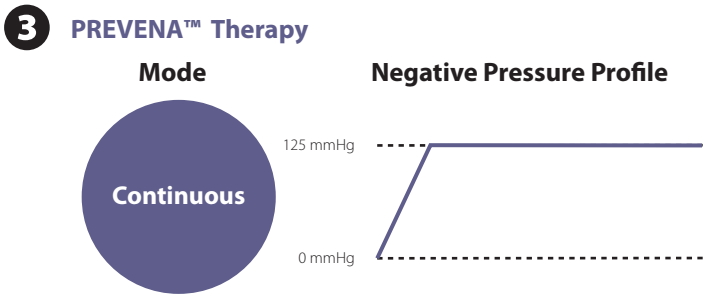


* SEAL CHECK™ Leak Detector

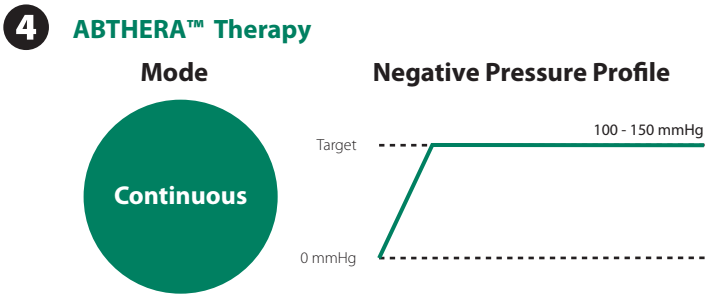
** Fill Assist allows the user to monitor initial wound fill by manually starting and stopping instillation to determine correct instill volume after dressing is applied. Once determined, this volume will be the set point for each subsequent instill phase of V.A.C. VERAFLO™ Therapy.

*** Continuous and DPC Therapy negative pressure modes are available with V.A.C. VERAFLO™ Therapy.

PREVENA™ Incision Management Therapy (**3**):

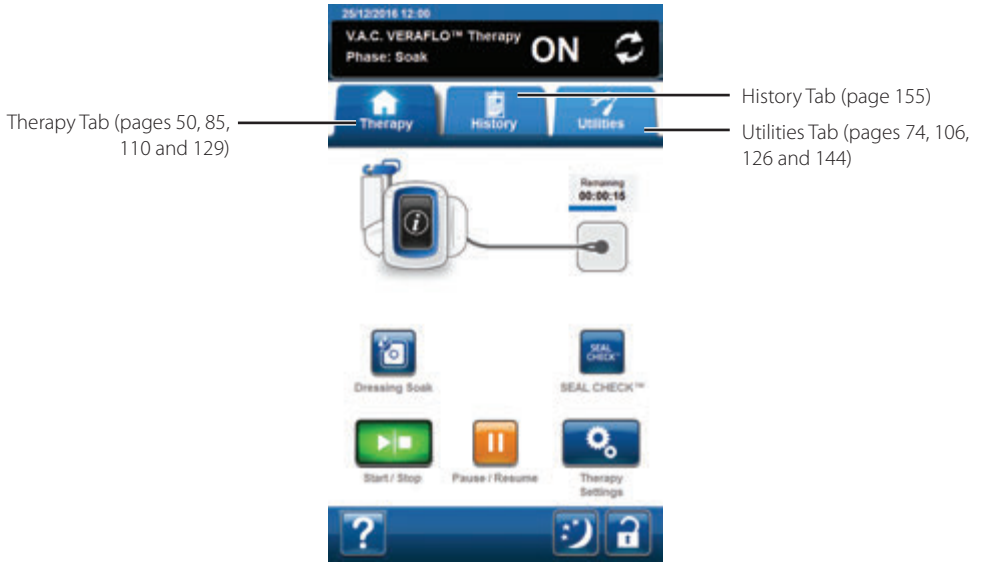


ABTHERA™ SENSAT.R.A.C.™ Open Abdomen Therapy (**4**):



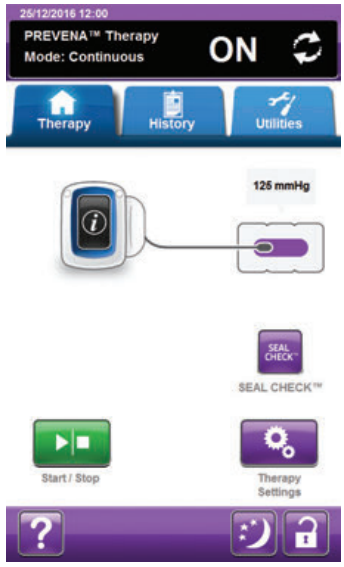
Touch Screen - Tabs

The touch screen is divided into three sections, each marked by a separate tab. These tabs allow access to the different areas of the V.A.C.ULTA™ Therapy Unit's software.



V.A.C. VERAFLO™ Therapy *Home* Screen

V.A.C.® Therapy *Home* Screen



PREVENA™ Therapy *Home* Screen

ABTHERA™ Therapy *Home* Screen

Therapy Tab - (pages 50, 85, 110 and 129) Use to access the ***Home*** screen, therapy settings, features and active therapy summary information. Use the **Therapy Settings** button on the Therapy Tab to select prescribed therapy (**V.A.C. VERAFLO™ Therapy**, **V.A.C.® Therapy**, **PREVENA™ Therapy** or **ABTHERA™ Therapy**).

History Tab - (page 155) Use to access to all therapy history for the patient.

Utilities Tab - (pages 74, 106, 126, 144) Use to access therapy related features and to set system preferences including language, unit of measure, date, screen brightness, etc. KCI contact information and software version can also be viewed.

Common Touch Screen Buttons

Most screens have one or more common control buttons. These are:

Help - Access Help screens

Screen Guard / Settings Lock- Activate the **Screen Guard** feature to prevent unintentional changes. This feature should be used when cleaning the touch screen (page 192). Select and hold for more than five seconds to activate or deactivate **Settings Lock**. Settings Lock prevents patient access to therapy settings.

Night Mode - Activate Night Mode feature to darken the touch screen. When Night Mode is active, the display will turn on at lowest brightness setting when the touchscreen is touched. To cancel Night Mode, select **Night Mode** to return to previous brightness setting.

OK - Confirm selection

Exit - Close pop-up screen

Cancel - Cancel operation

Back - Return to previous screen

Forward - Advance to next screen

+ or **-** - Use **+** / **-** to adjust above or below values shown.

Information - Select to view ***Therapy Summary*** and ***Current Settings*** screens for the active therapy.

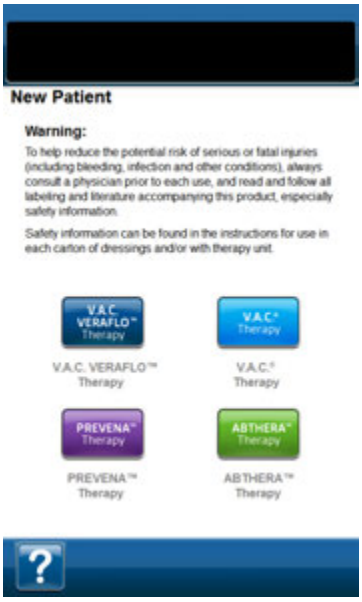
Start / Stop - Select to restart therapy (**V.A.C.® Therapy**, **PREVENA™ Therapy**, **ABTHERA™ Therapy**).

Pause / Resume - Select to restart therapy (**V.A.C. VERAFLO™ Therapy**).

Power the V.A.C.ULTA™ Therapy Unit On or Off

The **Power** button is located in the upper left hand corner on the front of the unit (page 18). Press and hold the **Power** button until the light comes on to turn the V.A.C.ULTA™ Therapy Unit on. The unit will go through a self-check routine and then present the ***Startup*** screen. Press and hold the **Power** button until the display turns off to turn the V.A.C.ULTA™ Therapy Unit off.

The ***Startup*** screen will be displayed one of two ways:



The first time the V.A.C.ULTA™ Therapy System is used following a quality checklist inspection and cleaning, the ***New Patient*** screen will be displayed.

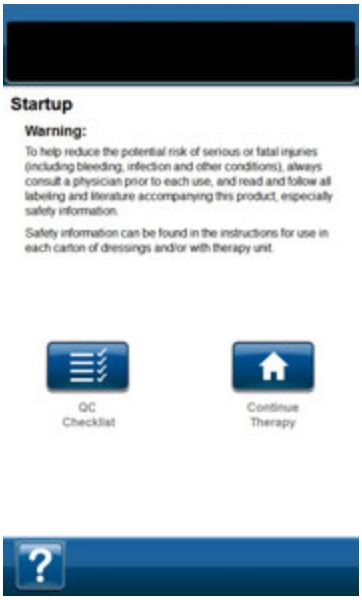
Select **V.A.C. VERAFLO™ Therapy** to configure the therapy unit for use with **V.A.C. VERAFLO™ Therapy** (page 44).

Select **V.A.C.® Therapy** to configure the therapy unit for use with **V.A.C.® Therapy** (page 81).

Select **PREVENA™ Therapy** to configure the therapy unit for use with **PREVENA™ Therapy** (page 109).

Select **ABTHERA™ Therapy** to configure the therapy unit for use with **ABTHERA™ Therapy** (page 127).

A new therapy mode can not be selected until the current therapy mode is stopped. The selection button for the inactive therapies will not be available.



If the V.A.C.ULTA™ Therapy Unit has been previously set up and the unit is power cycled (turned off then back on), the ***Startup*** Screen will display **Continue Therapy** and **QC Checklist**.

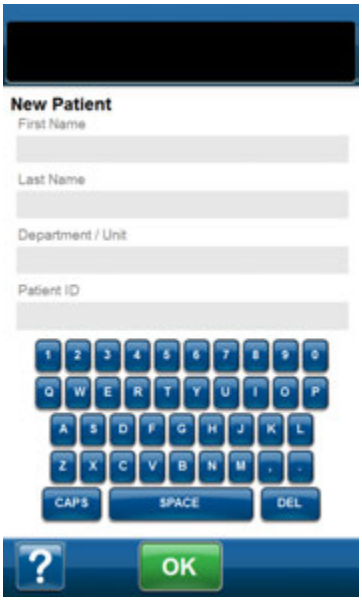
Continue Therapy - Select to accept **Warning** and return to previously used therapy ***Home*** screen (pages 50, 85, 110 and 129).

QC Checklist - Select to accept the **Warning** and proceed to Quality Checklist inspection process.

Accompanying Service Documentation is required to use QC Checklist functions. Please contact KCI for more information.

New Patient Screen

Use this screen to enter the patient's information into the V.A.C.ULTA™ Therapy Unit. Patient information is encrypted.



Therapy configuration may not display this screen.

Use the onscreen keyboard to enter the following:

- Patient's First Name
- Patient's Last Name
- Patient's Department / Unit
- Patient's (Identification) ID

Once this information has been entered, select **OK** to continue to the ***Choose Therapy*** screen.

At least one character must be entered into each entry row.

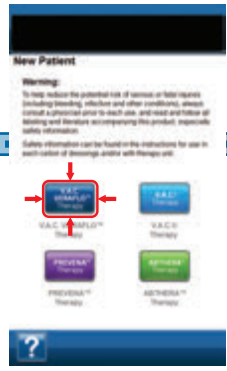
V.A.C. VERAFLO™ Therapy Configuration - Default Settings Overview

The following flow chart shows the basic steps required to configure **V.A.C. VERAFLO™ Therapy** using the **Default** settings. Refer to the pages listed for detailed information about individual screens and options.

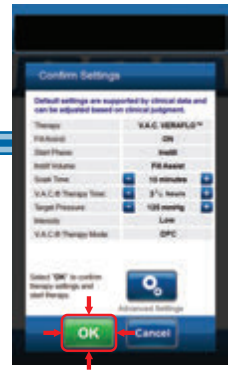
Press and hold **Power** button until light comes on.

Required for V.A.C. VERAFLO™ Therapy:

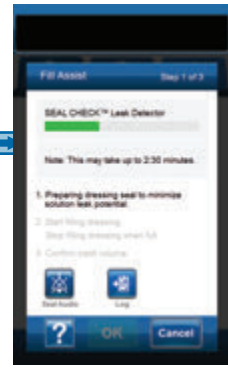
- Canister
- V.A.C. VERAFLO™ Dressing
- V.A.C. VERALINK™ Cassette 100 - 1000 mL solution bag / bottle



Select **V.A.C. VERAFLO™ Therapy** (page 42).

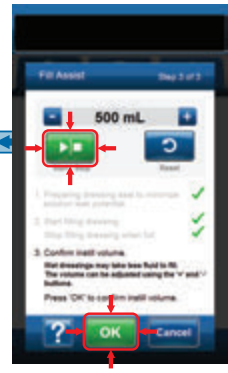


Select **OK** to accept default settings.

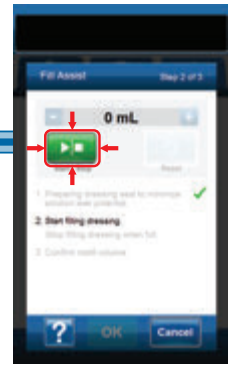


Fill Assist procedure will begin (could take up to 2 1/2 minutes to prepare the dressing seal and minimize solution leak potential).

Home Screen - **V.A.C. VERAFLO™ Therapy**.



Select **OK** to accept settings and begin **V.A.C. VERAFLO™ Therapy**.



Select **Start / Stop** to start instilling fluid into dressing. Select **Start / Stop** again to stop instilling fluid into the dressing.

Screen shots shown above are for representation only. Refer to the page numbers listed for a more detailed view and more detailed information.

Settings displayed will vary depending on settings defined by user.

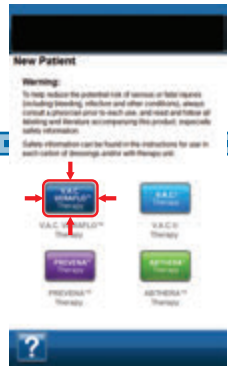
V.A.C. VERAFLO™ Therapy Configuration - Advanced User Defined Settings Overview

The following flow chart shows the basic steps required to configure **V.A.C. VERAFLO™ Therapy** with User defined settings including turning Fill Assist OFF. Refer to the following pages for detailed information about individual screens and options.

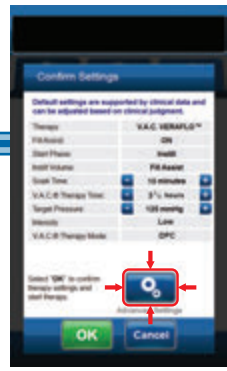
Press and hold **Power** button until light comes on.

Required for V.A.C. VERAFLO™ Therapy:

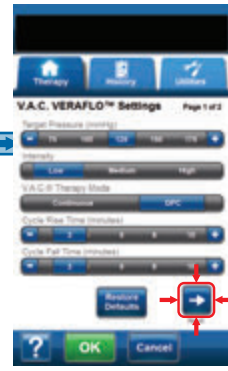
- Canister
- V.A.C. VERALINK™ Cassette 100 - 1000 mL solution bag / bottle



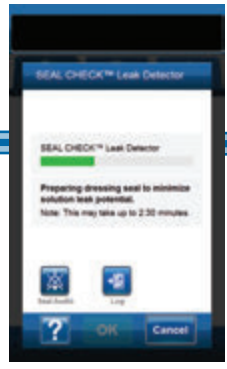
Select **V.A.C. VERAFLO™ Therapy** (page 42).



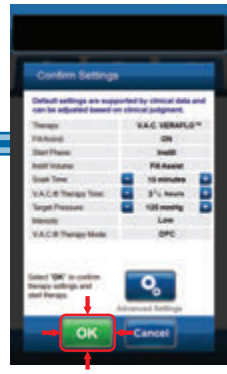
Select **Advanced Settings**.



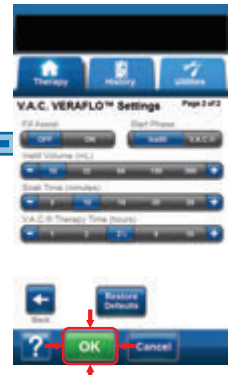
Configure **V.A.C.® Therapy** phase of **V.A.C. VERAFLO™ Therapy** as prescribed (page 46). Select **Next**.



Drawdown begins.



Select **OK** to accept settings..



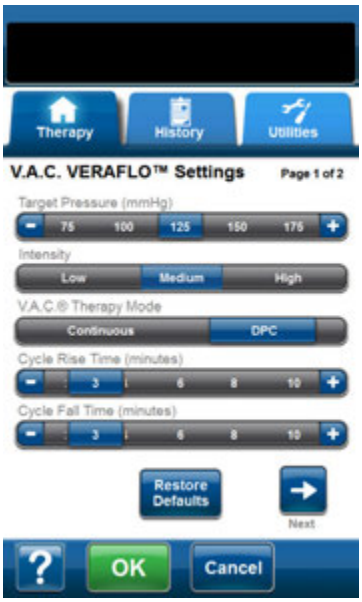
Configure Instill phase of **V.A.C. VERAFLO™ Therapy** as prescribed (page 46). Select **OK**.

Home screen - **V.A.C VeraFlo™ Therapy**

Screen shots shown above are for representation only. Refer to the page numbers listed for a more detailed view and more detailed information.

Settings displayed will vary depending on settings defined by user.

Configure V.A.C. VERAFLO™ Therapy - Advanced User Defined Settings



These screens are used to configure the V.A.C.ULTA™ Therapy Unit to deliver **V.A.C. VERAFLO™ Therapy**:

- **Target Pressure (mmHg)** - (**Default = 125 mmHg**) Prescribed negative pressure level for V.A.C.® Therapy phase. Target Pressure can be set from 50 - 200 mmHg in 25 mmHg increments.
- **Intensity** - (**Default = Medium**) Related to the time it takes to reach the target pressure after the initiation of therapy. The lower the intensity setting, the slower the target pressure will be reached. It is recommended that new patients begin therapy at the lowest intensity setting as this allows for slower increase of negative pressure once the foam is compressed in the wound. The intensity can remain at the minimum setting throughout the entire length of treatment, if desired.
- **V.A.C.® Therapy Mode** - (**Default = Continuous**) Available modes include **Continuous** and **DPC**. Continuous provides constant negative pressure at selected Target Pressure. DPC provides negative pressure between preset low pressure (25 mmHg) and selected Target Pressure.
- Cycle Rise Time - (Default = 3 minutes) Time used to transition from the preset low pressure (25 mmHg) to the selected target pressure while using DPC. Cycle Rise Time can be set from one minute to 10 minutes in one minute increments.
- Cycle Fall Time - (Default = 3 minutes) Time used to transition from the selected target pressure to the preset low pressure (25 mmHg) while using DPC. Cycle Fall Time can be set from one minute to 10 minutes in one minute increments.

1. Select desired value by selecting or sliding finger / stylus along bar. Use **+** / **-** to adjust above or below values shown.

- **Fill Assist** - (**Default = ON**) Fill Assist allows the user to monitor initial wound fill by manually starting and stopping instillation to determine correct instill volume after dressing is applied. Once determined, this volume will be the set point for each subsequent instill phase of **V.A.C. VERAFLO™ Therapy** (page 48).
- **Start Phase** - (**Default = Instill**) (**Default = 10 mL** if Fill Assist is Off). Sets first phase of **V.A.C. VERAFLO™ Therapy** (pages 14 and 38).
- **Soak Time (minutes)** - (**Default = 10 minutes**) Duration of time instilled solution will remain in wound during each soak phase of **V.A.C. VERAFLO™ Therapy**. Soak Time can be set from 1 second to 30 minutes with varying increments.
- **V.A.C.® Therapy Time (hours)** - (**Default = 3 1/2 hours**) Duration of time that negative pressure will be applied during each **V.A.C.® Therapy** phase of **V.A.C. VERAFLO™ Therapy**. **V.A.C.® Therapy** Time can be set from 3 minutes to 12 hours with varying increments.

2. Select **Next** to continue to the ***V.A.C. VERAFLO™ Settings (page 2 of 2)*** screen.

Select **Restore Defaults** to return all therapy settings to their defaults.

3. Once all settings have been entered or defaults restored, select **OK** to continue to the ***Confirm Settings*** screen. This screen allows the user to review the therapy settings that were selected on the ***V.A.C. VERAFLO™ Settings*** screen.

4. Use + / - to adjust above or below values shown.

Select **Advanced Settings** to return to the ***V.A.C. VERAFLO™ Therapy Settings*** screen to make any required adjustments.

5. Select **OK** to initiate therapy and continue to the ***SEAL CHECK™ Leak Detector*** screen.

OR

6. Select **Cancel** to return to the ***New Patient*** screen.

Fill Assist Screens

These screens will display the status of the Fill Assist sequence.

Drawdown can take up to two minutes and thirty seconds to prepare the dressing seal to minimize solution leak potential. During this drawdown, observe the dressing for leaks. The SEAL CHECK™ Leak Detector time is designed to help minimize the potential for leaks by pulling the drape against the skin and allowing the adhesive time to cure.

1. Fill Assist (**1**) will begin to draw down the dressing to prepare the dressing seal to minimize solution leak potential. Once the V.A.C.ULTA™ Therapy Unit has reached target pressure and determined that the dressing air leaks are small enough to continue **V.A.C. VERAFLO™ Therapy**, the therapy unit will continue to the ***Fill Assist*** screen.

Seal Audio - (**Default = OFF**) Audible tone used to find and repair leaks. Select to turn seal audio tone on or off.

Log - Used to record disposable component change (page 150).

2. Select **Start / Stop** on the ***Fill Assist*** screen to begin delivering solution to the wound (**2**).

During the use of Fill Assist it is possible to exceed the soak time for a solution. Consider elapsed time in comparison to the selected soak time while using this tool.

3. **Monitor the wound as it fills with solution.**

4. Select **Start / Stop** again to stop solution delivery when suitable fill volume has been delivered to the wound bed.

Overfilling wound may compromise dressing seals.

5. Use **+** / **-** to adjust the fluid volume if required.

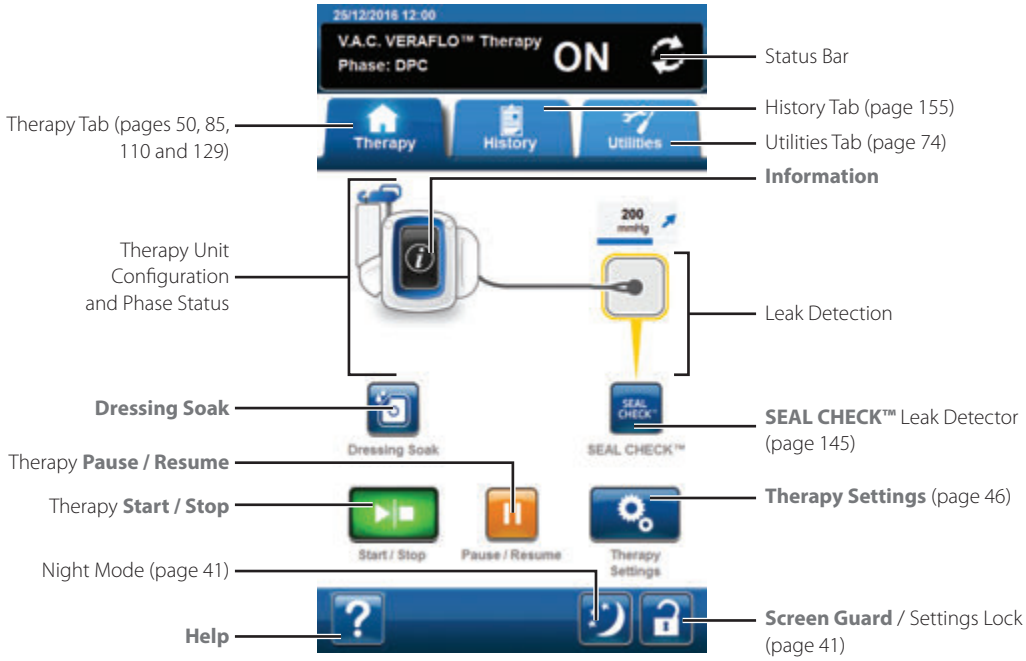
6. Select **OK** (**3**) to confirm the determined fluid volume as displayed on the ***Fill Assist*** screen and return to the ***Home*** screen (page 50). The therapy unit will then begin the soak phase.

If OK is not selected within 15 minutes of starting Fill Assist or within 15 minutes of stopping Fill Assist, the V.A.C.ULTA™ Therapy Unit will transition to V.A.C.® Therapy phase and the Fill Assist volume will not be recorded.

7. If wound has been over-filled, solution needs to be removed, or Fill Assist needs to be restarted, select **Reset** to remove solution from the wound and return to the ***Fill Assist*** screen.

Home Screen - V.A.C. VERAFLO™ Therapy

This ***Home*** screen is the main screen displayed by the V.A.C.ULTA™ Therapy Unit during **V.A.C. VERAFLO™ Therapy**. It is used to access important information about the Therapy Status.



Therapy phase and status (**ON**, **OFF** or **PAUSED**) will be displayed in the status bar at the top of the screen. The current therapy phase will also appear under the icon of the therapy unit or above the dressing.

The following options are available from the ***Home*** screen:

Therapy Settings - Use to change current therapy settings.

SEAL CHECK™ Leak Detector - An on-screen bar graph will indicate leak level and an audible tone will sound if unit detects a significant leak (page 145).

Information - Use to view a summary of therapy history and current therapy settings (page 51).

Start / Stop - Use to start or stop therapy.

Pause / Resume - Use to pause or resume therapy.

Help - Use to access the V.A.C.ULTA™ Therapy Unit's on-screen help features.

Leak Detection - If the therapy unit detects a leak in the system temporarily above the Leak Alarm threshold, the ***Home*** screen for **V.A.C. VERAFLO™ Therapy** will display a yellow box around the dressing. Refer to the instructions for use provided with the dressings for information on using excess drape material to seal any leak areas.

Refer to page 41 for a list of **Common Touch Screen Buttons** not described here.

Information Screens - V.A.C. VERAFLO™ Therapy

These screens will display the current therapy settings and a summary of therapy applied to the patient.

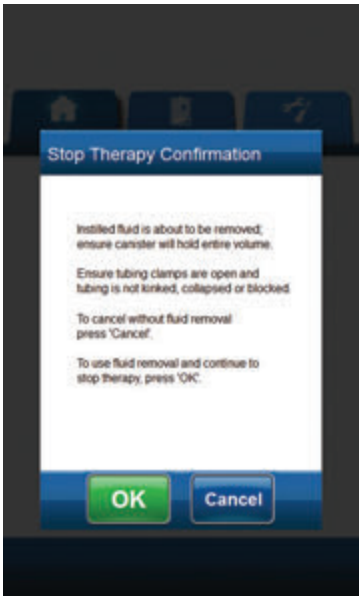
1. Select **Information** from the ***Home*** screen to continue to the ***Therapy Summary*** tab. Use this tab to review the Therapy Start Date, Therapy Time, V.A.C.® Time, Soak Time, Therapy Cycles and Instilled Volume. If the Log feature is used, the date and time for Canister Last Changed, Cassette Last Changed, Dressing Last Changed and Solution Last Changed will also be displayed.

2. Select **Current Settings** to continue to the ***Current Settings*** screen. Use this tab to review the current therapy settings.

3. Select **Change Settings** to continue to the ***Confirm Settings*** screen (page 47).

4. Select ***Exit*** to return to the ***Home*** screen for **V.A.C. VERAFLO™ Therapy**.

Stop V.A.C. VERAFLO™ Therapy Confirmation

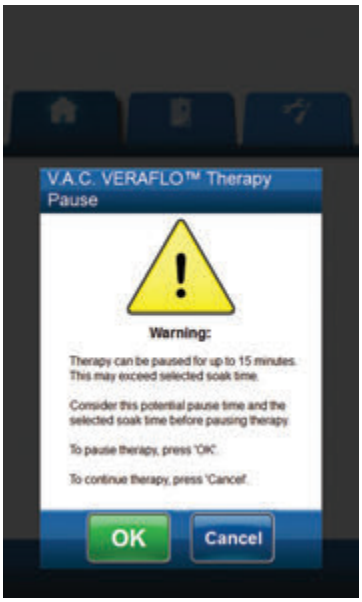


1. If therapy is being provided, select **Start / Stop** from the ***Home*** screen to continue to the ***Stop Therapy Confirmation*** screen.

2. Select **OK** to stop therapy. Select **Cancel** to return to the ***Home*** screen without stopping therapy.

Instilled fluid will be removed; ensure canister can hold the entire volume. Ensure tubing clamps are open and tubing is not kinked, collapsed or blocked.

V.A.C. VERAFLO™ Therapy Paused



1. If therapy is being provided, select **Pause / Resume** from the ***Home*** screen to continue to the ***V.A.C. VERAFLO™ Therapy Pause*** screen.

2. Select **OK** to pause therapy. Select **Cancel** to return to the ***Home*** screen for **V.A.C. VERAFLO™ Therapy** without pausing therapy.

Therapy can be paused for up to 15 minutes. This may exceed selected soak time. Consider this pause time and the selected soak time before pausing therapy.

V.A.C. VERAFLO™ Therapy Alerts and Alarms

The following alerts and alarms may appear on the touch screen during **V.A.C. VERAFLO™ Therapy**.

Alerts and alarms are accompanied by a repeating audible tone.

Following initiation of therapy, if an audible tone is not heard when SEAL CHECK™ Leak Detector is displayed and Seal Audio tone is turned ON, the alarms may not be working properly. Contact KCI for more information. Alarms are intended to be heard when facing the therapy unit at a maximum of one meter away. If two or more alarm conditions are present, only the highest priority alarm will be displayed.

Low Priority Alert Condition - Displayed on the touch screen when the V.A.C.ULTA™ Therapy Unit detects a condition that requires attention. Alerts will be accompanied by a repeating audible tone approximately every 20 seconds (two beeps).

Medium Priority Alarm Condition - Displayed on the touch screen when the V.A.C.ULTA™ Therapy Unit detects a condition that requires prompt attention in order to ensure the prescribed therapy is being delivered. Alarms will be accompanied by a repeating audible tone approximately every two seconds (three beeps) and a flashing screen title.

Select **Seal Audio** to turn the audible tone ON.

Select **Help** for more information regarding alarm resolution.

If alert or alarm conditions cannot be resolved, contact KCI.

V.A.C. VERAFLO™ Therapy Blockage Alert

Low Priority Alert - This alert screen appears when the V.A.C.ULTA™ Therapy Unit has detected a potential blockage in the V.A.C.® Therapy line. This alert will be accompanied by a repeating audible tone.

To resolve this alert:

1. Select **Audio Pause** to silence alert for two minutes during troubleshooting.

2. Ensure clamps on the V.A.C.® Therapy tubing on the V.A.C. VERAT.R.A.C.™ Pad or V.A.C. VERAT.R.A.C. DUO™ Tube Set and canister tubing are open.

3. Ensure tubing is not kinked, crimped, or blocked in any way.

4. If the ***V.A.C.® Therapy Blockage Alert*** remains after completing steps 2 and 3, lower the therapy unit and tubing to be level with or below the wound site. If the alert is resolved by lowering the unit, normal use may resume.

5. Select **Reset** to return to the ***Home*** screen.

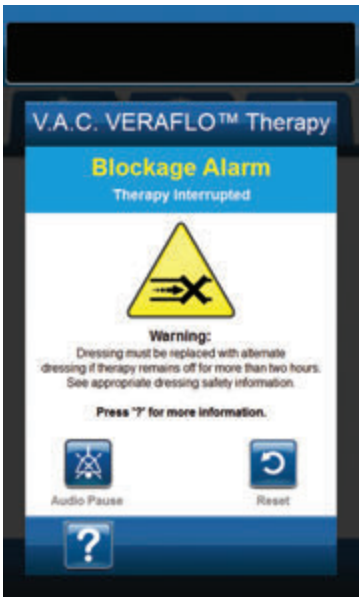
6. Ensure therapy is ON by checking the status bar (page 50). If not, select **Start / Stop** to restart therapy.

The V.A.C.ULTA™ Therapy Unit will continue to attempt to apply therapy during this alert.

If alarm condition cannot be resolved, contact KCI.

V.A.C. VERAFLO™ Therapy Blockage Alarm (Therapy Interrupted)

Medium Priority Alarm - This alarm screen appears when a blockage is present in the V.A.C.® Therapy line. This alarm will be accompanied by a repeating audible tone.



To resolve this alarm:

1. Select **Audio Pause** to silence alarm for two minutes during troubleshooting.

2. Ensure clamps on the V.A.C.® Therapy tubing on the V.A.C. VERAT.R.A.C.™ Pad or V.A.C. VERAT.R.A.C. DUO™ Tube Set and canister tubing are open.

3. Ensure tubing is not kinked, crimped, or blocked in any way.

4. If the ***V.A.C.® Therapy Blockage Alarm (Therapy Interrupted)*** remains after completing steps 2 and 3, lower the therapy unit and tubing to be level with or below the wound site. If the alarm is resolved by lowering the unit, normal use may resume.

5. Select **Reset** to return to the ***Home*** screen.

6. Ensure therapy is ON by checking the status bar (page 50). If not, select **Start / Stop** to restart therapy.

Therapy unit remains on; however, negative pressure at the wound site may be below therapeutic value.

If alarm condition cannot be resolved, contact KCI.

Certain KCI Dressings must be replaced with an alternate dressing if therapy is interrupted or off for more than two hours. See the Safety Information Sheet provided with the individual dressing for further information.

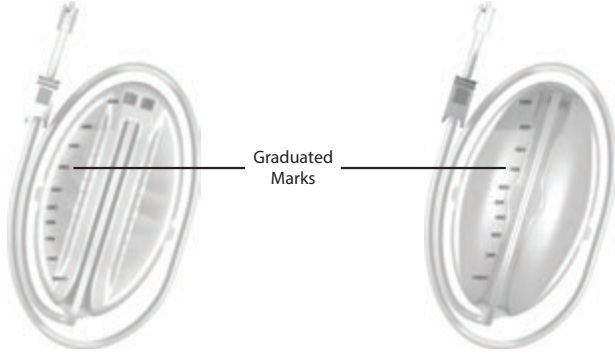
V.A.C. VERAFLO™ Therapy Canister Full Alarm (Therapy Interrupted)

Medium Priority Alarm - This alarm screen appears when the canister is full and should be replaced. This alarm will be accompanied by a repeating audible tone.

To resolve this alarm:

1. Select **Audio Pause** to silence alarm for two minutes during troubleshooting.

2. Check if canister is full by comparing the level of fluid to the graduated marks on the canister.



A full canister is approximately 300 mL, 500 mL or 1000 mL depending on canister used. Canister release button will be flashing.

3. If canister is not full, select **Reset** to return to the ***Home*** screen.

4. If canister is full, change canister and select **Reset** on this screen to return to the ***Home*** screen. See the **Changing the Canister** section of this manual (page 34) for additional information.

5. Select **Pause / Resume** to restart therapy.

Certain KCI Dressings must be replaced with an alternate dressing if therapy is interrupted or off for more than two hours. See the Safety Information Sheet provided with the individual dressing for further information.

V.A.C. VERAFLO™ Therapy Canister Not Engaged Alarm

Medium Priority Alarm - This alarm screen appears when the canister is not fully inserted and / or properly latched. This alarm will be accompanied by a repeating audible tone.

To resolve this alarm:

1. Select **Audio Pause** to silence alarm for two minutes during troubleshooting.

2. Remove the canister by pressing the **Canister Release** button (page 18) on the unit.

3. Inspect the canister and V.A.C.ULTA™ Therapy Unit to ensure no foreign objects or debris interfere with the canister and therapy unit's mating surfaces.

4. Ensure both seals are present and seated completely (page 19). If seals are missing or damaged, contact KCI.

5. Re-attach the canister to the V.A.C.ULTA™ Therapy Unit ensuring that the canister is fully engaged and latched (page 32). An audible click indicates that the canister is properly installed.

6. Select **Reset** to return to the ***Home*** screen.

7. Select **Pause / Resume** to restart therapy.

8. If this alarm continues to appear, repeat steps 2 - 7 with a new canister.

If alarm condition cannot be resolved, contact KCI.

V.A.C. VERAFLO™ Therapy Therapy Inactive Alarm

Medium Priority Alarm - This alarm screen appears when therapy (**V.A.C. VERAFLO™ Therapy**) has been off or paused for more than 15 minutes (with the unit powered on) . This alarm will be accompanied by a repeating audible tone.

To resolve this alarm:

1. Select **Audio Pause** to silence alarm for two minutes during troubleshooting.

2. Select **Reset** to return to the ***Home*** screen.

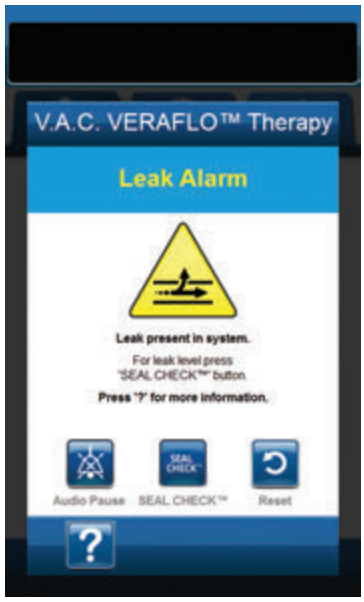
3. Select **Start / Stop** to restart therapy.

4. If therapy is not desired, turn the V.A.C.ULTA™ Therapy Unit off by using the **Power** button on the front of the unit.

Certain KCI Dressings must be replaced with an alternate dressing if therapy is interrupted or off for more than two hours. See the Safety Information Sheet provided with the individual dressing for further information.

V.A.C. VERAFLO™ Therapy Leak Alarm

Medium Priority Alarm - This alarm screen appears when a significant negative pressure leak has been detected. If this alarm is not resolved in three minutes, therapy will be interrupted. This alarm will be accompanied by a repeating audible tone.



To resolve this alarm:

1. Select **Audio Pause** to silence alarm for two minutes during troubleshooting.

2. Ensure connector between dressing tubing and canister tubing is properly locked.

3. Ensure canister is fully engaged. (See **Canister Not Engaged Alarm**, page 57).

4. Select **SEAL CHECK™** to access the SEAL CHECK™ Leak Detector. Refer to the **SEAL CHECK™ Leak Detector** section (page 145) of this manual for details on how to use the SEAL CHECK™ Leak Detector and how to repair leaks.

5. Once the leak is resolved using the SEAL CHECK™ Leak Detector, select **Exit** on the ***SEAL CHECK™ Leak Detector*** screen to return to the ***V.A.C. VERAFLO™ Therapy Leak Alarm*** screen.

6. Select **Reset** to return to the ***Home*** screen.

7. Ensure therapy is ON by checking the Status Bar (page 50). If not, select **Start / Stop** to restart therapy.

If this alarm is not resolved within three minutes, the V.A.C. VERAFLO™ Therapy Leak Alarm (Therapy Interrupted) will appear and therapy will stop.

Refer to V.A.C. VERAFLO™ Therapy Leak Alarm (Therapy Interrupted) section of this manual (page 60) for procedures to restart therapy.

V.A.C. VERAFLO™ Therapy Leak Alarm (Therapy Interrupted)

Medium Priority Alarm - This alarm screen appears when a detected negative pressure leak has not been resolved and therapy has been interrupted. This alarm will be accompanied by a repeating audible tone.

To resolve this alarm:

1. Select **Audio Pause** to silence alarm for two minutes during troubleshooting.
2. Ensure connector between dressing tubing and canister tubing is properly locked.
3. Ensure canister is fully engaged. (See **Canister Not Engaged Alarm**, page 57).

4. Select **Reset** to return to the ***Home*** screen.

5. Restart therapy by selecting **Start / Stop**.

6. Select **SEAL CHECK™** to access the SEAL CHECK™ Leak Detector. Refer to the **SEAL CHECK™ Leak Detector** section (page 145) of this manual for details on how to use the SEAL CHECK™ Leak Detector and how to repair leaks.
7. Once the leak is resolved using the SEAL CHECK™ Leak Detector, select **Exit** on the ***SEAL CHECK™ Leak Detector*** screen to return to the ***Home*** screen.

If the leak condition is not resolved, an alarm screen will reappear after several minutes.

If alarm condition cannot be resolved, contact KCI.

Certain KCI Dressings must be replaced with an alternate dressing if therapy is interrupted or off for more than two hours. See the Safety Information Sheet provided with the individual dressing for further information.

V.A.C. VERAFLO™ Therapy Low Pressure Alarm (Therapy Interrupted)

Medium Priority Alarm - This alarm screen appears when the V.A.C.ULTA™ Therapy Unit has not reached the target therapy negative pressure setting and negative pressure at the wound may be below set pressure, potentially compromising therapeutic benefits. This alarm is accompanied by a repeating audible tone.

To resolve this alarm:

1. Select **Audio Pause** to silence alarm for two minutes during troubleshooting.

2. Ensure clamps on the V.A.C.® Therapy tubing on the V.A.C. VERAT.R.A.C.™ Pad or V.A.C. VERAT.R.A.C. DUO™ Tube Set and canister tubing are open.

3. Ensure tubing is not kinked, crimped, or blocked in any way.

4. If the ***V.A.C.® Therapy Low Pressure Alarm (Therapy Interrupted)*** remains after completing steps 2 and 3, lower the therapy unit and tubing to be level with or below the wound site. If the alarm is resolved by lowering the unit, normal use may resume.

5. Select **Reset** to return to the ***Home Screen***.

6. Ensure therapy is ON by checking the status bar (page 50). If not, select **Start / Stop** to restart therapy.

Therapy unit remains on; however, negative pressure at the wound site may be below therapeutic value.

If alert condition cannot be resolved, contact KCI.

Certain KCI Dressings must be replaced with an alternate dressing if therapy is interrupted or off for more than two hours. See the Safety Information Sheet provided with the individual dressing for further information.

V.A.C. VERAFLO™ Therapy V.A.C. VERALINK™ Not Engaged Alert

Low Priority Alert - This alert screen appears when the V.A.C. VERALINK™ Cassette is not fully seated and / or properly latched. This alert will be accompanied by a repeating audible tone.

During V.A.C. VERAFLO™ Therapy the V.A.C.ULTA™ Therapy Unit will transition to the Soak Phase upon initiation of this alert and will continue to the V.A.C.® Therapy Phase before repeating the cycle. If V.A.C. VERALINK™ Cassette is correctly engaged prior to the completion of the V.A.C.® Therapy Phase, the V.A.C. VERAFLO™ Therapy cycle will not be interrupted.

To resolve this alert:

1. Select **Audio Pause** to silence alert for two minutes during troubleshooting.
2. Remove the V.A.C. VERALINK™ Cassette from the unit by pushing down on the cassette latch release tab (page 28).
3. Inspect the V.A.C. VERALINK™ Cassette and the V.A.C.ULTA™ Therapy Unit to ensure no foreign objects or debris interfere with the cassette and the therapy unit connection points.
4. Ensure the cassette's pivot connection (on the end with the tubing spike) is securely engaged within the pivot slot on the therapy unit (page 28).
5. Re-attach the V.A.C. VERALINK™ Cassette to the therapy unit ensuring that the cassette is fully engaged and latched (page 28). An audible click indicates that the cassette is properly installed.

Once the V.A.C. VERALINK™ Cassette is properly installed, the V.A.C. VERALINK™ Not Engaged Alert screen will automatically clear.

OR

6. Select **Reset** to return to the ***Home*** screen.
7. Ensure therapy is ON by checking the status bar (page 50). If not, select **Start / Stop** to restart therapy.
8. If this alert condition continues to appear, repeat steps 2 - 7 with a new V.A.C. VERALINK™ Cassette.

If alert condition cannot be resolved, contact KCI.

V.A.C. VERAFLO™ Therapy Solution Bag / Bottle Empty Alert

Low Priority Alert -This alert screen appears when there is no instillation fluid in the solution bag / bottle. This alert will be accompanied by a repeating audible tone.

During V.A.C. VERAFLO™ Therapy the V.A.C.ULTA™ Therapy Unit will transition to the Soak Phase upon initiation of this alert and will continue to the V.A.C.® Therapy Phase before repeating the cycle. If solution bag / bottle is changed prior to the completion of the V.A.C.® Therapy Phase, the V.A.C. VERAFLO™ Therapy cycle will not be interrupted.

To resolve this alert:

1. Select **Audio Pause** to silence alert for two minutes during troubleshooting.
2. Remove empty solution bag / bottle from V.A.C. VERALINK™ Cassette.
3. Attach new solution bag / bottle. Refer to **Hang Solution Container Bag / Bottle** section of this manual (page 30) for more information.
4. Place new bag / bottle on the adjustable solution container hanger arm (page 30).
5. Select **Log** to enter the solution bag / bottle change. Refer to the ***Log*** screen section (page 150) for more information.
6. Select **Reset** to return to the ***Home*** screen.
7. Ensure therapy is ON by checking the status bar (page 50). If not, select **Start / Stop** to restart therapy.

V.A.C. VERAFLO™ Therapy Fill Assist Inactive Alert

Low Priority Alert - This alert screen appears if the Fill Assist volume has not been accepted within 15 minutes of using Fill Assist. This alert will be accompanied by a repeating audible tone

To resolve this alert:

1. Select **Audio Pause** to silence alert for two minutes during troubleshooting.

2. Select **Reset** to return to the ***Home*** screen.

3. Select **Therapy Settings** on the ***Home*** screen (page 50).

4. Reconfigure therapy (page 46).

If alert condition cannot be resolved, contact KCI.

V.A.C. VERAFLO™ Therapy Pressure Deviation Alarm (Therapy Interrupted)

Medium Priority Alarm - This alarm screen appears when the wound site positive pressure has exceeded its allowable limits. This alarm will be accompanied by a repeating audible tone.

During V.A.C. VERAFLO™ Therapy the V.A.C.ULTA™ Therapy Unit will transition to the Soak Phase upon initiation of this alarm and will continue to the V.A.C.® Therapy Phase before repeating the cycle. If pressure deviation condition is resolved prior to completion of the V.A.C.® Therapy Phase, the V.A.C. VERAFLO™ Therapy cycle will not be interrupted.

To resolve this alarm:

1. Select **Audio Pause** to silence alarm for two minutes during troubleshooting.
2. Ensure clamps on the V.A.C. VERAT.R.A.C.™ Pad or the V.A.C. VERAT.R.A.C. DUO™ Tube Set and V.A.C. VERALINK™ Cassette tubing are open.
3. Ensure that the tubing is not kinked, crimped or blocked in any way.
4. If the V.A.C. VERAFLO™ Therapy Pressure Deviation Alarm (Therapy Interrupted) remains after completing steps 2 and 3, check patient positioning or any external compression devices that may impede flow. Remove external compression device.
5. Select **Reset** to return to the ***Home*** screen.
6. Ensure therapy is ON by checking the status bar (page 50). If not, select **Start / Stop** to restart therapy.

If alarm condition cannot be resolved, contact KCI.

Certain KCI Dressings must be replaced with an alternate dressing if therapy is interrupted or off for more than two hours. See the Safety Information Sheet provided with the individual dressing for further information.

V.A.C. VERAFLO™ Therapy Instill Tube Blockage Alert (Therapy Interrupted)

Low Priority Alert - This alert screen appears when a blockage is present in the instillation line of the V.A.C. VERAT.R.A.C.™ Pad or V.A.C. VERAT.R.A.C. DUO™ Tube Set. This alert will be accompanied by a repeating audible tone.

During V.A.C. VERAFLO™ Therapy the V.A.C.ULTA™ Therapy Unit will transition to the Soak Phase upon initiation of this alert and will continue to the V.A.C.® Therapy Phase before repeating the cycle. If blockage is resolved prior to completion of the V.A.C.® Therapy Phase, the V.A.C. VERAFLO™ Therapy cycle will not be interrupted.

To resolve this alert:

1. Select **Audio Pause** to silence alert for two minutes during troubleshooting.
2. Ensure clamps on the V.A.C. VERAT.R.A.C.™ Pad or V.A.C. VERAT.R.A.C. DUO™ Tube Set and V.A.C. VERALINK™ Cassette are open.
3. Ensure that the tubing is not kinked, crimped, or blocked in any way.
4. Ensure the V.A.C. VERALINK™ Cassette is fully engaged and latched. See the **Attaching the V.A.C. VERALINK™ Cassette to the V.A.C.ULTA™ Therapy Unit** section (page 28) of this manual for more information.
5. Ensure that the instillation solution in the V.A.C. VERALINK™ Cassette tubing is still liquid and flows freely. If the solution has degraded to a thicker consistency, change any or all of the following:
   - V.A.C. VERALINK™ Cassette
   - V.A.C. VERAT.R.A.C.™ Pad or V.A.C. VERAT.R.A.C. DUO™ Tube Set
   - Solution bag / bottle
6. If the V.A.C. VERAFLO™ Therapy Instill Tube Blockage Alert remains after completing steps 2 - 5, check patient positioning or any external compression devices that may impede flow. If applicable, remove external compression device.
7. Select **Reset** to return to the ***Home*** screen.

Alert screen will clear when the blockage is corrected.

8. Ensure therapy is ON by checking the status bar (page 50). If not, select **Start / Stop** to restart therapy.

If alarm condition cannot be resolved, contact KCI.

Certain KCI Dressings must be replaced with an alternate dressing if therapy is interrupted or off for more than two hours. See the Safety Information Sheet provided with the individual dressing for further information.

V.A.C. VERAFLO™ Therapy Battery Low Alert

Low Priority Alert - This alert screen appears approximately two hours before the battery power level is too low to support continued operation of the V.A.C.ULTA™ Therapy Unit. This alert will be accompanied by a repeating audible tone.

To resolve this alert:

1. Select **Audio Pause** to silence alarm for two minutes during troubleshooting.

2. Connect the therapy unit to a wall outlet using the KCI supplied power supply to recharge battery. An amber light at the bottom of the touch screen and a battery charge icon indicate the unit is charging. Refer to the **Charge Battery** section of this manual (page 23) for more information.

Once the V.A.C.ULTA™ Therapy Unit is plugged into a wall outlet, the Battery Low Alert screen will automatically clear.

OR

3. Select **Reset** to return to the ***Home*** screen.

Therapy continues.

V.A.C. VERAFLO™ Therapy Battery Critical Alarm

Medium Priority Alarm - This alarm screen appears approximately 30 minutes before the battery power level is too low to support continued operation of the V.A.C.ULTA™ Therapy Unit. This alarm will be accompanied by a repeating audible tone.

To resolve this alarm:

1. Select **Audio Pause** to silence alarm for two minutes during troubleshooting.

2. Connect the therapy unit to a wall outlet using KCI supplied power supply to recharge battery. An amber light at the bottom of the touch screen and a battery charge icon indicates the unit is charging. Refer to the **Charge Battery** section of this manual (page 23) for more information.

Once the V.A.C.ULTA™ Therapy Unit is plugged into a wall outlet, the Battery Critical Alarm screen will automatically clear.

3. If the ***Battery Critical Alarm*** screen does not automatically clear, select **Reset** to return to the ***Home*** screen.

V.A.C.® Therapy continues and V.A.C. VERAFLO™ Therapy transitions to V.A.C.® Therapy phase after approximately five minutes; however, if this alarm is not resolved within approximately thirty minutes, therapy will be interrupted.

4. Ensure therapy is ON by checking the status bar (page 50). If not, select **Start / Stop** to restart therapy.

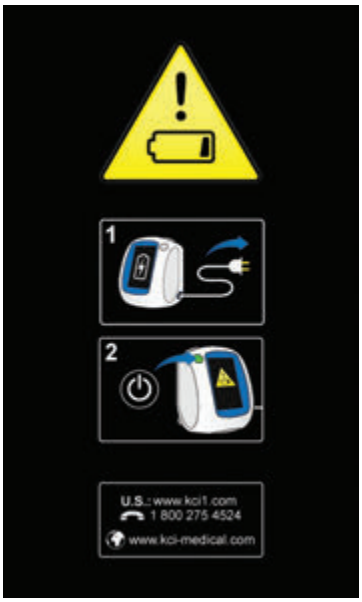
The V.A.C.ULTA™ Therapy must be plugged into a wall outlet in order to continue therapy.

Alarm logs and settings are not lost in the case of a total power loss or if the unit is power cycled (turned off then back on).

Certain KCI Dressings must be replaced with an alternate dressing if therapy is interrupted or off for more than two hours. See the Safety Information Sheet provided with the individual dressing for further information.

Battery Exhausted Alarm

Medium Priority Alarm - This alarm screen appears when the battery power level is too low to power on the V.A.C.ULTA™ Therapy Unit.



To resolve this alarm:

1. Connect the therapy unit to a wall outlet using KCI supplied power supply to recharge battery. An amber light at the bottom of the touch screen and a battery charge icon indicates the unit is charging. Refer to the **Charge Battery** section of this manual (page 23) for more information.

2. Power the V.A.C.ULTA™ Therapy Unit on and initiate therapy. Refer to the **Power the V.A.C.ULTA™ Therapy Unit On or Off** section of this manual (page 42) for more information.

V.A.C. VERAFLO™ Therapy Internal Temperature Alert

Low Priority Alert - This alert screen appears when the internal temperature of the V.A.C.ULTA™ Therapy Unit is outside its specified limits. This alert will be accompanied by a repeating audible tone.

Therapy will continue while this alert is active. The touch screen will be turned off after five minutes of inactivity. The screen will illuminate when touched. Battery charging is stopped.

To resolve this alert:

1. Select **Audio Pause** to silence alert for two minutes during troubleshooting.

2. Move the therapy unit to an environment with an operational temperature range as detailed in the **Specifications** section of this manual (page 194).

It may take up to two hours for the therapy unit to return to operating temperatures.

3. Select **Reset** to return to the ***Home*** screen.

Therapy continues.

If alarm condition cannot be resolved, contact KCI.

Certain KCI Dressings must be replaced with an alternate dressing if therapy is interrupted or off for more than two hours. See the Safety Information Sheet provided with the individual dressing for further information.

V.A.C. VERAFLO™ Therapy System Error Alarm (Therapy Interrupted) (after Power On)

Medium Priority Alarm - This alarm screen appears when there is a system fault within the V.A.C.ULTA™ Therapy Unit after it has been powered on. Several different types of system errors may occur. A number will appear next to **Error Code** that represents the diagnostic code of the system fault. This alarm will be accompanied by a repeating audible tone.

To resolve this alarm:

1. Select **Audio Pause** to silence alarm for two minutes during troubleshooting.
2. Record the Error Code number.
3. Power the unit off and then on using the **Power** button on the front of the unit (page 18).

If alarm condition cannot be resolved, contact KCI.

Certain KCI Dressings must be replaced with an alternate dressing if therapy is interrupted or off for more than two hours. See the Safety Information Sheet provided with the individual dressing for further information.

System Error Alarm (at Power On)

Medium Priority Alarm - This alarm screen appears when there is a system fault within the V.A.C.ULTA™ Therapy Unit while the unit is powering on. "00000001" represents the diagnostic code of the system fault. This alarm will be accompanied by a repeating audible tone.

To resolve this alarm:

1. Record the Error Code number (00000001).

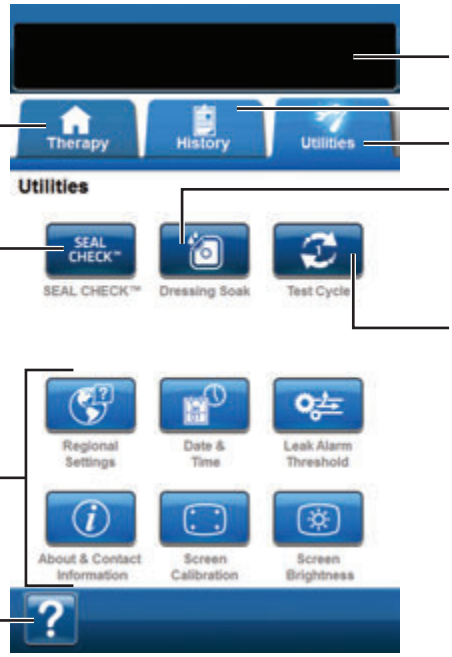
2. Power the unit off and then on using the **Power** button on the front of the unit (page 18).

If alarm condition cannot be resolved, contact KCI.

Certain KCI Dressings must be replaced with an alternate dressing if therapy is interrupted or off for more than two hours. See the Safety Information Sheet provided with the individual dressing for further information.

Utilities Tab - V.A.C. VERAFLO™ Therapy

Use the ***Utilities Tab*** screen to set preferences for the V.A.C.ULTA™ Therapy Unit. Certain selections are available no matter what therapy is active. Those selections are discussed in the **Utilities Tab** chapter. Selections that are unique to the selected therapy are detailed below.



The following options are available from the ***Utilities Tab*** Home screen:

SEAL CHECK™ Leak Detector - An on-screen bar graph will indicate leak level and an audible tone will sound if unit detects a significant leak (page 146).

Dressing Soak - Use to soak the dressing with solution in preparation for a dressing change (page 75).

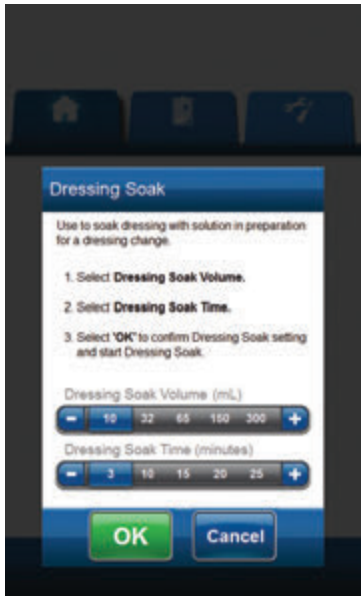
Test Cycle - Use to complete an abbreviated V.A.C. VERAFLO™ Therapy cycle. Each phase of the cycle will be tested to ensure system is set up and functioning correctly (page 79).

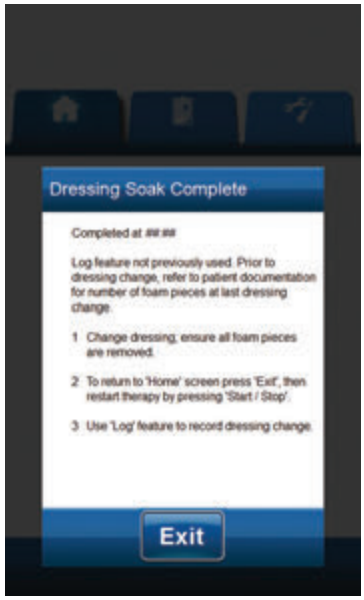
Help - Use to access the V.A.C.ULTA™ Therapy Unit's on-screen help features.

Dressing Soak

Use to soak the dressing with solution in preparation for a dressing change.

If the Dressing Soak tool is available for selection, the Dressing Soak icon on the Home screen or Utilities Tab (V.A.C. VERAFLO™ Therapy and V.A.C.® Therapy only) will be blue.





Dressing Soak selected while therapy is idle:

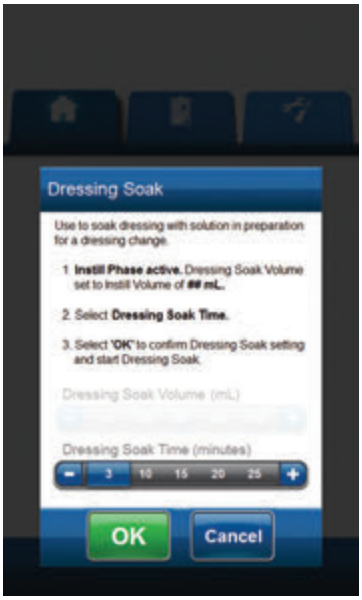
1. Ensure that both the V.A.C.® canister tubing and instillation line are properly connected.
2. Ensure that all four tubing clamps are open.
3. Ensure that the V.A.C. VERALINK™ Cassette is properly installed (page 28).
4. Ensure that the canister has adequate capacity remaining for the dressing change.

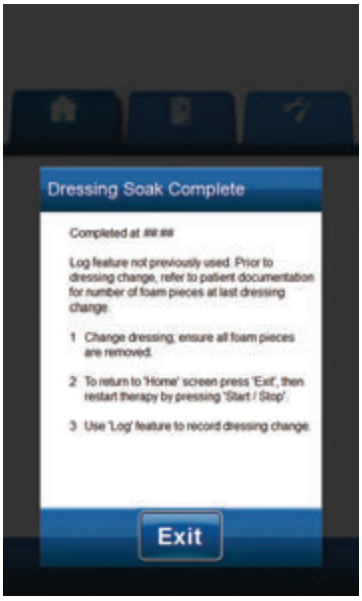
5. Select **Dressing Soak** from the ***Home*** screen or ***Utilities Tab*** to continue to the ***Dressing Soak*** screen.
6. Select the target **Dressing Soak Volume (mL)**.
7. Select the target **Dressing Soak Time (minutes)**.

8. Select **OK** to confirm settings and return to the ***Home*** screen or ***Utilities Tab***.
9. The V.A.C.ULTA™ Therapy Unit will complete the Instill, Soak, and fluid removal phases. Therapy phase will be displayed in the status bar (page 50) at the top of the screen. The current therapy status will also appear under the icon of the therapy unit along with time or fluid amount (during the **Instill** phase) remaining.
10. Once the Dressing Soak fluid removal phase is complete, the dressing can be removed.

11. Select **Exit** to return to the ***Home*** screen or ***Utilities Tab***.

Refer to the appropriate dressing Instructions for Use for safety information and procedures to change the dressing.





Dressing Soak selected during Instill Phase:

1. Select **Dressing Soak** from the ***Home*** screen or ***Utilities Tab*** to continue to the ***Dressing Soak*** screen.

2. Ensure that both the V.A.C.® canister tubing and instillation line are properly connected.

3. Ensure that all four tubing clamps are open.

4. Ensure that the canister has adequate capacity remaining for the dressing change.

5. Select the target **Dressing Soak Time (minutes)**.

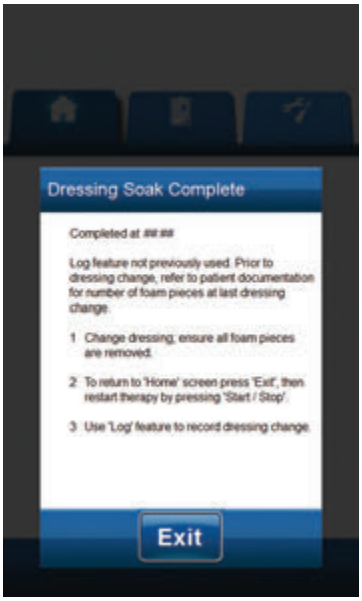
6. Select **OK** to confirm settings and return to the ***Home*** screen or ***Utilities Tab***.

7. The V.A.C.ULTA™ Therapy Unit will complete the Instill, Soak, and fluid removal phases. Therapy will be displayed in the status bar (page 50) at the top of the screen. The current therapy status will also appear under the icon of the therapy unit along with time or fluid amount (during the **Instill** phase) remaining.

8. Once the Dressing Soak fluid removal phase is complete, the dressing can be removed.

9. Select **Exit** to return to the ***Home*** screen or ***Utilities Tab***.

Refer to the appropriate dressing Instructions for Use for safety information and procedures to change the dressing.



Dressing Soak selected during Soak Phase:

1. Select **Dressing Soak** from the ***Home*** screen or ***Utilities Tab*** to begin Dressing Soak.

2. Ensure that both the V.A.C.® canister tubing and instillation line are properly connected.

3. Ensure that all four tubing clamps are open.

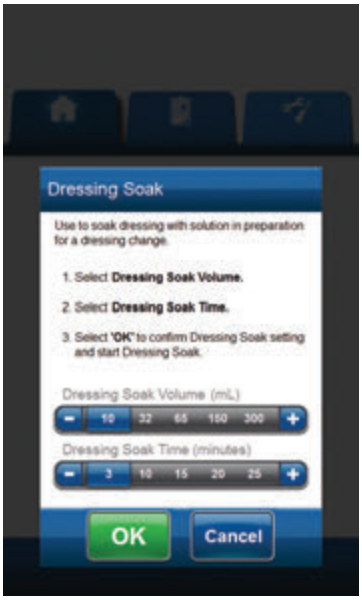
4. Ensure that the canister has adequate capacity remaining for the dressing change.

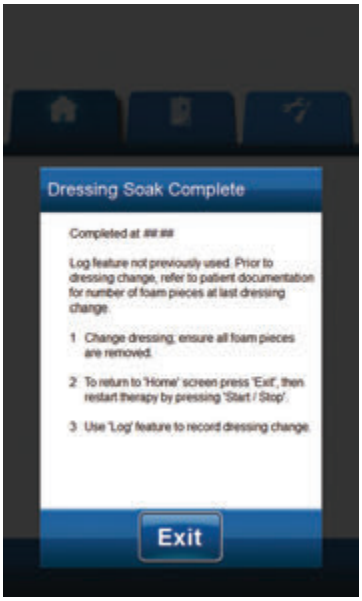
5. The V.A.C.ULTA™ Therapy Unit will complete the Soak and fluid removal phases. Therapy will be displayed in the status bar (page 50) at the top of the screen. The current therapy status will also appear under the icon of the therapy unit along with time or fluid amount (during the **Instill** phase) remaining.

6. Once the Dressing Soak fluid removal phase is complete, the dressing can be removed.

7. Select **Exit** to return to the ***Home*** screen or ***Utilities Tab***.

Refer to the appropriate dressing Instructions for Use for safety information and procedures to change the dressing.





Dressing Soak selected during V.A.C.® Therapy Phase:

1. Ensure that the instillation line is properly connected.
2. Ensure that all four tubing clamps are open.
3. Ensure that the V.A.C. VERALINK™ Cassette is properly installed (page 28).
4. Ensure that the canister has adequate capacity remaining for the dressing change.

5. Select **Dressing Soak** from the ***Home*** screen or ***Utilities Tab*** to continue to the ***Dressing Soak*** screen.
6. Select the target **Dressing Soak Volume (mL)**.
7. Select the target **Dressing Soak Time (minutes)**.

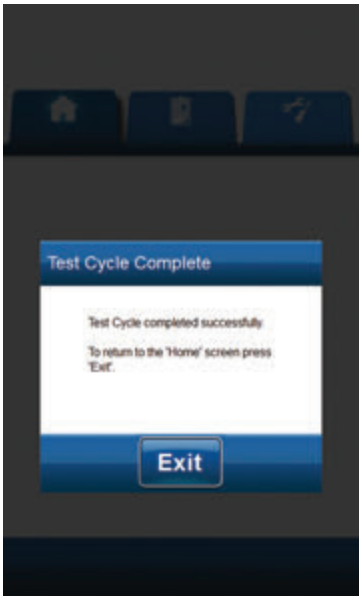
8. Select **OK** to confirm settings and return to the ***Home*** screen or ***Utilities Tab***.
9. The V.A.C.ULTA™ Therapy Unit will complete the Instill, Soak, and fluid removal phases. Therapy phase will be displayed in the status bar (page 50) at the top of the screen. The current therapy status will also appear under the icon of the therapy unit along with time or fluid amount (during the **Instill** phase) remaining.
10. Once the Dressing Soak fluid removal phase is complete, the dressing can be removed.

11. Select **Exit** to return to the ***Home*** screen or ***Utilities Tab***.

Refer to the appropriate dressing Instructions for Use for safety information and procedures to change the dressing.

Test Cycle

Use to complete an abbreviated **V.A.C. VERAFLO™ Therapy** cycle. Each phase of the cycle will be tested to ensure system is set up and functioning correctly.



1. Ensure that both the V.A.C.® Canister tubing and instillation line are properly connected (page 31).

2. Ensure that all four tubing clamps are open (pages 31 and 33).

3. Ensure the V.A.C. VERALINK™ Cassette is properly installed (page 28).

4. Ensure that the canister is properly installed (page 32).

5. Ensure solution bag / bottle is properly installed (page 29).

6. If unit has never been configured for V.A.C. VERAFLO™ Therapy, configure unit as described in the **V.A.C. VERAFLO™ Therapy Configuration - Overview** section (pages 44 - 47).

Test Cycle is only available while configured for V.A.C. VERAFLO™ Therapy.

If the user does not select any therapy settings, the V.A.C.ULTA™ Therapy Unit will default to factory settings.

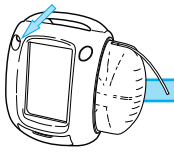
7. Select **Test Cycle** from ***Utilities*** screen (page 74).

8. Once Test Cycle is complete, select **EXIT** to go to the V.A.C.® Therapy phase.

V.A.C.® Therapy Configuration - Default Settings Overview

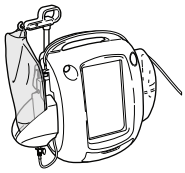
The following flow chart shows the basic steps required to configure **V.A.C.® Therapy** using the default settings. Refer to the following pages for detailed information about individual screens and options.

Press and hold **Power** buton until light comes on.



Required for V.A.C.® Therapy:

- Canister
- V.A.C.® Dressing

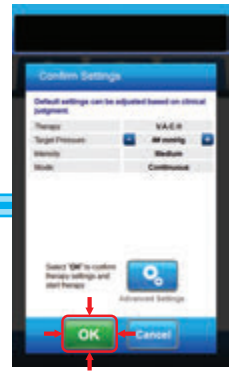


In order to use the Dressing Soak tool, a V.A.C. VERALINK™ Cassette must be installed (page 28).

New Patient screen

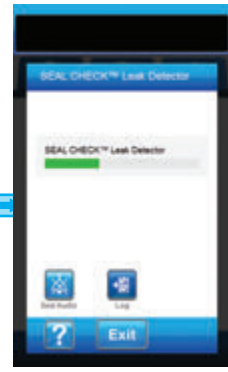
Select **V.A.C.® Therapy**. (page 42)

Confirm Settings screen



Select **OK** to accept default settings.

SEAL CHECK™ Leak Detector screen



Drawdown begins.

Home screen - **V.A.C.® Therapy**

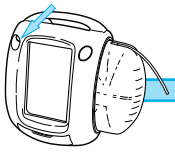
Screen shots shown above are for representation only. Refer to the page numbers listed for a more detailed view and more detailed information.

Settings displayed will vary depending on settings defined by user.

V.A.C.® Therapy Configuration - Advanced User Defined Settings Overview

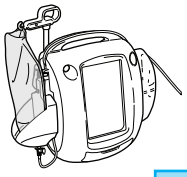
The following flow chart shows the basic steps required to configure **V.A.C.® Therapy** with User defined settings. Refer to the following pages for detailed information about individual screens and options.

Press and hold **Power** button until light comes on.



Required for V.A.C.® Therapy:

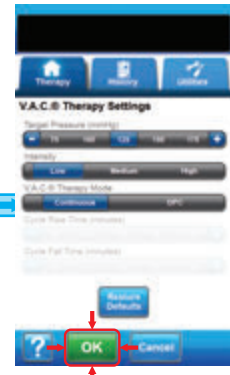
- Canister
- V.A.C.® Dressing



In order to use the Dressing Soak tool, a V.A.C. VERALINK™ Cassette must be installed (page 28).

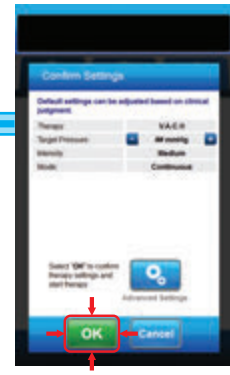
Select **V.A.C.® Therapy** (page 42).

Select **Advanced Settings**.



Configure **V.A.C.® Therapy** as prescribed (page 83). Select **OK** to continue to the ***Confirm Settings*** screen.

Drawdown begins.



Select **OK** to accept settings.

Home screen - **V.A.C.® Therapy**

Screen shots shown above are for representation only. Refer to the page numbers listed for a more detailed view and more detailed information.

Settings displayed will vary depending on settings defined by user.

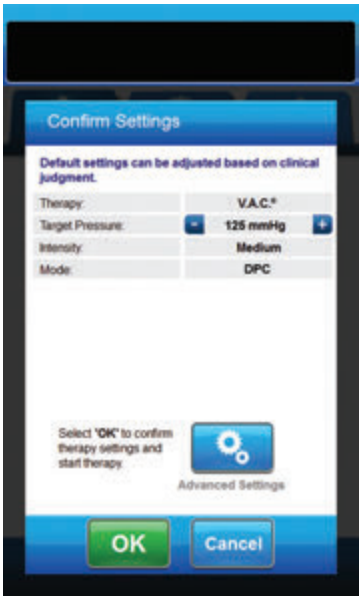
V.A.C.® Therapy Settings Screen

This screen allows the user to configure the V.A.C.ULTA™ Therapy Unit to deliver **V.A.C.® Therapy**:

- **Target Pressure (mmHg)** - (**Default = 125 mmHg**) Prescribed negative pressure level for **V.A.C.® Therapy**. Target Pressure can be set from 25 - 200 mmHg in 25 mmHg increments.
- **Intensity** - (**Default = Low**) Related to the time it takes to reach the target pressure after the initiation of therapy. The lower the intensity setting, the slower the target pressure will be reached. It is recommended that new patients begin therapy at the lowest intensity setting as this allows for slower increase of negative pressure once the foam is compressed in the wound. The intensity can remain at the minimum setting throughout the entire length of treatment, if desired.
- **V.A.C.® Therapy Mode** - (**Default = Continuous**) Available modes include **Continuous** and **DPC**. Continuous provides constant negative pressure at selected Target Pressure. DPC provides negative pressure between preset low pressure (25 mmHg) and selected Target Pressure.
- **Cycle Rise Time** - (**Default = 3 minutes**) Time used to transition from the preset low pressure (25 mmHg) to the selected target pressure while using DPC. Cycle Rise Time can be set from one minute to 10 minutes in one minute increments.
- **Cycle Fall Time** - (**Default = 3 minutes**) Time used to transition from the selected target pressure to the preset low pressure (25 mmHg) while using DPC. Cycle Fall Time can be set from one minute to 10 minutes in one minute increments.

1. Select desired value by selecting or sliding finger / stylus along bar. Use **+** / **-** to adjust above or below values shown.

Select **Restore Defaults** to reset therapy settings to the default values.



2. Once all settings have been entered, select **OK** to continue to the ***Confirm Settings*** screen. This screen allows the user to review the therapy settings that were selected on the ***V.A.C.® Therapy Settings*** screen.

3. Use + / - to adjust above or below values shown.

Select **Advanced Settings** to return to the ***V.A.C.® Therapy Settings*** screen to make any required adjustments.

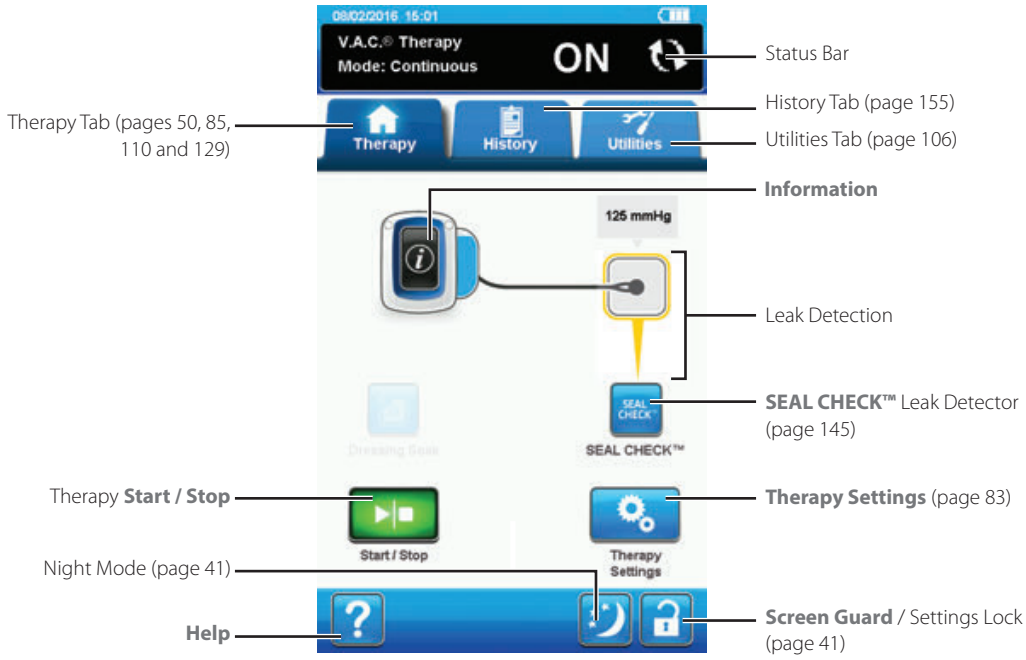
4. Select **OK** to initiate therapy and continue to the ***SEAL CHECK™ Leak Detector*** screen for **V.A.C.® Therapy.**

OR

5. Select **Cancel** to return to the ***Choose Therapy*** screen.

Home Screen - V.A.C.® Therapy

This ***Home*** screen is the main screen displayed by the V.A.C.ULTA™ Therapy Unit during **V.A.C.® Therapy**. It is used to access important information about the status of therapy.



Therapy mode and status (**ON** or **OFF**) will be displayed in the status bar at the top of the screen. The current therapy pressure will also appear above the icon of the dressing.

The following options are available from the ***Home*** screen for **V.A.C.® Therapy**:

Therapy Settings - Use to change current therapy settings.

SEAL CHECK™ Leak Detector - An on-screen bar graph will indicate leak level and an audible tone will sound if unit detects a significant leak (page 145).

Information - Use to view a summary of therapy history and current therapy settings (page 86).

Start / Stop - Use to start or stop therapy.

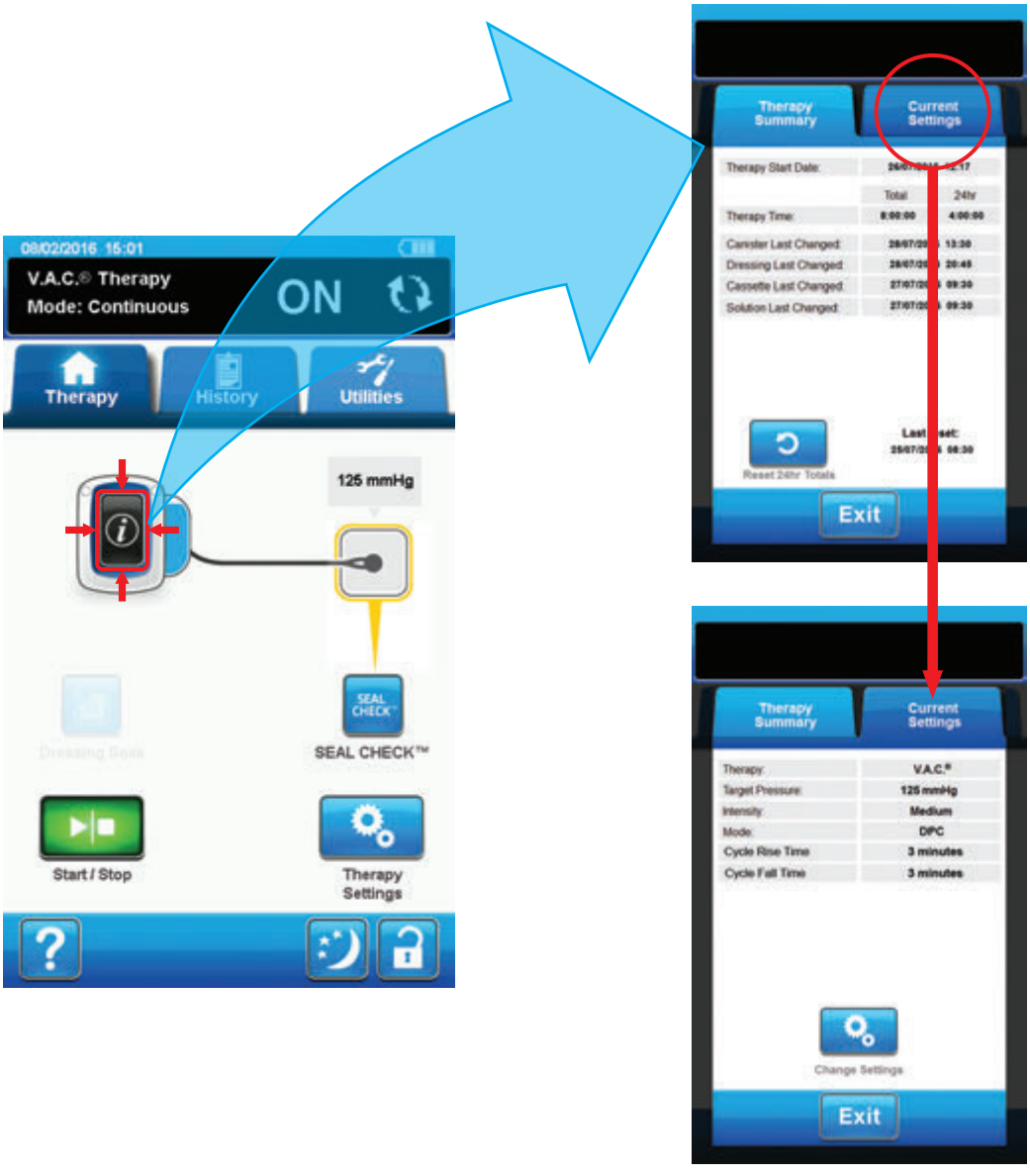
Help - Use to access to the V.A.C.ULTA™ Therapy Unit's on-screen help features.

Leak Detection - If the therapy unit detects a leak in the system temporarily above the Leak Alarm threshold, the ***Home*** screen for **V.A.C.®Therapy** will display a yellow box around the dressing. Refer to the instructions for use provided with the dressings for information on using excess drape material to seal any leak areas.

Refer to page 41 for a list of **Common Touch Screen Buttons** not described here.

Information Screens - V.A.C.® Therapy

These screens will display the current therapy settings and a summary of therapy applied to the patient.



1. Select **Information** from the ***Home*** screen to continue to the ***Therapy Summary*** tab. Use this tab to review the Therapy Start Date and Therapy Time. If the Log feature is used, the date and time for Canister Last Changed, Cassette Last Changed, Dressing Last Changed and Solution Last Changed will also be displayed.

2. Select **Current Settings** to continue to the ***Current Settings*** screen. Use this tab to review the current therapy settings.

3. Select **Change Settings** to continue to the ***Confirm Settings*** screen (page 84).

4. Select ***Exit*** to return to the ***Home*** screen for **V.A.C.® Therapy**.

V.A.C.® Therapy Alerts and Alarms

The following alerts and alarms may appear on the touch screen during **V.A.C.® Therapy**.

Alerts and alarms are accompanied by a repeating audible tone.

Following initiation of therapy, if an audible tone is not heard when SEAL CHECK™ Leak Detector is displayed and Seal Audio tone is turned ON, the alarms may not be working properly. Contact KCI for more information. Alarms are intended to be heard when facing the therapy unit at a maximum of one meter away. If two or more alarm conditions are present, only the highest priority alarm will be displayed.

Low Priority Alert Condition - Displayed on the touch screen when the V.A.C.ULTA™ Therapy Unit detects a condition that requires attention. Alerts will be accompanied by a repeating audible tone approximately every 20 seconds (two beeps).

Medium Priority Alarm Condition - Displayed on the touch screen when the V.A.C.ULTA™ Therapy Unit detects a condition that requires prompt attention in order to ensure the prescribed therapy is being delivered. Alarms will be accompanied by a repeating audible tone approximately every two seconds (three beeps) and a flashing screen title.

Select **Seal Audio** to turn the audible tone ON.

Select **Help** for more information regarding alarm resolution.

If alarm conditions cannot be resolved, contact KCI.

V.A.C.® Therapy Blockage Alert

Low Priority Alert - This alert screen appears when the V.A.C.ULTA™ Therapy Unit has detected a potential blockage. This alert will be accompanied by a repeating audible tone.

To resolve this alert:

1. Select **Audio Pause** to silence alert for two minutes during troubleshooting.

2. Ensure clamps on the V.A.C.® Therapy tubing on the SENSAT.R.A.C.™ Pad and canister tubing are open.

3. Ensure tubing is not kinked, crimped, or blocked in any way.

4. If the ***V.A.C.® Therapy Blockage Alert*** remains after completing steps 2 and 3, lower the therapy unit and tubing to be level with or below the wound site. If the alert is resolved by lowering the unit, normal use may resume.

5. Select **Reset** to return to the ***Home*** screen.

6. Ensure therapy is ON by checking the status bar (page 85). If not, select **Start / Stop** to restart therapy.

The V.A.C.ULTA™ Therapy Unit will continue to attempt to apply therapy during this alert.

If alarm condition cannot be resolved, contact KCI.

V.A.C.® Therapy Blockage Alarm (Therapy Interrupted)

Medium Priority Alarm - This alarm screen appears when a blockage is present in the V.A.C.® Therapy line. This alarm will be accompanied by a repeating audible tone.

To resolve this alarm:

1. Select **Audio Pause** to silence alarm for two minutes during troubleshooting.

2. Ensure clamps on the V.A.C.® Therapy tubing on the SENSAT.R.A.C.™ Pad and canister tubing are open.

3. Ensure tubing is not kinked, crimped, or blocked in any way.

4. If the ***V.A.C.® Therapy Blockage Alarm (Therapy Interrupted)*** remains after completing steps 2 and 3, lower the therapy unit and tubing to be level with or below the wound site. If the alarm is resolved by lowering the unit, normal use may resume.

5. Select **Reset** to return to the ***Home*** screen.

6. Ensure therapy is ON by checking the status bar (page 85). If not, select **Start / Stop** to restart therapy.

Therapy unit remains on; however, negative pressure at the wound site may be below therapeutic value.

If alarm condition cannot be resolved, contact KCI.

Certain KCI Dressings must be replaced with an alternate dressing if therapy is interrupted or off for more than two hours. See the Safety Information Sheet provided with the individual dressing for further information.

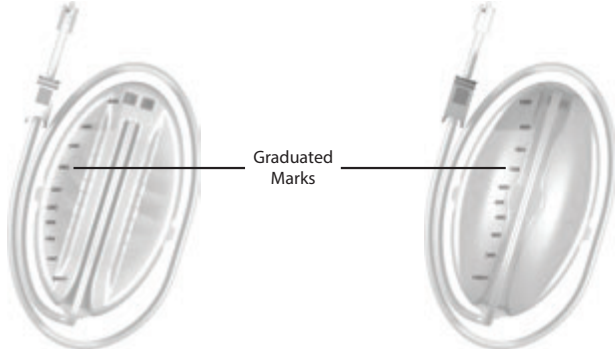
V.A.C.® Therapy Canister Full Alarm (Therapy Interrupted)

Medium Priority Alarm - This alarm screen appears when the canister is full and should be replaced. This alarm will be accompanied by a repeating audible tone.

To resolve this alarm:

1. Select **Audio Pause** to silence alarm for two minutes during troubleshooting.

2. Check if canister is full by comparing the level of fluid to the graduated marks on the canister.



A full canister is approximately 300 mL, 500 mL or 1000 mL depending on canister used. Canister release button will be flashing.

3. If canister is not full, select **Reset** to return to the ***Home*** screen.

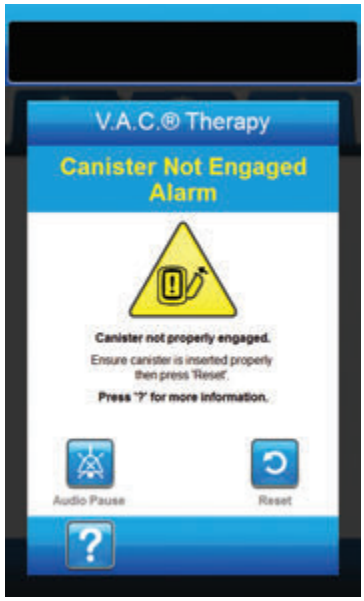
4. If canister is full, change canister and select **Reset** on this screen to return to the ***Home*** screen. See the **Changing the Canister** section of this manual (page 34) for additional information.

5. Select **Start / Stop** to restart therapy.

Certain KCI Dressings must be replaced with an alternate dressing if therapy is interrupted or off for more than two hours. See the Safety Information Sheet provided with the individual dressing for further information.

V.A.C.® Therapy Canister Not Engaged Alarm

Medium Priority Alarm - This alarm screen appears when the canister is not fully inserted and / or properly latched. This alarm will be accompanied by a repeating audible tone.



To resolve this alarm:

1. Select **Audio Pause** to silence alarm for two minutes during troubleshooting.

2. Remove the canister by pressing the **Canister Release** button (page 18) on the unit.

3. Inspect the canister and V.A.C.ULTA™ Therapy Unit to ensure no foreign objects or debris interfere with the canister and therapy unit's mating surfaces.

4. Ensure both seals are present and seated completely (page 19). If seals are missing or damaged, contact KCI.

5. Re-attach the canister to the V.A.C.ULTA™ Therapy Unit ensuring that the canister is fully engaged and latched (page 32). An audible click indicates that the canister is properly installed.

6. Select **Reset** to return to the ***Home*** screen.

7. Select **Start / Stop** to restart therapy.

8. If this alarm continues to appear, repeat steps 2 - 7 with a new canister.

If alarm condition cannot be resolved, contact KCI.

V.A.C.® Therapy Therapy Inactive Alarm

Medium Priority Alarm - This alarm screen appears when therapy (**V.A.C.® Therapy**) has been off or paused for more than 15 minutes (with the unit powered on). This alarm will be accompanied by a repeating audible tone.

To resolve this alarm:

1. Select **Audio Pause** to silence alarm for two minutes during troubleshooting.

2. Select **Reset** to return to the ***Home*** screen.

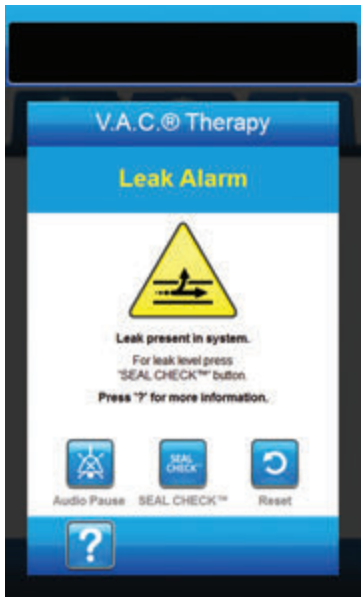
3. Select **Start / Stop** to restart therapy.

4. If therapy is not desired, turn the V.A.C.ULTA™ Therapy Unit off by using the **Power** button on the front of the unit.

Certain KCI Dressings must be replaced with an alternate dressing if therapy is interrupted or off for more than two hours. See the Safety Information Sheet provided with the individual dressing for further information.

V.A.C.® Therapy Leak Alarm

Medium Priority Alarm - This alarm screen appears when a significant negative pressure leak has been detected. If this alarm is not resolved in three minutes, therapy will be interrupted. This alarm will be accompanied by a repeating audible tone.



To resolve this alarm:

1. Select **Audio Pause** to silence alarm for two minutes during troubleshooting.

2. Ensure connector between dressing tubing and canister tubing is properly locked.

3. Ensure canister is fully engaged. (See **Canister Not Engaged Alarm**, page 91).

4. Select **SEAL CHECK™** to access the SEAL CHECK™ Leak Detector. Refer to the **SEAL CHECK™ Leak Detector** section (page 145) of this manual for details on how to use the SEAL CHECK™ Leak Detector and how to repair leaks.

5. Once the leak is resolved using the SEAL CHECK™ Leak Detector, select **Exit** on the ***SEAL CHECK™ Leak Detector*** screen to return to the ***V.A.C.® Therapy Leak Alarm*** screen.

6. Select **Reset** to return to the ***Home*** screen.

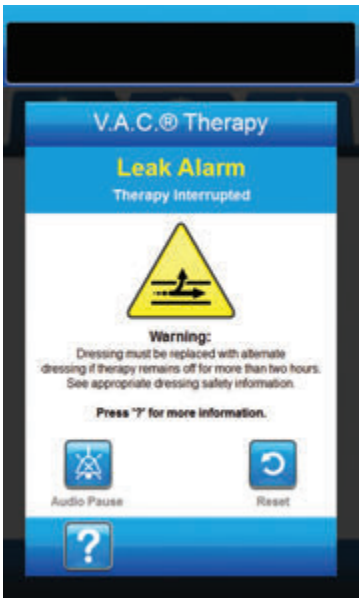
7. Ensure therapy is ON by checking the Status Bar (page 85). If not, select **Start / Stop** to restart therapy.

If this alarm is not resolved within three minutes, the V.A.C.® Therapy Leak Alarm (Therapy Interrupted) will appear and therapy will stop.

Refer to V.A.C.® Therapy Leak Alarm (Therapy Interrupted) section of this manual (page 94) for procedures to restart therapy.

V.A.C.® Therapy Leak Alarm (Therapy Interrupted)

Medium Priority Alarm - This alarm screen appears when a detected negative pressure leak has not been resolved and therapy has been interrupted. This alarm will be accompanied by a repeating audible tone.



To resolve this alarm:

1. Select **Audio Pause** to silence alarm for two minutes during troubleshooting.
2. Ensure connector between dressing tubing and canister tubing is properly locked.
3. Ensure canister is fully engaged. (See **Canister Not Engaged Alarm**, page 91).

4. Select **Reset** to return to the ***Home*** screen.

5. Restart therapy by selecting **Start / Stop**.

6. Select **SEAL CHECK™** to access the SEAL CHECK™ Leak Detector. Refer to the **SEAL CHECK™ Leak Detector** section (page 145) of this manual for details on how to use the SEAL CHECK™ Leak Detector and how to repair leaks.
7. Once the leak is resolved using the SEAL CHECK™ Leak Detector, select **Exit** on the ***SEAL CHECK™ Leak Detector*** screen to return to the ***Home*** screen.

If the leak condition is not resolved, an alarm screen will reappear after several minutes.

If alarm condition cannot be resolved, contact KCI.

Certain KCI Dressings must be replaced with an alternate dressing if therapy is interrupted or off for more than two hours. See the Safety Information Sheet provided with the individual dressing for further information.

V.A.C.® Therapy Low Pressure Alarm (Therapy Interrupted)

Medium Priority Alarm - This alarm screen appears when the V.A.C.ULTA™ Therapy Unit has not reached the target therapy negative pressure setting and negative pressure at the wound may be below set pressure, potentially compromising therapeutic benefits. This alarm is accompanied by a repeating audible tone.

To resolve this alarm:

1. Select **Audio Pause** to silence alarm for two minutes during troubleshooting.

2. Ensure clamps on the V.A.C.® Therapy tubing on the SENSAT.R.A.C.™ Pad and canister tubing are open.

3. Ensure tubing is not kinked, crimped, or blocked in any way.

4. If the ***V.A.C.® Therapy Low Pressure Alarm (Therapy Interrupted***) remains after completing steps 2 and 3, lower the therapy unit and tubing to be level with or below the wound site. If the alarm is resolved by lowering the unit, normal use may resume.

5. Select **Reset** to return to the ***Home Screen***.

6. Ensure therapy is ON by checking the status bar (page 85). If not, select **Start / Stop** to restart therapy.

Therapy unit remains on; however, negative pressure at the wound site may be below therapeutic value.

If alarm condition cannot be resolved, contact KCI.

Certain KCI Dressings must be replaced with an alternate dressing if therapy is interrupted or off for more than two hours. See the Safety Information Sheet provided with the individual dressing for further information.

V.A.C.® Therapy V.A.C. VERALINK™ Not Engaged Alert

Low Priority Alert - This alert screen appears when the V.A.C. VERALINK™ Cassette is not fully seated and / or properly latched. This alert will be accompanied by a repeating audible tone.

The V.A.C.ULTA™ Therapy Unit will continue to attempt to apply therapy during this alert.

To resolve this alert:

1. Select **Audio Pause** to silence alert for two minutes during troubleshooting.
2. Remove the V.A.C. VERALINK™ Cassette from the unit by pushing down on the cassette latch release tab (page 28).
3. Inspect the V.A.C. VERALINK™ Cassette and the V.A.C.ULTA™ Therapy Unit to ensure no foreign objects or debris interfere with the cassette and the therapy unit connection points.
4. Ensure the cassette's pivot connection (on the end with the tubing spike) is securely engaged within the pivot slot on the therapy unit (page 28).
5. Re-attach the V.A.C. VERALINK™ Cassette to the therapy unit ensuring that the cassette is fully engaged and latched (page 28). An audible click indicates that the cassette is properly installed.

Once the V.A.C. VERALINK™ Cassette is properly installed, the V.A.C. VERALINK™ Not Engaged Alert screen will automatically clear.

OR

6. Select **Reset** to return to the ***Home*** screen.
7. Ensure therapy is ON by checking the status bar (page 85). If not, select **Start / Stop** to restart therapy.
8. If this alert condition continues to appear, repeat steps 2 - 7 with a new V.A.C. VERALINK™ Cassette.

If alert condition cannot be resolved, contact KCI.

V.A.C.® Therapy Solution Bag / Bottle Empty Alert

Low Priority Alert -This alert screen appears when there is no instillation fluid in the solution bag / bottle. This alert will be accompanied by a repeating audible tone.

To resolve this alert:

1. Select **Audio Pause** to silence alert for two minutes during troubleshooting.

2. Remove empty solution bag / bottle from V.A.C. VERALINK™ Cassette.

3. Attach new solution bag / bottle. Refer to **Hang Solution Container Bag / Bottle** section of this manual (page 30) for more information.

4. Place new bag / bottle on the adjustable solution container hanger arm (page 30).

5. Select **Log** to enter the solution bag / bottle change. Refer to the ***Log*** screen section (page 151) for more information.

6. Select **Reset** to return to the ***Home*** screen.

7. Ensure therapy is ON by checking the status bar (page 85). If not, select **Start / Stop** to restart therapy.

V.A.C.® Therapy Pressure Deviation Alarm (Therapy Interrupted)

Medium Priority Alarm - This alarm screen appears when the wound site positive pressure has exceeded its allowable limits. This alarm will be accompanied by a repeating audible tone.

To resolve this alarm:

1. Select **Audio Pause** to silence alarm for two minutes during troubleshooting.

2. Ensure clamps on the V.A.C. VERAT.R.A.C.™ Pad or the V.A.C. VERAT.R.A.C. DUO™ Tube Set and V.A.C. VERALINK™ Cassette tubing are open.

3. Ensure that the tubing is not kinked, crimped or blocked in any way.

4. If the V.A.C.® Therapy Pressure Deviation Alarm (Therapy Interrupted) remains after completing steps 2 and 3, check patient positioning or any external compression devices that may impede flow. Remove external compression device.

5. Select **Reset** to return to the ***Home*** screen.

6. Ensure therapy is ON by checking the status bar (page 85). If not, select **Start / Stop** to restart therapy.

If alarm condition cannot be resolved, contact KCI.

Certain KCI Dressings must be replaced with an alternate dressing if therapy is interrupted or off for more than two hours. See the Safety Information Sheet provided with the individual dressing for further information.

V.A.C.® Therapy Instill Tube Blockage Alert (Therapy Interrupted)

Low Priority Alert - This alert screen appears when a blockage is present in the instillation line of the V.A.C. VERAT.R.A.C.™ Pad or V.A.C. VERAT.R.A.C. DUO™ Tube Set. This alert will be accompanied by a repeating audible tone.

To resolve this alert:

1. Select **Audio Pause** to silence alert for two minutes during troubleshooting.
2. Ensure clamps on the V.A.C. VERAT.R.A.C.™ Pad or V.A.C. VERAT.R.A.C. DUO™ Tube Set and V.A.C. VERALINK™ Cassette are open.
3. Ensure that the tubing is not kinked, crimped, or blocked in any way.
4. Ensure the V.A.C. VERALINK™ Cassette is fully engaged and latched. See the **Attaching the V.A.C. VERALINK™ Cassette to the V.A.C.ULTA™ Therapy Unit** section (page 28) of this manual for more information.
5. Ensure that the instillation solution in the V.A.C. VERALINK™ Cassette tubing is still liquid and flows freely. If the solution has degraded to a thicker consistency, change any or all of the following:
   - V.A.C. VERALINK™ Cassette
   - V.A.C. VERAT.R.A.C.™ Pad or V.A.C. VERAT.R.A.C. DUO™ Tube Set
   - Solution bag / bottle
6. If the V.A.C.® Therapy Instill Tube Blockage Alert remains after completing steps 2 - 5, check patient positioning or any external compression devices that may impede flow. If applicable, remove external compression device.
7. Select **Reset** to return to the ***Home*** screen.

Alert screen will clear when the blockage is corrected.

V.A.C.® Therapy Battery Low Alert

Low Priority Alert - This alert screen appears approximately two hours before the battery power level is too low to support continued operation of the V.A.C.ULTA™ Therapy Unit. This alert will be accompanied by a repeating audible tone.

To resolve this alert:

1. Select **Audio Pause** to silence alert for two minutes during troubleshooting.

2. Connect the therapy unit to a wall outlet using the KCI supplied power supply to recharge battery. An amber light at the bottom of the touch screen and a battery charge icon indicate the unit is charging. Refer to the **Charge Battery** section of this manual (page 23) for more information.

Once the V.A.C.ULTA™ Therapy Unit is plugged into a wall outlet, the Battery Low Alert screen will automatically clear.

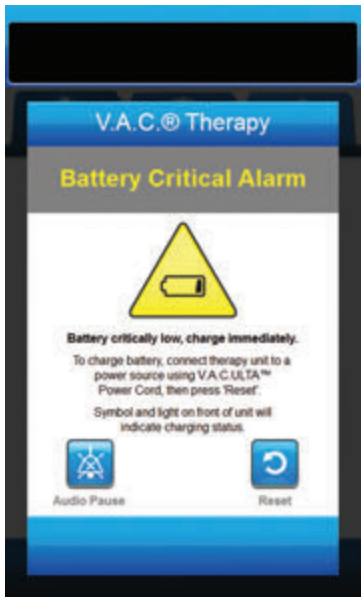
OR

3. Select **Reset** to return to the ***Home*** screen.

Therapy continues.

V.A.C.® Therapy Battery Critical Alarm

Medium Priority Alarm - This alarm screen appears approximately 30 minutes before the battery power level is too low to support continued operation of the V.A.C.ULTA™ Therapy Unit. This alarm will be accompanied by a repeating audible tone.



To resolve this alarm:

1. Select **Audio Pause** to silence alarm for two minutes during troubleshooting.

2. Connect the therapy unit to a wall outlet using KCI supplied power supply to recharge battery. An amber light at the bottom of the touch screen and a battery charge icon indicates the unit is charging. Refer to the **Charge Battery** section of this manual (page 23) for more information.

Once the V.A.C.ULTA™ Therapy Unit is plugged into a wall outlet, the Battery Critical Alarm screen will automatically clear.

3. If the ***Battery Critical Alarm*** screen does not automatically clear, select **Reset** to return to the ***Home*** screen.

V.A.C.® Therapy continues, however, if this alarm is not resolved within approximately thirty minutes, therapy will be interrupted.

4. Ensure therapy is ON by checking the status bar (page 85). If not, select **Start / Stop** to restart therapy.

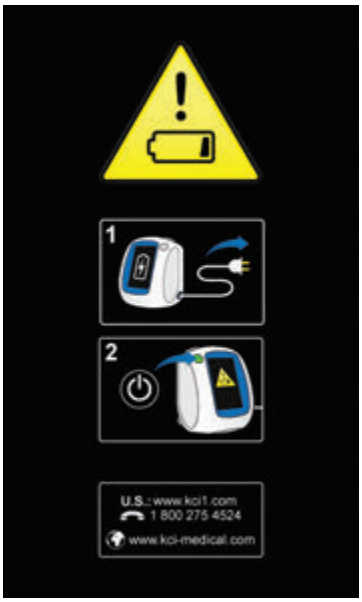
The V.A.C.ULTA™ Therapy must be plugged into a wall outlet in order to continue therapy.

Alarm logs and settings are not lost in the case of a total power loss or if the unit is power cycled (turned off then back on).

Certain KCI Dressings must be replaced with an alternate dressing if therapy is interrupted or off for more than two hours. See the Safety Information Sheet provided with the individual dressing for further information.

Battery Exhausted

Medium Priority Alarm - This alarm screen appears when the battery power level is too low to power on the V.A.C.ULTA™ Therapy Unit.



To resolve this alarm:

1. Connect the therapy unit to a wall outlet using KCI supplied power supply to recharge battery. An amber light at the bottom of the touch screen and a battery charge icon indicates the unit is charging. Refer to the **Charge Battery** section of this manual (page 23) for more information.

2. Power the V.A.C.ULTA™ Therapy Unit on and initiate therapy. Refer to the **Power the V.A.C.ULTA™ Therapy Unit On or Off** section of this manual (page 42) for more information.

V.A.C.® Therapy Internal Temperature Alert

Low Priority Alert - This alert screen appears when the internal temperature of the V.A.C.ULTA™ Therapy Unit is outside its specified limits. This alert will be accompanied by a repeating audible tone.

Therapy will continue while this alert is active. The touch screen will be turned off after five minutes of inactivity. The screen will illuminate when touched. Battery charging is stopped.

To resolve this alert:

1. Select **Audio Pause** to silence alert for two minutes during troubleshooting.

2. Move the therapy unit to an environment with an operational temperature range as detailed in the **Specifications** section of this manual (page 194).

It may take up to two hours for the therapy unit to return to operating temperatures.

3. Select **Reset** to return to the ***Home*** screen.

Therapy continues.

If alarm condition cannot be resolved, contact KCI.

Certain KCI Dressings must be replaced with an alternate dressing if therapy is interrupted or off for more than two hours. See the Safety Information Sheet provided with the individual dressing for further information.

V.A.C.® Therapy System Error Alarm (Therapy Interrupted) (after Power On)

Medium Priority Alarm - This alarm screen appears when there is a system fault within the V.A.C.ULTA™ Therapy Unit after it has been powered on. Several different types of system errors may occur. A number will appear next to **Error Code** that represents the diagnostic code of the system fault. This alarm will be accompanied by a repeating audible tone.

To resolve this alarm:

1. Select **Audio Pause** to silence alarm for two minutes during troubleshooting.
2. Record the Error Code number.
3. Power the unit off and then on using the **Power** button on the front of the unit (page 18).

If alarm condition cannot be resolved, contact KCI.

Certain KCI Dressings must be replaced with an alternate dressing if therapy is interrupted or off for more than two hours. See the Safety Information Sheet provided with the individual dressing for further information.

System Error Alarm (at Power On)

Medium Priority Alarm - This alarm screen appears when there is a system fault within the V.A.C.ULTA™ Therapy Unit while the unit is powering on. "00000001" represents the diagnostic code of the system fault. This alarm will be accompanied by a repeating audible tone.

To resolve this alarm:

1. Record the Error Code number (00000001).

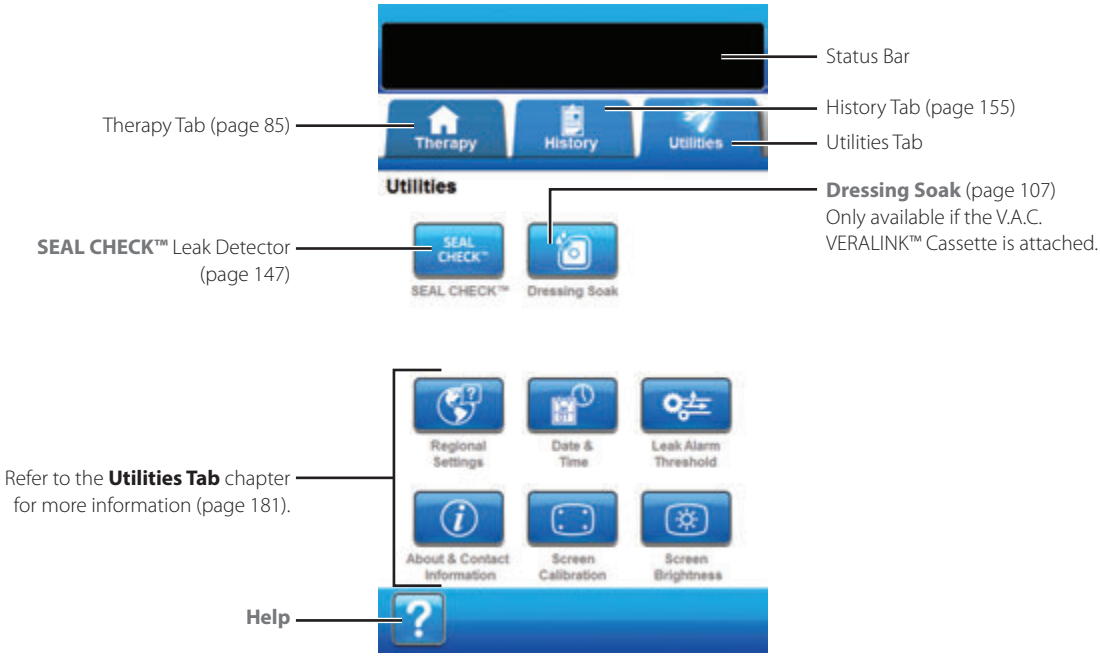
2. Power the unit off and then on using the **Power** button on the front of the unit (page 18).

If alarm condition cannot be resolved, contact KCI.

Certain KCI Dressings must be replaced with an alternate dressing if therapy is interrupted or off for more than two hours. See the Safety Information Sheet provided with the individual dressing for further information.

Utilities Tab - V.A.C.® Therapy

Use the ***Utilities Tab*** screen to set preferences for the V.A.C.ULTA™ Therapy Unit. Certain selections are available no matter what therapy is active. Those selections are discussed in the **Utilities Tab** chapter. Selections that are unique to the selected therapy are detailed below.



The following options are available from the ***Utilities Tab*** Home screen:

SEAL CHECK™ Leak Detector - An on-screen bar graph will indicate leak level and an audible tone will sound if unit detects a significant leak (page 145).

Dressing Soak - Use to soak the dressing with solution in preparation for a dressing change (page 107).

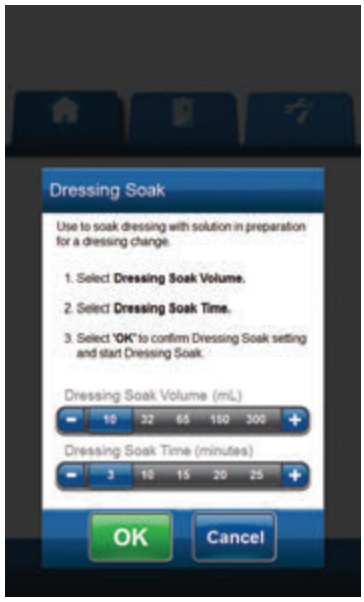
The V.A.C. VERALINK™ Cassette (page 28) must be installed for the Dressing Soak tool to be available.

Help - Use to access the V.A.C.ULTA™ Therapy Unit's on-screen help features.

Dressing Soak

Use Dressing Soak to soak the dressing with solution in preparation for a dressing change.

The V.A.C. VERALINK™ Cassette (page 28) must be installed for the Dressing Soak tool to be available.

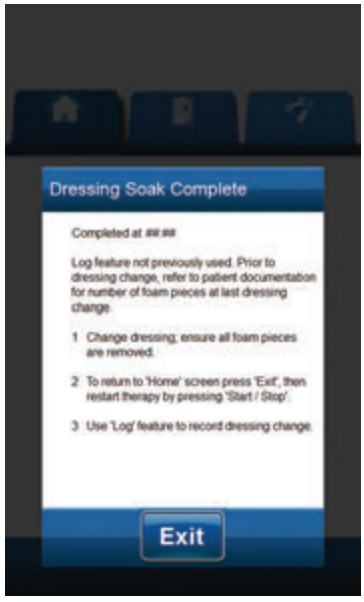


1. Ensure that the instillation line is properly connected.
2. Ensure that all four tubing clamps are open.
3. Ensure that the V.A.C. VERALINK™ Cassette is properly installed (page 28).
4. Ensure that the canister has adequate capacity remaining for the dressing change.

5. Select **Dressing Soak** from the ***Home*** screen to continue to the ***Dressing Soak*** screen.
6. Select the target **Dressing Soak Volume (mL)**.
7. Select the target **Dressing Soak Time (minutes)**.

8. Select **OK** to confirm settings and return to the ***Home*** screen.
9. The V.A.C.ULTA™ Therapy Unit will complete the Instill, Soak, and fluid removal phases. Therapy phase will be displayed in the status bar (page 85) at the top of the screen. The current therapy status will also appear under the icon of the therapy unit along with time or fluid amount (during the **Instill** phase) remaining.
10. Once the Dressing Soak fluid removal phase is complete, the dressing can be removed.

11. Select **Exit** to return to the ***Home*** screen.

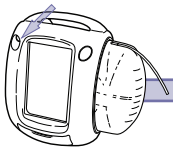


Refer to the appropriate dressing Instructions for Use for safety information and procedures to change the dressing.

PREVENA™ Therapy Configuration - Overview

The following flow chart shows the basic steps required to configure **PREVENA™ Therapy**. Refer to the following pages for detailed information about individual screens and options.

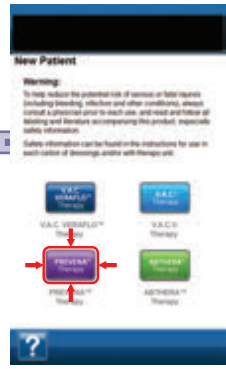
Press and hold **Power** buton until light comes on.



Required for PREVENA™ Therapy:

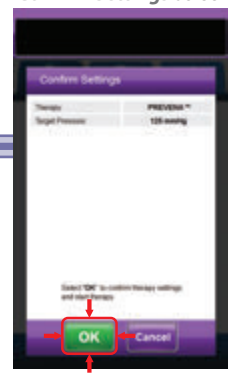
- Canister
- PREVENA™ Dressing

New Patient screen



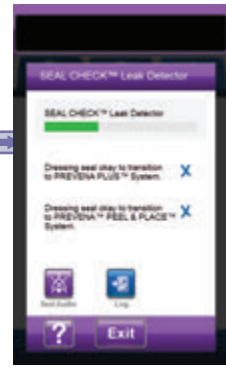
Select **PREVENA™ Therapy**. (page 42)

Confirm Settings screen

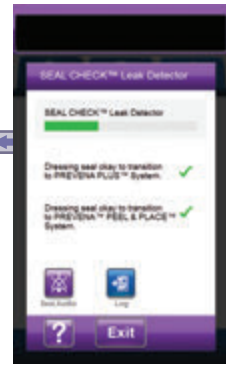


Select **OK** to begin SEAL CHECK™ Leak Detector (page 148)

SEAL CHECK™ Leak Detector screen



Drawdown begins.



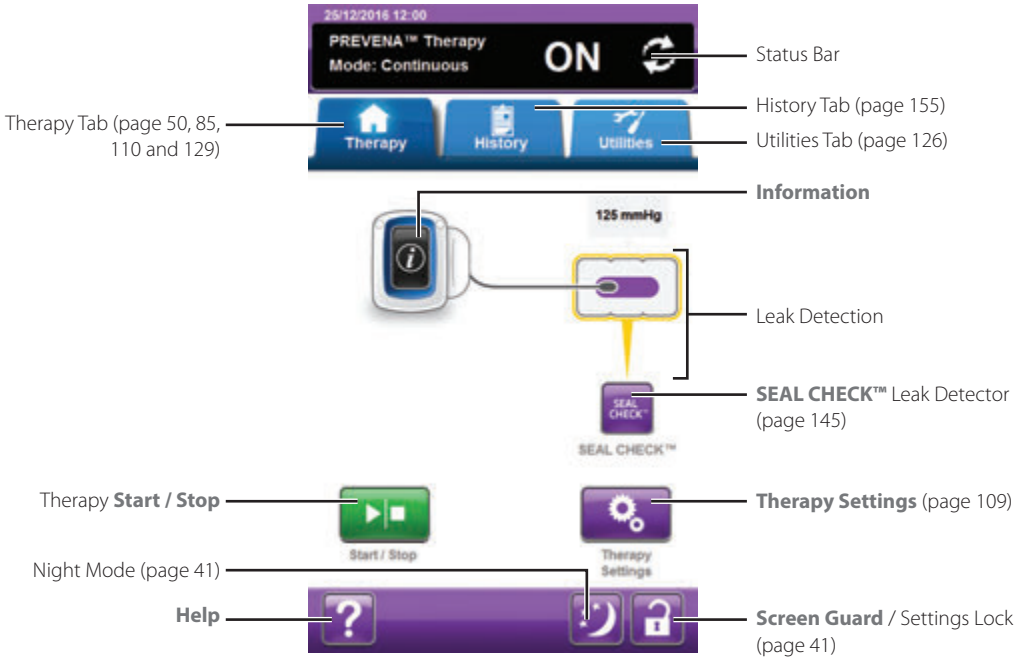
Home screen - **PREVENA™ Therapy**

Screen shots shown above are for representation only. Refer to the page numbers listed for a more detailed view and more detailed information.

Settings displayed will vary depending on settings defined by user.

Home Screen - PREVENA™ Therapy

This ***Home*** screen is the main screen displayed by the V.A.C.ULTA™ Therapy Unit during **PREVENA™ Therapy**. It is used to access important information about the status of therapy.



Therapy phase and status (ON or OFF) will be displayed in the status bar at the top of the screen. The current therapy pressure will also appear above the icon of the dressing.

The following selections are available from the ***Home*** screen for **PREVENA™ Therapy**:

Therapy Settings - Use to view current therapy settings.

SEAL CHECK™ Leak Detector - An on-screen bar graph will indicate leak level and an audible tone will sound if unit detects a significant leak (page 145).

Information - Use to view a summary of therapy history and current therapy settings (page 111).

Start / Stop - Use to start or stop therapy.

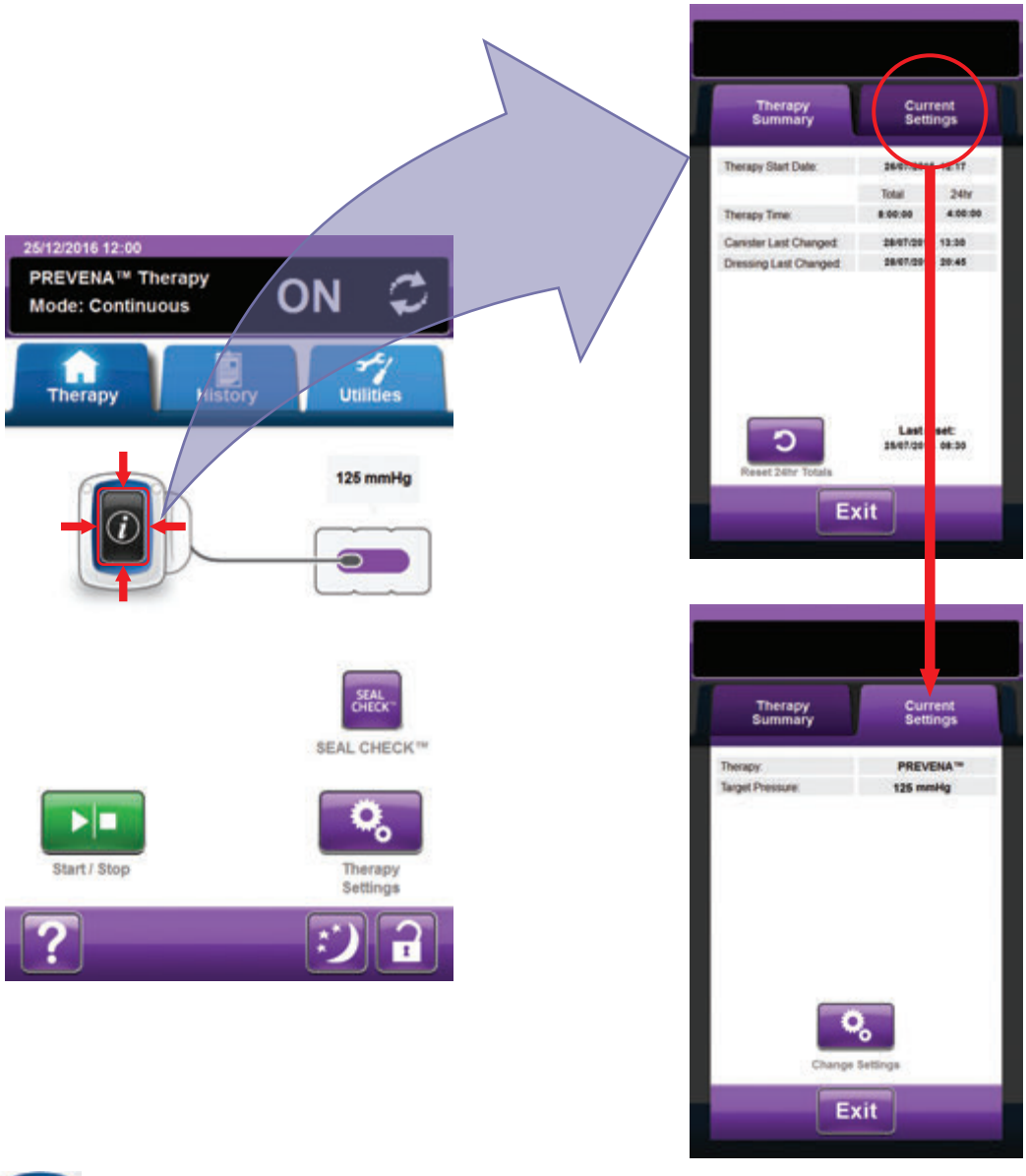
Help - Use to access the V.A.C.ULTA™ Therapy Unit's on-screen help features.

Leak Detection - If the therapy unit detects a leak in the system temporarily above the Leak Alarm threshold, the ***Home*** screen for **PREVENA™ Therapy** will display a yellow box around the dressing. Refer to the instructions for use provided with the dressings for information on using excess drape material to seal any leak areas.

Refer to page 41 for a list of **Common Touch Screen Buttons** not described here.

Information Screens - PREVENA™ Therapy

These screens will display the current therapy settings and a summary of therapy applied to the patient.



1. Select **Information** from the ***Home*** screen to continue to the ***Therapy Summary*** tab. Use this tab to review the Therapy Start Date and Therapy Time. If the Log feature is used, the date and time for Canister Last Changed and Dressing Last Changed will also be displayed.

2. Select **Current Settings** to continue to the ***Current Settings*** screen. Use this tab to review the current therapy settings.

3. Select **Change Settings** to continue to the ***Confirm Settings*** screen (page 109).

4. Select ***Cancel*** to return to the ***Home*** screen for **PREVENA™ Therapy**.

PREVENA™ Therapy Alerts

The following alerts may appear on the touch screen during **PREVENA™ Therapy**.

Alerts are accompanied by a repeating audible tone.

Following initiation of therapy, if an audible tone is not heard when SEAL CHECK™ Leak Detector is displayed and Seal Audio tone is turned ON, the alerts may not be working properly. Contact KCI for more information. Alerts are intended to be heard when facing the therapy unit at a maximum of one meter away. If two or more alert conditions are present, only the highest priority alert will be displayed.

Low Priority Alert Condition - Displayed on the touch screen when the V.A.C.ULTA™ Therapy Unit detects a condition that requires attention. Alerts will be accompanied by a repeating audible tone approximately every 20 seconds (two beeps).

Select **Seal Audio** to turn the audible tone ON.

Select **Help** for more information regarding alert resolution.

If alert conditions cannot be resolved, contact KCI.

PREVENA™ Therapy Blockage Alert

Low Priority Alert - This alert screen appears when the V.A.C.ULTA™ Therapy Unit has detected a potential blockage. This alert will be accompanied by a repeating audible tone.

To resolve this alert:

1. Select **Audio Pause** to silence alert for two minutes during troubleshooting.

2. Ensure clamps on the dressing tubing and canister tubing are open.

3. Ensure tubing is not kinked, crimped, or blocked in any way.

4. If the ***PREVENA™ Therapy Blockage Alert*** remains after completing steps 2 and 3, lower the therapy unit and tubing to be level with or below the wound site. If the alert is resolved by lowering the unit, normal use may resume.

5. Select **Reset** to return to the ***Home*** screen.

6. Ensure therapy is ON by checking the status bar (page 110). If not, select **Start / Stop** to restart therapy.

The V.A.C.ULTA™ Therapy Unit will continue to attempt to apply therapy during this alert.

If alert condition cannot be resolved, contact KCI.

PREVENA™ Therapy Blockage Alert (Therapy Interrupted)

Low Priority Alert - This alert screen appears when a blockage is present. This alert will be accompanied by a repeating audible tone.

To resolve this alert:

1. Select **Audio Pause** to silence alert for two minutes during troubleshooting.

2. Ensure clamps on the dressing tubing and canister tubing are open.

3. Ensure tubing is not kinked, crimped, or blocked in any way.

4. If the ***PREVENA™ Therapy Blockage Alert (Therapy Interrupted)*** remains after completing steps 2 and 3, lower the therapy unit and tubing to be level with or below the wound site. If the alert is resolved by lowering the unit, normal use may resume.

5. Select **Reset** to return to the ***Home*** screen.

6. Ensure therapy is ON by checking the status bar (page 110). If not, select **Start / Stop** to restart therapy.

Therapy unit remains on; however, negative pressure at the wound site may be below therapeutic value.

If alert condition cannot be resolved, contact KCI.

PREVENA™ Therapy Canister Full Alert

Low Priority Alert - This alert screen appears when the canister is full and should be replaced. This alert will be accompanied by a repeating audible tone.

To resolve this alert:

1. Select **Audio Pause** to silence alert for two minutes during troubleshooting.

2. Check if canister is full by comparing the level of fluid to the graduated marks on the canister.

A full canister is approximately 300 mL or 500 mL depending on canister used. Canister release button will be flashing.

3. If canister is not full, select **Reset** to return to the ***Home*** screen.

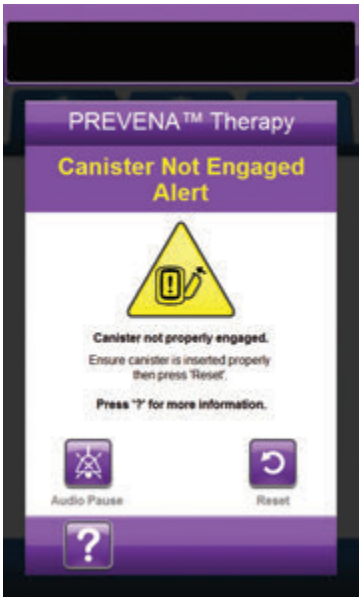
4. If canister is full or near full **call the treating physician immediately** for additional instructions.

5. Select **Reset** to return to the ***Home*** screen.

6. Select **Start / Stop** to restart therapy.

PREVENA™ Therapy Canister Not Engaged Alert

Low Priority Alert - This alert screen appears when the canister is not fully inserted and / or properly latched. This alert will be accompanied by a repeating audible tone.



To resolve this alert:

1. Select **Audio Pause** to silence alert for two minutes during troubleshooting.

2. Remove the canister by pressing the **Canister Release** button (page 18) on the unit.

3. Inspect the canister and V.A.C.ULTA™ Therapy Unit to ensure no foreign objects or debris interfere with the canister and therapy unit's mating surfaces.

4. Ensure both seals are present and seated completely (page 19). If seals are missing or damaged, contact KCI.

5. Re-attach the canister to the V.A.C.ULTA™ Therapy Unit ensuring that the canister is fully engaged and latched (page 32). An audible click indicates that the canister is properly installed.

6. Select **Reset** to return to the ***Home*** screen.

7. Select **Start / Stop** to restart therapy.

8. If this alert continues to appear, repeat steps 2 - 7 with a new canister.

If alert condition cannot be resolved, contact KCI.

Low Priority Alert - This alert screen appears when therapy (**PREVENA™ Therapy**) has been off or paused for more than 15 minutes (with the unit powered on) . This alert will be accompanied by a repeating audible tone.

To resolve this alert:

1. Select **Audio Pause** to silence alert for two minutes during troubleshooting.

2. Select **Reset** to return to the ***Home*** screen.

3. Select **Start / Stop** to restart therapy.

4. If therapy is not desired, turn the V.A.C.ULTA™ Therapy Unit off by using the **Power** button on the front of the unit.

PREVENA™ Therapy Leak Alert

Low Priority Alert - This alert screen appears when a significant negative pressure leak has been detected. This alert will be accompanied by a repeating audible tone.

To resolve this alert:

1. Select **Audio Pause** to silence alert for two minutes during troubleshooting.

2. Ensure connector between dressing tubing and canister tubing are properly locked.

3. Ensure canister is fully engaged. (See **Canister Not Engaged Alert**, page 117).

4. Select **SEAL CHECK™** to access the SEAL CHECK™ Leak Detector. Refer to the **SEAL CHECK™ Leak Detector** section (page 145) of this manual for details on how to use the SEAL CHECK™ Leak Detector and how to repair leaks.

5. Once the leak is resolved using the SEAL CHECK™ Leak Detector, select **Exit** on the ***SEAL CHECK™ Leak Detector*** screen to return to the ***PREVENA™ Therapy Leak Alert*** screen.

6. Select **Reset** to return to the ***Home*** screen.

7. Ensure therapy is ON by checking the Status Bar (page 110). If not, select **Start / Stop** to restart therapy.

The V.A.C.ULTA™ Therapy Unit will continue to attempt to apply therapy during this alert.

If alert condition cannot be resolved, contact KCI.

Low Priority Alert - This alert screen appears approximately two hours before the battery power level is too low to support continued operation of the V.A.C.ULTA™ Therapy Unit. This alert will be accompanied by a repeating audible tone.

To resolve this alert:

1. Select **Audio Pause** to silence alert for two minutes during troubleshooting.

2. Connect the therapy unit to a wall outlet using the KCI supplied power supply to recharge battery. An amber light at the bottom of the touch screen and a battery charge icon indicate the unit is charging. Refer to the **Charge Battery** section of this manual (page 23) for more information.

Once the V.A.C.ULTA™ Therapy Unit is plugged into a wall outlet, the Battery Low Alert screen will automatically clear.

OR

3. Select **Reset** to return to the ***Home*** screen.

Therapy continues.

PREVENA™ Therapy Battery Critical Alert

Low Priority Alert - This alert screen appears approximately 30 minutes before the battery power level is too low to support continued operation of the V.A.C.ULTA™ Therapy Unit. This alert will be accompanied by a repeating audible tone.

To resolve this alert:

1. Select **Audio Pause** to silence alert for two minutes during troubleshooting.

2. Connect the therapy unit to a wall outlet using KCI supplied power supply to recharge battery. An amber light at the bottom of the touch screen and a battery charge icon indicates the unit is charging. Refer to the **Charge Battery** section of this manual (page 23) for more information.

Once the V.A.C.ULTA™ Therapy Unit is plugged into a wall outlet, the Battery Critical Alert screen will automatically clear.

OR

3. Select **Reset** to return to the ***Home*** screen.

PREVENA™ Therapy continues, however, if this alert is not resolved within approximately thirty minutes, therapy will be interrupted.

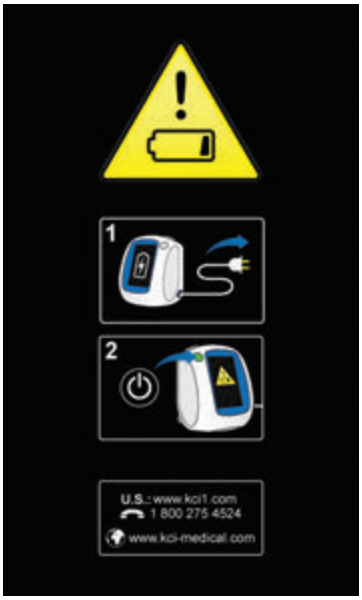
4. Ensure therapy is ON by checking the status bar (page 110). If not, select **Start / Stop** to restart therapy.

The V.A.C.ULTA™ Therapy must be plugged into a wall outlet in order to continue therapy.

Alert logs and settings are not lost in the case of a total power loss or if the unit is power cycled (turned off then back on).

Battery Exhausted

Low Priority Alert - This alert screen appears when the battery power level is too low to power on the V.A.C.ULTA™ Therapy Unit.



To resolve this alert:

1. Connect the therapy unit to a wall outlet using KCI supplied power supply to recharge battery. An amber light at the bottom of the touch screen and a battery charge icon indicates the unit is charging. Refer to the **Charge Battery** section of this manual (page 23) for more information.

2. Power the V.A.C.ULTA™ Therapy Unit on and initiate therapy. Refer to the **Power the V.A.C.ULTA™ Therapy Unit On or Off** section of this manual (page 42) for more information.

PREVENA™ Therapy Internal Temperature Alert

Low Priority Alert - This alert screen appears when the internal temperature of the V.A.C.ULTA™ Therapy Unit is outside its specified limits. This alert will be accompanied by a repeating audible tone.

Therapy will continue while this alert is active. The touch screen will be turned off after five minutes of inactivity. The screen will illuminate when touched. Battery charging is stopped.

To resolve this alert:

1. Select **Audio Pause** to silence alert for two minutes during troubleshooting.

2. Move the therapy unit to an environment with an operational temperature range as detailed in the **Specifications** section of this manual (page 194).

It may take up to two hours for the therapy unit to return to operating temperatures.

3. Select **Reset** to return to the ***Home*** screen.

Therapy continues.

If alert condition cannot be resolved, contact KCI.

PREVENA™ Therapy System Error Alert (Therapy Interrupted) (after Power On)

Low Priority Alert - This alert screen appears when there is a system fault within the V.A.C.ULTA™ Therapy Unit after it has been powered on. Several different types of system errors may occur. A number will appear next to Error Code: that represents the diagnostic code of the system fault. This alert will be accompanied by a repeating audible tone.

To resolve this alert:

1. Select **Audio Pause** to silence alert for two minutes during troubleshooting.
2. Record the Error Code number.
3. Power the unit off and then on using the **Power** button on the front of the unit (page 18).

If alert condition cannot be resolved, contact KCI.

System Error Alert (at Power On)

Low Priority Alert - This alert screen appears when there is a system fault within the V.A.C.ULTA™ Therapy Unit while the unit is powering on. "00000001" represents the diagnostic code of the system fault. This alert will be accompanied by a repeating audible tone.

To resolve this alert:

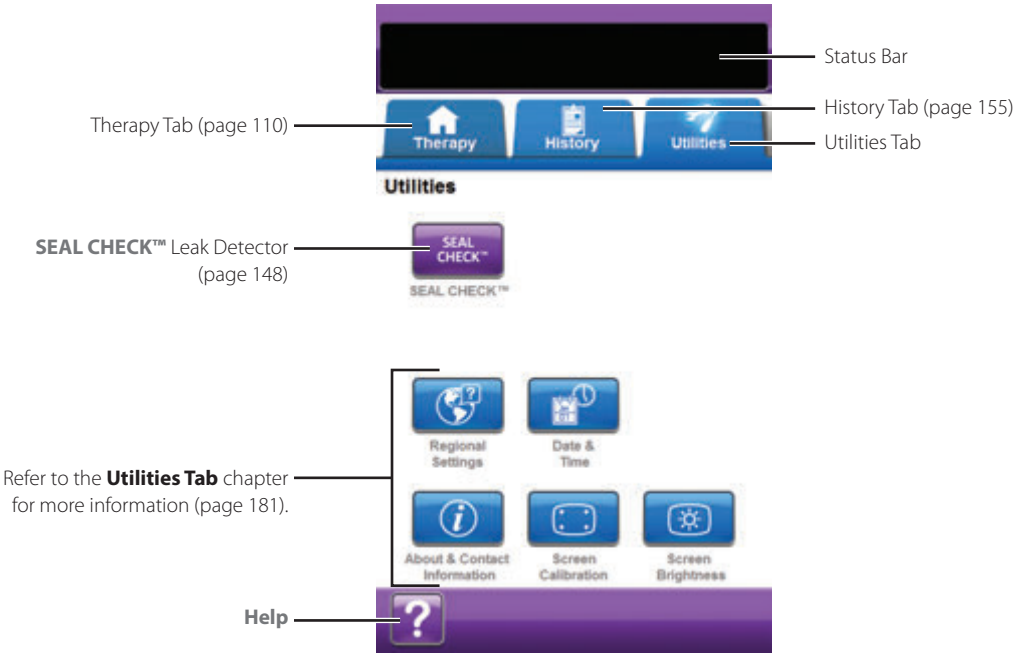
1. Record the Error Code number (00000001).

2. Power the unit off and then on using the **Power** button on the front of the unit (page 18).

If alert condition cannot be resolved, contact KCI.

Utilities Tab - PREVENA™ Therapy

Use the ***Utilities Tab*** screen to set preferences for the V.A.C.ULTA™ Therapy Unit. Certain selections are available no matter what therapy is active. Those selections are discussed in the **Utilities Tab** chapter. Selections that are unique to the selected therapy are detailed below.



The following options are available from the ***Utilities Tab*** Home screen:

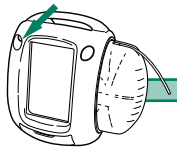
SEAL CHECK™ Leak Detector - An on-screen bar graph will indicate leak level and an audible tone will sound if unit detects a significant leak (page 145).

Help - Use to access the V.A.C.ULTA™ Therapy Unit's on-screen help features.

ABTHERA™ Therapy Overview

The following flow chart shows the basic steps required to configure **ABTHERA™ Therapy**. Refer to the following pages for detailed information about individual screens and options.

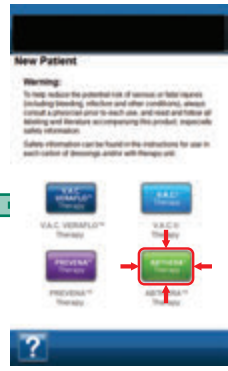
Press and hold **Power** buton until light comes on.



Required for ABTHERA™ Therapy:

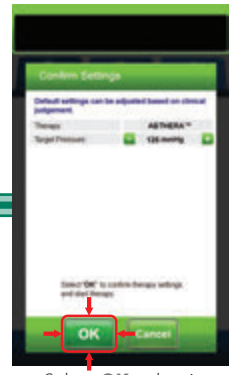
- Canister
- ABTHERA™ SENSAT.R.A.C.™ Open Abdomen Dressing

Startup screen



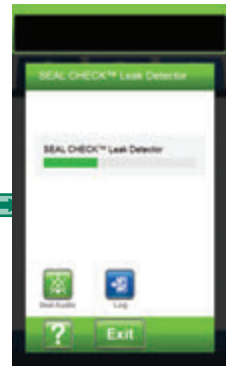
Select **ABTHERA™ Therapy**. (page 42)

Confirm Settings screen



Select **OK** to begin SEAL CHECK™ Leak Detector. (page 149)

SEAL CHECK™ Leak Detector screen

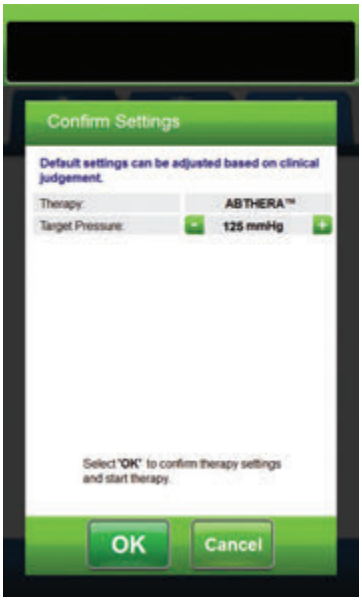


Drawdown begins.

Home screen - **ABTHERA™ Therapy**

Screen shots shown above are for representation only. Refer to the page numbers listed for a more detailed view and more detailed information.

Settings displayed will vary depending on settings defined by user.



This screen allows the user to adjust the Target Pressure the V.A.C.ULTA™ Therapy Unit will deliver during **ABTHERA™ Therapy**:

- **Target Pressure (mmHg)** - (**Default = 125 mmHg**) Prescribed negative pressure level for **ABTHERA™ Therapy**. Target Pressure can be set to 100, 125 or 150 mmHg.

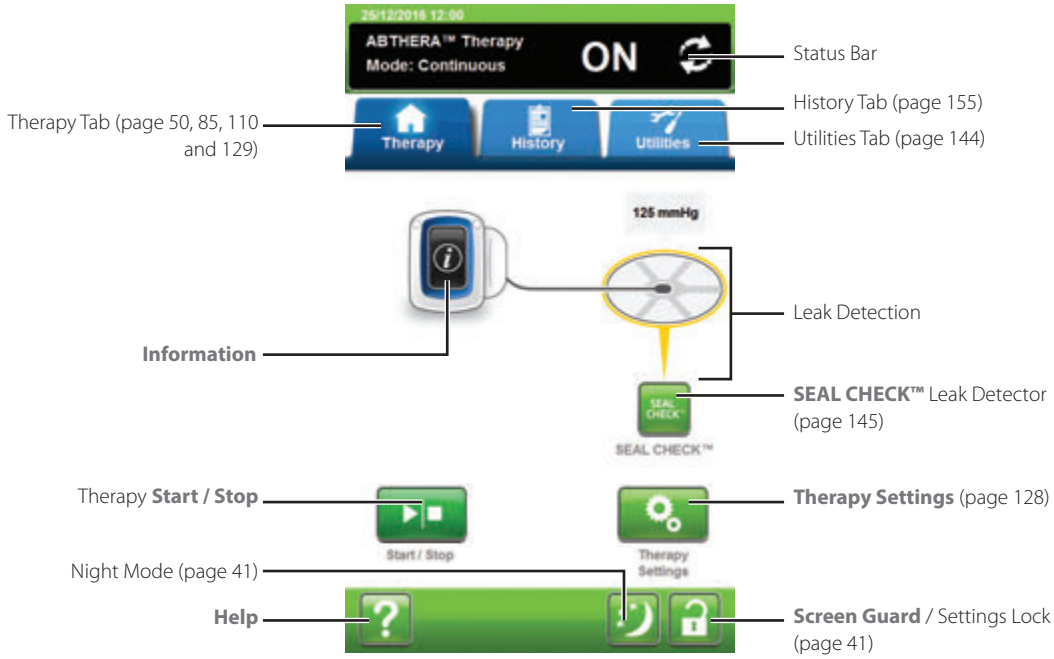
1. Use + / - to select desired value for **ABTHERA™ Therapy**.

2. Once Target Pressure has been entered, select **OK** to initiate therapy and continue to the ***SEAL CHECK™ Leak Detector*** screen for **ABTHERA™ Therapy**.

3. Select **Cancel** to return to the ***Choose Therapy*** screen.

Home Screen - ABTHERA™ Therapy

This ***Home*** screen is the main screen displayed by the V.A.C.ULTA™ Therapy Unit during **ABTHERA™ Therapy**. It is used to access important information about the status of therapy.



Therapy mode and status (**ON** or **OFF**) will be displayed in the status bar at the top of the screen. The current therapy pressure will also appear above the icon of dressing.

The following options are available from the ***Home*** screen for **ABTHERA™ Therapy**:

Therapy Settings - Use to change current therapy settings.

SEAL CHECK™ Leak Detector - An on-screen bar graph will indicate leak level and an audible tone will sound if unit detects a significant leak (page 145).

Information - Use to view a summary of therapy history and current therapy settings (page 130).

Start / Stop - Use to start or stop therapy.

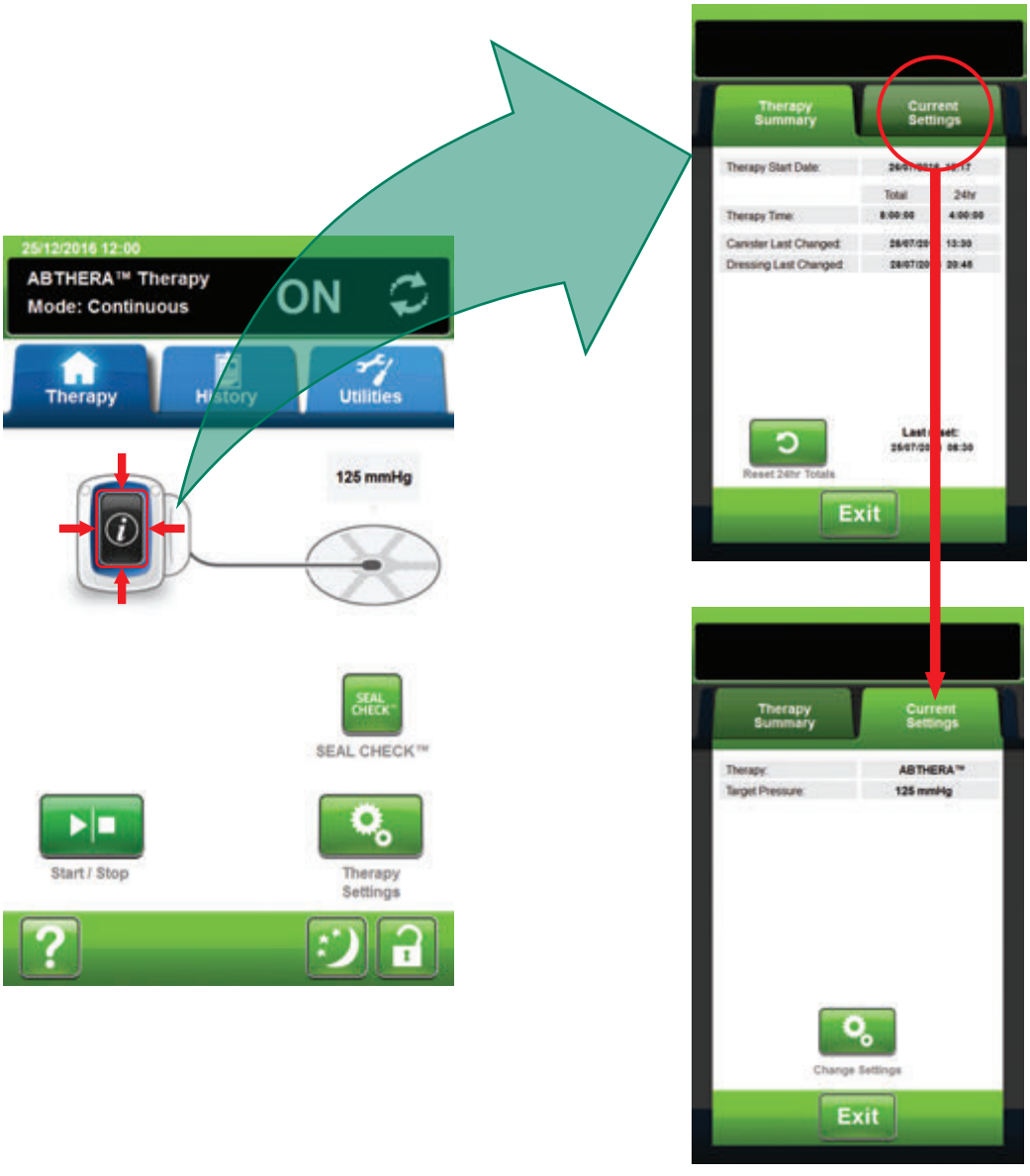
Help - Use to access to the V.A.C.ULTA™ Therapy Unit's on-screen help features.

Leak Detection - If the therapy unit detects a leak in the system temporarily above the Leak Alarm threshold, the ***Home*** screen for **ABTHERA™ Therapy** will display a yellow box around the dressing. Refer to the instructions for use provided with the dressings for information on using excess drape material to seal any leak areas.

Refer to page 41 for a list of **Common Touch Screen Buttons** not described here.

Information Screens - ABTHERA™ Therapy

These screens will display the current therapy settings and a summary of therapy applied to the patient.



1. Select **Information** from the ***Home*** screen to continue to the ***Therapy Summary*** tab. Use this tab to review the Therapy Start Date and Therapy Time. If the Log feature is used, the date and time for Canister Last Changed and Dressing Last Changed will also be displayed.

2. Select **Current Settings** to continue to the ***Current Settings*** screen. Use this tab to review the current therapy settings.

3. Select **Change Settings** to continue to the ***Confirm Settings*** screen (page 128).

4. Select ***Cancel*** on the ***Confirm Settings*** screen to return to the ***Home*** screen for **ABTHERA™ Therapy**.

ABTHERA™ Therapy Alerts

The following alerts may appear on the touch screen during **ABTHERA™ Therapy**.

Alerts are accompanied by a repeating audible tone.

Following initiation of therapy, if an audible tone is not heard when SEAL CHECK™ Leak Detector is displayed and Seal Audio tone is turned ON, the alerts may not be working properly. Contact KCI for more information. Alerts are intended to be heard when facing the therapy unit at a maximum of one meter away. If two or more alert conditions are present, only the highest priority alert will be displayed.

Low Priority Alert Condition - Displayed on the touch screen when the V.A.C.ULTA™ Therapy Unit detects a condition that requires attention. Alerts will be accompanied by a repeating audible tone approximately every 20 seconds (two beeps).

Select **Seal Audio** to turn audible tone ON.

Select **Help** for more information regarding alert resolution.

If alert conditions cannot be resolved, contact KCI.

ABTHERA™ Therapy Blockage Alert

Low Priority Alert - This alert screen appears when the V.A.C.ULTA™ Therapy Unit has detected a potential blockage. This alert will be accompanied by a repeating audible tone.

To resolve this alert:

1. Select **Audio Pause** to silence alert for two minutes during troubleshooting.

2. Ensure clamps on the tubing on the SENSAT.R.A.C.™ Pad and canister tubing are open.

3. Ensure tubing is not kinked, crimped, or blocked in any way.

4. If the **ABTHERA™ Therapy Blockage Alert** remains after completing steps 2 and 3, lower the therapy unit and tubing to be level with or below the wound site. If the alert is resolved by lowering the unit, normal use may resume.

5. Select **Reset** to return to the ***Home*** screen.

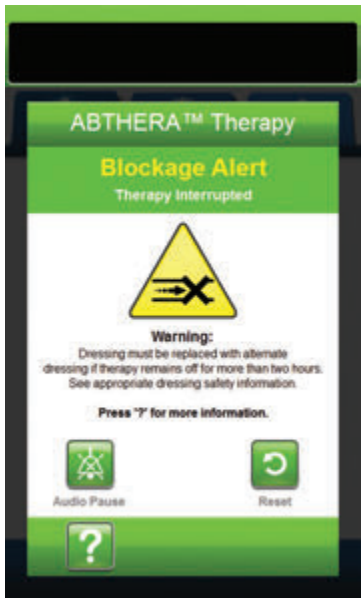
6. Ensure therapy is ON by checking the status bar (page 129). If not, select **Start / Stop** to restart therapy.

The V.A.C.ULTA™ Therapy Unit will continue to attempt to apply therapy during this alert.

If alert condition cannot be resolved, contact KCI.

ABTHERA™ Therapy Blockage Alert (Therapy Interrupted)

Low Priority Alert - This alert screen appears when a blockage is present. This alert will be accompanied by a repeating audible tone.



To resolve this alert:

1. Select **Audio Pause** to silence alert for two minutes during troubleshooting.

2. Ensure clamps on the tubing on the SENSAT.R.A.C.™ Pad and canister tubing are open.

3. Ensure tubing is not kinked, crimped, or blocked in any way.

4. If the **ABTHERA™ Therapy Blockage Alert (Therapy Interrupted)** remains after completing steps 2 and 3, lower the therapy unit and tubing to be level with or below the wound site. If the alert is resolved by lowering the unit, normal use may resume.

5. Select **Reset** to return to the ***Home*** screen.

6. Ensure therapy is ON by checking the status bar (page 129). If not, select **Start / Stop** to restart therapy.

Therapy unit remains on; however, negative pressure at the wound site may be below therapeutic value.

If alert condition cannot be resolved, contact KCI.

Certain KCI Dressings must be replaced with an alternate dressing if therapy is interrupted or off for more than two hours. See the Safety Information Sheet provided with the individual dressing for further information.

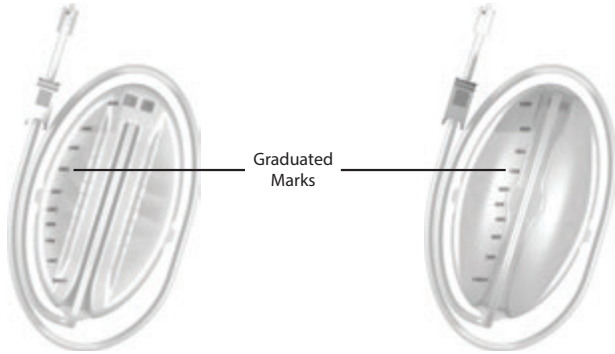
ABTHERA™ Therapy Canister Full Alert

Low Priority Alert - This alert screen appears when the canister is full and should be replaced. This alert will be accompanied by a repeating audible tone.

To resolve this alert:

1. Select **Audio Pause** to silence alert for two minutes during troubleshooting.

2. Check if canister is full by comparing the level of fluid to the graduated marks on the canister.



A full canister is approximately 300 mL, 500 mL or 1000 mL depending on canister used. Canister release button will be flashing.

3. If canister is not full, select **Reset** to return to the ***Home*** screen.

4. If canister is full, change canister and select **Reset** on this screen to return to the ***Home*** screen. See the **Changing the Canister** section of this manual (page 34) for additional information.

5. Select **Start / Stop** to restart therapy.

Certain KCI Dressings must be replaced with an alternate dressing if therapy is interrupted or off for more than two hours. See the Safety Information Sheet provided with the individual dressing for further information.

ABTHERA™ Therapy Canister Not Engaged Alert

Low Priority Alert - This alert screen appears when the canister is not fully inserted and / or properly latched. This alert will be accompanied by a repeating audible tone.

To resolve this alert:

1. Select **Audio Pause** to silence alert for two minutes during troubleshooting.

2. Remove the canister by pressing the **Canister Release** button (page 18) on the unit.

3. Inspect the canister and V.A.C.ULTA™ Therapy Unit to ensure no foreign objects or debris interfere with the canister and therapy unit's mating surfaces.

4. Ensure both seals are present and seated completely (page 19). If seals are missing or damaged, contact KCI.

5. Re-attach the canister to the V.A.C.ULTA™ Therapy Unit ensuring that the canister is fully engaged and latched (page 32). An audible click indicates that the canister is properly installed.

6. Select **Reset** to return to the ***Home*** screen.

7. Select **Start / Stop** to restart therapy.

8. If this alert continues to appear, repeat steps 2 - 7 with a new canister.

If alert condition cannot be resolved, contact KCI.

ABTHERA™ Therapy Therapy Inactive Alert

Low Priority Alert - This alert screen appears when therapy (**ABTHERA™ Therapy**) has been off or paused for more than 15 minutes (with the unit powered on). This alert will be accompanied by a repeating audible tone.

To resolve this alert:

1. Select **Audio Pause** to silence alert for two minutes during troubleshooting.

2. Select **Reset** to return to the ***Home*** screen.

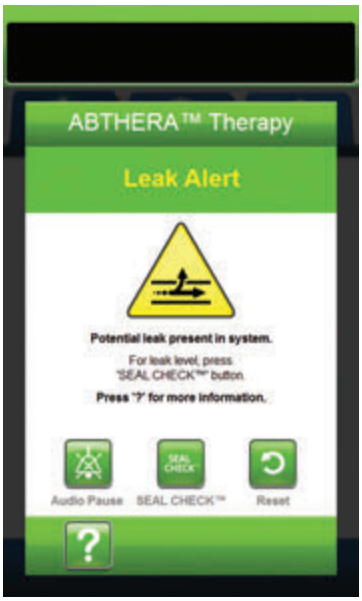
3. Select **Start / Stop** to restart therapy.

4. If therapy is not desired, turn the V.A.C.ULTA™ Therapy Unit off by using the **Power** button on the front of the unit.

Certain KCI Dressings must be replaced with an alternate dressing if therapy is interrupted or off for more than two hours. See the Safety Information Sheet provided with the individual dressing for further information.

ABTHERA™ Therapy Leak Alert

Low Priority Alert - This alert screen appears when a significant negative pressure leak has been detected. This alert will be accompanied by a repeating audible tone.



To resolve this alert:

1. Select **Audio Pause** to silence alert for two minutes during troubleshooting.

2. Ensure connector between dressing tubing and canister tubing is properly locked.

3. Ensure canister is fully engaged. (See **Canister Not Engaged Alert**, page 135).

4. Select **SEAL CHECK™** to access the SEAL CHECK™ Leak Detector. Refer to the **SEAL CHECK™ Leak Detector** section (page 145) of this manage for details on how to use the SEAL CHECK™ Leak Detector and how to repair leaks.

5. Once the leak is resolved using the SEAL CHECK™ Leak Detector, select **Exit** on the ***SEAL CHECK™ Leak Detector*** screen to return to the ***ABTHERA™ Therapy Leak Alert*** screen.

6. Select **Reset** to return to the ***Home*** screen.

7. Ensure therapy is ON by checking the Status Bar (page 129). If not, select **Start / Stop** to restart therapy.

The V.A.C.ULTA™ Therapy Unit will continue to attempt to apply therapy during this alert.

If alert condition cannot be resolved, contact KCI.

ABTHERA™ Therapy Battery Low Alert

Low Priority Alert - This alert screen appears approximately two hours before the battery power level is too low to support continued operation of the V.A.C.ULTA™ Therapy Unit. This alert will be accompanied by a repeating audible tone.

To resolve this alert:

1. Select **Audio Pause** to silence alert for two minutes during troubleshooting.

2. Connect the therapy unit to a wall outlet using the KCI supplied power supply to recharge battery. An amber light at the bottom of the touch screen and a battery charge icon indicate the unit is charging. Refer to the **Charge Battery** section of this manual (page 23) for more information.

Once the V.A.C.ULTA™ Therapy Unit is plugged into a wall outlet, the Battery Low Alert screen will automatically clear.

OR

3. Select **Reset** to return to the ***Home*** screen.

Therapy continues.

ABTHERA™ Therapy Battery Critical Alert

Low Priority Alert - This alert screen appears approximately 30 minutes before the battery power level is too low to support continued operation of the V.A.C.ULTA™ Therapy Unit. This alert will be accompanied by a repeating audible tone.

To resolve this alert:

1. Select **Audio Pause** to silence alert for two minutes during troubleshooting.

2. Connect the therapy unit to a wall outlet using KCI supplied power supply to recharge battery. An amber light at the bottom of the touch screen and a battery charge icon indicates the unit is charging. Refer to the **Charge Battery** section of this manual (page 23) for more information.

Once the V.A.C.ULTA™ Therapy Unit is plugged into a wall outlet, the Battery Critical Alert screen will automatically clear.

OR

3. Select **Reset** to return to the ***Home*** screen.

ABTHERA™ Therapy continues, however, if this alert is not resolved within approximately thirty minutes, therapy will be interrupted.

4. Ensure therapy is ON by checking the status bar (page 129). If not, select **Start / Stop** to restart therapy.

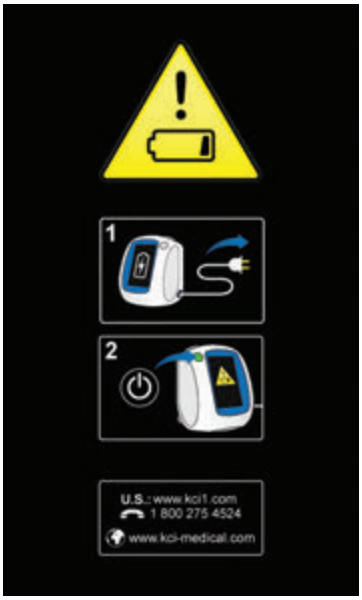
The V.A.C.ULTA™ Therapy must be plugged into a wall outlet in order to continue therapy.

Alert logs and settings are not lost in the case of a total power loss or if the unit is power cycled (turned off then back on).

Certain KCI Dressings must be replaced with an alternate dressing if therapy is interrupted or off for more than two hours. See the Safety Information Sheet provided with the individual dressing for further information.

Battery Exhausted

Low Priority Alert - This alert screen appears when the battery power level is too low to power on the V.A.C.ULTA™ Therapy Unit.



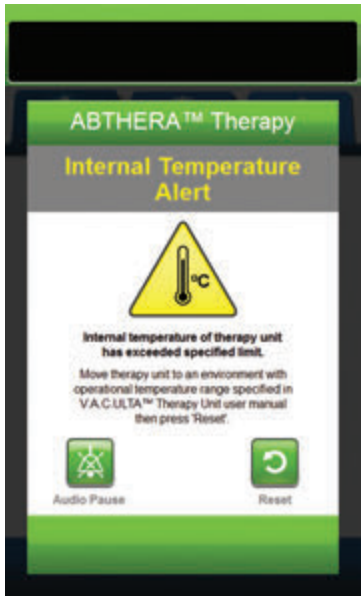
To resolve this alert:

1. Connect the therapy unit to a wall outlet using KCI supplied power supply to recharge battery. An amber light at the bottom of the touch screen and a battery charge icon indicates the unit is charging. Refer to the **Charge Battery** section of this manual (page 23) for more information.

2. Power the V.A.C.ULTA™ Therapy Unit on and initiate therapy. Refer to the **Power the V.A.C.ULTA™ Therapy Unit On or Off** section of this manual (page 42) for more information.

ABTHERA™ Therapy Internal Temperature Alert

Low Priority Alert - This alert screen appears when the internal temperature of the V.A.C.ULTA™ Therapy Unit is outside its specified limits. This alert will be accompanied by a repeating audible tone.



Therapy will continue while this alert is active. The touch screen will be turned off after five minutes of inactivity. The screen will illuminate when touched. Battery charging is stopped.

To resolve this alert:

1. Select **Audio Pause** to silence alert for two minutes during troubleshooting.

2. Move the therapy unit to an environment with an operational temperature range as detailed in the **Specifications** section of this manual (page 194).

It may take up to two hours for the therapy unit to return to operating temperatures.

3. Select **Reset** to return to the ***Home*** screen.

Therapy continues.

If alert condition cannot be resolved, contact KCI.

Certain KCI Dressings must be replaced with an alternate dressing if therapy is interrupted or off for more than two hours. See the Safety Information Sheet provided with the individual dressing for further information.

ABTHERA™ Therapy System Error Alert (Therapy Interrupted) (after Power On)

Low Priority Alert - This alert screen appears when there is a system fault within the V.A.C.ULTA™ Therapy Unit after it has been powered on. Several different types of system errors may occur. A number will appear next to Error Code: that represents the diagnostic code of the system fault. This alert will be accompanied by a repeating audible tone.

To resolve this alert:

1. Select **Audio Pause** to silence alarm for two minutes during troubleshooting.
2. Record the Error Code number.
3. Power the unit off and then on using the **Power** button on the front of the unit (page 18).

If alert condition cannot be resolved, contact KCI.

Certain KCI Dressings must be replaced with an alternate dressing if therapy is interrupted or off for more than two hours. See the Safety Information Sheet provided with the individual dressing for further information.

System Error Alert (at Power On)

Low Priority Alert - This alert screen appears when there is a system fault within the V.A.C.ULTA™ Therapy Unit while the unit is powering on. "00000001" represents the diagnostic code of the system fault. This alert will be accompanied by a repeating audible tone.

To resolve this alert:

1. Record the Error Code number (00000001).

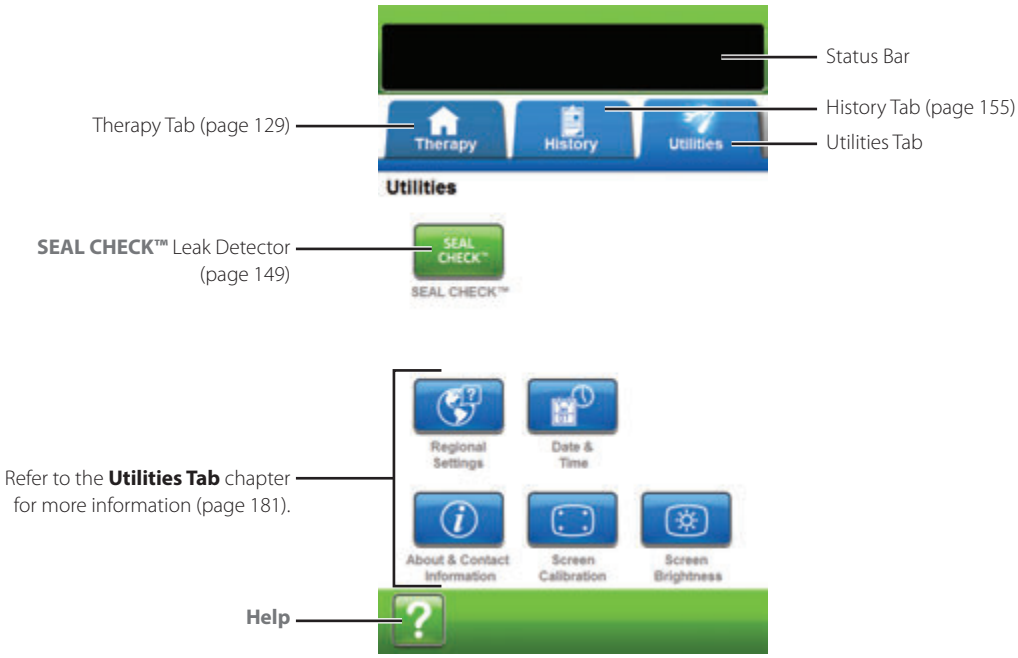
2. Power the unit off and then on using the **Power** button on the front of the unit (page 18).

If alert condition cannot be resolved, contact KCI.

Certain KCI Dressings must be replaced with an alternate dressing if therapy is interrupted or off for more than two hours. See the Safety Information Sheet provided with the individual dressing for further information.

Utilities Tab - ABTHERA™ Therapy

Use the ***Utilities Tab*** screen to set preferences for the V.A.C.ULTA™ Therapy Unit. Certain selections are available no matter what therapy is active. Those selections are discussed in the **Utilities Tab** chapter. Selections that are unique to the selected therapy are detailed below.



The following options are available from the ***Utilities Tab*** Home screen:

SEAL CHECK™ Leak Detector - An on-screen bar graph will indicate leak level and an audible tone will sound if unit detects a significant leak (page 145).

Help - Use to access the V.A.C.ULTA™ Therapy Unit's on-screen help features.

SEAL CHECK™ Leak Detector Overview

The SEAL CHECK™ Leak Detector is used to help find negative pressure leaks.

Access the SEAL CHECK™ Leak Detector from the ***Home*** screen. The SEAL CHECK™ Leak Detector will also automatically run during the initial Drawdown phase once therapy has been initiated.

Most leaks occur:

- where the drape meets the skin.
- where the V.A.C. VERAT.R.A.C.™ Pad, V.A.C. VERAT.R.A.C. DUO™ Tube Set pads or SENSAT.R.A.C.™ Pad is attached to the drape, if applicable.
- at tubing connections.
- if canister is not fully seated to therapy unit.

Seal Audio default is set to OFF.

1. Ensure that both the V.A.C.® Canister tubing and instillation line are properly connected.

2. Ensure that all four tubing clamps are open.

3. Ensure the V.A.C. VERALINK™ Cassette is properly installed (page 28), if applicable.

4. Ensure that the canister is properly installed (page 32).

5. Once therapy has been initiated, select **SEAL CHECK™** Leak Detector.

The SEAL CHECK™ Leak Detector uses an audible tone and bar graph to assist in finding leaks. The frequency of the audible tone and length of the bar graph will reflect the leak rate. The audible tone slows down and the bar graph decreases in length as the leak is found.

The bar graph will be yellow if a significant leak is detected. A green bar graph indicates the V.A.C.ULTA™ Therapy Unit is operating normally. The line on the bar graph is the transition point from yellow to green.

During initial dressing draw down, the bar graph should turn yellow and then return to a green state if there are no significant leaks.

6. Select **Seal Audio** to turn seal audio tone on or off. **Seal Audio default is set to OFF**.

7. While therapy is on and using light pressure, move your hand and fingers slowly around the edges of the drape and tubing pads. The bar graph will decrease and change from yellow to green and the frequency of the audible tone (if Seal Audio is on) will decrease when a leak is found and repaired.

8. Refer to the instructions for use provided with the dressings for information on using excess drape material to seal any leak areas.

9. Select **Exit** to return to the ***Home*** screen.

1. Ensure that the V.A.C.® Canister tubing is properly connected.

2. Ensure that both tubing clamps are open.

3. Ensure that the canister is properly installed (page 32).

4. Once therapy has been initiated, select **SEAL CHECK™** Leak Detector.

The SEAL CHECK™ Leak Detector uses an audible tone and bar graph to assist in finding leaks. The frequency of the audible tone and length of the bar graph will reflect the leak rate. The audible tone slows down and the bar graph decreases in length as the leak is found.

The bar graph will be yellow if a significant leak is detected. A green bar graph indicates the V.A.C.ULTA™ Therapy Unit is operating normally. The line on the bar graph is the transition point from yellow to green.

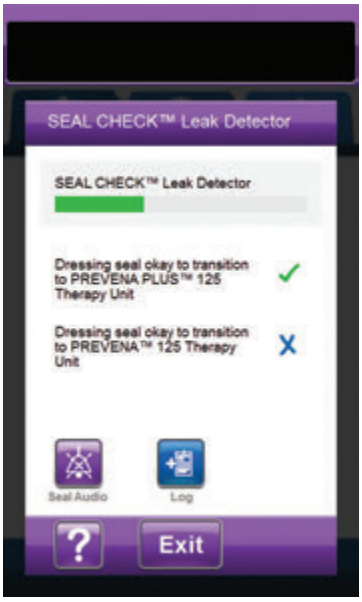
During initial dressing draw down, the bar graph should turn yellow and then return to a green state if there are no significant leaks.

5. Select **Seal Audio** to turn seal audio tone on or off. **Seal Audio default is set to OFF**.

6. While therapy is on and using light pressure, move your hand and fingers slowly around the edges of the drape and tubing pad. The bar graph will decrease and change from yellow to green and the frequency of the audible tone (if Seal Audio is on) will decrease when a leak is found and repaired.

7. Refer to the instructions for use provided with the dressings for information on using excess drape material to seal any leak areas.

Select **Exit** to return to the ***Home*** screen.



1. Ensure that the V.A.C.® Canister tubing is properly connected.
2. Ensure that both tubing clamps are open.
3. Ensure that the canister is properly installed (page 32).

4. Once therapy has been initiated, select **SEAL CHECK™** Leak Detector.

The SEAL CHECK™ Leak Detector uses an audible tone and bar graph to assist in finding leaks. The frequency of the audible tone and length of the bar graph will reflect the leak rate. The audible tone slows down and the bar graph decreases in length as the leak is palpated.

The bar graph will be yellow if a significant leak is detected. A green bar graph indicates the V.A.C.ULTA™ Therapy Unit is operating normally. The line on the bar graph is the transition point from yellow to green.

If the patient will be transitioned to a PREVENA™ Therapy Unit:

The ***SEAL CHECK™ Leak Detector*** screen will display an **X** if the dressing seal is not adequate for use with the associated **PREVENA™ Therapy Unit**. The **PREVENA™ Therapy Unit** may sound a Leak Alarm when connected.

The ***SEAL CHECK™ Leak Detector*** screen will display a **Check Mark** if the dressing seal is adequate for use with the associated **PREVENA™ Therapy Unit**. The **PREVENA™ Therapy Unit** should not sound a Leak Alarm when connected.

During initial dressing draw down, the bar graph should turn yellow and then return to a green state if there are no significant leaks.

5. Select **Seal Audio** to turn seal audio tone on or off. **Seal Audio default is set to OFF**.
6. While therapy is on and using light pressure, move your hand and fingers slowly around the edges of the dressing and drape. The bar graph will decrease and change from yellow to green and the frequency of the audible tone (if Seal Audio is on) will decrease when a leak is found and repaired.
7. Refer to the instructions for use provided with the dressings for information on using excess drape material to seal any leak areas.

8. Select **Exit** to return to the ***Home*** screen.

1. Ensure that the V.A.C.® Canister tubing is properly connected.

2. Ensure that both tubing clamps are open.

3. Ensure that the canister is properly installed (page 32).

4. Once therapy has been initiated, select **SEAL CHECK™** Leak Detector.

The SEAL CHECK™ Leak Detector uses an audible tone and bar graph to assist in finding leaks. The frequency of the audible tone and length of the bar graph will reflect the leak rate. The audible tone slows down and the bar graph decreases in length as the leak is found.

The bar graph will be yellow if a significant leak is detected. A green bar graph indicates the V.A.C.ULTA™ Therapy Unit is operating normally. The line on the bar graph is the transition point from yellow to green.

During initial dressing draw down, the bar graph should turn yellow and then return to a green state if there are no significant leaks.

5. Select **Seal Audio** to turn seal audio tone on or off. **Seal Audio default is set to OFF**.

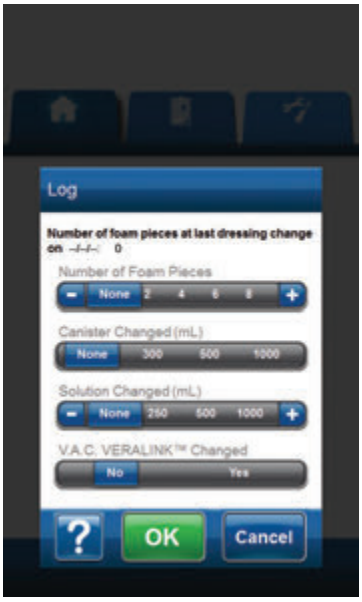
6. While therapy is on and using light pressure, move your hand and fingers slowly around the edges of the drape and tubing pad. The bar graph will decrease and change from yellow to green and the frequency of the audible tone (if Seal Audio is on) will decrease when a leak is found and repaired.

7. Refer to the instructions for use provided with the dressings for information on using excess drape material to seal any leak areas.

8. Select **Exit** to return to the ***Home*** screen.

Log - V.A.C. VERAFLO™ Therapy

Use this tool to record important information about dressing and component application / changes. The information will be recorded in the Therapy History Report (page 177).



Number of Foam Pieces - Select the number of foam pieces used in the wound at dressing application or dressing change. Use **+** / **-** , as applicable to adjust above or below the values shown.

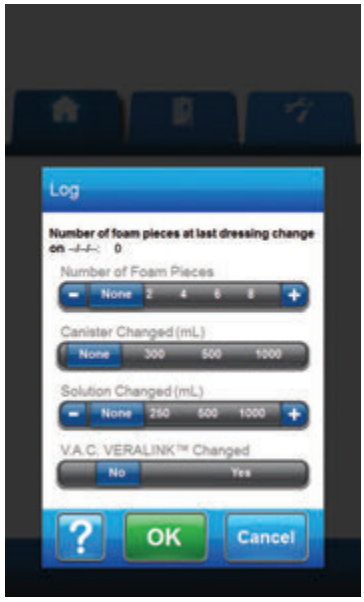
Canister Changed (mL) - Select which canister (300 mL, 500 mL or 1000 mL) was installed or changed.

Solution Changed (mL) - Select the size (100 to 1000 mL) of solution bag / bottle that was installed. Use **+** / **-** , as applicable to adjust above or below the values shown.

V.A.C. VERALINK™ Changed - Select **Yes** or **No** to indicate whether or not a V.A.C. VERALINK™ Cassette was installed or changed.

Log - V.A.C.® Therapy

Use this tool to record important information about dressing and component application / changes. The information will be recorded in the Therapy History Report (page 177).



Number of Foam Pieces - Select the number of foam pieces used in the wound at dressing application or dressing change. Use **+** / **-** , as applicable to adjust above or below the values shown.

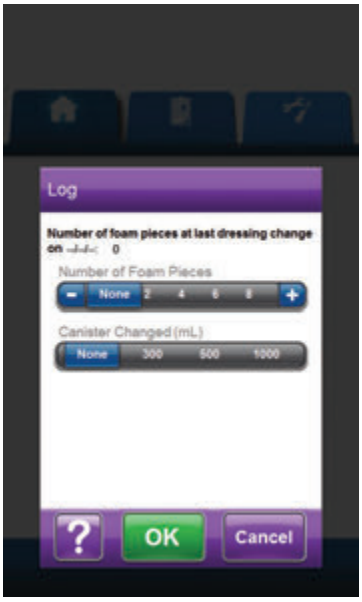
Canister Changed (mL) - Select which canister (300 mL, 500 mL or 1000 mL) was installed or changed.

Solution Changed (mL) - Select the size (100 to 1000 mL) of solution bag / bottle that was installed. Use **+** / **-** , as applicable to adjust above or below the values shown.

V.A.C. VERALINK™ Changed - Select **Yes** or **No** to indicate whether or not a V.A.C. VERALINK™ Cassette was installed or changed.

Log - PREVENA™ Therapy

Use this tool to record important information about dressing and component application / changes. The information will be recorded in the Therapy History Report (page 177).

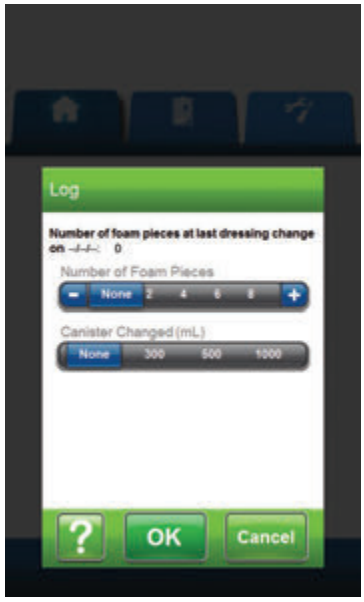


Number of Foam Pieces - Select the number of foam pieces used in the wound at dressing application or dressing change. Use + / - , as applicable to adjust above or below the values shown.

Canister Changed (mL) - Select which canister (300 mL, 500 mL or 1000 mL) was installed or changed.

Log - ABTHERA™ Therapy

Use this tool to record important information about dressing and component application / changes. The information will be recorded in the Therapy History Report (page 177).

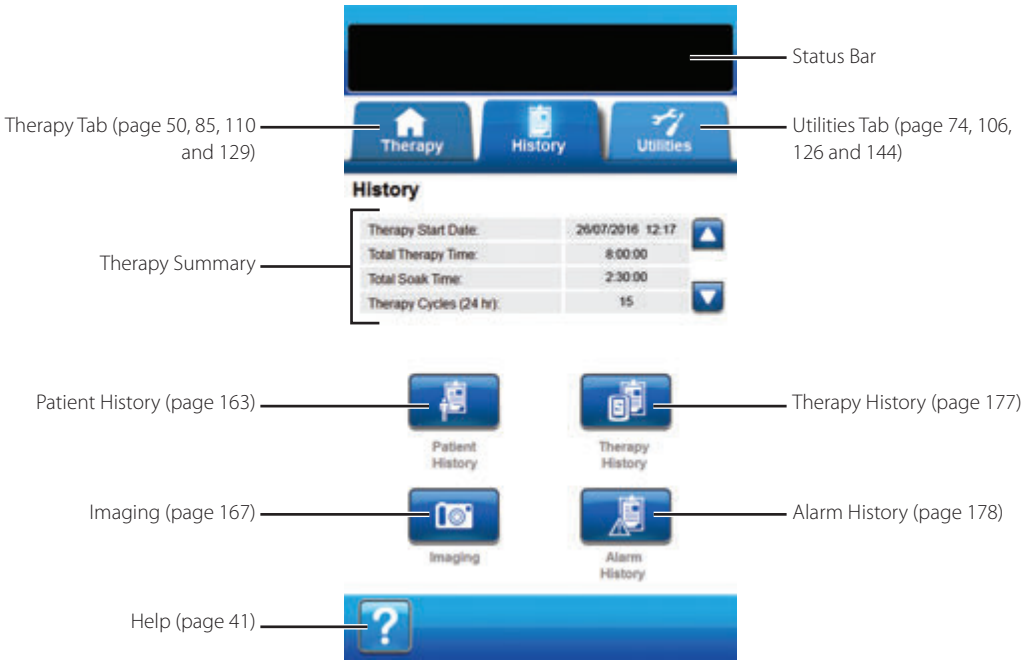


Number of Foam Pieces - Select the number of foam pieces used in the wound at dressing application or dressing change. Use + / - , as applicable to adjust above or below the values shown.

Canister Changed (mL) - Select which canister (300 mL, 500 mL or 1000 mL) was installed or changed.

History Tab Screen

Use the ***History Tab*** screen to access History (Patient, Therapy and Alarm) and the Wound Imaging Tool.



The following options are available from the ***History Tab*** screen:

Patient History - The Patient History screen displays the patient's information in date, time and event columns. The date is in descending order and time is displayed using the twenty-four hour clock format.

Imaging - The Wound Imaging feature aids in recording the wound healing process. Use to upload digital wound images for on-screen viewing or surface area and volume trending.

Therapy History - The Therapy History screen displays the patient's therapy information in date, time and event columns. The date is in descending order and time is displayed using the twenty-four hour clock format.

Alarm History - The Alarm History screen displays the alarm information from the V.A.C.ULTA™ Therapy Unit in date, time and event columns. The date is in descending order and time is displayed using the twenty-four hour clock format.

Help - Use to access the V.A.C.ULTA™ Therapy Unit's on-screen help features.

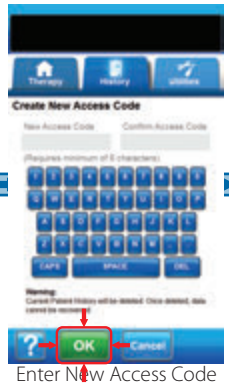
Patient History or Imaging Configuration (First Time Use) - Overview

The following flow charts show the basic steps required to establish an access code and start a new patient history log. Refer to the following pages for more detailed information about individual screens and options.

History Tab screen

With **History Tab** selected select **Patient History** (page 155).

Create New Access Code screen



Enter New Access Code and Confirm. Select **OK** (page 158)

Create New Patient ID screen

Enter Patient ID. Select **OK** (page 158).

Patient History screen

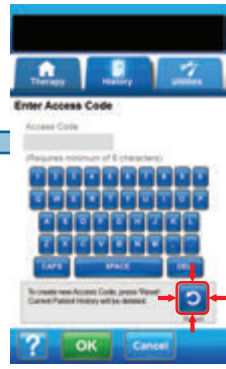
Patient History screen is displayed (page 162).

Screen shots shown above are for representation only. Refer to the page numbers listed for a more detailed view and more detailed information.

History Tab screen

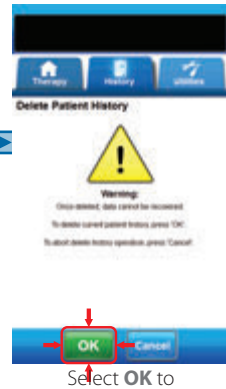
With **History Tab** selected, select **Patient History** button (page 155).

Enter Access Code screen.



Select **Reset** (page 160) to create a new Patient History log.

Create Patient History screen.

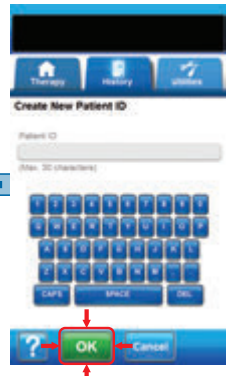


Select **OK** to delete current Patient History (page 160).

Patient History screen.

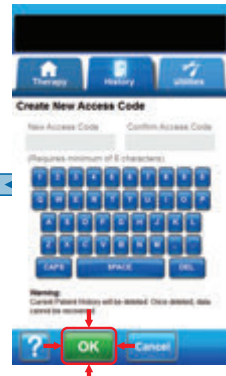
Patient History screen is displayed (page 162).

Create New Patient ID screen.



Enter Patient ID. Select **OK** (page 161).

Create New Access Code screen.

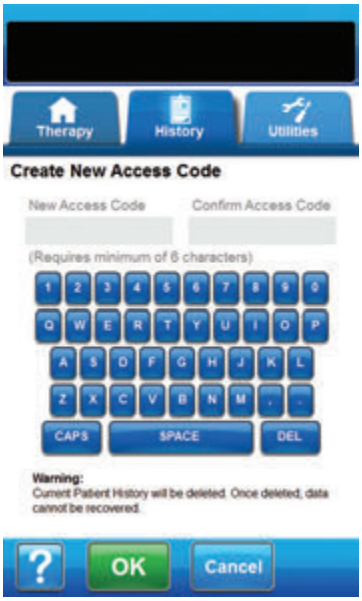


Enter New Access Code and confirm. Select **OK** (page 161).

Patient History

Use the Patient History screens to create a new access code and start a new patient history log, view patient history, delete patient history, export patient history, and view a wound image area graph.

Create New Patient History



1. Select the **History** tab (page 155).

2. Select **Patient History** from the ***History Tab*** screen (page 155) to continue to the ***Create New Access Code*** screen.

3. Select the **New Access Code** field and use the on-screen keyboard to enter an access code. The access code must be at least six characters long.

Record the access code. It will be needed each time patient history is accessed.

4. Select the **Confirm Access Code** field and re-enter the access code entered in the **New Access Code** field.

5. Select **OK** to continue to the ***Create New Patient ID*** screen.

6. Select the **Patient ID** field and use the on-screen keyboard to enter the patient's identification (ID). The patient's ID must be 30 characters or less.

7. Select **OK** to continue to the ***Patient History*** screen (page 162).

For security purposes, the V.A.C.ULTA™ Therapy Unit will only allow one patient record at a time to be active. If a new access code is entered, the current access code is overwritten and all patient history associated with it is deleted.

All information will be automatically deleted when the unit is returned to KCI.

Access Patient History

Once an access code is created, it must be entered to access Patient History.

1. Select the **History** tab (page 155).

2. Select **Patient History** from the ***History Tab*** screen (page 155) to continue to the ***Enter Access Code*** screen.

3. Select the **Access Code** field and use the on-screen keyboard to enter the Patient History access code.

4. Select **OK** to continue to the ***Patient History*** screen (page 162).

For security purposes, the V.A.C.ULTA™ Therapy Unit will only allow one patient record at a time to be active. If a new access code is entered, the current access code is overwritten and all patient history associated with it is deleted.

All information will be automatically deleted when the unit is returned to KCI.

For security purposes, if an incorrect access code is entered 12 times, access to Patient History will be disabled. If this happens, contact KCI.

Create New Access Code

In order to create a second patient history log, a new access code must be created. When a second access code is created, all previously recorded patient history will be deleted.

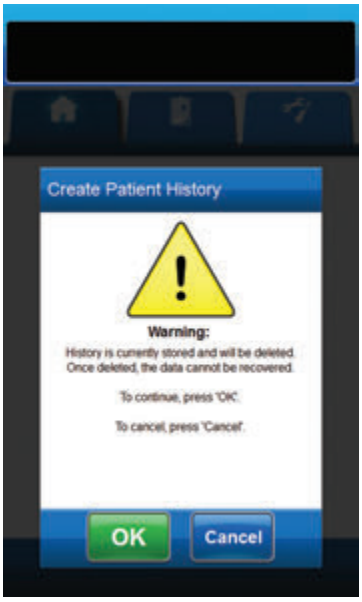
1. Select the **History** tab (page 155).

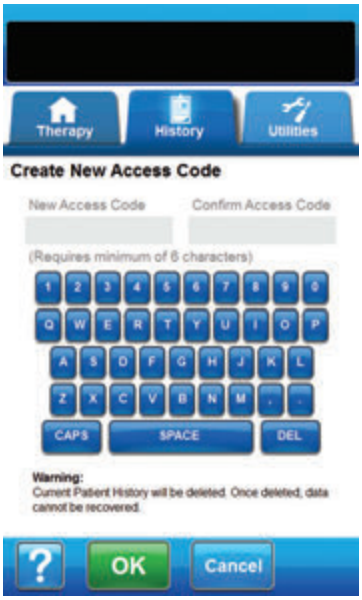
2. Select **Patient History** from the ***History Tab*** screen (page 155) to continue to the ***Enter Access Code*** screen.

3. Select **Reset** to create a new access code.

For security purposes, the V.A.C.ULTA™ Therapy Unit will only allow one patient record at a time to be active. If a new access code is entered, the current access code is overwritten and all patient history associated with it is deleted.

4. Select **OK** on the ***Create Patient History*** warning screen to continue to the ***Create New Access Code*** screen and delete the currently stored history.





5. Select the **New Access Code** field and use the on-screen keyboard to enter an access code. The access code must be at least six characters long.

Record the access code. It will be needed each time patient history is accessed.

6. Select the **Confirm Access Code** field and re-enter the access code entered in the **New Access Code** field.

7. Select **OK** to continue to the ***Create New Patient ID*** screen.

8. Select the **Patient ID** field and use the on-screen keyboard to enter the patient's identification (ID). The patient's ID must be 30 characters or less.

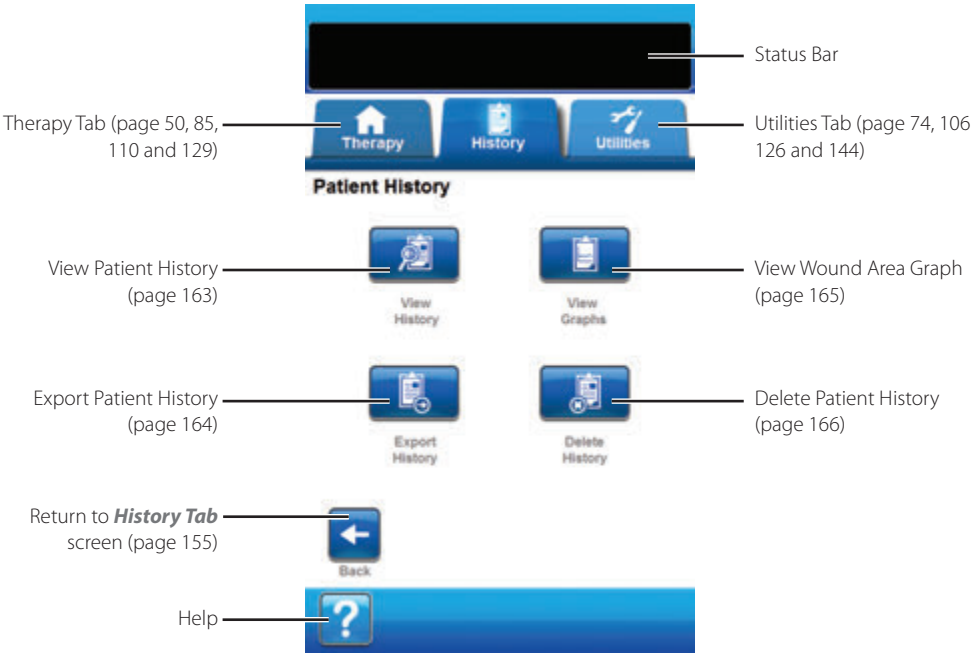
9. Select **OK** to continue to the ***Patient History*** screen (page 162).

For security purposes, the V.A.C.ULTA™ Therapy Unit will only allow one patient record at a time to be active. If a new access code is entered, the current access code is overwritten and all patient history associated with it is deleted.

All information will be automatically deleted when the unit is returned to KCI.

Patient History Screen

Use the Patient History Screen to view, export, or delete a Patient History log (e.g. wound imaging information and disposable component changes).



The following options are available from the ***Patient History*** screen:

View History - Use to view patient history and add short notes about the patient's treatment. For a new patient history log, this screen will not have any event entries.

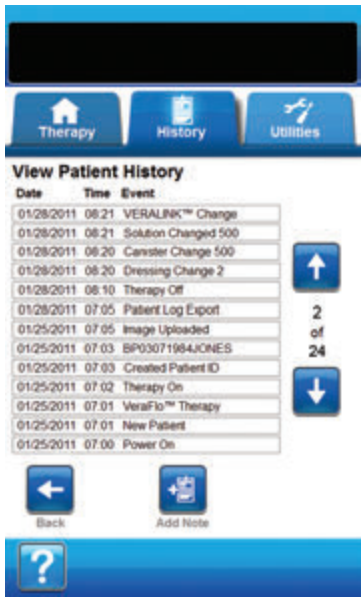
Export History - Use to export all patient history to a USB Drive or SD Card.

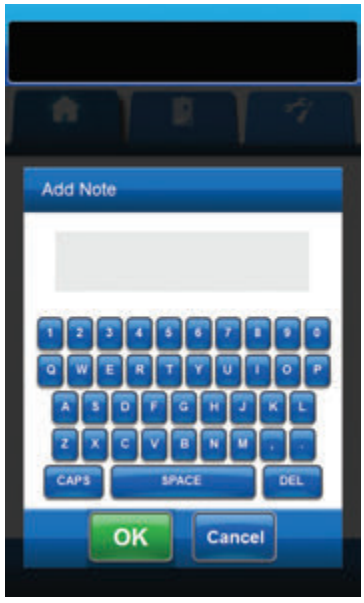
View Graph - Use to view a graph of the measured wound area over time.

Delete History - Use to delete the patient history data from the V.A.C.ULTA™ Therapy Unit's memory.

View Patient History Screen

Use the ***View Patient History*** screen to view and add short notes about the patient's treatment. For a new patient history log, this screen will not have any event entries.





1. Select **View History** from the ***Patient History*** screen (page 162) to continue to the ***View Patient History*** screen.

2. Use the **Up** and **Down** arrows to scroll through the patient's history.

3. Select **Add Note** to continue to the ***Add Note*** screen.

4. Use the on-screen keyboard to add notes about the patient's history. The note has a maximum of 90 characters.

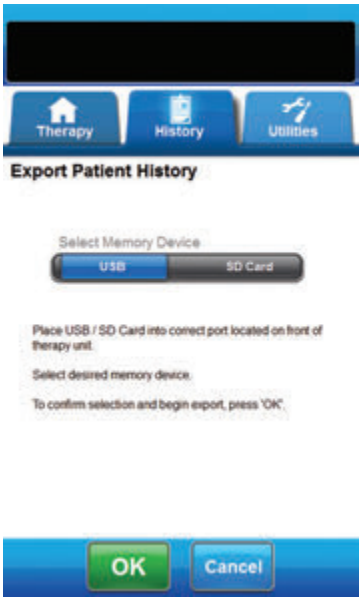
5. Select **OK** to add the note, or **Cancel** to return to the ***View Patient History*** screen without adding the note.

6. Select **Back** to return to the ***Patient History*** screen.

Each Instillation cycle is not recorded in the history log. Only the initial settings selected during set up are recorded.

Export Patient History Screen

Use the ***Export Patient History*** screen to export patient history to a USB Drive or SD Card.



1. Select **Export History** from the ***Patient History*** screen (page 162) to continue to the ***Export Patient History*** screen.

2. Insert the desired memory device (USB Drive or SD Card) into the proper port on the front of the V.A.C.ULTA™ Therapy Unit (page 18).

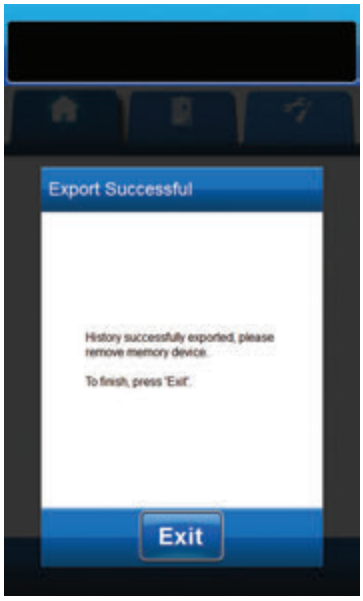
Use only non-powered USB devices.

3. On the ***Export Patient History*** screen, select the memory device being used, **USB** or **SD Card**.

4. Select **OK** to begin exporting patient history to the memory device or select **Cancel** to return to the ***Patient History*** screen without exporting patient history.

5. The V.A.C.ULTA™ Therapy Unit will begin exporting patient history. A bar graph will display transfer progress.

If the V.A.C.ULTA™ Therapy Unit detects an error during transfer, the Export Transfer Error screen will appear. Refer to the Data Transfer Errors section (page 180) of this manual for information about resolving this error.



6. Once all patient history is successfully transferred to the memory device, select **Exit** on the ***Export Successful*** screen to return to the ***Patient History*** screen.

View Graph - Wound Area (cm^2) Screen

Use the ***View Graph - Wound Area (cm^2)*** screen to view a graph of the measured wound area over time.

1. Select **View Graph** from the ***Patient History*** screen (page 162) to continue to the ***View Graph - Wound Area (cm^2)*** screen.

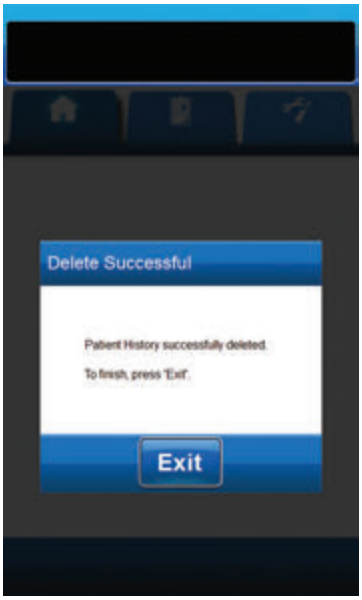
A graph cannot be constructed if the patient history file has been deleted.

A graph cannot be constructed unless measurements of the wound area have been previously saved in the patient's history. At least two measurements from different days are required (area of the image against time) for a graph to be constructed. Refer to the Wound Imaging section (page 167) of this manual for complete details about entering this information in the patient's history.

2. Select **Back** to return to the ***Patient History*** screen.

Delete Patient History Screen

Use the ***Delete Patient History*** screen to delete patient history data from the V.A.C.ULTA™ Therapy Unit's memory.



1. Select **Delete History** from the ***Patient History*** screen (page 162) to continue to the ***Delete Patient History*** warning screen.

2. Select **OK** to confirm deletion or **Cancel** to return to the ***Patient History*** screen without deleting patient history.

3. Once the deletion is complete, select **Exit** on the ***Delete Successful*** screen to return to the ***Patient History*** screen.

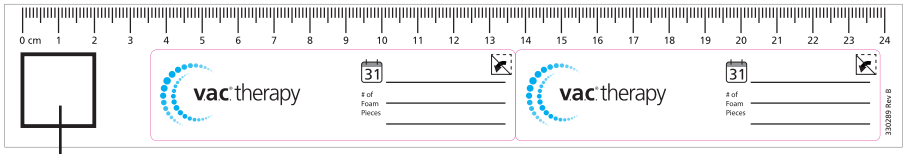
Wound Imaging

Use the Wound Imaging feature to aid in recording the wound healing process.

Wound imaging area and volume calculation features are not intended to be exact measurements and are not intended for use in the diagnosis and treatment of wounds.

Accessories required to use this feature include:

- Digital camera with at least two megapixel resolution and that uses an SD Memory Card
- An SD Memory Card
- Calibration Reference Square - located on the ruler in the dressing kit. This reference square is needed for the V.A.C.ULTA™ Therapy Unit to calculate wound measurements.



Calibration Reference Square

- Stylus - located inside the door on the front of the V.A.C.ULTA™ Therapy Unit (page 18).

The touch screen should only be operated by finger or the supplied stylus. Using pens or other pointing devices will damage the screen and may affect correct device function.

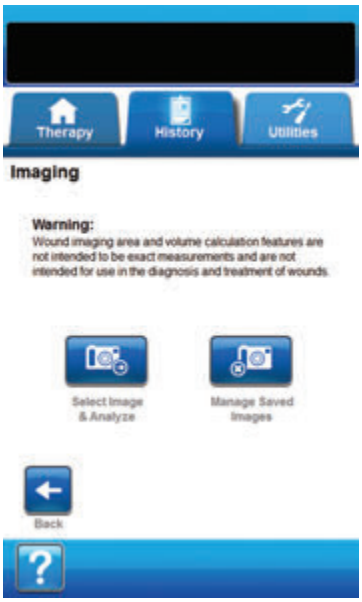
For optimal operation of the Wound Imaging feature, it is recommended that:

- A new sterile Calibration Reference Square be placed in the same location on the wound each time an image is taken.
- All images be taken directly above the wound.
- The wound and Calibration Reference Square fill as much of the image as possible.
- The image be taken in good lighting conditions.
- Image files must be in a JPEG (.jpg) format.

Using a camera that has a date and time function will allow for easier tracking of images.

Imaging Screen

Use the ***Imaging*** screen to upload images for calculating wound area and volume and to delete images from the V.A.C.ULTA™ Therapy Unit.



Uploading Images

1. From the ***History Tab*** screen (page 155), select **Imaging** to continue to the ***Imaging*** screen.

2. Enter Patient History access code (page 159).

A Patient History Log must be created prior to using the Imaging feature. Refer to the Create New Patient History section (page 158) of this manual for more information.

3. Insert memory device into the proper slot on front of the V.A.C.ULTA™ Therapy Unit (page 18).

Use only non-powered USB devices.

4. Select **Select Image & Analyze** to continue to the ***Upload Image*** screen.

5. Select the memory device that contains the images from the ***Upload Images*** screen. Select **USB**, **SD Card**, or **Unit Memory**.

There will be short delay while the images are accessed from the V.A.C.ULTA™ Therapy Unit's memory or the memory card.

When selecting unit memory, the Select Image screen will be blank unless images have been previously uploaded and saved in unit memory.

6. Select **OK** to continue to the ***Select Image*** screen. Select **Cancel** to return to the ***Imaging*** screen.

7. Use the **Up** and **Down** arrows to display the desired folder or image in the window.

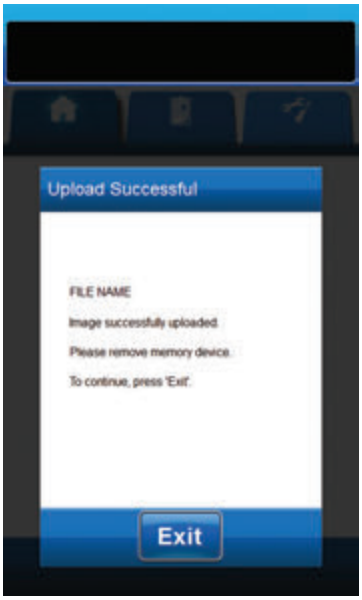
8. If the desired image is in a folder, display the available folders with the **Up** and **Down** arrows and select the desired **Folder**. Use the **Up** and **Down** arrows to display the desired image.

Select **Back** to back out of the folder.

9. When the desired image is displayed, select **OK** to load the image into the V.A.C.ULTA™ Therapy Unit's memory.

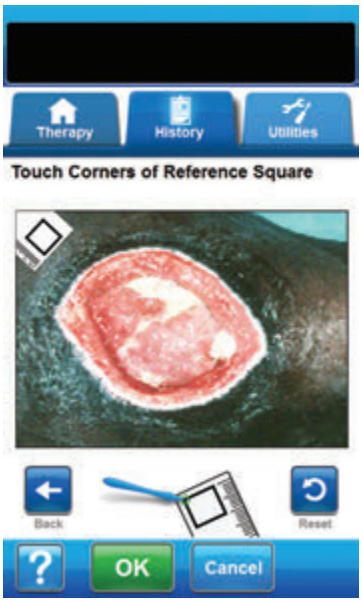
10. The V.A.C.ULTA™ Therapy Unit will begin uploading the image. A bar graph will display transfer progress.

If the V.A.C.ULTA™ Therapy Unit detects an error during transfer, the Upload Transfer Error screen will appear. Refer to the Data Transfer Errors section (page 180) of this manual for information about resolving this error.



11. Once image is successfully transferred, remove the memory device.

12. Select **Exit** on the ***Upload Successful*** screen to continue to the ***Touch Corners of Reference Square*** screen.



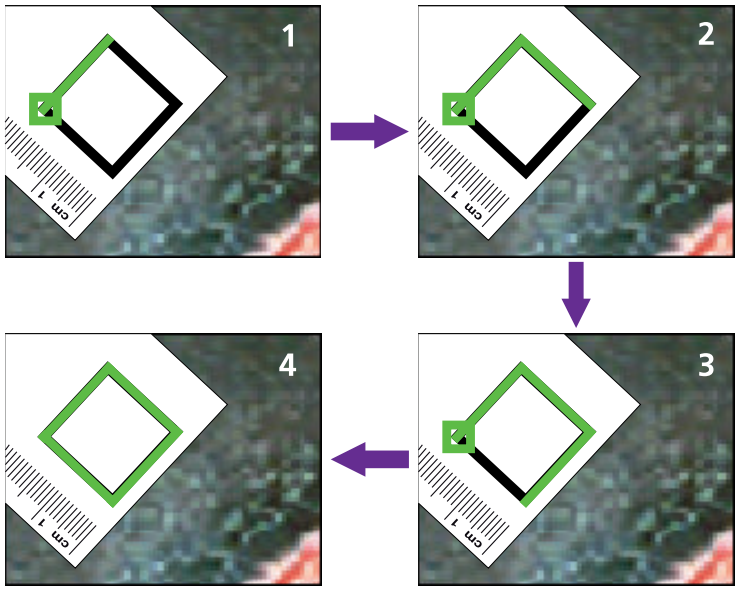
Use the supplied stylus to touch each corner of the reference square displayed in the image window on the ***Touch Corners of Reference Square*** screen.

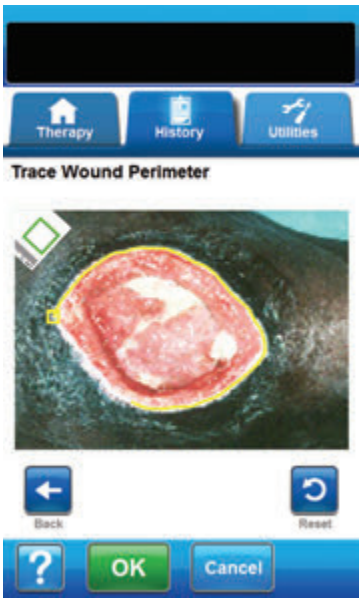
When the last corner of the reference square is touched, the corner points will be joined by a highlighted line.

The touch screen should only be operated by finger or the supplied stylus. Using pens or other pointing devices will damage the screen and may affect correct device function.

It is important to select corners in either a clockwise or counter-clockwise manner. Incorrect sequence will lead to a calibration error.

13. Once all the corners of the reference square have been touched, select **OK** to continue to the ***Trace Wound Perimeter*** screen.



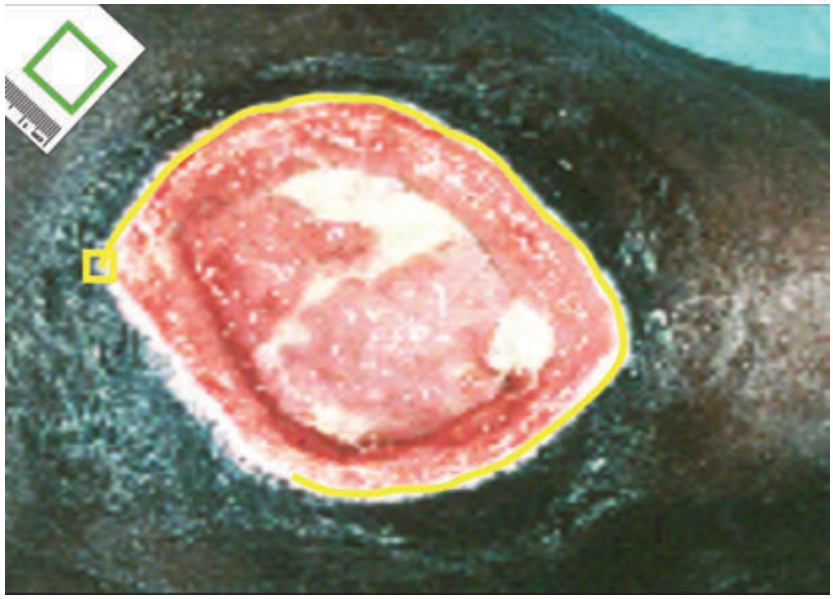


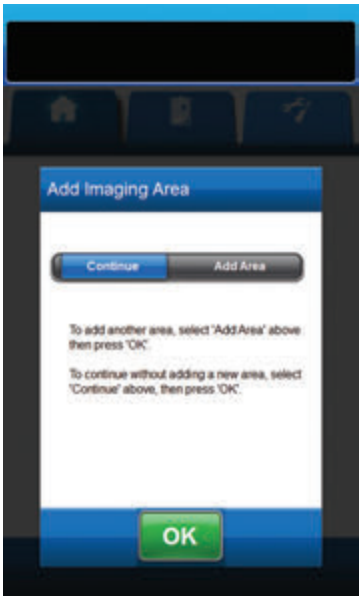
1. Use the supplied stylus to trace a line around the wound area to be analyzed in the image window on the ***Trace Wound Perimeter*** screen.

   If an error is made during tracing, select **Reset** to trace the wound area again.

The touch screen should only be operated by finger or the supplied stylus. Using pens or other pointing devices will damage the screen and may affect correct device function.

A square will appear at the start of the trace. The trace is completed when the end of the line returns to the start point.





2. Once the wound area has been traced, select **OK** to continue to the ***Add Imaging Area*** screen.

3. Select **Add Area** to continue back to the ***Trace Wound Perimeter*** screen if there is an additional wound area to be traced.

   OR

4. Select **Continue** if all wound area(s) have been traced.

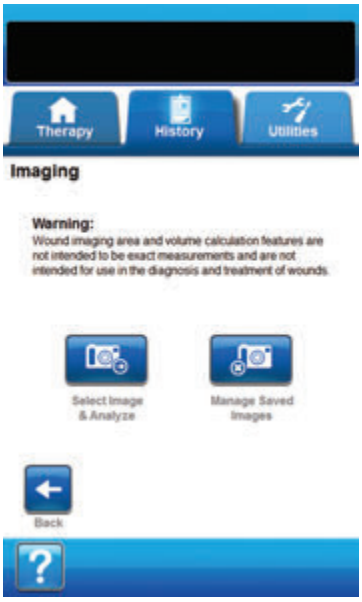
5. Select **OK** to continue to the ***Image Area Depth*** screen.

1. Select the approximate depth of each wound area traced. Use + / -, as applicable to adjust above and below values shown.

2. Select **Back** to return to the ***Add Imaging Area*** screen.

3. Select **OK** to save wound imaging data to the patient's history.

4. Select **Cancel** to return to the ***Upload Image*** screen.



1. From the ***History Tab*** screen (page 155), select **Imaging** to continue to the ***Imaging*** screen.

2. Enter Patient History access code.

A Patient History Log must be created prior to using the Imaging feature. Refer to the Create New Patient History section (page 158) of this manual for more information.

3. Select **Manage Saved Images** to continue to the ***Select Image for Deletion*** screen.

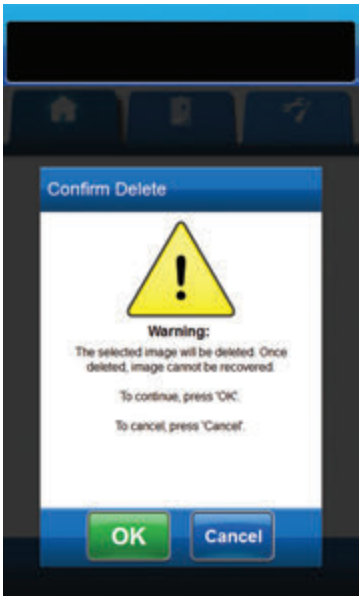
There will be short delay while the images are accessed from the V.A.C.ULTA™ Therapy Unit's memory.

4. Use the **Up** and **Down** arrows to display the desired image in the window.

5. When the desired image is displayed, select **OK** to continue to the ***Confirm Delete*** screen.

OR

6. Select **Back** to return to the ***Imaging*** screen.



7. Select **OK** to delete the image from the V.A.C.ULTA™ Therapy Unit's memory.

OR

8. Select **Cancel** to return to the ***Select Image for Deletion*** screen.

9. Once the image is successfully deleted, the ***Select Image for Deletion*** screen will be displayed. Select another image to delete, or select **Back** to return to the ***Imaging*** screen.

10. Select the **History** Tab to return to the ***History Tab*** screen.

Therapy History Screen

The ***View Therapy History*** screen displays the patient's therapy information in date, time and event columns (e.g. therapy starts / stops, therapy settings and disposable component changes). The date is in descending order and time is displayed using the twenty-four hour clock format.

1. From the ***History Tab*** screen (page 155), select **Therapy History** to continue to the ***View Therapy History*** screen.

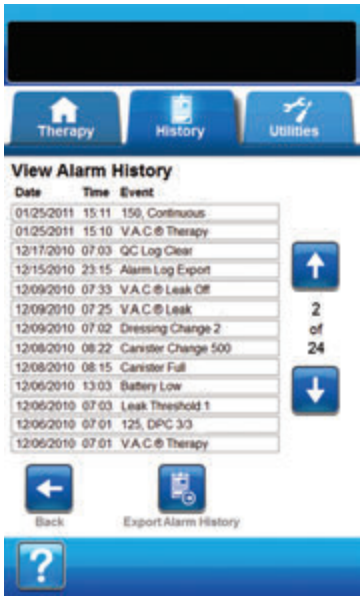
2. Use the **Up** and **Down** arrows to scroll through the therapy history.

3. Select **Back** to return to the ***History Tab*** screen.

4. Select **Export Therapy History** to continue to the ***Export History*** screen (page 179).

Alarm History Screen

The ***View Alarm History*** screen displays alarm information for the V.A.C.ULTA™ Therapy Unit in date, time and event columns (e.g. alarms and disposable component changes). The date is in descending order and time is displayed using the twenty-four hour clock format.



1. From the ***History Tab*** screen (page 155), select **Alarm History** to continue to the ***View Alarm History*** screen.

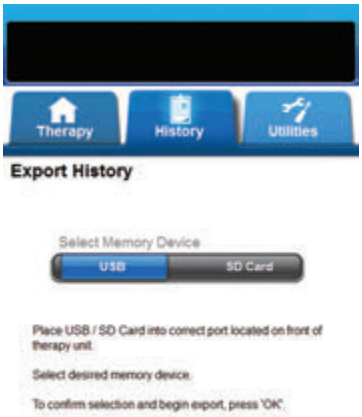
2. Use the **Up** and **Down** arrows to scroll through the alarm history.

3. Select **Back** to return to the ***History Tab*** screen.

4. Select **Export Alarm History** to continue to the ***Export History*** screen (page 179).

Export History Screen

Use the ***Export History*** screen to export therapy and alarm history to a memory device (USB or SD Card).



1. Insert the desired memory device (USB or SD Card) into the proper port on the front of the V.A.C.ULTA™ Therapy Unit (page 18).

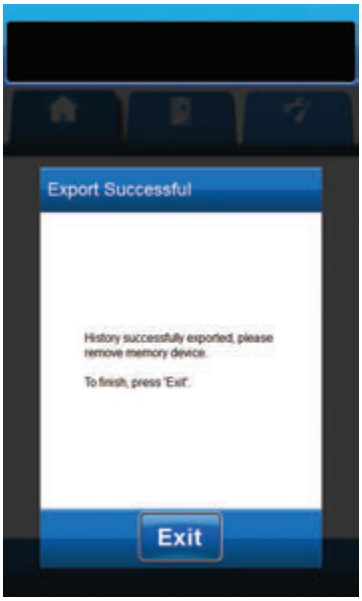
Use only non-powered USB devices.

2. From the ***History Tab*** screen (page 155), select **Therapy History** to continue to the ***View Therapy History*** screen.

3. Select **Export Therapy History** to continue to the ***Export History*** screen.

4. On the ***Export History*** screen, select the memory device being used, **USB** or **SD Card**.

5. Select **OK** to begin exporting history to the memory device or select **Cancel** to return to the ***View Therapy*** or ***Alarm History*** screen without exporting history.



6. The V.A.C.ULTA™ Therapy Unit will begin exporting history. A bar graph will display transfer progress.

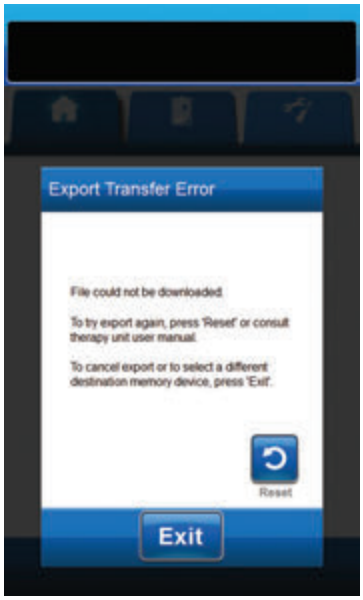
If the V.A.C.ULTA™ Therapy Unit detects an error during transfer, the Export Transfer Error screen will appear. Refer to the Data Transfer Errors section (page 180) of this manual for information about resolving this error.

7. Once all history is successfully transferred to the memory device, select **Exit** on the ***Export Successful*** screen to return to the ***History Tab*** screen.

Data Transfer Errors

If the V.A.C.ULTA™ Therapy Unit detects an error during data transfer, the unit will display a Transfer Error screen.

The V.A.C.ULTA™ Therapy Unit is not compatible with USB Drives or SD Cards which have U3 software pre-installed. U3 software must be uninstalled prior to use.

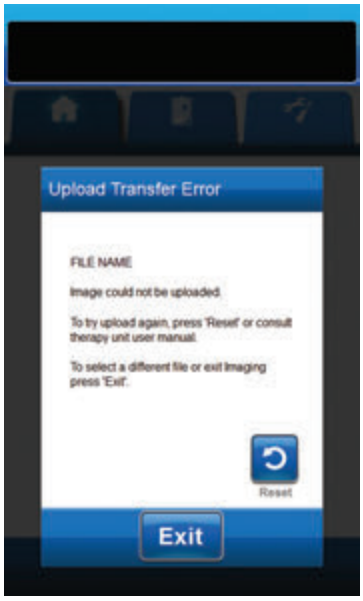


If the ***Export Transfer Error*** screen appears, the possible reasons for transfer errors are:

- SD Card / USB Drive not inserted properly.
- Incorrect SD card / USB drive format.
- Incorrect type of device connected.

1. Select **Reset** to return to try the export again.

2. Select **Exit** to cancel the export or to select a different destination device.



If the ***Upload Transfer Error*** screen appears, the possible reasons for transfer errors are:

- SD Card / USB Drive not inserted properly.
- Incorrect SD card / USB drive format.
- Incorrect type of device connected.
- V.A.C.ULTA™ Therapy Unit's memory is full.

If therapy unit's memory is full, delete any unused photos to free memory. Refer to Delete Images section (page 175) for information on deleting images.

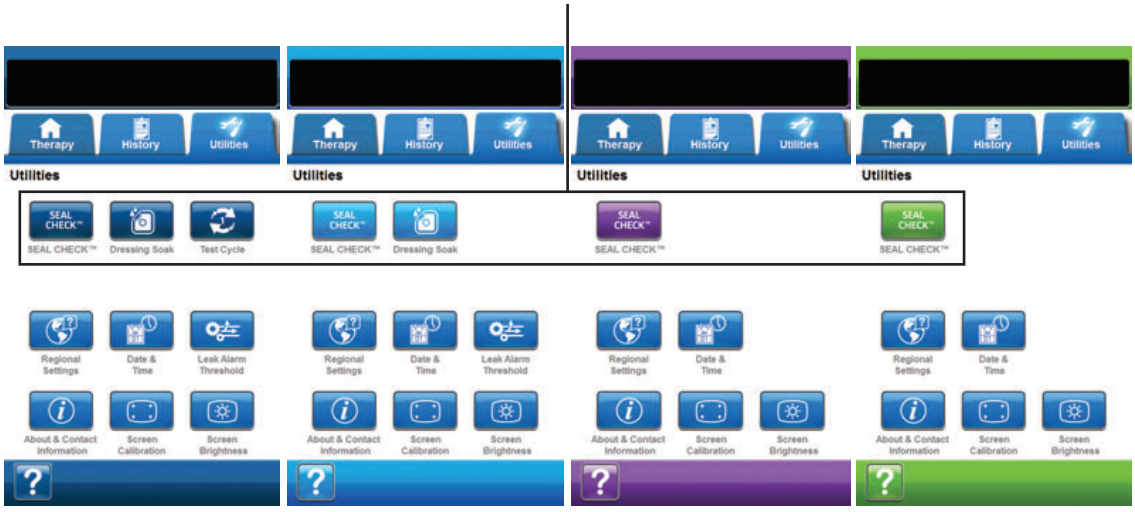
1. Select **Reset** to return to try the upload again.

2. Select **Exit** to select a different image (page 168) or to exit Imaging.

Utilities Tab

Use the ***Utilities Tab*** screen to set preferences for the V.A.C.ULTA™ Therapy Unit.

Refer to pages 74, 106, 126 and 144 for details on features.



V.A.C. VERAFLO™ Therapy | **V.A.C.® Therapy** | **PREVENA™ Therapy** | **ABTHERA™ Therapy**

The following options are available from any therapy mode on the ***Utilities Tab*** Home screen:

Regional Settings - Use to set the language, units of measure, number format and date format displayed by the V.A.C.ULTA™ Therapy Unit.

Screen Calibration - Use to calibrate the V.A.C.ULTA™ Therapy Unit's touch screen.

About and Contact Information - Use to access information about the V.A.C.ULTA™ Therapy Unit, including the software version and KCI contact information.

Date and Time - Use to set the current date and time.

Screen Brightness - Use to adjust the brightness of the V.A.C.ULTA™ Therapy Unit's touch screen.

Leak Alarm Threshold - Use to set the leak rate threshold that triggers the Leak Alarm (**V.A.C.® Therapy** and **V.A.C. VERAFLO™ Therapy** only).

Help - Use to access the V.A.C.ULTA™ Therapy Unit's on-screen help features.

Regional Settings Screen

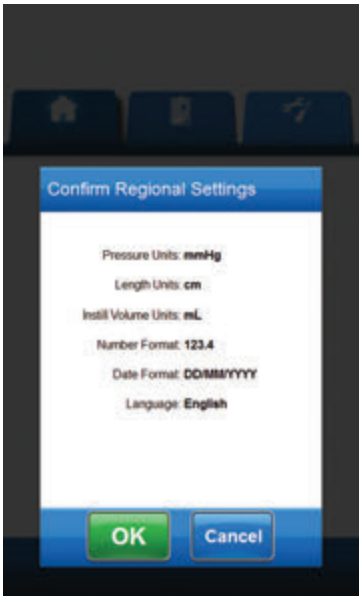
Use the ***Regional Settings*** screen to set the language, unit of measure, number format and date format displayed by the V.A.C.ULTA™ Therapy Unit.

1. Select the **Utilities** tab (page 181).

2. Select **Regional Settings** from the ***Utilities Tab*** screen (page 181) to continue to the ***Regional Settings*** screen.

3. Set the following options:

   - **Pressure Units** - Select between **mmHg** (millimeters of mercury) or **kPa** (kilo-Pascals).
   - **Length Units** - Select between **cm** (centimeters) or **inch** (inches).
   - **Instill Volume Units** - Select between **mL** (milliliters) or **cc** (cubic centimeters).
   - **Number Format** - Select decimal separator "." or "," (**123.4** or **123,4**).
   - **Date Format** - Select between **DD/MM/YYYY** or **MM/DD/YYYY**.
   - **Language** - Select the display language for the V.A.C.ULTA™ Therapy Unit.

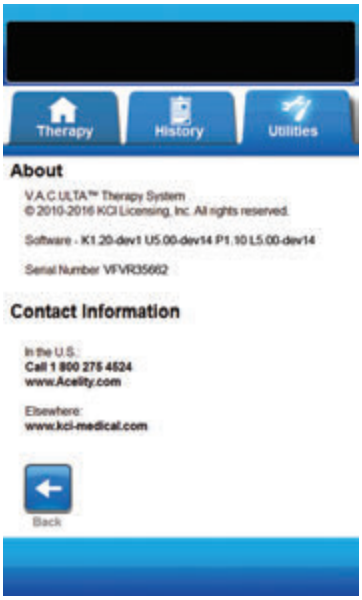


4. Once all options have been selected, select **OK** to continue to the ***Confirm Regional Settings*** screen.

5. Select **OK** to confirm settings and return to the ***Utilities Tab*** screen. Select **Cancel** to return to the ***Regional Settings*** screen to make any required adjustments.

About and Contact Information Screen

Use the ***About*** and ***Contact Information*** screen to access information about the V.A.C.ULTA™ Therapy Unit, including the software version and KCI contact information.



1. Select the **Utilities** tab (page 181).

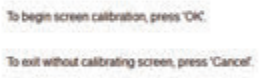
2. Select **About & Contact Information** from the ***Utilities Tab*** screen (page 181) to continue to the ***About*** and ***Contact Information*** screen.

   - About - Shows current software version information
   - Contact Information - Shows KCI contact information

3. Select **Back** to return to the ***Utilities Tab*** screen.

Screen Calibration Screen

Use the ***Screen Calibration*** screen to calibrate the V.A.C.ULTA™ Therapy Unit's touch screen. If screen inputs are not correctly recognized, it may be necessary to calibrate the touch screen.

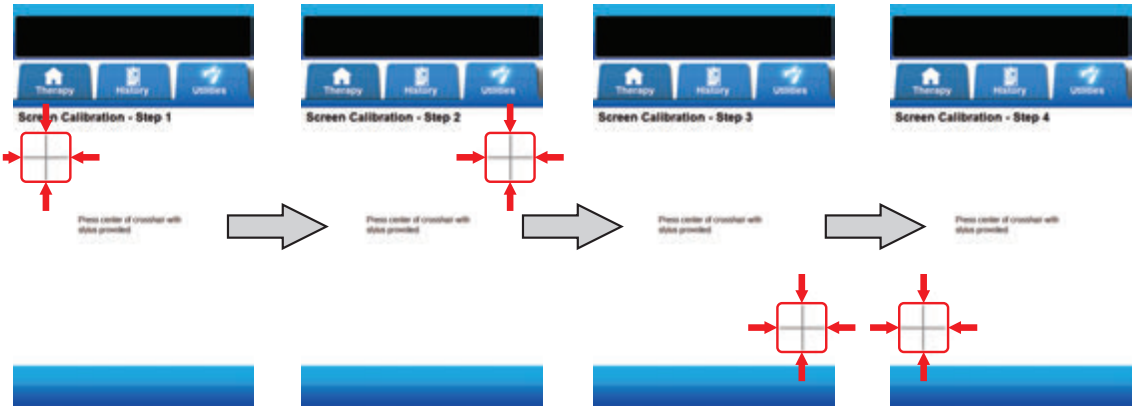


1. Select the **Utilities** tab (page 181).

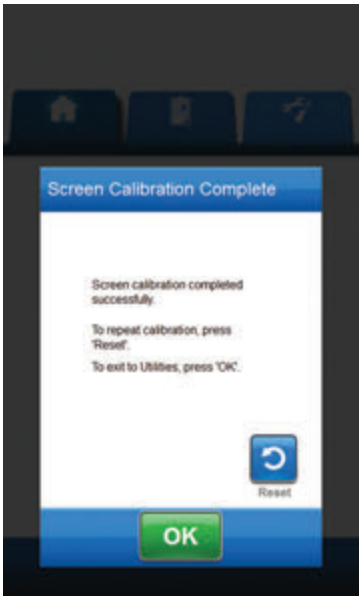
2. Select **Screen Calibration** from the ***Utilities Tab*** screen (page 181) to continue to the ***Screen Calibration*** screen.

3. Select **OK** to begin calibrating the touch screen.

4. Using the supplied stylus, touch and hold the center of each cross as it is displayed on the touch screen.



The touch screen should only be operated by finger or the supplied stylus. Using pens or other pointing devices will damage the screen and may affect correct device function.

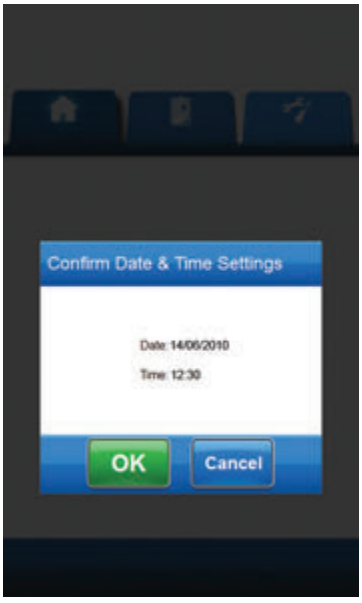


5. Once Step 4 of screen calibration is complete, the ***Screen Calibration Complete*** screen will appear. If necessary, select **Reset** on the ***Screen Calibration Complete*** screen to repeat calibration.

6. Select **OK** to return to the ***Utilities Tab*** screen.

Date & Time Settings Screen

Use the ***Date & Time Settings*** screen to set the current date and time.



1. Select the **Utilities** tab (page 181).

2. Select **Date & Time** from the ***Utilities Tab*** screen (page 181) to continue to the ***Date & Time Settings*** screen.

3. Set the following options:

   - **Day** - Select the current day. Use **+** / **-** to adjust above and below values shown.
   - **Month** - Select the current month. Use **+** / **-** to adjust above and below values shown.
   - **Year** - Select the current year. Use **+** / **-** to adjust above and below values shown.
   - **Hour** - Select the current hour of the current time. Use **+** / **-** to adjust above and below values shown.
   - **Minute** - Select the current minute of the current time. Use **+** / **-** to adjust above and below values shown.

4. Once all options have been selected, select **OK** to continue to the ***Confirm Date & Time Settings*** screen.

5. Select **OK** to confirm settings and return to the ***Utilities Tab*** screen. Select **Cancel** to return to the ***Utilities Tab*** screen without making any adjustments to the date and time.

Screen Brightness Screen

Use the ***Screen Brightness*** screen to adjust the brightness of the V.A.C.ULTA™ Therapy Unit's touch screen.

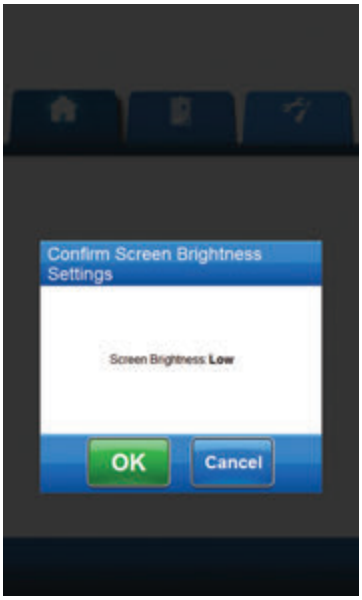
1. Select the **Utilities** tab (page 181).

2. Select **Screen Brightness** from the ***Utilities Tab*** screen (page 181) to continue to the ***Screen Brightness*** screen.

3. Select the desired screen brightness - **Low**, **Medium**, or **High**.

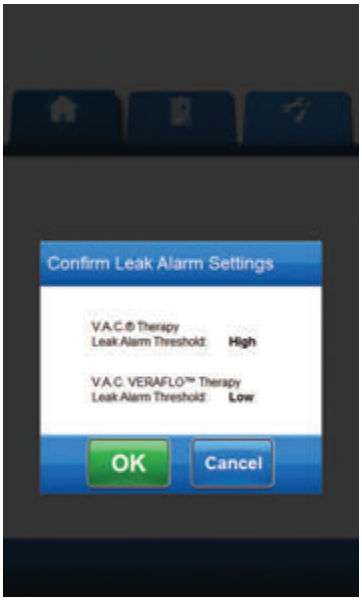
4. Once the desired screen brightness has been selected, select **OK** to continue to the ***Confirm Screen Brightness Settings*** screen.

5. Select **OK** to confirm settings and return to the ***Utilities Tab*** screen. Select **Cancel** to return to the ***Utilities Tab*** screen without making any adjustments to the screen brightness.



Leak Alarm Threshold Screen

Use the ***Leak Alarm Threshold*** screen to set the leak rate threshold that triggers the Leak Alarm. This option is available in the V.A.C. VERAFLO™ Therapy and V.A.C.® Therapy modes only.



1. Select the **Utilities** tab (page 181).

2. Select **Leak Alarm Threshold** from the ***Utilities Tab*** screen (page 181) to continue to the ***Leak Alarm Threshold*** screen.

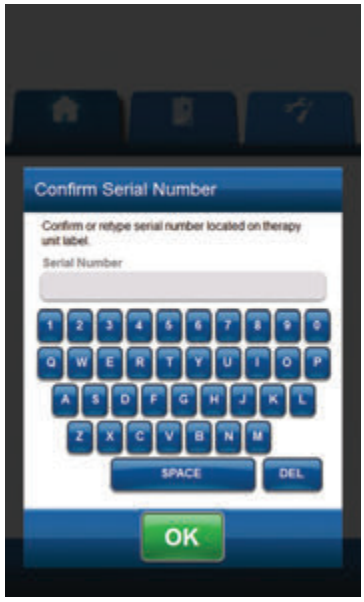
3. Select the desired negative pressure leak alarm threshold for V.A.C.® Therapy and V.A.C. VERAFLO™ Therapy. Threshold options are **Low** or **High**. Low is approximately equal to one liter per minute. High is approximately equal to two liters per minute.

4. Once the desired negative pressure leak alarm thresholds have been selected, select **OK** to continue to the ***Confirm Leak Alarm Settings*** screen.

5. Select **OK** to confirm settings and return to the ***Utilities Tab*** screen. Select **Cancel** to return to the ***Utilities Tab*** screen without making any adjustments to the negative pressure leak alarm thresholds.

Confirm Serial Number

This screen appears when the V.A.C.ULTA™ Therapy Unit is powered on and the serial number stored in the unit's memory is corrupt or missing.



To resolve:

1. Compare serial number on unit's serial number label (page 18) to displayed serial number.

2. If serial number is incorrect, use the on-screen keyboard to re-enter the unit's serial number label.

3. Select **OK** to continue to the ***Startup*** screen.

Care and Cleaning

Standard Precautions

The following are the KCI recommended daily and weekly cleaning and infection control procedures for the V.A.C.ULTA™ Therapy Unit.

Always follow Standard Precautions.

Standard Precautions are designed to reduce the risk of transmission of microorganisms from both known and unknown sources of infection. These precautions can be applied to all patients, regardless of their diagnosis or presumed infection status, and should be used when contact is anticipated with blood and all body fluids. This also includes secretions and excretions (except sweat) regardless of whether blood is visible or not, non-intact skin (i.e., open wounds) and mucous membranes.

Waste Disposal

Discard all disposable items (all tubing, connectors, clamps, used canister, used dressings, etc.) in accordance with local medical waste disposal regulations. Improper disposal may run the risk of regulatory non-compliance.

Cleaning the V.A.C.ULTA™ Therapy Unit

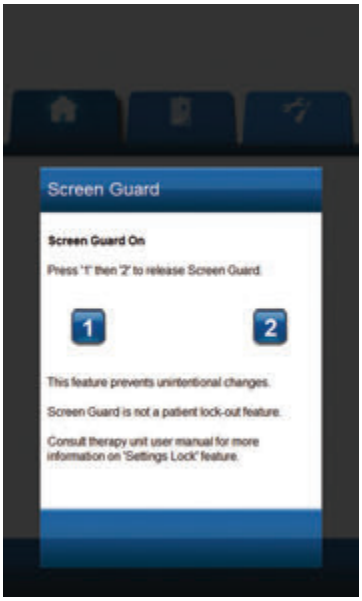
Cleaning and disinfection of the V.A.C.ULTA™ Therapy Unit includes wipe down of all hard surface components. Follow institutional procedures used for cleaning and disinfection of other hard surface durable electronic medical equipment. The V.A.C.ULTA™ Therapy Unit must be cleaned and disinfected:

- If it becomes soiled during patient use.
- At least weekly.

Ensure that the V.A.C.ULTA™ Therapy Unit is powered off and disconnected from AC power when using cleaning fluids of any nature.

KCI recommends the following regarding cleaning and disinfecting KCI V.A.C.® Therapy devices:

- To help reduce risk of infection and contact with blood and body fluids, use personal protective equipment (PPE) such as medical procedure gloves.
- Clean all organic material (visible soil or body secretions) from the therapy unit prior to disinfection.
- Use hospital-grade cleaners and disinfectants.
- Do not immerse or saturate the therapy unit with fluids to avoid damage to the electronics in the device.
- Do not use alcohol based solutions around the touchscreen edges or near gasket and power switches since alcohol based solutions will easily wick up into the screen and may cause equipment malfunction.



1. Select **Lock** on the ***Home*** screen (page 50, 85, 110 and 129) to activate Screen Guard. The **Lock** icon will close.

2. Use a soft, non-abrasive cloth to gently clean the touch screen.

Do not use any liquid to clean the touch screen.

Do not use excessive force to clean the touch screen. Pressing too hard may cause damage.

3. To unlock the touch screen, touch the screen to display the ***Screen Guard*** screen.

4. Select the **1**, then the **2** on the ***Screen Guard*** screen to return to the ***Home*** screen.

Explanation of Symbols Used

Warning or Caution statement of possible hazard to system, patient or staff

Important Operational Information

Refer to User Manual

IPX1

No protection against ingress of solid forcing objects. Protected against ingress of vertically dripping water.

Conforms with the Waste Electrical and Electronic Equipment Directive (2002/96/EC). At the end of useful life, dispose of all waste according to local requirements, or contact your local KCI subsidiary or agent for advice. This product is designated for separate collection at an appropriate collection point. Do not dispose of in normal waste stream.

Type BF Applied Part

MR Unsafe - Keep the V.A.C.ULTA™ Therapy Unit away from magnetic resonance imaging (MRI) equipment

Rx Only

CAUTION: Federal (US) law restricts this device to sale/rental by or on the order of a physician

Manufacturer

Catalog Number

Authorized Representative in the European Community

3182664

ETL Listed, Conforms to AAMI ES60601-1 1st edition, CSA C22.2#60601-1 3rd edition and IEC 60601-1 3rd edition

Specifications

Specifications subject to change without notice.

Classification

Equipment not suitable for use in the presence of a flammable anesthetic mixture with air, oxygen or nitrous oxide, or an oxygen enriched environment.

V.A.C.ULTA™ Therapy Unit

Continuous Operation
Type BF Applied Part
Class I equipment
IPX1

Power Supply

Class I Equipment
Ordinary Equipment

V.A.C.ULTA™ Therapy Unit

Dimensions ..... 217mm X 260mm X 191mm (8.55in X 10.25in X 7.5in)
Weight ..... 3.35kg (7.4 lbs)

Electrical Data (Power Supply)

External Power Supply Input: ..... 100 - 240 VAC, 1.6A, 50Hz - 60Hz
External Power Supply Output 15V, 4.8A

Alarm Volume

Minimum of 72 dBA at 1 meter in maximum volume orientation.

Environmental Conditions

Transport and Storage Temperature Range ..... -20 °C to 60 °C (-4°F to 140°F)
Operational Temperature Range ..... 10 °C to 30 °C (50°F to 86°F)
Relative Humidity Range ..... 10% to 85% non-condensing
Barometric Pressure Range ..... 700 hPa to 1060 hPa

Instill Pump Volumetric Accuracy

6 - 10 ml ± 2 ml
12 - 50 ml ± 20%
55 - 500 ml ± 15%

Accuracy Testing performed under the following conditions

Room Temperature ..... 22.5°C ± 2°C
Solution ..... 1000 mL bag of 0.9% saline fluid located on solution container hanger arm
Downstream pressure ..... 0 psi with discharge height at pump rotor centerline
Testing Duration ..... V.A.C. VERALINK™ Cassette usage up to 72 hours

The disposable components of the V.A.C.ULTA™ Therapy System are considered Applied Parts under IEC 60601-1 Third Edition.

Electromagnetic Compatibility

Electromagnetic Interference - Although this equipment conforms with the intent of the directive 2004/108/EC in relation to Electromagnetic Compatibility (EMC), all electrical equipment may produce interference. If interference is suspected, move equipment away from sensitive devices or contact the manufacturer.

Portable and mobile RF communications equipment can effect medical electrical equipment.

Radios, cell phones and similar devices may affect this equipment and should be kept at least 6.5 feet (2 meters) away from the equipment.

Medical electrical equipment needs special precautions regarding EMC and needs to be installed and put into service according to the EMC information in the following tables.

Other medical equipment or systems can produce electromagnetic emissions and therefore can interfere with the functionality of the V.A.C.ULTA™ Therapy Unit. Care should be used when operating the V.A.C.ULTA™ Therapy Unit adjacent to or stacked with other equipment. If adjacent or stacked use is necessary, the V.A.C.ULTA™ Therapy Unit should initially be observed to verify normal operation in the configuration in which it will be used.

The following tables document compliance levels and guidance from the IEC 60601-1-2 2007 Standard, for the electromagnetic environment in which the V.A.C.ULTA™ Therapy Unit should be used in a clinical environment.

Guidance and Manufacturer's Declaration - Electromagnetic Emissions		
The V.A.C.ULTA™ Therapy Unit is intended for use in the electromagnetic environment specified below. The customer or user of the V.A.C.ULTA™ Therapy Unit should assure that it is used in such an environment.		
Emission Test	Compliance	Electromagnetic environment
RF emissions CISPR 11	Group 1 Class A	The V.A.C.ULTA™ Therapy Unit uses RF energy only for its internal function. Therefore, its RF emissions are very low and are not likely to cause any interference in nearby electronic equipment
Conducted emissions CISPR 11	Group 1 Class A	
Harmonic emissions IEC 61000-3-2	Class A	
Voltage fluctuations / flicker emissions IEC 61000-3-3	Yes	

Guidance and Manufacturer's Declaration - Electromagnetic Immunity			
The V.A.C.ULTA™ Therapy Unit is intended for use in the electromagnetic environment specified below. The customer or user of the V.A.C.ULTA™ Therapy Unit should assure that it is used in such an environment.			
Immunity Test	IEC 60601 Test Level	Compliance level	Electromagnetic Environment Guidance
Electrostatic discharge (ESD) IEC 61000-4-2	±6kV Contact ±8kV Air	±6kV Contact ±8kV Air	In accordance with IEC 60601-1-2: 2007, floors are covered with synthetic material, the relative humidity should be at least (30)%.
Electrical fast transient / burst IEC 61000-4-4	±1kV Cables ±2kV Power	±1kV Cables ±2kV Power	
Surge IEC 61000-4-5	1kV line(s) to line(s) 2kV line(s) to earth	1kV line(s) to line(s) 2kV line(s) to earth	
Voltage dips, short interruptions and voltage variations on power supply input lines IEC 61000-4-11	5% half cycle 40% 5 cycles 70% 25 cycles 5% for 5 seconds	5% half cycle 40% 5 cycles 70% 25 cycles 5% for 5 seconds	
Power frequency (50Hz / 60Hz) magnetic field IEC 61000-4-8	3A/M	3A/M	Power frequency magnetic fields should be at levels characteristic of a typical location in a typical commercial or hospital environment.
NOTE: U_r is the a.c. mains voltage prior to application of the test level.			

Recommended separation distances between portable and mobile RF communications equipment and the V.A.C.ULTA™ Therapy Unit			
The V.A.C.ULTA™ Therapy Unit is intended for use in an electromagnetic environment in which radiated RF disturbances are controlled. The customer or the user of the V.A.C.ULTA™ Therapy Unit can help prevent electromagnetic interference by maintaining a minimum distance between portable and mobile RF communications equipment (transmitters) and the V.A.C.ULTA™ Therapy Unit as recommended below, according to the maximum output power of the communications equipment.			
Rated maximum output power of transmitter	**Separation distance according to frequency of transmitter meters**		
	150 kHz to 80 MHz	**80 MHz to 800 MHz**	**800 MHz to 2.5 GHz**
W	**d =** $1.2\sqrt{P}$	**d =** $1.2\sqrt{P}$	**d =** $2.3\sqrt{P}$
0.01	0.12	0.12	0.23
0.1	0.38	0.37	0.74
1	1.2	1.2	2.3
10	3.8	3.7	7.4
100	12	12	23
For transmitters rated at a maximum output power not listed above, the recommended separate distance d in meters (m) can be estimated using the equation applicable to the frequency of the transmitter, where P is the maximum output power rating of the transmitter in watts (W) according to the transmitter manufacturer. NOTE 1: At 80 MHz and 800 MHz, the separation distance for the higher frequency range applies. NOTE 2: These guidelines may not apply in all situations. Electromagnetic propagation is affected by absorption and reflection from surfaces, objects and people.			

Guidance and Manufacturer's Declaration - Electromagnetic Immunity			
The V.A.C.ULTA™ Therapy Unit is intended for use in an electromagnetic environment specified below. The customer or user of the V.A.C.ULTA™ Therapy Unit should assure that it is used in such an environment.			
Immunity Test	IEC 60601 Test Level	Compliance Level	Electromagnetic Environment Guidance
Conducted RF IEC 61000-4-6	3Vrms 150K - 80 MHz	3Vrms 150K - 80 MHz	Portable and mobile RF communications equipment should be used no closer to any part of the V.A.C.ULTA™ Therapy Unit, including cables, than the recommended separation distance calculated from the equation application to the frequency of the transmitter. Recommended Separation Distance Battery Operated Device **d =** 1.2 $\sqrt{P}$
Radiated RF IEC 61000-4-3	3V/meter 80 MHz - 2.5 GHz	3V/meter 80 MHz - 2.5 GHz	**d =** 1.2 $\sqrt{P}$ 80 MHz to 800 MHz **d =** 2.3 $\sqrt{P}$ 800 MHz to 2.5 GHz Where P is the maximum output power rating of the transmitter in watts (W) according to the transmitter manufacturer and d is the recommended separation distance in meters (m) Field strengths from fixed RF transmitters, as determined by an electromagnetic site survey 1, should be less than the compliance level in each frequency range. 2 Interference may occur in the vicinity of equipment marked with the following symbol: 
NOTE 1: At 80 MHz and 800 MHz, the higher frequency range applies. NOTE 2: These guidelines may not apply in all situations. Electromagnetic propagation is affected by absorption and reflection from structures, objects and people.			
[1] Field strengths from fixed transmitters, such as base stations for radio (cellular/cordless) telephones and land mobile radios, amateur radio, AM and FM radio broadcast and TV broadcast cannot be predicted theoretically with accuracy. To asses the electromagnetic environment due to fixed RF transmitters, an electromagnetic site survey should be considered. If the measured field strength in the location in which the V.A.C.ULTA™ Therapy Unit is used exceeds the applicable RF compliance level above, the V.A.C.ULTA™ Therapy Unit should be observed to verify normal operation. If abnormal performance is observed, additional measures may be necessary, such as re-orienting or relocating the V.A.C.ULTA™ Therapy Unit. [2] Over the frequency range 150kHz, field strengths should be less than 3V/m.			

Power Cord	Description	Cord Specifications	Max Length (inches)
350084	Cord, VAC Ulta AC Power	3 x 18 AWG, SJT, 10A / 125V	78.74
360080	Cord, VAC Via Power, IT-220V	H05VVF-3G, 10A / 250V	79.00
360074	Cord, VAC Via Power, EU-220V	H05VVF-3G, 10A / 250V	79.00
350753	Cord, VAC Ulta Power, UK-240V	H05VVF-3G, 10A / 250V	78.74
350758	Cord, VAC Ulta Power, DK-220V	H05VVF-3G, 10A / 250V	78.74
360081	Cord, VAC Via Power, CH-220V	H05VVF-3G, 10A / 250V	79.00
360122	Cord, VACVia Power South Africa / India	H05VVF-3G, 10A / 250V	79.00
360076	Cord, VAC Via Power, AU / NZ-240V	H05VVF-3G, 10A / 250V	79.00
4103887	Cord, Power Brazil	H05VVF-3G, 10A / 250V	79.00

The use of electrical cables and accessories other than those specified in this manual or referenced documents may result in increased electromagnetic emissions from the V.A.C.ULTA™ Therapy Unit or decreased electromagnetic immunity of the V.A.C.ULTA™ Therapy Unit.

Customer Contact Information

For questions regarding this product, supplies, maintenance, or additional information about KCI products and services, please contact KCI or a KCI authorized representative, or:

In the US call 1-800-275-4524 or visit www.acelity.com, www.veraflo.com or www.vaculta.com
KCI USA, Inc. 12930 IH 10 West, San Antonio, TX 78249

Outside the US visit www.kci-medical.com

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Comparison of the Effects of Different Negative Pressure Wound Therapy Modes—Continuous, Noncontinuous, and With Instillation—on Porcine Excisional Wounds

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Keywords: dynamic NPWT, negative pressure wound therapy with instillation, preclinical model, variable NPWT, wound cleansing

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Objective: Negative pressure wound therapy (NPWT) can be delivered in continuous or noncontinuous modes, while NPWT with instillation (NPWTi) couples NPWT with automated delivery and removal of topical wound treatment solutions and suspensions. This porcine study compared granulation response of NPWTi (instillation foam dressing with saline) to NPWT (standard foam dressing) in continuous and noncontinuous modes. **Methods:** Full-thickness dorsal excisional wounds in pigs were treated with continuous NPWT, intermittent NPWT, dynamic (controlled variable) NPWT, and NPWTi with saline (n = 10 per group). Wound dimensions were determined from 3D images collected on days 0, 2, 5, and 7. On day 7, animals were euthanized and specimens were harvested for histopathological review. **Results:** Average granulation thickness was not statistically different among continuous (3.29 ± 0.33 mm), intermittent (3.03 ± 0.47 mm), and dynamic (3.40 ± 0.34 mm) NPWT wounds at day 7. Average granulation thickness of NPWTi wounds (4.75 ± 0.54 mm), however, was statistically greater ($P < .05$) by 44%, 57%, and 40%, respectively, than that of wounds treated with continuous, intermittent, and dynamic NPWT. Analysis of 3D images revealed a greater reduction in wound area and perimeter in NPWTi wounds compared to all NPWT wounds ($P < .05$). In addition, the average wound fill rate for NPWTi wounds was faster than that for continuous (40%; $P < .05$), intermittent (25%; $P > .05$), and dynamic (65%; $P < .05$) NPWT wounds. **Conclusions:** Although not confirmed in humans, these porcine data suggest that NPWTi with saline may stimulate a faster rate of wound granulation than NPWT in continuous and noncontinuous modes.

Negative pressure wound therapy (NPWT) creates an environment that promotes wound healing by preparing the wound bed for closure, reducing edema, promoting

granulation tissue formation and perfusion, and by removing exudate and infectious material.[1] These mechanisms and other effects of NPWT have been evaluated in various experimental and clinical studies, ranging from computer models,[2] to in vitro[3,4] and in vivo[5-7] models, to randomized controlled clinical trials.[8,9] Depending on the clinician's preference, NPWT can be delivered as continuous pressure or noncontinuous pressure. Two types of noncontinuous NPWT currently exist: intermittent NPWT, in which negative pressure alternates between a set pressure and no pressure for programmed periods of time; and dynamic (variable) NPWT, in which negative pressure transitions between a high pressure and a low pressure following programmed rise and fall times.

In addition, negative pressure wound therapy with instillation (NPWTi) is indicated for patients who would benefit from NPWT as well as controlled delivery and vacuum assisted drainage of topical wound treatment solutions and suspensions, including wound cleansers, over the wound bed.[10,11] NPWTi cycles between 3 discrete phases in the following order:

- Instillation—The topical wound treatment solution or suspension is delivered to the wound bed.
- Soak—The topical wound treatment solution or suspension is held in the wound bed for a prescribed period of time.
- NPWT—The topical wound solution, treatment solution or suspension, wound exudates, and infectious materials are removed from the wound bed as NPWT is delivered for a user-selected interval; when the NPWT phase is complete, the cycle begins again with instillation.

Compared to NPWT, NPWTi is a more recent addition to the wound care toolkit and its mechanisms of action are less understood. However, several publications suggest that NPWTi with the appropriate topical wound cleansing solution may help with wound bioburden management.[10-13] Published preclinical studies suggest that noncontaminated wounds may benefit from NPWTi as well.[14,15] Lessing et al[14] showed that porcine excisional wounds treated with NPWTi with saline had 43% more granulation than the wounds treated with continuous NPWT after 7 days of therapy.

Negative pressure is, by design, interrupted during the instillation and soak phases of NPWTi to prevent immediate aspiration of the topical wound treatment solution or suspension. Bench studies suggest that interruption of negative pressure and the introduction of a soak phase is essential for uniform coverage of the wound with the topical wound treatment solution, especially when complex wound geometries are present; if the negative pressure is not stopped while the solution is being delivered, coverage of the wound with the instilled solution may be incomplete.[16] Thus, this difference between instillation (fluid delivery with a soak phase) and irrigation (fluid delivery without a soak phase) is critical if the topical wound treatment solution requires a prescribed contact time in the wound bed to have a desired effect (eg, to loosen soluble debris, for antisepsis, etc).

Both researchers and device manufacturers claim that all NPWT systems are not created the same, and several studies have suggested that noncontinuous NPWT (intermittent or variable pressure modes) may result in more granulation tissue than continuous NPWT.[5,17,18] However, a separate study in diabetic mice suggested that the granulation response to continuous NPWT is superior to noncontinuous (intermittent and dynamic) NPWT modes.[7] As such, it is unclear whether the increased granulation tissue observed

by Lessing et al[14] was due to the enhanced wound cleansing provided by NPWTi or the noncontinuous nature of the interrupted negative pressure that is characteristic of NPWTi.

The present study uses a well-controlled porcine model to compare the granulation response of wounds treated with NPWTi (V.A.C. VeraFlo Therapy; KCI USA, Inc, San Antonio, Texas) to those treated with continuous and noncontinuous (intermittent and dynamic) NPWT.

METHODS

All animal procedures were performed under a protocol approved by the Institutional Animal Care and Use Committee at the test facility. Five female domestic swine (weight range, 65-75 kg) were fully anesthetized and physiological parameters including heart rate, blood pressure, body temperature, and respiratory rate were monitored during the surgical procedure and postsurgical recovery. Each animal received 10 paraspinal (5 per side) dorsal full-thickness 5-cm diameter excisional wounds to the muscle fascia, with the epidermal, dermal, subdermal fat, and subcutaneous fat layers removed. Light pressure with saline moistened gauze was applied to the wound to stop bleeding post excision, as needed. Adjacent or contralateral wounds, as appropriate, were dressed and bridged together as pairs. Bridged wound pairs were assigned to one of the following treatment groups (Fig 1), with each pig having one of every treatment group:

Continuous NPWT

Following the manufacturer's instructions for use, reticulated open-cell foam (ROCF) dressings (ROCF-G; V.A.C. GranuFoam Dressing; KCI USA, Inc, San Antonio, Texas) were applied to the wounds, bridged together as a pair by overlaying additional ROCF-G, and then covered with drape (V.A.C. Drape; KCI USA, Inc, San Antonio, Texas). The bridged wound pair was connected to a therapy unit (V.A.C.ULTA Therapy System, KCI USA, Inc, San Antonio, Texas) set to deliver continuous NPWT at −125 mm Hg.

Intermittent NPWT

Wound pairs were dressed as mentioned earlier. The bridged wound pair was connected to a therapy unit (InfoV.A.C. Therapy System, KCI USA, Inc, San Antonio, Texas; Note: the V.A.C.ULTA Therapy System does not provide intermittent NPWT as an option) set to deliver intermittent NPWT, with each cycle consisting of 5 minutes at −125 mm Hg followed by 2 minutes at 0 mm Hg.

Dynamic (controlled variable) NPWT

Wound pairs were dressed as mentioned earlier. The bridged wound pair was connected to a therapy unit (V.A.C.ULTA Therapy System) that delivered dynamic NPWT, with each cycle consisting of a controlled 3-minute rise to −125 mm Hg followed by a controlled 3-minute fall to −25 mm Hg.

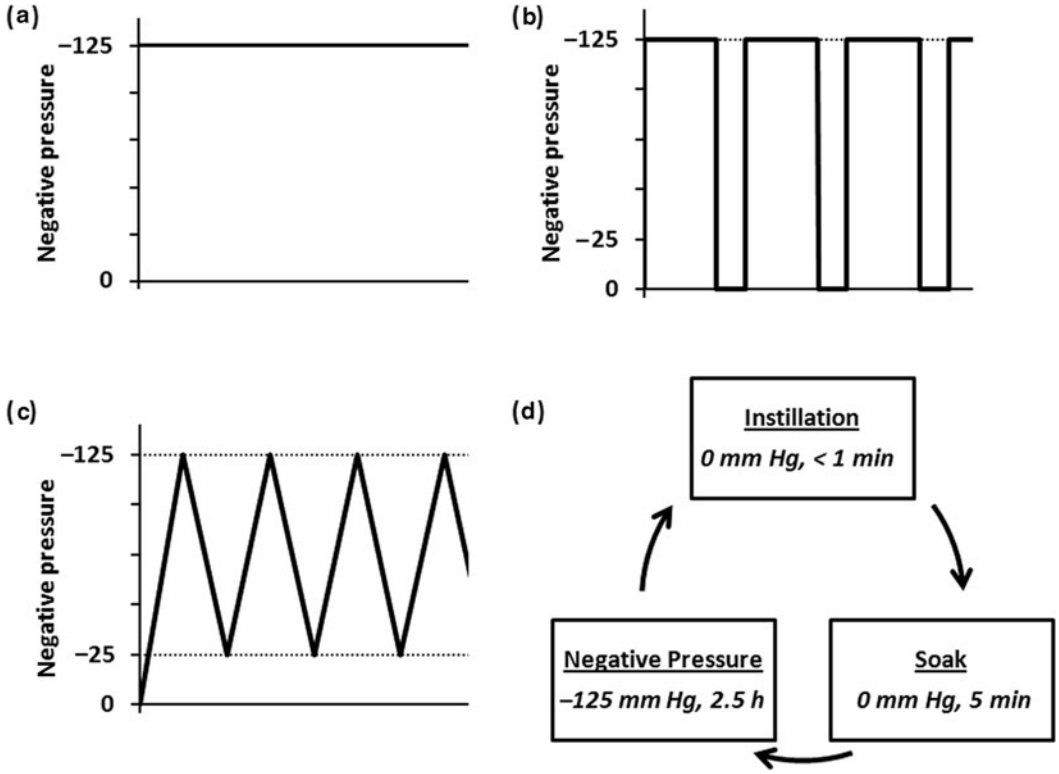

Figure 1. Schematics of negative pressure profiles evaluated in this study: (*a*) continuous NPWT at −125 mm Hg; (*b*) intermittent NPWT with cycles of 5 minutes at −125 mm Hg followed by 2 minutes of 0 mm Hg; (*c*) dynamic NPWT with a 3-minute rise to −125 mm Hg followed by a 3-minute fall to −25 mm Hg; and (*d*) NPWTi with each cycle consisting of a short instillation phase, following by a 5-minute soak phase, followed by a 2.5-h negative pressure phase.

NPWTi

Following the manufacturer's instructions for use, wounds were dressed with ROCF-V (V.A.C. VeraFlo Dressing; KCI USA, Inc, San Antonio, Texas), bridged together as a pair by overlaying additional ROCF-V, and then covered with drape. The bridged wound pair was connected to a therapy unit (V.A.C.ULTA Therapy System) set to deliver NPWTi with each cycle consisting of instillation of 55 mL of sterile normal saline (instillation phase), a 5-minute soak of saline in the wound (soak phase) and 2.5 hours of negative pressure at −125 mm Hg (NPWT phase). Cycling among these 3 phases continued for the duration of the study period.

A fifth negative pressure treatment mode not commercially available was tested but is not reported here. In total, each treatment group was assigned n = 10 wounds. Dressings were changed on days 2 and 5. Therapy systems were connected to a monitoring system, and alarms were addressed by on-call staff to minimize therapy interruptions. Animals were euthanized on day 7.

Wounds were photographed on Days 0, 2, 5, and 7, and three-dimensional reconstructions of the wounds were generated (3D LifeViz System; QuantifiCare S.A., Sophia

Antipolis, France). Wound perimeter and surface area were measured on reconstructions from days 0, 2, 5, and 7. The change in wound volume (percent fill normalized to day 0 wound volume) from day 5 to day 7 was calculated to determine the daily rate of granulation tissue formation during the granulation phase of healing.

After euthanasia, wound tissue was excised en bloc to include underlying musculature and surrounding unwounded tissue. Tissues were fixed in 10% neutral buffered formalin, paraffin embedded, thinly sectioned, and stained with hematoxylin and eosin. Histological sections were evaluated by a board-certified histopathologist. Granulation tissue thickness was measured from the base of the wound to the top of the granulation layer, at 2-mm increments across the entire cross section of the wound; the incremental measurements were averaged together to determine the average granulation thickness for each wound.

Univariate analyses were performed for all data (wound area and perimeter, wound fill, and granulation thickness) and treatment group means with standard error of the mean are presented. Hierarchical, or nested, models were used to compare the treatment group means by including a random intercept to adjust for the potential of animal variation in wound healing. All inferential statistical analyses were performed using a 2-tailed test at $\alpha = .05$ significance; no adjustments for multiple comparisons were made. All statistical analyses were performed using Statistical Analysis System software (Version 9.3; SAS Institute Inc, Cary, North Carolina).

RESULTS

Wound images

A representative time course of images of a continuous NPWT-treated wound is shown in Figure 2. The 5-mm full-thickness excisional wound immediately following creation has clearly defined edges with the smooth fascia of the underlying muscle intact. At the first dressing change (after 2 days of therapy), the wound appears more pink and with some texture present, but no granulation tissue has formed. By day 5 and continuing to day 7, the wound bed is covered with beefy red granulation tissue.

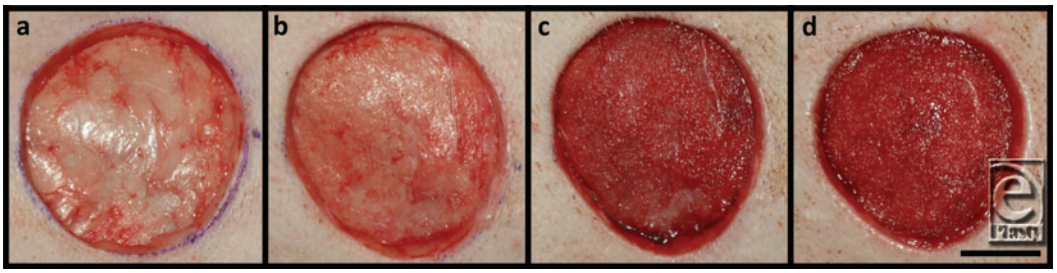

Figure 2. Progression of a single representative wound at (*a*) day 0 creation, (*b*) day 2 dressing change, (*c*) day 5 dressing change, and (*d*) day 7 termination. Note the paucity of granulation tissue at day 2, suggesting the wound has not fully left the inflammatory phase of healing. However, the wound enters the granulation phase of healing by day 5, and a robust granulation layer is present by day 7. (Wound shown was treated with continuous NPWT, scale bar = 2 cm.)

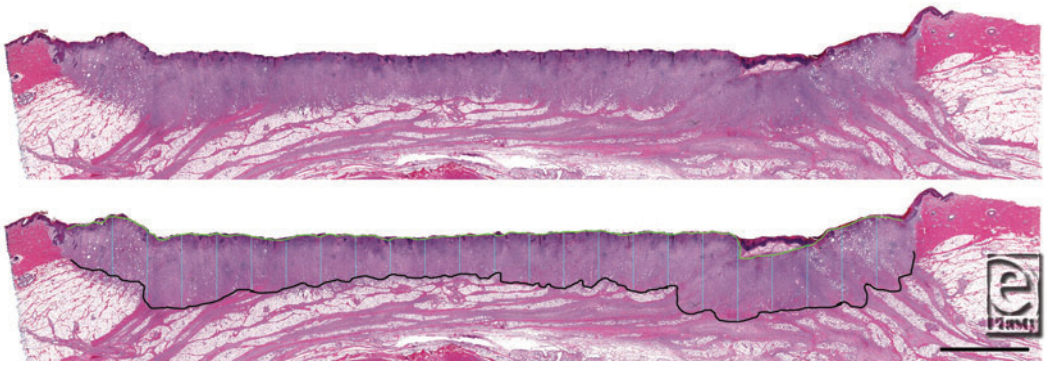

Figure 3. Representative photomicrograph of a wound treated with continuous NPWT. The top image shows the histological section stained with hematoxylin and eosin. The bottom image shows the same section with the bottom (black tracing) and top (green tracing) of the granulation tissue marked. The vertical blue lines are the incremental granulation tissue thickness measurements, spaced every 2 mm. These increments are averaged to determine the average granulation tissue thickness for this wound. (Scale bar = 5 mm)

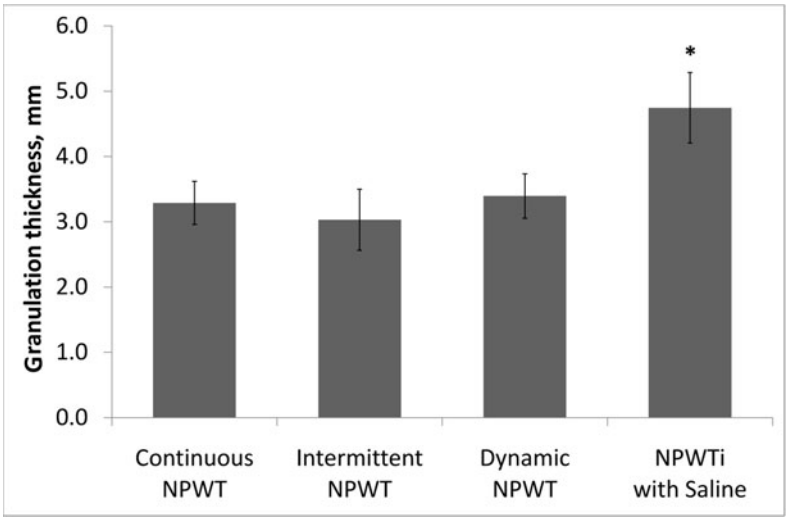

Figure 4. Average granulation tissue thickness measured in histology specimens at day 7. Data are shown as mean ± standard error of the mean. (n = 10 wounds per group; $^{*}P < .05$ for NPWTi compared to all NPWT groups)

Histomorphometry and histopathology

A representative photomicrograph of a continuous NPWT-treated wound is shown in Figure 3, with incremental granulation tissue thickness measurements indicated. The average granulation tissue thickness at day 7 for each treatment group is shown in Figure 4. There was no statistical difference between the 3 NPWT treatment groups (continuous NPWT [3.29 ± 0.33 mm], intermittent NPWT [3.03 ± 0.47 mm], or dynamic NPWT [3.40 ± 0.34 mm]). However, the NPWTi with saline treatment group

(4.75 ± 0.54 mm) was significantly greater than all of these ($P < .05$). The granulation tissue in the NPWTi with saline treatment group was 44% thicker than in continuous NPWT, 57% thicker than in intermittent NPWT, and 40% thicker than in dynamic NPWT.

Three-dimensional wound reconstruction measurements

Changes in wound perimeter and wound surface area from day 0 to day 7 are shown in Figure 5. These figures show a decrease in wound perimeter and wound surface area with statistically significant smaller mean values at day 7 for wounds treated with NPWTi with saline compared to wounds treated with continuous, intermittent, or dynamic NPWT modalities ($P < .05$).

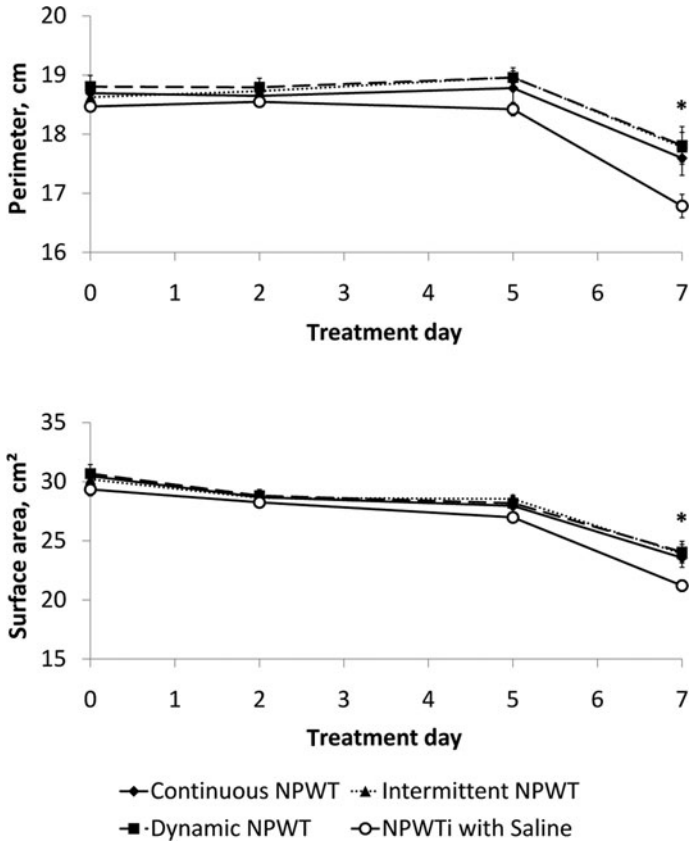

Figure 5. Changes in wound perimeter (*top*) and surface area (*bottom*) calculated from 3D wound reconstructions. Data are shown as mean ± standard error of the mean. (n = 10 wounds per group, $^{*}P < .05$ for NPWTi compared to all NPWT groups.)

The rates of wound volume (percent fill per day) from day 5 to day 7 were: continuous NPWT, 18.6% ± 3.0% per day; intermittent NPWT, 20.9% ± 4.1% per day; dynamic NPWT, 15.8% ± 2.7% per day; and NPWTi with saline, 26.1% ± 1.8% per day (Fig 6). The rate of wound fill with NPWTi with saline was statistically faster ($P < .05$) than with

continuous NPWT (40% faster) or dynamic NPWT (65% faster); however, the difference in wound fill rate between NPWTi with saline and intermittent NPWT treatment group was not statistically significant (25%, $P > .05$).

DISCUSSION

The first documented uses of NPWTi have suggested the therapy to be important in the management of contaminated wounds with measurable bioburden.[13,19] However, several preclinical studies have suggested that the cleansing provided by NPWTi may also benefit noncontaminated wounds. In 2010, Leung et al published a study on pigs showing that NPWTi with saline elicited a faster rate of wound filling with granulation and increased collagen content compared to continuous NPWT.[15] In subsequent work by Lessing et al,[14] the differences in granulation were more pronounced: the granulation tissue in porcine wounds treated with NPWTi with saline was 43% thicker than in wounds treated with continuous NPWT after 7 days of therapy.[14] However, as mentioned previously, these studies were interpreted with caution, because it was unknown whether the increase in granulation tissue was due to wound washing and cleansing or due to the noncontinuous nature of NPWTi.

This study compares, for the first time, continuous and noncontinuous (intermittent and dynamic) NPWT profiles to NPWTi. Despite prior reports by Morykwas et al[5] and Malmsjo et al[17] associating noncontinuous negative pressure with more granulation tissue than continuous negative pressure, no significant differences were observed between the continuous and noncontinuous NPWT groups for all evaluated outcomes in this study.

A limitation of the NPWT systems used in the studies of Morykwas et al[5] and Malmsjo et al[17] could explain this difference: less sophisticated NPWT systems measure the pressure at or near the pump, but not at the wound bed. Pressure measurement at the wound is critical to the pump's adjustment to challenges that develop in the tubing during the course of therapy, such as changes in exudate volume and viscosity, the vertical distance between the pump and the wound (referred to as *head height*), leaks, and blockages. Studies have shown that, when faced with these challenges, negative pressure systems or other vacuum sources that did not measure the pressure at the wound failed to deliver the set negative pressure level to the wound bed.[20,21] As stated by Ahearn[18] in 2009 review, "suboptimal strain in wounds may result in suboptimal healing." The therapy units used in the present study measured pressure at the wound bed, and review of the therapy and alarm logs indicate that there were no persistent therapy interruptions or deviations.

Continuous NPWT and NPWTi have been shown to create an environment that supports wound healing by promoting granulation tissue formation, so a subset of the analyses were designed to determine the rate of new tissue formation during this granulation phase. The canonical understanding of skin wound healing states that healing occurs in discrete, but overlapping, phases following injury: hemostasis (complete in the first minutes to hours postinjury), inflammation (beginning at injury but continuing for several days), proliferation and granulation (beginning 3-5 days postinjury), and remodeling (beginning several weeks postinjury).[22] Thus, the day 0 and day 2 time points were excluded from the evaluation of the rate of granulation tissue formation. No statistically significant differences in the rate of change of wound volume (percent fill increase) were observed between day 5 and

day 7 in the continuous and noncontinuous NPWT groups (Fig 6); however, NPWTi-treated wounds exhibited a faster increase in wound volume fill compared to the continuous and noncontinuous NPWT groups. Furthermore, wounds treated with NPWTi showed larger reductions in wound perimeter and surface area than with either continuous or noncontinuous NPWT, suggesting faster wound size reductions in NPWTi-treated wounds.

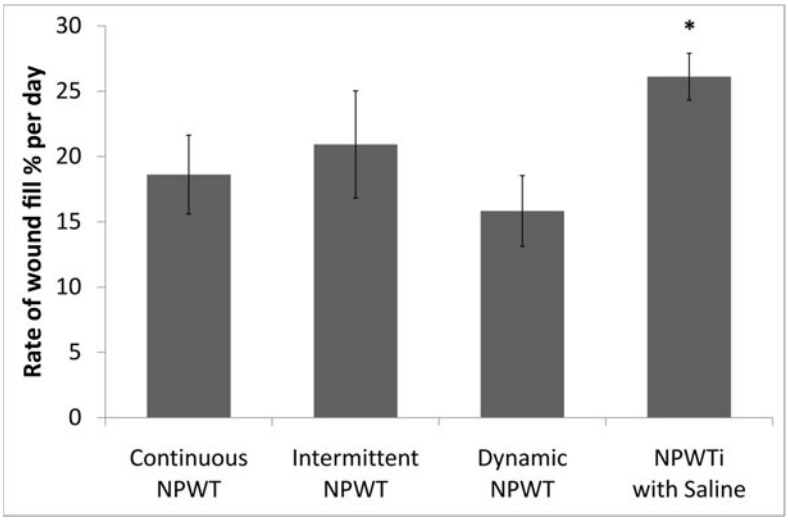

Figure 6. The rate of change of wound volume, calculated as percent fill per day. Data are shown as mean ± standard error of the mean. (n = 10 wounds per group, $^{*}P < .05$ for NPWTi compared to continuous NPWT and dynamic NPWT.)

These data support the hypothesis that the mechanism for the increased granulation response with NPWTi is extended, deliberate wound cleansing beyond the initial debridement rather than the intermittent nature of the therapy. The layer of exudate on a wound has evolved to serve as a barrier to infection, and its components play important roles in wound healing: for example, cytokines attract host cells including immune and inflammatory cells, reactive oxygen species target microorganisms, and proteolytic enzymes including matrix-metalloproteinases break down devitalized tissue. However, when uncontrolled, these exudate components contribute to wound chronicity. Consequently, exudate management is a pillar of modern wound bed preparation, along with debridement and bioburden management.[23] NPWTi dilutes and removes excess wound exudates and infectious materials, and it can be considered as an extension of the initial wound debridement and cleansing. A clean wound environment may allow the limited cellular metabolic and energetic resources in the wound to be dedicated to healing pathways, including cell proliferation and matrix production, as opposed to immune and inflammatory responses.

After NPWTi is prescribed, a topical wound treatment solution must be selected and a protocol developed. Considerations for selection of a solution should include: wound type and overall status, known or suspected bioburden (level and type), goals of therapy, patient allergies, and recommendations of the solution manufacturer related to solution soak time and application frequency. Given the complexity and number of permutations of these

factors, each wound should be evaluated individually and its NPWTi treatment program developed and revised as the wound progresses.

Compatibility of the solution with the NPWTi system and its components (including the tubing, dressing, drape, and adhesive) should also be considered, as reactive topical wound solutions could have adverse interactions with the components. A list of compatible solutions can be obtained from the manufacturer.

Recent clinical publications report the use of NPWTi-compatible topical wound treatment solutions, including the following.

- Polyhexanide on osteomyelitis of the pelvis or lower extremity,[24] skin and soft tissue wounds,[25] chronic or acute orthopedic wounds,[12] and infected and surgically debrided wounds[26]
- Saline or sterile water on complex wounds and wounds where conventional NPWT was ineffective[27]
- Hypochlorite-based solutions on venous stasis ulcers[28] and various other wounds[11]
- Silver nitrate on complex wounds.[29]

Other NPWTi-compatible solutions include mafenide acetate, octenidine dihydrochloride, acetic acid (ethanoic acid), and benzalkonium chloride; anecdotal reports of their use on individual patients are not yet available in the peer-reviewed literature. It is unknown how solutions other than saline may affect granulation tissue formation clinically.

Noncontinuous pressure modes will continue to play an important role in NPWT. At the subcellular level, the cytoskeleton of many cell types can adapt rather quickly to microdeformational changes.[30,31] As such, intermittent NPWT is, anecdotally, used to jump-start stalled wounds that have quit responding to continuous NPWT. However, intermittent NPWT is not commonly used at the beginning of a wound-treatment program because of the potential of patient discomfort associated with the contraction and expansion of dressings that occurs as negative pressure transitions between the therapeutic set point and 0 mm Hg. Dynamic NPWT has been developed to increase patient comfort during noncontinuous NPWT—the rate of pressure change is controlled, and the pressure does not drop below −25 mm Hg, preventing expansion of the dressing. Additional studies are needed to assess the effectiveness of intermittent and dynamic NPWT modes and their role as a clinical option for chronic and stalled wounds.

As with any preclinical evaluation of a medical device, the relevance of the model is open for discussion. The porcine excisional wound model is an acute injury in a young, healthy animal, and these wounds will generally heal without requiring advanced therapies; however, the porcine model is the accepted preclinical model for wound healing.[32] Even with the limitations of the model, demonstration of a difference between advanced treatments is noteworthy; each treatment group was represented in duplicate in each pig, so internal controls were present. This study would be challenging to repeat in humans, because the heterogeneity of clinical wounds and lack of internal controls would require much larger sample sizes. Also, determination of granulation tissue thickness is only possible as a destructive measurement (ie, tissue must be collected as a biopsy or other excisional method to determine the thickness).

Finally, as dressing choice is often a topic of discussion in the literature, it should also be mentioned here that new ROCF dressings have been specially designed for use

with NPWTi.[14] These dressings have both increased mechanical properties to reduce the likelihood of tearing and fragmentation and reduced hydrophobicity, which improves their ability to distribute fluids within the wound bed.

Together these preclinical data suggest that wounds treated with NPWTi with saline instillation may exhibit faster granulation rates than wounds treated with either continuous or noncontinuous NPWT. The granulation response of NPWT may be tied to many factors, including wound microstrain, increased perfusion, edema reduction, and removal of exudate and debris that may impair wound healing. NPWTi provides these factors as well as automated delivery and removal of topical wound treatment solutions and suspensions with a controlled soak time. The soak phase provided by NPWTi also allows for controlled solution exposure times and may help to loosen soluble debris and exudate while increasing solution coverage of the wound bed, providing a cleaner environment for healing. Ultimately, further investigations to understand mechanisms of action of NPWTi and noncontinuous NPWT are warranted, and the significance of these findings must be confirmed in clinical studies.

Acknowledgments

The authors thank B. Collins, D. Kilpadi, L. Clausen, and E. Gacke for their contributions to this study and A. Goodwin for her editing assistance with this manuscript.

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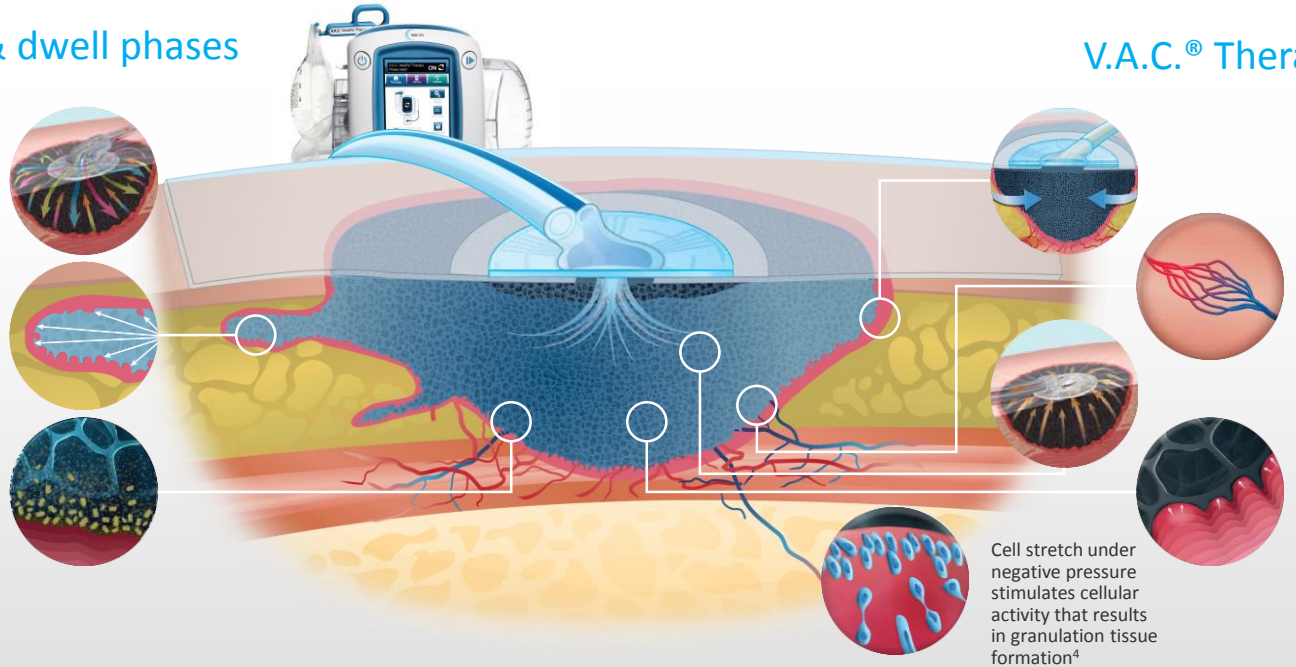
V.A.C. VERAFLO™ Therapy delivers enhanced mechanisms of action

Instillation & dwell phases

Solution Instillation
Cleanses wound with cyclic delivery, dwell and removal of topical wound solutions

Provides thorough wound coverage with topical solution during selected dwell time[1]

Solution Dwell
Dilutes and solubilizes infectious material and wound debris



Cell stretch under negative pressure stimulates cellular activity that results in granulation tissue formation[4]

V.A.C.® Therapy phases

Macrostrain
Draws wound edges together

Promotes perfusion and reduces edema

Removes exudate and infection material

Microstrain
In vitro/in vivo studies show that foam contact with tissue creates micro-deformation that leads to cell stretch[2,3]

REF

KCI
AN ACELITY COMPANY

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Center - WO66-G609
Silver Spring, MD 20993-0002

June 20, 2016

Kci Usa, Inc. (kinetic Concepts, Inc.)
% Melanie Avila
Senior Manager, Regulatory Affairs
Kci Usa, Inc.
6203 Farinon Drive
San Antonio, Texas 78249

Re: K160451
Trade/Device Name: V. A.c. Veraflo Cleanse Choice Dressing System For Use With The V.a.c. Ulta ...
Regulation Number: 21 CFR 878.4780
Regulation Name: Powered Suction Pump
Regulatory Class: Class II
Product Code: OMP
Dated: February 16, 2016
Received: February 18, 2016

Dear Melanie Avila:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in

the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801), please contact the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

David Krause -S

for Binita S. Ashar, M.D., M.B.A., F.A.C.S.
Director
Division of Surgical Devices
Office of Device Evaluation
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: January 31, 2017
See PRA Statement below.

510(k) Number *(if known)*
K160451

Device Name
V. A.C. VeraFlo Cleanse Choice Dressing System for use with the V.A.C. Ulta Negative Pressure Wound Therapy System

Indications for Use *(Describe)*
The V.A.C. Ulta Negative Pressure Wound Therapy System is an integrated wound management system that provides Negative Pressure Wound Therapy with an instillation option.

Negative Pressure Wound Therapy in the absence of instillation 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 instillation option is indicated for patients who would benefit from vacuum assisted drainage and controlled delivery of topical wound treatment solutions and suspensions over the wound bed.

The V.A.C. Ulta Negative Pressure Wound Therapy System with and without instillation is indicated for patients with chronic, acute, traumatic, sub-acute and dehisced wounds, partial-thickness burns, ulcers (such as diabetic, pressure and venous insufficiency), flaps and grafts.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

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In accordance with 21 CFR 807.87(h) and 21 CFR 807.92, the 510(k) Summary for the V.A.C. VeraFlo Cleanse Choice Dressing System is provided below.

1. SUBMITTER

KCI USA, Inc.
6203 Farinon Drive
San Antonio, TX 78249

Contact Person:
Melanie Avila
Senior Manager, Regulatory Affairs
KCI USA, Inc.
Telephone: 210-515-4059
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Date Prepared: February 16, 2016

2. DEVICE

Name of Device: V.A.C. VeraFlo Cleanse Choice Dressing System for use with the V.A.C. Ulta Negative Pressure Wound Therapy (NPWT) System
Common Name: Negative Pressure Wound Therapy Powered Suction Pump
Classification Regulation: 21 CFR 878.4780
Regulatory Class: II
Product Code: OMP
Panel: General and Plastic Surgery

3. PREDICATE DEVICE

Predicate Device: VeraFlo Cleanse Dressing System (K103156)

4. DEVICE DESCRIPTION

The V.A.C. VeraFlo Cleanse Choice Dressing System is intended for use with the V.A.C. Ulta Negative Pressure Wound Therapy System to deliver negative pressure wound therapy (NPWT) as well as facilitate the instillation of fluid to the wound.

The V.A.C. VeraFlo Cleanse Choice Dressing System has the same basic components as the predicate V.A.C. VeraFlo Cleanse Dressing cleared under K103156. The only difference between the two systems is the configuration of the dressing.

The subject system has a dressing that is designed with 3 separate layers. The predicate dressing, on the other hand, is a single spiral shaped rod configuration. The materials of the dressing are the same.

5. INDICATIONS FOR USE

The V.A.C. VeraFlo Cleanse Choice Dressing System is intended to be used with the V.A.C. Ulta Negative Pressure Wound Therapy System. The indications for use as follows:

> The V.A.C. Ulta Negative Pressure Wound Therapy System is an integrated wound management system that provides Negative Pressure Wound Therapy with an instillation option.
>
> Negative Pressure Wound Therapy in the absence of instillation 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 instillation option is indicated for patients who would benefit from vacuum assisted drainage and controlled delivery of topical wound treatment solutions and suspensions over the wound bed.
>
> The V.A.C. Ulta Negative Pressure Wound Therapy System with and without instillation is indicated for patients with chronic, acute, traumatic, sub-acute and dehisced wounds, partial-thickness burns, ulcers (such as diabetic, pressure and venous insufficiency), flaps and grafts.

Both the subject system and the predicate system are intended for use with the V.A.C. Ulta Negative Pressure Wound Therapy System. Both systems have the ability to deliver topical wound solutions and suspensions in the wound bed as well as delivery of negative pressure wound therapy. There is no change to the indications for use.

6. COMPARISON OF TECHNOLOGICAL CHARACTERISTICS

6.1. Similarities

The V.A.C VeraFlo Cleanse Choice Dressing System is nearly identical to that of the predicate V.A.C VeraFlo Cleanse Dressing System (cleared under K103156). Both systems have the same materials, sterilization, and packaging.

The subject V.A.C. VeraFlo Cleanse Choice Dressing System has the same basic components as the predicate V.A.C. VeraFlo Cleanse Dressing System cleared under K103156. Both dressings of these systems are made from the identical open cell, reticulated, grey polyurethane ester foam stock material.

6.2. Differences

The only difference between the proposed and the predicate system is the configuration of the dressing component. The subject system has a dressing that is provided in three separate layers in an oval shape to allow for flexibility in treating wounds of various depths. The predicate dressing is a tubular shaped rod and is split along the longitudinal axis by the user for ease of configuring.

For convenience purposes, the table below compares the subject and predicate systems.

	Proposed Device	**Predicate Device**
510(k) Number	K160451	K103156
Applicant	Same as predicate	KCI USA, Inc.
Trade name	V. A.C. VeraFlo Cleanse Choice Dressing System for use with the V.A.C. Ulta Negative Pressure Wound Therapy System	V. A.C. VeraFlo Cleanse Dressing System for use with the V.A.C. Ulta Negative Pressure Wound Therapy System
Classification Regulation	Same as predicate	878.4780
Product Code	Same as predicate	OMP
Indications for Use	Same as predicate	The V.A.C.Ulta Negative Pressure Wound Therapy System is an integrated wound management system that provides Negative Pressure Wound Therapy with an instillation option. The V.A.C.Ulta Negative Pressure Wound Therapy System in the absence of instillation 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 instillation option is indicated for patients who would benefit from vacuum assisted drainage and controlled delivery of topical wound treatment solutions and suspensions over the wound bed. The V.A.C.Ulta Negative Pressure Wound Therapy System with and without instillation is indicated for patients with chronic, acute, traumatic, sub-acute and dehisced wounds, partial-thickness burns, ulcers (such as diabetic, pressure and venous insufficiency), flaps and grafts.
Dressing System Components	Same as predicate	V.A.C. VeraT.R.A.C. Pad Assembly
	V.A.C. VeraFlo Cleanse Choice Dressing has 3 layer design	V.A.C. VeraFlo Cleanse Dressing has a tubular shaped rod design
	Same as predicate	V.A.C. Ruler
	Same as predicate	3M ™ Cavilon™ Skin Prep
	Same as predicate	V.A.C. Advanced Drape
NPWT Therapy System Design	Same as predicate	The VeraFlo Cleanse Dressing System is intended for use with the V.A.C. Ulta NPWT system. The NPWT system consists of: • Software controlled therapy unit • Canister

	Proposed Device	**Predicate Device**
		• Negative pressure tubing and sensing pad • Instillation tubing and pad • Foam wound dressing and polyurethane occlusive drape
NPWT System Operating Principle	Same as predicate	The V.A.C. Ulta NPWT system delivers software controlled negative pressure to the wound site. The open cells of the foam dressing to which the therapy unit is connected enable distribution of the negative pressure across the surface of the wound, while the tubing transfers accumulated fluids to the canister. The NPWT system also provides automated delivery of instillation fluids into the wound bed between negative pressure therapy cycles.
Materials	Skin contact material: Same as predicate	Skin contact material: Occlusive drape (polyurethane film with acrylic adhesive)
	Wound contact material: Same as predicate	Wound contact material: Polyurethane ester foam
	Same as predicate	0.1% w/v carbon black colorant
	Same as predicate	Density in lb/ft3: 5.1 - 6.3
Performance Testing	Same as predicate	Verification testing was performed to confirm: • mechanical properties (tensile testing) • the dressing, as part of the V.A.C. Ulta Negative Pressure Wound Therapy System, delivers negative pressure • the dressing distributes instillation solution throughout the wound surface
Mechanical Properties (Tensile Strength)	Pass	≥230kPa
Sterilization	Same as predicate	Gamma Irradiation to SAL of 10^{-6}
Sterile Packaging	Same as predicate	Thermoformed tray of PETG with a Tyvek lid
Shelf life	Same as predicate	2 years

7. PERFORMANCE DATA

Bench Verification testing was performed to confirm:

- mechanical properties (tensile testing)
- the dressing, as part of the V.A.C. Ulta Negative Pressure Wound Therapy System creates negative pressure within the sealed wound bed
- the dressing distributes instillation solution throughout the wound surface

8. CONCLUSIONS

The only difference between the proposed and the predicate dressing systems is the configuration of the dressing. The subject system has a dressing that is provided in three separate layers in an oval shape to allow for flexibility in treating wounds of various depths. The predicate dressing is a tubular shaped rod and is split along the longitudinal axis by the user for ease of configuring.

Bench and animal testing have demonstrated that the subject V.A.C VeraFlo Cleanse Choice Dressing System is substantially equivalent to the predicate V.A.C VeraFlo Cleanse Dressing System (K103156).

K103156
p. 1/3

510(k) SUMMARY
V.A.C. VeraFlo Cleanse Dressing System

MAR 14 2011

Date prepared	February 16, 2011
510(k) owner	KCI, Inc.
Name	KCI USA, Inc. (Kinetic Concepts, Inc.)
Address	6203 Farinon Drive; San Antonio, Texas 78249
Fax number	210 255-6727
Name of contact person	Margaret Marsh
Contact telephone number	1 800 275-4524; Request Regulatory Affairs.
Name of the device	
Trade or proprietary name	V.A.C. VeraFlo Cleanse Dressing System
Common or usual name	Negative pressure wound therapy dressing
Classification name	Dressing component for use with a Negative Pressure Wound Therapy Powered Suction Pump
Legally marketed device(s) to which equivalence is claimed	V.A.C. VeraFlo Dressing, a component of the V.A.C.Ulta Negative Pressure Wound Therapy System (K100657)
Device description	A dressing component of a negative pressure wound therapy system with an instillation feature which allows controlled delivery and drainage of topical wound treatment solutions and suspensions
Device design	Negative pressure wound therapy system, in which instillation of topical wound treatment solutions and suspensions and negative pressure wound therapy is provided via software controlled pumps. Instillation solutions and negative pressure are delivered through tubing to foam dressings in the wound covered by an occlusive drape. Software provides controls for both negative pressure wound therapy and delivery of instillation therapy. Software also provides controls for help and alarm functions.

Intended use of the device	The V.A.C.Ulta Negative Pressure Wound Therapy System is an integrated wound management system that provides Negative Pressure Wound Therapy with an instillation option. Negative Pressure Wound Therapy in the absence of instillation 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 instillation option is indicated for patients who would benefit from vacuum assisted drainage and controlled delivery of topical wound treatment solutions and suspensions over the wound bed. The V.A.C.Ulta Negative Pressure Wound Therapy System with and without instillation is indicated for patients with chronic, acute, traumatic, sub-acute and dehisced wounds, partial-thickness burns, ulcers (such as diabetic, pressure and venous insufficiency), flaps and grafts.		
Summary of the technological characteristics of the device compared to the predicate device.	**Feature**	**VeraFlo Cleanse Dressing**	**VeraFlo Dressing (predicate)**
	Dressing system components	Same as predicate	Foam based dressing with occlusive drape and negative pressure/ instillation tubing
	Patient contact materials of construction	Same as predicate, except for slightly less colorant	Polyurethane ester foam with polyurethane drape

Summary of tests conducted	The V.A.C. VeraFlo Cleanse System was evaluated under a number of design verification and validation tests that assure conformance to design specifications. The following tests were conducted on the V.A.C. VeraFlo Cleanse System: • Negative pressure distribution measurements (bench test with simulated wound model). • Visual observation of fluid distribution in the dressing and simulated wound bed (bench test with simulated wound model). • Mechanical properties (tensile and tear strength per ASTM 3574-08 tests) • Granulation tissue formation and wound fill response in an acute swine model. • Cytotoxicity, irritation, and sensitization testing was performed in accordance to ISO 10993-1 standards, and results demonstrated that the device is biocompatible according to these standards. The device was shown to meet all performance requirements.
Conclusions drawn	Testing demonstrates that the V.A.C. VeraFlo Cleanse System is substantially equivalent in terms of both indications for use and technology to the predicate product.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Room W-O66-0609
Silver Spring, MD 20993-0002

KCI USA
% Ms. Margaret Marsh
Regulatory Affairs Technical Director
6203 Farinon Drive
San Antonio, Texas 78249

MAR 14 2011

Re: K103156
Trade/Device Name: V.A.C. VeraFlo Cleanse Dressing System
Regulation Number: 21 CFR 878.4780
Regulation Name: Powered suction pump
Regulatory Class: II
Product Code: OMP
Dated: February 16, 2011
Received: February 17, 2011

Dear Ms. Marsh:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21

CFR Part 807); labeling (21 CFR Part 801); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801), please go to http://www.fda.gov/AboutFDA/CentersOffices/CDRH/CDRHOffices/ucm115809.htm for the Center for Devices and Radiological Health's (CDRH's) Office of Compliance. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

Mark N. Melkerson
Director
Division of Surgical, Orthopedic
and Restorative Devices
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosure

K103156

INDICATIONS FOR USE

510(k) Number (if known): _____

Device Name: V.A.C. VeraFlo Cleanse Dressing System

Indications for Use:

The V.A.C.Ulta Negative Pressure Wound Therapy System is an integrated wound management system that provides Negative Pressure Wound Therapy with an instillation option.

Negative Pressure Wound Therapy in the absence of instillation 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 instillation option is indicated for patients who would benefit from vacuum assisted drainage and controlled delivery of topical wound treatment solutions and suspensions over the wound bed.

The V.A.C.Ulta Negative Pressure Wound Therapy System with and without instillation is indicated for patients with chronic, acute, traumatic, sub-acute and dehisced wounds, partial-thickness burns, ulcers (such as diabetic, pressure and venous insufficiency), flaps and grafts.

Prescription Use ___X___ (Part 21 CFR 801 Subpart D) AND/OR Over-The-Counter Use _____ (21 CFR 801 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE OF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)

David Krause for MKM

(Division Sign-Off) Page __ of ___

Division of Surgical, Orthopedic, and Restorative Devices

510(k) Number K103156

(Posted November 13, 2003)

K100657
pg 1 of 3

510(k) SUMMARY

V.A.C.Ulta™ Negative Pressure Wound Therapy System

SEP 17 2010

Date prepared	July 26, 2010
510(k) owner	KCI USA, Inc.
Name	KCI USA, Inc. (Kinetic Concepts, Inc.)
Address	6203 Farinon Drive; San Antonio, Texas 78249
Fax number	210 255-6727
Name of contact person	Margaret Marsh
Contact telephone number	1 800 275-4524; Request Regulatory Affairs.
Name of the device	
Trade or proprietary name	V.A.C.Ulta™ Negative Pressure Wound Therapy System (V.A.C.Ulta™ Therapy System)
Common or usual name	Instillation and negative pressure wound therapy system
Classification name	Negative Pressure Wound Therapy Powered Suction Pump (and components)
Legally marketed device(s) to which equivalence is claimed	V.A.C. Instillamat Device (K021501 and K091585)
Device description	A negative pressure wound therapy system with an instillation feature which allows controlled delivery and drainage of topical wound treatment solutions and suspensions
Device design	Negative pressure wound therapy system, in which instillation of topical wound treatment solutions and suspensions and negative pressure wound therapy is provided via software controlled pumps. Instillation solutions and negative pressure are delivered through tubing to foam dressings in the wound covered by an occlusive drape. Software monitors both negative pressure during negative pressure wound therapy as well as positive pressure during instillation of fluids to the wound bed. Software also provides controls for help and alarm functions.

<table>
<tr><td>Intended use of the device</td><td colspan="3">The V.A.C.Ulta Negative Pressure Wound Therapy System is an integrated wound management system that provides Negative Pressure Wound Therapy with an instillation option.

Negative Pressure Wound Therapy in the absence of instillation 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 instillation option is indicated for patients who would benefit from vacuum assisted drainage and controlled delivery of topical wound treatment solutions and suspensions over the wound bed.

The V.A.C.Ulta™ Negative Pressure Wound Therapy System with and without instillation is indicated for patients with chronic, acute, traumatic, sub-acute and dehisced wounds, partial-thickness burns, ulcers (such as diabetic, pressure and venous insufficiency), flaps and grafts.</td></tr>
<tr><td rowspan="4">Summary of the technological characteristics of the device compared to the predicate device</td><td>Feature</td><td>V.A.C.Ulta Therapy System</td><td>V.A.C. Instill Therapy System</td></tr>
<tr><td>Dressing system</td><td>Same as predicate</td><td>Foam based dressing with occlusive drape</td></tr>
<tr><td>Pressure sensing</td><td>Same as predicate</td><td>Via sensing pad in tubing line</td></tr>
<tr><td>Therapy unit</td><td>Same as predicate</td><td>Software controlled pumps for delivery of negative pressure wound therapy and controlled delivery of instillation fluids</td></tr>
<tr><td>Summary of tests conducted</td><td colspan="3">The V.A.C.Ulta Therapy System and components were evaluated under a number of design verification and validation tests that assure conformance to design specifications.
The following bench tests were conducted on the V.A.C.Ulta Therapy System:
• Ability of the V.A.C.Ulta System to deliver NPWT in a comparable manner to currently marketed V.A.C. NPWT Systems was assessed at -50, -125 and -200 mmHg. Testing demonstrated that the V.A.C.Ulta System delivers equivalent negative pressure wound therapy.
• The ability of the V.A.C.Ulta System to deliver both NPWT and intermittent fluid instillation within specification was assessed over a continuous 96 hours period. Testing demonstrated the system met performance specifications.
• Testing was conducted to confirm the ability of the therapy unit to instill fluids within specified ranges and volumes, to provide alarms and controls during negative pressure and instillation therapy, and to provide a maximum flow rate that is equivalent to that provided by the predicate. Testing demonstrated that all requirements were met.
• Mechanical properties testing of the new foam dressing (under wet and dry conditions) indicate that the dressing has the</td></tr>
</table>

	appropriate mechanical properties for use during instillation. • Peel force testing of the new drape documents that it is equivalent to the currently marketed V.A.C. Drape. • Software verification and validation testing confirms that the software meets the requirements of the software requirements specification. Biocompatibility testing was performed in accordance to ISO 10993-1 standards, and results demonstrated that the device is biocompatible according to these standards.
Conclusions drawn	Testing demonstrates that the V.A.C.Ulta™ Therapy System is substantially equivalent in terms of both indications for use and technology to the predicate product.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Room –WO66-G609
Silver Spring, MD 20993-0002

KCI USA, Inc.
% Ms. Margaret Marsh
Regulatory Affairs Technical Director
6203 Farinon Drive
San Antonio, Texas 78249

SEP 17 2010

Re: K100657
Trade/Device Name: V.A.C. Ulta Negative Pressure Wound Therapy System
Regulation Number: 21 CFR 878.4780
Regulation Name: Powered suction pump
Regulatory Class: II
Product Code: OMP
Dated: July 26, 2010
Received: July 28, 2010

Dear Ms. Marsh:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21

CFR Part 807); labeling (21 CFR Part 801); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801), please go to http://www.fda.gov/AboutFDA/CentersOffices/CDRH/CDRHOffices/ucm115809.htm for the Center for Devices and Radiological Health's (CDRH's) Office of Compliance. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

For

Mark N. Melkerson
Director
Division of Surgical, Orthopedic
and Restorative Devices
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosure

K100657

INDICATIONS FOR USE

510(k) Number (if known): K100657
Device Name: V.A.C.Ulta Negative Pressure Wound Therapy System

SEP 17 2010

Indications for Use:

The V.A.C.Ulta Negative Pressure Wound Therapy System is an integrated wound management system that provides Negative Pressure Wound Therapy with an instillation option.

Negative Pressure Wound Therapy in the absence of instillation 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 instillation option is indicated for patients who would benefit from vacuum assisted drainage and controlled delivery of topical wound treatment solutions and suspensions over the wound bed.

The V.A.C.Ulta™ Negative Pressure Wound Therapy System with and without instillation is indicated for patients with chronic, acute, traumatic, sub-acute and dehisced wounds, partial-thickness burns, ulcers (such as diabetic, pressure and venous insufficiency), flaps and grafts.

Prescription Use ___X___ (Part 21 CFR 801 Subpart D) AND/OR Over-The-Counter Use _____ (21 CFR 801 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE OF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)

David Krum for MKM

(Division Sign-Off)
Division of Surgical, Orthopedic, and Restorative Devices

(Posted November 13, 2003)

510(k) Number K100657

Cureus

Open Access Original Article

DOI: 10.7759/cureus.9047

Comparison of Negative Pressure Wound Therapy With and Without Instillation of Saline in the Management of Infected Wounds

Paul J. Kim [1], Ronald Silverman [2, 3], Christopher E. Attinger [4], Leah Griffin [5]

1. Plastic Surgery, University of Texas Southwestern Medical Center, Dallas, USA 2. Plastic Surgery, University of Maryland, Baltimore, USA 3. Medical Solutions Division, 3M, San Antonio, USA 4. Plastic Surgery, MedStar Georgetown University Hospital, Washington, DC, USA 5. Health Economics and Reimbursement, 3M, San Antonio, USA

Corresponding author: Paul J. Kim, paul.kim@utsouthwestern.edu

Abstract

Background

Negative pressure wound therapy (NPWT) with instillation and dwell time (NPWTi-d) includes periodic instillation of topical solution into the wound followed by a negative pressure. Our objective was to evaluate potential differences in wound outcomes in patients receiving NPWT and those receiving NPWTi-d using saline.

Methods

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 NPWT-treated patients with 42 NPWTi-d-treated patients.

Results

Patient demographics and comorbidities, wound etiologies, and anatomical locations of wounds were similar between groups, although a significantly higher percentage of NPWT-treated patients had end-stage renal disease (P = 0.0119). Compared with patients treated with standard NPWT, NPWTi-d-treated patients had a significantly lower number of operations (P = 0.0048), shorter length of hospital stay (P = 0.0443), shorter time to final surgical procedure (P = 0.0001), higher percentage of closed wounds (P = 0.0004), and a higher percentage of wounds that remained closed at one month (P = 0.0001).

Conclusions

The results of this analysis suggest that management of infected wounds with NPWTi-d using saline leads to favorable wound outcomes when compared to those managed with NPWT.

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Review began 06/29/2020
Review ended 06/30/2020
Published 07/07/2020

Categories: General Surgery, Healthcare Technology
Keywords: negative pressure wound therapy, instillation, chronic wounds, wound healing

Introduction

Increased patient morbidity and mortality, length of hospital stay, and costs are associated with

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infection in both acute and chronic wounds [1]. Wound infection management strategies include the use of antibiotics and the removal of infectious materials. While numerous advanced wound care products assist in the management of wound infection, negative pressure wound therapy (NPWT) utilizes negative pressure to remove exudate and infectious materials from wounds. The resulting negative pressure draws wound edges together and promotes angiogenesis and granulation tissue formation in the wound bed [2-5].

NPWT has evolved to include the periodic instillation of topical wound solutions directly over the wound bed, followed by removal using negative pressure. This NPWT with instillation and dwell time (NPWTi-d) utilizes the same properties of NPWT with the added benefit of wound cleansing [6]. NPWTi-d has been reported to promote wound cleansing, granulation tissue development, and healing in wounds that did not respond to traditional NPWT [7-9]. The comparative effectiveness of NPWTi-d using normal saline, a recommended first-line NPWTi-d solution, versus standard NPWT has not been adequately assessed in previous studies [10-12]. Our objective was to evaluate potential differences in wound outcomes in patients at an institution receiving NPWT and those receiving NPWTi-d with saline.

Materials And Methods

An analysis was performed using two independent previously published studies from a single investigator and hospital to compare patient characteristics and clinical outcomes of infected wounds from 74 NPWT-treated patients from the article's retrospective control cohort (control group) with 42 NPWTi-d-treated patients from the article's per protocol population (study group) [13,14]. As previously described, all patients underwent excisional debridement in the operating room and received parenteral or oral antibiotics [13,14]. The control group received continuous negative pressure at -125 mmHg using NPWT (INFOV.A.C.™ Therapy System, KCI, San Antonio, TX) [13]. The study group received NPWTi-d (V.A.C. VERAFLO™ Therapy, KCI, San Antonio, TX) with instillation of 0.9% saline with a dwell time of 20 minutes followed by two hours of negative pressure (-125 mmHg) [14]. Outcomes assessed included the number of operations, time to final surgery, length of hospital stay, wound closure, and percentage of wounds that remained closed at one month. Wound closure was defined as coverage of wound through delayed primary closure, skin graft, or flap. Statistical significance was determined using a t-test for continuous variables or Fisher's exact test for categorical values. Results were considered statistically significant at a P-value $\leqslant 0.05$.

Results

The mean age of patients in the control group (n = 74) and the study group (n = 42) was 58.0 ± 13.0 years and 60.7 ± 15.1 years, respectively (Table *1*). Patient demographics, comorbidities, wound etiologies, and anatomical locations of wounds were similar between groups, although a significantly higher percentage of NPWT-treated patients had end-stage renal disease (P = 0.0119) (Tables *1*, *2*).

Characteristics	Control Group (n = 74)	Study Group (n = 42)	P-value
Age, years (mean ± SD)	58.0 ± 13.0	60.7 ± 15.1	0.3202
BMI, kg/m^2 (mean ± SD)	32 ± 9.1	29.1 ± 8.2	0.0913
Gender, n (%)			0.2429
Male	38 (51.0)	27 (64.0)	
Female	36 (49.0)	15 (36.0)	
Race, n (%)			0.0995
African American	21 (28.0)	19 (51.4)	
Caucasian	39 (53.0)	17 (45.9)	
Hispanic	2 (6.0)	0 (0)	
Asian	1 (3.0)	1 (2.7)	
Other race	6 (8.0)	0 (0)	
Comorbidities, n (%)			
ESRD	22 (30.0)	4 (9.5)	0.0119
PVD	27 (36.0)	9 (21.4)	0.1004
History of cancer	6 (8.0)	6 (14.3)	0.3477

TABLE 1: Patient demographics and comorbidities

BMI = body mass index; ESRD = end-stage renal disease; PVD = peripheral vascular disease; SD = standard deviation

Characteristic	Control Group (n = 74)	Study Group (n = 42)
Wound type, n (%)		
Ischemic	17 (23.0)	6 (14.3)
Neuropathic	16 (22.0)	14 (33.3)
Decubitus	16 (22.0)	4 (9.5)
Surgical	17 (23.0)	13 (31)
Venous insufficiency	3 (4.0)	2 (4.8)
Traumatic	4 (5.0)	1 (2.4)
Other	3 (4.0)	1 (4.8)
Anatomical location, n (%)		
Forefoot	12 (16.0)	10 (23.8)
Midfoot	12 (16.0)	2 (4.8)
Hindfoot	22 (30.0)	3 (7.1)
TMA site	1 (1.0)	6 (14.3)
Ankle	7 (9.0)	7 (16.7)
Lower leg	7 (9.0)	5 (11.9)
BKA/AKA	1 (1.0)	1 (2.4)
Knee	1 (1.0)	3 (7.1)
Thigh	3 (4.0)	0 (0)
Back/buttock	2 (3.0)	3 (7.1)
Abdomen	5 (7.0)	2 (4.8)
Arm	1 (1.0)	0 (0)

TABLE 2: Wound type and anatomical location

AKA = above-knee amputation; BKA = below-knee amputation; TMA = transmetatarsal amputation

Compared with the control group patients, the study group patients had a significantly lower number of operations (P = 0.0048), shorter length of hospital stay (P = 0.0443), and shorter time to final surgical procedure (P = 0.0001). Additionally, higher percentage of closed wounds (P = 0.0004) and higher percentage of wounds that remained closed at one month (P = 0.0001) were observed in the study group (Table *3*).

Characteristic	Control Group (n = 74)	Study Group (n = 42)	P-value
Number of operations (mean ± SD)	3.0 ± 0.9	2.5 ± 0.9	0.0048
Length of hospital stay, days (mean ± SD)	14.9 ± 9.2	11.7 ± 6.0	0.0443
Time to final procedure, days (mean ± SD)	9.2 ± 5.2	5.6 ± 3.6	0.0001
Wound closure/coverage, n (%)	46 (62)	39 (92.9)	0.0004
Wounds remained closed at one month, n (%)	28 (37.8)	32 (82.1)	0.0001

TABLE 3: Clinical outcomes

SD = standard deviation

Discussion

Wound infection can create a barrier to healing and increase patient morbidity and healthcare costs [1]. While treatment includes the use of bacteria-specific antibiotics, advanced wound therapies play an important role in wound management during treatment. NPWT can help manage wounds through the use of negative pressure to remove exudate and infectious materials. NPWT use in infected wounds has been reported as safe for patients [15,16]. Product advancements have led to the addition of wound cleansing to NPWT, which may provide an additional wound management option to patients with infected wounds. This study examined differences in wound outcomes in patients with infected wounds at one institution receiving either NPWT or NPWTi-d using saline.

NPWT uses macrostrain and microstrain resulting from negative pressure to draw wound edges together, remove infectious materials and exudate, reduce edema, and promote angiogenesis and granulation tissue formation in the wound bed [2-5]. NPWTi-d utilizes these same properties with the added benefit of wound cleansing with the instillation of topical wound solutions [6]. However, while the clinical benefit of NPWTi-d use has been shown, limited published evidence exists for NPWTi-d use in infected wounds.

In this study, significantly lower number of operations, shorter length of hospital stay, shortened time to final procedure, higher percentage of closed wounds, and higher percentage of wounds that remained closed at the one-month follow-up visit were reported in the NPWTi-d group. These results are similar to those reported by Gabriel et al. and Omar et al. [11,12]. However, patients received either saline or a polyhexanide instillation solution in the Gabriel et al. study. Additionally, while a shorter hospital stay and time to wound closure were observed in the NPWTi-d group in the Omar et al. study, these were not statistically significant compared to the NPWT group [12]. The results of this analysis suggest that management of infected wounds with NPWTi-d using saline leads to favorable wound outcomes when compared to those managed with NPWT.

The retrospective nature and the analysis of only two previously published studies are limitations to this work. Limited data exist for the use of NPWTi-d in infected wounds [13,14]. The publications that were available for comparison used polyhexanide and saline instillation solutions with limited numbers of patients in each. Instead of a meta-analysis, we opted to assess patients treated by one clinician at one hospital using to provide a more direct

comparison. Caution should be used when interpreting the conclusions of this study due to the limited scope of the analysis. Future, large-scale, controlled cohort studies are warranted to further assess the potential benefits associated with NPWTi-d use in the management of infected wounds.

Conclusions

The results indicate that wound cleansing combined with NPWT may provide an additional clinical benefit in the management of infected wounds. However, due to the limited analysis, conclusions should be interpreted with caution. Future studies assessing the potential benefits of NPWTi-d use in the management of infected wounds are necessary.

Additional Information

Disclosures

Human subjects: All authors have confirmed that this study did not involve human participants or tissue. **Animal subjects:** All authors have confirmed that this study did not involve animal subjects or tissue. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** PJ Kim and CE Attinger are consultants for KCI. R Silverman and L Griffin are employees of 3M. . **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

Acknowledgements

The authors thank Julie M. Robertson, PhD (3M) and John D. Short, PhD (3M) for assistance with manuscript preparation and editing.

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Comparison of Outcomes for Normal Saline and an Antiseptic Solution for Negative-Pressure Wound Therapy with Instillation

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Background: Negative-pressure wound therapy with instillation is an adjunctive treatment that uses periodic instillation of a solution and negative pressure for a wide diversity of wounds. A variety of solutions have been reported, with topical antiseptics as the most frequently chosen option. The objective of this study was to compare the outcomes of normal saline versus an antiseptic solution for negative-pressure wound therapy with instillation for the adjunctive treatment of infected wounds.

Methods: This was a prospective, randomized, effectiveness study comparing 0.9% normal saline versus 0.1% polyhexanide plus 0.1% betaine for the adjunctive treatment of infected wounds that required hospital admission and operative débridement. One hundred twenty-three patients were eligible, with 100 patients randomized for the intention-to-treat analysis and 83 patients for the per-protocol analysis. The surrogate outcomes measured were number of operative visits, length of hospital stay, time to final surgical procedure, proportion of closed or covered wounds, and proportion of wounds that remained closed or covered at the 30-day follow-up.

Results: There were no statistically significant differences in the demographic profiles in the two cohorts except for a larger proportion of male patients ($p = 0.004$). There was no statistically significant difference in the surrogate outcomes with the exception of the time to final surgical procedure favoring normal saline ($p = 0.038$).

Conclusion: The authors' results suggest that 0.9% normal saline may be as effective as an antiseptic (0.1% polyhexanide plus 0.1% betaine) for negative-pressure wound therapy with instillation for the adjunctive inpatient management of infected wounds. (*Plast. Reconstr. Surg.* 136: 657e, 2015.)

CLINICAL QUESTION/LEVEL OF EVIDENCE: Therapeutic, II.

Negative-pressure wound therapy with instillation combines periodic instillation of a solution and negative pressure. This therapy is designed to be applied over a wound surface in a similar way to standard negative-pressure wound therapy, with the additional component of instilling a selected solution over the wound surface for a preprogrammed period. Fleischmann et al. in 1998 described this concept using a polyvinyl alcohol sponge, drainage tubes, and vacuum pump as an adjunct therapy for a variety of acutely and chronically infected wounds.[1] They alternated two different antiseptic solutions, neomycin/bacitracin and polyhexanidum.

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Since this early publication, there have been a variety of reports using many different instillation solutions. Predominantly, the solutions reported in the literature are considered antimicrobial, such as hypochlorite, silver nitrate, dilute povidone-iodine, bacitracin, antibiotic cocktails, and polyhexanide.[2–8] However, others report positive clinical outcomes using 0.9% normal saline despite its lack of antimicrobial activity.[9,10] A prospective, randomized comparison of the effectiveness or efficacy has never been reported. Thus, it is not clear whether an antimicrobial solution is required to maximize the effects of negative-pressure wound therapy with instillation in the adjunctive treatment of wounds. The primary goal of this study was to compare the outcomes of 0.9% normal saline and 0.1% polyhexanide plus 0.1% betaine with negative-pressure wound therapy with instillation for the adjunctive treatment of infected wounds.

PATIENTS AND METHODS

This is a single-institution, prospective, randomized, comparative effectiveness clinical study examining the outcomes for negative-pressure wound therapy with instillation using normal saline versus 0.1% polyhexanide plus 0.1% betaine. Patients admitted to a tertiary wound referral academic hospital with an infected wound requiring surgical débridement in the operating room and who consented to participate were enrolled in this study. All patients were excisionally débrided in the operating room in the customary fashion using sharp technique by four surgeons within 48 hours of admission (P.J.K., C.E.A., J.S.S., and K.K.E.). Devitalized and infected tissue was removed, and tunnels and abscess pockets were explored and decompressed. Pulsatile irrigation was performed on the wound using approximately 3 liters of 0.9% normal saline. After irrigation, the area was redraped in sterile fashion and a new set of sterile instruments were used for hemostasis and further débridement if needed. Negative-pressure wound therapy with instillation was then applied to the wound surface. Patients were then readmitted to the inpatient floor for medical monitoring and management. All patients received qualitative culture sensitivity–driven parenteral or oral antibiotics. Patients were brought back to the operating room serially every 2 to 4 days for débridement. The final operation was performed after resolution of the infection based on the surgeon's judgment influenced by the following: scant or no growth on the postdébridement qualitative cultures taken from the prior operating room visit, clinical signs of infection clearance from the wound bed and surrounding tissue, and normalization of laboratory markers of infection. This final procedure was primary closure of the wound, local or free flap coverage, application of a xenograft or a split-thickness skin graft, or débridement alone based on the surgeon's judgment. The primary team then discharged patients with follow-up in the outpatient wound center clinic.

After patients consented to participate in the study, the patients were randomized into the normal saline or the 0.1% polyhexanide plus 0.1% betaine group immediately before the first operation. Randomization was performed a priori by a research assistant using a simple scheme of 1:1 allocation using a random number generator producing a list of 100 discrete spreadsheet cells, with 1 representing normal saline and 2 representing 0.1% polyhexanide plus 0.1% betaine (Excel; Microsoft Corp., Redmond, Wash.). The negative-pressure wound therapy with instillation device (V.A.C. Ulta System with Veraflo; Acelity, San Antonio, Texas) was applied in the operating room in the customary fashion. The device settings were preprogrammed for 20 minutes of dwelling of solution and 2 hours of negative pressure. The solution was contained in a 1-liter bottle labeled with the assigned solution. The normal saline group solution was an isotonic 0.9% saline and the 0.1% polyhexanide plus 0.1% betaine solution was Prontosan (B. Braun, Bethlehem, Pa.). The investigators or patients were not blinded to the treatment once applied. A new, sterile drape and foam were applied at each operating room visit and a new bottle of solution was hung if necessary.

Study data that were collected included the following: (1) subject demographics, (2) comorbidities and smoking history, (3) wound location and cause, and (4) surrogate wound outcomes. The surrogate wound outcome endpoints consisted of the following: (1) number of operating room visits, (2) length of hospital stay in days, (3) time to final surgical procedure during the admission in days, (4) the proportion (percentage) of wounds closed/covered during the admission, and (5) the proportion (percentage) of wounds that remained closed or covered approximately 30 days after hospital discharge. Both intention-to-treat and per-protocol statistical analysis was performed on the demographics and outcomes for the two cohorts. Chi-square test was performed for analysis on proportions as represented by percentages. Means were statistically compared with

a t test ($p < 0.05$ indicates statistical significance). This study was approved by the Georgetown University Medical Center Institutional Review Board (no. 2013-0865). Patients were not compensated for their participation in this study.

RESULTS

A total of 123 patients were assessed for eligibility. Twenty-three patients were excluded, with five patients not meeting the eligibility criteria and 18 refusing to participate. A total of 100 patients were randomized and enrolled in this study. For the intention-to-treat analysis, there were 49 patients in the normal saline cohort and 51 patients in the 0.1% polyhexanide plus 0.1% betaine cohort. For the per-protocol analysis, there were 42 patients in the normal saline cohort and 41 patients in the 0.1% polyhexanide plus 0.1% betaine cohort (total attrition rate, 17 percent). Seven patients were removed in the normal saline cohort and 10 patients were removed from the 0.1% polyhexanide plus 0.1% betaine cohort for one of the following reasons: (1) greater than 30-day length of stay (normal saline, $n = 2$; 0.1% polyhexanide plus 0.1% betaine, $n = 3$), (2) lost to follow-up after discharge (normal saline, $n = 4$; 0.1% polyhexanide plus 0.1% betaine, $n = 5$), or (3) had less than two visits to the operating room (normal saline, $n = 1$; 0.1% polyhexanide plus 0.1% betaine, $n = 2$) (Fig. 1).

Demographics were similar in each cohort for both the intention-to-treat and per-protocol analyses, with the only statistically significant difference being more male and fewer female patients in the 0.1% polyhexanide plus 0.1% betaine cohort compared with the normal saline cohort ($p = 0.004$) (Table 1). There was also no statistically significant difference in comorbidities including smoking history between the two cohorts for both the intention-to-treat and per-protocol analyses. There was no statistically significant difference in the wound location or wound cause for both the intention-to-treat and per-protocol analyses between the two cohorts (Tables 2 and 3).

The outcome data reveal no statistically significant difference between the normal saline and 0.1% polyhexanide plus 0.1% betaine cohorts for the number of operating room visits, length of hospital stay, proportion of wounds closed/covered, and proportion of wounds that remained closed at the 30-day follow-up for both the intention-to-treat and per-protocol analyses (Table 4). There was a statistically significant difference between the normal saline and the 0.1% polyhexanide plus 0.1% betaine cohorts for the time to final surgical procedure [intention-to-treat, 5.73 (SD, 3.75) and

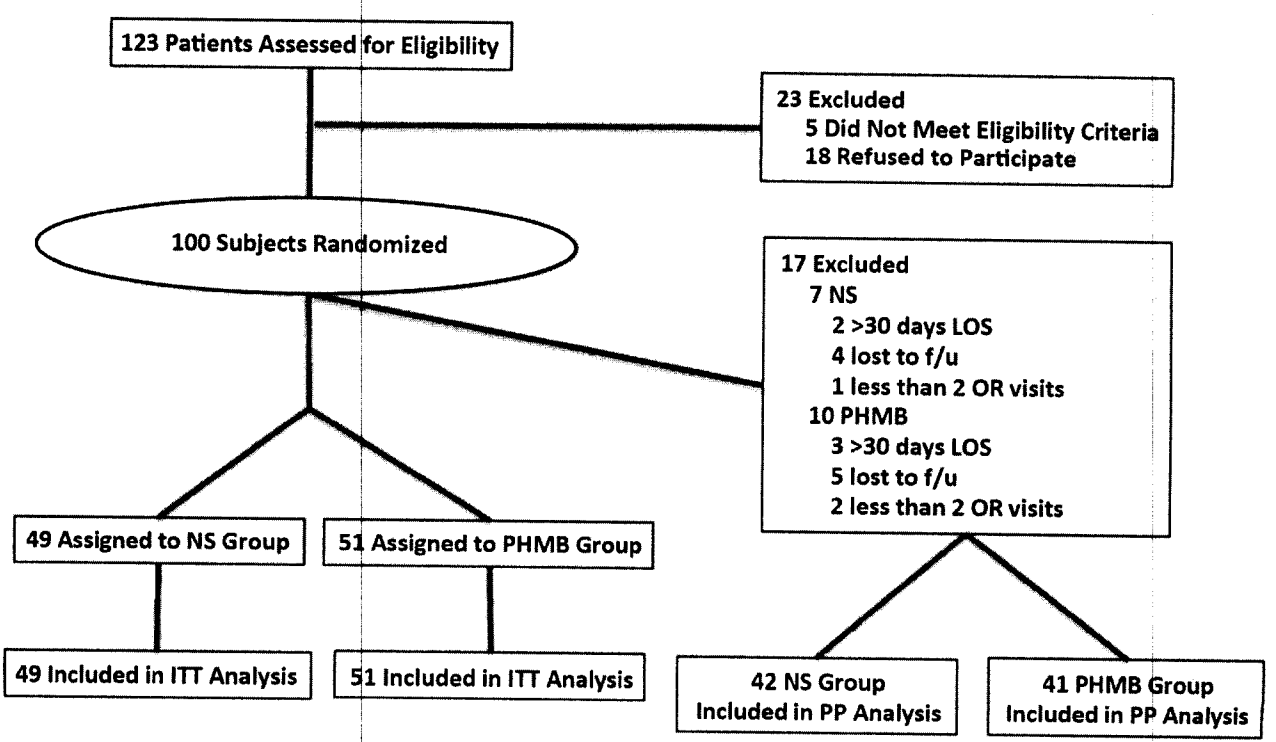

Fig. 1. Consolidated Standards of Reporting Trials flow diagram. *NS*, 0.9% normal saline; *PHMB*, 0.1% polyhexanide plus 0.1% betaine; *ITT*, intention-to-treat; *PP*, per protocol; *LOS*, length of hospital stay; *f/u*, follow-up; *OR*, operating room.

Table 1. Demographics and Comorbidities*

	NS (%)	PHMB (%)	*p*
ITT			
No. of patients	49	51	
Sex			0.004†
Male	28 (57.1)	43 (84.3)	
Female	21 (42.9)	8 (15.7)	
Age, yr			0.21
Mean	59.64	55.94	
SD	15.4	13.9	
BMI, kg/m²			0.98
Mean	29.39	29.46	
SD	7.9	13.9	
Race			
African American	21 (42.9)	21 (41.2)	0.99
Caucasian	22 (44.9)	23 (45.1)	0.99
Asian	1 (2.0)	5 (9.8)	0.21
Amp Hx	18 (36.7)	21 (41.2)	0.69
CA Hx	8 (16.3)	5 (9.8)	0.38
DM	26 (53.1)	29 (56.9)	0.84
ESRD	6 (12.2)	5 (9.8)	0.76
CAD	1 (2.0)	4 (7.8)	0.36
CVA Hx	3 (6.1)	4 (7.8)	0.99
HEP	6 (12.2)	3 (5.9)	0.31
RA	2 (4.1)	2 (3.9)	0.99
PVD	9 (18.4)	12 (23.5)	0.63
Transplant Hx	2 (4.1)	3 (5.9)	0.99
Smoking Hx	21 (42.9)	19 (37.3)	0.69
PP			
No. of patients	42	41	
Sex			0.08
Male	27 (64)	34 (83)	
Female	15 (36)	7 (17)	
Age, yr			0.43
Mean	60.66	58.24	
SD	15.1	12.4	
BMI, kg/m²			0.68
Mean	29.10	29.80	
SD	8.2	7	
Race			
African American	19 (51.4)	15 (38.4)	0.51
Caucasian	17 (45.9)	19 (48.7)	0.66
Asian	1 (2.7)	5 (12.8)	0.11
Amp Hx	16 (38.1)	17 (41.5)	0.82
CA Hx	6 (14.3)	5 (12.2)	0.99
DM	22 (52.4)	24 (58.5)	0.66
ESRD	4 (9.5)	3 (7.3)	0.99
CAD	1 (2.4)	3 (7.3)	0.36
CVA Hx	2 (4.8)	4 (9.8)	0.43
HEP	3 (7.1)	2 (4.9)	0.99
RA	1 (2.4)	2 (4.9)	0.62
PVD	9 (21.4)	9 (22.0)	0.99
Transplant Hx	1 (2.4)	2 (4.9)	0.62
Smoking Hx	17 (40.5)	16 (39.0)	0.99

NS, 0.9% normal saline; PHMB, 0.1% polyhexanide plus 0.1% betaine; ITT, intention-to-treat; BMI, body mass index; Amp Hx, amputation history; CA Hx, cancer history; DM, diabetes mellitus type 1 or 2; ESRD, end-stage renal disease; CAD, coronary artery disease; CVA Hx, cardiovascular accident history; HEP, hepatitis; RA, rheumatoid arthritis; PVD, peripheral vascular disease; Transplant Hx, solid organ transplant history; Smoking Hx, current or history of smoking; PP, per-protocol.

*Patients are counted more than once if multiple comorbidities existed.

†Statistically significant ($p < 0.05$).

7.73 (SD, 5.49), respectively, $p = 0.038$; per-protocol, 5.57 (SD, 3.61) and 7.46 (SD, 4.42), respectively, $p = 0.035$].

Table 2. Wound Location

	NS (%)	PHMB (%)	*p*
ITT			
No. of patients	49	51	
Forefoot	10 (20.4)	15 (29.4)	0.36
Midfoot	3 (6.1)	5 (9.8)	0.72
Hindfoot/heel	5 (10.2)	6 (11.8)	0.99
TMA site	5 (10.2)	1 (2)	0.11
Ankle	9 (18.4)	10 (19.6)	0.99
Lower leg	5 (10.2)	2 (3.9)	0.26
BKA, AKA site	1 (2.0)	5 (9.8)	0.21
Knee	3 (6.1)	3 (5.9)	0.99
Thigh	1 (2)	1 (2)	0.99
Back, buttock	4 (8.2)	0	—
Abdomen	3 (6.1)	3 (5.9)	0.99
PP			
No.	42	41	
Forefoot	10 (23.8)	13 (31.7)	0.47
Midfoot	2 (4.8)	3 (7.3)	0.68
Hindfoot/heel	3 (7.1)	5 (12.2)	0.48
TMA site	6 (14.3)	1 (2.4)	0.11
Ankle	7 (16.7)	9 (22)	0.59
Lower leg	5 (11.9)	1 (2.4)	0.20
BKA, AKA site	1 (2.4)	4 (9.8)	0.20
Knee	3 (7.1)	1 (2.4)	0.62
Thigh	0	1 (2.4)	—
Back, buttock	3 (7.1)	0	—
Abdomen	2 (4.8)	3 (7.3)	0.68

NS, 0.9% normal saline; PHMB, 0.1% polyhexanide plus 0.1% betaine; ITT, intention-to-treat; TMA, transmetatarsal amputation; BKA, below-knee amputation; AKA, above-knee amputation; PP, per-protocol; —, statistically not analyzed.

Table 3. Wound Cause

	NS (%)	PHMB (%)	*p*
ITT			
No.	49	51	
Neuropathic	14 (28.6)	17 (33.3)	0.67
Surgical	16 (32.7)	20 (39.2)	0.54
Venous	3 (6.1)	2 (3.9)	0.68
Ischemic	6 (12.2)	6 (11.8)	0.99
Decubitus	7 (14.3)	4 (7.8)	0.35
Trauma	1 (2.1)	1 (2.0)	0.99
Other	2 (4.1)	1 (2.0)	0.61
PP	42	41	
No.			
Neuropathic	14 (33.3)	13 (31.7)	0.99
Surgical	13 (31.0)	16 (39)	0.50
Venous	2 (4.8)	2 (4.9)	0.99
Ischemic	6 (14.3)	5 (12.2)	0.99
Decubitus	4 (9.5)	4 (9.8)	0.99
Trauma	1 (2.4)	0	—
Other	1 (4.8)	1 (2.4)	0.99

NS, 0.9% normal saline; PHMB, 0.1% polyhexanide plus 0.1% betaine; ITT, intention-to-treat; PP, per protocol; —, statistically not analyzed.

DISCUSSION

Negative-pressure wound therapy with instillation is an adjunctive therapy commonly used for wounds with a history of acute or chronic infection. Thus, defining the most effective selection of a topical solution for negative-pressure wound therapy with instillation is logical. The published

Table 4. Outcomes

	NS (%)	PHMB (%)	*p*
ITT			
No. of patients	49	51	
No. of operations			0.19
Mean	2.5	2.8	
SD	0.9	0.9	
LOS			0.68
Mean	13.6	14.5	
SD	11.7	9	
Time to FSP			0.04*
Mean	5.7	7.7	
SD	3.8	5.5	
CC	42 (85.7)	47 (92.2)	0.35
F/U CC	34 (69)	33 (65)	0.83
PP			
No.	42	41	
No. of operations			0.19
Mean	2.5	2.8	
SD	0.9	0.7	
LOS, days			0.08
Mean	11.7	14.2	
SD	6	6.6	
Time to FSP, days			0.04*
Mean	5.6	7.5	
SD	3.6	4.4	
CC	39 (92.9)	39 (95.1)	0.99
F/U CC	32 (82.1)	30 (76.9)	0.90

NS, 0.9% normal saline; PHMB, 0.1% polyhexanide plus 0.1% betaine; ITT, intention-to-treat; LOS, length of hospital stay (days); FSP, final surgical procedure (days); CC, closed, covered; F/U, follow-up at 1 mo; PP, per-protocol.
*Statistically significant ($p < 0.05$).

clinical literature on this topic predominantly report and encourage the use of antimicrobial solutions.[1–3,5–8,11,12] Specifically, 0.1% polyhexanide plus 0.1% betaine has been studied extensively as having a broad spectrum of activity and being well tolerated in both solution and gel formulations.[13–19] Animal models also validate the use of antiseptics for negative-pressure wound therapy with instillation. Phillips et al., in a porcine explant *Pseudomonas aeruginosa* biofilm wound model of negative-pressure wound therapy with instillation, report no colony-forming unit log reduction for normal saline but report a 4-log reduction for 0.1% polyhexanide plus 0.1% betaine.[20] Davis et al., in an in vivo *Pseudomonas aeruginosa*–inoculated porcine wound model, also reported a trend for a greater reduction in bacterial counts for 0.1% polyhexanide plus 0.1% betaine compared with normal saline.[21] An international consensus article led by the study authors also preferentially recommended the use of antiseptics with negative-pressure wound therapy with instillation.[22] In a noncomparative observational study, Lehner et al. report artificial joint replacement salvage rate of 86.4 percent (19 of 22) in the environment of acute infection and an 80 percent (eight of 10) salvage rate in the environment of a chronic infection using 0.04% polyhexanide.[6] The authors published a 142-patient retrospective, comparative cohort study reporting the effectiveness of negative-pressure wound therapy with instillation with 0.1% polyhexanide plus 0.1% betaine compared with negative-pressure wound therapy.[23] We reported that the number of operating room visits, length of hospital stay, time to final surgical procedure, and the proportion of wounds closed was superior for the negative-pressure wound therapy with instillation of 0.1% polyhexanide plus 0.1% betaine cohort compared with negative-pressure wound therapy. The vast majority of the publications on negative-pressure wound therapy with instillation with antiseptics are small case studies, case series, and expert opinion using various antiseptic and antibiotic solutions.[5,7,8,11] There is a paucity of robust studies examining the outcomes of negative-pressure wound therapy with instillation, and inconsistency as to the optimal solution choice. Nevertheless, there is a clear bias toward the use of antiseptics.

This is the first randomized, prospective, comparative effectiveness study examining the outcomes with the use of negative-pressure wound therapy with instillation using two different solutions. The results of this study suggest that the outcomes following the use of negative-pressure wound therapy with instillation using normal saline are comparable to those of 0.1% polyhexanide plus 0.1% betaine. The only difference in outcomes is the time to final surgical procedure, which interestingly favored the normal saline cohort. Brinkert et al. also report positive outcomes for the use of normal saline with negative-pressure wound therapy with instillation.[9] They report a wound closure rate of 98 percent in their case series of 131 patients with a variety of infected and contaminated wounds. This study may have been biased by the fact that there are few choices available to the authors for instillation solution selection, and normal saline was a default choice. Furthermore, 35 percent of patients received standard negative-pressure wound therapy before they received negative-pressure wound therapy with instillation, and 48.8 percent received negative-pressure wound therapy after receiving negative-pressure wound therapy with instillation, which may have skewed their results.

We used surrogate outcome endpoints to determine the effect of negative-pressure wound therapy with instillation on wounds. Thus, the direct effectiveness/efficacy of negative-pressure wound therapy with instillation with either solution cannot be definitely established with our

results. However, our surrogate outcome endpoints of number of operating room visits, length of hospital stay, time to final surgical procedure, proportion of closed/covered wounds, and proportion of wounds that remain closed at the 30-day follow-up are relevant to the inpatient surgical management of infected wounds. These surrogate outcome endpoints reflect both clinical and economic realities. Another important variable that was not reported concerned the qualitative cultures taken before and after débridement at each operating room visit. We did report these data in our retrospective study but elected not to include the results in this study because of the difficulty in interpretation and variability of the microbiology culture results. We do not have strong confidence in qualitative culture results. The results may reflect inconsistent technique, prior antibiotic therapy, and institutionally established selective growth of specific bacterial species. For this study and as part of our routine clinical decision-making algorithm, we take into account the quality of the wound (color, odor, and pliability), serologic markers, radiographic findings, histologic reports, and qualitative cultures.

There are other significant potential flaws to our study that may impact the interpretation of our results. First, there is an ingrained institutional bias for aggressive serial excisional débridement. Therefore, the reliance on an antiseptic solution between operating room visits may be less important in our institution. Second, there was no control group used in this study, so we cannot determine whether the results reflect the experimental intervention of negative-pressure wound therapy with instillation. In other words, we cannot definitively determine whether these subjects would have had similar outcomes without the use of negative-pressure wound therapy with instillation. Third, investigator bias may have also skewed the results. From our prior published work, we observed that 0.1% polyhexanide plus 0.1% betaine resulted in good outcomes. Thus, potential candidates for this study may have been excluded because of the chance that the patient may have been randomized to the normal saline group. Every attempt was made to include all patients that met the very broad eligibility criteria, but the worst wounds or sickest patients may have been excluded from this study. However, this would have affected the cohorts equally. Thus, the principal focus of this study to compare solutions is uncontaminated. Finally, this was not a blinded study. Thus, investigator bias may have also influenced the decision by the surgeon that the wound was sufficiently prepared for closure or coverage. Again, this bias would have favored 0.1% polyhexanide plus 0.1% betaine based on prior experience. However, the 30-day follow-up data showed no difference in proportion of closed wounds. This implies that we did not favor one solution or another because, if we did bias for faster closure, we would most likely have seen a lower proportion of closed or covered wounds at the 30-day follow-up for the 0.1% polyhexanide plus 0.1% betaine cohort. Furthermore, the number of operating room visits was not different between the two cohorts. This indicates that closure/coverage decisions were similar in both groups.

Another limitation of this study is its overall study design. This study is best defined as an effectiveness study rather than an efficacy study. Although conducted in a randomized, prospective fashion, the broad eligibility criteria encompassing all wound causes, wound sizes, and anatomical locations preclude our study from being identified as a typical comparative efficacy study. Thus, the reader should acknowledge this lack of homogeneity of the study population and lack of adherence to the rules that govern a classic efficacy study design. However, we believe these results are meaningful because they reflect a real-world application of this type of therapy.

Our data suggest that the choice of solution may not be critical to the success or failure of this adjunctive therapy. One possible contribution to the positive clinical results may be related to a fundamental concept of negative-pressure wound therapy. Morykwas et al. reported that *intermittent* negative pressure improves local tissue perfusion, thus creating a more ideal environment for wound healing compared with continuous negative pressure.[24,25] Negative-pressure wound therapy with instillation inherently provides intermittency because of the periods of solution dwell. As an aside, many wound care providers use the *continuous* setting for negative-pressure wound therapy for a variety of pragmatic reasons, including the concern for leaks during intermittent periods of no negative pressure. Perhaps the positive effect observed with negative-pressure wound therapy with instillation reflects this intermittent negative-pressure application phenomenon rather than anything to do with instillation of a solution. A more recent publication by Lessing et al. reported that negative-pressure wound therapy with instillation with normal saline significantly increases granulation thickness by almost 2 mm over intermittent or continuous negative pressure in an animal model.[26] Thus, intermittency does

not appear to be the sole reason for negative-pressure wound therapy with instillation efficacy. The mechanism(s) of action of negative-pressure wound therapy with instillation appears to be more complicated and elusive. The choice of solution may play a role, but other factors including the mechanical effect of fluid dynamics disrupting biofilm formation and the removal of inflammatory factors may also be important. Further work is needed to elucidate the mechanism of action of negative-pressure wound therapy with instillation to identify key contributors to positive outcome.

CONCLUSIONS

Our results provide important information regarding the choice of instillation solutions for negative-pressure wound therapy with instillation. Specifically, our data suggest that normal saline may be as effective as 0.1% polyhexanide plus 0.1% betaine when used as the solution for negative-pressure wound therapy with instillation. However, because of the limitations of our study as discussed above, definitive conclusions cannot be drawn. Ultimately, clinical effects, spectrum of activity, safety, and cost will be the driving factors for the choice of instillation solution. Normal saline conforms well to most of the above criteria despite its lack of direct antimicrobial activity.

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The Impact of Negative-Pressure Wound Therapy with Instillation Compared with Standard Negative-Pressure Wound Therapy: A Retrospective, Historical, Cohort, Controlled Study

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Background: Negative-pressure wound therapy with instillation is a novel wound therapy that combines negative pressure with instillation of a topical solution.
Methods: This retrospective, historical, cohort-control study examined the impact of negative-pressure wound therapy with and without instillation.
Results: One hundred forty-two patients (negative-pressure wound therapy, $n = 74$; therapy with instillation, 6-minute dwell time, $n = 34$; and therapy with instillation, 20-minute dwell time, $n = 34$) were included in the analysis. Number of operative visits was significantly lower for the 6- and 20-minute dwell time groups (2.4 ± 0.9 and 2.6 ± 0.9, respectively) compared with the no-instillation group (3.0 ± 0.9) ($p \leq 0.05$). Hospital stay was significantly shorter for the 20-minute dwell time group (11.4 ± 5.1 days) compared with the no-instillation group (14.92 ± 9.23 days) ($p \leq 0.05$). Time to final surgical procedure was significantly shorter for the 6- and 20-minute dwell time groups (7.8 ± 5.2 and 7.5 ± 3.1 days, respectively) compared with the no-instillation group (9.23 ± 5.2 days) ($p \leq 0.05$). Percentage of wounds closed before discharge and culture improvement for Gram-positive bacteria was significantly higher for the 6-minute dwell time group (94 and 90 percent, respectively) compared with the no-instillation group (62 and 63 percent, respectively) ($p \leq 0.05$).
Conclusion: The authors' results suggest that negative-pressure wound therapy with instillation (6- or 20-minute dwell time) is more beneficial than standard negative-pressure wound therapy for the adjunctive treatment of acutely and chronically infected wounds that require hospital admission. (*Plast. Reconstr. Surg.* 133: 709, 2014.)
CLINICAL QUESTION/LEVEL OF EVIDENCE: Therapeutic, III.

Negative-pressure wound therapy with instillation combines localized subatmospheric pressure with delivery of a topical solution. Negative-pressure wound therapy has been widely used for decades as an effective adjunctive treatment of acute and chronic wounds.[1–7] Negative-pressure wound therapy with instillation provides an additional dimension to negative-pressure wound therapy, with the ability to deliver a solution to the wound bed in a preprogrammed manner. The interval, duration of negative pressure, solution dwell time, and type of solution can be precisely prescribed.

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To date, there are minimal data examining the efficacy or effectiveness of negative-pressure wound therapy with instillation in the adjunctive treatment of wounds, mostly limited to small case series and uncontrolled studies.[8–17] The purpose of this study was to compare the outcomes for patients who received negative-pressure wound therapy with instillation versus a historical control cohort of patients who received traditional negative-pressure wound therapy without instillation. The variables examined were the (1) the number of operating room visits, (2) length of hospital stay, (3) time to final surgical procedure during the admission period, (4) percentage of wounds surgically closed before discharge, (5) percentage of wounds that remained closed 30 days after discharge, and (6) reduction in microorganisms.

PATIENTS AND METHODS

This is a retrospective, historical, cohort, controlled study comparing negative-pressure wound therapy with negative-pressure wound therapy with instillation. Data were collected from inpatient electronic medical records from a single institution (MedStar Georgetown University Hospital). All patients with infected wounds requiring admission with at least two operative débridements and that received either negative-pressure wound therapy or negative-pressure wound therapy with instillation application at the time of the initial operation, were included in this analysis. An infected wound was defined by clinically evident infection and positive culture results at the time of the initial operation. The need for hospital admission was determined through clinical judgment (e.g., systemic signs of infection, wound quality including the presence of purulence), elevated white blood cell count, and/or radiographic evidence of infection (e.g., cortical erosion, fluid/emphysema). Comorbidities were identified from clinical diagnoses that were designated in the patients' medical records. Negative-pressure wound therapy was compared with negative-pressure wound therapy with instillation using 6 or 20 minutes of dwell time. The negative-pressure wound therapy group was compared with the negative-pressure wound therapy with instillation group for the same 6-month period separated by exactly 1 year. The following criteria were used to exclude patients from the analysis from both the negative-pressure wound therapy and the negative-pressure wound therapy with instillation groups: (1) cultures not taken or documented during sequential operative visits, (2) culture results of no growth at the first operative visit, or (3) an extended hospital stay greater than 30 days because of medical complications unrelated to the infected wound. The primary wound cause was defined as the principal reason for the development of the wound and subsequent infection. Each subject's data were counted once in the analysis.

The device used for negative-pressure wound therapy was the InfoV.A.C. Therapy System (Kinetic Concepts, Inc., San Antonio, Texas) and the negative-pressure wound therapy with instillation device was the V.A.C. Ulta with VeraFlo Instillation Therapy (Kinetic Concepts). The instillation solution used for both negative-pressure wound therapy with instillation groups was Prontosan (B. Braun, Inc., Bethlehem, Pa.). The setting for both the negative-pressure wound therapy and negative-pressure wound therapy with instillation group was −125 mmHg continuous negative pressure. Sufficient volume of instillation was determined by observing foam saturation through a change in color of the foam to a darker black. The dwell time (the period in which the solution is contained in the foam/wound interface while no negative pressure is being applied) was programmed for 6 or 20 minutes. The negative pressure time was 3.5 hours for the 6-minute dwell time group and 2 hours for the 20-minute dwell time group. The application of the foam and drape to the wound surface was performed in a similar fashion for all groups. Negative-pressure wound therapy or negative-pressure wound therapy with instillation was applied at the initial operative visit immediately after the débridement was performed while in the operating room. Negative-pressure wound therapy or negative-pressure wound therapy with instillation was applied at each subsequent operating room visit until the wound was deemed ready for closure or the patient was discharged from the hospital because the infection was determined to be cleared.

Four surgeons performed all surgical procedures as part of the same limb salvage team (P.J.K., C.E.A., J.S.S., and K.K.E.). Operative débridement of nonviable tissue was performed in a similar manner using scalpels, curettes, rongeurs, scissors, and/or hydrosurgical scalpel. The following operative approach sequence was used: (1) predébridement deep wound culture specimens obtained, (2) sharp excisional débridement performed, (3) pulsatile irrigation using 3 liters of normal saline, (4) redraping of the sterile field with new surgical gloves, (5) new surgical instruments

and instrument table used, (6) postdébridement deep wound culture specimens obtained, and (7) application of negative-pressure wound therapy/negative-pressure wound therapy with instillation or closure. Intraoperative wound culture specimens obtained from the deepest margin were sent for qualitative assessment. Improvement in culture results (postdebridement cultures from the first operative visit compared with predébridement cultures from the second operative visit) was defined as a progression to no growth or a decrease in cultured microorganism amount (e.g., heavy growth progressing to scant growth). All patients received parenteral antibiotics at the time of hospital admission, and antibiotic therapy was adjusted to the sensitivities of the bacterial cultures throughout the hospital stay.

The number of operative visits includes any time the patient was taken to the operating room for wound débridement or closure. The length of hospital stay was calculated in days from the date of admission to the date of discharge. The time to final surgical procedure was calculated in days from the date of admission to the date of the final procedure during the admission period. Clinical judgment, laboratory values, radiographic evidence, and qualitative culture results were used by the surgeon to determine whether the wound was ready for closure. Closure was defined as covering the wound by delayed primary closure, skin graft, or flap. A single follow-up time point at 1 month after discharge from the hospital was used to determine whether the wound remained closed. A closed wound was defined by the absence of a break in the skin as determined by the surgeon.

Statistical calculation was performed using StatPlus:mac LE.2009 (AnalystSoft, Inc., Vancouver, British Columbia, Canada). We used multivariate analysis of variance to compare the three treatment arms for the length of hospital stay (days), the time to final surgical procedure (days), and the number of operative visits. We then performed post hoc pairwise comparison using the least significant difference test. Statistical comparisons of percentages (proportional analysis) were performed using Fisher's exact test (two-tailed). The Georgetown University Medical Center Institutional Review Board approved this study.

RESULTS

A total of 142 patients, 74 subjects in the negative-pressure wound therapy group, 34 subjects in the 6-minute dwell time negative-pressure wound therapy with instillation group, and 34 subjects in the 20-minute dwell time negative-pressure wound therapy with instillation group were included in the analysis. Age, sex, body mass index, current smoking status, and medical comorbidities were not statistically different between the negative-pressure wound therapy group and the 6- or 20-minute dwell time negative-pressure wound therapy with instillation groups (Table1). The only difference was a statistically higher percentage of African Americans in the 6-minute dwell time negative-pressure wound therapy with instillation group compared with the negative-pressure wound therapy group ($p = 0.03$).

There was no difference between the negative-pressure wound therapy group and the 6- or 20-minute dwell time negative-pressure wound therapy with instillation group in the primary wound cause. There was a statistically significant difference between the anatomical location of the wound in negative-pressure wound therapy group and the 20-minute dwell time negative-pressure wound therapy with instillation group for the forefoot and hindfoot/heel ($p = 0.04$ and $p = 0.03$, respectively). There was a higher percentage of forefoot wounds and a lower percentage of hindfoot/heel wounds for the 20-minute dwell time negative-pressure wound therapy with instillation group compared with the negative-pressure wound therapy group (Table 2).

There is a statistically significant difference in the following outcomes: (1) length of hospital stay between the negative-pressure wound therapy group and the 20-minute dwell time negative-pressure wound therapy with instillation group ($p = 0.034$; 95 percent CI, 0.27 to 6.86), (2) number of operative visits between the negative-pressure wound therapy group and the 6-minute dwell time negative-pressure wound therapy with instillation group ($p = 0.043$; 95 percent CI, 0.014 to 0.75) and between the negative-pressure wound therapy group and the 20-minute dwell time negative-pressure wound therapy with instillation group ($p = 0.003$; 95 percent CI, 0.19 to 0.93), (3) time to final surgical procedure between the negative-pressure wound therapy group and the 6-minute dwell time negative-pressure wound therapy group ($p = 0.043$; 95 percent CI, 0.065 to 4.04) and between the negative-pressure wound therapy group and the 20-minute dwell time negative-pressure wound therapy with instillation group ($p = 0.0019$; 95 percent CI, 0.39 to 4.36) (Table 3).

The percentage of wounds closed before discharge was significantly higher in the 6-minute dwell

Table 1. Demographics

	NPWT	NPWTi 6		NPWTi 20	
	Value (%)	Value (%)	*p**	Value (%)	*p*†
Age, yr					
Mean ± SD	58 ± 13	63 ± 16		55 ± 17	
Range	18–95	20–88	0.11	18–90	0.43
Male sex	38 (51)	20 (59)	0.54	22 (65)	0.22
Race					
African American	21 (28)	17 (50)	0.03	15 (44)	0.13
Caucasian	39 (53)	16 (47)	0.68	14 (41)	0.30
Hispanic	2 (6)	1 (3)	1.0	0 (0)	
Asian	1 (3)	1 (1)	1.0	1 (3)	1.0
Other	6 (8)	5 (15)	0.32	4 (12)	0.72
BMI, kg/m^2	32 ± 9.14	29.6 ± 6.77	0.17	32.9 ± 8.89	0.63
Current smoker	7 (9)	2 (6)	0.72	1 (3)	0.74
Comorbidities					
Diabetes type 1	7 (9)	2 (6)	0.72	4 (12)	0.74
Diabetes type 2	35 (47)	18 (53)	0.54	16 (47)	1.0
ESRD	22 (30)	12 (35)	0.66	4 (12)	0.05
PVD	27 (36)	10 (29)	0.52	11 (32)	0.83
Autoimmune disease	4 (5)	4 (12)	0.26	3 (9)	0.68
Hemiparalysis	1 (1)	2 (6)	0.23	1 (3)	0.53
History of cancer	6 (8)	2 (6)	1.0	3 (9)	1.0
Kidney/pancreas transplant	3 (4)	1 (3)	1.0	1 (3)	1.0

NPWT, negative-pressure wound therapy; NPWTi 6, negative-pressure with instillation 6-minute dwell time; NPWTi 20, negative pressure with instillation 20-minute dwell time; BMI, body mass index; ESRD, end-stage renal disease; PVD, peripheral vascular disease.
*Comparison of NPWT and NPWTi 6.
†Comparison of NPWT and NPWTi 20.

Table 2. Wound Cause and Anatomical Location

	NPWT	NPWTi 6		NPWTi 20	
	Value (%)	Value (%)	*p**	Value (%)	*p*†
Primary cause					
Ischemic wound	17 (23)	7 (21)	1.0	8 (24)	1.0
Neuropathic wound	16 (22)	6 (18)	0.80	7 (21)	1.0
Decubitus wound	16 (22)	6 (18)	0.80	4 (12)	0.29
Surgical wound	17 (23)	9 (26)	0.81	10 (29)	0.48
Venous	3 (4)	2 (6)	0.65	1 (3)	1.0
Traumatic	4 (5)	2 (6)	1.0	1 (3)	1.0
Other (unclear)	3 (4)	2 (6)	0.65	3 (9)	0.38
Anatomical location					
Forefoot	12 (16)	6 (18)	1.0	12 (35)	0.04
Midfoot	12 (16)	3 (9)	0.38	3 (9)	0.38
Hindfoot/heel	22 (30)	6 (18)	0.24	3 (9)	0.03
Transmetatarsal amputation site	1 (1)	2 (6)	0.23	2 (6)	0.23
Ankle	7 (9)	4 (12)	0.74	3 (9)	1.0
Leg	7 (9)	4 (12)	0.74	6 (18)	0.40
Below-knee amputation site	1 (1)	2 (6)	0.23	0 (0)	
Knee	1 (1)	1 (3)	0.53	2 (6)	0.23
Thigh	3 (4)	1 (3)	1.0	0 (0)	
Back/buttock	2 (3)	2 (6)	0.59	3 (9)	0.32
Abdomen	5 (7)	3 (9)	0.71	0 (0)	
Arm	1 (1)	0 (0)	1.0	0 (0)	

NPWT, negative-pressure wound therapy; NPWTi 6, negative-pressure with instillation 6-minute dwell time; NPWTi 20, negative pressure with instillation 20-minute dwell time.
*Comparison of NPWT and NPWTi 6.
†Comparison of NPWT and NPWTi 20.

time negative-pressure wound therapy with instillation group compared with the negative-pressure wound therapy group ($p = 0.0004$). The overall wound culture improvement was not different between the negative-pressure wound therapy group and the 6- or 20-minute dwell time negative-pressure wound therapy with instillation groups; however, when Gram-negative bacteria, *Corynebacterium*, and yeast were excluded from analysis, there was a significantly greater improvement in

Table 3. Outcomes

	NPWT	NPWTi 6		NPWTi 20	
	Value (%)	Value (%)	*p**	Value (%)	*p*†
No. of OR visits	3.0 ± 0.9	2.4 ± 0.9	0.04	2.6 ± 0.9	0.003
Length of hospital stay	14.92 ± 9.2	11.9 ± 7.8	0.10	11.4 ± 5.1	0.03
Time to final surgical procedure	9.23 ± 5.2	7.8 ± 5.2	0.04	7.5 ± 3.1	0.002
Closed	46 (62)	32 (94)	0.0004	27 (80)	0.08
Remained closed at 1 mo	28 (61)	24 (75)	0.23	14 (52)	0.47
Overall culture improvement	28 (38)	20 (59)	0.06	17 (50)	0.30
Culture improvement with Gram-negative, *Corynebacterium*, and yeast excluded	17 (63)	19 (90)	0.0001	13 (65)	0.77

NPWT, negative-pressure wound therapy; NPWTi 6, negative-pressure with instillation 6-minute dwell time; NPWTi 20, negative pressure with instillation 20-minute dwell time; OR, operating room.
*Comparison of NPWT and NPWTi 6.
†Comparison of NPWT and NPWTi 20.

the 6-minute dwell time negative-pressure wound therapy with instillation group than in the negative-pressure wound therapy group ($p = 0.0001$) (Table 3).

DISCUSSION

To date, this is the most systematic examination of the impact of negative-pressure wound therapy with instillation in the adjunctive treatment of the acutely infected wound in an inpatient setting, and is the only study to compare traditional negative-pressure wound therapy and negative-pressure wound therapy with instillation. Previous publications using negative-pressure wound therapy with instillation use "standard" wound care as the comparator.[14,17] In these studies, it is difficult to determine whether there is any additional benefit from instillation or whether the superior results are simply because of the effectiveness of traditional negative-pressure wound therapy. Although the primary benefit of negative-pressure wound therapy is in the promotion of wound healing and wound bed preparation, there is some evidence that negative-pressure wound therapy may inhibit bacterial growth and reduce infection.[18,19] The use of antiseptic solutions for irrigation of infected wounds has been well established.[20] Our results suggest that adding instillation therapy to negative-pressure wound therapy enhances the effectiveness of both of these treatment modalities.

There are several limitations to this study, including inherent limitations related to the retrospective study design. Comorbidities were identified from the patients' medical records; thus, definitive diagnosis is unconfirmed by diagnostic modalities. For our study, this is less important because both negative-pressure wound therapy and negative-pressure wound therapy with instillation would have been impacted in the same manner. Furthermore, there is the potential for selection bias for the use of negative-pressure wound therapy with instillation and negative-pressure wound therapy. The observed benefit of negative-pressure wound therapy with instillation could have prompted its selective use for wounds that were potentially more infected or when the surgeon suspected that the débridement was inadequate. Contrarily, the negative-pressure wound therapy group could have been biased toward less infected wounds or when the débridement was performed adequately. The retrospective nature of this study makes it impossible to determine whether there was selection bias and the direction and degree of impact on the results.

Although conclusive statements of superior efficacy cannot be made because of a lack of rigid prospective comparative trial design, our approach reflects a "real-world" effectiveness examination of negative-pressure wound therapy with instillation. The important variables of length of hospital stay, number of operating room visits, and time to final closure during the admission period reflect significant clinical and economic comparative effectiveness endpoints. Although the length of hospital stay is heavily influenced by factors unrelated to the wound, the number of operating room visits and time to final surgical closure are less encumbered by these factors.

We found a significantly higher percentage of closed wounds before discharge in the 6-minute dwell negative-pressure wound therapy with instillation group and a strong trend in the 20-minute dwell time negative-pressure wound therapy with instillation group compared with the negative-pressure wound therapy group. Furthermore, there was a statistically significant decrease in time to final surgical procedure for both negative-pressure wound therapy with

instillation groups compared with the negative-pressure wound therapy group. It is possible that the higher percentage of closed wounds and a reduced time to final surgical closure in the negative-pressure wound therapy with instillation groups reflects a bias by the surgeons to close the wounds earlier. However, the percentage closed at the 30-day follow-up did not reflect an inherent bias of premature wound closure because both groups had statistically similar rates of closure. Furthermore, our qualitative culture data suggest that if there had been a bias, there should have been a smaller percentage of culture improvement for the negative-pressure wound therapy with instillation groups compared with the negative-pressure wound therapy group. In other words, a rush to closure would more likely translate to cultures worsening. Although the overall culture data showed no statistically significant difference between the negative-pressure wound therapy and the negative-pressure wound therapy with instillation groups, there was a trend toward greater improvement in favor of the negative-pressure wound therapy with instillation groups. This also suggests that there may be a positive effect of negative-pressure wound therapy with instillation on microorganisms.

We found no difference between the negative-pressure wound therapy with instillation groups and the negative-pressure wound therapy group in overall microorganism improvement, which may reflect the limitations of swab cultures rather than the lack of superior effectiveness of negative-pressure wound therapy with instillation. This includes the lack of consistency in the way the cultures were obtained in the operating room or the fact that swab cultures were selective for a limited number of specific types of bacteria.[21] It is interesting that the 6-minute dwell negative-pressure wound therapy with instillation group but not the 20-minute dwell time negative-pressure wound therapy with instillation group showed a statistically significant culture improvement compared with negative-pressure wound therapy group. Again, this may reflect the limitations of swab cultures.

Polyhexanide has been reported to have positive effects on wound healing, presumably by reducing infection or through biofilm eradication.[22–25] Koburger et al. report that polyhexanide is immediately effective against pathogens in vitro.[26] Furthermore, they report in vitro that the longer the solution is in contact with bacteria such as *Streptococcus aureus*, *Pseudomonas aeruginosa*, and *Candida albicans*, the lower the concentration of polyhexanide that is needed to be effective. Our results suggest that a longer dwell time has no significant bearing on culture improvement. Lee et al. suggest that, in an inoculated agar plate model, polyhexanide is less effective against Gram-negative bacteria compared with Gram-positive bacteria.[27] This is consistent with our results, where we found that excluding Gram-negative bacteria from our analysis yielded a statistically significant difference in culture improvement in the 6-minute dwell time negative-pressure wound therapy with instillation group compared with the negative-pressure wound therapy group. The reason why this was not found for the 20-minute dwell time negative-pressure wound therapy with instillation group is unclear but may again reflect the limitations of swab cultures.

The published literature is not consistent about the most appropriate dwell time, with ranges varying from 1 second to 30 minutes.[13–15] Initially, 6 minutes of dwell time was selected based on reported positive results with shorter durations.[14,15] Furthermore, there was initial concern of longer dwell times increasing the chance of leaks and macerating the surrounding tissue. As these problems did not occur, we progressed to the 20-minute dwell time based on published literature that suggested 10- to 30-minute dwell time.[1,15,17] Fleischmann et al. report 7-day treatment of negative-pressure wound therapy with gravity-fed intermittent instillation for soft-tissue and bone infections using alternating regimens of antibiotic solution (neomycin and bacitracin) with an antiseptic (polyhexanide 0.04%) for 30 minutes of instillation.[13] Lehner et al. report 5 to 30 minutes of dwell time with polyhexanide 0.04% for periprosthetic implant infections, resulting in a salvage rate of 80 percent for acute infections and 86.4 percent for chronic infections.[15] Timmers et al. report using 10 to 15 minutes of dwell time with polyhexanide 0.04% for traumatic bone infections.[17] They report a 10 percent infection recurrence rate using negative-pressure wound therapy with instillation versus a historical control that had a 58.5 percent infection recurrence rate. Furthermore, they report a significantly shorter median duration of hospital stay (36 days versus 73 days) and fewer surgical procedures (two versus five). Our results suggest that there is not an overall difference in using 6 or 20 minutes of dwell time compared with negative-pressure wound therapy. The wide range of dwell times reported in the literature with positive outcomes, and our own findings, suggest that an exact dwell time may not be an important contributing factor

to the overall effectiveness of negative-pressure wound therapy with instillation.

The choice of instillation solution may also play a significant role. We used Prontosan as our choice of instillation solution because of the combined benefit of 0.1% polyhexanide (antimicrobial) and 0.1% betaine (surfactant). Prontosan has a high tolerability profile with in vivo and in vitro benefits at low concentrations and efficacy against a wide variety pathogens.[23] However, many other solutions and combinations of solutions have been reported in the literature, including Dakin's solution, silver nitrate, and mixed antibiotic solution.[11,12,14] Others have suggested that normal saline be used as the instillation solution.[28,29] Perhaps the choice of instillation solution is not as critical as the fact that a solution is being bathed over the wound.

Other factors that may have influenced our results include the duration of negative pressure, volume of instillation solution, and the minimum or maximum duration of therapy. The published literature provides little guidance as to the most appropriate duration of negative pressure, varying from 45 minutes to 6 hours.[9,10] Furthermore, the volume of instillation used varied on the size and location of the wound. It is likely that the subjective determination of "sufficient" volume was inaccurate and the wound was not completely bathed by the instillation solution, which could have changed our results. The volume of instillation used is not generally reported in the published literature, except for two publications where ranges were reported from 3 to 75 ml.[14,17] Establishing the minimum and maximum duration of negative-pressure wound therapy with instillation was not a principal goal of our study and thus was not captured. The literature again reports a wide range from 2 to 60 days.[8,17] Based on our data, we generally used negative-pressure wound therapy with instillation or negative-pressure wound therapy for a minimum of 2 days and a maximum of 10 days.

CONCLUSIONS

Our results suggest that negative-pressure wound therapy with instillation is superior to negative-pressure wound therapy for inpatient adjunctive treatment of the acutely infected wound. However, there are many remaining questions regarding the efficacy and effectiveness of negative-pressure wound therapy with instillation. The data presented in this article add to the body of knowledge regarding this novel technology while simultaneously raising many questions. A robust, prospective, randomized, controlled study is needed to better delineate the most appropriate use of negative-pressure wound therapy with instillation.

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Pro-forma Response

External Assessment Centre Report factual check

V.A.C. VERAFLO Therapy System for acute infected or chronic wounds that are failing to heal

Please find enclosed the assessment report prepared for this assessment by the External Assessment Centre (EAC).

You are asked to check the assessment report from Newcastle External Assessment Centre to ensure there are no factual inaccuracies contained within it. If you do identify any factual inaccuracies you must inform NICE by 12pm, **Friday 31 July 2020** using the below proforma comments table. All your comments on factual inaccuracies will receive a response from the EAC and when appropriate, will be amended in the EAC report. This table, including EAC responses will be presented to the Medical Technologies Advisory Committee and will subsequently be published on the NICE website with the Assessment report.

28 July 2020

Issue 1

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Reliance upon Kim 2020 to drive the Economic Model and to consider statistical significance in outcomes between V.A.C. VERAFLO™ Therapy and NPWT is inappropriate. Kim 2020 is represented in the EAC report as a level 1 RCT 32 times. It is in fact a pilot feasibility study used to assist the authors to identify the numbers needed to power a future RCT study. It was never designed or conducted to collect the outcomes the EAC has elected to draw upon and therefore the facts are at risk of having been distorted. We feel this is a misrepresentation of the status of this publication. Stating that it is an RCT is factually incorrect.	The report should correctly define the status of Kim 2020 ((Kim et al., 2020) pilot RCT) and incorporate data from other publications submitted by the company.	Factually incorrect and misrepresentation of the status of the publication. Which is further supported by https://www.jospt.org/doi/10.2519/jospt.2014.0110	The title of the paper is "The impact of negative-pressure wound therapy with instillation on wounds requiring operative debridement: Pilot *randomised, controlled trial*" [EAC emphasis]. This study was clearly a parallel RCT featuring randomization and intention to treat analysis. In the opinion of the EAC, it was the study that had the best internal validity of those available for analysis. It was found to have reasonably good methodological quality following critical appraisal using the Cochrane checklist. Furthermore, it was the largest study, and, as it included patients with both acute and chronic wounds, was the most generalisable. In comparison, other studies included in the submission were observational, and in most cases had retrospective designs which made it difficult

			to establish causality of the intervention with the outcomes. Most of these studies were set in highly specific populations and settings which caused issues with generalizability, particularly as none were set in the UK. The EAC would add that it did not consider that the RCT by Kim 2020 answered all the issues with the decision problem adequately. However, the EAC maintains it was the best evidence available and hence weighted it accordingly, according to standard practice on the hierarchy of evidence. The EAC notes that the company appeared to agree that the Kim study provided possibly the most robust evidence, stating (EAC emphasis "*We agree with the EAC that Kim 2020 could possibly be the most robust piece of evidence for lower limb subgroup comparing NPWTi to NPWT*. However, we note that the paper is a draft and still subject to the peer-

			review process. Therefore, we excluded it from the economic modelling on the basis that we wanted to include published peer-reviewed evidence in our cost-analysis model." This paper has since been published. No change required.

Issue 2

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
The cases within the Kim 2020 paper do not fully represent the scope, particularly the sub-groups, and it is therefore factually incorrect to draw the heterogenous conclusions made and apply these to the economic model. For example in table 4.4 in (Kim et al., 2020) pilot RCT it is stated that 43.1% of wounds were Diabetic ulcers and 17.1% Pressure ulcers.	A wider selection of papers that include data from all of the sub-groups should be used to inform the economic model, which also demonstrates the total population.	Potential bias related to inclusion of a high amount of data from one particular sub-group.	The Kim study was the only RCT that reported experimentally on a relevant comparison, and was the largest study available. It included patients with both chronic and acute wounds, indicated for treatment with VAC VeraFlo. In the opinion of the EAC, it represented the best evidence on the technology. However, it is misleading to state other studies were not considered in the clinical and economic evidence. All the company's included studies were appraised and considered. None were excluded from the EAC's economic analysis. No change required.

Issue 3

NICE National Institute for Health and Care Excellence

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response

The EAC have suggested that the care given to patients in the VERAFLO arm of the (Kim et al., 2020) pilot RCT study reflects standard care and that the results can therefore be applied to all wound types. This is factually incorrect as Prontosan was used as the only instillation solution for all these patients. It is generally well known that Prontosan, is the initial treatment when a wound is infected, before reverting to normal saline, as Prontosan delays the formation of granulation tissue. Suggesting that the outcomes from (Kim et al., 2020) pilot RCT are therefore representative of standard care is incorrect and misleading. In addition the EAC has not commented on the fact that patient recruitment for this trial was begun in 2013. The International consensus guidelines (Kim et al) update published in 2019 stated that "normal saline was recommended as the first choice of instilled topical	The report should clearly state that the use of Prontosan in the VERAFLO arm of (Kim et al., 2020) pilot RCT may have increased lengths of therapy and healing times, which may not have been the case if saline or other recommended instillation fluids were used. The report should clearly state that the use of Prontosan is not reflective of international guidelines.	Potential introduction of poorer outcomes through a non-standard use of the therapy. Potentially artificially skewing data in favour of the NPWT comparator. Misleading the committee to believe that Prontosan use is standard practice in V.A.C VERAFLO™ Therapy internationally.	Prontosan is one of the recommended instillation agents for use with VAC VeraFlo, as highlighted by consensus guidelines. The earlier Kim RCT (2015) compared Prontosan with normal saline and found no significant difference in results. Furthermore, many of the other studies included in the submission utilised antiseptic solutions, including Prontosan and Dakin's solution. This included the large observational study by Kim et al. (2014, used Prontosan). The company has not advocated their exclusion. At no point in the submission does the company suggest antiseptic solutions should be excluded, including in the scope. No change required.

solution with negative pressure wound therapy, with instillation for most wounds, vs topical antiseptic solutions, which were previously used more often as first-line instilled topical solutions". Inclusion of this data is therefore not representative of UK practice or Kim's standard practice so it is factually incorrect to utilise the outcomes and economic calculations of this paper alone as a means to draw conclusions about the clinical and cost effectiveness of V.A.C VERAFLO™ Therapy.			

Issue 4

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
The EAC has made an assumption that in the absence of LOS (Length of Stay) data in (Kim et al., 2020) pilot RCT then LOT (Length of Therapy) can be used as an appropriate substitute. We do not accept that this is a valid modelling methodology and	Data from the paper referenced here should be used in the economic model.	Use of LOT as a substitute for LOS in (Kim et al., 2020) pilot RCT is invalid particularly as a further publication relevant to the outcomes in the scope has been published.	The Lack of LoS data from the Kim study was listed as a limitation of this study. However, in correspondence with Prof Kim he acknowledged there was no significant difference in LoS between the arms, so the EAC considered it was justifiable to make the assumption LoS was equivalent to LoT, with the caveats provided.

believe it distorts the facts about the care patients received and their outcomes. This is especially disappointing given that during the Covid-19 time delay, a further peer reviewed paper by Kim has been published. This contains data directly related to the scope showing statistically significant differences between V.A.C VERAFLO™ Therapy and NPWT for both LOS and the number of operations patients underwent. This paper drew upon data used in Kim et al 2014 and 2015 both of which were retained by the EAC following their literature review. https://www.cureus.com/articles/35306-comparison-of-negative-pressure-wound-therapy-with-and-without-instillation-of-saline-in-the-management-of-infected-wounds			We did not receive the newer Kim analysis as part of the submission. However, we would advise caution when interpreting this paper as, unlike the Kim 2020 study, it does not appear to be an RCT. Retrospective studies of this nature are prone to bias and confounding. No change required.

Issue 5

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
We note that the EAC contacted the principle author to seek clarification on his findings and in particular data not disclosed in his publication. We are concerned that by doing so and not contacting authors of other publications, where the EAC suggested there was ambiguity, this has potentially introduced bias into the data the EAC has reviewed and that this altered the facts available for them to consider.	The statements made by the principle author should be removed from the report.	Introduction of potential bias as the EAC sought information that had not been included in the (Kim et al., 2020) pilot RCT paper from the author.	The EAC clarified with Prof Kim that there was no significant difference between the study arms in terms of LoS (total cohort). This was justified because in our model we had to make the assumption LoS was the same in both arms. No quantitative analysis was performed as a result of our communication with Prof Kim. No change required.

Issue 6

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response

Section 1.2 Intervention, page 10 The report inaccurately states that “The predecessor technology to V.A.C.®Therapy was V.A.C. INSTILL™ Therapy System which differs from V.A.C. VERAFLO™ Therapy in some potentially important ways, such as the use of gravity assisted instillation rather than active instillation of controlled volumes of fluid through pumps and software control”. Whilst V.A.C. VERAFLO™ Therapy constitutes a further development of the V.A.C. INSTILL™ Therapy System, in terms of battery life, design, weight, and it’s expected life-time,the mechanisms of action used by both systems remains unchanged.It combines the benefits of the conventional V.A.C.® Therapy with the topical wound solution distribution in, and removal from, the wound bed. In addition, the same categories of solutions can be chosen,	The report should recognise that the evolution of the V.A.C. INSTILL™ Therapy system in terms of mechanism of therapy, battery life, weight, and lifetime have not changed its clinical operation and that therefore in order to provide further evidence of its benefits, in terms of the outcomes in the Scope, these studies (Gabriel et al., 2008, Timmers et al., 2009) and their data, should once again be included in the review.	Incorrect conclusion that the V.A.C. VERAFLO™ Therapy differs from its predecessor V.A.C. INSTILL™ Therapy system.	One potentially important difference between the VAC VeraFlo system and its predecessor is the fact that VAC Instill uses gravity assisted instillation rather than active pump driven instillation. This could be an important technical difference which could lead to system benefits through increased reliability and reproducibility. Additionally, the VAC VeraFlo uses different dressings which the company stated “improves their ability to distribute fluids across the wound bed, and the new dressings come in different shapes and configurations that allow for more wound types to be addressed”. It is perhaps surprising that the company does not acknowledge these incremental improvements might lead to improved performance? As such, it was decided early in the process, that the predecessor system would not be included in the EAC’s clinical assessment; but, we do not believe this disbenefits the assessment of VAC VeraFlo. However, data from VAC Instill studies were included in the economic analyses.

selected and applied according to the surgeon`s clinical judgement and practice for both systems. A detailed and in-depth comparison of the V.A.C.VERAFLO™ Therapy and the V.A.C. INSTILL™ Therapy System reveals, and unambiguously shows, that both therapy systems are directly correlated to each other and perform physically, mechanistically and thus clinically in the same way. The name change was as a result of a marketing decision and for no other reason and the improvement in instillation mechanism was to promote ease of use. Both therapies – regardless of the name under which they are marketed – work with the same therapy phases, that are: [1.] Approximation of wound edges [2.] Conveying instillation solution to the wound bed.			In summary, the EAC would consider the VAC VeraFlo to be incrementally improved compared with VAC Instill. Nevertheless, the EAC has clarified the incremental changes in this section and has acknowledged the company's view point (see Section 1.2 of the Assessment Report, page 13). No further change required.

[3.] Soaking the wound bed in the corresponding instillation solution in order to dilute and solubilizes infectious material and wound debris [4.] V.A.C. ® Therapy – this step promotes perfusion, reduces oedema, removes exudate and infection material (steps 2 to 4 are repetitive) We believe that this evolution is no different to that of PICO and PICO 7 where improvements in the product were accepted as natural development by the MTG committee. We are working on the assumption that in line with NICE's rigorous and fair processes our product will be assessed in the same way as other devices. The principle mechanism of action for the updated V.A.C. VERAFLO™ Therapy is the same as the V.A.C. INSTILL™ Therapy System, the former is an evolution or an improvement of the latter. For these reasons we believe			

it is factually incorrect to exclude studies related to earlier versions of this product.			

Issue 7

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response

Section 3.1 Clinical Guidelines, page 13. The report makes a factually incorrect statement about comparator technologies and raises concerns that the EAC has regrettably not fully understood the aetiology and nature of the wounds that are suitable for V.A.C. VERAFLO™ Therapy. To help infom the preparation of the guideline, we have inserted images of the wounds that would be suitable for V.A.C. VERAFLO™ Therapy at the end of this document. We have also included images of wounds that would be treated by the comparators suggested in the EAC report. These products are not comparators for V.A.C. VERAFLO™ Therapy and therefore this section should be amended. The closest comparator is NPWT for open wounds, but not open abdomens as per IPG467 as V.A.C. VERAFLO™ Therapy is contraindicated for open	The report should remove the technologies currently proposed as comparators as they are not recommended for care of these types of wound. The report should clarify that due to the complexity of the wounds that receive V.A.C. VERAFLO™ Therapy the comparator should be NPWT used in a hospital setting.	The proposed comparators are not recommended for use on the wound types suitable for V.A.C. VERAFLO™ Therapy.	The purpose of this section was to briefly summarise UK clinical guidelines with respect to wound care. The EAC took advice from NICE clinical advisors when undertaking this task. Clearly, a full and comprehensive description of the complexity of wound care management is beyond the scope of the assessment; further detail are provided in the external communication log where NICE clinical advisors describe pathways in different patient groups by speciality. Patient heterogeneity is a recurring issue. At no point in this section does the EAC suggest the listed devices are comparators to VAC VeraFlo. The comparators for VAC VeraFlo are discussed in Section 1.3 (NPWT without instillation and advance wound care dressings). No change required.

abdomens. “The two former technologies (subject of MTG43 and MTG5) listed may be regarded as comparators in some patient populations; whereas the latter two (MTG17 and MIB173) technologies may be used in conjunction with NPWTi. In all instances, these technologies might impact on the economics of wound healing”. MTG43 (PICO), as stated in your document is for closed surgical incisions. The wounds to which V.A.C. VERAFLO™ Therapy is applied are open rather than closed and it is not appropriate for closed wounds. These open wounds can be acute or chronic, typically have high bioburden, and are failing to heal. Furthermore, PICO’s negative pressure (-75mmHg0 compared to V.A.C. VERAFLO™ Therapy (-125mmHg) is less than optimal and it does not have any cleansing ability. MTG5 (MIST Therapy) has an			

entirely different method of action and has no contact with the wound. It is not a continuous therapy and does not apply the benefit of NPWT with instillation and dwell time like V.A.C. VERAFLO™ Therapy. NICE's own guidance for MTG17 states that "The case for adopting the Debrisoft monofilament debridement pad as part of the management of acute or chronic wounds in the community is supported by the evidence". It is recommended for use on sloughy wounds and hyperkeratotic skin and does not replicate the sharp/surgical debridement required for black necrotic tissue. These wounds are entirely different from the wounds that require V.A.C. VERAFLO™ Therapy. Debrisoft is only ever used in a clinic setting to undertake superficial and gentle debridement as opposed to a much more sophisticated and advanced therapy like V.A.C.			

VERAFLO™ Therapy. MIB173 (Prevena) is a management system for closed surgical incisions only and it is not appropriate for open wounds. Whilst it delivers NPWT of -125mmHg it delivers no cleansing capability. MIB1 (Versajet II) is used for surgical debridement in the operating room rather than the clinic or bedside. Unlike V.A.C. VERAFLO™ Therapy it is not a continuous therapy and does not deliver NPWT or cyclical cleansing.			

Issue 8

NICE National Institute for Health and Care Excellence

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response

Section 3.2 Use of Debridement in Wound Healing, page 14. Whilst this description and subsequent diagram is an accurate representation of the Wounds UK consensus guidelines, which were developed for use by generalist nurses, they once again give the impression that patients who would benefit from V.A.C. VERAFLO™ Therapy would follow a pathway where options such as mechanical, ultrasonic and hydro surgical debridement are likely to be appropriate, which is not the case. This section of the report is therefore factually "light" and fails to recognise the critical importance of "aggressive" surgical debridement in the healing of the type of severe wounds that respond to V.A.C. VERAFLO™ Therapy. The European Wound Management Association Position Document (https://ewma.org/fileadmin/us	The document needs to accurately reflect the debridement pathway that patients who require V.A.C. VERAFLO™ Therapy will follow. Also removing the statement that the significance upon outcomes of the decrease of bacterial count should. Be removed as this is clearly evident in literature.	The proposed pathway is incorrect and was developed for use by generalist nurses. It is factually incorrect to question the impact of bacterial bioburden upon wound outcomes.	This section is intended to be a brief summary of the wound care options available; it is not intended to be an exhaustive description of wound care in the UK. The EAC has reported on published sources of wound care management and included relevant opinion from NICE clinical experts, as documented in the external communications log. The consensus of these experts were that that repeated microbiological culture and debridement under general anaesthesia is not a feature of routine NHS care, although it may occur during complex wound management. The EAC does not dispute that the presence of bioburden does potentially impair healing and that VAC VeraFlo reduces this bioburden. This is discussed in Section 5.3.1 of the report "Colonisation with antimicrobial resistant pathogens". However, this was a surrogate outcome that could not be directly related to clinical or economic outcomes. The EAC therefore stated in its summary table "The available evidence suggests

er_upload/EWMA.org/Position_documents_2002-2008/pos_doc_English_final_04.pdf) confirms that the presence of necrotic or compromised tissue is common in chronic non healing wounds and that its removal, by debridement, takes away non-vascularised tissue, bacteria and cells that impede the healing process. This provides an environment that stimulates the build-up of healthy tissue. The position statement confirms that bacterial bioburden of 106 organisms/g of tissue, as is frequently seen in chronic non-healing wounds, seriously impairs wound healing https://pubmed.ncbi.nlm.nih.gov/9194884/. Bowler et al, which has been cited nearly 2000 times in literature illustrated the importance of reducing bacterial counts, debridement and cleansing in healing wounds. https://pubmed.ncbi.nlm.nih.gov/11292638/. We therefore believe that the EAC statement			that NPWTi reduces bacterial bioburden compared with NPWT alone. However, the significance of this on clinical outcomes is unclear. Additionally, this effect may be dependent on the type of instillation fluid used", which we consider to be a fair comment as the company had not attempted to link this surrogate outcome with tangible clinical outcomes. No change required.

that the significance on outcomes of the decrease in bacterial count reported in (Kim et al., 2020) pilot RCT and Goss 2008 on outcomes is unclear, is, factually incorrect as there is clear evidence of its impact. Particularly the fact that if bioburden is not reduced, wounds remain in the inflammatory stage. The EAC document is factually incorrect as it does not appear to recognise that within NHS pathways, severe and chronic wounds are likely to need repeated surgical debridement in order to reduce bioburden and support preparation of the wound bed. Due to the nature of these wounds clinical experts have stated that these can only be performed in the operating room under anaesthetic as reported by Kim 2014 and Gabriel 2008.			

Issue 9

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Section 3.4 Special Considerations, page 23. The EAC have stated that no specific equality issues were identified by the EAC for this technology. This statement is factually incorrect as there is clear evidence that some citizens are more prone to poor wound healing than others. The EAC report for MTG43 stated that 'Certain ethnic groups are more prone to poor wound healing due to increased risk of diabetes or keloid formation. Older people are also more at risk of poor wound healing. Sex, race, and age are protected characteristics under the equality act 2010.' We concur with this statement and feel that these factors should also be recognised for the population likely to benefit from V.A.C. VERAFLO™ Therapy.	The equality issues related to people with poor wound healing should be included in the report.	It is factually incorrect to state that there are no equality issues.	Whilst it is true that poor healing may be related to particular patient demographics, this is not a protected characteristic *per se*. We therefore feel the statement given in Section 3.4 is accurate. No change required.

Issue 10

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response

Executive summary, page 6. "The model was informed from selected comparative observational studies identified in the clinical literature" gives an impression that the company preferred observational studies over RCTs. This is inaccurate. Whenever there was an RCT (Jurkovic 2019 in surgical site infection subgroup), it was preferred over observational studies	"The model was informed from selected comparative observational studies identified in the clinical literature whenever RCTs were not available".	Accuracy	This is misleading because this statement was not made in the clinical or economic submission. The study by Jurkovic et al. (2019) was not included by the EAC as it was published in non-English language that was not considered to appraisable. This was a small study (n = 41) that primarily reported economic outcomes. Nevertheless it was included in the EAC's economic analysis (for instance see Table 9.4 of the Assessment Report). The one directly relevant RCT (Kim et al. 2020) that was available was not selected, although the EAC appreciates this was prepublication at the time. The EAC also notes that some of the observational studies with non-significant results were not included by the company in their economic analysis (e.g. the study by Omar et al. 2016). There did not appear to be a justification for this and the EAC retains its claim that there was some evidence of potential bias in how the studies were chosen and interpreted. No change required.

Issue 11

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Section 3.4 Special considerations, page 23 "Additionally, diabetes is a known risk factor for poor wound healing, and this condition is associated people of some ethnicities."	"... and this condition is associated <u>with</u> people of some ethnicities."	Missing word	Thank you, we will add this.

Issue 12

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Section 8 Interpretation of the clinical evidence, page 60. "The first of these 6 studies showed statistically significant reductions in the number of surgical debridements"	"The first six of these studies showed statistically significant reductions in the number of surgical debridements"	This was factually inaccurate as the other five studies reported statistically significant reductions	Thank you. We will fix this.

Issue 13

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Section 9.2 Company de novo cost analysis, page 71. "The company reported developed …"	"The company developed …"	Extra verb	Thank you. We will fix this.

Issue 14

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Section 9.2.3 Economic model parameters, page 79. "Their omission suggests that a degree of cherry picking of studies may have occurred"	Omission	The current sentence infers that the company excluded studies without reasons. This is factually inaccurate. Omar was excluded due to low sample size, and Kim 2020 was excluded as it was neither published nor peer-reviewed at the time plus other outcomes (LoS) were not reported	The submission does not give a rationale for the exclusion of Omar et al. (2016). Although this had a small sample size (n = 20), this was true of many of the other studies included. Additionally, Omar et al. (2016) was described as prospective. The omission of Kim et al. (2020) has been discussed. However, in the interests of avoiding perjorative terminology, the EAC will remove the term cherry picking and replace with “study selection”.

Issue 15

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Section 9.2.6 Sensitivity analysis, page 84. " … for instance seeking to incorporate all available evidence, rather than selectively picking single sources and using best-practice methods to avoid potential biases"	Omission	The sentence infers that the company picked certain studies rather than others without giving reasons. This is factually inaccurate as the company reported transparently the limitations of each relevant study in Section 2 of the submission	This is a matter of opinion. The company's critical appraisal of the selected studies was limited or absent, with no attempt made to put potential sources of bias or confounding in context. However, it is the EAC's contention that the clinical evidence base used to inform the clinical and economic analysis was lacking in the necessary quality to make robust conclusions. The EAC has made it clear that this is due to a lack of evidence, rather than evidence of no benefit. This is a matter of opinion rather than an issue that can be factually challenged. No change required.

Issue 16

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Section 9.2.7 EAC changes to model, page 86. "Data from the small observational study by Omar et al. (2106) …"	"Data from the small observational study by Omar et al. (2016) …"	Wrong year	Thank you. We will fix this.

Issue 17

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Page 80. – shows in Table 9.1 (Relevant economic outcomes reported in omitted studies.) a population stating just "Patients with chronic and acute wounds (n = 181)"	This is misrepresenting the study, as it should be demonstrating the anatomical sites as the EAC have done in other tables, such as OMAR in Table 9.1	Accuracy	We will add ("mainly of the lower limb") for the sake of clarity.

Issue 18

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Page 83. However, even within an HRG the complexity of patient clinical needs vary, as well as the availability of social care on discharge, as sometimes medically fit patients cannot be discharged due to delays in setting up support packages.	This leads the reader to believe that social care is included in the HRG coding and therefore tariff, which is not accurate. This sentence needs to say. “However, even within an HRG the complexity of patient clinical needs vary. Also the availability of social care on discharge, sometimes for medically fit patients cannot be discharged due to delays in setting up support packages.”	Accuracy	The EAC disagree with this assertion. The point about social care was a separate, essentially unquantifiable, issue. No change required.

Issue19

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Page 83. It should be noted that because the costs associated with a day of LoS were roughly twice as costly as one surgical debridement procedure, and because LoS was significantly higher in comparator groups compared with NPWTi in most scenarios, this parameter was the main driver of the model.	This is misleading the reader, as it infers that possibly the LoS cost or debridement is too high. However, on page 83 under debridement it had already been confirmed by NICE and a KOL that the costs were accurately reflected and possibly underestimated.	Accuracy	No such inference was intended. This text was written to add some clarity about what costs were driving the model. No change required.

Issue 20

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Page 84. Where these could not be calculated, the company assumed the standard error was 20%.The EAC considered this value was arbitrary unlikely to cover the feasible range of variability in poorly evidenced parameters, thus it did not usefully inform the degree of uncertainty in the model (Briggs et al., 2012).	The percentage used was in support of the NICE methods and processes documentation and therefore applied in line with guidance. Therefore, this should be removed or reflect the NICE guidance which was followed.	Accuracy	As per the included reference, adjusting costs by 20% in deterministic analysis does not explore the full range of plausible values when there is significant uncertainty. No change required.

Issue 21

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Page 86. Not all studies reported all the informing parameters. In the absence of data, crude assumptions were made, namely that LoS was the same as LoT. This assumption disbenefits NPWTi, as the assumption in the model is that, whilst NPWTi is more costly than its comparators, it introduces savings by reducing LoS.	Until we can see the studies and model from the EAC, we are unable to validate what was used here. However this would be considered inappropriate statistical analysis. Due to no other study having the same LOS and LOT reported throughout the cohort of studies either included or excluded by the EAC.	Accuracy	The EAC did not have access to the LoS data from the Kim 2020 RCT, although the EAC was informed there was no significant difference between arms. The EAC has indicated this is a clear limitation of the analysis for this population. No changer required.

Issue 22

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Page 86. Of these, the study by Kim et al. (2020) was regarded the most robust and was the closest that could be considered a “base case”. This was because this was a relatively high quality experimental study, it was conducted in a well-defined population (case mix of patients with acute and chronic wounds), and it was the largest study (n = 181).	The EAC have applied an inappropriate statistical analysis deciding that Kim 2020 was a base case to consider its findings. Due to the limitations of the study of both a pilot to prove power, along with the population being significantly skewed to Lower limb, this would not be appropriate to be considered as a base case. Therefore, the EAC would need to consider a suitable alternative to a base case, as we have done, due to the broad range of conditions suggested in the scope by NICE.	Accuracy	The EAC has critiqued the company’s base case in the Assessment Report. In our opinion the company’s analysis was flawed for the reasons stated. Rather than estimate an aggregated “base case”, the EAC considered that it was most appropriate to use empirical data reported from single studies. In the opinion of the EAC, data from Kim et al. (2020) was most robust, although the EAC has been careful to emphasise the limitations of this approach too. In the opinion of the EAC, the economic analysis is insufficient to draw firm conclusions from. That is, the cost saving potential of VAC VeraFlo has not been quantified with sufficient certainty. No change required.

Issue 23

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Page 90. It is notable in the model that the cost of an overnight stay (average cost £407) was almost double the cost of a surgical debridement (£237), and there were more excess overnight stays than excess debridement procedures.	This is a replication of issue 5 – which again should be removed or reworded to not mislead the reader into a possible consideration.	Accuracy	This text explains the drivers of the model. No change required.

Issue 24

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Page 93. And fourthly, the method of reporting the base case results was unsatisfactory, as it was not directly based on appropriate empirical data and was not accordingly weighted to reflect this. The EAC also considered that the scale of the structural and parameter uncertainty in the model meant that sensitivity analyses were uninformative.	This is opinion and misleading of the reader as the use of a Pilot study could also be considered to be based on empirical data and was not accordingly weighted to reflect the broad population from a lower limb main study of Kim 2020.	Accuracy	The patients recruited by Kim et al. 2020 were not exclusively lower limb wounds. As discussed, the EAC considered it was more appropriate to inform the economic model directly from empirical evidence. The EAC also noted that in some cases the patients from studies informing the company's scenarios did not have wounds in that anatomical location or of that type. No change required.

Issue 25

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Page 94. The main alteration was to use data from the RCT by Kim et al. (2020), which the EAC considered was the most robust evidence available.	This needs to be removed and reworked by the EAC as it is not statistically correct to use a single study to inform a base case when the study is a clear subset of the overall population. It has not been considered by the EAC that the broadness of the population is not possible to report at a global level and therefore is not accurate and misleads the reader.	Accuracy	The EAC has explained the limitations of all the studies, including that of Kim et al. 2020. However, it remains the case this study was the only RCT that performed a relevant comparison. It was judged by the EAC to be of good quality and was the largest study identified. No change required.

Issue 26

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Page 94. The main limitation to this analysis was that the RCT did not report LoS, so this was assumed to be the same as LoT.	The use of LoT to reflect LoS is not an accurate marker for the LoS findings, as none of the studies submitted or included by the EAC reflect this finding. Therefore, to use a numerical value which is not reflective of the 19 studies included, is misleading and inaccurate. The EAC needs to revise this, however until we can see the model from the EAC we are unable to model the full impact. Also, none of the Kim et al's. prior papers showed this outcome and the sub group of dehiscence wounds in the Kim 2020 study shows a reduction in length of stay for those patients treated with NPWTi, even with the use of Prontosan.	Accuracy	As discussed, in the opinion of the EAC aggregating data from observational studies exhibiting high levels of heterogeneity was no appropriate. The EAC does not try to extrapolate beyond the patients enrolled in this study. LoS data from this cohort was not available. The limitations of this approach have been fully explained in the Assessment Report. No change required.

Issue 27

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Page 75 One issue was that in the NHS, NPWTi must be performed as an inpatient procedure, meaning it could lead to paradoxical increases in LoS by preventing earlier discharge to community care.	It is inappropriate to state that a by-product of using V.A.C. VERAFLO™ Therapy or any other medical device would intrinsically be linked to an increase in LoS. This is misleading the reader and is not factual and therefore should be removed.	Accuracy	This comment arose from a NICE clinical advisor. There was consensus that in the NHS patients are discharged to receive NPWT in community settings, this comment is highlighting this fact. No change required.

Issue 28

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Page 74. The EAC accepted clinical data for NPWT from any technology, although the costing used in the economic modelling was restricted to the VAC Ulta device.	The EAC accepted clinical data for NPWT from any technology. This was reflected in the economic costing model which included both the VAC Ulta device and other NPWT products available in the NHS.	Accuracy and was referenced in the EAC/NICE and company email log dated 17/04/2020	We are unclear what the issue is here, the text states the costs for NPWT were derived from VAC Ulta which is true. No change required.

Issue 29

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Page 82. All costs were verified by the EAC and, where found to be incorrect, they were updated or changed for the EAC's base case model (see Table C4).	All costs were verified by the EAC and were correct (2019/20 prices)	Accuracy – All costs, were correct at the time of model sign off.	The EAC cross referenced these costs and updated these where required. Technology costs made little material difference to the overall economic results. No change required.

Issue 30

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Page 137. Table C4. *Summary of EAC's modifications to the model (see also Table C3a and C3b).*	Update table to reflect 2019/20 NHSSC costs	The incorrect prices were applied in the EAC model, as they used 2020/21 prices. It is not clear if these are the buy-in or sell-out prices.	The EAC has used the correct prices. No change required.

[redacted]