Healthcare Improvement Scotland | SHTG Advice on health technologies

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In response to enquiry from Tissue Viability, NHS Greater Glasgow and Clyde

What is the clinical and cost effectiveness of Negative Pressure Wound Therapy (NPWT) in chronic, acute and surgical wounds?

What is an evidence note?

Evidence notes are rapid reviews of clinical and cost-effectiveness evidence on health technologies under consideration by decision makers within NHSScotland. They are intended to provide information quickly to support time-sensitive decisions. Information is available to the topic referrer within a 6-month period and the process of peer review and final publication of the associated advice is usually complete within 6–12 months. Evidence notes are not comprehensive systematic reviews. They are based on the best evidence that Healthcare Improvement Scotland could identify and retrieve within the time available. The evidence notes are subject to peer review. Evidence notes do not make recommendations for NHSScotland, however the Scottish Health Technologies Group (SHTG) produces an Advice Statement to accompany all evidence reviews.

Key points

- There is moderate-quality evidence from randomised controlled trials (RCTs) supporting the use of negative pressure wound therapy (NPWT) for people with diabetes who require treatment for either post-operative foot wounds or foot ulcers. Some authors of the systematic reviews noted the need for robust RCTs in this patient group to consolidate the existing evidence.
- With regards to clinical effectiveness, there is a lack of robust and/or consistent evidence from RCTs supporting or refuting the use of NPWT in the following wound types: pressure ulcers; venous leg ulcers; burns; open abdomen; wounds healing by primary intention (including split thickness skin grafts, caesarean section wounds and closed incision wounds); surgical wounds healing by secondary intention; and sternal wound infections after cardiothoracic surgery.
- A good quality systematic review reported that for open fracture wounds there was no statistically significant difference between NPWT and standard care for wound healing at

6 weeks (based on one robust RCT). The review also reported that it is uncertain whether there is a difference in risk of wound infection, adverse events, time to closure or coverage surgery, pain or health-related quality of life between NPWT and standard care for any type of open traumatic wound.

- A good quality systematic review reported on one robust RCT which concluded that NPWT was unlikely to be a cost-effective treatment for open fracture wounds.
- The evidence is insufficient to draw definitive conclusions on the cost-effectiveness of NPWT in all other wound types.
- To supplement this evidence note, and to address concerns of over-use in NHSScotland, a group of clinical experts have produced consensus statements to guide the appropriate use of NPWT.

Literature search

A systematic search of the secondary literature was carried out between 9 and 17 May 2018 to identify systematic reviews and guidelines published between 2013 and 2018. The Medline, Medline in process and Embase databases were also searched for systematic reviews and meta-analyses.

The primary literature was systematically searched on 21 August 2018 using the following databases: Medline, Medline in process, and Embase. Results were limited to Randomised Controlled Trials (RCTs) in English from 2013-2018. An update search for economic studies was completed on 26 and 27 of September 2018 using the above limits and databases.

Key websites were searched for guidelines, policy documents, clinical summaries, economic studies and ongoing trials.

Concepts used in all searches included: NPWT (negative pressure wound therapy), TNP (topical negative pressure), vacuum assisted closure technique (VAC therapy). A full list of resources searched and terms used are available on request.

This evidence note was based on a high-level, rapid review of the literature. Therefore, searches were limited to systematic reviews and RCTs published between 2013 and 2018.

Introduction

Negative pressure wound therapy (NPWT) is a widely used treatment in NHSScotland for acute, chronic and surgical wounds.

In 2010, NHS Quality Improvement Scotland produced a health technology assessment (HTA) on NPWT[1]. While the HTA concluded that the evidence base was weak for this technology, it noted some areas of application where NPWT may improve clinical outcomes.

This review was referred to the Scottish Health Technologies Group (SHTG) in March 2018. Initial exploratory work was conducted which highlighted anecdotal concerns that NPWT was being over-used in Scotland, often when conventional dressings would be the more appropriate treatment choice. There also appeared to be concerns that NPWT was sometimes being used on wounds/patients for which the technology was contraindicated. The initial exploratory work included a high-level scope of the literature, which suggested that there was a lack of published evidence to support or guide the current extent of NPWT use in NHSScotland.

A decision was made to produce an evidence note on NPWT, updating the clinical and cost-effectiveness evidence presented in the 2010 HTA. The primary question to be addressed was: 'What is the clinical and cost effectiveness of NPWT in chronic, acute and surgical wounds?' Based on the initial exploratory work, it was apparent however that the issues of inconsistent use, over-use, and possibly unsafe use of NPWT were unlikely to be satisfactorily addressed by a review of the published evidence and conclusions about an insufficient evidence base would be unlikely to change practice.

To help guide appropriate and safe use of NPWT in Scotland, a group of clinical experts was convened to produce best practice consensus statements. These consensus statements have been published as a supplement to this evidence note.

Health technology description

NPWT has been used to treat wounds since the late 1990s[2].

A NPWT system comprises a sealed dressing over a wound, a suction pump and a drainage tube going from inside the dressing or its surface to a canister within the pump unit. The wound is covered or packed with an open-cell foam or gauze dressing and sealed with an occlusive drape. Dressings are typically changed two to three times per week. NPWT is delivered by a stationary or portable vacuum pump, and pressure can be applied either continuously or intermittently. Negative pressure settings range from -50 mmHg to -125 mmHg[2].

NPWT is thought to progress a wound towards healing by:

- Maintaining a moist wound environment
- Improving blood flow
- Removing waste exudate

- Promoting the formulation of granulation tissue
- Increasing the rate of epithelial tissue growth
- Reducing infection
- Pulling the wound edges together

Several manufacturers produce NPWT devices in differing formats, all of which have different applications, wear times, costs and fluid handling properties.

Epidemiology

NPWT is a rapidly evolving therapy, used in a broad range of specialities. It is currently used for a number of different applications, including:

- Chronic wounds (pressure ulcers, foot wounds associated with diabetes, venous leg ulcers, pilonidal sinus or any other chronic wound);
- Acute wounds (trauma and burns);
- Surgical wounds (open abdomen, sternal wounds, skin flap/grafts, surgical closure failures, amputations, surgical incisions and reconstruction).

NPWT is used to promote healing, but also prophylactically in certain patient groups to prevent surgical site complications. It may also be used as a temporary dressing.

NPWT is an NHSScotland contract item and it costs approximately £1 million per annum. Total spend between September 2017 and August 2018 was £1,106,733. Of this total, £178,173 was on pump hire, and the rest was on consumables (dressings). Pumps are either hired from the manufacturers, or provided by the manufacturers free of charge with volume commitment on dressings purchases (Alex Little, Commodity Manager, NHS National Services Scotland. Personal Communication. 12 October 2018).

Clinical effectiveness

The review of clinical-effectiveness evidence for this evidence note was very large. Therefore, a summary is presented here. The full review is available as an appendix (Appendix 1).

In this section, the evidence for different wound types has been considered separately. The volume of literature was large, and categorising it by wound type was challenging owing to overlap in the patient groups included in the studies.

An HTA on NPWT was published by Healthcare Improvement Scotland (then NHS Quality Improvement Scotland) in 2010. For each of the wound types, the main conclusions from the 2010 HTA have been summarised, followed by a description of the evidence published more recently. The review is intended to provide a rapid summary of the evidence, therefore the literature searches

were limited to secondary evidence published in the last 5 years (2013-2018), and randomised controlled trials (RCTs) which were not included in the systematic reviews.

Systematic reviews and RCTs that considered solely home-made NPWT devices, or comparing different types of commercial NPWT systems were not eligible for inclusion. Some reviews had broad inclusion criteria however, including studies on home-made devices, and these reviews have been included. Reviews and RCTs were included if they compared NPWT to 'conventional treatment', which might be standard or advanced dressings, or surgery depending on the application. All outcomes reported on in the literature were included.

The term 'negative pressure wound therapy' (NPWT) has been used in this review. However, other terms in the literature, for the same technology, include 'topical negative pressure' (TNP) and 'vacuum assisted closure' (VAC). The language used by the review/RCT authors has been retained.

Chronic wounds: pressure ulcers

The HTA published in 2010 identified some RCT evidence relating to the use of NPWT in pressure ulcers[1]. However the methodological quality of the studies was poor, and the results were inconsistent.

Literature published after 2010 HTA

A search for secondary evidence highlighted a Cochrane review by Dumville *et al* (2015) which assessed the effects of NPWT for treating pressure ulcers. It included four RCTs, encompassing 149 participants, of very low quality. The authors concluded that "high uncertainty remains about the potential benefits or harms, or both, of using this treatment for pressure ulcer management"[3].

Two additional systematic reviews were identified, but these do not alter the conclusions of the Cochrane review[4, 5].

Guidance from the National Institute for Health and Care Excellence (NICE) from 2014 states that there is limited evidence to support the use of NPWT on pressure ulcers[6]. NICE makes the following two recommendations:

- "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)."
- "Do not routinely use negative pressure wound therapy to treat a pressure ulcer in neonates, infants, children and young people."

Our literature search did not identify any RCTs on the use of NPWT in pressure ulcers not already included in the systematic reviews.

Current position in light of new evidence

NPWT is used on pressure ulcers in NHSScotland, however there is limited evidence to support this use. The HTA from 2010 noted a lack of good quality evidence, and this conclusion was echoed in the Cochrane review from 2015.

Chronic wounds: venous leg ulcers

The HTA published in 2010 identified one 'reasonable quality' RCT (n=60) which suggested that venous leg ulcers receiving a split-thickness pinch skin graft may heal more quickly when pre-treated with NPWT rather than hydrogel/alginate with compression[1]. For venous leg ulcers not being grafted, no useful evidence was found on NPWT. A Scottish Intercollegiate Guidelines Network (SIGN) guideline published in the same year, based on the same RCT, concluded that "there is insufficient evidence on which to base a recommendation for TNP/VAC in chronic venous leg ulcer"[7].

Literature published after 2010 HTA

A Cochrane review by Dumville *et al* (2015) assessed the effects of NPWT for treating leg ulcers in any care setting[8]. The review highlighted only the RCT that was included in the 2010 HTA and SIGN guidelines, and so reported the same conclusions as the 2010 publications.

Three older systematic reviews were identified but these did not include any RCTs other than the one already identified[4, 5, 9].

The literature search did not identify any RCTs on the use of NPWT in venous leg ulcers not already included in the systematic reviews.

Current position in light of new evidence

NPWT is used on venous leg ulcers in NHSScotland, however there is limited evidence to support this use. Systematic reviews published since the 2010 HTA found no new RCT evidence. Therefore, the conclusion that there is insufficient evidence on which to base advice, remains unchanged.

Chronic wounds: wounds associated with diabetes mellitus

For wounds associated with diabetes mellitus, the main conclusion of the HTA published in 2010 was that foot wounds "may be more likely to heal, and heal more quickly, when treated with TNP versus other modalities"[1]. This was largely based on four RCTs (three of which were described as having methodological flaws, and one described as 'reasonable' in quality). In the same year, SIGN produced guidelines on the management of diabetes, and recommended that NPWT "should be considered in patients with active diabetic foot ulcers or postoperative wounds"[10]. Similarly, NICE guidelines from 2010 recommended that NPWT is considered after surgical debridement of foot ulcers associated with diabetes.

Literature published after 2010 HTA

A recent search highlighted eight systematic reviews which evaluated the use of NPWT in people with wounds associated with diabetes mellitus[4, 5, 9, 11-15].

The most recent was a systematic review (with meta-analyses) from 2017[14]. The aim was to: "assess the clinical efficacy, safety, and cost-effectiveness of NPWT in the treatment of diabetic foot ulcers"[14]. The review appears to be of good quality, with clearly described methodology. It included 11 RCTs (encompassing 1044 patients), nearly all of which were rated as having an unclear risk of bias relating to the blinding of study participants and personnel, and blinding of outcome assessment. The authors of the review stated that the comparator was 'standard dressing changes'. The authors performed meta-analyses and reported statistically significant improvements with NPWT for the following outcomes: complete healing rate; time to complete healing; change in ulcer size; and amputation. The results from three studies suggested that there was no significant difference in treatment-related adverse events.

The authors concluded that "this meta-analysis of eleven RCTs extends support for the use of NPWT in the treatment of DFUs [*diabetic foot ulcers*] and post-operative wounds in diabetic patients. Additional robust RCT research is necessary to solidify support for the treatment."[14]

Similar conclusions were reached in six of the other reviews, which generally agreed that there is moderate-quality evidence supporting the use of NPWT compared to conventional treatments in wounds associated with diabetes. Some of the reviews also suggested that the current RCT evidence was limited, with possible bias, and that further trials were required[4, 9, 11-13, 15]. The remaining review evaluated the efficacy and safety of NPWT for the treatment of chronic wounds in the home setting. The authors only identified three observational studies, and concluded that they were "unable to draw conclusions about the efficacy or safety of NPWT for the treatment of chronic wounds in the home setting…"[5].

Guidelines from NICE on the prevention and management of diabetic foot problems (2015) recommended that NPWT should be considered after surgical debridement for foot ulcers associated with diabetes, on the advice of the multidisciplinary foot care service[16].

Our literature search did not identify any RCTs on the use of NPWT in ulcers associated with diabetes not already included in the systematic reviews.

Current position in light of new evidence

The recent RCTs and systematic reviews published since the HTA in 2010 support the use of NPWT in people who have wounds associated with diabetes mellitus. However, the authors of reviews have highlighted the need for robust RCT research.

Acute wounds: burns

The 2010 HTA included a Cochrane review, which included one 'methodologically weak' RCT on NPWT for burns published as an abstract. Therefore, the HTA concluded that there was no useful evidence on the use of NPWT as the primary treatment of burns[1].

Literature published after 2010 HTA

A Cochrane review by Dumville *et al* (2014) only identified an RCT published as a conference abstract, and which had previously been included in the 2010 review and HTA. Therefore the authors stated that in the absence of completed RCTs on NPWT for partial-thickness burn injury, conclusions cannot be drawn on the merits – or otherwise – of this treatment[17]. A HTA from Malaysia, published in 2013, reiterated the same conclusions as the 2010 HTA and review by Dumville et al (2014)4.

Current position in light of new evidence

The recent literature search did not identify any additional RCTs on the use of NPWT in burns. It is not possible to support or refute the use of NPWT in this patient group.

Acute wounds: trauma wounds

Based on two randomised studies by the same author, the 2010 HTA concluded that: "Trauma wounds may drain more quickly with TNP than pressure dressings. No difference was found in wound infections and breakdown. For surgical incisions or fractures deemed at high risk of healing problems, wounds may drain more quickly with TNP. No difference was found in wound infections or repeat surgery."[1]

Literature published after 2010 HTA

For open fracture wounds that have been debrided but are still waiting for soft tissue cover, NICE guidance recommends that NPWT is considered as an intermediate wound dressing prior to further surgical intervention[18]. This is based on evidence that was rated as low or very low in quality.

A good quality systematic review from 2018 by Liu *et al* evaluated the use of NPWT in open fractures compared with conventional wound dressings[19]. It included eight RCTs (encompassing 421 patients) and six retrospective cohort studies (encompassing 488 patients). All RCTs were rated as having an unclear risk of bias, apart from two that had a high risk of bias.

The authors are appropriately cautious in their conclusions, noting the potential for bias in the included studies, and the need for good quality RCTs before robust conclusions are possible (particularly with regards to effects on flaps, fracture healing and patient quality of life). They state that there is some evidence which indicates that NPWT reduces the risk of infection in the treatment of open fractures and accelerates their wound healing process. They also note that there is some (but not much) evidence that NPWT may help reduce the risk of amputation.

A systematic review published in 2015 included one RCT and 12 retrospective studies[20]. Only the RCT and three of the retrospective cohorts were included in Liu *et al*. It aimed to assess whether: NPWT

in Grade IIIB tibia factures lead to fewer infections compared with gauze dressings; NPWT allowed flap procedures to be performed beyond 72 hours without increased infection rates; and whether NPWT was associated with fewer local or free flap procedures. The conclusions are similar to those reported by Liu *et al*: "There is an association with decreased infection rates with negative pressure wound therapy compared with gauze dressings. There is evidence to support negative pressure wound therapy beyond 72 hours without increased infection rates and to support a reduction in flap rates...However, negative pressure wound therapy use for Grade IIIB tibia fractures requires extensive additional study."

An RCT by Costa *et al* (2018), aimed to assess disability, rate of deep infection, and quality of life in patients with severe open fracture of the lower limb treated with NPWT compared with standard wound management after the first surgical debridement of the wound[21]. The study included 460 patients, 226 of which were treated with NPWT. The authors concluded that there were no statistically significant differences in the patients' Disability Rating Index score at 12 months; in the number of deep surgical site infections; in the proportions of wounds healed at 6 weeks; and in quality of life. This study appears to have been well conducted, with transparent and clear reporting of the methods and results.

After this evidence note was drafted, a Cochrane review was published on the use of NPWT in treating open traumatic wounds (Iheozor-Ejiofor Z et al, 2018)[22]. The authors evaluated the evidence for open fracture wounds and other open traumatic wounds (no broken bones) separately. For open fracture wounds, four studies were included (including Costa et al). For risk of wound infection, pooled data from the four studies (n=596) highlighted no statistically significant difference between groups treated with NPWT at 125mmHg and standard care (relative risk (RR) 0.48, 95% confidence interval (CI) 0.20 to 1.13; I^2=56%; very low certainty evidence). Other outcomes were reported from the individual studies – but have already been covered in this evidence note. For other traumatic wounds, data from two studies were pooled (n=509), also suggesting no clear difference in risk of wound infection between open traumatic wounds treated with NPWT at 125mmHg or standard care (RR 0.61, 95% CI 0.31 to 1.18; low certainty evidence). The authors concluded that for open fracture wounds there was moderate-certainty evidence of no clear difference between NPWT and standard care in the proportion of wounds healed at 6 weeks (based on the Costa et al study). They also conclude that there is moderate certainty evidence that NPWT is not a cost-effective treatment for open fracture wounds (also based on the Costa et al study – see cost effectiveness section for more details). Finally, the review authors conclude that "it is uncertain whether there is a difference in risk of wound infection, adverse events, time to closure or coverage surgery, pain or health-related quality of life between NPWT and standard care for any type of open traumatic wound".

Current position in light of new evidence

Recently published systematic reviews include RCTs which, for some outcomes, support the use of NPWT in the treatment of open fractures/grade IIIB tibia fractures, particularly with regards to decreased infection rates. However, these RCTs were rated as having an unclear or high risk of bias by the systematic review authors. In addition, results from a good quality RCT published after the systematic reviews do not support the use of NPWT in severe open fractures of the lower limbs.

Surgical wounds: open abdomen

The 2010 HTA identified four systematic reviews on the use of NPWT in open abdominal wounds, but these included a small number of studies that were methodologically weak. Based on these systematic reviews, the HTA concluded that open abdominal wounds with peritonitis may be associated with lower mortality when treated with NPWT compared with conventional therapy. However, the need for good quality trials was noted[1].

Literature published after 2010 HTA

A systematic review by Cirocchi *et al* (2016) evaluated the effectiveness of NPWT compared to non-NPWT therapies in patients treated with open abdomen technique[23]. It included eight studies (two randomised, two prospective cohorts, and four retrospective cohorts), encompassing 723 patients who had NPWT and 502 patients who did not. The authors stated that the risk of bias in the RCTs was high, and all but one of the cohort studies were rated as 'fair' quality. Clinical heterogeneity between the studies was also noted, for example with respect to the variability in NPWT systems and in the comparator groups.

Comparing the NPWT group to the group that did not receive NPWT, there was no statistically significant difference in fascial closure, postoperative enteroatmospheric fistulae rate, postoperative bleeding rate, or postoperative abdominal abscess rate. However, there was a statistically significant difference between the groups for postoperative mortality rate and length of stay in the intensive care unit, favouring NPWT.

The authors note that for several outcomes, the confidence intervals were wide, and inconsistency was high. Based on the results they conclude that from the current available data NPWT seems to be associated with a trend toward better outcomes compared to the use of no NPWT. However, they stress the need for caution given the weaknesses in the studies and the clinical and statistical heterogeneity. They highlight the need for RCTs in this area. This review is well reported, and the conclusions are appropriately cautious.

NICE Interventional Procedures Guidance (2013) states that the current evidence on NPWT for the open abdomen "is adequate to support the use of this procedure provided that normal arrangements are in place for consent, audit and clinical governance"[24]. The guidance also states that the procedure should only be carried out by healthcare professionals with specific training, and encourages further research into the role of NPWT for the open abdomen. The guidance is based on a systematic review from 2012, two RCTs (one of which is included in the 2012 systematic review), two non-randomised comparative studies and two case series.

Our literature search did not identify any additional RCTs on the use of NPWT in open abdomen.

Current position in light of new evidence

The evidence supporting the use of NPWT in the open abdomen is weak, but suggests that it may be associated with better outcomes compared to the use of no NPWT.

Surgical wounds: skin grafts and surgical wounds healing by primary intention

Apart from skin grafts, this patient group was not included in the 2010 HTA[1]. For skin grafts, six systematic reviews that evaluated the use of NPWT were cited in the 2010 HTA. However, all systematic reviews seemed to draw on the same RCTs, two of which met the inclusion criteria of the HTA. One RCT (n=60) reported that in a burns unit NPWT led to less graft loss, reduced frequency of regrafting, and reduced time from intervention to patient discharge. The other RCT (n=22) compared NPWT with bolster dressings and reported that NPWT did not significantly improve skin graft take rates - although it appeared to offer an advantage in the quality of graft take. Some additional non-randomised trials were included, but the results were inconsistent.

Literature published after HTA

The most comprehensive review identified for this patient group was a Cochrane review from 2014 (Webster *et al*), which assessed the effects of NPWT on surgical wounds that were expected to heal by primary intention (primary closure, skin grafting or flap closure)[2]. Fifteen additional reviews were identified, considering a variety of different patient groups[25-37]. In addition, seven RCTs not included in the reviews were identified. Synthesising the reviews and RCTs was challenging, largely because the patient group they considered varied and overlapped. The literature has been split into categories based on the patient groups/interventions as described by the authors. These categories are imperfect and the overlap should be noted. The overall conclusion, of insufficient/inconsistent evidence, is the same for all categories. Given the disparity of the studies, for simplicity they have been summarised in table 1.

Current position in light of new evidence

The most comprehensive review for this patient group (skin grafts and surgical wounds healing by primary intention) concluded that: “In closed surgical wounds, the evidence for the effects of NPWT for reducing surgical site infection (SSI) and wound dehiscence remains unclear, as does the effect of NPWT on time to complete healing”[2].

A small number of reviews reported positive results with NPWT (for example, increased graft take and reduced rate of reoperation with split thickness skin grafts; and reduced incidence of wound infection in closed incision wounds). However, several of the reviews consistently reported the need for good quality trials, and so confidence in these positive findings is low.

Additional RCTs were identified but the results from these are inconsistent and trial authors’ often reported the need for additional well-conducted RCTs before definitive conclusions were possible. One well-reported RCT found no significant differences in superficial SSIs or deep SSIs between NPWT and standard dressings in patients who underwent open resection for intra-abdominal neoplasms.

Table 1: Summary of reviews and RCTs on skin grafts and surgical wounds healing by primary intention

Patient group	Review references	RCT references	Overall conclusions
Wounds healing by primary intention	Webster *et al* (2014)[2]	0	In closed surgical wounds, the evidence for the effects of NPWT for reducing surgical site infection (SSI) and wound dehiscence remains unclear, as does the effect of NPWT on time to complete healing.
Split thickness skin grafts	Yin *et al* (2018)[34]; Azzopardi *et al* (2013)[25]	0	The most recent review (Yin *et al,* 2018) concluded that compared with conventional therapy, NPWT significantly increased the rate of graft take and reduced the rate of reoperation when applied to cover the wound bed with split thickness skin graft; but no impact on wound infection was found. An older review (Azzopardi *et al,* 2013) also reported positive results, stating that NPWT may impart considerable advantage over traditional dressings in quality and quantity of take. In both reviews the authors note the lack of high-quality RCTs.
Skin flaps	Yu *et al* (2017)[36]	0	One review, for which the full text was not obtainable and so not critically appraised, concluded that NPWT may facilitate flap transfer and help to rescue flaps threatened by infection and venous congestion.
Caesarean wounds	Yu *et al* (2018)[35]; Smid *et al* (2017)[33]	Hyldig *et al* (2018)[38]; Wihbey *et al* (2018)[39]	Two reviews were identified that evaluated the prophylactic use of NPWT after caesarean sections. They included largely the same evidence base, although analysed the data differently. Yu *et al* concluded that studies were heterogeneous but suggested a reduction in SSI and overall wound complications. The conclusions from Smid *et al* were less positive, with the authors stating that the current evidence does not support the prophylactic use of NPWT after caesarean sections in obese women. Two additional RCTs were identified, but the results of these were inconsistent, making any robust conclusions impossible.
Closed incision wounds	Cahill *et al* (2018)[27]; Strugala *et* al (2017)[37]; Hyldig	Crist *et al* (2018)[40]; Engelhardt *et al* (2018)[41];	Seven reviews evaluated the prophylactic use of NPWT for closed surgical incisions. The most recent review (Cahill *et* al) reported a decrease in perineal wound complications after abdominoperineal resection. The next two most recent reviews (Hyldig *et al* and

NB The reviews/RCTs in this category evaluated the prophylactic use of NPWT for closed surgical incisions (or talked about the use of incisional NPWT).	*et al* (2016)[28]; Scalise *et al* (2016)[31]; Sandy-Hodgetts *et al* (2015)[30]; Semsarzadeh *et al* (2015)[32]; Ingargiola *et al* (2013)[29]; CADTH (2013)[26]	Gombert *et al* (2018)[42]; Kwon *et al* (2018)[43]; Lee *et al* (2017)[44]; Pleger *et al* (2018)[45]; Suh *et al* (2016)[46]	Scalise *et al*) reported similar conclusions: compared to standard care, NPWT was associated with reductions in wound infection and seroma formation, but not in dehiscence. The review authors also note weaknesses in the evidence base, meaning definitive conclusions are not possible. The four older reviews are generally in agreement. Seven additional RCTs were identified, six of these relating to the use of NPWT on closed wounds after vascular surgery. The results of these were inconsistent. Some reported reduced rates of infection with NPWT, but the differences were not statistically significant. Two studies reported statistically significant reductions in wound complications and re-operations/revisions.
Prophylactic use in other closed surgical wounds	De Vries *et al* (2016)[47]; Swanson *et al* (2016)[48]	O'Leary *et al* (2017)[49]; Shen *et al* (2017)[50]; Manoharan *et al* (2016)[51]	One review evaluated the prophylactic use of NPWT in clean and contaminated surgery generally (De Vries *et al*) and another considered its use after ventral hernia repair only (Swanson *et al*). There was overlap in the included studies, although De Vries *et al* had broader inclusion criteria. De Vries *et al* reported that summary estimates showed a benefit of NPWT over conventional dressings in reducing SSIs, although cautioned that their confidence in this estimate was low and that more research was required. Swanson *et al* also reported a reduction in SSIs, and the need for more high-quality research. Three additional RCTs were identified. The first included 50 patients and compared prophylactic NPWT with standard dressings on postoperative SSI rates in closed laparotomy wounds (no statistically significant difference). The second RCT included 256 patients who underwent open resection of intra-abdominal neoplasms, and the authors reported no difference in superficial or deep SSI rates between the standard dressing and NPWT group. The last RCT included 21 patients having bilateral knee arthroplasty, and the authors reported no benefit in wound healing, but improvements in wound leakage and wound protection in the NPWT group (compared to conventional dry dressings).

Surgical wounds: wounds healing by secondary intention

The HTA from 2010 did not include a section on surgical wounds healing by secondary intention[1].

Literature published after 2010 HTA

A good quality Cochrane review from 2015 assessed the effects of NPWT on surgical wounds healing by secondary intention (excluding open abdomen wounds) in any care setting (Dumville *et al,* 2015)[52]. It included two RCTs encompassing 69 patients. One compared NPWT with an alginate dressing in the treatment of open and infected groin wounds; and one compared NPWT with a silicone dressings in the treatment of excised pilonidal sinus. The authors of the review noted that the trials reported limited outcome data for healing, adverse events and resource use. The first study (n=20) suggested that time to healing was shorter for participants in the NPWT group (57 days), compared to the alginate group (104 days), and reported no difference for number of amputations or number of deaths. The second study reported shorter median time of healing in the NPWT group (84 days) compared to the silicone dressing group (93 days). The review authors concluded that the potential benefits and harms of using this treatment for this wound type remain largely uncertain.

Current position in light of new evidence

While the evidence suggests that there may be a benefit of using NPWT on wounds healing by secondary intention, it is too weak to definitively support or refute its use in this patient group.

Surgical wounds: sternal wound infections

The HTA from 2010 stated that no RCTs were identified on the use of NPWT for sternal wound infections that developed after cardiothoracic surgery[1]. Some non-randomised trials and retrospective reviews were included, which suggested that NPWT may be associated with reduced mortality. The overall evidence to endorse NPWT in the routine management of deep sternal wound infections after cardiac surgery was too weak to base any firm conclusions.

Literature published after 2010 HTA

Two systematic reviews from 2013 were identified which evaluated the use of NPWT on patients with sternal wound infections after cardiothoracic surgery[53, 54].

The first systematic review, by Falagas *et al* (2013), included 22 retrospective cohorts encompassing 2,467 patients[53]. The authors combined the data in meta-analyses and reported that patients treated with NPWT had lower mortality compared to patients treated without NPWT. They also reported that NPWT was associated with fewer recurrences, but no difference in length of stay. The authors concluded that "the currently available data from retrospective cohort studies suggest that the use of VAC therapy [*NPWT*] was associated with lower mortality than non-VAC therapy for the treatment of patients with deep sternal wound infections after cardiovascular surgery". However, they also note that the retrospective nature of the studies means that the results need to be treated with caution, and that good-quality RCTs are required.

The second systematic review, by Pan *et al* (2013), aimed to compare NPWT to conventional therapy (standard debridement and drainage therapy) in the treatment of deep surgical site infections, particularly post-sternotomy infections[54]. The authors included 12 'low quality' cohort studies, which together suggest that NPWT might be more effective that standard therapy in the cure of post-

sternotomy mediastinitis and deep-sternal wound infections. However, in line with Falagas *et al.*¸ the authors note the need for good quality RCTs, and the "strong need for actual investigation rather than just observation".

Current position in light of new evidence

The currently available evidence on the use of NPWT in sternal wound infections after cardiothoracic surgery is weak, but suggests that outcomes (including mortality) may be better with NPWT compared to standard therapy.

Surgical wounds: other

Three other systematic reviews were identified, relating to other types of surgical wounds. The reviews evaluated the effectiveness of NPWT in patients with a spinal wound[55]; for enterocutaneous fistula[56]; and the healing of complicated breast wounds[57]. All three concluded that there was a need for further studies.

In addition, a search for RCTs published since the systematic reviews identified a further study that did not fit under the other chapter headings (Johnson *et al*, 2018)[58]. This small RCT included 10 participants (14 wounds) who underwent an extremity fasciotomy following trauma. The aim of the study was to examine the effectiveness of the 'shoelace' technique compared with NPWT on achieving primary skin closure of fasciotomy wounds. The authors reported that after interim analyses, the study was closed early with all five wounds treated with the shoelace technique closed primarily, compared with only one out of nine wounds treated with NPWT.

Current position in light of new evidence

For all other surgical wounds, the evidence is insufficient to support or refute the use of NPWT.

Safety

Safety outcomes reported in the systematic review and RCTs are included in the clinical effectiveness section.

According to documentation from the European Wound Management Association (EWMA) in 2017[59] the following contraindications for NPWT have been established:

- Clotting disorders (risk of bleeding) and acute mild to moderate bleeding in the wound region after injury/debridement. Suction could result in a continuous removal of blood leading to significant blood loss.
- Exposed organs, vessels and vascular anastomoses, which might be altered or damaged by NPWT.
- Necrotic wound bed. Necrotic tissue acts as a barrier to new tissue growth. The use of NPWT must therefore be preceded by radical debridement.
- Untreated osteomyelitis. Due to the deep extension of a potential osteomyelitic focus, simple surface treatment is unlikely to be successful.

- Neoplastic tissue in the wound area. NPWT is thought to enhance granulation tissue formation, and so should not be used in the presence of malignant neoplastic tissue. However, the EWMA document suggests that an exception to this contraindication may be the use of NPWT as a purely palliative measure, as it allows wounds to be covered in a hygienic and clean manner, and may be more comfortable for the patient.

Several manufacturers produce NPWT devices in differing formats, all of which have different applications, wear times, costs and fluid handling properties. Device-specific contraindications and precautions may be detailed in manufacturer guidance, and NPWT users should refer to these.

Patient and social aspects

The HTA from 2010 included a review of the literature, and some primary qualitative research with patients who had experience of NPWT. The findings reported in the HTA are still relevant.

Peer review comments were received from the patient organisation Diabetes Scotland (Linda McGlynn, Regional Engagement Manager Scotland, Diabetes Scotland; 2 November 2018). Patient issues highlighted included:

- There are many differing types of NPWT device available, and this can be confusing.
- In order to make informed decisions, patients and their families/carers should be advised of the benefits and risks associated with NPWT, what alternative treatment options there are, and what to expect with treatment (for example, frequency of dressing changes and the need for analgesia prior to dressing changes).
- Patients should be made aware that the noise made by NPWT devices may change as they move, or as the wound heals, and this does not necessarily mean the device is not working.

Cost effectiveness

The HTA in 2010 included three economic studies[1]. The studies evaluated the use of NPWT for the treatment of foot ulcers or post-amputation wounds in people with diabetes, but only one of the studies evaluated the relative cost effectiveness. The other two studies reported on health outcomes and costs separately. All three studies were conducted in the US care setting, thus the relevance of their comparators and their generalisability to NHSScotland was unclear. Overall, the HTA concluded that there was insufficient evidence to draw conclusions on the cost effectiveness of NPWT.

A literature search conducted for economic studies published between 2013 and 2018 highlighted an additional seven studies[60-66]. One study was UK-based[65].

The UK-based study evaluated the cost effectiveness of single-use NPWT in patients undergoing primary hip and knee replacements[65]. A decision analytic model was developed, with a 6 week post-operative time horizon. The clinical-effectiveness data used in the analysis came from a single RCT (Karlakki et al, 2016[37]). The RCT (n=220) reported a reduction in dressing changes (1.79 fewer; p=0.002), surgical site complications (2% versus 8.4%; p=0.06) and length of hospital stay (3.8 days

versus 4.7 days; p=0.07) in favour of single-use NPWT compared with standard care. It should be noted that the latter two outcomes were not statistically significant at the 5% level.

Single-use NPWT was associated with a 0.0014 increase in Quality-Adjusted Life Years (QALYs) and 0.07 fewer wound-related complications compared to standard care. These small differences in health outcomes likely reflect the non-statistically significant findings from the RCT by Karlakki *et al*. The model predicted a reduction of £1,132 in total mean treatment cost per patient (£5,602 for single-use NPWT and £6,713 for standard care). This would make single-use NPWT a cost saving intervention, although it was unclear from the analysis whether the difference in costs can be attributed to lower incidence of complications or a reduction in resource use. Results of the sensitivity analysis showed that the model was most sensitive to mean length of hospital stay associated with standard care. Varying the mean length of hospital stay for patients receiving standard care from 4.7 to 4.1 days reduced the difference in costs to £348. The findings of this analysis should therefore be treated with caution given the uncertainty around some of the model parameters.

The remaining six economic studies were from the US[60, 61, 63, 64], Denmark[62] or Australia[66], and so their generalisability to the context in NHSScotland is unclear. The main findings from the studies are presented here for information:

- Chopra *et al* (2016): This US-based cost-utility analysis compared closed-incision NPWT with standard dressings following closure of abdominal incisions in high-risk patients[60]. The authors concluded that closed-incision NPWT is cost-saving following closure of abdominal incisions in high-risk patients. However, the cost-utility analysis was partly informed by a meta-analysis of low quality studies[32].
- Lewis *et al* (2014): This US-based study aimed to determine the reduction in the rate of wound complications that would render the use of prophylactic NPWT cost saving compared to routine care following laparotomy for gynaecologic malignancy. A decision tree was designed from a payer perspective. The authors concluded that if the wound complication rate can be reduced by one-third, prophylactic NPWT is potentially cost saving in high-risk women undergoing laparotomy for gynaecologic malignancy[64].
- Echebiri *et al* (2015): This US-based cost-benefit analysis suggested that NPWT should not be used on closed laparotomy incisions in patients with low risk of post caesarean delivery SSIs. However, the analysis also suggested that "among patients with a high risk of surgical site infections prophylactic negative pressure wound therapy is potentially cost-beneficial"[61].
- Tuffaha *et al* (2015): This study aimed to evaluate the cost-effectiveness of NPWT compared with standard dressings in preventing SSI in obese women undergoing elective caesarean sections. The analysis was from the perspective of Queensland Health, Australia, and used a decision model. Parameters were obtained from the existing published studies, a pilot clinical trial and expert opinion. Based on the parameters used in the model NPWT appeared to be cost effective. However, the authors also acknowledge that the evidence used was not robust, and that there was a need for further research to establish clinical effectiveness before conclusions on cost effectiveness were possible[66].

- Hampton *et al* (2015): This study, from Denmark, included nine patients with leg ulcers or pressure ulcers that had been slow in healing. The study reported costs and health outcomes separately. The authors concluded that "wounds decreased in size and healed more quickly under NPWT treatment that under standard treatment" and that "additional NPWT costs can be quickly offset by faster healing and a shortened treatment period"[62].
- Kempton *et al* (2015): This retrospective US-based study compared NPWT to conventional compressive dressings for spit-thickness skin grafts placed on healthy, low-risk wounds. As well as reporting on clinical outcomes, the authors reported on the cost difference. This study included 195 people who had received split-thickness skin grafts, though 35 were lost to follow-up, leaving 120 treated with NPWT and 40 with compressive dressings. The authors reported high rates of healing in both groups (91/120 in NPWT group and 37/40 in the compressive dressing group). Patients treated with compressive dressings had a higher likelihood of healing relative to those treated with NPWT (p=0.018). NPWT was the more expensive treatment, costing $2,370 (approximately £1,827) more per patient. Based on these findings, the authors concluded that "the increased cost of NPDs [*NPWTs*] is not justified in wounds that are at low risk of developing STSG [*split thickness skin graft*] failure"[63].

In summary, based on the published literature, it is not possible to make robust conclusions on the cost-effectiveness of NPWT in any wound type.

After this evidence note was drafted, a Cochrane review was published on the use of NPWT in treating open traumatic wounds (Iheozor-Ejiofor Z et al, 2018)[22]. The main results from this have been detailed in the clinical effectiveness section. However, it also reported cost-effectiveness data from an RCT (Costa et al, 2018). This RCT has been included in the clinical effectiveness section, but the economic data was in press at the time of writing. Therefore the details presented here have been taken from the Cochrane review rather than the primary study.

Costa et al compared NPWT to standard wound management in patients with severe open fracture of the lower limb. They reported that it was unlikely that NPWT was a cost-effective treatment. The mean total cost of resource was £678 (95% CI -1,082 to 2,438) more in the NPWT group. Incremental mean QALYs were slightly higher in the NPWT group (0.002, 95% CI -0.0054 to 0.059). This gives an incremental cost-effectiveness ratio (ICER) of £267,910. The authors also assessed the probability of NPWT being cost effective for open fracture wounds at cost-per-QALY thresholds of £15,000 to £30,000. The probability of NPWT being cost effective at these thresholds was never more than 27%. The Cochrane review rated this evidence as 'moderate-certainty'.

Conclusion

The HTA published in 2010 highlighted the need for good quality RCTs on NPWT, and this has been echoed in more recently published systematic reviews. Unfortunately, the lack of RCTs for most wound types has not changed since the 2010 HTA.

This review of the clinical effectiveness evidence highlighted that there is still insufficient (or inconsistent) evidence from RCTs on which to give robust advice on the use of NPWT for most wound types. It was also not possible to draw conclusions on the cost effectiveness of NPWT across different wound types.

NPWT has been used to treat wounds for approximately 20 years, and its use in NHSScotland has expanded in that time to include a broad range of specialities. While it was originally used for harder to heal chronic wounds, it is now a widely diffused treatment which is often used prophylactically, or on wounds which may heal equally as well with conventional dressings. In addition, there are anecdotal concerns that with this spread of use, NPWT is occasionally being used on wounds for which it is contraindicated, or where precautions are required. There is strong support from the clinical community for NPWT, and in certain wound types (notably foot wounds in people with diabetes) there is some evidence backing its use. It is feasible that NPWT could improve clinical outcomes in other wound types, however this is yet to be demonstrated in robust clinical trials.

In the absence of robust RCT evidence it is not possible to give advice regarding the use of NPWT for most wound types. This conclusion is unlikely to help address the possible over-use of this technology in NHSScotland. Therefore, a group of clinical experts, including various specialities and NHS boards, was convened to produce a set of consensus statements to guide the appropriate use of NPWT in Scotland. These statements have been published as a supplement to this evidence note and the associated advice from SHTG.

Identified research gaps

There is a need for good quality RCT evidence on the use of NPWT in most wound types.

Equality and diversity

Healthcare Improvement Scotland is committed to equality and diversity in respect of the nine equality groups defined by age, disability, gender reassignment, marriage and civil partnership, pregnancy and maternity, race, religion, sex, and sexual orientation.

The process for producing evidence notes has been assessed and no adverse impact across any of these groups is expected. The completed equality and diversity checklist is available on www.healthcareimprovementscotland.org

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References can be accessed via the internet (where addresses are provided), via the NHS Knowledge Network www.knowledge.scot.nhs.uk, or by contacting your local library and information service. A glossary of commonly used terms in Health Technology Assessment is available from htaglossary.net.

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Abbreviations

cNPWT	Closed incision negative pressure wound dressing
HTA	Health technology assessment
NPWT	Negative pressure wound dressing
RCT	Randomised controlled trial
STSG	Split thickness skin graft
SSI	Surgical site infection
TNP	Topic negative pressure (different term for NPWT)