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Synopsis

Clinical and cost-effectiveness of negative pressure wound therapy versus usual care for surgical wounds healing by secondary intention: the SWHSI 2 pragmatic RCT

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Abstract

Background: Surgical wounds healing by secondary intention occur if a surgical wound is not closed or dehisces following primary closure.

Surgical wounds healing by secondary intention are common and adversely affect patients' quality of life. Treatment is often prolonged, complex and expensive.

Negative pressure wound therapy applies a controlled vacuum to the wound and is increasingly used to promote surgical wound healing by secondary intention despite limited rigorous evidence for the clinical and cost-effectiveness of negative pressure wound therapy to augment surgical wound healing by secondary intention.

Objective: Assess the clinical and cost-effectiveness of negative pressure wound therapy versus usual care (no negative pressure wound therapy) in treating surgical wounds healing by secondary intention.

Design and methods: A pragmatic, two-arm, parallel-group, randomised controlled superiority trial. Twenty-eight UK NHS Trusts randomised adult patients with a surgical wounds healing by secondary intention to receive negative pressure wound therapy or usual care (no negative pressure wound therapy). The planned sample size was 696 participants.

Participants were followed up for 12 months via weekly telephone contact to collect the primary outcome (time to healing: full cover with no scab in days since randomisation) and clinical secondary outcomes: wound healing, surgical site infection, pain, hospital re-admission, current treatment and reasons for treatment change (if applicable), reoperation, amputation, antibiotic use, death.

Patient-reported outcomes (pain, health-related quality of life and resource use) were collected by postal questionnaire at 3, 6 and 12 months. Validation of the Bluebelle Wound Healing Questionnaire, a patient-reported measure of surgical site infection, was also undertaken.

A cost-effectiveness decision model considering all available evidence, and a within-trial cost-utility analysis, was also undertaken to evaluate the cost-effectiveness of negative pressure wound therapy against usual care.

Neither participants nor the investigators were blind to treatment allocation.

Results: Between 15 May 2019 and 13 January 2023, 686 participants were recruited, randomised and included in the analysis (negative pressure wound therapy $n = 349$; usual care $n = 337$). Most participants had a single surgical wound healing by secondary intention ($n = 622$, 90.7%), located on the foot ($n = 551$, 80.3%) or leg ($n = 69$, 10.1%) arising following vascular surgery ($n = 619$, 90.2%). Most participants had comorbidities; diabetes ($n = 549$, 80.0%), cardiovascular disease ($n = 446$, 65.0%) and/or peripheral vascular disease ($n = 349$, 50.9%).

Median time to healing was 187 days (negative pressure wound therapy) versus 195 days (usual care), with no evidence that negative pressure wound therapy reduced the time to wound healing compared to usual care (hazard ratio 1.08, 95% CI 0.88 to 1.32; $p = 0.47$).

Odds of re-admission, reoperation, surgical site infection and antibiotic use were slightly higher, and odds of amputation or death slightly lower for negative pressure wound therapy participants. These results were not clinically or statistically significant. Bluebelle Wound Healing Questionnaire, quality of life and wound pain scores were not statistically significantly different at any time point. Serious adverse events were rare (nine negative pressure wound therapy vs. five usual-care participants).

Both cost-effectiveness analyses concluded that negative pressure wound therapy generates higher costs and marginally higher quality-adjusted life-years than usual care, although findings were statistically insignificant. The probability of negative pressure wound therapy being cost-effective was under the recommended National Institute for Health and Care Excellence cost-effectiveness thresholds.

The Bluebelle Wound Healing Questionnaire was acceptable to participants, had low levels of missing data and demonstrated good levels of sensitivity and specificity in the detection of surgical site infection in surgical wounds healing by secondary intention.

Limitations: The trial included a high proportion of diabetic participants with foot wounds, which may affect study generalisability. Negative pressure wound therapy use for 'wound management', common in certain surgical specialties, was not assessed in this study.

Conclusions: Negative pressure wound therapy is not clinically or cost-effective in augmenting healing in patients with surgical wounds healing by secondary intention, particularly those with comorbidities.

Future work: Evaluation of methods to treat or prevent infection of surgical wounds healing by secondary intention and evaluation of negative pressure wound therapy for 'wound management' are recommended.

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A plain language summary of this synopsis is available on the NIHR Journals Library Website <https://doi.org/10.3310/GJIC1716>.

Introduction

Background and rationale

Following an operation, wounds are usually closed with stitches, glue or clips (healing by primary intention). When this is not possible, or a closed wound breaks open (dehiscence), wounds may be left open to heal through the formation of granulation tissue from the bottom upwards (healing by secondary intention).

With a large number of surgical operations taking place in the NHS, surgical wounds healing by secondary intention (SWHSI) are common, estimated at 4.1 per 10,000 population.¹

Treatment of these wounds is often prolonged, complex and expensive. In a cohort study of SWHSI wounds, median time to healing was 86 days, with foot and leg wounds taking almost twice as long to heal as wounds in other locations (182 and 127 days, respectively).² Infections, hospital re-admission and the need for further surgical procedures as a result of SWHSI are common.² Prolonged time to healing and wound complications adversely affect patients' quality of life.^{3,4}

Negative pressure wound therapy (NPWT) devices may be used as part of the treatment pathway for SWHSI. These devices apply a controlled negative pressure (vacuum) to wounds via a special dressing. Manufacturers suggest

that the negative pressure generated aids wound healing by: removing exudate and infective materials; reducing oedema; and increasing perfusion and granulation.⁵ The cost of NPWT treatment has previously been estimated to be £1323 per month compared to £441 per month for standard wound dressings.⁶

Negative pressure wound therapy use as a treatment for SWHSI has increased greatly over recent years.⁷ Despite this, a Cochrane Systematic Review of the use of NPWT for treatment of SWHSI identified no rigorous randomised controlled trial (RCT) evidence on the clinical effectiveness of NPWT and therefore the benefits and harms of the treatment remained uncertain.⁸ The review found only two RCTs ($n = 69$ participants) comparing NPWT with standard care.^{9,10} In both studies, the data were poorly analysed and reported, and therefore caution in the interpretation of any results was advised.⁸ A further review of NPWT for diabetic foot wounds,¹¹ identified a further RCT ($n = 76$ participants).¹² Again caution in interpretation of the findings was advised given the population was not necessarily generalisable to all diabetic foot wound patients, was commercially funded and at risk of performance bias.¹¹

Given the increased use of NPWT for SWHSI in routine clinical practice, despite the absence of effectiveness evidence, an adequately powered RCT was warranted to investigate if NPWT was superior to usual care in treating SWHSI in relation to time to wound healing. To ensure the best use of future NHS resources, the study also needed to determine the cost-effectiveness and the potential harms and benefits of NPWT compared to usual-care dressings.

Objective

To assess the clinical and cost-effectiveness of NPWT as compared to usual care (no NPWT) in treating SWHSI.

Methods

Design, participants and interventions

We undertook a pragmatic, cross surgical specialty, two arm, parallel-group, randomised controlled superiority trial in 27 UK NHS secondary care hospitals and one community NHS trust in England. The study also included a 6-month internal pilot phase to assess site set up, participant randomisation, intervention delivery and follow-up rates.

As summarised in [Figure 1](#), adult patients with a SWHSI who met the eligibility criteria as set out in the protocol,¹³ were randomised to receive either NPWT or usual care and were followed up for 12 months. Randomisation was stratified by wound location (foot, ankle, leg, abdomen or other), wound area ($< 28 \text{ cm}^2$, $\geq 28 \text{ cm}^2$) and study centre.

Data including demographics, comorbidities, smoking status, surgical procedure details and a wound photograph were collected at baseline.

The choice of NPWT device (providing pressure of 60–150 mmHg), wound dressing and co-intervention treatment choices were left to the discretion of the clinical care team.

Clinical effectiveness outcomes

Primary outcome

Patient and public input identified faster healing was a key outcome for patients with a SWHSI. The primary outcome was therefore chosen to be the time to healing in days since randomisation (defined as complete epithelial cover in the absence of a scab). Participants were contacted weekly by a research nurse and asked if a healthcare professional had indicated that their wound had healed.

Initially, healing was planned to be verified by face-to-face clinical assessments at research nurse visits for 3 consecutive weeks with a photograph taken at each visit to facilitate independent blinded review of healing. During the trial, to ease the burden on both participants and research nurses, healing verification was modified to be by a single in-person assessment followed by two subsequent weekly telephone calls to the participant. During the COVID-19 pandemic, where in-person visits could not be undertaken safely, the options of a video call (capturing an image of the wound via screenshot) or a phone call (with request for a photograph to be sent by the participant) were implemented for the first healing verification visit.

Due to redeployment and pressures resulting from the COVID-19 pandemic and/or where site capacity was reduced for any reason, the coordinating centre (York Trials Unit, University of York) undertook weekly participant follow-up and post-healing assessments by telephone. For participants who withdrew from follow-up, with participant consent, the research nurses continued to access clinical notes to obtain a date of wound healing. The same approach was used for participants lost to follow-up.

Secondary outcomes

Clinical secondary outcomes were collected during weekly assessments with participants and review of medical notes, and included:

- antibiotic treatment
- hospital re-admission
- treatment status
- reoperation
- amputation

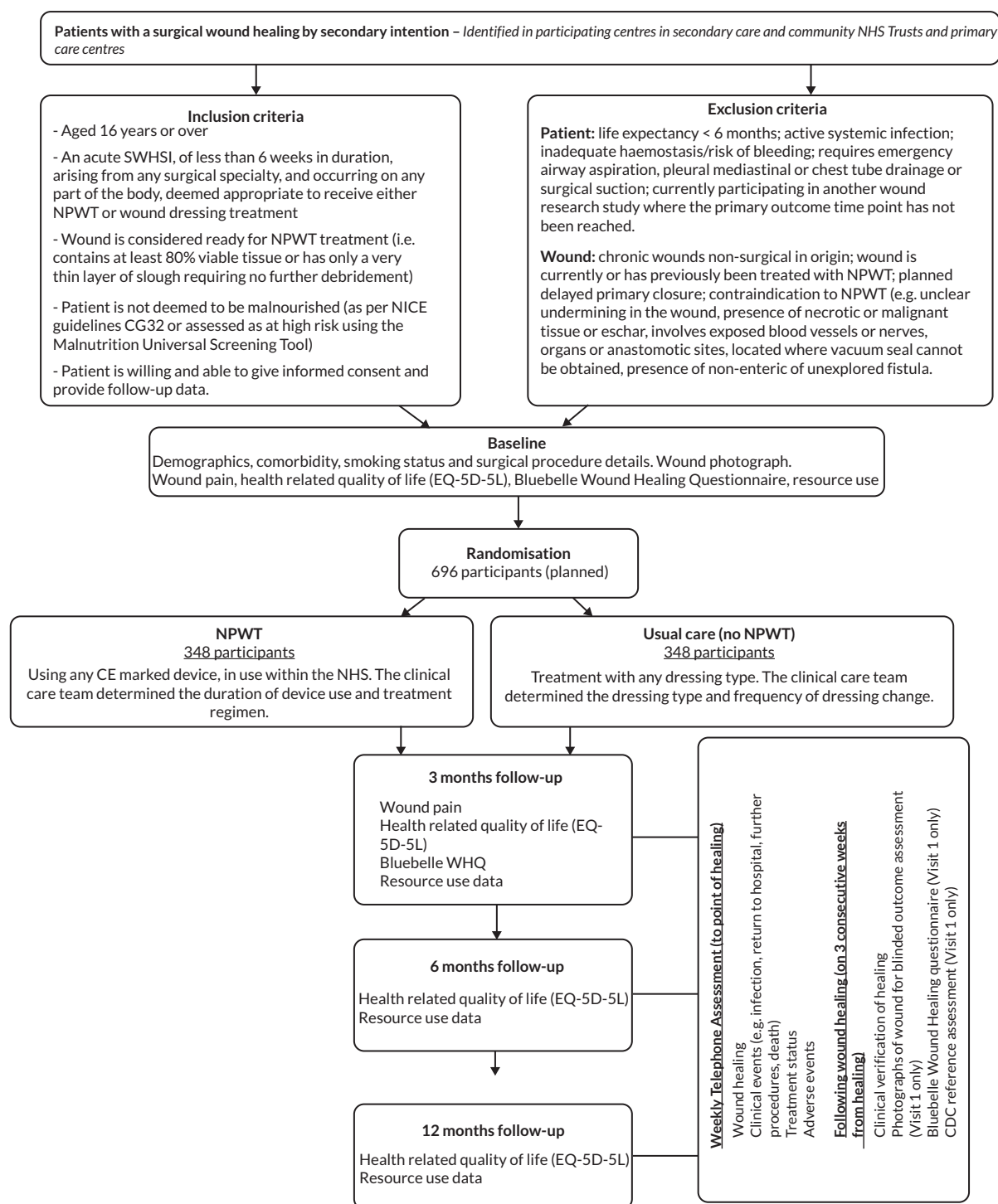


FIGURE 1 Study flow diagram. CDC, Centre for Disease Control and Prevention; EQ-5D-5L, EuroQol-5 Dimensions, five-level version; NICE, National Institute for Health and Care Excellence; WHQ, Wound Healing Questionnaire

- death
- accident and emergency (A&E) and outpatient appointments
- additional treatments and medications.

Blinded assessment of wound healing photographs was completed to verify wound healing status,¹⁴ given that participants, the clinical and research teams were unblinded to treatment allocation and outcome assessment.

Patient-reported wound pain, as a clinical effectiveness outcome, was completed by participants at baseline, 3, 6 and 12 months* using a visual analogue scale: range 0 (no pain) to 100 (worst imaginable pain).

Cost-effectiveness outcomes

- Health-related quality of life [(HRQoL; using EuroQol-5 Dimensions, five-level version (EQ-5D-5L)] across five dimensions (mobility, self-care, usual

activities, pain/discomfort and anxiety/depression) and using five severity levels (no problems, slight problems, moderate problems, severe problems and unable/extreme problems). A visual analogue scale records overall health evaluation ranging from 100 (best imaginable health) to 0 (worst imaginable health).¹⁵

- Resource use (wound-related NHS consultations and support).

Additional patient-reported outcomes: questionnaire validation

Surgical site infection (SSI) using a modified Bluebelle Wound Healing Questionnaire (WHQ):¹⁶ range 0–33; lower scores represent fewer problems.*

*To improve participant questionnaire response rates partway through the trial, the Bluebelle WHQ and wound pain measures ceased to be collected at 6 and 12 months with the aim of reducing participant burden (See [Appendix 1](#), [Table 7](#)).

Sample size, randomisation and analysis

The planned sample size of the trial was 696 participants based on detecting a 25% reduction in median time to healing with 90% power and allowing for 20% attrition. This assumed a median time to healing of 86 days in the usual-care group.² The 25% reduction in time in healing was selected based on cost-effectiveness models from observational data,⁶ research literature^{9,10,12,17} and significance to patients, through patient and public involvement (PPI). This equated to an estimated 21-day reduction in time to healing. The attrition rate was based on rates in similar previous studies.^{2,12,18}

Randomisation to NPWT or usual care (1 : 1) was stratified by wound location (foot and ankle, leg, abdomen or other), wound area (< 28 cm², ≥ 28 cm²) and study centre, using variable block sizes (two, four, six and eight). The allocation sequence was independently generated by the trial statistician and was implemented using a centralised secure internet randomisation service hosted by York Trials Unit, University of York.

Analyses were completed in R version 4.4.0 (The R Foundation for Statistical Computing, Vienna, Austria) and Stata version 18 (StataCorp LP, College Station, TX, USA) on an intention to treat basis using two two-sided significance tests at the 5% significance level, with parameter estimates presented with associated 95% confidence intervals (CI) and *p*-values as appropriate.

Prespecified statistical and health economics analysis plans were developed prior to the completion of data collection (see [Report Supplementary Materials 1 and 2](#) and www.isrctn.com/ISRCTN26277546).

The primary outcome (time to reference wound healing) was assessed using a Kaplan–Meier curve, the median time to healing and hazard ratio (HR) with 95% CIs calculated using a proportional hazards Cox regression model. The model adjusted for baseline wound size, wound duration and wound location (fixed effects) and centre (shared frailty effect). For eight missing baseline wound area measurements and three wound durations, mean imputation was used. Time to healing was right-censored at the last point at which the wound was known to still be unhealed, that is the earliest of 12 months post randomisation, loss-to-follow-up, full withdrawal, death or amputation of the SWHSI.

Sensitivity analyses were completed to account for death and amputation as competing risks, to correct for stratification errors, and to adjust for baseline imbalances in smoking and alcohol consumption.¹⁹ Compliance was assessed with a Complier Average Causal Effect analysis using an instrumental variable approach,²⁰ and a prespecified subgroup analysis was completed to account for previous history of SWHSI. The primary analysis was also repeated using outcomes derived from blinded wound healing assessments with other wounds treated as healed in the primary analysis censored at the date of healing.

Wound Healing Questionnaire and wound pain scores were analysed using a covariance pattern linear mixed model adjusting for baseline measure, wound size, wound duration and location as fixed effects and site and participant as random effects. Clinical events were analysed using a mixed effect logistic regression model adjusting for wound size at baseline, duration of wound in days and wound location as fixed effects, and site as a random effect. Adverse events were summarised by trial arm and overall.

Under the UK NHS perspective, the cost-effectiveness of NPWT was evaluated using a decision-analytic Markov cohort model, extrapolating the SWHSI-2 trial results and considering other relevant evidence, in order to estimate the lifetime costs and outcomes [quality-adjusted life-years (QALYs)] of NPWT and usual care using a time horizon of 30 years. The model's structure was based on inputs related to the key health states of patients with SWHSI: healed SWHSI, unhealed SWHSI and death and considered three main health state transitions: from unhealed to healed

SWHSI, from unhealed SWHSI to death and from healed SWHSI to death. Systematic literature reviews were undertaken to inform key model parameters, including clinical effectiveness, HRQoL, costs and resource use and mortality. When possible, evidence on these parameters was synthesised using Bayesian meta-analyses. The economic model structure, components, and data sources are presented in [Appendix 4, Figure 3](#). The net monetary benefit (NMB) and probability of cost-effectiveness were estimated, and extensive scenario analyses were conducted to evaluate the robustness of results and the degree of uncertainty. In addition, a within-trial cost-utility analysis was performed within the trial's follow-up period of 12 months. Total QALYs and costs were aggregated and analysed for each treatment group with missing data imputed via multiple imputation by chained equations, adjusted for participant baseline characteristics, baseline EQ-5D index scores and baseline costs. Missing data on QALYs and costs were assumed to be missing at random (MAR). The adjusted mean difference in QALYs and costs between the treatment groups was estimated via seemingly unrelated regressions of 10,000 bootstrapped samples, to estimate the incremental QALYs and the incremental costs. Sensitivity analyses were undertaken, including complete-case analysis (SA.1), exclusion of participants who died during the study's follow-up period (SA.2) and addressing treatment crossover effects (SA.3). See [Appendix 4](#).

Cost estimates for both NPWT and usual care were obtained following the collection and analysis of resource use data. Questionnaires completed by trial participants at baseline, 3, 6 and 12 months of follow-up, provided information about primary care service use (e.g. general practitioner (GP) surgery visits, nurse home visits) and medication use (e.g. antibiotics, analgesics). Secondary care health resource use data (e.g. hospital admissions with/without an overnight stay, hospital outpatient appointments and A&E visits) were collected using an annual investigator-completed resource use questionnaire. [Appendix 4 \(Tables 11–13\)](#) presents the unit costs used for both economic analyses. Costs in both economic analyses are expressed

in 2022 prices. The EQ-5D-5L questionnaire was used as an instrument to evaluate HRQoL. Participants completed the EQ-5D-5L questionnaire at baseline, 3, 6 and 12 months of follow-up. Participant responses to the EQ-5D-5L questionnaire were valued through mapping to the corresponding Three Levels questionnaire, in line with National Institute for Health and Care Excellence (NICE) guidance. EQ-5D index scores range from 1 (full health) to 0 (death), with negative values representing a HRQoL worse than death. QALYs for the within-trial cost-utility analysis were estimated using the area under the curve approach according to the EQ-5D scores at baseline and follow-up points. QALYs and costs associated with NPWT and usual care were not discounted in the within-trial cost-utility analysis due to the 12-month time horizon; however, both QALYs and costs were discounted at 3.5% per year in the long-term Markov cohort decision model in line with NICE guidance.

Analysis and validation of the Bluebelle WHQ was assessed by comparing participants' Bluebelle WHQ total score with the surgical site infection (SSI) reference assessment [based on the Centres for Disease Control and Prevention (CDC) criteria/classification system].²¹ A contingency table of WHQ total score and the binary reference assessment of SSI was examined, with sensitivity and specificity values and 95% CIs calculated for a range of WHQ thresholds. Sensitivity and one-specificity values were used to plot a receiver operating characteristic (ROC) curve. Acceptability of the WHQ was assessed using (1) questionnaire return rates at each time point, (2) levels of missing data, (3) answers to additional questions about acceptability collected as part of the study at the post-healing visit.

Results summary

Internal pilot

Using a pre-specified traffic light grading system, the internal pilot phase was assessed including activity occurring up to 3 January 2020. Performance against the prespecified criteria is summarised in [Table 1](#).

TABLE 1 Surgical wounds healing by secondary intention-2 pilot criteria and performance

Criteria		Status on 3 January 2020
Set up at least 10 sites	Green > 80% Amber 60–80% Red < 60%	Green – 120%; 12 sites opened to recruitment
Randomise 100 participants		Amber – 63%; 63 participants recruited
Intervention delivery within 48 hours		Green – 96%; 26 participants received intervention within 48 hours (of 27 recruited to intervention)
Non-response rate to postal follow-up (3 months)	Green ≤ 15% Amber 15–20% Red > 20%	Red – 38%

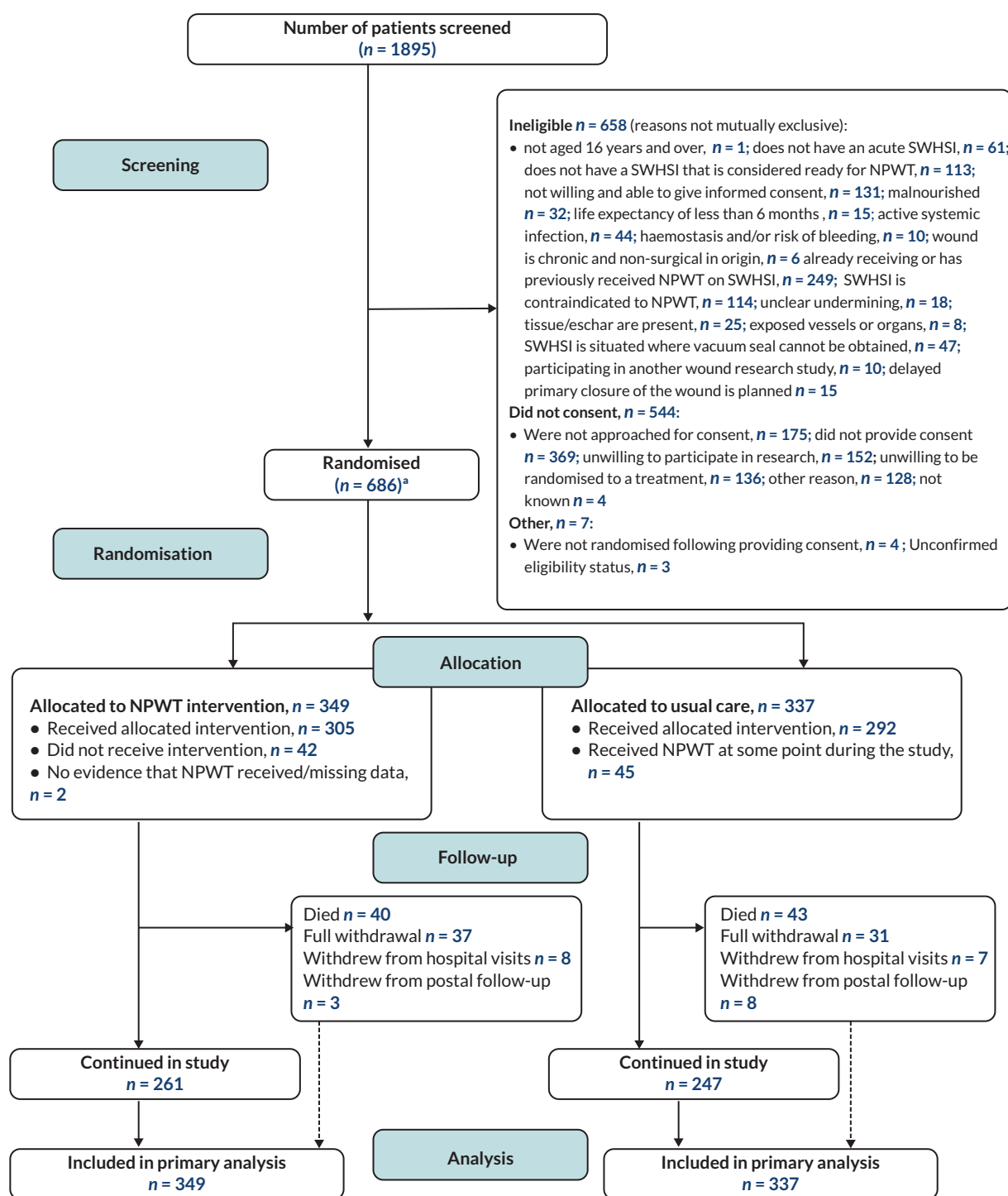


FIGURE 2 Trial CONSORT diagram. a, There were 6 system randomisation errors where the same participant was randomised multiple times. These were removed from any analysis leaving 686 participants.

Where assessment indicated an amber or red rating (i.e. randomisation and follow-up), mitigations for the lower than anticipated performance were identified.²² For recruitment, mitigations included two sites having not been open for sufficient time to contribute to recruitment and three sites yet to commence recruitment. Follow-up mitigations included the fact that there were only data available for a small number of participants at the time of reporting (n = 21) and there was no missing time to

healing data for participants randomised.²³ As a result, approval was obtained for the study to continue progress to full trial.²²

Clinical results

Results of the trial have been published separately.²³ In summary, between 15 May 2019 and 13 January 2023, 1895 patients with a SWHSI were screened and of these 686 (36.2%) were consented and randomly assigned to

receive NPWT ($n = 349$) or usual care that is standard dressings without NPWT ($n = 337$). Participants were followed up for 12 months following randomisation, with final follow-up completed on 13 January 2024.

As shown in [Table 2](#), the baseline characteristics of participants were considered balanced across groups for all categories, except for smoking status and alcohol consumption. The median participant age was 63 years [interquartile range (IQR) 55–72 years], most participants were male ($n = 513$, 74.8%) and of White ethnicity ($n = 630$, 91.8%).

Most participants had a single SWHSI ($n = 622$, 90.7%), with most wounds arising following vascular surgery ($n = 619$, 90.2%) and located on the foot or leg ($n = 620$, 90.4%).

Most participants were diabetic ($n = 549$, 80.0%), and approximately two-thirds of participants had cardiovascular disease (CVD; $n = 446$, 65.0%) and half had peripheral vascular disease (PVD; $n = 349$, 50.9%).

Participants who were randomised to receive NPWT, received this for a mean duration of 46.6 days [standard error (SE) = 4.1], following which they received usual-care dressings. Approximately 50% of participants ([Table 3](#)) received a Renasys NPWT system (Smith and Nephew), with most of the remaining participants ($n = 131$, 44%) receiving a KCI NPWT system. Single-use NPWT dressings (PICO, Smith and Nephew) were only used by a limited number of participants. Continuous pressure was widely used with a mean pressure of 101.4 mmHg (min 40 mmHg; max 125 mmHg).

Participants allocated to receive usual care received standard dressings for a mean duration of 164.3 days (SE = 4.7).

By 12 months, wound healing had occurred in 202 participants (57.9%) allocated to NPWT and 196 participants (58.2%) allocated to usual care, with a difference of 8 days in the median time to healing (187 days NPWT vs. 195 usual care). One hundred and fifty-nine participants were censored in the analysis due to death, amputation, withdrawal or loss to follow-up.

The primary analysis HR for time to wound healing was 1.08 (95% CI 0.88 to 1.32, $p = 0.47$). Findings were similar for all prespecified sensitivity and subgroup analyses (see [Appendix 2](#), [Tables 8](#) and [9](#)), and for the secondary outcome of blinded outcome assessment of healing (HR 1.13, 95% CI 0.87 to 1.47).

As shown in [Table 4](#), the odds of hospital admission, reoperation, SSI and antibiotic use were slightly higher for NPWT participants compared to usual care. The odds of amputation and death were slightly lower in the NPWT group.

As shown in [Table 5](#), there was no evidence of a difference in WHQ (SSI) scores or wound pain any time point between the trial groups.

Across the two groups, rates of adverse events were similar [NPWT 150/349 (43.0%) vs. usual care 139/337 (41.2%), risk difference -1.7% (95% CI -9.1 to 5.7%), [Table 6](#)]. SSI was the most common adverse event reported with total events similar between the two groups (NPWT 43% vs. usual care 41.2%). Fourteen serious adverse events were reported [NPWT $n = 9$; usual care $n = 5$, risk difference -1.3 (95% CI -3.4 to 0.6)]. Major SSI was the most common type of serious adverse event, with the majority deemed unrelated or unlikely to be related to study treatment ($n = 10$, 71.4%).

Cost-effectiveness results

The within-trial economic analysis found that NPWT increased QALYs by 0.007 (95% CI -0.024 to 0.038) and increased healthcare costs by £251.44 (95% CI $-£2192.63$ to £2695.52) over the 12-month study period, although these results were not statistically significant. The probability of NPWT being cost-effective is less than 50% at £20,000 and £30,000 cost-effectiveness thresholds. As detailed in [Appendix 4](#), sensitivity analysis confirms the low probability of NPWT being cost-effective when participants who died during the study were excluded from the analysis (SA.2), and when treatment crossover effects were considered (SA.3). The complete case analysis (SA.1) suggests that NPWT might be cost-effective, but due to the extent of missing data (75.7%), and the fact that the QALY and cost data are unlikely to be missing completely at random (MCAR) following logistic regressions of missing QALYs and costs (see [Appendix 4](#), [Table 14](#)), these findings are likely to be biased. [Appendix 4](#) presents the proportions of EQ-5D-5L dimensions by intervention group at each follow-up point (see [Appendix 4](#), [Table 15](#)), EQ-5D scores by intervention group at each follow-up point and QALYs [see [Appendix 4](#), [Table 16](#) (complete data) and [Table 17](#) (multiply imputed data)], as well as the total costs over the 12-month follow-up period for each intervention group [see [Appendix 4](#), [Table 18](#) (complete data) and [Table 19](#) (multiply imputed data)]. Moreover, [Appendix 4](#), [Tables 20–23](#) and [Figures 4–11](#) present the findings from the within-trial base-case analysis and the sensitivity analyses, including incremental NMB, cost-effectiveness planes and cost-effectiveness acceptability curves (CEAC).

TABLE 2 Baseline characteristics of randomised and analysed participants by treatment group

	NPWT (N = 349)	Usual care (N = 337)
Age (years)	62.00 (54.0, 71.0)	64.00 (55.0, 72.0)
Median (IQR)		
Gender		
Male	267 (76.5%)	246 (73.0%)
Female	79 (22.6%)	91 (27.0%)
Missing data	3 (0.9%)	0 (0.0%)
Ethnicity		
White	317 (90.8%)	313 (92.9%)
Asian or Asian British	14 (4.0%)	14 (4.2%)
Black or Black British	11 (3.2%)	9 (2.7%)
Other ethnicity	1 (0.3%)	0 (0.0%)
Missing data	6 (1.7%)	1 (0.3%)
Smoking status		
Never	121 (34.7%)	143 (42.4%)
Current	66 (18.9%)	53 (15.7%)
Previous	158 (45.3%)	140 (41.5%)
Missing data	4 (1.1%)	1 (0.3%)
Routine alcohol consumption		
Yes	125 (35.8%)	128 (38.0%)
Comorbidities		
CVD (hypertension, myocardial infarction, angina or heart failure)	218 (66.3%)	228 (71.9%)
PVD	181 (55.0%)	168 (53.0%)
Diabetes	281 (85.4%)	268 (84.5%)
Surgery type		
Vascular	314 (90.0%)	305 (90.5%)
Colorectal	9 (2.6%)	14 (4.2%)
Plastics	2 (0.6%)	1 (0.3%)

continued

TABLE 2 Baseline characteristics of randomised and analysed participants by treatment group (*continued*)

	NPWT (N = 349)	Usual care (N = 337)
Other	21 (6.0%)	17 (5.0%)
Missing data	3 (0.9%)	0 (0.0%)
Urgency of surgery		
Elective	141 (40.4%)	143 (42.4%)
Emergency	205 (58.7%)	194 (57.6%)
Missing data	3 (0.9%)	0 (0.0%)
Contamination level of surgery (as defined by CDC criteria)¹²⁴		
Clean	94 (26.9%)	77 (22.8%)
Clean contaminated	36 (10.3%)	30 (8.9%)
Contaminated	26 (7.4%)	20 (5.9%)
Dirty	190 (54.4%)	210 (62.3%)
Missing data	3 (0.9%)	0 (0.0%)
Wound area in cm² Mean (SD)	26.41 (30.4)	27.53 (41.3)
Wound location		
Foot	279 (79.9%)	272 (80.7%)
Leg	40 (11.5%)	29 (8.6%)
Abdomen	11 (3.2%)	13 (3.9%)
Other	19 (5.4%)	23 (6.8%)
Number of SWHSIs		
1	318 (91.1%)	304 (90.2%)
2	21 (6.0%)	28 (8.3%)
3 or more	7 (2.0%)	5 (1.5%)
Missing data	3 (0.9%)	0 (0.0%)
Previous history of SWHSI	57 (17.6%)	51 (16.0%)
SWHSI currently infected (based on clinical opinion)	54 (15.6%)	41 (12.2%)

The bold text is used to distinguish the overarching variable from the response options provided.

TABLE 3 Negative pressure wound therapy devices used

Type of NPWT machine used	NPWT (n = 349)
V.A.C Ultra (KCI)	38 (13%)
V.A.C Via (KCI)	9 (3%)
InfoV.A.C (KCI)	5 (2%)
ActiV.A.C (KCI)	79 (26%)
Renasys (Smith and Nephew)	149 (49%)
PICO (Smith and Nephew)	21 (7%)
Other	1 (0%)
Machine type not reported	3
Did not receive NPWT	44

TABLE 4 Clinical secondary outcomes for NPWT and usual-care groups

Clinical event	NPWT n/N%		Usual care n/N%		Treatment difference (95% CI) ^a	p-value
Hospital admission	320	63/320 (19.7%)	320	58/320 (18.1%)	1.13 (0.76 to 1.69)	0.54
Reoperation	320	78/320 (24.4%)	320	69/320 (21.6%)	1.20 (0.82 to 1.74)	0.35
Amputation	320	35/320 (10.9%)	320	36/320 (11.2%)	0.98 (0.60 to 1.62)	0.95
SSI	320	102/320 (31.9%)	320	100/320 (31.2%)	1.05 (0.75 to 1.48)	0.77
Antibiotic use (for SWHSI)	320	211/320 (65.9%)	320	210/320 (65.6%)	1.01 (0.70 to 1.45)	0.96
Death	349	40/349 (11.5%)	337	43/337 (12.8%)	0.89 (0.56 to 1.41)	0.61

^a Odds ratio adjusted for wound size, duration of wound and wound location as fixed effects and centre as a random effect, analysed via logistic regression using events over 12-month follow-up.

TABLE 5 Patient-reported secondary outcomes for NPWT and usual-care groups

	NPWT n/N%		Usual care n/N%		Treatment difference (95% CI) ^a	p-value
WHQ baseline	263	7.77 (5.28)	263	8.08 (5.31)	–	–
WHQ 3 months	195	7.01 (5.08)	190	7.15 (5.72)	0.29 (–1.01 to 1.58)	0.66
WHQ 6 months	132	4.71 (4.33)	118	4.94 (5.67)	0.29 (–1.19 to 1.77)	0.70
WHQ 12 months	86	5.75 (5.76)	74	5.52 (5.60)	1.09 (–0.65 to 2.83)	0.22
Wound pain baseline	340	27.9 (29.8)	324	26.3 (28.9)	–	–
Wound pain 3 months	197	18.9 (24.7)	202	17.4 (23.1)	–0.58 (–6.45 to 5.30)	0.85
Wound pain 6 months	139	17.6 (27.3)	124	15.3 (24.3)	–0.28 (–7.11 to 6.54)	0.94
Wound pain 12 months	90	15.9 (24.4)	83	11.5 (18.3)	1.03 (–7.02 to 9.08)	0.80

^a Mean difference, adjusted for baseline score wound size, duration of wound and wound location as fixed effects and centre and participant as a random effect analysed via mixed-effects linear regression.

TABLE 6 Adverse and serious adverse events

	NPWT (N = 349)	Usual care (N = 337)	Risk difference (95% CI)
Number of patients experiencing adverse events of special interest (AESI)	48 (13.8%)	47(13.9%)	0.2% (–5.0 to 5.4%)
Amputation (major) ^a	33 (%)	38 (%)	
Amputation (minor) ^a	7 (2.0%)	3 (0.9%)	
Revascularisation – angioplasty	7 (2.0%)	5 (1.5%)	
Revascularisation – angioplasty (failed)	0 (0%)	1 (0.3%)	
Revascularisation – surgical (CFA endarterectomy)	1 (0.3%)	0 (0%)	
Number of participants experiencing at least 1 SAE	9 (2.6%)	4 (1.2%)	–1.3 (–3.4 to 0.6)
SAE category			
Death ^b	1 (11%)	0 (0%)	
Medication overdose	0 (0%)	1 (20%)	
Revascularisation – angioplasty	1 (11%)	1 (20%)	
Wound bleeding	1 (11%)	0 (0%)	
SSI (major – debridement)	4 (44%)	0 (0%)	
SSI (major – endarterectomy)	0 (0%)	1 (20%)	
SSI (major – revascularisation)	0 (0%)	2 (40%)	
SSI (moderate)	1 (11%)	0 (0%)	
SSI (severe)	1 (11%)	0 (0%)	
Total deaths including those reported elsewhere	40 (11.5%)	43 (12.8%)	1.3% (–3.6 to 6.2%)

a Amputations might not exactly correspond to those reported as secondary outcomes. These are amputations at any location regardless of the SWHSI location and at any point during the study (rather than within 12 months of randomisation).

b Deaths include those reported on both serious adverse event forms and in other case report forms.

Over the longer-term, the implemented cost-effectiveness decision model,²⁵ which consider a wider range of evidence and followed a 30-year time horizon, identified that the average QALY gains for NPWT compared to usual care to be 0.01 (95% CI –0.02 to 0.05). Healthcare resource use during healing, dependent on the treatment received, was on average lower for NPWT than for usual care while unhealed, except for nurse surgery appointments where it was higher [NPWT 1.39 (SE = 0.22); usual care: 1.26 (SE = 0.19)]. Thus, usual care had the highest average NMB and indicated that NPWT is not cost-effective at cost-effectiveness thresholds between £20,000 and £30,000/QALY gained. This was supported by the low probability estimates of NPWT being cost-effective (28.9% to 29.5%). These results are highly influenced by the uncertain pooled relative treatment effectiveness which considered all the available evidence [HR 1.07 (95% CI 0.82 to 1.71)]; for NPWT to be considered cost-effective, NPWT would need to increase the probability of wound healing by 16% relative to standard dressings. Findings were similar for scenario analyses that explored the

sensitivity of results to model assumptions. The exception was use of cohort resource use data,² which identified that NPWT would be considered cost-effective over usual care. [Appendix 4, Tables 24–26](#) present the main inputs used for the cost-effectiveness decision model, the key model assumptions and the lifetime cost-effectiveness results.

In a Value of Information analysis, using an effective technology time horizon of 5 years and an annual target population in England and Wales of 410 per million individuals, the population Expected Value of Perfect Information was estimated at approximately £245M²⁶ at a £30,000 threshold value, indicating high uncertainty in the model.

Validation of the Bluebelle Wound Healing Questionnaire

Acceptability

Wound Healing Questionnaire return rates were highest at the baseline face-to-face assessment (672/686;

98.0%).²⁷ Response rates to the 3-, 6- and 12-month postal questionnaire were lower and decreased over time to the 12-month follow-up point [186/296 (62.8%)]. Overall, there was no difference in participant socio-demographic or clinical characteristics between those that returned a questionnaire and those that did not. The exception was socioeconomic deprivation score, with higher proportions of non-responders observed in those from areas with higher deprivation.

Very low levels of missing data were observed at the follow-up time points (< 3.5%), with slightly higher levels of missingness at baseline. Commonly missing data items included those relating to wound care interventions such as use of antibiotics, drainage of pus/abscess, reoperation, debridement or seeking of wound care advice.

Criterion validity

Evaluation of the relationship between WHQ total scores and the reference SSI assessment based on the CDC criteria found that most participants classified as not having had an SSI had low WHQ scores (WHQ ≤ 6 , $n = 145/185$; 78%). Participants classified in reference data as having had an SSI had higher WHQ scores (WHQ ≥ 8 , $n = 46/71$; 65%). The area under the ROC curve indicated good sensitivity and specificity of the measure for discriminating between SSI/No SSI compared to the reference standard (0.796).

Research papers included in synopsis

1. Chetter IC, Arundel CE, Corbacho-Martin B, Hewitt C, Fairhurst C, Joshi K, *et al.* Negative pressure wound therapy versus usual care for surgical wounds healing by secondary intention (SWHSI-2 trial): study protocol for a pragmatic, multicentre, cross surgical specialty, randomised controlled trial. *Trials* 2021;**22**:739. <https://doi.org/10.1186/s13063-021-05662-2>

2. Arundel CE, Mandefield L, Fairhurst C, Baird K, Gkekas A, Saramago P, *et al.* Negative pressure wound therapy versus usual care in patients with surgical wound healing by secondary intention in the UK (SWHSI-2): an open-label, multicentre, parallel-group, randomised controlled trial. *Lancet* 2025;**405**:1689–99. [https://doi.org/10.1016/S0140-6736\(25\)00143-6](https://doi.org/10.1016/S0140-6736(25)00143-6)

3. Saramago P, Gkekas A, Arundel CE, Chetter I. Negative pressure wound therapy for surgical wounds healing by secondary intention is not cost-effective. *Br J Surg* 2025;**12**:znaf077. <https://doi.org/10.1093/bjs/znaf077>

4. Macefield R, Mandefield L, Blazeby JM, Fairhurst C, Baird K, Arundel C, *et al.* Modification and validation of

the Bluebelle Wound Healing Questionnaire (WHQ) for assessing surgical site infection in wounds healing by secondary intention. *J Tissue Viability* 2025;**34**:100889. <https://doi.org/10.1016/j.jtv.2025.100889>

5. Arundel C, Zahra S, Chetter I; SWHSI-2 Trial Investigators. Surgical wounds healing by secondary intention 2 trial: outcomes and learning from the internal pilot phase and main trial. *Pilot Feasibility Stud* 2025;**11**:90. <https://doi.org/10.1186/s40814-025-01658-w>

Discussion

Previous research has identified that the treatment of SWHSI is often prolonged, complex and expensive.^{2,4,6} This has a significant impact on patient HRQoL and healthcare resource use.^{3,4,6}

Previously reported time to healing of SWHSI, derived from an observational cohort, was a median of 86 days (95% CI 75 to 103); however, there was high variability around this estimate (5 days to 1 year 7 months following censoring).² Compared with this finding, the SWHSI-2 trial has found that time to healing SWHSI may be more prolonged than originally reported [median time to healing NPWT group: 187 days (95% CI 169 to 226); usual care: 195 days (95% CI 158 to 213)], particularly in patients with wounds on the foot or leg, and with diabetes, cardiovascular disease (CVD and/or PVD).

The SWHSI-2 trial data has also indicated that a proportion of included participants (42.8%) did not achieve complete wound healing within 12 months following randomisation.²³ This again differs to previous research, where 15.9% of participants remained unhealed at the end of study follow-up (650 days).² The differences in proportion of wounds healed and time to wound healing observed in SWHSI-2 are likely due to the high proportion of foot or leg wounds in vascular patients included (90.4%),²³ compared to the proportions included in previous research (29.8%), given previous research has found that foot and leg wounds took longer to heal than wounds in other locations (182 and 127 days, respectively).² This is further amplified by the predominance of participants with one or more of diabetes, CVD or PVD which can also be attributed to a prolonged wound healing duration.^{28,29}

When the SWHSI-2 trial commenced, information from associated manufacturers suggested that NPWT promotes wound healing.⁵ Previous available evidence suggested that NPWT may augment the healing of SWHSI,^{9,10,12} however, these studies were of low quality and therefore caution in interpretation of the findings was

recommended. The SWHSI-2 trial has found no convincing evidence that NPWT significantly accelerates healing of SWHSI compared to usual care (no NPWT) particularly in populations with wounds on the foot or leg, and with diabetes, CVD and/or PVD.²³

The SWHSI-2 trial has found that in this patient group, there were small increased chances of hospital admission, reoperation and SSI in the NPWT group, and increased chances of amputation or death in the usual-care group; however, there is uncertainty around these estimates which could have occurred by chance.²³ The SWHSI-2 trial therefore corresponds to previous studies which found no differences in SSI, amputation or death rates when NPWT was compared to other dressing types (alginate and silicone dressings respectively), although these studies were of low quality.^{9,10}

A further and more recent meta-analysis of NPWT for wounds healing by secondary intention has found differences (in favour of NPWT) for hospital re-admission and stay, but no difference with regard mortality, SSI, amputation or pain.³⁰ As with the previous meta-analysis, a significant proportion of the included studies were at high risk of bias (85%) limiting the interpretation of the findings. Furthermore, the population included in this meta-analysis is not directly comparable to the SWHSI-2 population given that non-SWHSI were also included (e.g. pressure ulcers, venous leg ulcers, diabetic foot ulcers, traumatic wounds). As no subgroup analysis of wound type (surgical vs. non-surgical) was undertaken, the results of this meta-analysis cannot be compared or reflected upon in the context of the SWHSI-2 results.

The cost-effectiveness decision model identified that the expected NMB was higher for usual care than for NPWT, indicating that for standard threshold values NPWT is not cost-effective for the treatment of SWHSI patients.²⁵ This aligns to previous research in this area;^{6,7} however, the level of uncertainty in the result differs between the two studies. The within-trial cost-utility analysis also concluded NPWT not to be cost-effective, particularly those with a lower limb SWHSI, and/or with comorbidities such as diabetes, CVD and/or PVD, since NPWT was found to be more costly and produced marginally higher QALYs than usual care, although these results were not statistically significant.

Included in the SWHSI-2 trial was the validation of a modified Bluebelle WHQ for the assessment of SSI.²⁷ This questionnaire has previously been developed and validated in patients with primary closed wounds.^{16,31} As

with previous studies in patients with closed wounds, the WHQ was found to be acceptable and demonstrated good sensitivity and specificity for discriminating between SSI and no SSI compared to a face-to-face reference assessment using CDC criteria. This therefore suggests that a modified WHQ can be a valuable tool for the assessment of SSI in SWHSI patients.²⁷

Inclusion of an internal pilot phase to the study was crucial in facilitating the early identification and mitigation or minimisation of recruitment and retention difficulties. Working agilely to support the needs of sites during both the pilot and main trial phase were crucial to facilitating successful trial conduct.²² Additional to this, ensuring equipoise balance at the outset and during a trial, providing opportunities for peer-to-peer support, employing a range of follow-up methods are all recommended considerations for future research.²² In accordance with previous recommendations,³² these have been reported for the benefit of researchers both in the field of wound care and trial conduct more broadly.²²

Strengths and limitations of the study

Strengths

Given the limitations of previous research regarding NPWT as a treatment for SWHSI,⁸ the SWHSI-2 trial provides the first robust evaluation of NPWT as a treatment for SWHSI.

Development of the SWHSI-2 trial utilised the findings of a previous external pilot to inform the design and conduct of this study.³³ An internal pilot was also included to allow for the early evaluation and adaptation of recruitment and retention methods. This helped to ensure that potential challenges were identified early and rectified quickly. The agile management of the study by a UK Clinical Research Collaboration registered Trials Unit (York Trials Unit, University of York; Registration 40) and the wider study management team was integral to the successful delivery of the study.

Study recruitment was conducted at 28 UK sites, located in both larger urban areas with a diverse population and in more rural areas which helped to ensure a heterogeneous pool of participants were recruited. This combination of sites has enabled the study to recruit from across the demographics of the UK population. The study also utilised the National Institute for Health and Care Research (NIHR) Associate Principal Investigator (API) scheme, which helped support recruitment and provide individual development opportunities. During the study, eight individuals participated as an API, including four surgical trainees, two nurses, one podiatrist and one

clinical lecturer. The diversity of individuals involved in this role in SWHSI-2 will have helped to develop future research capabilities in both surgical and wound care.

The study permitted use of any NPWT device, available within the local NHS site and which provided 60–150 mmHg as treatment for the study, on the basis that the principles of any NPWT device are similar and there is no evidence to suggest clinical or cost-effectiveness differences between devices. The findings of this research are applicable to all marketed NPWT devices.

Given the primary outcome (time to wound healing), this enabled data from all participants to be included in the primary outcome analysis. As it was not possible to blind patients, researchers and treating healthcare practitioners to the treatment allocation, the study also included a secondary outcome of blinded assessment using wound photography to supplement the unblinded primary outcome assessment.¹⁴

The Bayesian meta-analysis developed to evaluate cost-effectiveness has made best use of all available RCT evidence for the effectiveness of NPWT for SWHSI. Both individual patient data (IPD) and aggregate data were used to maximise the data available for this analysis, with the inclusion of IPD format data enabling comprehensive modelling of relevant evidence.

The contribution of PPI members throughout the study from conception to study design, conduct and dissemination has ensured a consistent patient perspective to the research. A wide range of strategies were used throughout the study to maintain PPI contributions during the study.

Engagement with other stakeholders has also been an integral part of study conduct. This has included engagement with organisations relevant to the use of NPWT (e.g. National Wound Care Strategy Programme, Society of Tissue Viability) as well as more focused organisations (e.g. Society of Vascular Nurses, Vascular Society of Great Britain & Ireland). A broad dissemination strategy across all groups is planned, with engagement also planned with further stakeholders to ensure that the results can be implemented appropriately both nationally and internationally.

Limitations

The study reported a longer time to healing of SWHSI than previously reported.² This may be due to the fact that 80% of the included SWHSI in this study being located on the foot, which previous research has reported as increasing the time to wound healing.² As a result, there is an

under-representation of SWHSI in other sites on the body. This is likely due to equipoise difficulties in non-vascular surgical specialties, something which was identified in the earlier external pilot, and which remained a persistent issue in SWHSI-2 despite numerous strategies implemented to promote study engagement and to raise the study profile. The study population also had high levels of comorbidities (including diabetes, CVD and/or PVD) resulting in these patients being at high risk of impaired wound healing. As a result, generalisability of the findings across surgical specialties or in patient populations without comorbidities may be limited.

The role of NPWT for wound or exudate management was not evaluated in this study, although these may be common reasons for using NPWT in certain surgical specialties. Further research is therefore required to address the role of NPWT in relation of wound or exudate management.

Wound size in SWHSI-2 was calculated by multiplying length by width measured using a ruler. This method of measurement may overestimate wound size.³³ Caution should therefore be taken when considering initial wound area measurements as used for randomisation.

The cost-effectiveness analysis identified the considerable uncertainty over the pooled relative treatment effect. This reflects the fact that many of the included studies were small, with wide CIs and with many of the studies ($n = 5/6$) being deemed to be at moderate or high risk of bias.

The Bluebelle WHQ was collected via postal questionnaire at the majority of time points, and so the analysis of this, and other patient-reported outcome measures (pain, EQ-5D-5L¹⁵) may have been limited by the lower than anticipated response rates to the postal questionnaires although response rates were similar in both groups. Given mobility issues for patients with a SWHSI, particularly on the foot or leg, which was highly prevalent in this study, assessment of the acceptability and validity of the measure for use in electronic data collection may be beneficial. This work is currently ongoing.^{34,35} Although the measure was deemed to be both acceptable and valid, acceptability was assessed through quantitative rather than qualitative means. Additional qualitative assessment may have further enhanced the understanding of acceptability in relation to the measure.

The within-trial cost-utility analysis was subject to a significant proportion of missing data in resource use items and EQ-5D-5L scores, ranging from 8.3% (secondary healthcare resource use) to 50.6% (medication resource use). This implied that the complete-case analysis (Appendix 4 SA.1) could only consider 167/686 (24.3%)

participants. This is because a complete-case analysis requires all data on resource items and EQ-5D-5L scores to be complete for QALYs and costs to be derived for each participant. This analysis, in contrast to the base-case cost-utility analysis, suggested that NPWT may be a cost-effective treatment for SWHSI patients, in relation to standard dressings. However, logistic regressions performed on missing QALYs and missing costs (see [Appendix 4, Table 14](#)) identified that missingness on QALYs was significantly associated with baseline EQ-5D-5L scores, age and area of SWHSI, whereas missingness for total costs was significantly associated with full thickness skin loss, duration of SWHSI and baseline EQ-5D-5L scores. Such findings imply that the MCAR assumption, a necessary condition for complete-case analyses to be statistically valid, was not met. Therefore, the MAR assumption, a necessary condition for base-case analyses based on multiple imputations to be reliable, is likely to be valid.

Generic HRQoL and pain assessments were collected via postal questionnaire and so analyses of these measures was also impacted by lower than anticipated response rates. Participants reported that these assessments were irrelevant following healing or amputation of the SWHSI. Changes were subsequently made to questionnaires, by placing the generic quality-of-life assessment at the start of the form and removing the pain and Bluebelle WHQ measures, which did improve responses rates. Future studies should carefully consider the ordering of patient-reported outcomes to maximise response rates.

Only generic HRQoL was assessed in the SWHSI-2 trial, given the absence of appropriate validated wound-related quality-of-life measures for this population. As a result, quality-of-life assessment may not adequately reflect the intricacies of the impacts of an open wound on quality of life. Work to identify appropriate wound-related quality of life measures is ongoing.³⁶

Patient and public involvement

Patient and public involvement was utilised in the SWHSI-2 trial to ensure that a patient perspective was included in both formulating the research question, and the subsequent design, conduct and dissemination of the study, given the significant impacts that SWHSI wounds may have on patient quality of life.^{3,4}

Study design

Patient perspectives, obtained during the previous NIHR PGfAR (RP-PG-0609-1017) exploring the epidemiology, management and impacts of SWHSI, were integral in

developing the SWHSI-2 proposal.⁷ Qualitative semi-structured interviews conducted as part of the PGfAR identified wound healing as the most important outcome measure for SWHSI-2.⁴ Members of the PGfAR PPI group also supported wound healing as being a key outcome for patients.

A member of the PGfAR PPI group was included in SWHSI-2 as a co-applicant. They reviewed and confirmed that the proposed research question and outcome measures were relevant and important to patients, and contributed to study design, trial procedures and discussions in relation to sample size parameters for the SWHSI-2 trial. Input continued during the trial through attendance at Trial Management Group meetings to provide a patient perspective to discussions particularly with regard participant documentation, procedures and contacts during the study.

As the PGfAR PPI group had been established for more than a decade at the time SWHSI-2 commenced, it was necessary to establish further PPI contributors for the SWHSI-2 trial. In February 2019, the 'People in Research' website was used to advertise for PPI expressions of interest. Six individuals expressed an interest in participation, of which three members (all female and with lived experience of a SWHSI) formed our PPI group. Two further members (one male, one female) were involved in the study as PPI contributors to the Trial Steering Committee. All activities of PPI members were reimbursed according to NIHR/INVOLVE guidelines.³⁷

Study delivery

Throughout the trial, draft patient facing documentation were reviewed by the PPI group. This included review and contribution to the:

- Participant photography procedure to help participants of taking photo of their wound themselves.
- Participant recruitment information sheet and infographic.
- Follow up questionnaire cover letters.
- Supplementary diaries to help recall of wound-related visits.

Patient and public involvement review of these documents ensured that these were appropriate to study participants and were written in lay language. Where possible, changes based on PPI input were made to documents prior to submission for ethical approval.

To further expand the PPI group, an expression of interest was subsequently included with the 12-month participant

follow-up questionnaire. This resulted in 43 additional expressions of interest, from which 1 patient (male, lived experience of SWHSI) joined the PPI group during the dissemination stage. Engagement of PPI members was maintained throughout the trial through dissemination of bi-annual newsletter updates and sending of seasonal greetings cards at the end of each year.

Study dissemination

Patient and public involvement input throughout SWHSI-2 has provided continued confirmation that the research question remains important to patients with a SWHSI.

To ensure a patient perspective to the interpretation of the study results, these have been shared and discussed with PPI members. The group have advised writing findings of study outcomes in an order that is most relevant to patients with a SWHSI.

The PPI group have identified the best ways to disseminate the SWHSI-2 trial findings to participants, stakeholders and the wider population. On their advice we have developed a combination of a written summary, a visual aid and an animation. Results dissemination outputs were prepared and shared with the PPI group members for review and comment before they were distributed to study participants and made available to other relevant stakeholders.

The PPI co-applicant will assist with the dissemination of study findings in peer-reviewed journals and at scientific conferences.

Equality diversity and inclusion

Participants

Most randomised participants in the SWHSI-2 trial were recruited in England (95.8%), with recruitment in Yorkshire and the Humber accounting for approximately a third of the total sample (32.4%).

Data relevant to monitoring of equality and diversity across the sample were collected for all participants at baseline and included age, gender, ethnicity and smoking status. As SWHSI-2 commenced prior to publication of the INCLUDE framework,³⁸ other equality and diversity criteria were not included.

Age

In accordance with INCLUDE framework, underserved groups include individuals under 18 years or over 75 years of age.³⁸ SWHSI-2 ensured diversity of patients by including

patients aged 16 years and over, with no upper age limit for inclusion. The age of participants recruited ranged from 21 to 93 years, which corresponds to patient demographics from previous research in this patient population (range 19–95 years)² and is therefore representative of the wider population of patients with a SWHSI.

Ethnicity

The ethnicity of the recruited population was 93% White, with 4% Asian/Asian British and 3% Black/Black British. Five participants reported another ethnicity, and data were missing for one participant. The UK government indicates that 82% of the general population are of White ethnicity; this ethnicity is therefore overrepresented in the SWHSI-2 population while Asian/Asian British and Black/Black British are under-represented (UK population 9% Asian, 4% Black).

Sex

Conditions associated with SWHSI (e.g. PVD, diabetes) are more common in men than women; however, SWHSI are also common following procedures such as caesarean section.³⁹ The SWHSI-2 population comprised 75% male participants, which suggests that females are under-represented in the study population. This is likely due to the high prevalence of foot or leg wounds, potentially arising because of diabetes and PVD, and the lack of patients with caesarean section wounds included in the study.

Socioeconomic status

The socioeconomic status of participants was assessed by mapping participants' residence postcodes to indices of multiple deprivation.^{40–42} More participants were resident in the most deprived areas, than were resident in the least deprived areas (65.6% most deprived, 34.4% least deprived), with 20% of participants living in areas defined by indices of multiple deprivation as level 1 (most deprived).

As noted in relation to sex, there was a high prevalence of foot and leg wounds in this study, potentially arising due to PVD. Previous evidence suggests that there is a link between low socioeconomic status and development of PVD due to increased prevalence of cardiovascular risk factors (e.g. smoking status).⁴³ As a result, it can be suggested that those living in areas of higher deprivation were more likely to have a SWHSI and so be eligible for study participation.

Smoking status

At baseline, 18% of participants reported being current smokers. A study in 2019 found that 14.7% of UK residents smoked,⁴⁴ with the proportion of UK smokers decreasing over time with 13.3% of the UK population

reported as smokers in 2021,⁴⁵ and with a relatively equal split between genders (3.9 million males, 56.1%). Current smokers are therefore slightly overrepresented in the SWHSI-2 population when compared to the overall UK population. The links between smoking status and healing of SWHSI were not further explored in the trial.

Research team and recruiting sites

Representativeness requirements for staff involved in the study at participating sites were not imposed; however, the representativeness of the research team is unlikely to have affected patient participation in SWHSI-2.

Beyond planned study specific training, and routine training updates provided during meetings with all sites, no specific training in relation to diverse recruitment or retention was provided as part of the SWHSI-2 Trial. This has potential to limit diverse recruitment; however, recruiting sites were encouraged to ensure that they offered the study to all patients with a SWHSI.

Sites were distributed throughout England ($n = 25$), Scotland ($n = 2$) and Wales ($n = 1$) and were located both in larger urban areas with a diverse population, and in more rural areas (see [Appendix 3, Table 10](#)). The mix of sites has therefore provided a good basis for recruiting from a representative demographic of the UK population.

Impact and learning

Negative pressure wound therapy is currently a widely used treatment in the NHS. Prior to the SWHSI-2 trial, there was limited robust evidence with regard the clinical or cost-effectiveness of this treatment.⁸ The SWHSI-2 trial provides the first robust assessment of NPWT compared to standard dressings for healing of SWHSI and has found that, based on the outcomes assessed, NPWT appears to offer no added benefit in both clinical and cost terms particularly when used to treat SWHSI located on the lower limb and/or in patients with comorbidities such as diabetes, CVD and/or PVD.²³ As a result, the main impact of this research will be through a change to clinical practice.

Key to enacting this change will be the revision of relevant NICE guidance. There is currently no specific guidance pertaining to the management and treatment of open surgical wounds; however, evidence from SWHSI-2 will contribute to other related guidance documents. These potentially include evidence summaries regarding chronic wounds and the use of advanced dressings which does not currently include NPWT as a treatment,⁴⁶ and NICE Guideline NG125 regarding treatment of SSI.⁴⁷ Relevant data from SWHSI-2 may also be appropriate to include in

NICE interventional procedures guidance focussed on the management of the open abdomen.

National Health Service Supply Chain and procurement groups should also reflect on the appropriateness for continued use of NPWT devices for the purpose of wound healing based on the findings from this research. The SWHSI-2 Trial Management Group have begun to approach these groups to share the study findings and to discuss how best to support their integration.

Change to guidance should result in changes to the future training curricula of doctors and nurses, both in the UK and internationally. Within the UK, engagement with the General Medical Council and Nursing and Midwifery Council will be necessary to ensure that these curricula are updated quickly and appropriately for current and future cohorts.

As outlined in a pre-specified Impact and Dissemination plan, there are further key stakeholders relevant to facilitating a change in practice with regard use of NPWT for SWHSI. These include surgical Royal Colleges, Society of Tissue Viability, surgical and nursing specialty groups, relevant charities, parliamentary groups (such as the Vascular All Party Parliamentary group) and healthcare professionals. The SWHSI-2 Trial Management Group have begun to approach these groups to share the study findings and to discuss how best to support their integration. The findings of each component of the study will also be disseminated through peer-reviewed publications, at relevant UK, European and international conferences, and to patients and the public.

Following integration of the SWHSI-2 results into routine clinical practice, we propose to assess impact by evaluating changes to NPWT use across the NHS. This may include use of Hospital Episode Statistics data, data on NPWT procurement from the NHS Supply Chain and/or through use of survey data to collect information on change in practice directly from healthcare professionals. We also propose to assess the impacts of this research on patients, by comparing patient preferences reported at baseline with patient treatment preferences following results dissemination to both study participants and the wider SWHSI patient population.

Negative pressure wound therapy was found to increase rates of hospital re-admission, SSI and further treatment,²³ which corresponds to previous similar findings.² Previous research has identified the detrimental impact that these events have on people's HRQoL.^{3,4} As a result, cessation of use of NPWT may confer health-related quality-of-life benefits to patients with a SWHSI, by reducing

the occurrence of these events. SWHSI-2 results in a population of primarily foot and leg wounds in patients with comorbidities such as diabetes, CVD and/or PVD have found that NPWT has no significant impact on SWHSI healing and incurs additional costs compared to usual care.²³ Cessation of use of NPWT as a treatment to accelerate healing of SWHSI will therefore incur cost savings to the NHS.

The SWHSI-2 trial recruited participants from 28 participating sites across the UK and included the involvement of a wide range of healthcare professionals in supporting the study. The NIHR API scheme was also utilised at participating sites to develop research capabilities. It is likely, therefore, that this trial has also served to further improve the quality and quantity of surgical and wound care clinical research in the UK. As a result, there is a potential for significantly benefit patients into the future.

The conduct of the SWHSI-2 trial has afforded additional learning with regard to trial design and delivery for both future wound care studies, and trials more generally.²² The inclusion of an internal pilot phase was crucial in minimising and mitigating barriers to recruitment and retention promptly, with continued review and evaluation used throughout the full trial life course. The ability to work agilely to support sites was crucial to facilitating successful conduct. Future studies should plan active review and evaluation accordingly. The SWHSI-2 trial also identified the importance of ensuring equipoise balance both at the outset of and during the trial to maximise engagement. This is particularly pertinent for interventions like NPWT which are already used in routine practice but without robust evaluation to support this. In accordance with previous recommendations,³² the lessons learnt within the SWHSI-2 trial have been reported to support future trial design and conduct.²²

The SWHSI-2 trial has provided the first robust evaluation of NPWT as a treatment for SWHSI. The previous Cochrane review of NPWT for SWHSI includes research data published before May 2015.⁸ As a result, this review requires updating to incorporate SWHSI-2 and other published data regarding NPWT for SWHSI. The SWHSI-2 Trial Management Group propose to undertake an update to this review in due course.

In addition to the direct impacts of the SWHSI-2 trial, there have also been additional components of work linked to and/or indirectly supported by the study. These include:

- Award of funding to evaluate assessment of wound-related quality of life for SWHSI patients.

This included a Research Design Service PPI award (Coapplicants: CA and IC) and has resulted in a peer reviewed publication.⁴⁸ Subsequently, a NIHR Doctoral Research Fellowship has been awarded to develop a SWHSI core outcome set and to evaluate and map the Wound QoL measure (SWHSI-3),^{36,49} supervised by IC and CA.

- Led by IC, a Vascular Society of Great Britain and Ireland Wounds Special Interest group has been established, which includes involvement of SWHSI-2 members CA and SD. This group were integral to the development of James Lind Alliance Vascular research priorities for wounds.⁵⁰
- Two studies within a trial (SWATs) were included in the SWHSI-2 trial – one evaluated the impact of an infographic plus patient information sheet (PIS) on recruitment when compared to PIS alone,⁵¹ the second evaluated the impact of a thank-you card pre-notification compared with no pre-notification, on participant retention.⁵² The findings of both SWATs will be published, with cumulative meta-analysis completed to combine data with previous replications (if appropriate).⁵³
- Additional papers relating to specific components of the SWHSI-2 trial are also proposed. These include an evaluation of future SWHSI research priorities, learning from the practical implementation of blinded outcome assessment, learning relating to adverse events in wound care, before and after evaluation of additional strategies implemented to improve retention, and a subsequent update to the Cochrane review in relation to NPWT for SWHSI.⁸
- A systematic review is ongoing to evaluate current evidence with regard to use of antimicrobial dressings to prevent SSI in SWHSI. This will inform consideration for the design of a future SWHSI research study (SWHSI-4).
- Further evaluation of wound dehiscence and subsequent healing by secondary intention has been included in the recently funded HAMLET RCT, comparing above knee and through knee amputations.⁵⁴
- Further validation of the Bluebelle WHQ which will improve its readiness for future studies in this area.

Implications for decision-makers

Currently NPWT is widely used in the NHS for SWHSI. SWHSI-2 results clearly demonstrate that NPWT is of no added clinical or cost benefit based on the outcomes and population assessed in this study.²³ As a result, NICE and other organisations should consider inclusion of these

findings in relevant guidance pertaining to the treatment of open surgical wounds.

Across healthcare delivery, individuals and groups involved in treatment procurement and supply, such as the NHS Supply Chain, should reflect on the appropriateness for continued use of NPWT devices for the purpose of wound healing based on the findings from this research. At an organisational level, secondary care NHS Trust-specific groups (for example prescribing committees), community NHS Trusts, community interest companies providing NHS services, and integrated care systems, will also need to consider the appropriateness of the continued provision of NPWT for the purposes of wound healing for SWHSI.

Historically, the commonly held clinical view has been that NPWT is associated with shorter wound healing times and fewer complications. As the SWHSI-2 findings do not corroborate this, healthcare practitioners should reflect on this evidence where any decision is to be made regarding wound healing treatments. This study did not measure the impact of NPWT on aspects of wound management such as exudate management so trial findings cannot be used to inform the use of NPWT for non-healing outcomes, where there is further uncertainty. Similarly the study population had high levels of comorbidities (including diabetes, CVD and/or PVD) resulting in these patients being at high risk of impaired wound healing. The relative cost of the treatment and the uncertainty on benefit for non-healing outcomes and NPWT use in other surgical specialties or in patient populations without comorbidities should be considered in decision-making.

The SWHSI-2 findings show that NPWT does not appear to be a clinically or cost-effective treatment for the healing of SWHSI but is in widespread use.^{23,25} This highlights the importance of undertaking timely randomised evaluations to inform practice. The lack of previous RCT evidence to support NPWT effectiveness has resulted in an ineffective and costly intervention being used in routine care for a considerable period. This raises serious questions about how innovation pertaining to non-medicinal products occurs in health care prior to a full trial.

Unlike the incremental pathway used for introducing new drugs (with phase 1 and phase 2 studies), for surgery it is possible to introduce new procedures and technologies without evidence of comparative effectiveness. This has risks. In research settings, patients are given information about uncertainties to inform consent for participation to take place; however, in routine clinical care, outside of research, it is possible that this does not happen. A recent study examined consultations between surgeons

and patients where innovative procedures were offered.⁵⁵ It demonstrated that despite surgeons' best intentions to be open in the consultations, limited information was conveyed about uncertainties, risks and effectiveness. Optimism bias instead prevailed. As a result, patients accepting the new procedure were sometimes unaware of the lack of evidence to support its effectiveness.⁵⁵ Given the SWHSI-2 findings, it is recommended that before any new intervention is widely used in the NHS, more detailed research and evaluation is needed. This will improve transparency for patients and lead to cost savings for the NHS because expensive new treatments will be compared with standard interventions before widespread use.

How interventions are evaluated before use in routine clinical care should also be considered. Our previous economic modelling work, using observational cohort data and involving an instrumental variable approach, reported that NPWT was expected to be less cost-effective and more costly than standard dressings.⁶ The uncertainty around the estimate was very small and even with use of advanced adjustment techniques reached the same conclusions.⁶ The lack of confidence in conclusions being derived from observational data, due to confounding, resulted in the SWHSI-2 trial being funded; however, there was scope for observational evidence to inform decision-making in the interim while the trial data were being generated, but the perceived limitations made implementation challenging. There is increasing focus on the value of high quality 'real world data' to inform decision-making especially when RCT data will take time to generate. In situations, such as with NPWT use for treating SWHSI where there was a dearth of evidence and widespread NHS use, consideration of such data should be supported. In general, and subject to their conduct and findings, robust economic evaluations which use all available evidence may therefore offer an alternative to costly RCTs.

Research recommendations

The SWHSI-2 trial has provided the first robust evaluation of NPWT as a treatment for SWHSI. Given that treatment for open SWHSI is often prolonged, complex and expensive and has a significant impact on patient quality of life and healthcare resource use,^{2-4,6} additional high-quality research remains warranted in this population.

The SWHSI-2 trial has identified that a widely used intervention may not be as effective as first thought at healing wounds. Given that the process for the introduction of new surgical interventions and wound

dressings is not as rigorous as the incremental pathway used for introducing new drugs (with phase 1 and phase 2 studies), it is imperative that any new intervention is subject to high-quality, rigorous evaluation to determine comparative effectiveness to existing treatments, before they are routinely implemented into the NHS. Research of these interventions should therefore be prioritised.

Surgical site infection

Within the SWHSI-2 trial population, SSI was common, with outcome data indicating 32% of patients had an infection during the healing trajectory.²³ Adverse event data estimated the percentage of infections to be higher (NPWT 43% vs. usual care 41.2%).²³ Irrespective of infection status, 66% of participants received antibiotics in relation to their wound during the postoperative healing process. The presence of infection has previously been reported to impair healing and increase morbidity and mortality⁵⁶ and is often attributable to subsequent hospitalisation and re-admission, particularly for open wounds.^{57,58} Given the detrimental impact of SSI on healing, in terms of both patient quality of life and healthcare resource use,^{2-4,6} research to evaluate SSI prevention and/or reduction in duration is warranted.

Evaluation of interventions to prevent SSI was priority eight in the recent James Lind Alliance Vascular Priority Setting Partnership (JLA-VPSP) for vascular wounds: 'How can wounds be prevented from becoming infected?'⁵⁰ Evaluation of methods to prevent SSI in these wounds is also likely to address JLA-VPSP priorities two, three, seven and nine: accelerating healing of wounds, improvement of HRQoL, consistency in assessment and management and optimising wound healing respectively.⁵⁰ Evaluation of SSI prevention could therefore make significant progress in addressing 5 of the top 10 JLA-VPSP priorities for vascular wounds. Consideration should be given to interventions used preoperatively, intraoperatively and postoperatively.

Preoperatively and intraoperatively, an exploration of the processes undertaken prior to and during surgery and variation in these is warranted to enable identification of methods to prevent SSI in the first instance. As outlined by the NICE SSI guideline, further research regarding nasal decolonisation, antiseptic skin preparations and use of antibiotics and antiseptics prior to wound closure is required.⁵⁹ Postoperatively, intervention options could include dialkylcarbomoyl chloride-coated dressings for SSI prevention, given this has previously been shown as a potentially beneficial intervention in chronic wounds,⁶⁰ and other antimicrobial dressings where, like NPWT, use has been increasing over time,⁶¹ despite a lack of evidence for effectiveness to support routine use. Given

the need to prevent SSI or reduce its duration, and given the lack of available evidence, these dressings may therefore be relevant and appropriate interventions for future assessment.

The importance of consistency in assessment, diagnosis and management of wounds was also identified by the JLA-VPSP wound special interest group to be a research priority (priority seven).⁵⁰ Validation of the Bluebelle WHQ within this study has demonstrated this to be an acceptable measure with good sensitivity and specificity for discriminating between SSI and no SSI compared to a face-to-face reference assessment using CDC criteria²⁷ and so is recommended for use in both research and routine clinical care. The measure was collected via postal questionnaire at most time points which was limited by lower than anticipated response rates, potentially because of mobility issues for patients with a SWHSI on the foot or leg. Further assessment of the acceptability and validity of the measure when administered through electronic data collection methods may be beneficial. Initial evaluation of electronic data collection is ongoing; however, both studies focus on primary closed wounds.^{34,35} Further assessment of methods of data collection for patients with open surgical wounds is therefore warranted. Additional qualitative assessment of acceptability in relation to the measure should also be considered, given the evaluation in the SWHSI-2 trial was through quantitative rather than qualitative means.

Treatment modalities and interventions

The SWHSI-2 trial evaluated only one treatment for SWHSI healing. Following on from an earlier PGfAR to explore the epidemiology, management and impact of SWHSI, there remains an absence of evidence as to the best ways to heal these wounds and therefore evaluation of other interventions remains warranted.⁷ Interventions, which have been shown to be effective for the healing of other wound types, may be beneficial to explore with regard to SWHSI healing. Potential interventions could include hyperbaric oxygen therapy, effective for healing of diabetic foot ulcers, and iodine or honey dressings, effective for healing in chronic or burn wounds.⁶²⁻⁶⁴ Interventions effective for other wound types or for outcomes other than healing may also be relevant to consider, for example, use of larvae which has previously been found to be effective for wound debridement in chronic wounds and venous leg ulcers.^{65,66} There also remains a significant number of other candidate interventions where evidence of effectiveness remains limited both for SWHSI patients and for patients with other wound types. These may therefore also warrant further exploration, for example topical oxygen therapy and extracorporeal shockwave therapy.⁶²

The SWHSI-2 trial found that time to healing for SWHSI may be longer than previously reported,² likely due to the high proportion of foot or leg wounds included in the study. These wounds primarily resulted from vascular surgeries where healing is often delayed due to patient factors. There was an under representation in this study of SWHSI in other locations and/or arising from other surgical specialties. As a result, future research into the use of NPWT as a treatment for wound healing in other locations may remain warranted. Other specialties often use NPWT for wound management or exudate outcomes rather than wound healing, and these outcomes were not assessed within SWHSI-2 and so there remains uncertainty around NPWT effectiveness for these outcomes. Further research may therefore consider the role of NPWT in relation to wound or exudate management rather than or in addition to wound healing.

At baseline, approximately 32% of participant's wounds were, in accordance with CDC criteria, classified as clean or clean contaminated. These wounds may therefore have been appropriate for alternative closure methods (e.g. primary closure, delayed primary closure or closure using skin grafting) rather than being left to heal from the bottom up. Further research may therefore be warranted to identify when clean or clean contaminated wounds may be appropriate for alternative closure methods rather than these being left open to heal from the bottom upwards.

Patient quality of life

Finally, only generic HRQoL was assessed in the SWHSI-2 trial, given the absence of appropriate validated wound-related quality-of-life measures for this population. As a result, quality-of-life assessment may not adequately reflect the intricacies of the impacts of an open wound on quality of life and may also not account for the presence of multiple co-morbidities. Identification of how quality of life could be improved in patients with open wounds was ranked as the third priority for research by the recent JLA-VPSP wounds group. Work to identify appropriate wound-related quality-of-life measures is ongoing, which will support evaluation of interventions related to this theme.³⁶ Further assessment of any measure identified by this work will likely be warranted before routine use in both research and clinical practice. Consideration should therefore be given to evaluation of potential outcome measures in future research.

Research priorities

Following on from the findings of the SWHSI-2 trial, we consider key future research priorities to be:

- How can SSI in SWHSI be prevented or best treated and does this augment healing?

- Which treatments (e.g. dressings, or surgical procedures) are clinically and cost-effective for the healing of SWHSI and does wound location impact on treatment clinical or cost-effectiveness?
- What is the clinical and cost-effectiveness of NPWT versus usual care for wound management or exudate control?
- What is the best outcome measure to evaluate health-related quality of life in patients with a SWHSI?
- Is electronic completion of the Bluebelle WHQ acceptable to SWHSI patients and how valid is this as a measure of SSI when completed electronically?
- Could the Bluebelle WHQ be sufficient to detect SSI in SWHSI to use as a primary outcome in a trial?

Conclusions

The SWHSI-2 trial has provided the first robust evaluation of the effectiveness of NPWT as a treatment, in terms of time to healing, for patients with a SWHSI particularly in patients with wounds on the foot or leg and with diabetes, CVD and/or PVD.

The study found no clear evidence that NPWT had a significant impact on time to wound healing when compared to standard dressings for people with a SWHSI primarily located on the foot or leg and who had existing comorbidities including diabetes, CVD and/or PVD.²³ There was no significant difference in the odds of re-admission, reoperation or amputation, SSI and antibiotic use, or death for NPWT participants compared to usual-care participants. There was also no significant difference observed in relation to patient-reported SSI symptoms or wound pain. Adverse event rates were similar irrespective of treatment group. NPWT incurs higher costs than usual care when used as a treatment for SWHSI and health economic analysis indicates that NPWT is not a cost-effective treatment for this patient population.²⁵

The SWHSI-2 trial also enabled the first validation assessment of the Bluebelle WHQ as a patient-reported outcome measure for the assessment of SSI.²⁷ The measure was found to be both acceptable and valid for use in this patient population and therefore is recommended for use with SWHSI-2 patients both in clinical practice and in future research studies.

Inclusion of an internal pilot phase to the study was crucial in facilitating the early identification and mitigation or minimisation of recruitment and retention difficulties. Details of the strategies used have been shared for the benefit of future research design and conduct.²²

Collectively, SWHSI-2 findings do not support the use of NPWT to augment healing particularly in patients with SWHSI on the foot or leg and with diabetes, CVD and/or PVD. The SWHSI-2 trial findings therefore pose a significant implication to clinical practice going forward given that key stakeholders, such as NICE, NHS Supply Chain, National Wound Care Strategy Programme and local procurement groups, will need to carefully reflect on the appropriateness of continued use of NPWT devices for wound healing based on the findings from this research.

Given the significant impacts of a SWHSI on people's HRQoL and healthcare resource use, additional research remains warranted in this population. Key focus of future research includes evaluation of the clinical and cost-effectiveness of other interventions to augment SWHSI healing, prevention and/or treatment of SSI, clinical and cost-effectiveness of NPWT use for wound or exudate management, methods for the evaluation of HRQoL in SWHSI patients and assessment of SSI through electronic data collection methods.

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Patient data statement

This work uses data provided by patients and collected by the NHS as part of their care and support. Using patient data is vital to improve health and care for everyone. There is huge potential to make better use of information from people's patient records, to understand more about disease, develop new treatments, monitor safety and plan NHS services. Patient data should be kept safe and secure, to protect everyone's privacy, and it's important that there are safeguards to make sure that they are stored and used responsibly. Everyone should be able to find out about how patient data are used. #datasaveslives You can find out more about the background to this citation here: <https://understandingpatientdata.org.uk/data-citation>

Data-sharing statement

Anonymised data are available from: https://osf.io/8mehf/?view_only=07643d8f208f45f18b214594ca645103.

All data requests should be submitted to the corresponding author for consideration. Sharing of this anonymised data is covered by original participant consent for the SWHSI-2 trial which permits sharing of data to support future research via sharing anonymously.

Ethics statement

The study was approved by the Leeds East Research Ethics Committee on 5 April 2019 (reference 19/YH/0054).

Information governance statement

Hull University Teaching Hospitals NHS Trust (Sponsor) and York Trials Unit, University of York (Clinical Trials Unit) are committed to handling all personal information in line with the UK Data Protection Act (2018) and the General Data Protection Regulation (EU GDPR) 2016/679.

Under the Data Protection legislation York Trials Unit, University of York is the Data Processor; Hull University Teaching Hospitals NHS Trust is the Data Controller and personal data were processed in accordance with their instructions. You can find out more about how we handle personal data, including how to exercise your individual rights and the contact details for Hull University Teaching Hospitals NHS Trust Data Protection Officer here hyp-tr.informationgovernance.huthnlag@nhs.net. www.hey.nhs.uk/privacy/data-protection/

Disclosure of interests

Full disclosure of interests: Completed ICMJE forms for all authors, including all related interests, are available in the toolkit on the NIHR Journals Library report publication page at <https://doi.org/10.3310/GJIC1716>.

Primary conflicts of interest: Catherine Arundel declares additional NIHR funding for projects outside of this work, and support for attendance to present the study at the Vascular Society of Great Britain and Ireland Annual Scientific Meetings in 2021 and 2024.

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Jo Dumville declares additional NIHR funding for projects outside of this work. Jo Dumville was also previously a member of the HTA General Committee and HTA Fast Track Committee (2021).

Catherine Hewitt declares payments made to the academic institution for membership in the NIHR HTA Commissioning committee (2015–22) and NIHR HTA General Committee (2023–present), Deputy Chair of the NIHR HTA Commissioning committee (2019–22) and as Chair of the NIHR HTA General committee (2023–present), funding as a NIHR Senior Investigator, and unpaid involvement as a member of the NIHR CTU SAC (2020–2). Catherine Hewitt was also a member of the HTA Commissioning Sub-Board (EOI), HTA Post-Funding Committee teleconference, HTA Funding Committee Policy Group (formerly CSG), HTA Commissioning Committee, NIHR CTU Standing Advisory Committee, HTA – Fast-Track Funding Committee, HTA Fast Track Committee (June 2021) and is a member of the CTUs funded by NIHR.

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All other named authors declare no conflict of interest.

Department of Health and Social Care disclaimer

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This synopsis was published based on current knowledge at the time and date of publication. NIHR is committed to being inclusive and will continually monitor best practice and guidance in relation to terminology and language to ensure that we remain relevant to our stakeholders.

Trial registration

This trial is registered as Current Controlled Trials ISRCTN 26277546.

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Award publications

This synopsis provided an overview of the research award A pragmatic multicentre randomised controlled trial to assess the clinical and cost effectiveness of negative pressure wound therapy versus usual care for surgical wounds healing by secondary intention (SWHSI 2).

Other articles published as part of this thread are:

Arundel CE, Mandefield L, Fairhurst C, Baird K, Gkekas A, Saramago P, *et al.* Negative pressure wound therapy versus usual care in patients with surgical wound healing by secondary intention in the UK (SWHSI-2): an open-label, multicentre, parallel-group, randomised controlled trial. *Lancet* 2025;405:1689–99. [https://doi.org/10.1016/S0140-6736\(25\)00143-6](https://doi.org/10.1016/S0140-6736(25)00143-6)

Arundel C, Zahra S, Chetter I; SWHSI-2 Trial Investigators. Surgical wounds healing by Secondary Intention-2 Trial: outcomes and learning from the internal pilot phase and main trial. *Pilot Feasibility Stud* 2025;11:90. <https://doi.org/10.1186/s40814-025-01658-w>

Saramago P, Gkekas A, Arundel CE, Chetter I; SWHSI-2 Trial Investigators. Negative pressure wound therapy for surgical wounds healing by secondary intention is not cost-effective. *Br J Surg* 2025;12:znaf077. <https://doi.org/10.1093/bjs/znaf077>

Macefield R, Mandefield L, Blazeby JM, Fairhurst C, Baird K, Arundel C, *et al.* Modification and validation of the Bluebelle Wound Healing Questionnaire (WHQ) for assessing surgical site infection in wounds healing by secondary intention. *J Tissue Viability* 2025;34:100889. <https://doi.org/10.1016/j.jtv.2025.100889>

For more information about this research, please view the award page (www.fundingawards.nihr.ac.uk/award/17/42/94).

Additional outputs

Chetter IC, Arundel CE, Corbacho-Martin B, Hewitt C, Fairhurst C, Joshi K, *et al.* Negative pressure wound therapy versus usual care for surgical wounds healing by secondary intention (SWHSI-2

trial): study protocol for a pragmatic, multicentre, cross surgical specialty, randomised controlled trial. *Trials* 2021;22:739. <https://doi.org/10.1186/s13063-021-05662-2>

Conferences

Chetter I. *Surgical Wounds Healing by Secondary Intention; Management Pathway – From Assessment to Treatment*. Charing Cross International Symposium, April 2019.

Arundel C. *Surgical Wound Healing by Secondary Intention Trial-2*. Wounds UK, November 2019.

Arundel C. *Surgical Wound Healing by Secondary Intention Trial-2*. National Research Collaborative Meeting, December 2019.

Chetter I. *The SWHSI Programme Grant and SWHSI-2 Trial*. Wounds Research Network – European Wound Management Association Conference, November 2020.

Arundel C. *Surgical Wound Healing by Secondary Intention Trial-2*. Wounds Research Network/Tissue Viability Society Conference, September 2021.

Arundel C. *Assessment of Healing in Open Surgical Wounds*. Wounds Research Network/Tissue Viability Society Conference, September 2021.

Arundel C. *Surgical Wound Healing by Secondary Intention Trial-2*. Vascular Society Annual Scientific Meeting, December 2021.

Arundel C. *Surgical Wound Healing by Secondary Intention Trial-2*. Yorkshire Vascular Forum, June 2022.

Chetter I. *A Decade of Surgical Wounds Research*. The Grey Turner Lecture – University of Newcastle, June 2024.

Arundel C, Chetter I, Dixon S. *Surgical Wound Healing by Secondary Intention Trial-2 Results*. Vascular Society Annual Scientific Meeting, November 2024.

Chetter I. *Surgical Wound Healing by Secondary Intention Trial-2 Results*. Vascular Society of Aotearoa New Zealand, February 2025.

Arundel C. *Surgical Wound Healing by Secondary Intention Trial-2 Results*. European Wound Management Association Conference, March 2025.

Arundel C. *Surgical Wound Healing by Secondary Intention Trial-2 Results*. Society of Tissue Viability Conference, May 2025.

Arundel C. *Surgical Wound Healing by Secondary Intention Trial-2 Results*. Association of Surgeons of Great Britain and Ireland Conference, May 2025.

Arundel C. *Surgical Wound Healing by Secondary Intention Trial-2 Results*. Surgical Infection Society – Europe, May 2025.

Seminars

Chetter I, Arundel C. *Surgical Wound Healing by Secondary Intention Trial-2*. National Wound Care Strategy – Evidence for Wound Care Seminar, July 2019.

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List of supplementary material

Report Supplementary Material 1

SWHSI-2 statistical analysis plan

Report Supplementary Material 2

SWHSI-2 health economics analysis plan

Supplementary material can be found on the NIHR Journals Library report page (<https://doi.org/10.3310/GJIC1716>).

Supplementary material has been provided by the authors to support the report and any files provided at submission will have been seen by peer reviewers, but not extensively reviewed. Any supplementary material provided at a later stage in the process may not have been peer reviewed.

The supplementary materials (which include but are not limited to related publications, patient information leaflets and questionnaires) are provided to support and contextualise the publication. Every effort has been made to obtain the necessary permissions for reproduction, to credit original sources appropriately, and to respect copyright requirements. However, despite our diligence, we acknowledge the possibility of unintentional omissions or errors and we welcome notifications of any concerns regarding copyright or permissions.

List of abbreviations

A&E	accident and emergency
API	Associate Principal Investigator
CDC	Centre for Disease Control and Prevention
CEAC	cost-effectiveness acceptability curves
COVID-19	coronavirus disease 2019
CVD	cardiovascular disease
EQ-5D-5L	EuroQol-5 Dimensions, five-level version
GP	general practitioner
HRQoL	health-related quality of life
IPD	individual patient data
JLA-VPSP	James Lind Alliance Vascular Priority Setting Partnership
MCAR	missing completely at random
NICE	National Institute for Health and Care Excellence

NIHR	National Institute for Health and Care Research
NMB	net monetary benefit
NPWT	negative pressure wound therapy
PPI	patient and public involvement
PIS	patient information sheet
PVD	peripheral vascular disease
QALY	quality-adjusted life-year
RCT	randomised controlled trial
ROC	receiver operating characteristic
SSI	surgical site infection
SWAT	study within a trial
SWHSI	surgical wounds healing by secondary intention
WHQ	Wound Healing Questionnaire

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Appendix 1 Summary of protocol amendments

TABLE 7 Summary of protocol amendments

Protocol (version/date)	Changes made	Sponsor approval (date)	REC approval (date)	HRA approval (date)	Date of issue
V1.1 21 March 2019	Change to Inclusion criteria relating to participant age. Reduced from 18 years to 16 years at request of the approving Research Ethics Committee	Pre-approval	Pre-approval	Pre-approval	21 March 19
v1.2 6 June 2019	Clarification on derivation of sample size Clarification to exclusion criteria Addition of details of engagement with sites Addition of wound photograph at Baseline Removal of CDC assessment at 3 months, in selected sites	7 June 2019	18 July 2019	5 August 2019	10 September 2019
v1.3 3 December 2019	Clarification to exclusion criteria Addition of two methodological SWATs Reduction of post wound healing photographs to one image at initial assessment Inclusion of patient taken post wound healing photograph where required Removal of right to erasure in accordance with GDPR for research	6 January 2020	24 January 2020	24 January 2020	28 January 2020
V1.4 31 July 2020	Addition of a participant newsletter Addition of pens with postal case report form (CRFs) Changes to participant photography procedure Addition of telephone follow-up Addition of PPI group invite	4 August 2020	7 September 2020	15 September 2020	20 October 2020
v1.5 15 July 2021	Change to allow consent to be obtained by any suitably qualified and experience member of the research team as agreed with local R&D and Sponsor	21 July 2021	N/A – notification only	2 September 2021	15 July 2021
v1.6 1 July 2022	Reordering and shortening of M3, M6 and M12 Patient CRFs	14 July 2022	17 August 2022	30 August 2022	10 October 2022

Appendix 2 Prespecified sensitivity and subgroup analyses

Sensitivity analysis of the primary outcome

TABLE 8 Sensitivity analyses on primary outcome

Description of analysis	n	HR (95% CI)	p-value
Competing risks model (death and amputation of SWHSI as competing events)	686	0.99 (0.80 to 1.24)	0.93
Wound location corrected (stratification errors)	686	1.10 (0.90 to 1.33)	0.38
Baseline imbalances (including smoking status and alcohol consumption)	686	1.08 (0.88 to 1.33)	0.45
Wound area calculation	686	1.08 (0.88 to 1.32)	0.48
Removal of covariates that violate the proportional hazards assumption	686	1.04 (0.85 to 1.27)	0.69
CACE analysis (using received NPWT as a complier)	686	1.08 (0.81 to 1.43)	0.61

Subgroup analysis

TABLE 9 Subgroup analysis

	<i>n</i>	HR (95% CI)	<i>p</i> -value
Subgroup: previous history of SWHSI ^a	641	1.00 (0.66 to 1.50)	0.98

^a Treatment effect is the interaction term between allocation and history of SWHSI (yes/no).

Appendix 3 Site list

TABLE 10 List of recruiting sites

SWHSI-2 Recruiting NHS Trusts

Aneurin Bevan University Health Board (Bwrdd Iechyd Prifysgol Aneurin Bevan)

Bradford Teaching Hospitals NHS Foundation Trust

Royal Cornwall Hospitals NHS Trust

Doncaster and Bassetlaw Teaching Hospitals NHS Foundation Trust

The Dudley Group NHS Foundation Trust

Frimley Health NHS Foundation Trust

Hull University Teaching Hospitals NHS Trust

Imperial College Healthcare NHS Trust

NHS Lanarkshire

The Leeds Teaching Hospitals NHS Trust

Liverpool University Hospitals NHS Foundation Trust

NHS Lothian

Manchester University NHS Foundation Trust

Mid Yorkshire Teaching NHS Trust

The Newcastle upon Tyne Hospitals NHS Foundation Trust

Northumbria Healthcare NHS Foundation Trust

Norfolk and Norwich University Hospitals NHS Foundation Trust

North Bristol NHS Trust

Northern Care Alliance Foundation Trust

The Queen Elizabeth Hospital King's Lynn NHS Foundation Trust

Royal Free London NHS Foundation Trust

The Shrewsbury and Telford Hospital NHS Trust

St George's University Hospitals NHS Foundation Trust

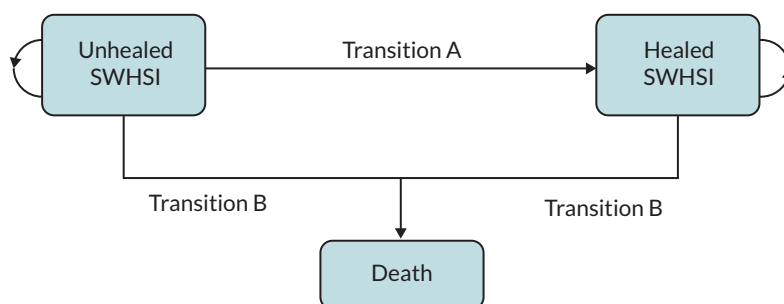
University Hospitals Birmingham NHS Foundation Trust

University Hospitals of Derby and Burton NHS Foundation Trust

University Hospitals of Leicester NHS Trust

Worcestershire Acute Hospitals NHS Trust

Appendix 4 Cost-effectiveness analyses



Overview of economic model components		Summary of data sources
Transition A – unhealed to healed SWHSI		Systematic literature review and meta-analysis on time to wound healing for SWHSI
Transition B – unhealed and healed SWHSI to death by any cause		Adjusted ONS general population mortality
Healed SWHSI HRQoL (QALYs)		Age and sex UK population utility values
Unhealed SWHSI HRQoL (QALYs)		Age and sex UK population utility values with decrement (derived from the SWHSI-2 trial) due to unhealed SWHSI
Healed SWHSI costs		Assumption – no cost
Unhealed SWHSI costs	NPWT costs	SWHSI-2 trial centre-specific estimates (Hull and Cornwall)
	Standard dressing costs	
	Medication	
	Primary care appointment (GP and nurse home/surgery, inc. dressing changes)	
	Secondary care appointments	
	Hospital stays	
	A&E visits	

FIGURE 3 Markov model for SWHSI over patients' lifetime.

Unit costs

TABLE 11 Unit costs of primary and secondary healthcare resources

Health resource	Unit cost	Description	Source
GP surgery appointment	£41.00	Based on £41/9.22 minutes. 9.22-minute appointment	PSSRU 2023
GP home appointment	£107.01	Based on £41/9.22 minutes. 11.4-minute home visit, 12 minutes of travel and 5 miles of travel assumed (£0.59 per mile)	PSSRU 2023
Nurse surgery appointment	£13.43	Based on £52/hours and 15.5 minutes of patient contact	PSSRU 2023
Nurse home appointment	£26.78	Based on minutes of travel and 5 miles of travel (£0.59/mile)	PSSRU 2023
Hospital outpatient appointment (diabetic foot clinic)	£183.00	Service code: 307 (Diabetes Service)	NHS Reference Costs 2021/2022

TABLE 11 Unit costs of primary and secondary healthcare resources (*continued*)

Health resource	Unit cost	Description	Source
Hospital outpatient appointment (Podiatry)	£93.00	Service code: 653 (Podiatry Service)	NHS Reference Costs 2021/2022
Hospital outpatient appointment (specialty dressing clinic)	£175.00	Currency code: JB71A (Cleansing and Dressing of Burn, 16 years and over)	NHS Reference Costs 2021/2022
Hospital outpatient appointment (vascular, colorectal or plastics)	£176.33	Average of service codes 104 (Colorectal Surgery Service), 107 (Vascular Surgery Service), 160 (Plastic Surgery Service)	NHS Reference Costs 2021/2022
Hospital admission without overnight	£1038.36	Average cost of elective hospital stays	NHS Reference Costs 2021/2022
Hospital inpatient nights (per night)	£492.19	Elective inpatient excess bed-days (£431). Inflation adjusted according to World Bank GDP deflator for UK	NHS Reference Costs 2017/2018
A&E	£242.00	Emergency care	NHS Reference Costs 2021/2022

PSSRU, Personal Social Services Research Unit.

TABLE 12 Unit costs of medications

Medication	Unit cost (per day)	Description	Source
Paracetamol	£0.19	Paracetamol 500 mg caplets, 100 tablets: £2.34. Max use: 8 tablets per day	BNF 2023
Co-codamol	£0.26	Co-codamol 8 mg/500 mg, 100 tablets: £3.27. Max use: 8 tablets per day	BNF 2023
Tramadol	£1.07	Zydol 50 mg soluble tablets, 100 tablets: £13.33 Max use: 8 tablets per day	BNF 2023
Codeine phosphate	£0.42	Codeine 15 mg tablets, 100 tablets: £2.64. Max use: 16 tablets per day	BNF 2023
Short acting morphine	£0.51	Morphine sulphate 20 mg tablets, 56 tablets: £9.50. Max use: Three 20 mg tablets per day	BNF 2023
Long-acting morphine	£0.41	Morphine sulphate 60 mg tablets, 60 tablets: £24.32. Max use: One 60 mg tablet per day	BNF 2023
Other morphine-based tablets	£0.45	Kaolin and Morphine mixture; 200 ml: £2.27 Max use: 40 ml per day	BNF 2023
Morphine oral suspension	£0.81	Morphine sulphate 10 mg/5 ml oral solution. 500 ml: £6.72. Max use: 120 mg per day, that is 60 ml	BNF 2023
Amitriptyline	£0.07	Amitriptyline 25 mg tablets. 28 tablets: £0.68. Max use: 75 mg per day (neuropathic pain), that is 3 tablets per day	BNF 2023
Pregabalin	£0.34	Pregabalin 75 mg tablets. 56 tablets: £4.79. Initially 150 mg daily in 2–3 divided doses, then increased if necessary to 300 mg daily in 2–3 divided doses, dose to be increased after 3–7 days, then increased, if necessary, up to 600 mg daily in 2–3 divided doses, dose to be increased after 7 days. Assume 300 mg per day, that is 4 tablets per day	BNF 2023
Gabapentin	£0.08	Gabapentin 300 mg capsules. 100 capsules: £2.55. Max use: 3 capsules (900 mg) per day	BNF 2023
Diclofenac	£2.91	Diclofenac. 74 mg per 1 ml. 200 ml: £12.95. Max use: 45 ml per day	BNF 2023
Aspirin	£1.63	Aspirin 300 mg tablets. 100 tablets: £12.56. Max use: 4 g per day for pyrexia (by mouth), that is 13 tablets	BNF 2023
Ibuprofen	£0.22	Ibuprofen 200 mg tablets. 250 tablets: £9.30. Max use: 1200 mg per day, that is 6 tablets per day	BNF 2023

continued

TABLE 12 Unit costs of medications (continued)

Medication	Unit cost (per day)	Description	Source
Antibiotics	£1.06	Weighted average of: - Flucloxacillin 500 mg capsules. 28 capsules: £2.01. Max use: 2 g/day, that is 4 tablets a day (£0.29) - Co-amoxiclav 500/125 mg capsules. 21 capsules. Max use: 500/125 mg every 8 hours for foot infection/leg ulcers, that is 3 tablets a day (£0.48) - Metronidazole 400 mg tablets. Max use: 400 mg every 8 hours for leg ulcers, that is 3 tablets a day (£0.15) - Clindamycin 300 mg tablets. Max use: 300 mg every 6 hours for foot infection, that is 4 tablets a day (£4.60) - Ciprofloxacin 500 mg tablets. Max use: 500 mg twice daily, that is 2 tablets a day (£0.20) - Doxycycline. Max use: 100 mg daily (200 mg day 1 and then 100 mg for another 6 days), that is 1 tablet a day on average (£0.61)	BNF 2023
Beta blockers	£0.03	Amlodipine 5 mg 28 tablets. Max use: 5 mg per day	BNF 2023
Anticoagulant	£0.18	Apixaban 5 mg 56 tablets. Max use: 10 mg twice daily, that is 2 tablets daily	BNF 2023
Atorvastatin	£0.06	Atorvastatin 20 mg 28 tablets Max use: 20 mg once daily	BNF 2023
Clopidogrel	£0.04	Clopidogrel 75 mg 28 tablets. Max use: 75 mg once daily	BNF 2023
Analgesics (oxycodone)	£8.94	Oxycodone modified released medicine 40 mg 56 tablets. Max use: 400 mg per day, that is 10 tablets per day	BNF 2023
Metformin	£0.02	Metformin 28 tablets (500 mg). Max use: 500 mg per day	BNF 2023
Omeprazole	£0.21	Omeprazole 28 tablets (20 mg). Max use: 20 mg per day	
Duloxetine	£0.31	Duloxetine 28 tablets (60 mg). Max dose: 60 mg per day	BNF 2023
Isosorbide mononitrate	£0.73	Isosorbide Mononitrate 56 tablets (40 mg). Max dose: 40 mg twice per day	BNF 2023
Perindopril	£0.04	Perindopril erbumine 30 tablets (4 mg). Max dose: 4 mg per day	BNF 2023
BNF, British National Formulary.			

TABLE 13 Intervention-related daily costs

	Unit cost	Source
Standard dressings		
<i>Type of dressing</i>		
Alginate dressing (advanced)	£2.46	BNF 2023
Hydrogel dressing (advanced)	£4.62	BNF 2023
Hydrocolloid dressing (advanced)	£3.37	BNF 2023
Basic wound contact dressing	£0.98	BNF 2023
Hydrofibre/spun Hydrocolloid dressing (advanced)	£4.19	BNF 2023
Foam dressing (advanced)	£4.13	BNF 2023

TABLE 13 Intervention-related daily costs (*continued*)

	Unit cost	Source
Soft Polymer dressing (advanced)	£5.55	BNF 2023
Cavity foam dressing	£3.49	BNF 2023
Silver containing	£10.79	BNF 2023
Iodine containing	£3.28	BNF 2023
Superabsorbent dressing (advanced)	£4.97	BNF 2023
Gauze Ribbon	£0.00	BNF 2023
Honey	£3.98	BNF 2023
PHMB	£7.24	BNF 2023
Protease modulating matrix	£6.16	BNF 2023
Vapour permeable	£1.51	BNF 2023
Average daily cost of standard dressings (SE)	£4.17 (£0.11)	
NPWT		
<i>Type of device</i>		
PICO7	£15.43	Data from Cornwall site
<i>Type of dressing</i>		
Medium dressing (Granufoam)	£11.03	Data from Cornwall site
Small dressing (Granufoam)	£9.48	Data from Cornwall site
White foam	£10.16	Data from Cornwall site
Gauze	£13.01	Data from Cornwall site
Small canister/Small foam dressing	£16.65	Data from Hull site
Small canister/Medium foam dressing	£17.21	Data from Hull site
Small canister/Large foam dressing	£17.89	Data from Hull site
Small canister/Gauze dressing	£13.71	Data from Hull site
Small canister/Polyvinyl dressing	£14.19	Data from Hull site
Medium canister/Small foam dressing	£18.98	Data from Hull site
Medium canister/Medium foam dressing	£19.54	Data from Hull site.
Medium canister/Large foam dressing	£20.22	Data from Hull site
Medium canister/Gauze dressing	£16.04	Data from Hull site
Medium canister/Polyvinyl dressing	£16.52	Data from Hull site
<i>Average daily cost of dressings</i>	<i>£15.18</i>	
<i>Average daily cost of device</i>	<i>£15.43</i>	
Average daily cost of NPWT (SE)	£30.61 (£3.41)	
BNF, <i>British National Formulary</i> .		
Note		
The average daily costs of dressings for both standard dressings and NPWT were based on the average of the presented daily unit costs of different types of dressings. Regarding NPWT, the average daily cost of the device is also incorporated to estimate its average daily cost. The presented costs aimed to cover the most realistic practices of delivering NPWT and standard dressings and thus to produce the most accurate daily costs of these treatments given the information available.		

TABLE 14 Logistic regressions (correlation between missing QALYs/missing costs and baseline variables)

	Odds ratio in logistic regression for missing data (95% CI; p-value)	
	Missing data on QALYs	Missing data on costs
Treatment allocation	1.04 [(95% CI 0.76 to 1.42); (p-value = 0.82)]	1.24 [(95% CI 0.87 to 1.76); (p-value = 0.24)]
Age	0.97 [(95% CI 0.96 to 0.98); (p-value = 0.00)]*	0.99 [(95% CI 0.97 to 1.00); (p-value = 0.11)]
Gender	0.83 [(95% CI 0.56 to 1.22); (p-value = 0.34)]	0.74 [(95% CI 0.47 to 1.16); (p-value = 0.19)]
EQ-5D-5L score (baseline)	0.48 [(95% CI 0.25 to 0.89); (p-value = 0.02)]*	0.36 [(95% CI 0.17 to 0.74); (p-value = 0.01)]*
Duration of SWHSI	1.00 [(95% CI 0.97 to 1.02); (p-value = 0.75)]	1.04 [(95% CI 1.00 to 1.08); (p-value = 0.04)]*
Number of SWHSI	1.06 [(95% CI 0.71 to 1.60); (p-value = 0.77)]	0.83 [(95% CI 0.53 to 1.32); (p-value = 0.44)]
Location of SWHSI	0.92 [(95% CI 0.73 to 1.17); (p-value = 0.50)]	0.93 [(95% CI 0.71 to 1.20); (p-value = 0.56)]
Area of SWHSI	0.99 [(95% CI 0.99 to 1.00); (p-value = 0.05)]*	1.00 [(95% CI 1.00 to 1.01); (p-value = 0.78)]
Treatment location	0.94 [(95% CI 0.85 to 1.04); (p-value = 0.20)]	1.04 [(95% CI 0.91 to 1.17); (p-value = 0.58)]
History of previous SWHSI	1.20 [(95% CI 0.76 to 1.89); (p-value = 0.42)]	1.69 [(95% CI 0.98 to 2.92); (p-value = 0.06)]**
Infection of SWHSI	1.10 [(95% CI 0.68 to 1.79); (p-value = 0.70)]	0.70 [(95% CI 0.41 to 1.18); (p-value = 0.18)]
Full-thickness skin loss	0.71 [(95% CI 0.50 to 1.01); (p-value = 0.06)]**	0.53 [(95% CI 0.36 to 0.80); (p-value = 0.00)]*
Subcutaneous issue exposed	1.29 [(95% CI 0.91 to 1.82); (p-value = 0.15)]	1.31 [(95% CI 0.89 to 1.92); (p-value = 0.18)]
Underlying muscle exposed	1.14 [(95% CI 0.78 to 1.66); (p-value = 0.51)]	1.04 [(95% CI 0.69 to 1.58); (p-value = 0.85)]
Underlying tendons exposed	1.09 [(95% CI 0.72 to 1.65); (p-value = 0.70)]	1.24 [(95% CI 0.77 to 1.99); (p-value = 0.39)]
Underlying bone exposed	0.86 [(95% CI 0.56 to 1.31); (p-value = 0.48)]	1.47 [(95% CI 0.89 to 2.42); (p-value = 0.14)]
Tissue involvement unclear due to devitalised tissue	0.68 [(95% CI 0.17 to 2.67); (p-value = 0.58)]	0.66 [(95% CI 0.15 to 2.87); (p-value = 0.58)]

TABLE 15 EuroQol-5 Dimensions, five-level version levels by dimension, intervention group and follow-up point

EQ-5D-5L scale		Baseline		3 months		6 months		12 months	
	Health state severity	NPWT	Usual care	NPWT	Usual care	NPWT	Usual care	NPWT	Usual care
Mobility	Level 1	58 (16.62%)	48 (14.24%)	50 (14.33%)	44 (13.06%)	52 (14.90%)	51 (15.13%)	42 (12.03%)	36 (10.68%)
	Level 2	83 (23.78%)	77 (22.85%)	35 (10.03%)	50 (14.84%)	43 (12.32%)	31 (9.20%)	44 (12.61%)	39 (11.57%)
	Level 3	81 (23.21%)	94 (27.89%)	62 (17.77%)	52 (15.43%)	50 (14.33%)	55 (16.32%)	45 (12.89%)	48 (14.24%)
	Level 4	62 (17.77%)	54 (16.02%)	35 (10.03%)	47 (13.95%)	36 (10.32%)	26 (7.72%)	30 (8.60%)	32 (9.50%)
	Level 5	56 (16.05%)	51 (15.13%)	22 (6.30%)	19 (5.64%)	25 (7.16%)	21 (6.23%)	25 (7.16%)	13 (3.86%)
	Missing	9 (2.58%)	13 (3.86%)	145 (41.55%)	125 (37.09%)	143 (40.97%)	153 (45.40%)	163 (46.70%)	169 (50.15%)
Self-care	Level 1	189 (54.15%)	157 (46.59%)	110 (31.52%)	107 (31.75%)	113 (32.38%)	93 (27.60%)	104 (29.80%)	91 (27.00%)
	Level 2	61 (17.48%)	74 (21.96%)	38 (10.89%)	40 (11.87%)	40 (11.46%)	41 (12.17%)	30 (8.60%)	27 (8.01%)
	Level 3	58 (16.62%)	62 (18.40%)	38 (10.89%)	44 (13.06%)	35 (10.03%)	37 (10.98%)	32 (9.17%)	34 (10.09%)
	Level 4	18 (5.16%)	19 (5.64%)	12 (3.44%)	11 (3.26%)	11 (3.15%)	8 (2.37%)	12 (3.44%)	12 (3.56%)
	Level 5	14 (4.01%)	13 (3.86%)	7 (2.01%)	11 (3.26%)	6 (1.72%)	5 (1.48%)	9 (2.58%)	4 (1.19%)
	Missing	9 (2.58%)	12 (3.56%)	144 (41.26%)	124 (36.80%)	144 (41.26%)	153 (45.40%)	162 (46.42%)	169 (50.15%)

TABLE 15 EuroQol-5 Dimensions, five-level version levels by dimension, intervention group and follow-up point (*continued*)

EQ-5D-5L scale		Baseline		3 months		6 months		12 months	
	Health state severity	NPWT	Usual care	NPWT	Usual care	NPWT	Usual care	NPWT	Usual care
Usual activities	Level 1	71 (20.34%)	60 (17.80%)	52 (14.90%)	48 (14.24%)	56 (16.05%)	56 (16.62%)	54 (15.47%)	40 (11.87%)
	Level 2	73 (20.92%)	72 (21.36%)	44 (12.61%)	45 (13.35%)	49 (14.04%)	38 (11.28%)	35 (10.03%)	38 (11.28%)
	Level 3	83 (23.78%)	61 (18.10%)	47 (13.47%)	52 (15.43%)	43 (12.32%)	35 (10.39%)	36 (10.32%)	40 (11.87%)
	Level 4	41 (11.75%)	49 (14.54%)	36 (10.32%)	36 (10.68%)	35 (10.03%)	28 (8.31%)	35 (10.03%)	28 (8.31%)
	Level 5	70 (20.06%)	81 (24.04%)	25 (7.16%)	33 (9.79%)	22 (6.30%)	28 (8.31%)	27 (7.74%)	22 (6.53%)
	Missing	11 (3.15%)	14 (4.15%)	145 (41.55%)	123 (36.50%)	144 (41.26%)	152 (45.10%)	162 (46.42%)	169 (50.15%)
Pain/discomfort	Level 1	102 (29.23%)	111 (32.94%)	66 (18.91%)	76 (22.55%)	70 (20.06%)	73 (21.66%)	62 (17.77%)	61 (18.10%)
	Level 2	107 (30.66%)	93 (27.60%)	52 (14.90%)	63 (18.69%)	67 (19.20%)	52 (15.43%)	61 (17.48%)	41 (12.17%)
	Level 3	76 (21.78%)	71 (21.07%)	58 (16.62%)	49 (14.54%)	48 (13.75%)	40 (11.87%)	38 (10.89%)	43 (12.76%)
	Level 4	42 (12.03%)	40 (11.87%)	24 (6.88%)	21 (6.23%)	17 (4.87%)	11 (3.26%)	24 (6.88%)	18 (5.34%)
	Level 5	14 (4.01%)	11 (3.26%)	4 (1.15%)	4 (1.19%)	4 (1.15%)	7 (2.08%)	3 (0.86%)	4 (1.19%)
	Missing	8 (2.29%)	11 (3.26%)	145 (41.55%)	124 (36.80%)	143 (40.97%)	154 (45.70%)	161 (46.13%)	170 (50.45%)
Anxiety/depression	Level 1	163 (46.70%)	158 (46.88%)	96 (27.51%)	106 (31.45%)	89 (25.50%)	95 (28.19%)	94 (26.93%)	87 (25.82%)
	Level 2	87 (24.93%)	81 (24.04%)	43 (12.32%)	46 (13.65%)	49 (14.04%)	42 (12.46%)	42 (12.03%)	30 (8.90%)
	Level 3	66 (18.91%)	53 (15.73%)	42 (12.03%)	38 (11.28%)	46 (13.18%)	29 (8.61%)	32 (9.17%)	28 (8.31%)
	Level 4	15 (4.30%)	23 (6.82%)	18 (5.16%)	13 (3.86%)	14 (4.01%)	13 (3.86%)	16 (4.58%)	14 (4.15%)
	Level 5	9 (2.58%)	10 (2.97%)	4 (1.15%)	10 (2.97%)	7 (2.01%)	5 (1.48%)	3 (0.86%)	8 (2.37%)
	Missing	9 (2.58%)	12 (3.56%)	146 (41.83%)	124 (36.80%)	144 (41.26%)	153 (45.40%)	162 (46.42%)	170 (50.45%)

TABLE 16 Summary of EQ-5D-5L utility scores and mean difference (95% CI) at each time point, based on all available cases

Health utility	NPWT (n = 349)		Usual care (n = 337)		Total (n = 686)		Mean difference (unadjusted)
	Mean (SE)	n (% missing)	Mean (SE)	n (% missing)	Mean (SE)	n (% missing)	
EQ-5D-5L score (baseline)	0.614 (0.015)	335 (4.0%)	0.601 (0.016)	321 (4.7%)	0.607 (0.011)	656 (4.4%)	0.012 (95% CI -0.030 to 0.055)
EQ-5D-5L score (3 months)	0.598 (0.022)	209 (40.1%)	0.581 (0.021)	228 (32.3%)	0.589 (0.015)	437 (36.3%)	0.017 (95% CI -0.043 to 0.077)
EQ-5D-5L score (6 months)	0.590 (0.022)	222 (36.4%)	0.572 (0.024)	210 (37.7%)	0.581 (0.016)	432 (37.0%)	0.019 (95% CI -0.045 to 0.083)
EQ-5D-5L score (12 months)	0.524 (0.025)	223 (36.1%)	0.514 (0.025)	207 (38.6%)	0.519 (0.017)	430 (37.3%)	0.010 (95% CI -0.059 to 0.078)
QALYs (all available)	0.575 (0.024)	151 (56.7%)	0.566 (0.024)	143 (57.6%)	0.571 (0.017)	294 (57.1%)	0.009 (95% CI -0.058 to 0.076)
SE, standard error.							

TABLE 17 Summary of EQ-5D-5L utility scores and mean difference (95% CI) at each time point, based on multiply imputed data set

Health utility	NPWT (n = 349)	Usual care (n = 337)	Total (n = 686)	Mean difference (unadjusted)
	Mean (SE)	Mean (SE)	Mean (SE)	
EQ-5D-5L score (baseline)	0.613 (0.014)	0.601 (0.015)	0.607 (0.010)	0.012 (95% CI -0.029 to 0.052)
EQ-5D-5L score (3 months)	0.590 (0.019)	0.563 (0.020)	0.577 (0.014)	0.027 (95% CI -0.027 to 0.082)
EQ-5D-5L score (6 months)	0.567 (0.021)	0.563 (0.020)	0.579 (0.014)	0.022 (95% CI -0.036 to 0.081)
EQ-5D-5L score (12 months)	0.541 (0.022)	0.532 (0.023)	0.536 (0.016)	0.009 (95% CI -0.055 to 0.073)
QALYs	0.581 (0.016)	0.562 (0.017)	0.571 (0.012)	0.019 (95% CI -0.027 to 0.065)

SE, standard error.

TABLE 18 Total mean costs based on all available cases, up to 12-month follow-up

Cost item	NPWT (n = 349)		Usual care (n = 337)		Total (n = 686)		Mean difference (unadjusted)
	Mean (SE)	n (% missing)	Mean (SE)	n (% missing)	Mean (SE)	n (% missing)	
GP surgery appointment	£29.87 (£10.59)	140 (59.9%)	£62.33 (£23.04)	123 (63.5%)	£45.05 (£12.17)	263 (61.7%)	-£32.46 (95% CI -£80.44 to £15.51)
GP home appointment	£18.58 (£6.18)	144 (58.7%)	£39.72 (£20.92)	132 (60.8%)	£28.69 (£10.51)	276 (59.8%)	-£21.15 (95% CI -£62.57 to £20.27)
Nurse surgery appointment	£122.56 (£23.69)	135 (61.3%)	£132.53 (£23.75)	114 (66.2%)	£127.13 (£16.80)	249 (63.7%)	-£9.97 (95% CI -£76.51 to £56.57)
Nurse home appointment	£533.62 (£74.63)	122 (65.0%)	£458.98 (£65.82)	108 (68.0%)	£498.57 (£50.17)	230 (66.5%)	£74.64 (95% CI -£123.65 to £272.94)
Hospital outpatient appointment (diabetic foot clinic)	£232.75 (£24.13)	320 (8.3%)	£272.49 (£25.21)	319 (5.3%)	£252.59 (£17.45)	639 (6.9%)	-£39.74 (95% CI -£108.27 to £28.79)
Hospital outpatient appointment (podiatry)	£32.55 (£6.72)	320 (8.3%)	£24.49 (£5.16)	319 (5.3%)	£28.53 (£4.24)	639 (6.9%)	£8.06 (95% CI -£8.58 to £24.70)
Hospital outpatient appointment (specialty dressing clinic)	£11.48 (£4.08)	320 (8.3%)	£18.10 (£6.21)	319 (5.3%)	£14.79 (£3.71)	639 (6.9%)	-£6.62 (95% CI -£21.20 to £7.96)
Hospital outpatient appointment (vascular, colorectal or plastics)	£38.57 (£5.20)	320 (8.3%)	£37.59 (£7.04)	319 (5.3%)	£38.08 (£4.37)	639 (6.9%)	£0.98 (95% CI -£16.18 to £18.15)
Hospital admission without overnight	£19.47 (£7.89)	320 (8.3%)	£29.30 (£10.69)	319 (5.3%)	£24.37 (£6.64)	639 (6.9%)	-£9.83 (95% CI -£35.90 to £16.24)
Hospital inpatient nights (per night)	£2934.01 (£824.34)	320 (8.3%)	£3621.22 (£964.58)	319 (5.3%)	£3277.08 (£633.91)	639 (6.9%)	-£687.21 (95% CI -£3178.22 to £1803.80)
A&E	£27.23 (£5.13)	320 (8.3%)	£40.97 (£8.76)	319 (5.3%)	£34.08 (£5.08)	639 (6.9%)	-£13.74 (95% CI -£33.66 to £6.18)
Medication costs	£90.05 (£13.94)	173 (50.4%)	£102.13 (£28.36)	166 (50.7%)	£95.96 (£15.58)	339 (50.6%)	-£12.08 (95% CI -£73.46 to £49.30)
Intervention costs	£1700.86 (£106.22)	349 (0.0%)	£967.26 (£69.77)	337 (0.0%)	£1340.48 (£65.46)	686 (0.0%)	£733.59 (95% CI £482.27 to £984.92)
Total costs	£4077.81 (£401.89)	104 (70.2%)	£6246.09 (£2347.22)	83 (75.4%)	£5040.20 (£1064.92)	187 (72.7%)	-£2168.29 (95% CI -£6396.65 to £2060.08)

SE, standard error.

TABLE 19 Total mean costs of health resources based on multiply imputed data set, up to 12-month follow-up

Cost item	NPWT (n = 349)	Usual care (n = 337)	Total (n = 686)	Mean difference (unadjusted)
	Mean (SE)	Mean (SE)	Mean (SE)	
GP surgery appointment	£35.88 (£11.71)	£48.23 (£13.58)	£41.95 (£8.88)	–£12.36 (95% CI –£47.92 to £23.20)
GP home appointment	£22.60 (£10.46)	£36.25 (£15.07)	£29.30 (£9.07)	–£13.65 (95% CI –£49.89 to £22.59)
Nurse surgery appointment	£115.95 (£19.34)	£121.42 (£19.32)	£118.64 (£14.02)	–£5.46 (95% CI –£58.13 to £47.20)
Nurse home appointment	£499.21 (£56.00)	£483.09 (£58.15)	£491.29 (£39.53)	£16.12 (95% CI –£146.99 to £179.24)
Hospital outpatient appointment (diabetic foot clinic)	£235.50 (£24.39)	£270.06 (£25.24)	£252.48 (£17.68)	–£34.56 (95% CI –£102.90 to £33.78)
Hospital outpatient appointment (podiatry)	£32.68 (£6.61)	£25.21 (£5.33)	£29.01 (£4.26)	£7.46 (95% CI –£9.26 to £24.19)
Hospital outpatient appointment (specialty dressing clinic)	£11.30 (£4.07)	£17.62 (£6.03)	£14.41 (£3.62)	–£6.32 (95% CI –£20.48 to £7.84)
Hospital outpatient appointment (vascular, colorectal or plastics)	£38.51 (£5.35)	£36.93 (£6.87)	£37.73 (£4.34)	£1.58 (95% CI –£15.42 to £18.58)
Hospital admission without overnight	£19.04 (£7.69)	£28.72 (£10.41)	£23.79 (£6.43)	–£9.68 (95% CI –£34.96 to £15.61)
Hospital inpatient nights (per night)	£2947.52 (£821.28)	£3618.22 (£954.87)	£3277.00 (£629.32)	–£670.70 (95% CI –£3132.41 to £1791.01)
A&E	£27.17 (£5.15)	£41.08 (£8.65)	£34.00 (£5.03)	–£13.91 (95% CI –£33.37 to £5.55)
Medication costs	£95.93 (£19.46)	£107.90 (£25.44)	£101.81 (£16.48)	–£11.97 (95% CI –£72.83 to £48.88)
Intervention costs	£1700.86 (£106.22)	£967.26 (£69.77)	£1340.48 (£65.46)	£733.59 (95% CI £482.27 to £984.92)
Total costs	£5782.14 (£830.36)	£5801.99 (£969.99)	£5791.89 (£637.49)	–£19.85 (95% CI –£2516.81 to £2477.11)

SE, standard error.

Main cost-utility results

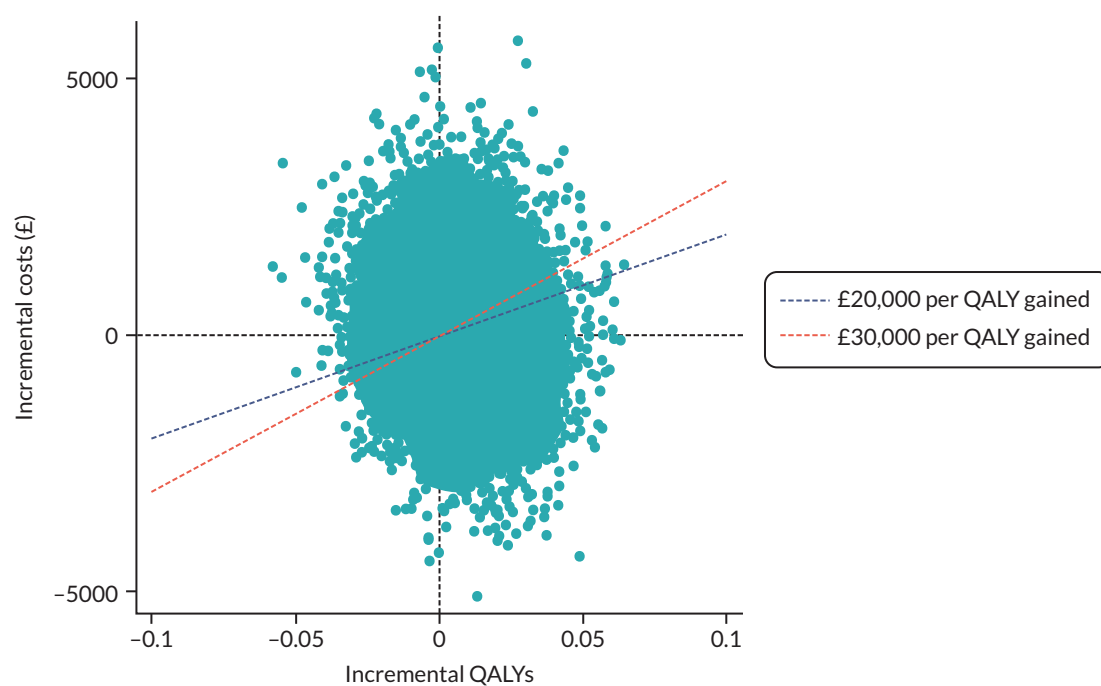
The within-trial economic analysis estimated the unadjusted mean per participant QALYs and mean per participant costs as 0.581 (95% CI 0.549 to 0.612) and £5782.13 (95% CI £4151.32 to £7412.95) for the NPWT group and 0.562 (95% CI 0.528 to 0.595) and £5801.99 (95% CI £3897.19 to £7706.78) for the usual-care group.

The mean difference-adjusted incremental QALYs and incremental costs suggest that NPWT increased QALYs by 0.007 (95% CI –0.024 to 0.038) and increased costs by £251.44 (95% CI –£2192.63 to £2695.52) over the 12-month study period. A cost-effectiveness plane ([Figure 4](#)) and a CEAC ([Figure 5](#)) graphically present the results of the base-case analysis.

TABLE 20 Cost-utility analysis (base-case analysis)

	NPWT (n = 349)	Usual care (n = 337)
Total QALYs	0.581 (95% CI 0.549 to 0.612)	0.562 (95% CI 0.528 to 0.595)
Incremental QALYs (adjusted) ^a	0.007 (95% CI -0.024 to 0.038)	
Total costs	£5782.13 (95% CI £4151.32 to £7412.95)	£5801.99 (95% CI £3897.19 to £7706.78)
Incremental costs (adjusted) ^a	£ 251.44 (95% CI -£2192.63 to £2695.52)	
Cost-utility results	£20,000 cost-effectiveness threshold	£30,000 cost-effectiveness threshold
Incremental NMB	-£93.22 (95% CI -£119.16 to -£67.28)	-£18.65 (95% CI -£45.85 to £8.55)
Probability of NPWT being cost-effective	47.2%	49.7%

^a Seemingly unrelated regression.

**FIGURE 4** Cost-effectiveness plane (base-case analysis).

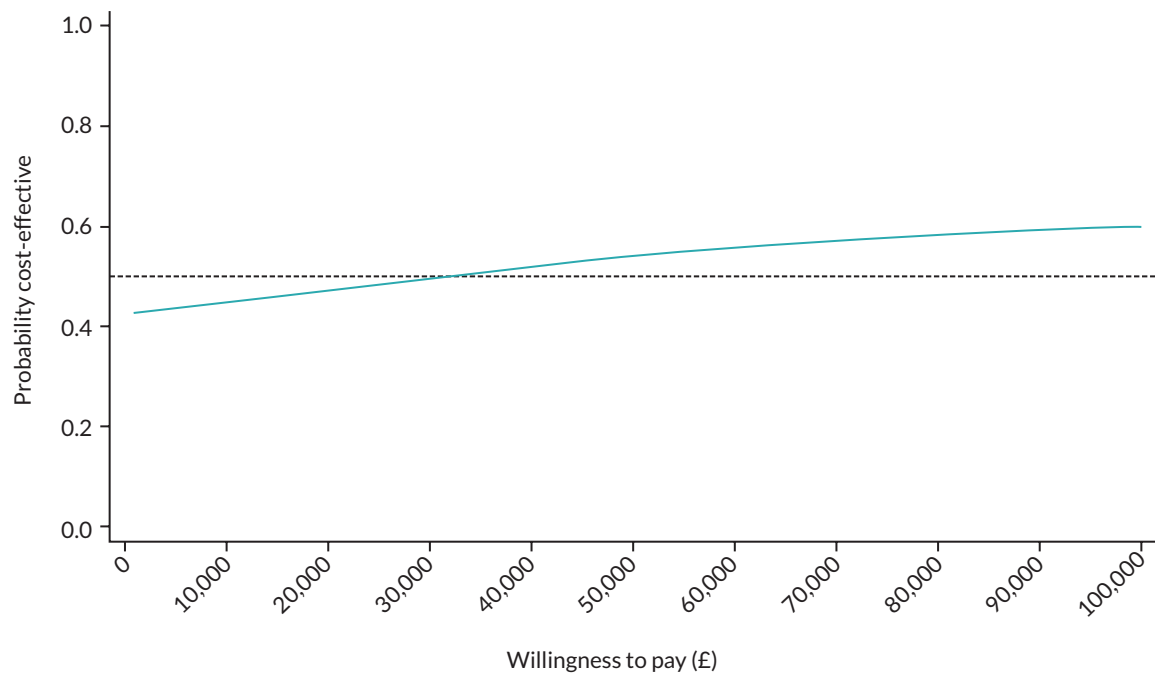


FIGURE 5 Cost-effectiveness acceptability curve (base-case analysis).

SA.1. Sensitivity analysis: complete-case analysis

Complete-case data were available for 167 participants (96 in the NPWT group and 71 in the usual-care group). The complete-case analysis estimated the unadjusted mean per participant QALYs and mean per participant costs as 0.669 (95% CI 0.623 to 0.715) and £4019.35 (95% CI £3237.10 to £4801.59) for the NPWT group and 0.678 (95% CI 0.624 to 0.732) and £6579.99 (95% CI £1128.59 to £12031.39) for the usual-care group. The mean difference-adjusted incremental QALYs and

incremental costs suggest that NPWT reduced QALYs by -0.000 (95% CI -0.059 to 0.058) and reduced costs by $-\text{£}1983.58$ (95% CI $-\text{£}6868.42$ to $\text{£}2901.24$) over the 12-month study period, although these results were not statistically significant. The Incremental Net Monetary Benefit (INMB) is £1956.77 and £1952.20 at the £20,000 and £30,000 cost-effectiveness thresholds respectively. The probability of cost-effectiveness of NPWT is 75.6% at the £20,000 threshold, and 74.6% at the £30,000 threshold. A cost-effectiveness plane and a CEAC present graphically these results (*Figures 6 and 7*).

TABLE 21 Cost-utility analysis (complete-case analysis)

Complete-case analysis (Intention to treat)		
	NPWT (n = 96)	Usual care (n = 71)
Total QALYs	0.669 (95% CI 0.623 to 0.715)	0.678 (95% CI 0.624 to 0.732)
Incremental QALYs (adjusted) ^a	-0.000 (95% CI -0.059 to 0.058)	
Total costs	£4019.35 (95% CI £3237.10 to £4801.59)	£6579.99 (95% CI £1128.59 to £12031.39)
Incremental costs (adjusted) ^a	$-\text{£}1983.58$ (95% CI $-\text{£}6868.42$ to $\text{£}2901.24$)	
Cost-utility results	£20,000 cost-effectiveness threshold	£30,000 cost-effectiveness threshold
Incremental NMB	£1956.77	£1952.20
Probability of NPWT being cost-effective	75.6%	74.6%

^a Seemingly unrelated regressions.

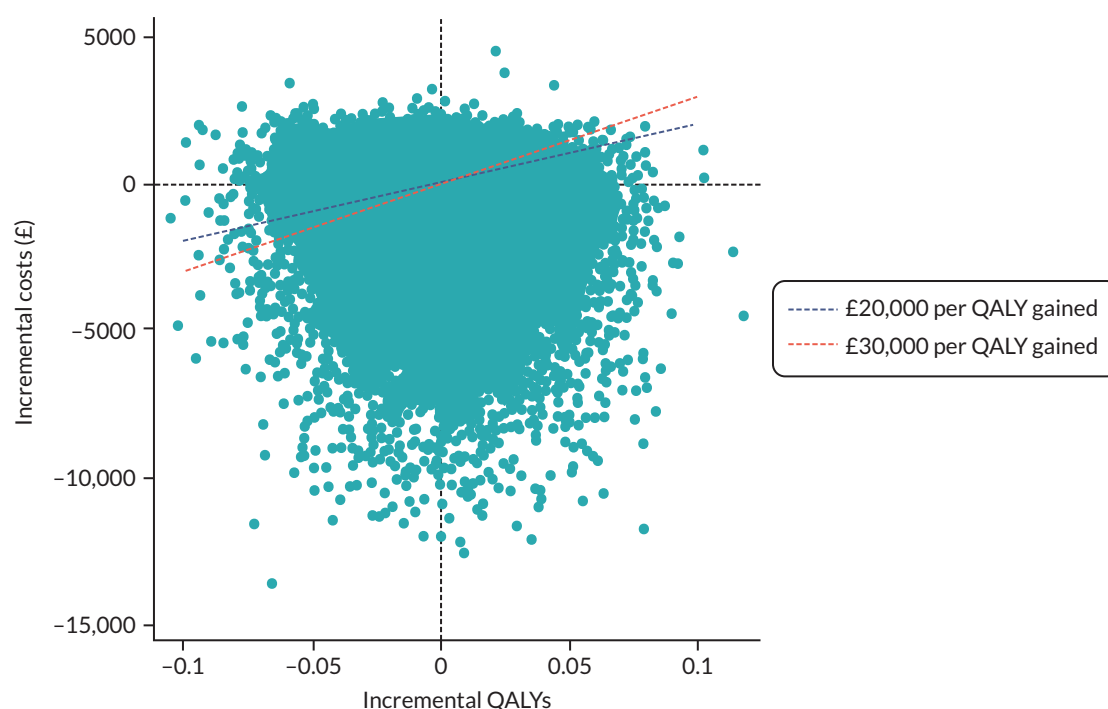


FIGURE 6 Cost-effectiveness plane (complete-case analysis).

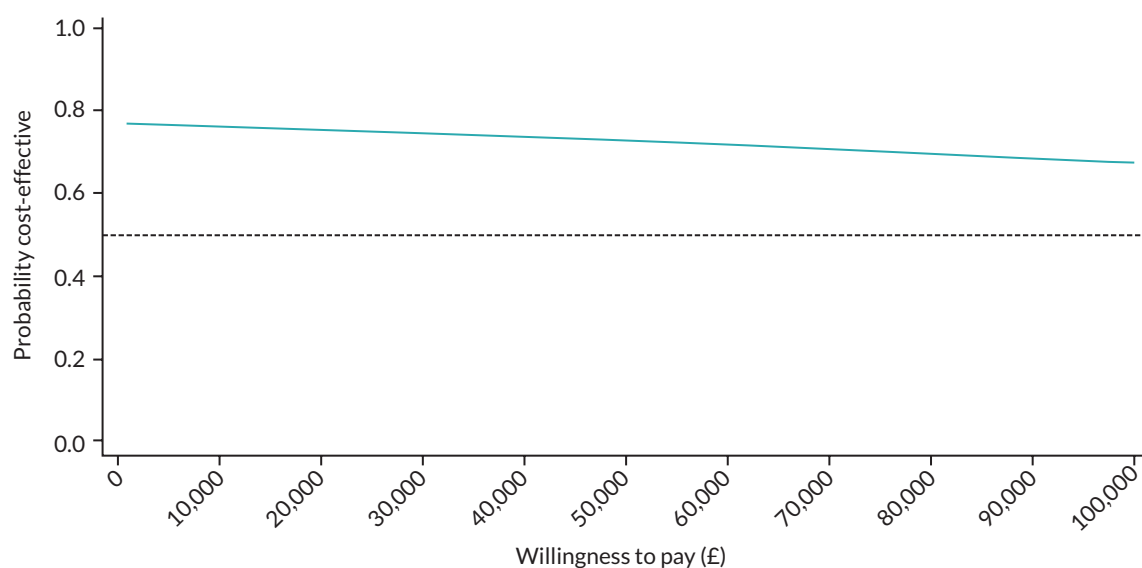


FIGURE 7 Cost-effectiveness acceptability curve (complete-case analysis).

SA.2. Sensitivity analysis: deaths excluded

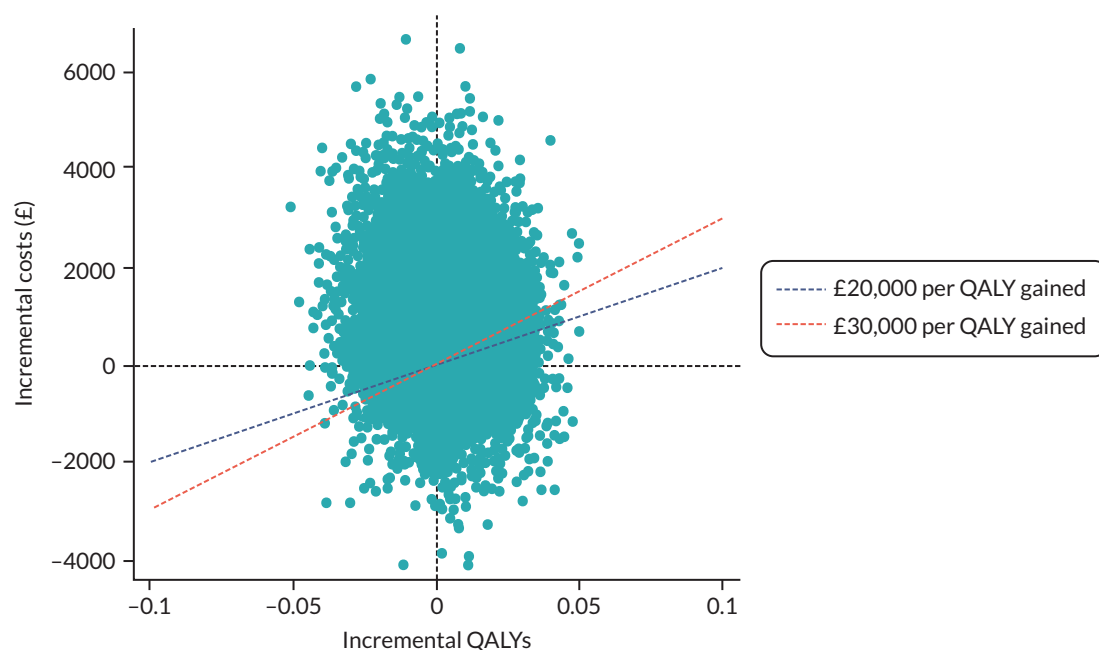
By excluding participants who died during the trial from the cost-utility analysis, the unadjusted mean per participant QALYs and mean per participant costs are 0.664 (95% CI 0.614 to 0.675) and £6173.83 (95% CI £4231.94 to £8115.73) for the NPWT group and 0.634 (95% CI 0.604 to 0.665) and £5610.79 (95% CI £3652.69 to £7568.88) for the usual-care group. The mean difference-adjusted incremental QALYs and incremental costs suggest that

NPWT increased QALYs by 0.002 (95% CI -0.026 to 0.029) and increased costs by £987.37 (95% CI -£1558.27 to £3533.02) over the 12-month study period, although these results were not statistically significant. The INMB is -£961.27 and -£942.45 at the £20,000 and £30,000 cost-effectiveness thresholds, respectively. The probability of cost-effectiveness of NPWT is 24.2% at the £20,000 threshold, and 25.5% at the £30,000 threshold. A cost-effectiveness plane and a CEAC graphically present these results (*Figures 8 and 9*).

TABLE 22 Cost-utility analysis (deaths excluded)

Deaths excluded (Intention to treat)		
	NPWT (n = 307)	Usual care (n = 295)
Total QALYs	0.664 (95% CI 0.614 to 0.675)	0.634 (95% CI 0.604 to 0.665)
Incremental QALYs (adjusted) ^a	0.002 (95% CI -0.026 to 0.029)	
Total costs	£ 6173.83 (95% CI £4231.94 to £8115.73)	£ 5610.79 (95% CI £3652.69 to £7568.88)
Incremental costs (adjusted) ^a	£987.37 (95% CI -£1558.27 to £3533.02)	
Cost-utility results	£20,000 cost-effectiveness threshold	£30,000 cost-effectiveness threshold
Incremental NMB	-£961.27	-£942.45
Probability of NPWT being cost-effective	24.2%	25.5%

^a Seemingly unrelated regressions.

**FIGURE 8** Cost-effectiveness plane (deaths excluded).

SA.3. Sensitivity analysis: NPWT ever received (no intention to treat)

By accounting for treatment crossover effects and participants who have ever received NPWT within the trial follow-up period, the unadjusted mean per participant QALYs and mean per participant costs are 0.590 (95% CI 0.557 to 0.622) and £6404.83 (95% CI £4555.69 to £8253.98) for the NPWT group and 0.555 (95% CI 0.522 to 0.587) and £5323.00 (95% CI £3470.69 to £7175.29) for the usual-care group. The mean difference-adjusted

incremental QALYs and incremental costs suggest that NPWT increased QALYs by 0.024 (95% CI -0.007 to 0.055) and increased costs by £1260.83 (95% CI -£1383.88 to £3905.54) over the 12-month study period, although these results were not statistically significant. The INMB is -£761.88 and -£516.18 at the £20,000 and £30,000 cost-effectiveness thresholds, respectively. The probability of cost-effectiveness of NPWT is 30.5% at the £20,000 threshold, and 37.3% at the £30,000 threshold. A cost-effectiveness plane and a CEAC graphically present these results (*Figures 10 and 11*).

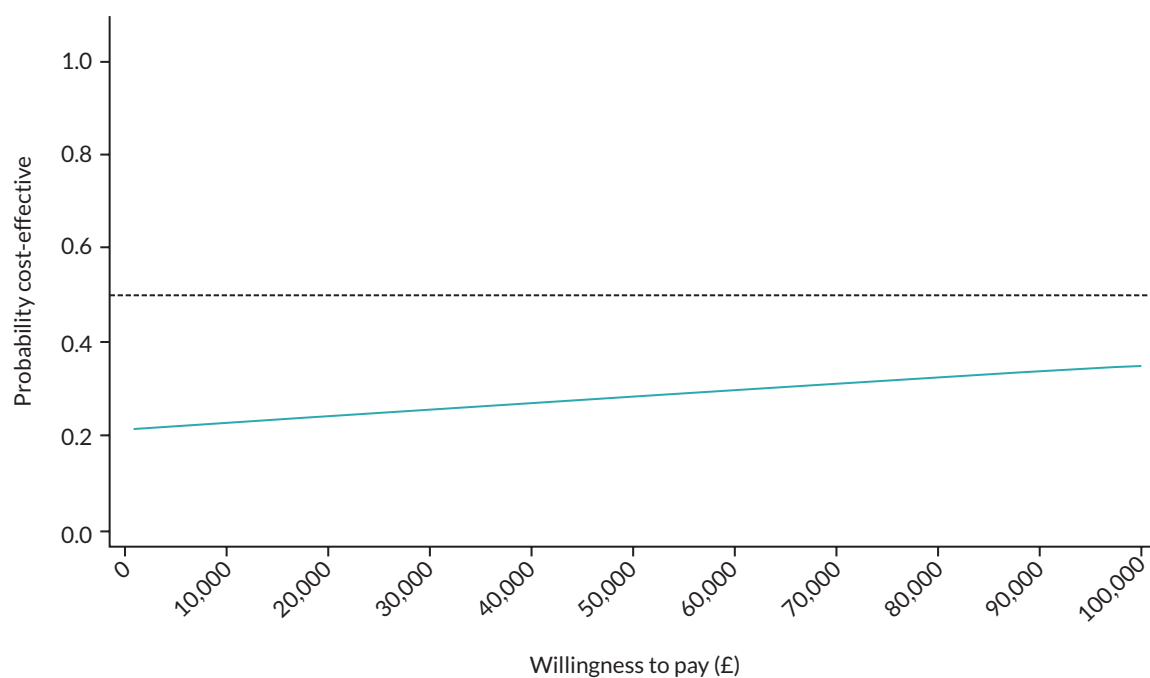


FIGURE 9 Cost-effectiveness acceptability curve (deaths excluded).

TABLE 23 Cost-utility analysis (NPWT ever received; no intention to treat)

NPWT ever received (no intention to treat)		
	NPWT (n = 333)	Usual care (n = 353)
Total QALYs	0.590 (95% CI 0.557 to 0.622)	0.555 (95% CI 0.522 to 0.587)
Incremental QALYs (adjusted) ^a	0.024 (95% CI -0.007 to 0.055)	
Total costs ^a	£6404.83 (95% CI £4555.69 to £8253.98)	£ 5323.00 (95% CI £3470.69 to £7175.29)
Incremental costs (adjusted)	£1260.83 (95% CI -£1383.88 to £3905.54)	
Cost-utility results	£20,000 cost-effectiveness threshold	£30,000 cost-effectiveness threshold
Incremental NMB	-£761.88	-£516.18
Probability of NPWT being cost-effective	30.5%	37.3%

^a Seemingly unrelated regressions.

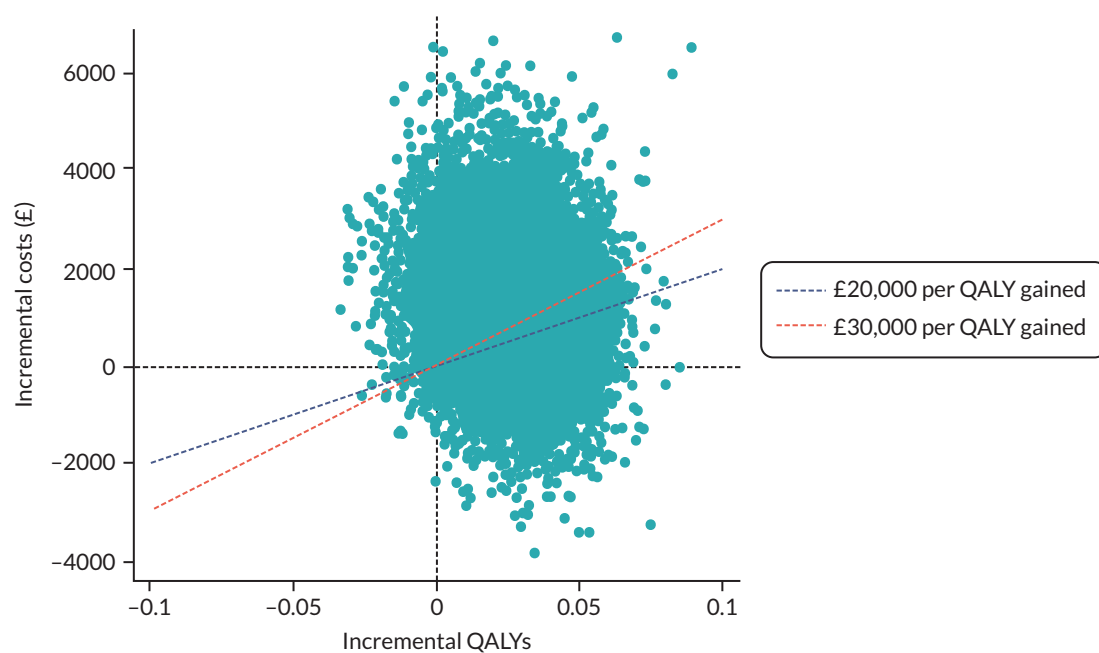


FIGURE 10 Cost-effectiveness plane (NPWT ever received; no intention to treat).

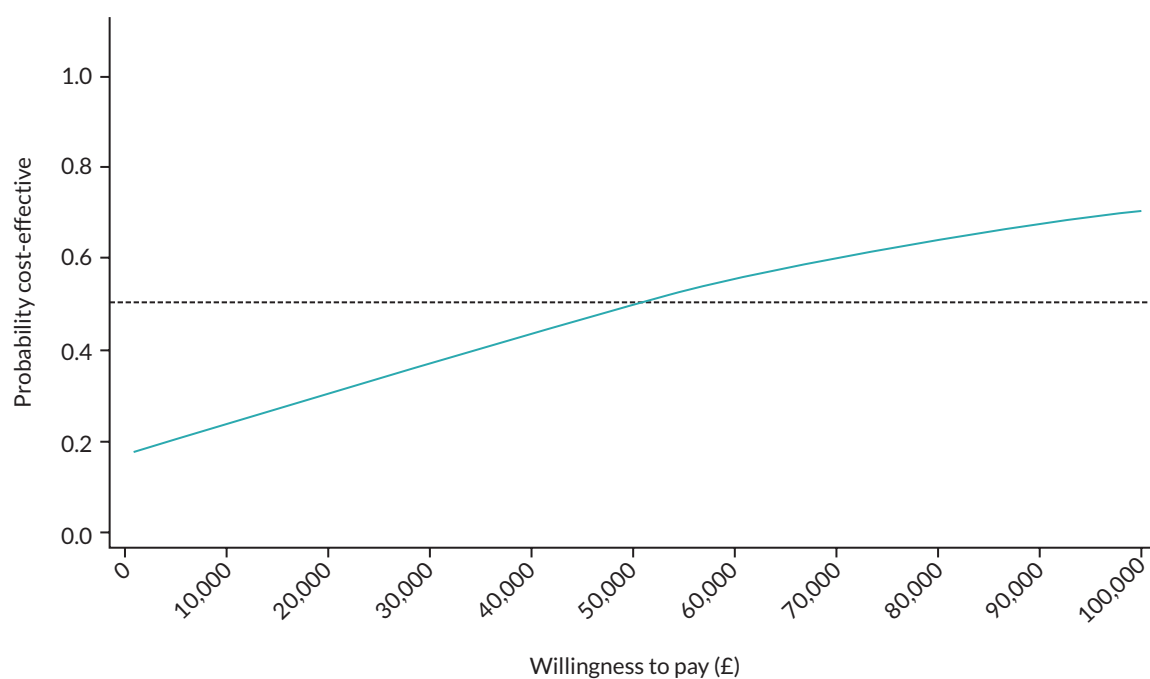


FIGURE 11 Cost-effectiveness acceptability curve (NPWT ever received; no intention to treat).

TABLE 24 Summary of parameters (cohort cost-effectiveness model for SWHSI patients)

Parameter	Value	Source
Specification of the patient population		
Baseline age [years, mean (SE)]	62.9 (12.6)	SWHSI-2 trial ⁸
Wound area > 25 cm ² , %	37.7	SWHSI-2 trial ⁸
Treatment location, % inpatient (versus outpatient)	83.1	SWHSI-2 trial ⁸
Tissue involvement, % skin and subcutaneous tissue loss (versus skin loss)	78.4	SWHSI-2 trial ⁸
SWHSI history, %	16.8	SWHSI-2 trial ⁸
Transition probabilities from unhealed wound to healed		
Pooled relative treatment effectiveness (posterior distribution), HR (95% CI)	1.07 (0.82 to 1.71)	Bayesian meta-analysis synthesising six studies from the literature and SWHSI-2 data ⁸
Transition to death		
Mortality risk	Adjusted general population mortality; 84 deaths (12.2%) (66 unhealed and 18 healed); SMR = 13.3 (additional mortality risk for an SWHSI patient compared with general population mortality)	ONS ²¹ (2022) SWHSI-2 trial ⁸
HRQoL		
General population utilities for healed patients (health-state utility)	Utility values of the UK population	Ara and Brazier ⁷ (2010)
Monthly utility decrement in the unhealed wound health state (health-state utility)	0.0095 (0.004)	Mixed-effect model using SWHSI-2 trial ⁸
Costs and resource use		
Time on treatment with NPWT (days)	46.6 (4.12)	SWHSI-2 trial ⁸
NPWT daily cost (£)	30.61 (0.18)	Centre-specific costings (Hull and Cornwall), assuming a combination of canister and dressing sizes and types, and based on the breakdown of dressings used and averaging the price of advanced dressings
Standard dressings daily cost (£)	4.17 (0.11)	Centre-specific costings (Hull and Cornwall), assuming a combination of canister and dressing sizes and types, and based on the breakdown of dressings used and averaging the price of advanced dressings
Monthly health resources while healed	0	Assumption
Monthly primary care health resources consumed while unhealed (resources assumed to be treatment dependent)		
GP surgery appointments (NPWT)	0.11 (0.03)	SWHSI-2 trial ⁸
GP surgery appointments (standard dressings)	0.13 (0.05)	SWHSI-2 trial ⁸
GP home appointments (NPWT)	0.05 (0.01)	SWHSI-2 trial ⁸
GP home appointments (standard dressings)	0.07 (0.04)	SWHSI-2 trial ⁸

TABLE 24 Summary of parameters (cohort cost-effectiveness model for SWHSI patients) (*continued*)

Parameter	Value	Source
Nurse surgery appointments (NPWT)	1.39 (0.22)	SWHSI-2 trial ⁸
Nurse surgery appointments (standard dressings)	1.26 (0.19)	SWHSI-2 trial ⁸
Nurse home appointments (NPWT)	3.65 (0.35)	SWHSI-2 trial ⁸
Nurse home appointments (standard dressings)	3.89 (0.45)	SWHSI-2 trial ⁸
Dressing change appointments (NPWT)	14.67 (2.44)	SWHSI-2 trial ⁸
Dressing change appointments (standard dressings)	12.82 (2.24)	SWHSI-2 trial ⁸
Monthly secondary care health resources consumed while unhealed (resources assumed to be treatment independent)		
Hospital outpatient appointments (diabetic foot clinic)	0.24 (0.02)	SWHSI-2 trial ⁸
Hospital outpatient appointments (podiatry)	0.06 (0.01)	SWHSI-2 trial ⁸
Hospital outpatient appointments (specialty dressing clinic)	0.01 (0.001)	SWHSI-2 trial ⁸
Hospital outpatient appointments (vascular, colorectal, or plastics)	0.01 (0.001)	SWHSI-2 trial ⁸
Hospital admissions without an overnight stay	0.01 (0.001)	SWHSI-2 trial ⁸
Hospital inpatient nights	0.74 (0.13)	SWHSI-2 trial ⁸
A&E service visits	0.02 (0.001)	SWHSI-2 trial ⁸
Medication cost while unhealed (£)	6.18 (0.65)	SWHSI-2 trial ⁸

ONS, Office for National Statistics; SE, standard error; SMR, standardised mortality ratio.

Note

Values are mean (SE) unless otherwise indicated.

TABLE 25 Input parameters (cohort SWHSI cost-effectiveness model)

Assumption	Description
Treatment groups	Assumed the treatment to which SWHSI-2 trial patients were randomised to, that is an intention-to-treat analysis
Patient population	Assumed that the SWHSI-2 trial population reflected the population of interest for this evaluation
Patients' HRQoL	To derive the quality-of-life decrement of being in the unhealed SWHSI health state, it was assumed that patients' HRQoL was conditional only on their healing status and not on other patient characteristics
Time on standard dressings and on NPWT	Patients in the standard dressings group were assumed to be treated with standard dressings while unhealed. Patients in the NPWT group were assumed to be treated with NPWT for a proportion of time while unhealed and with standard dressings for the remaining time, conditional on the time on NPWT treatment being shorter/longer than the estimated time to healing
Healed SWHSI costs	Assumed that, once healed, an SWHSI patient would be discharged and no further healthcare resources would be used and, thus, no costs would be incurred by the health system
Mortality	Assumed that the probability of death is equivalent for patients in the unhealed and healed SWHSI health states Assumed that the mortality of the SWHSI population is higher than the mortality of the general population, adjusted for age and sex

TABLE 26 Summary of cost-effectiveness results (cohort SWHSI cost-effectiveness model)

	NPWT	Standard dressings
Total QALYs	3.77 (3.63 to 3.87)	3.76 (3.62 to 3.86)
Total costs (£)	92,436 (70,470 to 114,516)	89,642 (73,038 to 110,037)
Healthcare costs	73,881 (53,603 to 94,824)	75,940 (59,773 to 95,890)
Intervention costs	18,554 (14,804 to 21,971)	13,702 (12,349 to 15,101)
Incremental costs (versus standard dressings) (£)	2794 (–11,916 to 13,559)	–
Incremental QALYs (versus standard dressings)	0.01 (–0.02 to 0.05)	–
£20,000/QALY gained cost-effectiveness threshold (willingness-to-pay)		
NMB (£)	–17,018 (–39,208 to 5672)	–14,414 (–34,318 to 3032)
Incremental NMB (£)	–2604 (–13,901 to 12,853)	–
Probability of NPWT being cost-effective, %	28.9	–
£30,000/QALY gained cost-effectiveness threshold (willingness-to-pay)		
NMB (£)	20,692 (–2053 to 44,054)	23,200 (2159 to 40,880)
Incremental NMB (£)	–2509 (–14,029 to 13,323)	–
Probability of NPWT being cost-effective, %	29.5	–
Note Values are mean (95% CI) unless otherwise indicated.		