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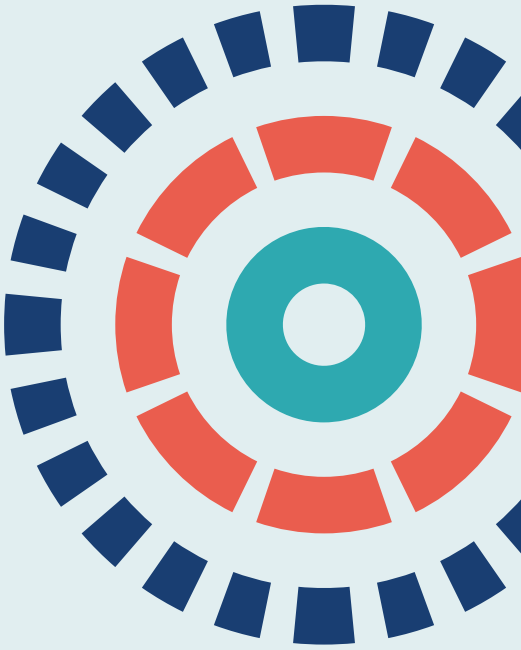

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The epidemiology, management and impact of surgical wounds healing by secondary intention: a research programme including the SWHSI feasibility RCT

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Abstract

The epidemiology, management and impact of surgical wounds healing by secondary intention: a research programme including the SWHSI feasibility RCT

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Background: Most surgical incisions heal by primary intention (i.e. wound edges are apposed with sutures, clips or glue); however, some heal by secondary intention (i.e. the wound is left open and heals by formation of granulation tissue). There is, however, a lack of evidence regarding the epidemiology, management and impact on patients' quality of life of these surgical wounds healing by secondary intention, resulting in uncertainty regarding effective treatments and difficulty in planning care and research.

Objectives: To derive a better understanding of the nature, extent, costs, impact and outcomes of surgical wounds healing by secondary intention, effective treatments, and the value and nature of further research.

Design: Cross-sectional survey; inception cohort; cost-effectiveness and value of implementation analyses; qualitative interviews; and pilot, feasibility randomised controlled trial.

Setting: Acute and community care settings in Leeds and Hull, Yorkshire, UK.

Participants: Adults (or for qualitative interviews, patients or practitioners) with previous experience of a surgical wound healing by secondary intention. Inclusion criteria varied between the individual workstreams.

Interventions: The pilot, feasibility randomised controlled trial compared negative-pressure wound therapy – a device applying a controlled vacuum to a wound via a dressing – with usual care (no negative-pressure wound therapy).

Results: Survey data estimated that treated surgical wounds healing by secondary intention have a point prevalence of 4.1 per 10,000 population (95% confidence interval 3.5 to 4.7 per 10,000 population). Surgical wounds healing by secondary intention most frequently occurred following colorectal surgery ($n = 80$, 42.8% cross-sectional survey; $n = 136$, 39.7% inception cohort) and were often planned before surgery ($n = 89$, 47.6% cross-sectional survey; $n = 236$, 60.1% inception cohort). Wound care was frequently delivered in community settings ($n = 109$, 58.3%) and most patients ($n = 184$, 98.4%) received active wound treatment. Cohort data identified hydrofibre dressings ($n = 259$, 65.9%) as the most common treatment, although 29.3% ($n = 115$) of participants used negative-pressure wound therapy at some time during the study. Surgical wounds healing by secondary intention occurred in 81.4% ($n = 320$) of participants at a median of 86 days (95% confidence interval 75 to 103 days). Baseline wound area ($p \leq 0.01$), surgical wound contamination (determined during surgery; $p = 0.04$) and wound infection at any time ($p \leq 0.01$) (i.e. at baseline or postoperatively) were found to be predictors of prolonged healing. Econometric models, using observational, cohort study data, identified that, with little uncertainty, negative-pressure wound therapy treatment is more costly and less effective than standard dressing treatment for the healing of open surgical wounds. Model A (ordinary least squares with imputation) effectiveness: 73 days longer than those who did not receive negative-pressure wound therapy (95% credible interval 33.8 to 112.8 days longer). Model A cost-effectiveness (associated incremental quality-adjusted life-years): observables –0.012 (standard error 0.005) and unobservables –0.008 (standard error 0.011). Model B (two-stage model, logistic and linear regression) effectiveness: 46 days longer than those who did not receive negative-pressure wound therapy (95% credible interval 19.6 to 72.5 days longer). Model B cost-effectiveness (associated incremental quality-adjusted life-years): observables –0.007 (standard error 0.004) and unobservables –0.027 (standard error 0.017). Patient interviews ($n = 20$) identified initial reactions to surgical wounds healing by secondary intention of shock and disbelief. Impaired quality of life characterised the long healing process, with particular impact on daily living for patients with families or in paid employment. Patients were willing to try any treatment promising wound healing. Health professionals ($n = 12$) had variable knowledge of surgical wound healing by secondary intention treatments and, frequently, favoured negative-pressure wound therapy, despite the lack of robust evidence. The pilot feasibility randomised controlled trial screened 248 patients for eligibility and subsequently recruited and randomised 40 participants to receive negative-pressure wound therapy or usual care (no negative-pressure wound therapy). Data indicated that it was feasible to complete a full randomised controlled trial to provide definitive evidence for the clinical effectiveness and cost-effectiveness of negative-pressure wound therapy as a treatment for surgical wounds healing by secondary intention. Key elements and recommendations for a larger randomised controlled trial were identified.

Limitations: This research programme was conducted in a single geographical area (i.e. Yorkshire and the Humber, UK) and local guidelines and practices may have affected treatment availability, and so may not represent UK-wide treatment choices. A wide range of wound types were included; however, some wound types may be under-represented, meaning that this research may not represent the overall surgical wound healing by secondary intention population. The lack of randomised controlled trial data on the relative effects of negative-pressure wound therapy in surgical wounds healing by secondary intention resulted in much of the economic modelling being based on observational data. Observational data, even with extensive adjustment, do not negate the potential for unresolved confounding to affect the results, which can reduce confidence in conclusions drawn from observational data. Definitive evidence from a randomised controlled trial may be the only way to overcome this lack of confidence.

Conclusions: This research has provided new information regarding the nature, extent, costs, impacts and outcomes of surgical wounds healing by secondary intention, treatment effectiveness, and the value and nature of future research, while addressing previous uncertainties regarding the problem of surgical wounds healing by secondary intention. Aspects of our research indicate that negative-pressure wound therapy is more costly and less effective than standard dressing for the healing of open surgical wounds. However, because this conclusion is based solely on observational data, it may be affected by unresolved confounding. Should a future randomised controlled trial be considered necessary, its design should reflect careful consideration of the findings of this programme of research.

Future work: This research signals the importance of further research on surgical wound healing by secondary intention. Key research questions raised by this programme of research include (1) which treatments are clinically effective and cost-effective for surgical wound healing by secondary intention for all patients or for particular patient subgroups? (2) Can particular prognostic factors predict time to healing of surgical wound healing by secondary intention? And (3) do psychosocial interventions have the potential to improve quality of life in people with hard-to-heal surgical wound healing by secondary intention? Given that negative-pressure wound therapy has been widely adopted, with relatively little evidence to support its use, the design and outcomes of a randomised controlled trial would need to be carefully considered. We focused in this research on wound healing, and maintain, based on the findings of patient interviews, that this is a key outcome for future research. Impacts of negative-pressure wound therapy on outcomes such as infection and reoperation should also be considered, as should patients' views of the treatment. The type of patient group recruited and the outcomes of interest will all influence the duration of follow-up of any planned study. The comparator in any future study will also need careful consideration.

Trial registration: Current Controlled Trials ISRCTN12761776.

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List of abbreviations

BMI	body mass index
BPI	Brief Pain Inventory
CI	confidence interval
CINAHL	Cumulative Index to Nursing and Allied Health Literature
CrI	credible interval
EQ-5D	EuroQol-5 Dimensions
EQ-5D-3L	EuroQol-5 Dimensions, three-level version
GP	general practitioner
HRQoL	health-related quality of life
IV	instrumental variable
MCS	mental component score
NICE	National Institute for Health and Care Excellence
NPWT	negative-pressure wound therapy
OLS	ordinary least squares
OR	odds ratio
PCS	physical component score
QALY	quality-adjusted life-year
RCT	randomised controlled trial
SD	standard deviation
SE	standard error
SF-12	Short Form questionnaire-12 items
SWHSI	surgical wound healing by secondary intention
VAS	visual analogue scale

Plain English summary

Surgical wounds healing by secondary intention are open wounds that are left to heal from the base up. At the start of this work, there was little information on these wounds, their management, impact on patients and which treatments offered best value for money. The overall aim of this research was therefore to describe, characterise and identify the nature and impact of surgical wounds healing by secondary intention and the current evidence for effective treatments.

This research found the following:

- Surgical wounds healing by secondary intention are very common and affects approximately 4 out of 10,000 adults in the general population.
- Patients may have their wound for a long time and this has an impact on their well-being and daily life.
- Patients are often shocked when they first see their wound and are concerned about what others think of it.
- Several factors are associated with delayed wound healing (e.g. wound infections and wound size).
- Wound dressings are often used as the first treatment, but sometimes a vacuum device called negative-pressure wound therapy is used. Health professionals are using this treatment more frequently.
- This research looked at how NHS patients receiving negative-pressure wound therapy fared when compared with patients receiving standard dressings. This research was not experimental: health professionals and patients chose the treatments they received.
- Definitive evidence about the comparative effects of negative-pressure wound therapy and standard dressing may still be required in the form of a large randomised clinical trial; our small pilot study has shown that such a study is possible.
- Further studies are required to assess other treatments for other surgical wounds healing by secondary intention and to improve patient well-being and care.
- Specialised analysis methods showed that negative-pressure wound therapy was less effective and did not offer value for money compared with standard wound dressings. It is possible that these findings are due to differences between the people receiving the different treatments, rather than the treatments themselves.

Scientific summary

Background

Surgical wounds healing by secondary intention are open wounds that heal from the base up. Healing by secondary intention may be planned (e.g. due to infection) or unplanned [e.g. when a wound has been closed but then opens (dehisces), either fully or partially]. Surgical wounds healing by secondary intention may remain open for many months, are prone to infection and may prolong or require further hospital stays, adversely affecting patients' quality of life and incurring substantial NHS costs.

The lack of available research evidence regarding surgical wounds healing by secondary intention at the start of this programme meant that clinicians and patients lacked evidence regarding surgical wounds healing by secondary intention management, what treatment options were most effective and which treatments were best value for money. The lack of basic data regarding the frequency, characteristics, current treatments, healing trajectory and impact meant that it was difficult to plan new primary research.

Objectives

The overall aim of the programme was to derive a better understanding of the nature, extent, costs, impact and outcomes of surgical wound healing by secondary intention, effective treatments, and the value and nature of further research. The objectives were as follows:

- Workstream 1 – to describe the number, characteristics, current treatments, impacts and health outcomes of patients with surgical wounds healing by secondary intention.
- Workstream 2 – to use all available research data to estimate the cost-effectiveness of current treatments for surgical wounds healing by secondary intention (identified in workstream 1) and to assess whether or not investment in future research on treatments for surgical wounds healing by secondary intention was likely to be worthwhile and, if so, what research woulds offer best value for money.
- Workstream 3 – to determine the impact of surgical wounds healing by secondary intention on patients, specifically their perspectives and experiences of living with a surgical wound healing by secondary intention, of wound management and relevant wound outcomes, and to determine NHS health-care professionals' views of surgical wounds healing by secondary intention treatments and outcomes to measure treatment effects.
- Workstream 4 – to determine the feasibility of conducting further primary research on surgical wounds healing by secondary intention through a pilot feasibility randomised controlled trial.

Methods and results

Workstream 1

An inception cohort approach was used to enable accurate assessment of time to healing and treatment use. Given the lack of information on patient numbers and care locations, the cohort study was preceded by a cross-sectional survey, which enabled point prevalence of treated surgical wounds healing by secondary intention to be assessed.

Our cross-sectional survey, conducted in East Yorkshire, UK, obtained 200 responses, with the majority of responses received from community or district nurses ($n = 77$, 41.2%), followed by research nurses ($n = 44$, 23.5%). Data from 187 patients were analysed, giving an estimated point prevalence of treated surgical wounds healing by secondary intention of 4.1 per 10,000 population (95% confidence interval 3.5 to 4.7

per 10,000 population). Most patients had only one surgical wound healing by secondary intention (87.7%) and the most common surgical procedure resulting in a surgical wound healing by secondary intention was for pilonidal sinuses/abscesses (15.0%). Half of surgical wounds healing by secondary intention were planned (47.6%) and the median wound duration at the point of survey was 28 (95% confidence interval 21 to 35) days. Most patients (98.4%) were receiving active treatment, most commonly wound dressings (93.4%), and care was frequently provided in community settings (58.3%).

Our cohort study, conducted in eight primary, secondary and community care sites in Yorkshire and the Humber, UK, recruited 396 participants, with 393 participants included in the analysis (three patients were subsequently ineligible). Participants were followed up for a minimum of 12 months and a maximum of 21 months to collect key clinical outcome data (including healing, surgical site infection, hospital readmission, treatments received, changes to study involvement) and quality-of-life and pain assessments. The median age of participants was 55 years (range 19–95 years), 69.5% of participants were overweight or obese and 28.5% were current smokers. The most common comorbidities were cardiovascular disease (38.4%), diabetes mellitus (26.2%) and peripheral vascular disease (14.5%). Most patients had only one surgical wound healing by secondary intention (91.0%), had no previous history of surgical wounds healing by secondary intention (72.0%) and had a surgical wound healing by secondary intention that was planned (60.1%), with the most common site being the abdomen (33.6%), reflecting that colorectal surgery was the most commonly represented surgical specialty (39.7%). The most common treatment was hydrofibre dressings (65.9%), and 29.3% of participants reported receiving negative-pressure wound therapy during the study.

In our cohort study, data indicated that surgical wounds healing by secondary intention healed for 81.4% of participants ($n = 320$), with a median time to healing of 86 days (95% confidence interval 75 to 103 days). Area greater than the baseline median (6 cm^2) ($p < 0.01$), surgical wound contamination level as determined at the point of surgery ($p = 0.04$) and surgical site infection at any point ($p < 0.01$) were significant predictors of prolonged time to healing. Quality of life remained constant during the study, whereas pain severity, interference and Short Form questionnaire-12 items scores improved over time.

Workstream 2

Econometric models were applied to cohort data collected in workstream 1 to assess the clinical effectiveness and cost-effectiveness of negative-pressure wound therapy, when compared with standard dressings; no published research data could be identified to complement the cohort data in the model. The lack of randomised controlled trial data on the relative effects of negative-pressure wound therapy in surgical wounds healing by secondary intention therefore resulted in much of the economic modelling being based on observational data. A Bayesian approach to inferences was used, computed using Markov chain Monte Carlo simulation. Time to healing was modelled using two approaches: ordinary least squares with imputation, using an instrumental variable regression to adjust for unobservable confounding (model A); and a two-stage model, using logistic regression followed by linear regression (model B). Instrumental variables were identified to adjust for unobservable confounding.

Model A identified that participants who received negative-pressure wound therapy were expected to take longer to heal than those who did not receive negative-pressure wound therapy: on average, 73 days longer (95% credible interval 33.8 to 112.8 days longer). This was maintained when interaction terms (treatment and surgical wound healing by secondary intention history) and expert opinions on censoring of healing times were included. Model B identified that participants who received negative-pressure wound therapy were estimated to have lower probability of healing (odds ratio 0.59, 95% credible interval 0.28 to 1.12) and time to healing was an additional 46 days (95% credible interval 19.6 to 72.5 days). Conclusions were similar in both approaches when adjusted for unobservables.

Cost-effectiveness estimates indicated that negative-pressure wound therapy was expected to be less cost-effective than standard dressings [associated incremental quality-adjusted life-years of –0.012 (standard error 0.005) (model A, observables) and –0.008 (standard error 0.011) (model A, unobservables),

–0.007 (standard error 0.004) (model B, observables) and –0.027 (standard error 0.017) (model B, unobservables)]. There was little decision uncertainty in this result.

Workstream 3

Semistructured qualitative interviews were conducted with 20 patients (with experience of a surgical wound healing by secondary intention), five surgeons and seven nurses, using topic guides. Interviews were audio-recorded, transcribed and analysed using a 'framework' approach.

Patients reported that unplanned surgical wounds healing by secondary intention resulted in feelings of alarm, shock, disbelief and disgust. Patients with previous experience of a surgical wound healing by secondary intention expected slow healing, whereas patients without previous surgical wound healing by secondary intention experience often had unrealistic expectations of time to healing. Patients were ever-hopeful that a new or untried treatment might accelerate or achieve wound healing, and there was a willingness to try any procedure or treatment to achieve this, even if it was unpleasant or lacked high-level evidence of efficacy. The main surgical wound healing by secondary intention treatments experienced were negative-pressure wound therapy, debridement, dressings and skin grafting. Patients would have liked more information in relation to the rationale for using different treatment methods and approaches.

Prolonged or multiple hospital admissions were not uncommon, and many patients reported feeling unsupported at the point of hospital discharge, owing to a lack of available information regarding follow-up care and infection management. Most patients received home visits from district, community or general practice nurses during their wound healing. Patients acknowledged that the nurses tried to attend to all needs during the visit, but felt that nurses had limited time to devote to each visit.

Wound-related symptoms had a negative impact on daily life, physical and psychosocial functioning, and well-being. Limited physical mobility was frustrating and disrupted normal activities, and patients felt unable to socialise due to concerns about their self-image. Disruption of roles and responsibilities within the family unit was common, and patients reported feeling burdensome and dependent. This appeared particularly difficult for younger male participants who were often the main earner in the family.

Surgeons and nurses agreed that a number of factors were associated with delayed healing, including surgical (e.g. reason for surgery, procedure type), patient comorbidity, systemic infection, medication, mobility and treatment compliance factors. In many instances, it was difficult to identify any specific reason for impaired wound healing. Specific wound factors reported to be associated with healing included wound size, presence of wound infection, slough and/or granulation tissue and condition of the wound edges. Nurses also emphasised psychosocial and practical issues that might have an impact on patients' quality of life, such as family support and patients' potential for self-care of the wound.

The majority of patients operated on by general surgeons had their wound care passed to nurses following discharge. Plastic and vascular surgeons were more likely to continue to care for 'their' patients through follow-up in specialist clinics. Surgeons relied on nurses to make appropriate dressing choices, which were influenced by wound-, patient- and dressing-specific factors. Surgeons or tissue viability specialists often initiated decisions regarding the use of negative-pressure wound therapy, as knowledge and expertise regarding negative-pressure wound therapy among general nurses was often limited. Tissue viability specialists were a frequent point of reference for nurses regarding the management of complex, non-healing open surgical wounds.

Surgeons reported that use of negative-pressure wound therapy was increasing and that complex, cavity wounds (e.g. extensive abdominal wounds) were ideally suited to benefit from negative-pressure wound therapy. Negative-pressure wound therapy was generally perceived as a cost-effective and transformative treatment, particularly for patients with hard-to-heal wounds. Surgeons noted the lack of research evidence relating to negative-pressure wound therapy, but felt that their own and colleagues' experiences supported its use.

Workstream 4

A pilot, feasibility randomised controlled trial was designed to test the methods and the feasibility of conducting a larger randomised controlled trial to assess clinical effectiveness and cost-effectiveness of negative-pressure wound therapy compared with usual care (no negative-pressure wound therapy). In total, 41 participants were recruited from two secondary and one community care NHS trust in the north of England. Forty participants were subsequently included in the analysis (one participant was randomised in error). Using a 1 : 1 ratio, participants were allocated to one of two groups: negative-pressure wound therapy ($n = 19$, 47.5%) and usual care (no negative-pressure wound therapy) ($n = 21$, 52.5%). Participants were recruited over 9 months and followed up for 3 months. An intention-to-treat analysis was conducted.

The proposed primary clinical outcome for a larger trial (time to wound healing) was assessed along with other clinical and feasibility outcomes, including recruitment and retention rates; time to treatment start; duration of and changes to negative-pressure wound therapy; clinical events; resource use data; documentation acceptability; and feasibility of blinded outcome assessment.

Of the 248 patients screened for eligibility, 186 (75.0%) were ineligible (including the patient randomised in error) and 22 (8.9%) were eligible but non-consenting. Common reasons for ineligibility included having previously received negative-pressure wound therapy on the surgical wound healing by secondary intention ($n = 45$, 18.1%), having received negative-pressure wound therapy in theatre for surgery resulting in the surgical wound healing by secondary intention ($n = 7$, 2.8%) or both ($n = 24$, 9.7%). Randomised participants received a median of eight (negative-pressure wound therapy) and seven (usual care) post-randomisation assessments. Participant questionnaire response rates were $\geq$ 78% at all time points.

Two of the 19 participants allocated to negative-pressure wound therapy (10.5%) did not receive negative-pressure wound therapy, 10 (52.6%) received negative-pressure wound therapy within 24 hours and 14 (73.7%) received it within 48 hours. The most common reason for delay was the machine being unavailable ($n = 6$, 85.7%). Participants received negative-pressure wound therapy for a median of 18 (range 0–72) days. Five usual-care participants (23.8%) received negative-pressure wound therapy at a median of 4 days after randomisation (range 0–17 days).

Ten wounds (25.0%) were deemed to have healed during the study and 17 participants (42.5%) experienced a wound infection. The mean total cost for negative-pressure wound therapy was £9490 (standard deviation £7346) and for usual-care it was £1153 (standard deviation £1806). A substantial proportion of negative-pressure wound therapy costs were attributed to hospital stays [£7710 (standard deviation £7557)].

Of those providing a response ($n = 31$), 28 participants (90.3%) found completing study questionnaires to be straightforward. Half of the eight nurse respondents ($n = 4$) found the case report forms to be straightforward and the majority ($n = 6$, 75.0%) found the frequency of clinical assessments to be manageable. There were mixed opinions regarding processes for identifying potential participants.

Blinded assessment of wound healing, by up to three reviewers, agreed with unblinded nurse healing assessment in 95.0% of cases. Treatment allocation was correctly identified in 37.5% of cases ($n = 15$, nine participants to negative-pressure wound therapy and six to usual care).

Conclusions

This research has provided new information regarding the nature, extent, costs, impacts and outcomes of surgical wounds healing by secondary intention, insights into uncertainty around current treatment effectiveness and the value and nature of future research in this area.

The cross-sectional survey of 187 patients in Hull and East Yorkshire, UK, has provided an estimate of treated surgical wound healing by secondary intention prevalence of 4.1 per 10,000 population (95% confidence interval 3.5 to 4.7 per 10,000 population) and inception cohort data has provided the first detailed analysis of surgical wound healing by secondary intention patients, treatments and wound healing trajectories. The heterogeneity of the surgical wound healing by secondary intention population, wide distributions of location sites of surgical wounds healing by secondary intention, surgeries resulting in surgical wound healing by secondary intention and treatments used, and predictors of slower healing of surgical wounds healing by secondary intention (wound area, surgical wound contamination as determined at the point of surgery and surgical site infection at any time), have also been identified as a result of this work.

Qualitative interviews identified the devastating effect that surgical wounds healing by secondary intention may have on patients' quality of life. Patients were focused on complete wound healing and were willing to try any treatment that promised this. Healing is therefore a crucial outcome for future research into treatments for surgical wounds healing by secondary intention.

Cost-effectiveness models, using the observational cohort data, demonstrated, with little uncertainty, that negative-pressure wound therapy is less effective and more costly than standard dressings. Should a lack of confidence in these conclusions from observational data mean that a future randomised controlled trial is considered necessary, the design of this trial should be informed by this programme of work.

Recruitment to a randomised controlled trial to assess clinical effectiveness and cost-effectiveness of negative-pressure wound therapy for patients with surgical wounds healing by secondary intention has been identified to be possible. This is therefore encouraging for future research, which we suggest should focus on enhancing evidence for clinically effective and cost-effective treatments for surgical wound healing by secondary intention, identifying factors predicting time to healing, assessing interventions to improve patient quality of life and potential improvements that could be made to care pathways for surgical wounds healing by secondary intention.

Trial registration

The pilot feasibility trial component is registered as ISRCTN12761776.

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SYNOPSIS

Introduction

More than 10 million surgical operations are conducted every year in the NHS, with the majority of these involving a wound created by surgical incision.[1] Most incised surgical wounds heal by primary intention, when the wound edges are closely apposed and sutured, clipped or glued together. However, not all surgical wounds heal in this way; some wounds are left open after surgery and heal from the bottom up by the formation of granulation tissue (known as healing by secondary intention). The surgical wounds healing by secondary intention (SWHSIs) may be planned (e.g. after significant tissue loss for which primary closure is not possible, or in the presence of infection). Alternatively, healing by secondary intention may be unplanned when a primarily closed wound opens or 'dehisces' (full or partial separation of wound edges). These SWHSIs, also called 'open surgical wounds', may remain open for many months, are prone to infection, may prolong hospital stays, and necessitate further hospital admissions and surgeries (delayed primary closure) or skin grafting,[2] all adversely affecting patients' quality of life and incurring substantial NHS costs.

Prevalence of SWHSIs

Although SWHSIs are thought to be relatively common, when we planned this research there were few national or international data regarding their epidemiology. Two published studies estimated that SWHSIs constituted approximately 28% of all prevalent surgical wounds.[3,4] From data collected in Hull and East Yorkshire, UK, Srinivasaiah *et al.*[4] reported 136 open surgical wounds and 74 dehisced surgical wounds, from a total population of 590,000 (a point prevalence of 0.36/1000 population). Further UK cross-sectional data from Bradford, UK, reported 111 wounds that were classed by the study authors as open surgical wounds and a further 88 that were classed by the study authors as having broken down post surgery.[3] However, the size of the underlying population and, hence, point prevalence for these wounds was not reported. A population-based estimate of the prevalence of SWHSIs alongside in-depth investigation of their origin, natural history, typical treatments and impact on patients and health services was needed.

Details of patient and wound characteristics

Previous research on wound prevalence by Vowden and Vowden[3] and Srinivasaiah *et al.*[4] focused on all wounds, rather than specific wound types. To the best of our knowledge, when we began this research, there was no high-quality information (national or international) describing patients with a SWHSI (age, sex, comorbidities, concomitant medications, surgical speciality); wound characteristics (site, size location, aetiology, whether or not the wounds were planned to be left open before surgery, frequency of wound infection); SWHSI treatments or healing rates in general and for specific patient groups (e.g. those with diabetes mellitus). Robust time to healing data were also limited and reports frequently presented inaccurately analysed data.[5–10] The generalisability of the existing research was also limited, as many trials reported time to healing rates in relation to subpopulations of SWHSI patients and treatments: one trial[5] of perineal wounds and foam dressing, two trials[7,8] of pilonidal sinus wounds and silastic foam dressing, and one trial[10] of below-knee amputation wounds and plaster cast with silicone sleeve or elastic compression. The lack of systematic data describing SWHSIs and their treatment and outcomes was matched by a lack of knowledge about the impact of SWHSIs on patients' quality of life or daily functioning, as well as the impact of these wounds on the use of health-care resources. This, in combination, made it almost impossible to assess the impact of SWHSIs and their treatments on patients, or to plan new research studies to assess the clinical effectiveness and cost-effectiveness of potential new or alternative treatments or interventions.

The treatment of SWHSIs

Management of SWHSIs often involves daily or more frequent dressing changes, sometimes with packing of the wound cavity. Many different dressing options are available, from simple dressings such as gauze (which can be painful to remove) to more modern options such as foam, hydrocolloid and alginate dressings. Wounds may also be treated by debridement (the removal of foreign material and devitalised tissue) or by skin grafting. When this research was conceived, the type and frequency of treatments being used for SWHSIs was not known. Randomised controlled trials (RCTs) in SWHSI patients are infrequent and often poorly designed, underpowered, utilise surrogate outcomes and often report limited or incorrectly analysed healing data, making interpretation of these data incredibly difficult. For example, a multicentre RCT comparing the effects of zinc oxide with placebo mesh on secondary-healing pilonidal wounds was underpowered, recruiting only 64 participants ($n = 33$ zinc and $n = 31$ placebo), and although it did not detect a difference in median healing times (54 days, interquartile range 42–71 days for zinc; 62 days, interquartile range 55–82 days for placebo; $p = 0.32$), this may have been due to the lack of power. In the same study, fewer postoperative antibiotics (a surrogate marker of wound infection) were prescribed in the zinc oxide group ($n = 3$) than in the placebo group ($n = 12$) ($p = 0.005$).[11]

In terms of evidence of effectiveness of different treatment options, Vermeulen *et al.*[12] explored the relative effects of dressings and topical agents for SWHSIs in a systematic review. They found only 13 RCTs, all of which were small, of poor quality and often conducted > 10 years previously. There was no evidence to indicate that the choice of dressing or topical treatment offered any benefit in terms of wound healing time, but the data were sparse. A systematic review, conducted to inform National Institute for Health and Care Excellence (NICE) clinical guidelines on surgical site infection, investigated the effects of topical antiseptics and antibiotics (including impregnated dressings) on the risk of wound infection in SWHSIs.[13] The four included studies were small and provided generally uncertain evidence on a range of uncommon treatment options. The guidelines recommend that chlorinated lime and boric acid [Edinburgh University Solution of Lime (EUSOL)] and gauze, moist cotton gauze or mercuric antiseptic solutions should not be used to prevent surgical site infection in the management of SWHSIs.[13]

Increasingly, more advanced and costly wound treatments have been extensively adopted into clinical practice, with inadequate supporting evidence. One example is negative-pressure wound therapy (NPWT), a device that applies a carefully controlled negative pressure (or vacuum) to the dressing, moving tissue fluid away from the treated wound area into a disposable canister.[14] The canister is removed and replaced either when it becomes full or at least once per week. The device is generally used as part of the SWHSI treatment pathway, rather than to the point of healing, and can be administered and removed by both nurses and surgeons.

Cost of treating SWHSIs

Surgical wounds healing by secondary intention can be large and may produce a significant volume of exudate, which can be difficult to manage, and frequent, time-consuming, dressing changes are common. In addition, SWHSIs must also be protected from infection and trauma during healing. It has been suggested that SWHSIs are at high risk of postoperative infection, with the wound providing an ideal environment for bacterial proliferation, which may be associated with delayed healing.[15] These factors, and the possible need for further surgery, suggest that the costs of treating patients with SWHSIs could be substantial. The lack of available epidemiological evidence in relation to SWHSIs had, however, made it difficult to ascertain the health and social care costs of treating these wounds.

SWHSIs: the patients' perspective

The lack of systematic data describing SWHSIs, their treatment and outcomes was matched by a scarcity of knowledge about the impact of SWHSIs on patients' quality of life. Little was known regarding patients' perspectives and experiences of living with a SWHSI, or their views, expectations and concerns regarding management and outcomes.

SWHSIs: the clinicians' perspective

A variety of clinicians, including surgeons, tissue viability nurses and general practice nurses, are all commonly involved in the management of patients with SWHSIs. As previously stated, there is a dearth of high-level evidence to guide the management of these patients, particularly regarding the clinical effectiveness and cost-effectiveness of different treatments or interventions. Greater clarity is required regarding assessment of these wounds and the factors that influence management decisions.

Summary

In summary, this research programme was undertaken recognising that SWHSIs may be common and costly but that there was a need for further exploration of the extent, nature, outcomes and impact of these wounds. The lack of international epidemiological data regarding these patients seriously impairs the development of new research studies in this area. There was also huge uncertainty regarding SWHSI management. Options ranged from inexpensive simple dressings to the more complex and costly NPWT, but accurate data regarding the frequency of use of specific treatments was non-existent. In addition, all treatment options for SWHSIs lacked robust, supportive evidence bases in terms of clinical effectiveness and cost-effectiveness, and the impact on patients' quality of life. As a result, clinicians and patients were uninformed about how to care for SWHSIs and, specifically, which treatment options were most effective and offered the best value for money. The need for research to fill these evidence gaps was also highlighted by the NICE guidance.[13]

Given the number of treatment options available, it is important that patients, carers and health professionals are involved in trial design, including the selection of significant outcome measures, and that research is conducted through sufficiently powered trials to detect significant differences in healing rates between treatments. However, the enormous cost of conducting the trials required to fill the evidence gaps means that a rush to undertake such studies, before obtaining additional key intelligence, would be hugely inefficient. There were several important unknowns: information about the natural history and epidemiology of SWHSIs; which treatments were being used most commonly and, thus, should be evaluated; whether or not the decision uncertainty associated with various treatments justifies an expensive trial; and whether or not a trial is feasible. In addition, little was known about which outcomes matter to patients with SWHSIs and what the desirable treatment characteristics are from the perspective of the staff treating them. We have undertaken research to generate vital data regarding an important, costly and hugely under-researched health problem. The research findings will aid in planning service delivery and future research, including economic modelling and primary studies.

Aims

We aimed to characterise and quantify SWHSIs, their outcomes and impact, and to begin to identify effective SWHSI treatments. The core aims of the research were achieved via four interdependent workstreams. The links between the four workstreams are shown in *Figure 1*.

Workstream 1

Workstream 1 aimed to describe the number, characteristics, current treatments, impacts and health outcomes of patients with SWHSIs. This was achieved using an initial prevalence survey and a subsequent inception cohort of patients with a SWHSI to collect naturalistic data regarding treatments used, rates of healing, adverse events and quality-of-life changes.

Workstream 2

Workstream 2 aimed to use all available research data to estimate the cost-effectiveness of current treatments for SWHSIs, as identified in workstream 1, and was completed using evidence synthesis and decision-analytic modelling. If assessments of cost-effectiveness suggested that there was decision uncertainty (i.e. uncertainty about which treatment offers best value to the NHS), we would extend analyses to assess whether or not investment in future research on treatments for SWHSIs was likely to be worthwhile and, if so, what research would offer best value for money.

Workstream 3

Workstream 3 aimed to determine the impact of SWHSIs on patients, specifically their perspectives and experiences of living with a SWHSI, of wound management and relevant wound outcomes. In addition, this workstream aimed to determine NHS professionals' views about SWHSI treatments and important outcomes to measure treatment effects. This was achieved through qualitative interviews with both patients and NHS professionals.

Workstream 4

Workstream 4 aimed to determine the feasibility of conducting further primary research on SWHSIs through a pilot, feasibility RCT.

This synopsis describes the results of our findings from all four workstreams. Publications arising from this research programme are listed in the *Acknowledgements*.

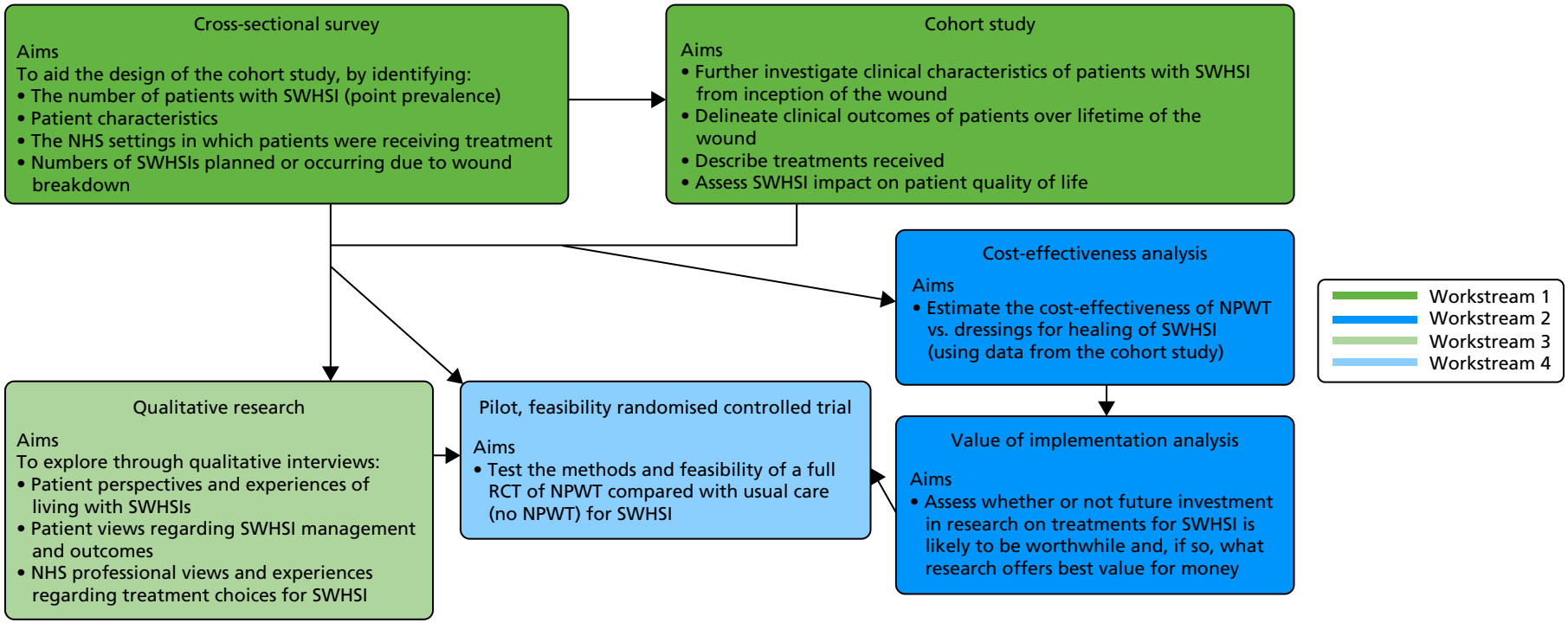

FIGURE 1 Overview of the whole research programme and its inter-relationships.

Patient and carer involvement

Involvement of patients and carers was identified at the outset as a priority for this research.

In workstream 1, two patient representatives contributed to the design of documentation for the cohort study and provided their perspective on study processes, questions and data interpretation through attendance at associated workstream meetings. A dedicated section of the meeting was devoted to patient feedback and the meeting was followed by an informal discussion between the research lead, a study research nurse and the patient representatives. When possible, any comments received from the patient representatives were incorporated into relevant study documentation or procedures. A newsletter to inform participants about the progress of the research was initiated by the patient representatives who assisted in the design and review of this document.

In workstream 3, the input of patient and carer representatives was crucial in the design and piloting of the interview topic guide, and the interpretation of the findings arising from the qualitative interviews, including review of the main study findings and input into the writing of the results. A summary of the results of the qualitative work was subsequently sent to participants, following review by the patient representatives.

Patient and carer involvement for this programme of work culminated in the development of a 'Patient User Group', convened at the start of workstream 4. This group was developed, following experiences in workstream 1, to increase the number of patient representatives involved and so reduce any burden on the two initial representatives involved. Ten patients or carers with experience of SWHSIs were invited to attend the inaugural meeting in March 2015, with five representatives subsequently attending. This resulted in a diverse group, with a mix of age, sex, SWHSI history and previous research experience. A further two meetings were convened during workstream 4 to provide comment on patient-facing documentation and study procedures and to discuss the interpretation of the results of the pilot, feasibility RCT. As in workstream 1, when possible, any comments received from the patient representatives were incorporated into study documentation or procedures. One member of the group was subsequently recruited to act as a patient and public representative for the workstream 4 Management Group meetings. The member provided a patient perspective on the trial processes and documentation, and made substantial contributions. This patient representative also contributed to and reviewed the summary of workstream 4 for this report and the associated papers arising from this workstream. In addition, a lay representative was also included in the workstream 4 Data Monitoring and Ethics Committee to provide patient input on data quality and patient safety and to advise on any issues arising during the trial.

The inclusion of patient and carer representatives has been instrumental in shaping this research programme and will undoubtedly be beneficial in shaping future research in this area. The mix of patients and carers providing input to the individual workstreams and in the Patient User Group provided the research programme team with a diverse range of experiences to draw on and consider when making decisions in relation to this research programme. Given the number of patient and public members involved in the various stages of this programme, there was naturally a range of views noted regarding patient and carer experiences, study procedures and documentation; however, in the vast majority of cases there was a consensus of opinion regarding progression of this research.

Workstream 1: cross-sectional survey and cohort study of SWHSIs

The dearth of national and international clinical and research information regarding the prevalence, patient characteristics and treatments for SWHSIs meant that we did not know the extent and nature of these wounds, how and where they were managed or the associated outcomes. To enable accurate assessment of time to healing and treatment use, we planned an inception cohort study to address key uncertainties. An inception cohort approach was essential to allow accurate assessment of SWHSI duration. Planning the cohort study was difficult, however, as there were no data regarding where most SWHSIs occurred. For example, were most SWHSIs left open in theatre or did they subsequently break down in hospital or in the community? We needed basic information regarding the numbers of patients with SWHSIs and their location in order to put adequate resources in place for the inception cohort study. We therefore preceded the cohort study with a cross-sectional survey. This approach facilitated the gathering of initial intelligence to support subsequent work and, in addition, the use of a cross-sectional design allowed us to estimate a point prevalence estimate for SWHSIs. The cross-sectional survey has been published (see *Appendix 1*).[16] The cohort study has also been published (see *Appendix 2*).[17]

Cross-sectional survey

Objectives

The cross-sectional survey aimed to capture information to aid the design of the cohort study. This included the:

- number of patients with a SWHSI (point prevalence), their characteristics and the NHS settings where they were receiving treatment
- proportions of SWHSIs planned prior to surgery and those that occurred as a result of wound breakdown (dehisced) after surgery.

Information was also collected on typical durations of SWHSIs, the types of surgery preceding the SWHSI and the treatments received by patients.

Methods

The cross-sectional survey was conducted over a 2-week period (spring 2012) in primary, secondary and community care settings in Hull and the East Riding of Yorkshire, UK. We asked health-care professionals to identify patients on their case load who had at least one SWHSI (i.e. a wound deliberately left open owing to infection, swelling, contamination or empty tissue space, a wound initially closed but subsequently dehisced or a wound arising from surgical debridement). When patients had multiple SWHSIs, the largest wound was deemed to be the 'reference SWHSI'. Detailed data were collected, including patient and wound characteristics, health-care provider, clinical and surgery details, and treatment events (see *Appendix 3*). As this survey was limited to secondary use of routinely collected information, Research Ethics Committee approval was not required.[18] Approval was, however, obtained from associated NHS trusts prior to commencement of data collection.

Data analysis was conducted using IBM SPSS Statistics, version 21 (IBM Corporation, Armonk, NY, USA). Categorical variables were summarised as frequencies and proportions, whereas continuous variables were summarised as medians and associated 95% confidence intervals (CIs) and ranges. The usual resident regional population aged ≥ 20 years, as taken from the 2011 census, was used as the denominator when calculating point prevalence.[19]

Results

Following removal of duplicate cases (identified through age, ethnicity and wound characteristics), data were analysed for 187 patients with a SWHSI. In total, 62% of patients were male, 95.2% were of white British ethnicity and the median age was 58.0 years (range 19–90 years), as detailed in *Table 1*.

We estimated the point prevalence of treated SWHSIs as 4.1 per 10,000 population (95% CI 3.5 to 4.7 per 10,000 population), using the resident regional population value as the denominator.[19] The observed maximum number of SWHSIs per patient was four (1/187, 0.5%), with the majority of patients (164/187, 87.7%) having only one SWHSI. Patients were more frequently treated in community than in secondary care settings (109/187, 58.3% vs. 56/187, 29.9%, respectively), with the remaining patients treated within primary care (8/187, 4.3%) or other care settings (2/187, 1.1%). There were 12 patients (12/187, 6.4%) for whom treatment location was not recorded.

We found that almost half of the SWHSIs were planned to heal by secondary intention ($n = 89$, 47.6%) and 77 (41.2%) were primarily closed wounds that had subsequently dehisced. A further six wounds (3.2%) were surgically opened, six (3.2%) arose for other reasons [surgical debridement ($n = 2$, 1.1%), sutures removed and left open to heal ($n = 1$, 0.5%), skin graft failure ($n = 1$, 0.5%), non-healing wound ($n = 1$, 0.5%) and necrotising fasciitis requiring debridement ($n = 1$, 0.5%)] and for nine patients (4.8%) the information was not known or was missing. The median time from surgery to wound breakdown was 9 (95% CI 7 to 10) days.

TABLE 1 Cross-sectional survey patient demographics

Variable	Patients ($N = 187$)
Sex, *n/N* (%)	
Male	116/187 (62.0)
Female	62/187 (33.2)
Age (years)	
Median (95% CI)	58.0 (55 to 61)
Minimum–maximum	19.0–90.0
Missing, *n/N* (%)	3/187 (1.6)
Ethnicity, *n/N* (%)	
White British	178/187 (95.2)
Asian Indian, Asian other, black other, other mixed background, white other, white and Asian and not specified	7/187 (3.7)
Missing	2/187 (1.1)
Number of SWHSI per patient, *n/N* (%)	
1	164/187 (87.7)
2	16/187 (8.6)
3	4/187 (2.1)
4	1/187 (0.5)
Missing	2/187 (1.1)

In addition, we found that the median duration of wounds at the point of survey was 28 days (95% CI 21 to 35 days). Fully dehisced SWHSIs had the longest median duration (35 days, 95% CI 15 to 150 days), and those with long wound durations were most frequently treated within primary care (median duration 112 days, 95% CI 21 to 469 days) and community settings (median duration 35 days, 95% CI 28 to 56 days) (*Table 2*).

In total, we identified 43 different surgical procedures that preceded the development of a SWHSI. The most common surgical procedures were for pilonidal sinuses/abscesses (28/187, 15.0%), lower-limb amputations (19/187, 10.2%) and laparotomy with bowel resection (19/187, 10.2%). As detailed in *Table 3*, the most common surgical specialties associated with SWHSIs were colorectal (80/187, 42.8%), plastic (24/187, 12.8%) and vascular (22/187, 11.8%) surgery.

TABLE 2 Duration of SWHSIs within different patient treatment settings

	Treatment setting		
Wound duration (days)[a]	Community	Secondary care	Primary care
n/*N*	89/109	56/56	7/8
Median (95% CI)	35.0 (28 to 56)	14.5 (6 to 21)	112.0 (21 to 469)
Minimum–maximum	1–560	1–238	21–896
Missing, *n* (%)	20 (18.3)	0 (0)	1 (12.5)

a Wound duration refers to the number of days elapsed between formation of the SWHSI and survey data collection.

TABLE 3 Surgical wounds healing by secondary intention categories according to type of surgical specialty

	Wound category (*n*)							
Surgical specialty	Planned	Partially dehisced[a]	Fully dehisced[a]	Surgically opened[a]	Other	Not known	Missing	Total (*n*)
Colorectal	51	16	8	1	1	2	1	80
Plastics	5	10	5		4			24
Vascular	14	3	4			1		22
Orthopaedic	4	3	2	2		1	2	14
Upper GI tract	2	7	2	1			1	13
Cardiothoracic	2	6		1		1		10
Urology		3	3					6
Obstetrics and gynaecology	2	2		1				5
Other[b]	5		1					6
Breast		2						2
Missing	4				1			5

GI, gastrointestinal.
a These wounds were initially closed surgically before they dehisced or were surgically opened to become a SWHSI.
b Other details: pressure sore requiring surgical debridement (*n* = 2); sutures removed in outpatient department clinic and wound now left open to heal by secondary intention (*n* = 1); skin graft that did not take (*n* = 1); non-healing wound (*n* = 1); necrotising fasciitis requiring surgical debridement (*n* = 1).

At the time of the survey, most patients (184/187, 98.4%) were receiving active treatment for their wound. Dressings were the most common single treatment, being received by 169 (93.4%) patients. Eleven (6.1%) patients were receiving NPWT (10 patients in secondary care and one patient in the community setting). One patient (0.5%) was receiving larval therapy.

Conclusions

This cross-sectional study is the first to characterise SWHSI patients and their wound origin, duration and treatment.

This study provided initial data on wound and treatment characteristics, for which there were limited data when the research programme was conceived. Identifying common surgical specialties (within secondary care) that lead to SWHSI, that almost 50% of SWHSIs were planned and that the most common treatment location was the community helped us to plan recruitment strategies (i.e. identification of planned SWHSIs in advance of surgery) and time frames for both the cohort study and the subsequent pilot, feasibility RCT (workstream 4), and will also help to inform research studies in the future.

A total of 43 surgical procedures preceding SWHSIs were identified, with common associated surgical specialties being colorectal, plastic and vascular surgeries. SWHSIs occur in a wide range of specialties; however, there are specific populations in whom SWHSIs more frequently occur and so these may be appropriate as the focus of further research.

Data collected in relation to wound duration at the point of the survey have enabled us to estimate the duration of follow-up required to capture healing events. Again, this information helped to inform our design of the cohort study and pilot, feasibility RCT (workstream 4).

When this research programme commenced, we had identified the need for a rigorous population-based estimate of SWHSI prevalence. This study has provided a population-based estimate of treated SWHSI prevalence, which has suggested that these wounds are relatively common. Given the prevalence observed, this therefore supports the need for further research into SWHSI epidemiology and treatments.

Cohort study

Objectives

Following the cross-sectional survey, we conducted a prospective, inception cohort study with the following objectives:

- to investigate the clinical characteristics of patients with SWHSIs from the point of inception of the wound
- to clearly delineate the clinical outcomes of patients with SWHSIs over the lifetime of their wound, with a particular focus on time to wound healing and associated determinants
- to describe the types of treatments received by those with a SWHSI
- to assess the measurable impact SWHSIs have on patients' quality of life.

Methods

The cohort study was conducted over a 21-month period (18 February 2013 to 30 November 2014) in primary, secondary and community care settings at eight study sites across Yorkshire and the Humber, UK. Prior to commencement of the study, approval was obtained from Yorkshire and Humber – Humber Bridge Research Ethics Committee (reference 12/YH/0350) and from the associated NHS trusts.

Patients were eligible for inclusion if they had a SWHSI, defined as 'an acute (< 3 weeks' duration) open wound, resulting from surgery and requiring treatment, which was healing from the bottom up by the formation of granulation tissue'. When patients had multiple SWHSIs, the largest wound was deemed to

be the 'reference SWHSI' and detailed data were collected for this one wound. Health-care professionals in primary, secondary and community care settings initially identified and screened patients for eligibility. Clinical areas identified as having a high prevalence of SWHSIs were targeted for recruitment, including colorectal and vascular surgical wards. Patients meeting the eligibility criteria were approached for informed consent by a research nurse before any data collection. A formal sample size calculation was not required for this study, although it was anticipated that 443 participants could be recruited over a 6-month period.

Data, including patient, surgery and wound information, quality of life and a wound photograph (used to assess wound features), were collected at baseline. Participants were followed up every 1–2 weeks for a minimum of 12 months and a maximum of 21 months to collect key clinical outcome data [including healing through either participant self-reporting or clinician observation, defined as 'complete epithelial cover in the absence of a scab (eschar)']; key clinical events such as surgical site infection (in accordance with Public Health England guidance on surgical site infection surveillance) or hospital admission;[20] SWHSI treatments received; and any changes to a participant's study involvement, including death. To ensure accurate data collection, healing status was further verified through a home visit to a sample of patients (10–20%). Participants also completed quality-of-life [Short Form questionnaire-12 item (SF-12)[21] and EuroQol-5 Dimensions, three-level version (EQ-5D-3L)[22]] and pain [Brief Pain Inventory (BPI)[23]] assessments via postal questionnaires at 3-monthly intervals for a minimum of 12 months and a maximum of 21 months.

Data analysis was conducted using Stata® version 13 (StataCorp LP, College Station, TX, USA). Summary statistics for all variables were generated. Association with healing was examined for prespecified variables and multivariate logistic regression analyses conducted. Kaplan–Meier curves and Cox proportional hazards model analyses were used to examine time to event data. SF-12,[21] EQ-5D-3L[22] and BPI[23] data were summarised, with SF-12[21] data subsequently analysed using linear mixed models.

Results

A total of 396 patients were recruited to the cohort study from primary and acute care settings in Yorkshire, UK, with 393 participants included in data analysis (three patients were found to be ineligible following recruitment and so were excluded from the analysis). Just over half of participants were male ($n = 222$, 56.5%), participants had a median age of 55 (range 19–95) years and 69.5% of the study population were classed as overweight or obese (31.3% and 38.17%, respectively). Current smokers made up 28.5% of participants (i.e. were currently smoking or had quit within the last year).

The most common comorbidities we observed were cardiovascular disease ($n = 151$, 38.4%), followed by diabetes mellitus ($n = 103$, 26.2%) and peripheral vascular disease ($n = 57$, 14.5%). The majority of participants had no previous history of SWHSIs ($n = 93$, 72.0%) and had only one SWHSI ($n = 358$, 91.0%), and their surgical wound had been planned to heal by secondary intention ($n = 236$, 60.1%). The median area of the reference SWHSI at baseline was 6 cm^2 (range 0.01–1200 cm^2). SWHSI location varied; however, the most common sites were the abdomen ($n = 132$, 33.6%), foot ($n = 59$, 15.0%) and leg ($n = 58$, 14.8%), linking the commonly represented surgical specialities of colorectal ($n = 136$, 39.7%) and vascular ($n = 82$, 20.9%). At baseline, 164 patients (41.7%) were receiving hydrofibre dressings and 89 patients (22.7%) were receiving NPWT. Further details of baseline demographics (patient, wound and surgery) and treatments received are presented in *Tables 4–7*.

The mean length of participant follow-up was 499 days [standard deviation (SD) 127.4 days], with a range of 13–651 days (median 528 days). Sixty-six participants (16.8%) were not followed up for the entire study duration (31 withdrew, 29 died and six were lost to follow-up). When the reference SWHSI was situated on a limb, this was amputated for 3.3% of participants ($n = 13$), of whom 61.5% had experienced an infection during follow-up ($n = 8$) and 76.9% had diabetes mellitus ($n = 10$). Infections were experienced by 32.1% of study participants ($n = 126$). Hospital admissions were reported for 97 participants (24.7%), of which 66 participants (68.0%) returned to the operating theatre. Thirty-six cases (38.1%) of hospital admissions were related to SWHSIs.

TABLE 4 Cohort patient baseline characteristics

Variable	Patients ($N = 393$)
Age (years), median (range)	55.0 (19.0–95.3)
Sex, *n* (%)	
Male	222 (56.5)
Female	171 (43.5)
BMI (kg/m^2), mean (SD)	28.9 (6.6)
History of SWHSI, *n* (%)	
Yes	93 (23.7)
No	283 (72.0)
Do not know	17 (4.3)
Tobacco use, *n* (%)	
None in last 10 years	219 (55.7)
None current, but in last 10 years	62 (15.8)
Current (less than one pack/day) or quit in last year	84 (21.4)
Current (more than one pack/day)	28 (7.1)
Baseline comorbidities	**Patients ($N = 286$), *n* (%)[a]**
Cardiovascular disease	151 (38.4)
Diabetes mellitus	103 (26.2)
Airways (e.g. asthma)	69 (17.6)
Arthritis	65 (16.5)
Peripheral vascular disease	57 (14.5)
Cancer	51 (13.0)
Orthopaedic (e.g. fractures)	27 (6.9)
Stroke	20 (5.1)
Autoimmune	19 (4.8)
Neurological	11 (2.8)
Other	31 (7.9)
Medications used	**Patients ($N = 272$), *n* (%)[b]**
Anticoagulants/antiplatelets	196 (49.9)
Vasodilator	111 (28.2)
NSAIDs	66 (16.8)
Corticosteroids	11 (2.8)
Immunosuppressant	9 (2.3)
Cytotoxic	5 (1.3)

BMI, body mass index; NSAID, non-steroidal anti-inflammatory drug; SD, standard deviation.
a *N* is less than total sample: 107 patients without associated comorbidity.
b *N* is less than total sample: 121 patients did not report medication use.

TABLE 5 Cohort wound baseline characteristics

Variable	Patients ($N = 393$)
Number of SWHSIs, median (range)	1 (1–6)
Area (cm^2), median (range)	6 (0.01–1200)
SWHSI location, *n* (%)	
Abdomen	132 (33.6)
Foot	59 (15.0)
Leg	58 (14.8)
Perianal	34 (8.7)
Back	19 (4.8)
Natal cleft	16 (4.1)
Buttocks	16 (4.1)
Breast	7 (1.8)
Arm	5 (1.3)
Perineum	5 (1.3)
Head	3 (0.8)
Hand	2 (0.5)
Neck	2 (0.5)
Missing	35 (8.9)
Aetiology, *n* (%)	
Planned	236 (60.0)
Dehisced	141 (35.9)
Surgically opened	16 (4.1)
Tissue involvement, *n* (%)	
Full thickness	235 (59.8)
Muscle, tendon or bone exposed	120 (30.5)
Organ exposed	1 (0.3)
Unsure	35 (8.9)
Missing	2 (0.5)
Infection at baseline, *n* (%)	
Yes	79 (20.1)
No	314 (79.9)
Antibiotics used, *n* (%)	
Yes	182 (46.3)
No	211 (53.7)
Dressing, *n* (%)	
Hydrofibre/spun hydrocolloid	164 (41.7)
Other	129 (32.8)
Wound contact	114 (29.0)

continued

TABLE 5 Cohort wound baseline characteristics (*continued*)

Variable	Patients (*N* = 393)
NPWT	89 (22.7)
Foam	36 (9.2)
Alginate	27 (6.9)
Silver containing	23 (5.9)
Iodine	19 (4.8)
Soft polymer	19 (4.8)
Hydrocolloid	10 (2.5)
Superabsorbent	7 (1.8)
Cavity foam	4 (1.0)
Hydrogel	1 (0.3)
Silver sulfadiazine	1 (0.3)
Treatment environment, *n* (%)	
Hospital inpatient	229 (58.3)
Home	88 (22.4)
GP	55 (14.0)
Hospital outpatient	11 (2.8)
Other	8 (2.0)
Missing	2 (0.5)

GP, general practitioner.

TABLE 6 Surgery baseline characteristics

Variable	Patients (*N* = 393), *n* (%)
Subspecialty	
Colorectal	156 (39.7)
Vascular	82 (20.9)
Other	50 (12.7)
Plastics	33 (8.4)
Orthopaedic	17 (4.3)
Obstetrics and gynaecology	13 (3.3)
Surgical debridement	11 (2.8)
Upper GI tract	7 (1.8)
Urology	7 (1.8)
Cardiothoracic	7 (1.8)
Neurosurgery	3 (0.8)
Thoracic	3 (0.8)
Breast	2 (0.5)
Trauma	1 (0.3)
Oral and maxillofacial	1 (0.3)

TABLE 6 Surgery baseline characteristics (*continued*)

Variable	Patients (*N* = 393), *n* (%)
Surgery type	
Emergency	236 (60.1)
Elective	135 (34.4)
Missing	22 (5.6)
Contamination level	
Dirty	247 (62.9)
Contaminated	65 (16.5)
Clean-contaminated	51 (13.0)
Clean	26 (6.6)
Missing	4 (1.0)

GI, gastrointestinal.

TABLE 7 Cohort treatment dressings received at any time

Treatment dressings received (at any time)	Patients (*N* = 393), *n* (%)[a]
Hydrofibre	259 (65.9)
Basic wound contact dressing	212 (53.9)
Other	196 (49.9)
NPWT	115 (29.3)
Foam	113 (28.8)
Silver-containing dressing	89 (22.7)
Soft polymer dressing	73 (18.6)
Iodine-containing dressing	71 (18.1)
Alginate dressing	49 (12.5)
Hydrogel	23 (5.9)
Hydrocolloid	22 (5.6)
Superabsorbent	21 (5.3)
Cavity	12 (3.1)
Polyhexamethylene biguanide dressing	8 (2.0)

a Values exceed total *N* due to multiple dressing changes and reasons throughout follow-up.

Data indicated that the reference SWHSI healed for 81.4% of participants (*n* = 320) during the study. Agreement between patient self-report and nurse assessment of healing status verification was relatively high (77.8% at 6 months and 74.2% at 12 months). Disagreements were present for four participants: three patients had healing confirmed during a visit but paperwork was not completed to this effect and one participant was not healed at the verification visit but healed shortly afterwards. The median time to healing for all cohort participants was 86 (95% CI 75 to 103) days, as presented in *Figure 2*. When we assessed time to healing against baseline participant and wound characteristics in a Cox proportional hazards model, baseline

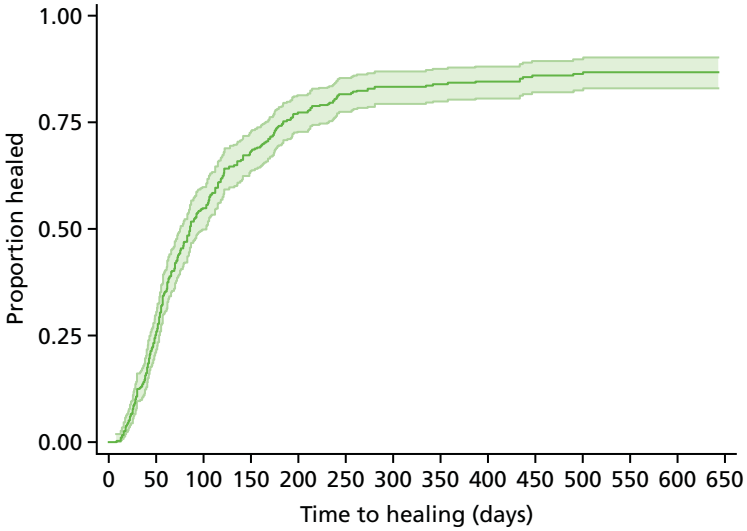

FIGURE 2 Cohort study: Kaplan–Meier curve of time to healing in days.

wound area above median ($p < 0.01$) and surgical wound contamination level as determined at the point of surgery ($p = 0.04$) were significant predictors of prolonged time to healing (see *Appendix 4*). Infection at any point was also found to be a significant predictor of prolonged time to healing ($p < 0.01$).

The most commonly received treatment throughout the study was hydrofibre dressings, with 65.9% ($n = 259$) of participants receiving this treatment at least once. Nearly one-third ($n = 115$, 29.3%) of participants received NPWT at some point during the study.

Health utility scores captured by the EuroQol-5 Dimensions (EQ-5D) measure[22] (in which 0 = death and 1 = perfect health) were a mean of 0.5 (SD 0.4) at baseline, increasing to a mean of 0.6 (SD 0.4) at 6 months and 0.6 (SD 0.4) at 12 months. Further details are provided in *Table 8*.

Pain, measured as BPI scores for pain severity (in which 0 = no pain and 10 = pain as bad as you can imagine) and pain interference (in which 0 = does not interfere and 10 = completely interferes)[23] reduced slightly over time. Mean pain severity reduced from 3.7 (SD 2.54) at baseline to 3.0 (SD 3.0) by 15 months; similarly, mean pain interference scores reduced from 4.2 (SD 2.54) at baseline to 3.1 (SD 3.17) at 15 months. Further details are provided in *Table 9*.

TABLE 8 Cohort EQ-5D utility scores by time point and healing status

		Healing status		
Time point	Overall	Healed	Not healed	*p*-value
Baseline, *n*	383	311	72	
Mean (SD)	0.5 (0.4)	0.5 (0.37)	0.4 (0.42)	0.07
3 months, *n*	258	223	35	
Mean (SD)	0.6 (0.4)	0.6 (0.38)	0.6 (0.33)	0.58
6 months, *n*	219	191	28	
Mean (SD)	0.6 (0.4)	0.6 (0.37)	0.5 (0.34)	0.08
12 months, *n*	185	166	19	
Mean (SD)	0.6 (0.4)	0.6 (0.35)	0.6 (0.38)	0.31

TABLE 9 Cohort BPI scores by time point and healing status

	BPI							
	Pain severity				Interference			
		Healing status				Healing status		
Time point	Overall	Healed	Not healed	*p*-value	Overall	Healed	Not healed	*p*-value
Baseline, *n*	385	313	72		390	318	72	
Mean (SD)	3.7 (2.54)	3.6 (2.53)	4.0 (2.53)	0.28	4.2 (3.12)	4.2 (3.14)	4.4 (3.05)	0.63
3 months, *n*	257	220	37		260	223	37	
Mean (SD)	3.3 (2.63)	3.3 (2.70)	3.4 (2.17)	0.83	3.8 (3.12)	3.7 (3.13)	4.3 (3.08)	0.30
6 months, *n*	210	182	28		214	186	28	
Mean (SD)	3.4 (2.67)	3.3 (2.71)	3.9 (2.38)	0.22	3.8 (3.18)	3.7 (3.20)	4.6 (2.97)	0.13
12 months, *n*	179	161	18		179	161	18	
Mean (SD)	3.4 (2.66)	3.3 (2.70)	4.0 (2.32)	0.29	3.6 (3.18)	3.5 (3.20)	4.3 (2.97)	0.36

Quality of life was measured using the SF-12 and presented as SF-12 physical component scores (PCSs) and mental component scores (MCSs).[21] At baseline, the mean PCS was 33.1 (SD 10.7) and the mean MCS was 42.2 (SD 12.35). At 15 months' follow-up, the mean PCS was 40.8 (SD 13.46) and the mean MCS was 48.3 (SD 10.73). Further details are provided in *Table 10*. A linear mixed model, adjusting for duration of SWHSI, baseline SWHSI area, location, participant age and baseline SF-12 subscale score, found follow-up time point, baseline score, age and SWHSI duration to be significant predictors of PCS ($p < 0.001$ in all cases) and MCS ($p = 0.03$ for time point and $p < 0.01$ for age, baseline score and SWHSI duration).

TABLE 10 Cohort SF-12 PCS and MCS by time point

	SF-12 dimensions (overall population)	
Time point	PCS	MCS
Baseline, *n*	390	390
Mean (SD)	33.1 (10.17)	42.2 (12.35)
3 months, *n*	255	255
Mean (SD)	37.7 (13.15)	45.1 (11.69)
6 months, *n*	223	223
Mean (SD)	39.2 (12.91)	45.1 (12.13)
9 months, *n*	210	210
Mean (SD)	39.4 (12.89)	46.4 (11.28)
12 months, *n*	187	187
Mean (SD)	38.8 (13.11)	47.2 (11.58)
15 months, *n*	147	147
Mean (SD)	40.8 (13.46)	48.3 (10.73)
18 months, *n*	78	78
Mean (SD)	39.4 (13.52)	47.3 (11.12)

Conclusions

This prospective inception cohort study in patients with SWHSIs is the first we have identified. Broad patient groups (patients undergoing abdominal colorectal surgery, lower-limb vascular surgery and a mixed group of other procedures and specialities) were identified, which were similar to those identified in our cross-sectional survey. This information flags populations of clinical relevance, as well as those likely to be the focus of further research.

The median time to healing for these wounds, of approximately 3 months, is new information, which highlights the extended period of time that patients might expect to cope with open surgical wounds. There was high variability, with time to healing ranging from 8 days to 1 year and 4 months (prior to censoring) and from 5 days to 1 year and 7 months (following censoring). The chronicity of these wounds is crucial for patients and carers to appreciate, in order for them to have realistic expectations regarding wound healing. The cohort also highlights the large number of adverse events that occur in SWHSI patients, with wound infection and readmission to hospital (with the associated care costs) being particularly common. This cohort study data clearly demonstrated that SWHSIs pose a distinctive management challenge that was previously unsupported by high-level evidence.

Adjusted analyses provide further initial insights into possible patient and wound 'risk' factors that might have a detrimental impact on healing, including wound infection at any point, baseline wound area and higher levels of surgical wound contamination, as determined at the point of surgery. The predictive baseline factors may be important for the stratification of randomisation or adjustment for prognostic factors in future trials; however, it should be noted that there are many other covariates that are associated and correlate with these predictors. The SF-12 data indicate that, at baseline, SWHSI patients have quality-of-life limitations comparable to patients with congestive cardiac failure; however, they were significantly younger.[24] This therefore demonstrates the potential impact that SWHSIs have on patient quality of life. However, as the improvements in SF-12 scores during the study demonstrate, quality of life may be improved by time or wound healing. The research to date is therefore building a picture of a relatively common wound type that takes a prolonged time to heal, negatively impacts quality of life and puts patients at high risk of infection and other adverse events.

The common treatments for SWHSIs, in the centres involved in this cohort that were treating SWHSI patients across Yorkshire and the Humber, UK, were dressings and NPWT. There is currently limited and generally low-quality evidence on how effective dressings are in terms of wound management and promoting optimal clinical outcomes in a cost-effective way.[14] A recent Cochrane systematic review found only two RCTs, with a total of 69 participants, that had investigated the relative effectiveness of NPWT on SWHSIs, both reporting limited outcome data, which prevents any firm conclusions to be made.[14] Given that all SWHSI patients in this cohort were receiving dressings and/or NPWT, further research to explore clinical effectiveness and cost-effectiveness of these treatments in one or more of the common surgical groups identified seems warranted, and so was considered appropriate for further assessment in workstream 2.

The prospective and observational design of this study allowed us to follow patients over time and to collect the important natural history, treatment and outcome data presented here. Although we tried to maintain a representative sample, the need for consent meant that the subset recruited might differ in some systematic way from the wider SWHSI patient population. Comparison of the cohort and the cross-sectional survey data may be useful here, as the survey data were captured away from the patient's bedside, did not require consent and thus may provide a more epidemiologically complete overview of the SWHSI population. In terms of patient, epidemiological, wound and surgery data, the populations in the survey and cohort appear similar; however, the findings from the survey may have influenced specific areas for focused recruitment into the cohort study (e.g. subspecialty-specific hospital wards). Some patient groups for whom wound problems are recognised nationally seem under-represented in the cohort study (e.g. post-caesarean wounds, for which dehiscence rates as high as 6% have been reported).[25]

The cohort study was conducted in a single geographical area (two large centres in Yorkshire, UK), and therefore the patient groups and the treatment availability observed may not be reflective of national or international patient populations or treatment availability. However, we have no reason to suspect that there are huge differences between these surgical patients and those elsewhere, particularly given the breadth of our inclusion criteria.

We also note that our analyses exploring the impact of factors on time to healing are based on our observational data set and thus these cannot be assumed to be causal relationships. Thus, firm conclusions regarding factors that may affect healing cannot be drawn. However, we are able to report the associations found between observed covariates and healing, and reflect on them. From the outset of the study, there was careful consideration regarding measured study variables, with the aim of capturing important data, including factors that had the potential to be prognostic in relation to healing. We consulted widely with clinical experts and extensively scoped the literature, with the aim of providing the most comprehensive analysis possible.

The further research conducted as part of this research programme (workstreams 2–4) focused on further investigation of interventions that may offer clinical effectiveness and cost-effective treatment options for SWHSIs (workstream 2), as well as more detailed exploration of patients' experiences of living with SWHSIs and health professionals' views of delivering care to patients with these challenging wounds.

Workstream 2: using evidence from observational research to estimate the value of negative-pressure wound therapy in SWHSIs

Following characterisation of SWHSI patients and their treatment in workstream 1, the evidence gap regarding the cost-effectiveness of SWHSI treatments remained. Data collected in workstream 1 indicated that a variety of interventions are used when treating and managing SWHSIs. Although the majority of participants in the cohort study received dressings throughout follow-up, 29.3% (115/393) received a significantly more expensive technology: NPWT.

Negative-pressure wound therapy devices apply a carefully controlled negative pressure (or vacuum) to a dressing, creating an air-tight seal and removing tissue fluid from the treated wound area into a disposable canister.[14] The canister is removed and replaced either when it becomes full or at least once a week. The device is generally used as part of the SWHSI treatment pathway, rather than to the point of healing, and can be administered and removed by both nurses and surgeons. It has been claimed that NPWT speeds up wound healing by removing excess fluid, increasing tissue perfusion and removing bacteria.[26] However, although a recent Cochrane systematic review identified two RCTs investigating the relative effectiveness of NPWT on SWHSIs,[14] it could not draw any conclusions, as the outcome data reported in both studies were very limited.

Given the current level of clinical use on SWHSIs, the cohort data collected in workstream 1 have been used here to evaluate the cost-effectiveness of NPWT for the healing of SWHSIs (the clinical outcome of wound treatments most valued by patients)[27] and the value of a future RCT. From this work, a paper highlighting methodological challenges of analysing observational evidence in this context has been published (see *Appendix 5*). The current chapter presents the clinical implications of the research.

Objectives

- To estimate the cost-effectiveness of NPWT compared with wound dressings for the healing of SWHSIs, using cohort data from workstream 1.
- To assess whether or not investment in further research on treatments for SWHSIs is likely to be worthwhile.

Methods

In this workstream, we evaluated if, after adjustment, NPWT was clinically effective and cost-effective when compared with standard dressings. For clinical effectiveness, we used wound healing as the outcome; for cost-effectiveness, we quantified the impact of differences in time to healing on quality-adjusted life-years (QALYs). This approach assumed that no mortality differences existed and, thus, any improvements in health-related quality of life (HRQoL) were associated with accelerated time to healing only. We also noted that any additional HRQoL improvements that may have arisen from treatment (independent of healing status) were expected to be transient and not to have a significant impact on HRQoL (which is a multidimensional concept that includes domains related to physical, mental, emotional and social functioning). For this reason, such effects were not considered here.

We hypothesised that NPWT could be cost-effective by reducing healing time, improving HRQoL and reducing treatment costs (via reduced healing time). We envisaged that if the total costs of treatment were higher with NPWT than for comparator treatments, NPWT would only be cost-effective if the incremental costs to QALY gains fell below the standard NICE £20,000–30,000 per QALY threshold.

Specifically, the cost-effectiveness analysis used cost per QALY gained as the cost-effectiveness outcome. A 1 year time horizon was considered and a NHS perspective was adopted. Formally, we aimed to quantify the impact of NPWT in expected time to healing. The difference in QALYs between the interventions was derived from the expected time to healing and the EQ-5D index score while healed/unhealed, the latter estimated using the multilevel model (described in supplementary material in *Appendix 5*). Incremental disease costs were calculated in an analogous way to incremental QALYs, making use of the cost estimates derived in the multilevel two-part modelling approach (see *Appendix 5*). Treatment-related costs considered that patients received some form of treatment up to healing. The daily costs associated with the 'non-NPWT' group were based on average costs of dressings in participants who had received other treatments and were calculated by multiplying this cost by the difference in time to healing. For patients receiving NPWT, an average daily cost of NPWT was applied to the mean time on NPWT treatment in the cohort study. In the remaining time, patients were assumed to use dressings, with a daily cost equal to patients in the 'non-NPWT' group.

The cohort data were analysed for evidence regarding the various aspects of treatment and wound healing, including the impact of treatment (NPWT vs. dressings) on the time to healing and the impact of this SWHSI healing on disease-specific costs and HRQoL, as is presented in *Figure 3*. To estimate the effect of treatment on healing, we attempted to control the confounding (and selection bias) inherent when using observational data in this context. We adjusted for observed confounding (i.e. for characteristics observed within the cohort study sample that determine time to healing and may have differed between the groups). We also attempted to account for any potential confounding from unobserved sources.

Health-related quality of life was assessed in the cohort study using the EQ-5D index score, obtained through a self-reported questionnaire, comprising five domains (mobility, self-care, usual activities, pain and discomfort, and anxiety and depression).[22] Participants were also asked to complete a resource use questionnaire quarterly.

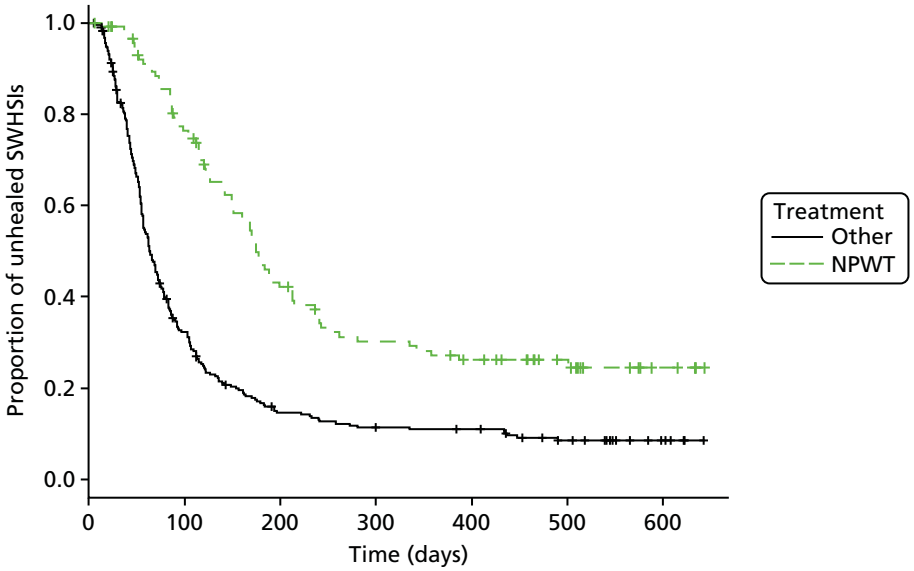

FIGURE 3 Time to healing: descriptive Kaplan–Meier curve. Reproduced with permission from Saramago *et al.*[28] This is an Open Access article distributed in accordance with the terms of the Creative Commons Attribution (CC BY 4.0) license, which permits others to distribute, remix, adapt and build upon this work, for commercial use, provided the original work is properly cited. See: http://creativecommons.org/licenses/by/4.0/. The figure includes minor additions and formatting changes to the original figure.

This questionnaire was developed for this study to allow costing of NHS resources specifically attributable to the SWHSIs and included collection of number of contacts with general practitioners (GPs), nurses and doctors in NHS institutions or the patient's home, as well as the number of nights spent as an inpatient between study follow-up time points. The costing used national sources and 2014 prices.[29]

Analyses required the application of econometric models to the cohort data. A Bayesian approach to inferences was utilised, computed using Markov chain Monte Carlo simulation, using WinBUGS version 1.4.3 (Medical Research Council Biostatistics Unit, Cambridge, UK).[30]

Identification of external evidence to supplement cohort data

To evaluate the existence of any external evidence to complement the cohort data, we also conducted the following range of systematic literature searches.

We conducted Cochrane systematic reviews of RCTs evaluating the treatment of SWHSIs, with any recognised form of NPWT.[14,31]

Using the general review methods and with the support of an information specialist and an expert systematic reviewer, we conducted systematic searches and identification of the following studies:

- any cohort studies evaluating the use of NPWT for SWHSIs
- any EQ-5D or related health utility data for people with SWHSIs
- any previous modelling work for the treatments of SWHSIs that might inform the planned work.

Details of the search strategies used are detailed in *Appendix 6*.

EuroQol-5 Dimensions index scores and disease-specific costs

A multilevel (or panel data) approach was used to model both EQ-5D index scores and quarterly costs that accounted not just for between-participant variation but also for within-participant variation across the quarterly observations. A time-dependent indicator of whether the participant had healed or not at each time point was used to capture the effect of healing. Changes from baseline EQ-5D index scores were modelled using a standard multilevel model based on the normal distribution (random intercept). For cost data, due to a high proportion of zero observations and the typical skewness associated with these data, a two-part model was used: the first part was a multilevel logistic regression (to explain the probability of observing zero costs over time) and the second was mixed gamma model with log-transformed costs (to evaluate the expected value of the non-zero observations). Both parts were multilevel models, to account for the repeated observations per participant.

We calculated the average daily cost of NPWT as £31.78 (according to centre-specific costings). For dressings, a unit cost of £2.39 per day was calculated (based on the mix of dressings used within the cohort data). The duration of NPWT treatment was evaluated from the cohort data (mean 37 days, SD 64.6 days) and was assumed to be independent of time to wound healing, as this treatment is rarely used up to the point of wound healing. NPWT patients were assumed to receive only dressings for the remainder of time unhealed.

Results indicated that healing was associated with a small (but statistically significant) increase in EQ-5D index score [mean 0.055, standard error (SE) 0.02]. Cost data, as presented in *Table 11*, indicated that healing significantly reduced quarterly wound-related costs (mean £865, SE £112).

Relative effectiveness (time to healing) of negative-pressure wound therapy and dressing-treated wounds

Based on the cohort data, we took two different approaches to modelling the time to healing and assessed robustness of our conclusions to the approach taken.

TABLE 11 EuroQol-5 Dimensions index scores and disease-related costs: regression analysis

Model	Mean	95% CrI
Expected EQ-5D (unhealed)	0.091	0.036 to 0.146
Expected EQ-5D (healed)	0.091 + 0.055 = 0.146	0.098 to 0.193
Difference in EQ-5D attributed to healing	0.055	0.015 to 0.094
Expected costs (£) (unhealed)	1124.45	916.9 to 1359.1
Expected costs (£) (healed)	258.91	208.1 to 317.7
Difference in costs (£) attributed to healing	865	674.2 to 1126.5

CrI, credible interval.

Modelling strategy A: ordinary least squares with imputation

Modelling strategy A used ordinary least squares (OLS) (or linear regression) to describe time to healing. OLS methods do not deal with censoring and 73 participants did not heal within the study follow-up period. To generate a complete data set on time to healing, the censored observations on time to wound healing were imputed, assuming their follow-up time plus an additional quantity, either 1 day (i.e. participants were conservatively assumed to have healed the day after they were censored) or expected healing time (data elicited from three experienced clinicians and pooled) (see *Appendix 5*). Note that by attributing an additional time to healing, elicited by clinical experts, to patients who have been censored in the study, we are also extrapolating beyond the study follow-up. Such extrapolation is required to allow achieving an unrestricted estimate of the effects of NPWT on mean time to healing, required for cost-effectiveness analysis.

Modelling strategy B: two-stage model

A second, more complex, modelling strategy (modelling strategy B) was also implemented, which explicitly considered the unhealed participants. Instead of OLS, it used a two-step modelling approach: a logistic regression estimated the probability of healing within the follow-up for each treatment, followed by linear regression, which estimated the expected time to healing for the population that healed within follow-up. This strategy reflected the possibility of there being a group of 'long-term non-healers' and allowed exploration of different determinants of the probability of healing and of time to wound healing, conditional on having healed in the adjustment for observables.

In terms of adjustment for observed confounding, and in the absence of evidence on determinants of healing in this patient group, a comprehensive variable selection process was undertaken using the cohort data sample. It aimed to identify predictors of treatment assignment with NPWT, predictors of healing and treatment effect modifiers. The selection criterion was based on goodness of fit (using the deviance information criteria at a widely used cut-off point of 5 deviance information criterion points).[32] All the predictors identified were used as adjustment covariates in the regression model for time to healing.

To account for unobservable confounding, instrumental variable (IV) regression was used. This method uses a variable (the instrument) that is associated with treatment assignment but not with outcome (except for any indirect effect on treatment assignment) to adjust for unobservable confounding. A range of instruments focused on the decisions of health professionals to use NPWT, that is use of NPWT on previous patient treated, perceptions of NPWT as effective treatment, likelihood of NPWT use for patients, desire to use NPWT more frequently, perceptions of NPWT as affordable and value for money, and company representative input, were considered (see *Appendix 5*). The selection of instruments was based on frequentist tests aimed at assessing aspects of validity and relevance (see *Appendix 5*). Previous treatment used by the treating health professional was the best-performing instrument.

The IV model used two regressions (two stages). The first stage regressed treatment allocation by the instrument and the set of relevant predictors of outcome (logistic regression) to predict the probability of each individual participant being assigned to NPWT. The predictions were then used as a covariate in the second-stage regression(s), which, again, conditions on the set of relevant predictors of outcome. Inferences were obtained using a Bayesian framework, so that uncertainty over predictions of treatment allocation was fully considered. Any external evidence located (from previous research) was to have been used as prior evidence to update the data obtained from the cohort.

Cost-effectiveness of negative-pressure wound therapy

The cost-effectiveness analysis uses cost per QALY gained as the cost-effectiveness outcome. A 1-year time horizon was considered and a NHS perspective was adopted. Formally, we aimed to quantify the impact of NPWT in expected time to healing. The difference in QALYs between the interventions was derived from the expected time to healing and the EQ-5D index score while healed or unhealed, the latter estimated by the multilevel model (described in the supplementary material in *Appendix 5*). Incremental disease costs were calculated in an analogous way to incremental QALYs, making use of the cost estimates derived in the multilevel two-part modelling approach described above (see *Appendix 5*). Treatment-related costs considered that patients received some form of treatment up to healing. The daily costs associated with the 'non-NPWT' group were based on average costs of dressings in participants who had received other treatments and were calculated by multiplying this cost by the difference in time to healing. For patients receiving NPWT, an average daily cost of NPWT was applied to the mean time on NPWT treatment in the cohort study. In the remaining time, patients were assumed to use dressings, with a daily cost equal to that for patients in the 'non-NPWT' group.

Results

Identification of external evidence to supplement cohort data

We screened 1477 citations from the literature searches and found no existing health utility data collected from patients with SWHSIs that could be used. Neither did we find any relevant published models exploring either the clinical effectiveness or the cost-effectiveness of treatments for SWHSIs. In terms of relative effects for NPWT compared with alternative treatments on healing, we located four potentially relevant RCTs[33–36] and no observational data.

Of the four trials, two explored the use of NPWT compared with standard dressings to treat foot wounds in patients with diabetes mellitus.[33,34] One trial[33] included 162 adult patients who had undergone a transmetatarsal amputation of the foot. It was not clear from the study whether or not the wounds had been left open following surgery. A second trial[34] included 342 adult patients who had undergone debridement of a foot wound and were randomised to receive NPWT or dressings (predominantly hydrogels and alginates). Although it was not clear whether or not the debridement of these wounds was surgical, we were advised by local clinicians that it was likely to be. Both trials of NPWT in foot wounds reported time to healing data; however, the data appeared to include wounds that had been closed by surgery following treatment with NPWT or dressings. The two trials were considered to be at high risk of performance bias, as unblinded health professionals had made key decisions regarding the treatment of wounds, such as closure surgery. This issue has been noted previously and the validity of combining wounds closed by secondary intention and those closed by surgery has been questioned.[37] The potential for high risk of bias in these studies, combined with the fact that the data from these trials related to only a subset of the heterogeneous group of patients of interest, meant that we felt that the relative healing data could not be reasonably combined with the adjusted estimates of the cohort data.

Two further trials were identified.[35,36] The first study,[35] with 20 participants, compared NPWT with an alginate dressing in the treatment of open, infected groin wounds. The second study,[36] with 49 participants, compared NPWT with a silicone dressing in the treatment of excised pilonidal sinus. No useable healing data were reported in either trial. For this reason, these studies did not provide relevant evidence to complement the cohort data.

Effectiveness results when adjusting for observables

Modelling strategy A: ordinary least squares with imputation

Relevant associations found with predictors of treatment assignment with NPWT were wound area > 25 cm^2, skin and subcutaneous tissue loss (a measure of tissue involvement) and inpatient (vs. outpatient) management. Relevant associations found with predictors of healing were inpatient (vs. outpatient) management and previous history of a SWHSI. The data also suggested that history of a SWHSI could be a relevant treatment effect modifier. Predictors of treatment assignment and predictors of healing were used to adjust all regressions within modelling strategy A.

In the model in which treatment effect modifiers were not considered, and censored observations were assumed to heal 1 day after follow-up, participants treated with NPWT were expected to take longer to heal than those who did not receive NPWT, on average 73 days longer [95% credible interval (CrI) 33.8 to 112.8 days longer] (*Table 12*). The addition of the interaction term between treatment and SWHSI history indicated that NPWT was still expected to increase time to healing compared with the use of dressings alone, but the magnitude of effect differed between the groups (181 days for participants with history of SWHSIs vs. 42 days for patients without history of a SWHSI). Results were similar when elicited expert opinion was used to impute censored healing times; however, the point estimates were even less favourable for NPWT (requiring, on average, 114 days additional days to wound healing compared with the use of standard dressings) and uncertainty was significantly increased.

TABLE 12 Effectiveness results: complete data set

	Model				
Model ID	**0**	**1**	**2**	**3**	**4**
Instrument used, *z*	None	None	None	Previous treatment	Previous treatment with interaction
Equation	TTH	TTH	TTH	(Stage 2) TTH	(Stage 2) TTH
Adjustment covariates	None	Observables	Observables + interaction	Observables	Observables + interaction
Area (> 25 cm^2), x_1		18.0 (95% CrI –23.1 to 58.0)	21.1 (95% CrI –20.3 to 62.1)	23.8 (95% CrI 29.8 to 43.7)	36.2 (95% CrI –23.7 to 56.3)
Treatment location,[a] x_2		45.3 (95% CrI 11.3 to 79.2)	43.8 (95% CrI 9.9 to 76.8)	48.9 (95% CrI 3.0 to 63.8)	55.3 (95% CrI 10.8 to 70.8)
Tissue involvement,[b] x_3		31.9 (95% CrI –1.5 to 65.0)	26.6 (95% CrI –5.3 to 58.7)	33.8 (95% CrI –8.0 to 73.1)	37.2 (95% CrI –2.0 to 50.6)
History, *w*		7.5 (95% CrI –28.4 to 42.9)	–29.3 (95% CrI –71.5 to 12.1)	7.2 (95% CrI –29.5 to 44.6)	–10.3 (95% CrI –61.4 to 7.4)
NPWT, *t*	108.0 (95% CrI 73.6 to 142.2)	73.2 (95% CrI 33.8 to 112.8)	41.9 (95% CrI –1.1 to 84.1)	56.9 (95% CrI –71.7 to 192.8)	9.1 (95% CrI –120.2 to 55.9)
NPWT × history, *w.t*			138.7 (95% CrI 56.9 to 221.8)		69.4 (95% CrI –67.5 to 118.0)
Constant	116.8 (95% CrI 97.9 to 135.2)	81.4 (95% CrI 53.3 to 110.0)	92.7 (95% CrI 64.5 to 120.8)	81.1 (95% CrI 52.3 to 109.1)	86.7 (95% CrI 56.7 to 97.0)
Observations	393	372	372	372	372

ID, identification; TTH, time to healing.
a Treatment location: inpatient (vs. outpatient).
b Tissue involvement: skin and subcutaneous tissue loss (vs. skin loss).
Notes
Imputation using minimum date of healing.

Modelling strategy B: two-stage model

This modelling approach explicitly modelled the probability of healing within follow-up and, in addition to the predictors of treatment assignment mentioned in *Modelling strategy A: ordinary least squares with imputation*, it identified associations with body mass index (BMI) and wound location being the foot (vs. other locations). For those healing within follow-up, time to healing was associated with surgery type (colorectal vs. other surgeries), wound duration and diabetic foot wounds. No evidence of relevant interaction terms was found. As detailed in *Table 13*, results indicated that participants treated with NPWT were estimated to have lower probability of healing than those who did not receive NPWT [odds ratio (OR) of healing with NPWT was 0.59 (95% CrI 0.28 to 1.12)]. The expected time to healing of NPWT-treated participants who healed compared with participants treated with dressings alone was an additional 46 days (95% CrI 19.6 to 72.5 days).

TABLE 13 Time to healing: extended modelling approach

	Model			
Model ID	**b0**		**b1**	
Equation	(Stage 2A) OR for healing	(Stage 2B) TTH	(Stage 2A) OR for healing	(Stage 2B) TTH
Type of regression model	Logit	OLS	IV, logit	IV, OLS
Adjustment	None	None	Adjustment set	Adjustment set
Area (> 25 cm^2), x_1			0.52 (95% CrI 0.24 to 0.99)	27.7 (95% CrI 0.6 to 54.5)
Treatment location,[a] x_2			0.52 (95% CrI 0.22 to 1.04)	30.9 (95% CrI 9.2 to 52.3)
Tissue involvement,[b] x_3			0.50 (95% CrI 0.25 to 0.91)	11.4 (95% CrI –8.1 to 30.9)
BMI (kg/m^3), v_1			1.04 (95% CrI 1.00 to 1.09)	
Location: foot, v_2			0.34 (95% CrI 0.16 to 0.64)	30.1 (95% CrI 9.2 to 52.3)
Surgery type, v_3				13.1 (95% CrI –6.1 to 32.4)
SWHSI duration (days), v_4				2.3 (95% CrI 0.6 to 4.0)
Diabetic feet, v_5				42.8 (95% CrI 9.1 to 76.3)
NPWT, t	0.35 (95% CrI 0.20 to 0.57)	69.0 (95% CrI 48.2 to 89.1)	0.59 (95% CrI 0.28 to 1.12)	46.0 (95% CrI 19.6 to 72.5)
Constant, γ_1	6.56 (95% CrI 4.70 to 9.37)	82.0 (95% CrI 71.9 to 92.1)	6.98 (95% CrI 1.62 to 29.55)	36.9 (95% CrI 12.4 to 61.3)
Observations	393		354	

ID, identification; TTH, time to healing.
a Treatment location: inpatient (vs. outpatient).
b Tissue involvement: skin and subcutaneous tissue loss (vs. skin loss).
Note
Extended modelling approach results. Results from OLS models reported as mean difference in time to healing (in days). Results from logit models reported as ORs for healing.

The table includes minor additions and formatting changes to the original table.

Effectiveness results when adjusting for observables and unobservables

Overall, conclusions were similar using modelling strategies A and B, and treatment effect estimates adjusted for unobservables were broadly consistent with the results we observed when adjusting only for observables. Participants treated with NPWT were predicted to take longer to heal, albeit with a high level of uncertainty in the estimates [e.g. modelling strategy B, second-stage regression: 46 days longer (95% CrI 19.6 to 72.5 days longer)].

Cost-effectiveness of negative-pressure wound therapy

The results for healing, utilities and costs were combined to generate cost-effectiveness estimates for NPWT. Evidence relating to the additional days until healing after censoring for unhealed patients within the follow-up period was elicited from three experts and used in an extended analysis, the results of which are shown in *Table 14*. Irrespective of the adjustment made (on either observables or unobservables), the results indicated that treatment with NPWT was expected to be less effective and a more costly use of NHS resources than treatment with standard dressings alone: associated incremental QALYs of –0.012 (SE 0.005) (model A, observables), –0.008 (SE 0.011) (model A, unobservables), –0.007 (SE 0.004) (model B, observables) and –0.027 (SE 0.017) (model B, unobservables). There was little decision uncertainty in this result. When losses arising from the displaced health-care resources were added to the direct health effects (by valuing 1 QALY at £20,000), the health consequences of using NPWT were evaluated at –0.111 (model A, observables), –0.095 (model A, unobservables), –0.087 (model B, observables) and –0.183 (model B, unobservables).

Data and analyses of the cohort study indicate, with little uncertainty, that treatment with NPWT is less effective and more costly than treatment with standard dressings alone.

Value of a future randomised controlled trial

Although there is uncertainty in the incremental cost and QALY estimates, our analyses consistently indicate that there is little uncertainty in the optimal decision (i.e. the probability of treatment with NPWT being considered cost-effective to the UK NHS was close to zero). This means that conducting a future study in order to reduce the associated uncertainty (in the costs and QALYs) would not change the optimal decision and therefore there is no value in conducting such a study for this purpose. For this reason, the value of information analyses originally planned were redundant: the value of information is zero.

TABLE 14 Elicited evidence on additional time to healing from follow-up for censored patients

	Elicited		Fitted values for parameters of a gamma distribution				
	50th percentile (days)	90th percentile (days)	Shape, first and third quartiles	Scale, first and third quartiles	Mean (days), first and third quartiles	50th percentile (days), first and third quartiles	90th percentile, (days), first and third quartiles
Expert 1	1044	3234	1.12	1290	1445	1031	3322
Expert 2	496	679	15.3	33.1	506	495	683
Expert 3	180	3650	0.23	5222	1201	176	3176
Pooled using formal synthesis (95% CrI)			1.79 (0.03 to 54.5)	615 (241 to 1615)	1038 (29 to 39,065)	559 (0 to 28,011)	1820 (15 to 37,161)

Negative-pressure wound therapy is currently widely used in clinical practice. The results from the observational study may contradict beliefs with regards the effectiveness of NPWT, but, given that our findings have been derived from observational research, there is the potential for unresolved confounding to affect the results and reduce confidence in them and the associated conclusions drawn. This lack of confidence may lead decision-makers and funders to justify calls for definitive evidence from a RCT. The value of conducting such research, to obtain definitive evidence, will be looked at next.

The value of a RCT to promote implementation was calculated here using a 'value of implementation' approach.[38] This assumes that the results of our research provide the best available evidence on the clinical effectiveness and cost-effectiveness of NPWT, and that the adjustments made for confounding returned unbiased estimates. Data from the cross-sectional survey conducted within this research programme (workstream 1) indicated a prevalence of treated SWHSIs of 4.1 per 10,000 population (95% CI 3.5 to 4.7 per 10,000 population). Using the observed median duration of wounds (28 days), the daily incidence of SWHSIs was estimated to be approximately 0.0146. Therefore, across England and Wales (population of 57,408,654, as per the Office for National Statistics' 2014 mid-year estimates),[39] we would expect 305,000 patients with a SWHSI per year. Cohort study data indicated that 29.3% (115/393) of incident patients received NPWT and so we would expect > 89,000 patients with a SWHSI receiving NPWT per year. Using this information, the value of implementation approach indicated, should definitive RCT evidence correspond to the findings of the modelling of observational data, that successful cessation of NPWT in clinical practice would have direct health benefits that would sum to between 719 and 2427 QALYs. When displaced health-care benefits were included (by valuing 1 QALY at £20,000), the value of a definitive trial increased to approximately 8500–16,400 QALYs per year (conditional on the findings of a future trial and their successful implementation).

Conclusions

This work compared the clinical effectiveness and cost-effectiveness of NPWT in healing of SWHSIs, relative to dressings, using advanced methods of adjustment for the potential selection effects expected with observational data. The published paper from this stream of work (see *Appendix 5*) covers methodological aspects of this research; thus, here we aimed to discuss the clinical implications of our results.

Results show that NPWT users in the cohort took longer to heal and this result (which did not reach conventional levels of statistical significance) sustains even after adjustment for differences in potential prognostic factors between the groups. A number of limitations of the data and methods of analyses were also tested (e.g. alternative assumptions on censoring), with none leading to different conclusions. Across all analyses, treatment with NPWT for SWHSIs was not clinically effective or cost-effective and there was little uncertainty over this result. Our treatment effect findings are derived from modelling of observational data and our results (and our interpretation of these) assume that inferences obtained (after adjustment) are unbiased. However, even extensive adjustment of observational data does not negate the potential for unresolved confounding to affect the results and the risk of this can reduce confidence in conclusions drawn from observational data. Definitive evidence from a RCT may be the only way to overcome this lack of confidence.

It is also important to emphasise that we evaluated the causal effects of NPWT on the healing of SWHSIs. Wound infection at baseline was explored in our analyses and was not found to be associated with either treatment allocation or wound healing. However, NPWT may have further direct effects on HRQoL (independent of healing), for example in prevention of wound infection or assisting with wound management. These other effects are likely to be less significant in magnitude and in duration, as NPWT is typically used for only a short duration of time. If future research further explores the effectiveness of NPWT on infection (prevention or treatment), it is important that this research is designed to also explore effects on healing.

There are other important clinical conclusions to be drawn from our analyses. First, patients treated with NPWT in the cohort study differ from those who were not; that is, there was significant selection into treatment with NPWT in the cohort study. Trying to understand how clinicians allocate treatment with

NPWT was, however, difficult. Wound area, level of tissue involvement and being an inpatient (rather than outpatient) seemed to have contributed to decisions on whether or not to use NPWT, but do not fully explain these treatment decisions.

Second, in adjusting for selection effects, it was important to consider relevant predictors of healing. However, given the absence of epidemiological research, there was no a priori evidence on what could predict healing in this patient group. The associations found within our work used a predefined process of model selection and indicated that being an inpatient (rather than outpatient) and having a history of a SWHSI may be relevant prognostic characteristics for healing. However, the sample of patients included in the cohort was very heterogeneous. For example, there was a range of anatomical sites for SWHSIs, with the most frequent being the abdomen (33.6%) and foot and leg wounds (30%); there was an approximately equal share of dehisced versus planned open wounds (60% vs. 40%, respectively) and an approximately equal share of wounds with superficial versus deeper tissue involvement (59% with skin involvement only vs. 41% with skin and subcutaneous tissue involvement). If determinants of healing differed across different subpopulations, then a more homogeneous sample would have meant that it was easier to identify these.

Third, our analyses of the cohort data suggest the existence of a subpopulation of 'hard-to-heal' patients: time to healing for those who healed (mean 99 days) was very different from the mean follow-up for those who did not heal (mean 416 days). Those who did not heal within follow-up also differed from those who did and our explorations indicate that BMI and foot wound location are associated with a lower probability of healing. Further research could continue to explore characteristics of 'hard-to-heal' patients who present with the biggest burden of disease and thus have a larger capacity to benefit from treatments.

Finally, our research also suggests that individuals with a history of SWHSIs treated with NPWT are expected to take even longer to heal than those who did not have a history of SWHSIs. Although we are not clear of the clinical plausibility of such an effect, future research on NPWT could explore the evidence for such treatment effect interaction.

The findings from this workstream have informed the final phase of work in our research programme: a pilot, feasibility RCT assessing NPWT compared with standard dressings.

Workstream 3: qualitative interviews to explore patient and clinician perspectives regarding SWHSIs

The absence of available literature meant that there was limited knowledge about patient experience of SWHSIs or their impact when we began this programme. There was also a lack of research about patient and professional opinions regarding wound management, treatment options and relevant outcomes in relation to measuring treatment effectiveness. These key elements were explored through qualitative interviews with both patients and health professionals (surgeons and nurses). A paper detailing findings from the patient interviews has been published (see *Appendix 7*).[40] A paper detailing findings from the clinician interviews has been published (see *Appendix 8*).

Objectives

To explore, using qualitative interviews:

- patients' perspectives and experiences of living with a SWHSI and to elicit their views regarding management and desirable outcomes
- NHS professionals' views and experiences concerning treatment choices for SWHSIs.

Methods

The purpose of this qualitative research was to explore the daily, lived experiences of patients with a SWHSI and to understand health-care professionals' perspectives of managing these wounds. The topic guide developed for use with patients (see *Appendix 9*) comprised a few key questions to encourage in-depth exploration of how a SWHSI might affect every aspect of patients' lives. Patient advisors were asked to comment on the content and clarity of the patient topic guide prior to its use. During interview, individual patients were encouraged to identify and speak freely about any issue related to their SWHSI that affected them. The clinicians' topic guide (see *Appendix 10*) similarly encouraged clinicians to fully express their own perspectives, with the topic guide acting as a flexible tool to guide the discussion.

Patients and clinicians were recruited from both acute and community nursing services in two settings in the north of England: one was a large city with an economically and ethnically diverse population and high levels of deprivation and the other was a smaller city, also with high levels of deprivation and ethnic diversity.

Patients were eligible to participate if they had a surgical wound considered to be healing by secondary intention by the referring clinician, were aged $\geq$ 18 years and able to give informed consent. Patients were purposively sampled to include those who had SWHSIs that were slow to heal or non-healing, and to ensure representation across sex, age, duration of wound and surgical discipline (e.g. general, vascular, orthopaedic surgery). We aimed for ethnic diversity within the patient sample and for a range of patients from both acute and community treatment settings. Potentially eligible patients were identified and approached regarding study participation by a member of their usual health-care team. Clinicians were purposively sampled from among those with responsibility for caring for patients with SWHSIs, and a range of clinicians from community and acute settings were selected for participation.

The backgrounds of the two researchers involved in the study differed: one was a registered nurse with extensive experience of applied health services research, whereas the other had a background in social sciences research. The two researchers, who were co-located in the same office, held regular, informal

meetings during data collection to discuss any differences and ensure consistency of approach. No significant differences were identified in the data collected by the two individuals.

Semistructured interviews were conducted in patients' homes and at the clinicians' place of work. Interviews with patients lasted approximately 1 hour (interviews with surgeons ranged from 30 to 45 minutes and those with nurses ranged from 60 to 75 minutes). All interviews were audio-recorded and fully transcribed before being analysed for thematic content using the 'framework' approach (see *Appendix 11*).[41] Interviews continued until no new information was forthcoming.[42] After familiarisation with the data set and initial identification of themes, a coding framework was developed to allow for linkage between participants and their responses and comparison across the full data set. This coding framework was modified during the initial phases of data analysis to accommodate new responses from patients. Interpretation relied on the abilities of the analysts to determine meaning, salience and connection.[43] The input of patient advisors was sought during the analytic process and advisors were asked to contribute to reflections on the meaning and interpretation of the data arising from the interviews.

The study received research ethics approval from Yorkshire and the Humber – Leeds Central Research Ethics Committee (reference 11/YH/0313) and written, informed consent was obtained from all patients prior to participation in the interviews.

Results

Patient interviews

Twenty patients with SWHSIs participated in the qualitative interviews. The mean age of patients was 53 (range 19–76) years, with an almost equal split in sex (11 women and nine men); 19 patients were of white British ethnicity and one was of South Asian ethnicity. The surgical procedure preceding the SWHSI was abdominal surgery (11 patients), vascular surgery (five patients), orthopaedic surgery (two patients) and excision of pilonidal sinus and drainage of abscess (one patient each). The median duration of SWHSIs was 5.5 (range 1.5–60) months. Further details of the sample are presented in *Table 15*.

Six emerging themes were identified through the interviews: (1) initial reactions, (2) wound symptoms, (3) expectations of wound healing, (4) psychosocial impact, (5) service provision and (6) SWHSI treatment.

Initial reaction

Unexpected SWHSIs (i.e. following emergency surgery or a dehisced wound) resulted in feelings of alarm, shock, disbelief and disgust among patients. This was most significant in patients whose SWHSIs resulted in the exposure of their internal organs. These patients frequently reported that they had presumed that their wound would be stitched closed and they were shocked and confused when this had not happened. When wounds were extensive, patients indicated their fear that the wound 'would never heal', to the extent that they could often recall the specific dimensions of their wound at various points in time.

In contrast, elective SWHSIs (e.g. from an elective partial foot amputation in a diabetic patient) resulted in less shock and alarm in relation to the initial appearance and immediate impact of the wound. These patients frequently viewed surgical intervention as a means of respite from pain, as well as offering a reduced risk of limb loss. Given the planned nature of these wounds, preoperative discussion with clinicians regarding their postoperative surgical wound was much more common in this group of patients, which is likely to have helped to manage patient expectations.

Wound-related symptoms

Wound-related symptoms were reported as having a negative impact on daily life, physical and psychosocial functioning, and sense of well-being. Frequently reported symptoms included pain and reduced mobility; leakage; smell; difficulties with personal hygiene; reduced appetite; disrupted sleep; lack of energy and low mood; skin problems; and side effects from wound-related medication (such as analgesia).

TABLE 15 Study participants' (patients') sociodemographic details

ID	Sex	Age (years)	Employment status	Wound type	Wound duration (months)	Comorbidities (self-reported)
P1	Female	58	Unemployed; registered disabled	Dehisced abdominal wound; had had multiple operations	6	Diabetes mellitus; Crohn's disease
P2	Female	73	Retired	Dehisced wound on upper thigh after bypass graft	2	Diabetes mellitus
P3	Female	19	Unemployed since surgery	Dehisced wound on leg after open fracture	3	
P4	Female	65	Retired	Open surgical wound following amputation of toes	12	Diabetes mellitus
P5	Male	30	Employed	Dehisced wound in groin after infection	3	
P6	Male	32	Unemployed since surgery	Open surgical wound after abdominal surgery	2	
P7	Female	44	Employed	Open surgical wound after drainage of abscess in axilla	1.5	
P8	Male	52	Unemployed since surgery	Dehisced abdominal wound	24	
P9	Male	76	Retired	Non-healing abdominal wound following surgery for bowel cancer	60	
P10	Male	64	Early retirement due to work injury	Open surgical wound following amputation of toes; had undergone skin graft	5	
P11	Male	45	Unemployed since surgery	Dehisced wound due to infection after surgery for Crohn's disease	3	Crohn's disease; necrotising fasciitis; pyoderma
P12	Female	72	Retired	Dehisced abdominal wound	8	
P13	Female	54	Employed	Dehisced abdominal wound	1.5	
P14	Female	47	Unemployed since surgery	Dehisced abdominal wound	4	
P15	Female	46	Unemployed since surgery	Dehisced abdominal wound	9	Crohn's disease
P16	Female	76	Retired	Dehisced abdominal wound	10	
P17	Male	44	Unemployed	Open surgical wound following partial amputation of foot	24	Diabetes mellitus
P18	Male	65	Employed	Non-healing abdominal wound	2	
P19	Male	25	Employed	Slow to heal wound following treatment for pilonidal sinus	30	
P20	Female	71	Retired	Dehisced wound following spinal surgery	9	Rheumatoid arthritis

ID, identification.

The limited physical mobility (and especially being unable to drive) was particularly frustrating for patients and disruptive of normal activities. In addition, patients felt unable to socialise, as they believed that the wound smell and exudate might be offensive to others.

Healing expectations

The majority of patients with open abdominal wounds feared that their wound would never heal. Patients reported frequently feeling disappointed, dismayed and frustrated with the slow healing process of their SWHSI and lack of, or delayed, healing also resulted in increased anxiety about future surgery for some patients. These feelings were intensified when patients had experienced healing delays due to infection. Many of those who had experienced previous SWHSIs expected healing to be a slow process, whereas patients without a previous SWHSI often had unrealistic expectations of time to healing. Patients' expectations often conflicted with information provided by health-care professionals. Comments from health-care professionals regarding the wound and its prospects of healing often had profound implications for patients. Positive remarks were a morale boost, whereas negative remarks frequently adversely affected the patients' general outlook. When conflicting information was provided, this was identified as a cause of confusion and consternation.

Patients were ever-hopeful that a new or untried treatment might accelerate or achieve healing of the wound, and they often looked to tissue viability nurses, regarded as experts in their field, to provide a solution for their unhealed wound. There was a willingness among patients to undergo almost any procedure or treatment if it might promise accelerated healing, even if it was unpleasant.

Psychosocial impact

Surgical wounds healing by secondary intention were frequently found to have a devastating effect on the lives of patients and their families, particularly following emergency surgery or if associated with a large cavity. Patients reported feeling uncertain and anxious following their surgery, particularly in relation to wound healing, physical health, financial concerns and relationships with others.

Patients felt that they had become isolated, withdrawn from society and confined to their homes while their SWHSI was healing. Patients receiving NPWT as a SWHSI treatment reported feeling unable to leave the house due to the pump and tubes associated with the device and concerns about their self-image in public. Feelings of isolation were particularly acute in patients who were incapable of driving after surgery, especially if they were the only car driver in the family. Disruption of established roles and responsibilities within the family unit was common and patients often reported feeling burdensome and dependent. Anxiety was also extremely common and often multifaceted.

The financial impact associated with SWHSIs was severe for some patients and their families, causing high levels of stress. The uncertainties and restrictions associated with SWHSIs appeared particularly difficult for younger male participants who were often the main earner in the family. Family members were also affected as they tried to balance maintaining the household income and acting as a carer for the patient. Out-of-pocket expenses in relation to transport to clinic appointments were troublesome for several patients, particularly for those who were unwilling to use public transport to attend appointments due to concerns about wound odour and who preferred to pay for private taxis.

Most participants described support from partners, family members, friends and neighbours as crucial, whether that support was practical (e.g. with transport and shopping) or emotional (helping them to adapt and adjust to living with their wound). Some older patients were, however, reluctant to ask their offspring for assistance, preferring to try to manage independently if they could.

Living with a SWHSI had a profound impact on patients' mental well-being. Almost one-quarter of patients indicated that they had become depressed as a result of factors associated with their SWHSI. This was sometimes associated with acceptance of the diagnosis of the condition (e.g. Crohn's disease) that had resulted in their SWHSI. Other patients did not report feeling depressed, but did acknowledge periods of low mood as a result of their experience of living with a SWHSI.

Service provision

Patients were managed in a variety of settings, including acute hospital and community settings, where district, community or general practice nurses predominantly gave patient care. Reported impressions of care were wide ranging, from 'brilliant' to 'rubbish'.

Prolonged or multiple hospital admissions were common. Duration of hospital admission ranged from an overnight stay (abscess drainage) to 9 months (spinal surgery). Patients indicated that timely provision of information, and regular contact with surgeons (especially those who had performed the operation) and nurses during this time, was important and valued. Comments from surgeons regarding general progress and wound healing were highly important to patients. Positive comments generated reassurance, whereas brusque and hurried interactions led to patients feeling unheard, dismissed and angry.

Several patients reported that their wound dressings had not been changed as frequently as they thought necessary while in hospital and a majority reported that their care on the wards was less than satisfactory. Significantly, many patients reported feeling dissatisfied and unsupported at the point of hospital discharge, due to a lack of available information relating to follow-up care and risks, symptoms and management of infection. Following discharge from hospital, however, only a minority of patients felt unsupported.

All patients expressed views about the district, community and general practice nursing service, with the majority having received home visits by district, community or general practice nurses during their healing pathway. It was widely perceived that the district, community or general practice nurses had limited time to devote to visits, leaving patients feeling that visits were rushed, although there was acknowledgement that the nurses had tried to attend to all needs during the visit. Patients also indicated that the unpredictability of visit timings caused substantial frustration and inconvenience, and for three patients, care via a general practice or treatment centre nurse was preferred, due to convenience and ongoing continuity of care.

With specific regard to district, community or general practice nursing services, patients were particularly troubled by a lack of continuity of care, with some patients claiming that they would 'never see the same nurse twice in a row'. Patients became anxious when they received conflicting information regarding the condition and likely healing and management of their wound, particularly if the information given was at variance to that provided by their surgeon.

SWHSI treatment

The main wound treatments experienced by study participants were NPWT, debridement, dressings and skin grafting.

Eleven patients had experience of NPWT, which they generally viewed as an effective treatment. The majority of patients receiving NPWT had undergone bowel or abdominal surgeries; however, patients also experienced NPWT for foot and orthopaedic surgical wounds. Perceived advantages of NPWT included reduced dressing change frequency, compared with 'traditional' dressings, and a reduced risk of wound infection. Patients did, however, note that NPWT dressing changes were painful when sponge or foam, rather than gauze, were used. Patients with prior experience of NPWT reported that some district, community and general practice nurses lacked appropriate knowledge, experience and expertise in NPWT and, in some instances, required guidance from the patient in its application. Perceptions concerning lack of nursing expertise in the use of this therapy were linked to feelings of anxiety by some patients. Several patients reported that they were disinclined to go out of the home with NPWT in situ, due to it being cumbersome or due to embarrassment about the equipment, and when they did leave the house they felt a need to somehow disguise the device. Patients also reported delay in discharge from hospital due to difficulty associated with obtaining NPWT within the community setting and they expressed the view that this treatment was more easily administered within a hospital environment as opposed to community settings.

Six patients had undergone wound debridement and described this as an extremely painful procedure. The rationale for and potential effectiveness of debridement were often poorly communicated to patients.

Three patients underwent skin grafting as a method of promoting healing, with a further two participants having discussed the possibility of a skin graft for their SWHSI. Views regarding the desirability of skin grafting were mixed, due to fears of infection and/or graft failure.

Patients reported that they would have liked more information from clinicians about the rationale for using different treatment methods and approaches, including different dressings, and they described nurses as rarely 'singing from the same hymn sheet' when selecting dressings.

Clinician interviews

Five surgeons and seven nurses participated in the qualitative interviews: two general surgeons, two vascular surgeons, one plastic surgeon, three tissue viability nurses, one general surgery nurse, two district nurses and one community staff nurse. Further details of the sample are presented in *Tables 16* and *17*.

Six themes were identified in the interview data: (1) factors influencing SWHSI development, (2) devolving care to nurses, (3) multifaceted assessment, (4) NPWT for specific types of SWHSI, (5) presumed cost-effectiveness and (6) dressing selection by nurses.

TABLE 16 Study participants' (nurses') demographic details

ID	Sex	Age (years)	Qualifications	Role	Specialist training
1	Female	49	RN; BA (Hons) nursing practice; postgraduate certificate nursing studies; community/specialist practitioner	Tissue viability nurse specialist (specialist assessment; care planning; evaluation; prescribing; liaison with surgeons; supporting nurses)	Diploma in wound care and ulcer management
2	Female	46	RN; BSc (Hons) health and social care; diploma in nursing	Clinical nurse specialist (education; training; support for colleagues)	No specialist training. Experience of working within the tissue viability team
3	Female	42	RN; BSc (Hons); district nursing qualification	Tissue viability nurse specialist (assessment of complex surgical wounds; instigation and monitoring of NPWT)	No specialist training. Experience of reading relevant research; 'peer shadowing'
4	Female	44	RN	Senior nurse working on acute general surgery ward caring for patients with abscess/fistulas/wound dehiscence	Training from employees of commercial company in use of NPWT
5	Female	39	RN; district nursing qualification	Senior treatment room nurse (seven treatment rooms city wide)	Study days; experience; leg ulcer management course
6	Female	38	RN; district nurse	District nurse; link nurse tissue viability	Link nurse tissue viability and related study sessions
7	Female	52	RN	Community staff nurse; general wound care	Wound management course

BA, Bachelor of Arts; BSc, Bachelor of Science; Hons, honours; ID, identification; RN, registered nurse.

TABLE 17 Study participants' (surgeons') demographic details

Surgeon	Specialty	Study site
1	General surgeon	1
2	Vascular surgeon	1
3	General surgeon	2
4	Plastic surgeon	1
5	Vascular surgeon	2

Factors influencing SWHSI development

Surgeons and nurses identified that the main types of SWHSIs encountered were extensive cavity wounds (e.g. from abdominal or pilonidal sinus surgery), open wounds on the feet of diabetic patients and wounds associated with lymph node removal (e.g. in the axilla and groin). Abdominal surgery wounds were regarded as being most likely to heal slowly or not to heal and were thought to be most likely to dehisce.

Both surgeons and nurses broadly agreed that there were a number of factors that predicted slow or no healing. These included surgical factors (e.g. emergency surgery, reason for surgery, type of procedure or presence of a foreign body), patient comorbidities or factors (e.g. obesity, diabetes mellitus, cancer, arterial and/or vascular disease, impaired immune system or Crohn's disease, nutritional status, smoking status and age), infection, medication, restricted mobility and lack of treatment compliance. It was, however, noted that in many instances it was difficult to identify any specific reason for impaired wound healing.

Wound healing was sometimes viewed as completely unpredictable: a wound was said to sometimes progress well, stop healing for a period, with no obvious explanation, and then recommence healing. It was suggested that a pause in healing might occur following removal of NPWT. Overgranulation was also mentioned as a factor that could delay the final stages of wound healing.

Devolving care to nurses versus 'looking after our own'

Surgeon involvement with the wound management of individual patients was related to wound-related factors, as well as the patient's general condition and the nature of the surgery. The two general surgeons included in the study indicated that usually their patients' wound care was passed on to nurses following discharge. However, the two vascular and one plastic surgeon interviewed said that they were more likely to continue to have personal involvement in wound care for 'their' patients through follow-up in specialist clinics, which they described as 'looking after our own'.

Surgeons and/or tissue viability nurse specialists generally initiated the decisions to use NPWT. Ward, district and community nurses indicated that there was limited knowledge and expertise about use of NPWT among general nurses working in both acute and community nursing settings. Tissue viability nurses reported that they were often regarded as the first port of call for expert advice in relation to complex non-healing wounds and use of NPWT.

Assessment is multifaceted and complex

Factors cited by the surgeons as associated with wound healing were the size of the wound; presence of wound infection, slough and/or granulation tissue; whether or not the wound appears to have healed superficially, but remains unhealed at a deeper level; level of exudate; the condition of the wound edges; the patients' general condition, including nutritional state and ability to mobilise; signs of overgranulation;

whether the wound seems 'static' and/or appears to be colonised; and blood supply at the wound site. Nurses described similar factors as affecting wound healing. They also emphasised psychosocial and practical issues that might have an impact on patients' quality of life, such as level of family support and patients' potential for self-care of the wound. Tissue viability nurses, for example, commented that they would adopt a holistic approach to assessment, by gathering background information about the history of the wound, as well as other relevant details about the patient's physical, social and psychological status.

Only one nurse mentioned using a wound-specific assessment tool – the TIME (Tissue, Infection, Moisture and wound Edge) tool – during the initial wound assessment.[45]

Perceived advantages and disadvantages of negative-pressure wound therapy

Negative-pressure wound therapy was favoured for a variety of reasons. Surgeons reported that the use of NPWT was increasing and that complex cavity wounds (e.g. extensive abdominal wounds) were ideally suited to benefit from NPWT. It was perceived that NPWT controlled exudate, contained and limited contamination (reducing infection risk), supported resolution of infection, promoted growth of granulation tissue, hastened wound healing and was liked by patients because it was convenient, promoted mobility, enhanced quality of life, shortened hospital stay and reduced the number of required dressing changes. Clinicians generally perceived NPWT as a cost-effective and transformative treatment, particularly for patients with hard-to-heal wounds.

One tissue viability nurse did, however, express strong reservations about the perceived 'espoused universal benefit' of NPWT, noting that it was not necessarily 'the answer to everything' and inappropriate for some patient groups. This view was supported by some surgeons and nurses who indicated that NPWT was an inappropriate treatment for some types of wound, particularly in patients following abdominal surgery who might be at risk of developing fistulae, as well as some patients who were unable to cope with the device. The same tissue viability nurse felt that NPWT was sometimes 'oversold' to patients, raising expectations unrealistically. This nurse also commented that longer-term healing of SWHSIs could be impeded by the use of NPWT due to the use of foam, rather than gauze dressings, which, they suggested, could result in the formation of less 'robust' granulation tissue. Further disadvantages, perceived by surgeons, included its lack of suitability for some patients who might be unable to cope with the equipment due to frailty or impairment, limited availability in the community, high cost, and the need for staff (predominantly nurse) training in its application. Disadvantages from a patient perspective mentioned by nurses were anxiety and disruption to sleep, and restrictions, even with 'portable' devices, when mobility increased in the time following surgery.

Presumed cost-effectiveness

Three surgeons noted the lack of research evidence relating to NPWT, but felt that their own and their colleagues' experiences supported its use. These surgeons perceived NPWT use as increasingly widespread and safe. They viewed NPWT as a cost-effective treatment option on the basis that patients with complex wounds could be discharged from hospital sooner, required less input from district, community or general practice nurses (in terms of dressing changes), once back in the community, and could return to work more quickly.

One surgeon was of the opinion that there was currently sufficient evidence to support the use of NPWT and referred to various studies (small scale, mainly case series) apparently demonstrating its effectiveness. This surgeon, the strongest advocate of NPWT among those interviewed, asserted that the advent of NPWT had 'changed practice considerably'.

Dressing selection usually devolved to nurses by surgeons in the study

Surgeons' knowledge concerning dressings was, by their own admission, limited, resulting in reliance on nurses to make appropriate dressing choices. The nurses described how wound, patient and general factors influenced wound management decisions. Nurses felt that they had adequate information to support wound management decisions for most routine SWHSIs, with choices determined by local guidance (formularies

and protocols), that purported to be evidence based, alongside an appreciation of the need for cost-effective treatment decisions, patient preference and likely concordance, and inclusive of the views of colleagues.

Nurses also commented that if they were uncertain about how to manage a complex, non-healing open surgical wound, they would contact tissue viability nurse specialists for advice and guidance. The tissue viability nurses noted that in these situations, they were able to draw on each other's knowledge and experience in dealing with difficult-to-heal wounds, through their involvement in close-knit clinical teams and other wound-focused clinical networks.

Similarities and differences between responses from surgeons and nurses

Surgeons and nurses were in broad agreement about the types of wounds likely to be slow to heal/non-healing and their symptom burden. During interview, tissue viability nurses focused, more than surgeons, on describing the possible psychosocial and financial consequences for patients of experiencing a SWHSI. Tissue viability nurses explained that they had more time than surgeons to explore the range of impacts of a SWHSI on the lives of individual patients and their family members; in their interviews, surgeons tended to focus mainly, though not exclusively, on clinical aspects of patients' surgical wounds and healing.

Tissue viability nurses reported their own first-hand experiences of the challenges of managing patients' hopes and expectations for healing. Nurses suggested that sometimes patients appeared ill-informed about likely healing projections after discharge from hospital and they said that sometimes there appeared to be a 'mismatch' between surgeons' and patients' expectations for healing (with patients holding unrealistic expectations).

Six of the seven nurses interviewed were in agreement with the study surgeons' views that NPWT is effective in the management of SWHSIs, particularly in the management of wound exudates, due to the good dressing seal that can be obtained and the potential for reduced likelihood of infection, resulting in perceived speedier healing of the wound. Reservations expressed by the seventh nurse related to the use of gauze rather than foam in the application of NPWT (she thought use of gauze caused less pain to patients) and the possibility of patients with an abdominal SWHSI developing an intestinal fistula connected to use of NPWT, a concern also noted by the general surgeons. Surgeons and nurses both commented that NPWT was not a suitable treatment for the very frail (who could find the equipment difficult to manage) and/or for patients with cognitive impairment.

During interview, surgeons were more likely than nurses to talk about perceived cost-effectiveness of NPWT in relation to length of hospital stay, reporting that use of NPWT allowed patients to be discharged from hospital sooner than with use of conventional dressings; surgeons also pointed to a reduced need for dressing changes by community-based nurses, which they perceived as beneficial in terms of reducing these nurses' workload and accrual of savings to the NHS. Variability in community and district nurses' expertise in application of NPWT, and the need for more widespread training in its application, were reported more frequently by nurses than surgeons, who appeared to be less aware of these issues.

Conclusions

To the best of our knowledge, this is the first study investigating patients' and clinicians' views about the management and treatment of SWHSIs, and patients' experiences of living with this condition. Findings from our study therefore lay the groundwork for further research in this important aspect of health care about which so little is known. For example, understanding more about what matters to patients helps to ensure that appropriate outcomes are captured in future trials.

Patients' initial reactions to their SWHSIs were of shock and disbelief, and the visual reminder following surgery of a 'violated' body intensified these feelings, particularly for patients with large abdominal cavity wounds. Having a SWHSI had a substantial impact on daily living and this impact was particularly important

for those patients with children or in employment, who constitute a younger demographic than seen in previous wound research associated with other wound types. As healing progressed, patients were concerned with both their own reaction to the wound and the reactions of others. The long healing process for many patients, characterised by a reduced quality of life and a constant need for treatment and care, concurs with previous evidence in relation to patients with other wound types or ulceration.[46–53] It is worth emphasising, however, that SWHSI patients are typically much younger than patients with leg or pressure ulcers and frequently have major caring and employment responsibilities: Cullum *et al.*[27] reported a mean age of 79.65 (SD 11.32) years for venous leg ulcer patients, a difference of 25 years when compared with the mean age observed in workstream 1 [54.1 (SD 18.2) years]. Wound care experiences among patients varied greatly, but most patients were willing to try any treatment that promised healing. Understanding the 'lived experience' of patients is crucial for clinicians to provide effective management and improve patient quality of life. Establishing a therapeutic relationship and listening to patient concerns is vital to meeting patient's physical, emotional and psychosocial needs during the wound healing process. The provision of additional information for patients in relation to the rationale of treatment choices is also an important element for consideration with regards future treatment delivery.

Clinicians had varying levels of knowledge in relation to wound care treatment options. Nurses were frequently responsible for dressing choice decisions, made on the basis of wound condition, clinical experience and recommendations. A treatment frequently favoured by clinicians was NPWT. The lack of robust evidence for this treatment option was noted by several of the study clinicians; however, for many, individual experiences of its use were deemed to sufficiently demonstrate the effectiveness of this treatment.[14]

The use of purposive sampling enabled us to obtain a diverse range of views from both patients and clinicians. It is noted, however, that only a limited number of interviews were conducted with clinicians. Therefore, further research may be warranted to build on these findings.

Generalisability in qualitative research involves thinking through what kind of relationship the study findings have with other populations and settings, and unpacking exactly what inferences can be drawn from the data analysis.[41] Our study yielded 'rich' data that captured a wide-ranging, yet in-depth, picture of significant issues relating to patients' and clinicians' views and experiences of SWHSIs. The study findings, therefore, promote and enhance understanding of the impact of a SWHSI on patients' lives, as well as describing the challenges faced by clinicians in managing these wounds, thereby adding to the evidence base by 'sensitising' readers, including the research community, to new ways of thinking about SWHSIs. Our study findings may be considered transferable to the 'parent populations' of patients with SWHSIs and the clinicians looking after them; however, decisions concerning broader extrapolation of the findings must take into account any study-specific contextual factors that may limit applicability.[41]

Workstreams 1–3: overall conclusions

Workstreams 1–3 have substantially contributed to the evidence base and understanding of SWHSIs, providing data about patient characteristics, wound origins, durations and treatments, alongside patient and clinician views of living with and treating SWHSIs.

Workstream 1 has identified the prevalence of treated SWHSIs and has provided extensive data on populations of clinical relevance for inclusion in further research. The median time to healing we observed in this workstream highlights the extended period of time that patients might expect to cope with open surgical wounds. This workstream has also highlighted the distinctive management challenge posed by SWHSIs.

Workstream 2 has identified that NPWT is not a clinically effective or cost-effective treatment for SWHSIs. However, because this uses observational research, even with adjustment, there is still the potential for unresolved confounding to affect the results and so reduce confidence in them. This lack of confidence may justify calls for definitive evidence from a RCT, which would be more likely to effect a change in clinical practice should the evidence support one.

Workstream 3 has provided the first evidence of clinicians' and patients' views about the management and treatment of SWHSIs, and patients' experiences of living with this condition. The impact of SWHSI on patients was evident in all interviews and the understanding of patient experiences will assist in providing effective management of this condition. The work conducted in workstream 3 has provided the necessary groundwork for further research in this area.

Interviews with clinicians identified increasing use of NPWT and illustrated the strength of support for NPWT among clinical staff, despite the lack of research. Surgeons and nurses perceived NPWT as safe and cost-effective; however, we have been unable to identify existing, or derive new, evidence to support this. Given the increasing use and perceived effectiveness of this treatment, it is crucial that further, robust evidence is obtained to support, or refute, the estimates derived from observational data in workstream 2.

In addition to the need to establish clinical effectiveness and cost-effectiveness of treatments, such as NPWT, the findings from workstreams 1–3 suggested that further research is necessary to understand the epidemiology of SWHSIs, prognostic factors for healing and the clinical effectiveness and cost-effectiveness of other treatment options. The findings of workstreams 1–3 helped formalise key components of the design of workstream 4 for this research programme, which comprised a pilot, feasibility RCT, required to assess feasibility of RCT assessment of NPWT compared with usual care (no NPWT), prior to a larger study being conducted.

Workstream 4: a pilot, feasibility randomised controlled trial of negative-pressure wound therapy compared with usual care

The results of workstream 2 indicated that NPWT was, with little uncertainty, not clinically effective or cost-effective. This conclusion was, however, based solely on observational data, which, even with extensive adjustment, may be subject to unresolved confounding, leading to a lack of confidence in the finding. A RCT may therefore be justified, to enable definitive, high-level evidence regarding the clinical effectiveness and cost-effectiveness of NPWT to be generated.

Given the difficulties in recruitment identified in previous studies of NPWT,[54,55] we conducted a pilot, feasibility study to assess the feasibility of conducting a larger RCT of this treatment. The study was registered as ISRCTN12761776 and the protocol has been published (see *Appendix 12*).[56] The results of this study have been published (see *Appendix 13*)[57] and the findings relating to nurse participation in the pilot, feasibility study have been published (see *Appendix 14*).

Objectives

- To test the methods and feasibility of a full RCT of NPWT compared with usual care (no NPWT) for SWHSI.
- Specifically, to determine:
    - likely recruitment rate, including potential participants' willingness to be randomised and if this depends on wound location and other factors
    - clinicians' willingness and ability to recruit and randomise participants
    - testing of inclusion and exclusion criteria
    - fitness for purpose of data collection methods, including across and between care settings
    - ability of sites and clinicians to supply NPWT to participants in a timely fashion, irrespective of care settings, and assess any training requirements
    - ability of community staff to manage participants randomised to NPWT
    - suitability of method of outcome ascertainment
    - adequacy of duration of follow-up
    - rates of withdrawal from treatment, response rates to questionnaires, attrition from the trial and likely rates of missing data for outcomes
    - other methodological issues, including feasibility of blinded outcome assessment and whether or not trial documentation is acceptable to NHS nurses collecting data
    - feasibility of collecting data for and conducting of economic analyses in a larger trial (through exploratory analyses).

Methods

The pilot, feasibility RCT was conducted over a 10-month period (20 November 2015 to 30 September 2016: recruitment 20 November 2015 to 30 June 2016 and follow-up 20 February 2016 to 30 September 2016) in acute and community settings at three study sites in Leeds and Hull, Yorkshire, UK. Prior to study activity commencing, approval was obtained from Yorkshire and the Humber – Leeds East Research Ethics Committee (reference 15-YH-0307) and from the associated NHS trusts.

Patients were eligible for inclusion if they were aged ≥ 18 years and able to give full informed consent; were receiving care from Hull and East Yorkshire Hospitals NHS Trust (now Hull University Teaching Hospitals NHS Trust), Leeds Teaching Hospitals NHS Trust or Leeds Community Healthcare NHS Trust; had a SWHSI that could be reasonably treated with NPWT and wound dressings; had a SWHSI that was considered ready for NPWT (i.e. minimum 80% viable tissue or thin layer of slough requiring no further debridement); and were receiving adequate nutrition (as assessed by the senior nurse responsible for nursing care). Patients were ineligible for inclusion if they had limited life expectancy; active systemic infection; inadequate haemostasis or risk of bleeding; chronic wounds (e.g. pressure or foot ulcers) that were non-surgical in origin but had been surgically debrided; or had wound characteristics that precluded the use of NPWT (e.g. unclear undermining, necrotic or malignant tissue, eschar, exposed blood vessels, organs, anastomotic sites or nerves). Patients were also excluded if they had previously been or were currently receiving NPWT on their SWHSIs (including applications while in theatre for the surgery resulting in the SWHSI), if the wound was located where a vacuum seal could not be obtained, if they had participated in a research study in the previous 4 weeks, or if they were unwilling to have wound photographs taken.

Health-care professionals initially identified and screened patients for eligibility. Those meeting eligibility criteria were approached with further details of the study by a clinical or research nurse (subject to patient consent to approach), prior to study consent being obtained. As the main aim of this study was to determine the feasibility of conducting a larger trial, rather than to detect a treatment effect, a formal sample size calculation was not required. We aimed to randomise 50 patients over a 7-month recruitment period.

Baseline data were collected, including participant, surgery and wound information, wound dimensions (measurements and wound tracing) and a photograph, pain assessment [using a visual analogue scale (VAS) and the BPI][23] and quality-of-life data (SF-12 and EQ-5D-3L).[21,22] As this was a feasibility trial, a primary outcome was not defined; rather, a range of feasibility (e.g. recruitment rate, time to intervention delivery) and clinical (e.g. time to wound healing) outcomes were collected to inform a future definitive trial. Participants were followed up for a maximum of 3 months, unless they withdrew consent, died or became lost to follow-up. Clinical outcomes were collected prospectively on a weekly to fortnightly basis at follow-up assessment visits conducted by the research nurses, including wound dimensions and photographs, healing status [defined as 'complete epithelial cover in the absence of a scab (eschar)'], infection, hospital admission, return to operating theatre and treatment changes. Participants also completed self-report postal questionnaires (EQ-5D-3L,[22] BPI,[23] SF-12[21] and resource use and pain via a VAS) at 2 weeks, 1 month and 3 months post randomisation. When consent was provided, participants were also contacted by text message on a weekly basis and asked to provide a numeric rating of their wound pain in the previous week. When participants failed to respond, one further message was sent before text message data collection discontinued. When participants' wounds were reported to have healed during the study, text messaging data collection ceased at the point of wound healing.

Information concerning acceptability of study participation was collected from participants using Likert scales. Data relating to acceptability of documentation and training requirements for NPWT were initially collected from research nurses, using a Likert scale. Qualitative interviews were then completed with the research nurses to ascertain additional information regarding acceptability of the study processes, documentation and delivery.

Participants were allocated (1 : 1) to the intervention (NPWT) or usual care (no NPWT), using random permuted blocks, with stratification by wound area (< 28 cm^2, ≥ 28 cm^2). Allocations were concealed through a central randomisation service at the University of York.

The study intervention (NPWT) was delivered using NPWT devices that were in use in the acute and community services in Hull and Leeds, which included V.A.C® (KCI Medical Asia Pte Ltd, Singapore), Renasys® (Smith & Nephew, London, UK) and PICO® (Smith & Nephew, London, UK) devices. The NPWT

treatment delivery (e.g. device type, pressure cycles, dressing change and canister emptying frequency, application and removal of the device and treatment duration) was as per the standard practice at the time to ensure that the pragmatic nature of the pilot feasibility study was maximised. This was therefore decided by the clinical care team in conjunction with the participant and nurse, with the only stipulation for NPWT being that use must be clinically appropriate.

The control group participants received usual care (wound dressings, no NPWT), with dressing type and frequency of change left to the discretion of the clinical care team. As there is no evidence to suggest that any one dressing is more clinically effective or cost-effective than another,[12] types of dressings were not stipulated for the trial.

Owing to the nature of the intervention, it was not possible to blind participants or health-care professionals to trial treatment; however, the feasibility of blinded outcome assessment of healing was assessed within the trial using study photographs. Initially, it was proposed that blinded review of healing would be completed for every participant photograph obtained, but this was reduced during the study to review of only the final photograph, due to time and resource constraints. Assessment of blinding to treatment allocation was conducted through review of photographs taken at the week 1 follow-up.

Data analysis was conducted using Stata, using the principles of intention to treat and two-sided statistical tests at the 5% significance level, when appropriate. Summary statistics for all variables were generated by trial arm and overall. Time to healing was defined as the number of days from randomisation to date of healing. Data were right censored at the date of the final assessment visit for participants not deemed to have healed. Time to healing was assessed using Kaplan–Meier curves, recognising that the study was not powered to detect a treatment effect. A Cox proportional hazards regression was used to investigate the impact of covariates (contamination level of surgery, wound infection, wound size, SWHSI history and location). Cost-effectiveness was explored using total mean resource use costs and mean QALYs per trial arm.

To understand improvements to trial processes, to support research nurses in conducting a larger RCT in this area, qualitative interviews with eight research nurses were completed. Interviews were audio-recorded and fully transcribed before being analysed for thematic content using a 'framework' approach.[41,58] Interpretation of the findings enabled linkage between individual nurses and their responses to account for variation between the type of study site (acute or community).

Prior to analysis, wound tracings were measured using Mouseyes software (R Taylor, Manchester, UK) to obtain perimeter and area estimates.[59] Both adjusted (length × width × Π)[60] and unadjusted (length × width) wound area (cm^2) measurements were calculated using ruler measurements obtained at clinical follow-up visits.

Results

Recruitment and participation

Recruitment to the study commenced on 20 November 2015 and continued until 30 June 2016. Delays in study set up, beyond the control of the research team, had an impact on recruitment rate in the early stages of the trial; there was only one recruiting site active until the two remaining sites were opened to recruitment in February and March 2016, respectively. The overall target recruitment rate for the study was seven participants per month and, following successful opening of all three recruitment sites, the study achieved this target in the final 4 months of recruitment (*Figure 4*). The flow of participants through the trial is shown in *Figure 5*.

Of 248 patients screened for eligibility, 75.0% (n = 186) were ineligible (including one participant found to be randomised in error). The most common reason for ineligibility was that the patient was receiving or had previously received NPWT on their current SWHSI (45/248, 18.1%), had NPWT applied while in

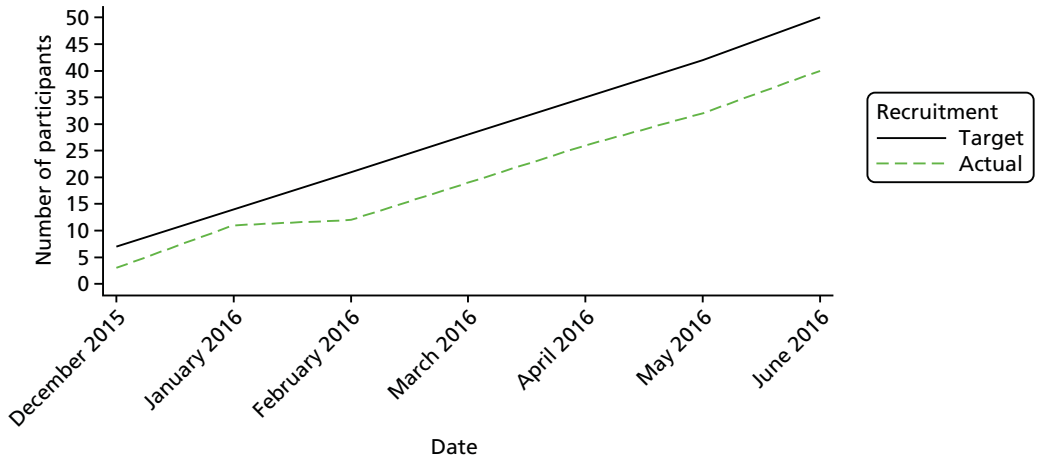

FIGURE 4 Cumulative target and actual participant recruitment.

theatre (*n* = 7/248, 2.8%) or both (24/248, 9.7%). Twenty-two participants were eligible but did not wish to consent to study participation; the most common reason for declination was not wishing to receive NPWT (5/22, 22.7%). Reasons for ineligibility were largely distributed across the observed wound locations, with the exception of 'receiving inadequate nutrition', which was only reported for five patients with abdominal wounds, and 'presence of exposed vessels or organs', which was reported for 11 abdominal and two leg wounds only.

Forty-one of the 248 screened patients (16.5%) were randomised to the pilot feasibility RCT, with 40 participants included in the study analyses (one patient was found to be ineligible following randomisation and so was withdrawn from study data collection and analysis). Of those correctly randomised, 19 out of 40 patients (47.5%) were allocated to NPWT and 21 out of 40 patients (52.5%) were allocated to usual care.

The mean age of participants was 57.8 (SD 14.4) years and just over half (*n* = 22, 55.0%) were male. Participants were, on average, overweight [mean BMI 29.1 (SD 5.7) kg/m^2], 60% (*n* = 24) were diabetic and 10 (25.0%) reported being a current smoker. The most common location of the wounds in recruited participants was the foot (*n* = 24, 60.0%), of which 19 out of 24 (79.2%) were due to toe or foot amputation, two (8.3%) were due to incision and drainage, two (8.3%) occurred following debridement (of amputation site, *n* = 1; of non-chronic ulcer, *n* = 1) and the cause of the remaining foot wound was unknown. Usual-care participants had their wound for a median of 12 days and over one-third (8/21, 38.1%) had a wound infection at baseline. NPWT participants had their wound for a median of 7 days and 26.3% (5/19) of participants had a wound infection at baseline. Baseline characteristics are summarised in *Table 18*.

Data collection methods

Twenty-six participants (65.0%) consented to data collection via text messaging; 20 participants (76.9%) subsequently provided at least one response (NPWT, *n* = 10; usual care, *n* = 10). Response rates to text messaging varied throughout the trial, ranging from 57.7% of those receiving a text in the week following randomisation to 100% of those receiving a text in week 12. Participants who responded to text messaging tended to be younger than those who did not respond (mean age 51 years vs. 60 years, respectively) and non-responders were predominantly male (85.7%). All non-responders had a foot wound, had at least one comorbidity and over half of those who did not respond to text messaging had been allocated to the control arm (57.1%). A range of wound locations were observed in those participants who did respond to text messages (e.g. foot wounds accounted for 36.8%) and 78.9% of participants had one or more comorbidities. Participants who responded to text messaging were almost evenly split between the intervention and control groups (52.6% vs. 47.4%, respectively).

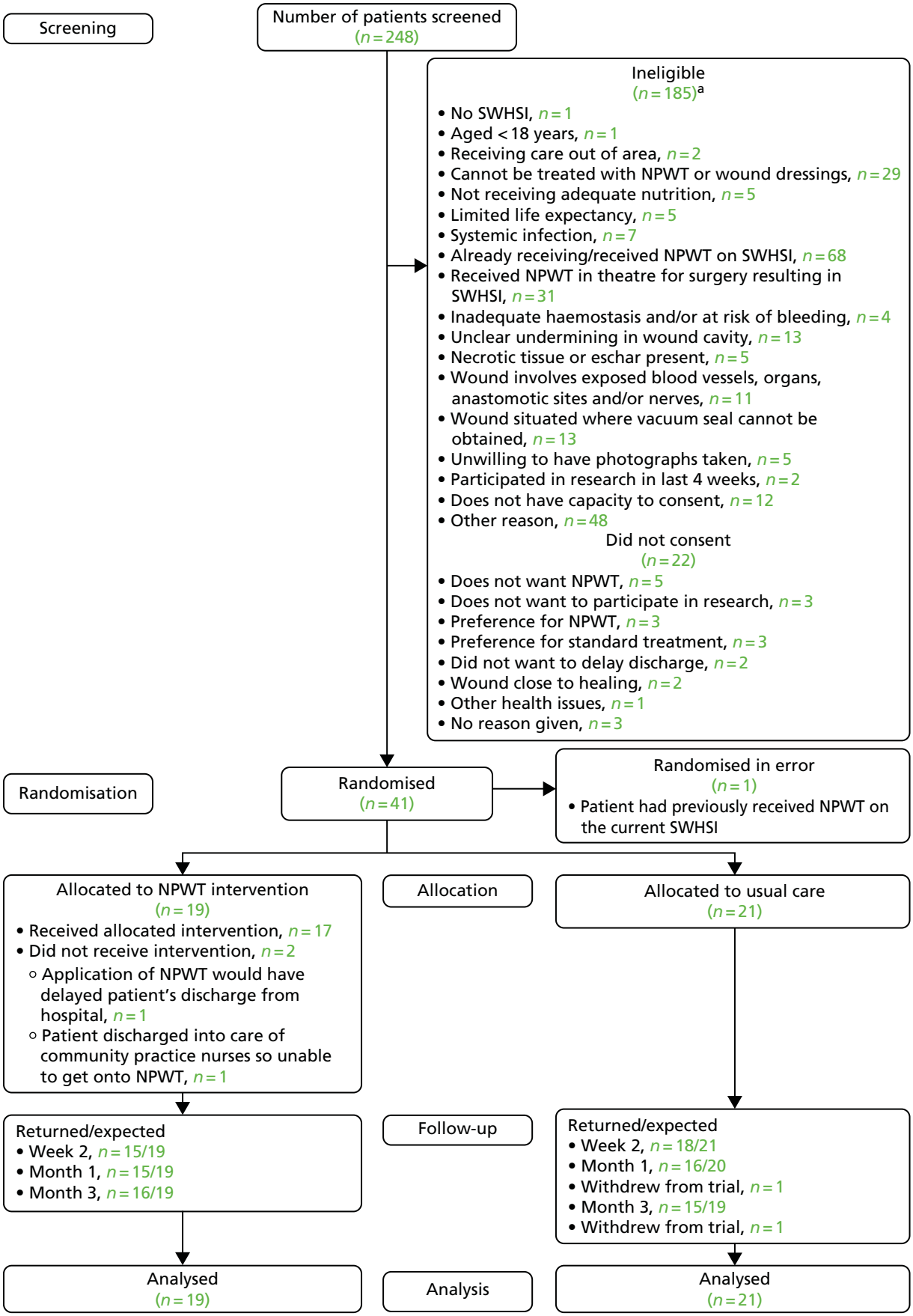

FIGURE 5 Pilot feasibility RCT: Consolidated Standards of Reporting Trials (CONSORT) flow diagram. a, Reasons not mutually exclusive.

TABLE 18 Pilot feasibility RCT: baseline characteristics of randomised participants by treatment group

Variable	Treatment group		
	NPWT ($N = 19$)	Usual care ($N = 21$)	Total ($N = 40$)
Age (years)			
Mean (SD)	58.8 (15.1)	56.9 (13.9)	57.8 (14.4)
Median (minimum, maximum)	62 (33, 88)	55 (35, 86)	58.5 (33, 88)
Sex, *n* (%)			
Male	11 (57.9)	11 (52.4)	22 (55.0)
Female	8 (42.1)	10 (47.6)	18 (45.0)
BMI (kg/m^2)			
Mean (SD)	29.2 (5.6)	29.0 (6.0)	29.1 (5.7)
Median (minimum, maximum)	28.6 (20.9, 39.9)	29.3 (13.7, 39.9)	28.7 (13.7, 39.9)
Diabetic, *n* (%)			
Yes	12 (63.2)	12 (57.1)	24 (60.0)
Peripheral vascular disease, *n* (%)			
Yes	7 (36.8)	7 (33.3)	14 (35.0)
Tobacco use, *n* (%)			
None	13 (68.4)	10 (47.6)	23 (57.5)
Ex-smoker	1 (5.3)	6 (28.6)	7 (17.5)
Current (less than or equal to one pack a day)	2 (10.5)	4 (19.1)	6 (15.0)
Current (more than one pack a day)	3 (15.8)	1 (4.8)	4 (10.0)
History of SWHSI, *n* (%)			
Yes	5 (26.3)	5 (23.8)	10 (25.0)
No	11 (57.9)	15 (71.4)	26 (65.0)
Do not know	3 (15.8)	1 (4.8)	4 (10.0)
Wound area (cm^2)			
< 28 cm^2, *n* (%)	10 (52.6)	11 (52.4)	21 (52.5)
≥ 28 cm^2, *n* (%)	9 (47.4)	10 (47.6)	19 (47.5)
Median (minimum, maximum)	18.2 (0.2, 122.5)	20.4 (2.3, 93.2)	19.3 (0.2, 122.5)
Wound duration (days)			
Median (minimum, maximum)	7 (0, 27)	12 (1, 142)	7 (0, 142)
Wound infected, *n* (%)			
Yes	5 (26.3)	8 (38.1)	13 (32.5)
No	14 (73.7)	13 (61.9)	27 (67.5)
Wound location, *n* (%)			
Foot	11 (57.9)	13 (61.9)	24 (60.0)
Abdomen	3 (15.8)	3 (14.3)	6 (15.0)
Leg	3 (15.8)	1 (4.8)	4 (10.0)
Breast	1 (5.3)	1 (4.8)	2 (5.0)
Groin	0 (0.0)	2 (9.5)	2 (5.0)
Buttocks	0 (0.0)	1 (4.8)	1 (2.5)
Perianal area	1 (5.3)	0 (0.0)	1 (2.5)

TABLE 18 Pilot feasibility RCT: baseline characteristics of randomised participants by treatment group (*continued*)

Variable	Treatment group		
	NPWT ($N = 19$)	Usual care ($N = 21$)	Total ($N = 40$)
Type of surgery, *n* (%)[a]			
Elective	12 (66.7)	18 (85.7)	30 (76.9)
Emergency	6 (33.3)	3 (14.3)	9 (23.1)
Contamination level of surgery, *n* (%)			
Clean	6 (31.6)	2 (9.5)	8 (20.0)
Clean/contaminated	9 (47.4)	12 (57.1)	21 (52.5)
Contaminated	4 (21.1)	7 (33.3)	11 (27.5)

a Totals for NPWT, usual care and overall total were $N = 18$, $N = 21$ and $N = 39$ for this category.

Wound area (cm^2) was collected by ruler measurement and wound tracing at each follow-up visit. Ruler measurements were found to overestimate the true area as obtained using wound tracings (mean difference 7.0 cm^2, SD 9.1 cm^2), even when an adjustment of '$\Pi/4$' was used. Wound area decreased in both treatment groups throughout the trial.

The movement of patients from acute to community settings did not substantially affect follow-up completion. In the majority of cases, follow-up continued as planned; however, qualitative interviews with the study nurses showed that, on occasion, it was impossible to assess the wound at follow-up visits. This was primarily due to community health-care professionals (e.g. district, community or general practice nurses) either having already attended and redressed the wound or not attending at the agreed time for the visit, meaning that research data could not be collected in full.

Negative-pressure wound therapy supply

Nineteen participants (of 40, 47.5%) were allocated to receive NPWT; however, two participants (of 19, 10.5%) did not receive the allocated intervention (one because NPWT would have caused delay in discharge and the other because all NPWT devices were with other patients in use in the community at that time). Approximately three-quarters of allocated participants (14/19, 73.7%) received NPWT within 48 hours of randomisation. Seven participants (of 19, 36.9%) did not receive NPWT within 24 hours of randomisation, with the primary reason for delay being lack of device availability (6/7, 85.7%). Participants received NPWT for a median of 18 (range 0–72) days, with eight participants discontinuing NPWT due to wound improvement. One participant recommenced NPWT following their initial cessation. Two participants (of 19, 10.5%) ceased NPWT therapy on the day they received it due to failure to maintain a seal. Twenty-one participants (of 40, 52.5%) were allocated to usual care, of whom more than half were initially treated with a hydrocolloid dressing (11/21, 52.4%), nine with a silver-containing ($n = 3$, 14.3%), iodine-containing ($n = 3$, 14.3%) or basic dressing ($n = 3$, 14.3%), and one with a soft polymer dressing (4.8%). Five usual-care participants (23.8%) switched to NPWT during the trial at a median of 4 (range 0–17) days after randomisation and subsequently remained on NPWT for a median of 31 (range 19–36) days. The most common reason for treatment crossover was wound deterioration (2/5, 40.0%).

Withdrawal and retention

During the trial, two participants (of 40, 5.0%) were fully withdrawn from the study due to amputation of the limb on which the reference wound was situated. The study protocol was revised following these withdrawals to enable continued data collection from participants after amputation, provided that they continued to give consent for this study. However, in the event, no further participants underwent amputation.

Participant questionnaire response rates were positive, achieving ≥ 77.5% at all time points, and 291 follow-up clinic visits were completed (NPWT, median 8; usual care, median 7) at intervals of between 4 and 33 days after randomisation (NPWT, median 7.5 days; usual care, median 9 days).

Blinded outcome assessment

In total, 308 photographs were taken as part of the study (38 at baseline, 270 at follow-up visits). Assessments of the final photographs for healing indicated that there was agreement between two reviewers for 29 (of 40, 72.5%) participants (NPWT, $n = 15$, 79.0%; usual care, $n = 14$, 66.7%), increasing to 38 participants (95.0%) following a third review. When healing status was recorded by one or more reviewers as 'unsure', this was due to poor photograph quality in 50.0% (4/8) of cases. For two participants (of 40, 5.0%), blinded outcome assessment of healing provided no consensus, with each reviewer recording a different healing status. The blinded assessors classed eight (of 40, 20.0%) wounds as healed (NPWT, $n = 3$, 15.8%; usual care, $n = 5$, 23.8%), of which seven (87.5%) were also recorded as healed by the unblinded investigators. Blinded assessors were unsure of healing status, or there was discordance between reviewers, for a further three wounds judged to have healed by the unblinded investigators.

The feasibility of blinding to treatment allocation was assessed using photographs taken at week 1, as the final photograph would not necessarily reflect the originally allocated treatment (given that NPWT is not necessarily used to the point of wound healing). In terms of blinding success, the assessors correctly identified treatment allocation for 15 participants (of 40, 37.5%): nine participants allocated to NPWT and six participants allocated to usual care. Allocation to NPWT was incorrectly identified in six cases (15.0%).

Documentation acceptability: nurses

Half of the eight research nurses who responded ($n = 4$, 50.0%) indicated that they found that the questionnaires asked all relevant questions and were straightforward to complete. There were mixed opinions on the ease of participant identification, with three nurses agreeing (agree or strongly agree), two nurses remaining impartial (neither agree nor disagree) and three strongly disagreeing. Half of the nurses ($n = 4$, 50%) indicated that trial processes were clear and the randomisation process was straightforward and just over half ($n = 5$, 62.5%) found that the assessments were straightforward to complete.

Qualitative interviews were subsequently conducted to ascertain further information on responses provided. Five face-to-face and three telephone interviews were conducted with research nurses across the three study sites, which identified key points of feedback on the trial procedures and processes:

- Trial documentation was found to be acceptable, straightforward and in keeping with expectations based on nurses' prior research experience. Amendments to clarify consistency in interpretation of eligibility criteria, processes for recording of wound depth and general minor amendments to study documentation were, however, suggested. The nurses acknowledged that the majority of issues encountered with the implementation of this pilot, feasibility RCT were not dissimilar to other new studies.
- Nurses based at the secondary care sites highlighted issues with engagement of consultants, due to concerns that randomisation could interfere with their preferred wound management plan. Nurses suggested that direct principal investigator involvement enabled more patients to be successfully screened at the preoperative stage. Nurses based within the community settings noted that the majority of patients were identified in the acute settings. Randomisation was regarded as an easy process, although availability of a 24-hour randomisation service would have been preferred.
- Given the geographical spread of participants at each study site, arranging visits to coincide with a patient's clinic appointment was the most efficient approach, although this was not always viable and often time was wasted waiting for district, community or general practice nurses at home visits. The frequency of follow-up visits was noted as having an impact on time available to recruit and the value of continued follow-up beyond wound healing (up to three visits completed post healing) was queried. Access to equipment was generally better in the acute setting than in the community setting, although there were occasions when equipment needed to be borrowed by the trial team across both acute and community settings to facilitate patient treatment.

- There was mixed feedback regarding nurses and consultants indirectly involved with the study. At one site, there was a perception that if NPWT was involved, some nurses would avoid a study due to a lack of confidence or training in its application and also the potential for additional work involved. At another site, it was reported that negative pressure is widely used and therefore there was a potential bias towards use of negative pressure. It was suggested that additional principal investigator involvement to promote the study, particularly during the set-up phase, would be helpful.
- All research nurses received training in the application of NPWT but, as a result of randomisation, not all nurses had the opportunity to apply it. Generally, there was confidence in the use of NPWT; however, staff turnover and levels of junior staffing were noted to highlight gaps in training. Nurses reported that for patient safety, patient lifestyle, in particular mobility requirements, should be taken into account during recruitment.

Study acceptability: patients

Feedback from participants indicated that taking part in the study had matched expectations (30/31, 96.8%), and that completing questionnaires had been straightforward (28/31, 90.3%) and manageable (29/31, 93.6%).

Clinical outcomes

Healing

Participants were followed for a median of 84 days after randomisation (range 13 to 105 days) to assess wound healing. During the study, 10 wounds (of 40, 25.0%) were deemed to have healed based on assessment at weekly follow-up [six in the NPWT group (31.8%) and four in the usual-care group (19.1%)]. Time to healing was summarised using Kaplan–Meier curves (*Figure 6*). Adjusted Cox proportional hazards models indicated that wound size ($p = 0.03$) and duration of wound ($p < 0.001$) were predictors of time to wound healing, with smaller and longer duration of wounds associated with increased time to healing (see *Appendix 13*).

Infection

During the trial, 17 participants (NPWT, $n = 6$, 31.6%; usual care, $n = 11$, 52.4%) experienced an infection. Of these, nine experienced infection at baseline only (NPWT, $n = 3$, 15.8%; usual care, $n = 6$, 28.6%), four during follow-up only (NPWT, $n = 1$, 5.3%; usual care, $n = 3$, 14.3%) and four both at baseline and during follow-up (NPWT, $n = 2$, 10.5%; usual care, $n = 2$, 9.5%).

Hospitalisation

Participants in the NPWT group spent a median of 29 nights in hospital during the trial and participants in the usual-care group spent a median of 10 nights in hospital.

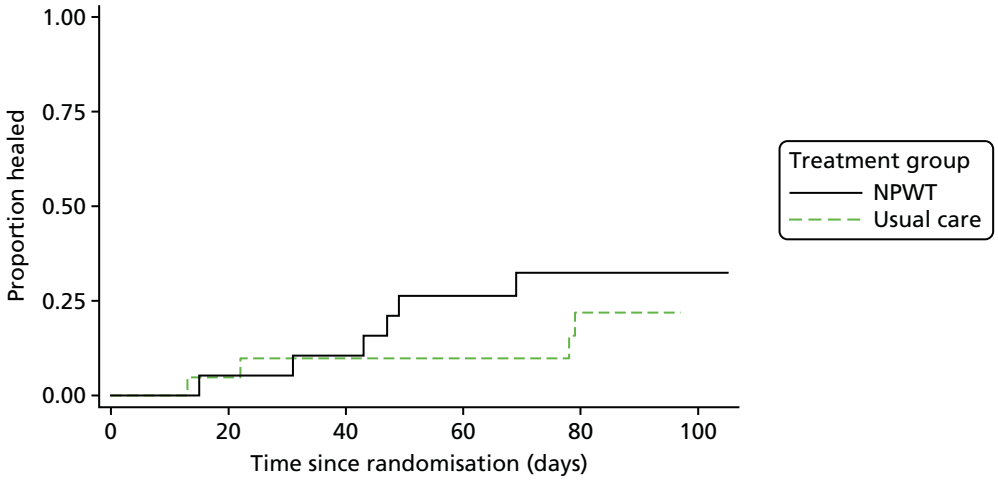

FIGURE 6 Pilot feasibility RCT: Kaplan–Meier curve – time from randomisation to healing.

There were five reported hospitalisations during the trial, all of which were associated with serious adverse events (as *Adverse events*). In four instances (of five, 80.0%) the participants were subsequently discharged and in one instance (20.0%) the participant was withdrawn from the study (due to amputation) and subsequently died, and so further information regarding hospital discharge was not collected.

Patient-reported outcomes

Participant-completed questionnaires indicated that pain severity (BPI),[23] interference and VAS wound pain reduced (improved outcome) in the NPWT group between baseline and month 1, but increased again (worse outcome) slightly at month 3 of follow-up. In the usual-care group, pain interference followed the same pattern as in the NPWT group, but VAS wound pain reduced consistently over time and BPI interference fluctuated between the follow-up time points. There was lower reported pain severity (improved outcome), interference scores (BPI)[23] and wound pain (VAS) for usual-care participants at all time points relative to the NPWT group (*Table 19*). A total of 20 participants provided at least one weekly text message providing a pain score (NPWT, $n = 10$; usual care, $n = 10$). Mean scores reduced between week 1 and month 3 (week 1 4.0, SD 3.0; week 12 1.6, SD 2.0); however, there was some fluctuation observed in scores during this time (see *Appendix 15*).

There was improvement (i.e. better health status) in the mean SF-12 PCS over time in both groups. MCSs reduced in the NPWT group over time, but improved initially in the usual-care group (between baseline and 1 month) before declining slightly at the month 3 follow-up visit. Further detail regarding these results is presented in *Table 20* (see also *Appendix 16*, *Figures 7* and *8*).

TABLE 19 Pilot feasibility RCT: pain scores by randomised group and time point

	Treatment group					
	NPWT ($N = 19$)		Usual care ($N = 21$)		Total ($N = 40$)	
	n	Mean (SD)	*n*	Mean (SD)	*n*	Mean (SD)
BPI severity						
Baseline	16	4.4 (2.8)	20	2.7 (2.8)	36	3.5 (2.9)
Week 2	15	3.7 (2.8)	17	2.5 (2.5)	32	3.0 (2.7)
Month 1	14	3.5 (3.4)	15	1.9 (2.6)	29	2.7 (3.1)
Month 3	14	4.3 (2.9)	13	2.1 (2.6)	27	3.2 (2.9)
BPI interference						
Baseline	15	5.0 (3.5)	16	2.8 (3.6)	31	3.8 (3.6)
Week 2	15	4.5 (3.5)	17	3.3 (3.3)	32	3.9 (3.4)
Month 1	14	4.2 (3.7)	15	2.3 (2.8)	29	3.2 (3.4)
Month 3	13	5.3 (2.8)	15	2.7 (3.4)	28	3.9 (3.4)
VAS wound pain						
Baseline	15	51.2 (32.1)	18	34.8 (32.7)	33	42.2 (33.0)
Week 2	13	32.4 (33.4)	17	26.5 (29.3)	30	29.1 (30.7)
Month 1	13	27.1 (31.1)	14	20.7 (26.7)	27	23.8 (28.5)
Month 3	12	30.8 (27.2)	15	13.5 (23.1)	27	21.1 (26.0)
VAS pain at dressing changes[a]						
Week 2	13	22.3 (25.5)	15	22.6 (24.5)	28	22.5 (24.5)
Month 1	13	26.5 (32.8)	14	16.4 (24.2)	27	21.2 (28.5)
Month 3	11	18.1 (20.2)	15	12.5 (27.0)	26	14.8 (24.1)

a Not measured at baseline.

TABLE 20 Pilot feasibility RCT: physical and mental composite scale scores derived from the SF-12 by randomised group and time point

SF-12	Treatment group		
	NPWT ($N = 19$)	Usual care ($N = 21$)	Total ($N = 40$)
PCS			
Baseline			
n	16	19	35
Mean (SD)	16, 28.9 (10.6)	19, 34.9 (11.4)	35, 32.1 (11.3)
Median (minimum, maximum)	28.0 (12.2, 47.9)	32.7 (15.5, 53.2)	32.4 (12.2, 53.2)
Month 1			
n	14	15	29
Mean (SD)	29.8 (10.1)	38.8 (12.1)	34.5 (11.9)
Median (minimum, maximum)	28.0 (14.9, 48.9)	39.8 (21.4, 55.1)	33.2 (14.9, 55.1)
Month 3			
n	14	14	28
Mean (SD)	30.4 (11.9)	42.8 (8.3)	36.6 (11.9)
Median (minimum, maximum)	26.6 (17.4, 51.0)	40.8 (30.5, 57.9)	37.5 (17.4, 57.9)
MCS			
Baseline			
n	16	19	35
Mean (SD)	44.7 (12.6)	42.2 (11.2)	43.3 (11.8)
Median (minimum, maximum)	44.2 (19.0, 62.4)	42.5 (18.8, 56.6)	43.4 (18.8, 62.4)
Month 1			
n	14	15	29
Mean (SD)	42.7 (13.8)	48.6 (11.7)	45.8 (12.9)
Median (minimum, maximum)	40.8 (21.8, 61.7)	46.8 (31.7, 67.5)	45.0 (21.8, 67.5)
Month 3			
n	14	14	28
Mean (SD)	41.5 (10.9)	47.1 (12.1)	44.3 (11.6)
Median (minimum, maximum)	41.5 (24.8, 62.3)	46.6 (29.8, 64.7)	42.1 (24.8, 64.7)

Adverse events

Adverse event data collection throughout the study identified 28 non-serious and five serious adverse events. Two serious adverse events were reported in the NPWT group from one participant and three in the usual care group from two participants. All five events were hospitalisations and only one (usual-care group) was classed as related to the reference wound. Three events (of five, 60.0%) were said to be possibly or probably related to treatment, all of which were recorded as expected. There were no suspected unexpected serious adverse reactions. The majority of non-serious adverse events related to the reference wound (25/28, 89.3%) and were reported as definitely related to treatment (19/28, 67.9%). The most common event type was 'other' (12/28, 42.9%), which included events such as skin irritation (3/12, 25.0%) and dressings falling off (3/12, 25.0%), followed by 'pump failure' (8/12, 28.6%).

Economic outcomes

Usual-care participants reported that they received a mean of 8.0 (SD 14.8) nurse visits at home and had a mean of 12.41 (SD 15.04) visits at the GP surgery for their SWHSIs. NPWT participants reported a limited number of nurse visits at the GP surgery (mean 1.14, SD 2.24), but additional nurse visits at home (mean 6.78, SD 9.82) and substantial mean inpatient hospital stays (mean 17.5, SD 19.8) and GP visits (mean 1.35, SD 2.70) (*Table 21*).

Costs associated with NHS and health-care resource use were calculated on a per-contact basis, using *NHS Reference Costs*[61] and *Unit Costs of Health and Social Care*[62] (see *Appendix 17*). The associated NHS and health-care costs were higher for the NPWT group: the mean total cost for the NPWT intervention was £9490 (SD £7346), compared with £1153 (SD £1806) for patients receiving usual care (*Table 22*).

TABLE 21 Pilot feasibility RCT: cost-effectiveness analyses and mean resource use, based on all available cases

	Treatment group			
	NPWT (*N* = 19)		Usual care (*N* = 21)	
Type of resource use	Mean (SD)	Missing, *n* (%)	Mean (SD)	Missing, *n* (%)
Doctor: hospital outpatient clinic				
Wound related	2.73 (3.23)	5 (25.0)	0.76 (1.16)	8 (38.0)
Not wound related	1.70 (2.00)	10 (50.0)	0.20 (0.63)	11 (52.0)
Nurse: hospital outpatient clinic				
Wound related	6.66 (10.35)	5 (25.0)	4.07 (10.07)	8 (38.0)
Not wound related	1.45 (2.39)	9 (45.0)	0 (0)	11 (52.0)
Day-case visit to the hospital				
Wound related	0.33 (0.88)	8 (40.0)	0.21 (0.80)	7 (33.3)
Not wound related	0.09 (0.30)	9 (45.0)	0 (0)	9 (43.0)
Nights stayed as hospital inpatient				
Wound related	17.5 (19.8)	6 (30.0)	0.90 (3.01)	10 (48.0)
Not wound related	14 (22.01)	10 (50.0)	0.54 (1.80)	10 (48.0)
GP visit at general practice				
Wound related	1.35 (2.70)	6 (30.0)	0.69 (1.31)	8 (38.0)
Not wound related	0.54 (1.03)	9 (45.0)	0.83 (1.19)	9 (43.0)
GP visit at home				
Wound related	0.28 (0.61)	6 (30.0)	0 (0)	9 (43.0)
Not wound related	0.15 (0.37)	7 (35.0)	0.08 (0.29)	9 (43.0)
Nurse visit at general practice				
Wound related	1.14 (2.24)	6 (30.0)	8.00 (14.8)	9 (43.0)
Not wound related	0.31 (0.75)	7 (35.0)	0.09 (0.30)	10 (48.0)
Nurse visit at home				
Wound related	6.78 (9.82)	6 (30.0)	12.41 (15.04)	9 (43.0)
Not wound related	1.91 (3.87)	8 (40.0)	0 (0)	11 (52.0)

TABLE 22 Total mean costs based on all available cases, up to 3 months' follow-up

Type of resource use	Treatment group, total mean cost (£) (SD) [*n*][a]		Incremental cost (£) (NPWT – usual care) (95% CI)[a]
	NPWT	Usual care	
Combined resource use	9490.00 (7346.00)	1153.00 (1806.00)	8333.00 (3311.13 to 13,362.96)
Doctor: hospital outpatient clinic	360.77 (427.59) [15]	101.53 (153.86) [13]	259.24 (1.63 to 516.84)
Nurse: hospital outpatient clinic	472.46 (733.90) [15]	288.93 (713.67) [13]	183.53 (–380.89 to 747.96)
Day-case visit to the hospital	240.26 (639.78) [12]	154.45 (577.90) [14]	85.80 (–407.07 to 578.69)
Nights stayed as hospital inpatient	6284.77 (7128.17) [14]	326.48 (1082.81) [11]	5958.29 (1452.14 to 10,464.44)
GP visit at general practice	59.71(119.07) [14]	30.46 (57.88) [13]	29.25 (–45.92 to 104.43)
GP visit at home	25.40 (54.35) [14]	0 (0) [13]	25.40 (–5.68 to 56.49)
Nurse visit at general practice	12.69 (24.97) [14]	88.88 (165.46) [12]	–76.19 (–168.35 to 15.98)
Nurse visit at home	158.31 (229.16) [14]	289.68 (350.93) [12]	–131.37 (–367.93 to 105.19)

a Costs expressed in Great British pounds using the price level of 2015 (£1 = €1.12).

Negative-pressure wound therapy participants reported a mean baseline EQ-5D-3L score of 0.34 (SD 0.10) and usual-care participants reported a mean baseline score of 0.54 (SD 0.08). At 3 months, following adjustment for baseline utility, mean scores had improved over time [NPWT participants 0.49 (SD 0.35) and usual-care participants 0.77 (SD 0.23)] (*Table 23*, see also *Appendices 18* and *19*).

The results show that NPWT had higher total NHS and health-care costs and also achieved lower QALY gains than usual care (complete-case analysis –0.007, 95% CI –0.04 to 0.02; multiple imputation analysis –0.004, 95% CI –0.03 to –0.02).

During the study, 1135 dressing changes were completed (NPWT, $n = 518$; usual care, $n = 617$). The average number of dressing changes completed was 27.26 for NPWT participants and 29.38 for usual-care participants. The majority of dressing changes were completed by district, community or general practice nurses (NPWT, $n = 253$; usual care, $n = 272$) or the participant's clinic nurse (NPWT, $n = 107$; usual care, $n = 167$). The distribution of dressing changes by group corresponds to the distribution by group of nursing visits received or attended by participants: nursing visits at home or at the GP clinic were higher for usual-care participants than those allocated to NPWT.

TABLE 23 Summary of EQ-5D utility scores at each time point (all available cases)

Time point	Treatment group				Mean difference (NPWT – usual care) (95% CI)	
	NPWT ($N = 19$)		Usual care ($N = 21$)			
	n	Mean (SD)	*n*	Mean (SD)	Unadjusted	Adjusted[a]
Baseline	16	0.34 (0.10)	21	0.54 (0.08)	–0.20 (–0.46 to 0.05)	
3 months	15	0.49 (0.35)	15	0.77 (0.23)	–0.28 (–0.50 to –0.06)	–0.05 (–0.31 to 0.20)

a The difference at 3 months is adjusted for baseline utility.

Conclusions

This pilot, feasibility RCT provides invaluable information on the feasibility of conducting a large-scale trial of NPWT for treatment of SWHSIs and identifies areas of key consideration in the planning of future research.

Recruitment, participation and retention

The consistent rate of recruitment observed following the opening of all sites to recruitment, demonstrates that it is possible to recruit participants to a trial of NPWT compared with usual care. A full trial would, however, need to ensure that an adequate number of recruiting sites are identified. On the basis of the recruitment rate observed (two patients per site per month), to recruit 400 participants to a similar trial over an 18-month recruitment period, 11 study sites would need to be opened to recruitment. This example is based on hypothetical detail and would therefore be subject to revision following full sample size calculations for a larger trial. A larger trial should consider the impact of, and account for in associated sample size calculations, the rates of participants randomised to, but subsequently not receiving, NPWT (10.5% of participants in the pilot feasibility RCT) and rates of crossover to NPWT (23.8% of usual-care participants in the pilot feasibility RCT).

Qualitative interviews indicated that nurses perceived the majority of SWHSI patients to be identified within acute care settings, highlighting that the primary source of recruitment in a future RCT may be best achieved in acute care settings. This distribution may, however, differ between individual localities and so work would be required prior to recruitment to ensure that appropriate and effective recruitment strategies and pathways were implemented at individual sites.

Having previously received, or currently receiving, NPWT for their SWHSI was found to be the most frequent reason for patients' ineligibility to take part in the study. Prior to undertaking a full RCT, it would be necessary to undertake some promotional work with clinical colleagues and research groups in order to fully engage surgeons and nurses within the study site, and to ensure consistent and continued referrals into the study. In addition, a future trial should recruit study sites where there is sufficient equipoise with regard to treatment of patients with SWHSIs, thus thorough evaluation of potential trial sites will be essential.

Work to engage clinical colleagues and research groups prior to recruitment commencement would also be crucial to allay resistance to trial recruitment from certain clinical groups. Anecdotal evidence from the study sites indicated some resistance to trial recruitment participation from colorectal surgeons, either because NPWT was primarily used for wound management rather than healing or because a surgeon's prior experience of NPWT had led them to feel that this treatment was inappropriate for use in this patient group. Given the small number of sites involved in this pilot feasibility study, it is impossible to draw firm conclusions on the likely resistance among specific clinical groups, which may be observed in a larger RCT. Promotional work with clinicians across potential research sites in advance of study commencement should, however, help to minimise any resistance to recruitment in a larger RCT. Where necessary, promotional work may need to be targeted to ensure that clinicians from a cross-section of surgical disciplines are aware of, and open to, recruitment for a larger trial.

Participant-reported questionnaire response rates in excess of 75% and the limited number of withdrawals observed also demonstrate that it is possible to retain participants in a RCT of NPWT compared with usual care. During the study, only two (5.0%) participants were withdrawn from the trial due to amputation of the limb on which the reference wound was situated. Data collection did not continue for these participants. The trial team subsequently amended the study protocol to reflect that clinical data collection would cease at the point of amputation, but participant-reported data could continue to be collected, subject to continued consent. A future trial should ensure that the process for continued data collection following amputation is discussed and is clearly defined prior to study recruitment commencing.

Data collection methods

Assessment of wound measurements indicated that ruler measurements, both with and without adjustment, overestimate wound size, compared with wound tracings. Wound tracings should therefore be chosen over ruler measurement in any future RCT.

We have shown how wound pain data can be successfully collected on a weekly basis using text messaging; however, there were limited numbers of participants who responded to this method of data collection and rates of response varied considerably throughout the study. Exploration of participant characteristics in relation to text message respondents and non-respondents indicated that collection of data using this method may be most effective in younger populations; those who routinely responded were, on average, almost 10 years younger than those who did not respond routinely. The use of text messaging data collection in a larger study should therefore be considered carefully, before implementation, to ensure that use of this method will provide sufficient data for analysis.

Negative-pressure wound therapy supply

Negative-pressure wound therapy delivery was largely completed within 48 hours; however, three participants did not receive NPWT within this time frame. Furthermore, two participants did not receive NPWT at all, due to delays to discharge and lack of intervention availability. A future RCT would therefore need to establish the availability of NPWT devices with sites from the outset, to ensure timely intervention delivery.

Nurses involved in the study reported that they had received sufficient training within their individual institutions to confidently apply NPWT. It was, however, noted that nursing colleagues were not always confident in using NPWT, which corresponds with findings from workstream 3 of this research programme. A future trial would therefore need to invest sufficient resource to ensure that NPWT training was provided to all staff who may be providing trial treatment to a participant.

Blinded outcome assessment

This pilot feasibility trial explored the feasibility of blinded outcome assessment in the context of NPWT for SWHSI healing. Blinded and unblinded investigator assessment in relation to wound healing agreed 87.5% of the time and so blinded outcome assessment can be deemed to be feasible and appropriate within a future RCT. Blinded assessment of healing was, however, often hampered by the quality of the wound photograph. A robust photography protocol would therefore be required for a full RCT to facilitate consistency of imaging throughout the study and accurate blinded healing assessment.

It was not possible within this study to blindly assess time to healing due to difficulties in transferring the necessary numbers of photographs required to complete this activity. Dependent on the outcomes included in a larger study, this may warrant further exploration and a robust and tested process for transfer of photographs to blinded assessors for review should be established prior to the study commencing.

It is important to note that assessors correctly identified treatment allocation in approximately one-third (37.5%) of cases when reviewing photographs taken in the first week of the study. Therefore, assessment of time to healing in a larger study may become biased through identification of treatment allocation and so inclusion of this assessment should be carefully considered before implementation.

Documentation acceptability

Participant questionnaires were largely well received and so limited changes would be required for data collection in a larger RCT. The variation in opinions from research nurses involved in the study regarding study documentation and study processes, especially frequency and method of follow-up visits, indicates that further work should be conducted during the design of a larger trial to develop and test data collection processes to ensure fitness for purpose.

Clinical events

Given the limited number of participants involved in this study, there were insufficient data to enable any true treatment effect of NPWT to be identified; and this was not the purpose of this study. A full RCT is therefore required to fully assess the clinical effectiveness and cost-effectiveness of NPWT as a treatment for patients with SWHSIs.

The cohort study undertaken before this pilot, feasibility RCT (workstream 1) estimated that a follow-up duration of 90 days should be sufficient to observe wound healing. However, in this pilot feasibility study, only 25% of participants healed, which meant that a median time to healing could not be calculated. As a result, a 3-month follow-up may be inadequate to reliably investigate and compare healing rate; therefore, a longer follow-up should be considered for future trials. The difference in time to healing between this pilot feasibility study and our cohort study may be explained by the greater proportion of participants with foot and leg wounds in the pilot feasibility study (usually secondary to diabetes mellitus). The complexities associated with wound healing in patients with diabetes mellitus[63] may explain these lower healing rates.

Regional arrangements for the supply of NPWT in community settings may have resulted in between-group differences in relation to nights spent as an inpatient. It is, however, worth noting that this may be due to specific regional arrangements present in the participating sites, rather than being an issue that would manifest in a larger national study. To ensure that inpatient stay is not distorted by regional arrangements, it is imperative to assess provisions for treatment delivery (e.g. local discharge arrangements and availability of NPWT within community settings) prior to commencing research activity at any study site. Associated with NPWT supply is the aforementioned requirement for training. Nurses noted that clinical colleagues were not always confident in using NPWT and so sufficient resource would be required to ensure full coverage of training across all those who may provide treatment to a participant.

This pilot feasibility study has clearly demonstrated the feasibility of completing a full RCT to provide definitive evidence in relation to NPWT effectiveness as a treatment for patients with SWHSIs. The pilot feasibility study has also identified key elements of, and recommendations for, recruitment, data collection, outcome measurement, trial design and safety reporting, which would need to be considered during the design of a larger RCT to investigate the clinical effectiveness and cost-effectiveness of NPWT compared with usual care.

Conclusions and recommendations

What do we now know about the SWHSI patient population?

This research programme emerged from clinical uncertainty about the best way of managing SWHSIs. To the best of our knowledge, there has been very little previous research on open surgical wounds, and what small amount there has been has focused only on dehisced surgical wounds;[64,65] we have now shown that these constitute approximately half of all SWHSIs. We have studied both dehisced surgical wounds and those intentionally left open after surgery because they present similar challenges for clinical management. We planned this research at a time (2009) when the use of a costly intervention, NPWT, was increasing; however, access to it varied hugely, based on clinical setting, local policies and resources. Prior to this research, little was known about the frequency of SWHSIs, the characteristics of the patients who experience them and longer-term outcomes. Without basic information about the frequency and prognosis of a health condition and how patients are affected by it, it is impossible to plan research on treatments.[66] Initially, we undertook a cross-sectional survey of the prevalence of treated SWHSIs, which had the dual purpose of deriving the first population-based estimate of prevalence, as well as identifying where and when SWHSIs occurred, to aid the planning of an inception cohort. The cross-sectional survey (conducted in 2012) was anonymised, completed away from the patient and did not require consent in order to optimise data capture. To the best of our knowledge, this survey provides the first estimate of the prevalence of treated SWHSIs, which we estimate at 4.1 per 10,000 of the population (95% CI 3.5 to 4.7).[16] There are several things worth noting about this estimate: the prevalence is similar to best estimates of the UK prevalence of leg ulcers (4.4 per 10,000),[27] almost half of SWHSIs (48%) were planned (before surgery) to be left open, the wounds had been present for a median of 28 days, the patients were mainly receiving care in primary and community care settings and 93% of patients were receiving wound dressings (6% had NPWT). Colorectal surgery was the most frequent type of surgery to precede the SWHSI, although plastic surgery and vascular surgery were also common.

This survey, although rather basic in design (lacking independent case ascertainment, for example, due to resourcing), provided crucial intelligence for planning the cohort study. Our median time from surgery to wound breakdown (in those whose wounds were not intentionally left open) of 9 days accords with previous studies of dehiscence.[64,67]

Our inception cohort collected data from 393 patients with SWHSIs and, to the best of our knowledge, is the first detailed analysis of this patient population, their wound treatments and healing trajectories. A notable difference between this and the cross-sectional survey (apart from the longitudinal follow-up) was the requirement for informed consent, which may have influenced participation. In total, 57% of the cohort were men, the overall median age was 55 years, 70% of the cohort were overweight or obese (higher than the 2015 national average of 63%)[68] and 29% were smokers or had quit in the last 12 months (compared with 19% of the adult population in Great Britain).[69] Common comorbidities were cardiovascular disease (in 38%), diabetes mellitus (in 26%) and peripheral vascular disease (in 14.5%). The wounds of 60% of the cohort participants were planned to be left open before surgery, higher than for the cross-sectional survey in which 48% were planned. This probably reflects the relative ease of recruitment of participants to the cohort, when it was known in advance that their wound would be open after surgery.

Our research illustrates, for the first time, the heterogeneous nature of the population of people with SWHSIs and of their wounds. Although it was anticipated that SWHSIs would stem from a range of surgical specialties, the distribution of SWHSI sites is noteworthy (34% abdominal, 15% feet, 15% leg) and anatomical site is very likely to influence the impact of the wound on quality of life (if it influences mobility or ability to drive, for example). The clinical specialty under whose auspices the preceding surgery took place was most commonly colorectal (40%), but also commonly vascular (21%). This information is

vital to the planning of future research to ensure that the studies are carried out in the populations most affected. Moreover, these subpopulations of people with SWHSIs are likely to demonstrate very different healing trajectories from one another (an open wound on the foot in somebody with peripheral vascular disease and/or diabetes mellitus is likely to heal differently from a partially dehisced abdominal wound post appendectomy). Those conducting future trials in this area will need to make decisions about trading off ease of recruitment of a heterogeneous population (with consequent 'noisy' healing data) with recruitment from smaller, focused patient populations. This is illustrated by our pilot trial, to which we recruited 40 eligible participants, 60% of whom had a SWHSI on the foot (compared with 15% in the cohort study). The nature of those recruited to the pilot trial meant that the time to healing was much longer than for the cohort study and far fewer healing events were observed (only 25% healed), despite the 90-day follow-up period. The reasons for the excess of patients with foot wounds in the pilot trial are unclear, but it is likely that they were more readily recruited for some reason. It is possible that the current enthusiasm for NPWT as a treatment for SWHSIs meant that some health professionals were not in equipoise and were unwilling to randomise, thus making it difficult to recruit specific patient subgroups.

Future trials will therefore need to be carefully planned, with a desired population in mind and appropriate targeted recruitment. The cohort study time to healing data will be invaluable to the planning of new research, particularly in relation to appropriate follow-up time frames.

Exploratory analysis of predictors of healing within the cohort identified larger-area surgical wound contamination classification (as judged at the point of surgery)[70] and infection at any time point as predictors of slower healing. The median time to healing of 86 (95% CI 75 to 103) days is very similar to that for venous leg ulcers (84 days in typical venous ulcer patients in a recent trial).[71] The typical healing trajectory for people with a SWHSI is not smooth, with episodes of infection and hospital readmission commonplace. The relatively young age of SWHSI patients compared with other patient groups with chronic wounds (e.g. leg and pressure ulcers) is particularly noteworthy. The wide-ranging impact on quality of life was detectable using the generic EQ-5D and SF-12 instruments, and was both physical and mental.[21,22] We heard directly from the patients themselves of the often devastating impact on their lives. Patients often felt isolated and confined to the home with disruption of working and caring responsibilities, causing feelings of dependency and burden. There were frequently financial impacts of the SWHSIs on the person and their family. To the best of our knowledge, the cost to the NHS of a SWHSI had not previously been estimated. We estimated that the mean cost of a SWHSI to health services was £1060 before the inclusion of treatment costs. Use of NPWT was estimated to cost, on average, an additional £1323 per month and use of dressings was estimated to cost, on average, an additional £441 per month.

What do we now know about treating SWHSIs?

Prior to this research, we had no information about treatments that were being used for SWHSIs. From our research we have learned that SWHSI treatments fall into three main categories: dressings, NPWT and further surgery. We observed a plethora of treatments being used for SWHSIs; however, hydrofibre dressings were the most commonly used (66% of patients received these at some time), alongside a high use of NPWT. Although the cross-sectional survey identified NPWT use in only 6% of patients, the cohort study indicated that a much larger proportion (29%) were treated with NPWT at some time.

Dressings are the cornerstone of treatment for complex wounds and there are many categories available, ranging from simple, basic wound contact dressings to 'advanced' dressings containing ingredients such as silver.[29] However, the evidence for the effectiveness of specific dressings and NPWT for SWHSIs is sparse and of low quality.[12] The most recent systematic review of the effects of dressings for open surgical wounds highlighted the paucity of evidence and a review of the effects of NPWT on open surgical wounds (search date June 2015) similarly concluded that there is currently no rigorous evidence available and therefore the benefits and harms are unclear.[14] There is an increasing amount of research regarding NPWT for the primary prevention of surgical site infections in closed surgical wounds; however, its effects in this

context also remain unclear.[72,73] There is some evidence of potential benefit of NPWT for foot wounds in diabetes mellitus; however, this evidence is of low certainty due to its low quality.[31]

We planned to construct a cost-effectiveness model for NPWT compared with dressings for open surgical wounds using a combination of published and cohort study data. We were unable to populate this model with published data as there were no data reporting time to healing as an outcome in RCTs of NPWT in this patient population. Using the cohort data alone to compare the effects of NPWT and dressings on time to healing effectiveness, and after using different approaches to adjust for confounding, we concluded that NPWT is less effective and more costly than wound dressings for SWHSIs. We had originally intended to conduct a value of information analysis to determine the potential impact of uncertainty on the decision regarding NPWT to treat SWHSIs. This analysis would assess the health and cost implications of the wrong decision being made and thus inform investments in future research to mitigate these uncertainties. However, our analyses showed that uncertainty around the decision not to use NPWT was very small. Even with the use of advanced adjustment techniques, such as those applied here, observational data may still affect the conclusions. Meta-analyses comparing the findings of RCTs and cohorts designed to answer the same clinical question give an OR of 1.04 (95% CI 0.89 to 1.21), highlighting the potential for agreement between the designs and the associated uncertainty.[74] The current economic evaluation uses all available evidence on the clinical effectiveness and cost-effectiveness of NPWT; thus, we argue that it should be seriously considered. However, the potential for unresolved confounding may limit confidence in the associated conclusions and therefore this may lead to justified calls for definitive RCT evidence to be obtained.

Interviews with patients and health professionals provided further insights into the use of, and views about, treatments for SWHSIs. The wide range of dressings used and inconsistency of use was noted by patients. Sharp, sometimes painful, debridement of SWHSIs was also reported by patients, despite the lack of high-quality evidence to support its use.[75] However, debridement was not measured explicitly as a treatment in the cohort study, so further data are needed on how widespread sharp debridement is as a treatment for SWHSIs. Finally, although our study participants generally viewed NPWT as an effective treatment, they reported various drawbacks, including pain during dressing changes. Some study participants reported feeling too embarrassed to go outside the home with NPWT in situ, due to the bulky appearance of the equipment and their fears that the exudate and odour might be detected by other people. Nurses' varying levels of expertise in use of NPWT appeared to provoke anxiety in patients. These findings mirror those from other small qualitative interview studies with patients receiving NPWT.[76–78]

What do we now know about living with a SWHSI?

The interviews with patients, together with the cohort HRQoL data, show the devastating effect that open surgical wounds can have on those affected. For those who did not expect to have an open wound after surgery, there were feelings of shock, fear and anxiety; these are feelings akin to those reported by people who have undergone life-changing trauma.[79] Significantly, the presence of an open wound resulted in the withdrawal of many people from normal employment, leisure and social activities. During interviews, participants indicated that their physical and mental resources had become depleted through the dominance of the wound in their lives.

We note the low baseline mean SF-12 PCSs and MCSs for SWHSI patients [mean PCS 33.1 (SD 10.17); mean MCS 42.2 (SD 12.35)]. These values, for people who have recently undergone surgery and who have an open wound, are lower than the mean PCS reported for an, on average, older venous leg ulcer population [mean PCS 38.4 (SD 11.2); mean MCS 48.6 (SD 12.0)],[71] and are also lower than mean scores for other patient groups, such as those with coronary heart disease and arthritis.[80,81] However, the SWHSI cohort mean scores are similar to postoperative SF-12 data from 85 participants with mainly closed wounds [mean PCS 35.1 (SD 7.8); mean MCS 43.5 (SD 12.4) 30 days post surgery].[82] Thus, it is difficult to separate the impact of surgery from the impact of an open wound on HRQoL. In the SWHSI cohort, we noted a significant improvement over time in both PCS and MCS, suggesting that the SF-12 is responsive to changes in HRQoL

in this population. Improved quality of life was likely to be the result of recovery from surgery, changes in the underlying condition the surgery aimed to ameliorate or resolve and wound healing. The baseline EQ-5D index score was found to be, on average, 0.43 (SD 0.45). Modelling results indicated that wound healing was associated with a small (but statistically significant) increase in EQ-5D index score (mean 0.055, SE 0.02). This level of improvement is smaller than what has been detected for the healing of other wound types,[71] but this may be due to different estimation methods. This value is also within the range of minimal clinically important differences evaluated across a wide range of conditions.[83,84]

Although baseline HRQoL was relatively poor in this SWHSI cohort, pain severity and interference scores of 4 (SD 3) (measured using the BPI)[23] were indicative of relatively mild pain when compared with, for example, the mean pain severity score of 7.0 (SD 1.8) and pain interference score of 7.6 (SD 2.0) reported in 440 patients with known chronic, non-malignant pain.[85] In addition, for the SWHSI cohort, mean pain scores reduced, on average, by only 1 point, to 3 points, by 15 months, follow-up. In interviews, some patients discussed pain and its impact, but it did not seem to be a key topic of concern and was not an obvious source for the overall poor HRQoL observed in those with a SWHSI.

Our findings, from exploring living with a SWHSI with patients, illuminate the significance of psychosocial effects, due to diminished sense of self, inability to fulfil social roles and obligations, and curtailment of normal social activities, especially when patients' hopes for healing are not met. Our study also highlights the impact of financial pressures on younger patients whose wound rendered them unfit for work, and their concerns about consequences for their family and implications for employment in the longer term.

From a patient perspective, the aspiration for complete wound healing was a major focus of all those interviewed. Healing was largely linked to return to some semblance of life prior to surgery, and was considered a sign that the body was returning to 'normality'. This focus on healing as a key outcome agrees with previous findings from interviews with 33 patients with a range of complex wounds, including leg ulcers, foot ulcers and surgical wounds.[27] Here, most people, again, said that being healed or 'cured' was their main goal, as did eight participants with complex wounds who, when responding to the question 'what did you most want from treatment?', reported that they most wanted the wound to heal.[46]

Health professionals' management of patient expectations is crucial to the patient experience. We know from our cohort study that, although the median time to healing was around 3 months, some people would live with a SWHSI for significantly longer than this. We heard how comments from health-care professionals regarding healing and the condition of their wound had profound impacts on patients. Positive feedback was a boost for morale and sustained the patient's hope for healing, whereas negative remarks adversely affected the patient's general outlook. Conflicting information led to feelings of confusion and consternation in patients. Even quite casual remarks from health-care professionals could have a profound impact, which has been noted in other recent research on patients with complex wounds.[86] Patients' expectations for wound healing may often appear unrealistic, yet clinicians need to manage these expectations within a framework that allows patients some measure of hope for healing, while avoiding the arousal of 'false hope', which may result in feelings of disappointment, disillusionment and distrust, which undermine professional–patient relationships.[46] Open, non-healing wounds that endure, such as SWHSIs, are associated with the 'forever healing' process, characterised by a constant need for treatment and care and a diminished quality of life, as described in patients with venous, diabetic and pressure ulceration.[47–51,53,87] This is challenging for clinicians, who must communicate uncertainty regarding wound progress and likely treatment outcomes without raising false hope or inducing a 'spiral of hopelessness' in patients.[51]

Given the severity of impact that these wounds have on patients' well-being, it is not clear whether or not psychological interventions may be useful in helping patients with hard-to-heal wounds to accept and adapt to their non-healing wound. Our findings also point to the need for improvements in communication with health-care professionals concerning the slow healing processes associated with SWHSIs; further research is required to investigate how, when and by whom information should be conveyed to patients

with these types of wounds. Study (nurse) participants also highlighted the need for patients to receive written, as well as verbal, information, including information about signs and symptoms of infection and what action to take should these occur.

Strengths of the research

A key strength of this research is the new information that has been captured and reported on this SWHSI patient population. Prior to this research, we did not know the prevalence of SWHSIs, the surgeries involved, how many SWHSIs were planned compared with how many formed spontaneously, how costly these wounds are to the health service, how best to treat these wounds and how best we might direct future research on SWHSIs. There was also an absence of rigorous data regarding SWHSI management in the UK, how long they took to heal and what the impact of these wounds is on patients and their families. This research has provided this information for one geographical area of the UK (Yorkshire and the Humber).

We present data and conclusions that address many of the uncertainties that were faced at the start of the work, which we aimed to address using the methodologies described here. This work should provide a solid foundation for the design and planning of further research in the field.

We have employed robust epidemiological, analytical and qualitative methodologies, as required. By conducting an inception cohort study (as opposed to a prevalence cohort study), we were able to obtain accurate estimates of time to event data on outcomes for this SWHSI patient group; we also obtained a full picture of treatments received over the natural history of the wound. Although a prevalence cohort would have allowed higher recruitment figures, it would have provided far less clarity on crucial outcomes, such as time to healing. We were unable to rely on retrospective extraction of routinely collected data on wound treatments and outcomes, as systematically collected data, especially in the community, are limited. Thus, obtaining robust data, such as we have, requires data collection to be embedded in an appropriately designed primary study from the inception of the wound.

Limitations of the research

Our cohort study was conducted in only two centres in the UK and we therefore acknowledge that practice may vary across different centres and that the prevalence rates observed may not reflect those observed across the UK.

We have noted previously that the generalisability of findings of the cohort study may have been reduced by the need for consent, which removes some of the patient group from the study group. Our cross-sectional survey findings reassured us, however, as there were no major differences in key demographic features, although more wounds in cohort participants were planned to be left open before surgery. Those patients treated with NPWT in the cohort study were found to differ from those who were not, therefore indicating potential treatment selection. Interviews with clinicians helped to explore how NPWT may be allocated; however, this did not provide a definitive explanation for treatment decisions.

The nature of the cross-sectional survey may have resulted in some cases of SWHSIs not being reported, resulting in an underestimation of treated SWHSI prevalence. The number of responses received was as we expected, and so we are confident that the number of missed wounds was low and not systematic, probably due to publicity of the survey and support provided for nurses to complete study activity.

Within the cohort study, 73 wounds (18.6%) did not heal by the end of the study follow-up period. Time to healing was used as the primary outcome, given that this is an important and recommended outcome in wounds research. However, when using this outcome, it is acknowledged that there will inevitably be some participants who do not heal by the end of the follow-up time point. We acknowledge that the lack

of healing data for these participants may have had an impact on the robustness of the findings; however, we expect this to be minimal, given the small number of participants this affected.

To meet the objective of our research programme, we opted to take a broad approach and collected data on a wide range of SWHSIs. This means that we have captured data on the heterogeneity of the wound type, but this also results in more limited data with which to investigate subgroups of SWHSIs in more detail, and this may be the focus of future work.

We present findings on the relative treatment effects of NPWT using observational data, given that there was a lack of RCT data available on relative effects of NPWT on SWHSIs. It is widely acknowledged that experimental data with groups formed by randomisation provide the least biased estimates of treatment effects. We implemented use of advanced adjustment approaches to try and reduce bias as much as possible, for both known (e.g. factors identified as prognostic for wound healing such as wound size, previous wound history or level of tissue involvement) and unknown confounders. However, even with adjustment, there is still the potential for unresolved confounding to affect the results and reduces confidence in them, leading to calls for definitive evidence from a RCT.

The relative treatment effects of NPWT were evaluated only on the healing of SWHSIs and so could not account for other direct effects on HRQoL (e.g. wound management). Again, these limitations may benefit from further assessment in a RCT.

The qualitative interviews conducted as part of this research programme identified a diverse range of views from both patients and clinicians. It is, however, noted that only a limited number of interviews were conducted with both clinicians (12 clinicians comprising seven nurses and five surgeons) and patients, which may limit the conclusions drawn. Interviews with both patients and clinicians continued until data saturation was achieved, thus ensuring comprehensive data. Further qualitative research may, however, be warranted to build on these findings.

Implications for practice

Findings from this research indicate that SWHSIs are relatively common, at least within the Yorkshire and the Humber region, UK (4.1 per 10,000 population), and such wounds frequently arise following colorectal, plastic or vascular surgery.

Data suggest that wounds will demonstrate different healing trajectories. Wounds with a large surface area, contaminated wounds (at the point of surgery) and infection at any time were found to predict slow healing. Furthermore, wound location and patient comorbidity may have an impact on wound healing trajectory.

This research has identified the vast range of treatments in use for SWHSIs and has identified increasing use of NPWT as a treatment during the wound healing pathway (rising from 6% to 29% over the course of approximately 3 years). Despite increasing use of this treatment within the NHS, RCT evidence supporting the use of this treatment for SWHSIs is sparse and of low quality. Our results indicate that NPWT has a negative impact on healing and is not cost-effective. However, as our results are based solely on observational data and, even after thorough adjustment, there may be unresolved confounding, the potential for which may limit confidence in the research findings.

Implications for research

This research signals the importance of, scope of, feasibility of and opportunity for further research on SWHSIs. As is the case across the wound care field, there are few good data on the prognostic factors for healing and on which factors may be amenable to treatment to promote better outcomes. NPWT, as with

other medical devices in wound care, has been adopted widely, with relatively little evidence to support its use. If decision-makers and funders call for definitive evidence derived from a RCT, the design of such a RCT would need to be carefully considered, based on data presented here. The overall population of those with SWHSIs is too heterogeneous for inclusion into a single trial and we would suggest that future research should focus on specific groups. Although people with open surgical wounds after colorectal surgery formed our largest subpopulation, careful engagement with colorectal surgeons and patients would be required for a full trial in this patient population given the difficulties and barriers outlined in the pilot trial.

Careful consideration also needs to be given to the outcomes measured in a full trial. We focused in this research on healing, and maintain, based on the findings of patient interviews, that this is a key outcome for future research. However, it is important to note that if NPWT is not cost-effective for healing, it may still offer worthwhile advantages for patients and health services, which need to be balanced against disbenefits and costs. Impacts of NPWT on outcomes such as infection and reoperation should also be considered, as should patients' view of the treatment. The type of patient group recruited and the outcomes of interest will all influence the duration of follow-up of any planned study.

In terms of how NPWT is evaluated, investigators must carefully consider the level of pragmatism that will be employed in any future trial.[88] There is a range of NPWT machines available for use, including those that use gauze dressings, foam dressings, single-use machines and repeat-use devices. There is no good evidence of any differences in the clinical effectiveness or cost-effectiveness of different machines, thus the trial design choice of whether to mandate use of a specific machine or allow sites to use their current NPWT provision will be down to the investigator. Although use of a single device will reduce the 'noise' in an evaluation, it is likely to limit the appeal of involvement to potential sites, as well as the potential generalisability of data. Thus, a pragmatic approach will arguably reflect effectiveness findings as they might be seen in the NHS and also make a large study more feasible. The same is true in terms of NPWT usage protocols (e.g. levels of pressure and cycle length), as well as how NPWT is used as part of the treatment pathway. The more prescriptive a future study is, the less pragmatic and feasible it may become but there would be less 'noise' in the findings.

Similar intervention issues also need to be considered in terms of the comparator in any future study. We know that SWHSI patients receive multiple dressings and there is no high-quality evidence that one dressing type is better than another for SWHSIs or any other complex wound type.[89] Use of a specific dressing type, such as hydrofibre, could be explored in a trial, but large deviations from use of a single dressing over the duration of a patient's SWHSI would be expected.

Blinded outcome assessment is crucial for studies with subjective outcomes, such as healing and infection.[90] We have demonstrated here that blinded outcome assessment in a NPWT trial in people with SWHSIs is possible, but protocols and equipment that ensure high-quality images are required. We also note the importance of taking photographs beyond the point at which the unblinded investigator considers a wound healed, so that a later healing date can be recorded by a blinded assessor should they disagree with the unblinded assessment.

Careful consideration should be given to use of data collection via text message in future trials investigating treatments for SWHSIs. Although this method has been identified as a simple, inexpensive, valid and acceptable method of data collection in previous studies,[91–93] our pilot, feasibility RCT suggested that data collection via text messaging was more successful in younger patients (respondents were, on average, almost 10 years younger than non-respondents). Other studies, which have successfully used text messaging for data collection have also included younger populations ranging from 22.0 (SD 1.47) years[93] to 44.0 (SD 13.4) years of age.[91] Future trials of SWHSI treatments should therefore consider the demographics of the target patient population prior to inclusion of such methods, to ensure that if utilised, data collection is likely to be successful and so provide sufficient data for analysis.

Questions for future research

We consider key research questions raised by this programme of research to be:

- Which treatments are clinically effective and cost-effective for SWHSIs for all patients or for particular patient subgroups?
- Can particular prognostic factors predict time to healing of SWHSIs?
- Do psychosocial interventions have the potential to improve quality of life in people with hard-to-heal SWHSIs?
- What are the current care pathways for people with SWHSIs, how do they vary nationally and can they be optimised to improve efficiencies and outcomes?
- Is the development of evidence-based practice guidelines for the management of SWHSI patients possible, in order to benefit and inform patients, clinicians and NHS commissioning?

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Ian Chetter (Professor, Vascular Surgery) was the chief investigator; led the research programme and chaired the Programme Management Group; and led workstreams 1 and 4.

Catherine Arundel (Research Fellow, Health Research and Trials) contributed to the design, conduct, analysis, interpretation and reporting of workstream 4.

Kerry Bell (Statistician, Health Research and Trials) undertook the statistical analysis and interpretation for workstream 1.

Hannah Buckley (Statistician, Health Research and Trials) undertook the statistical analysis and interpretation and advised on conduct for workstream 1, and advised on the design, conduct and statistical analysis for workstream 4.

Karl Claxton (Professor, Economics) oversaw all aspects of workstream 2 (design, conduct, analysis, interpretation and reporting).

Belen Corbacho Martin (Health Economist, Health Research and Trials) undertook the economic analysis and interpretation for workstream 4.

Nicky Cullum (Professor, Nursing) contributed to the conception, design, conduct, analysis and reporting of all workstreams and provided input to the programme management and strategy.

Jo Dumville (Senior Lecturer, Health Sciences) contributed to the design, conduct, analysis and reporting of all workstreams.

Caroline Fairhurst (Statistician, Health Research and Trials) undertook the statistical analysis for workstream 4.

Eileen Henderson (Assistant to Medical Director, NHS Needs) ensured that all workstreams met NHS needs and were relevant to NHS decision uncertainty.

Karen Lamb (Research Co-ordinator, Wound Research) contributed to the design and conduct of workstream 1 and the design, conduct, analysis and reporting of workstream 4.

Judith Long (Project Manager, Vascular Surgery Research) led and undertook qualitative data collection, analysis and reporting for workstream 4.

Dorothy McCaughan (Research Fellow, Health Research) led and undertook qualitative data collection, analysis and reporting for workstream 3.

Elizabeth McGinnis (Research Fellow, Wound Research) contributed to the design, conduct, analysis and reporting of workstreams 1 and 4.

Angela Oswald (Tissue Viability Matron, Wound Care and Research) provided clinical leadership and expertise in relation to NPWT.

Pedro Saramago Goncalves (Research Fellow, Health Economics) undertook the analyses in workstream 2 and contributed to the design, conduct, interpretation and reporting of workstream 2.

Laura Sheard (Senior Research Fellow, Health Research) undertook qualitative data collection and analysis for workstream 3.

Marta O Soares (Senior Research Fellow, Health Economics) supervised all aspects of workstream 2 (design, conduct, analysis, interpretation and reporting) and contributed to the design, conduct, analysis and reporting of workstreams 1 and 4.

Nikki Stubbs (Clinical Pathway Lead, Wound Research) contributed to the design, conduct, analysis and reporting of workstreams 1 and 4.

David Torgerson (Professor, Health Research and Trials) contributed to the management of the programme of work and the design, conduct, analysis, interpretation and reporting of workstreams 1 and 4.

Nicky Welton (Reader, Statistics and Health Economic Modelling) oversaw the design, interpretation and reporting of the analyses in workstream 2.

Publications

Workstream 1

Chetter C, Oswald A, Fletcher M, Dumville J, Cullum N. A survey of patients with surgical wounds healing by secondary intention; an assessment of prevalence, aetiology, duration and management. *J Tissue Viability* 2017;**26**:103–7.

Chetter I, Oswald AV, McGinnis E, Stubbs N, Arundel C, Buckley H, *et al.* Patients with surgical wounds healing by secondary intention: a prospective, cohort study. *Int J Nurs Stud* 2019;**89**:62–71.

Workstream 2

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Workstream 3

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McCaughan D, Sheard L, Dumville J, Cullum N. Nurses' and surgeons' views and experiences of surgical wounds healing by secondary intention: a qualitative study. *J Clin Nurs* 2020;**29**:2557–71.

Workstream 4

Arundel C, Buckley H, Clarke E, Cullum N, Dixon S, Dumville J, *et al.* Negative pressure wound therapy versus usual care for surgical wounds healing by secondary intention (SWHSI trial): study protocol for a randomised controlled pilot trial. *Trials* 2016;**17**:535.

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Long J, Meethan K, Arundel C, Clarke E, Firth A, Sylvester M, Chetter I. Exploring feedback from research nurses in relation to the design and conduct of a randomised controlled trial of wound care treatments: a sequential, dependent, mixed-methods study. *J Tissue Viability* 2020; in press.

Data-sharing statement

All data requests should be submitted to the corresponding author for consideration. Access to anonymised data may be granted following review.

Patient data

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 it is 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.

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Appendix 1 Cross-sectional survey publication

Chetter C, Oswald AV, Dumville JC, Cullum NA. A survey of patients with surgical wounds healing by secondary intention; an assessment of prevalence, aetiology, duration and management. *J Tissue Viability* 2017;**26**:103–7.[16]

Appendix 2 Cohort study publication

Chetter I, Oswald AV, McGinnis E, Stubbs N, Arundel C, Buckley H, *et al.* Patients with surgical wounds healing by secondary intention: a prospective, cohort study. *Int J Nurs Stud* 2019;**89**:62–71.[17]

Appendix 3 Cross-sectional survey data collection instrument

A survey of Surgical Wounds Healing by Secondary Intention (SWHSI) and their care: data capture form

Date of completion

DD MM YYYY

140 ☐☐ / ☐☐ / ☐☐☐☐

Section 1: Details of healthcare worker completing this form

1. Your Job title

☐ Community nurse ☐ Practice nurse ☐ Specialist nurse (Community) ☐ Podiatrist

☐ Hospital-based nurse (ward) ☐ Hospital-based nurse (outpatient)

☐ Other:_____

Section 2: Patient details

Patient's age ☐☐☐ years Patient's gender: Male ☐ Female ☐

Ethnicity:

White British	White Irish	White Other	Black African	Black Caribbean	Black Other
☐	☐	☐	☐	☐	☐

Asian Indian	Asian Pakistani	Asian Bangladeshi	Asian Other	White and black Caribbean
☐	☐	☐	☐	☐

White and black African	White and Asian	Other mixed background	Chinese	Other
☐	☐	☐	☐	☐

2. Where is this patient currently being treated? (Tick one box or all that apply)

CASTLEHILL: ☐ Hospital outpatient ☐ Hospital ward

If selected, give name and number of ward:

_____

HULL ROYAL INFIRMARY: ☐ Hospital outpatient ☐ Hospital ward

If selected, give name and number of ward:

_____

COMMUNITY: ☐ Podiatry clinic ☐ Nursing/care home ☐ GP practice

☐ Own/another's home ☐ Other Community clinic

☐ Other_____

Section 3: Wound details

3. How many surgical wounds healing by secondary intention (SWHSI) does this patient have?

1 2 3 4 5 6

IF THE PATIENT HAS MORE THAN ONE SWHSI PLEASE ANSWER THE FOLLOWING QUESTIONS FOR THE WOUND THAT YOU THINK IS THE LARGEST

4. How long has the patient had this SWHSI?

☐☐ weeks OR ☐☐ days

5. What type of surgery lead to this SWHSI?

☐ Orthopaedic ☐ Colorectal ☐ Breast ☐ Neurosurgery

☐ Trauma ☐ Plastics ☐ Cardiothoracic ☐ Oral and maxillofacial surgery

☐ Vascular ☐ Urology ☐ Upper GI ☐ Obs/gynaecological

☐ Other (please give details)_____ ☐ Don't know

6. Please also record the name of the specific type of surgery if possible

(e.g. hernia repair, c-section, pilonidal sinus) _____

7. If possible please record the date of original surgery that lead to the SWHSI:
Day ☐☐ **Month** ☐☐ **Year** ☐☐

8. Was this surgery: ☐ Emergency? ☐ Elective? ☐ Don't know?

9. Was the SWHSI a result of:

☐ A planned healing by secondary intention

☐ A surgically closed wound — **fully** broken open (**dehisced**) due to (for e.g.) infection or poor healing

☐ A surgically closed wound – **partially** broken open (**partially dehisced)**

☐ A surgically closed wound which was then **surgically opened** to become a surgical wound healing by secondary intention

☐ Other (please give details): _____

☐ Don't know

10. In your opinion, did infection significantly contribute to the development of the SWHSI?

☐ Yes ☐ No ☐ Don't Know

11. Is this patient receiving antibiotic therapy in relation to their SWHSI?

☐ Yes ☐ No ☐ Don't Know

12. If this wound was surgically closed and broke open (is a dehisced wound), please record how long after surgery the wound dehisced and where the patient was located when this occurred?

☐☐☐ Days

☐ In hospital ☐ In the community ☐ Don't know

13. What treatments is this patient's SWHSI currently receiving?

☐ Dressings

If selected, please indicate frequency of dressing changes = ☐☐ per day/week

☐ Negative pressure wound therapy

If selected, please indicate frequency of application = ☐☐ applications per day/week

☐ Other If other, please state which.

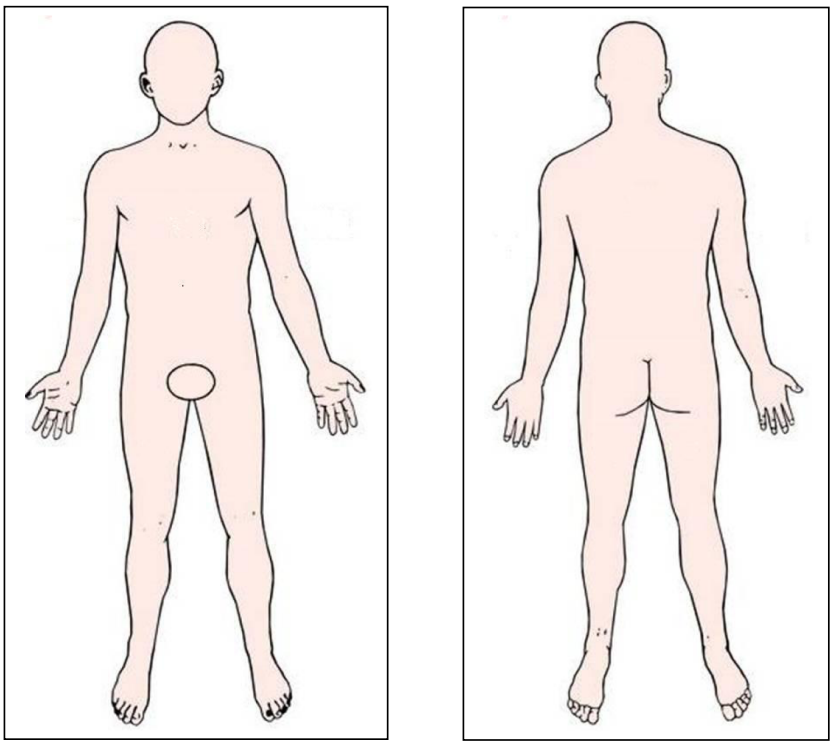
If selected, please indicate frequency of application = ☐☐ per day/week

14. Is this patient receiving treatment for their SWHSI elsewhere?

☐ Yes ☐ No ☐ Don't Know

If yes, please state where: _____

15. On the picture below, please draw and label clearly the location of all current SWHSI for this patient.



Please add any comments you may have regarding data collection in this patient population

Appendix 4 Cohort results: adjusted Cox proportional hazards model results for time to wound healing

	Hazard ratio (95% CI)	*p*-value
Diabetes mellitus present (vs. not)	0.81 (0.61 to 1.08)	0.16
Female (vs. male)	0.97 (0.77 to 1.22)	0.80
CVD present (vs. not)	1.03 (0.81 to 1.22)	0.79
Infection at any point (vs. not)	0.65 (0.51 to 0.84)	< 0.01
Baseline area above median (vs. below)	0.46 (0.36 to 0.59)	< 0.01
Reason for SWHSI[a]		
Planned due to infection	1.35 (0.96 to 1.89)	0.29
Planned for other reason	0.43 (0.10 to 1.76)	
Dehisced	1.16 (0.68 to 1.97)	
Partially dehisced	1.24 (0.89 to 1.75)	
Surgically opened	0.86 (0.46 to 1.61)	
Contamination level of surgery[b]		
Clean-contaminated	0.75 (0.46 to 1.25)	0.04
Contaminated	0.52 (0.32 to 0.86)	
Dirty	0.56 (0.36 to 0.89)	

CVD, cardiovascular disease.
a Reference category = planned due to being unable to approximate wound edges.
b Reference category = clean.

Appendix 5 Cost-effectiveness study publication

Saramago P, Claxton K, Welton NJ, Soares M. Bayesian econometric modelling of observational data for cost-effectiveness analysis: establishing the value of negative pressure wound therapy in the healing of open surgical wounds. *J R Statist Soc A* 2020; in press.[28]

Appendix 6 Search strategies for identification of external evidence to supplement cohort data

Search strategy: dressings

We searched the following electronic databases:

- Cochrane Wounds Group Specialised Register (date range searched: inception to 10 January 2012)
- Cochrane Central Register of Controlled Trials (date range searched: inception to The Cochrane Library, 2012, Issue 1)
- Ovid MEDLINE (date range searched: 1946 to 10 January 2012)
- Ovid EMBASE (date range searched: 1974 to 10 January 2012)
- EBSCO*host* Cumulative Index to Nursing and Allied Health Literature (CINAHL) (date range searched: 1982 to 10 January 2012).

Date searched: 10 January 2012.

Ovid MEDLINE search strategy

1. MeSH descriptor: [Bandages] explode all trees
2. MeSH descriptor: [Hydrogels] explode all trees
3. MeSH descriptor: [Alginates] explode all trees
4. (dressing* or hydrocolloid* or alginate* or hydrogel* or foam or bead or film or films or tulle or gauze or non-adherent or non adherent):ti,ab,kw (Word variations have been searched)
5. or/1-4
6. exp Surgical Wound Infection/
7. exp Surgical Wound Dehiscence/
8. (surg* adj5 infect*).tw.
9. (surg* adj5 wound*).tw.
10. (surg* adj5 site*).tw.
11. (surg* adj5 incision*).tw.
12. (surg* adj5 dehisc*).tw.
13. (wound* adj5 dehisc*).tw.
14. (wound* adj5 infect*).tw.
15. (wound adj5 disrupt*).tw.
16. wound complication*.tw.
17. or/6-16
18. (intent* or second* or heal* or complic*).tw.
19. ((open* or clos*) adj5 wound*).tw.
20. 25 or 26
21. 24 and 27
22. 12 and 28
23. randomised controlled trial.pt.
24. controlled clinical trial.pt.
25. randomi?ed.ab.
26. placebo.ab.
27. clinical trials as topic.sh.
28. randomly.ab.
29. trial.ti.

30. exp animals/ not humans.sh.
31. 29 and 37

Search strategy: cohort studies

We searched the following electronic databases:

- Ovid MEDLINE (date range searched: 1946 to 31 December 2013)
- Ovid EMBASE (date range searched: 1974 to 31 December 2013)
- EBSCO*host* CINAHL (date range searched: 1982 to 31 December 2013).

Date searched: 31 December 2013.

Ovid MEDLINE search strategy

1. exp Surgical Wound/
2. exp Surgical Wound Dehiscence/
3. (surg* adj5 wound*).ti,ab.
4. (surg* adj5 site*).ti,ab.
5. (surg* adj5 incision*).ti,ab.
6. (surg* adj5 dehisc*).ti,ab.
7. 1 or 2 or 3 or 4 or 5 or 6
8. (intent* or second*).ti,ab.
9. ((open* or clos*) adj5 wound*).ti,ab.
10. 8 or 9
11. 7 and 10
12. SWHSI.ti,ab.
13. 11 or 12
14. epidemiologic studies/
15. exp Case-Control Studies/
16. exp Cohort Studies/
17. case control.ti,ab.
18. (cohort adj (study or studies)).ti,ab.
19. Cohort analy$.ti,ab.
20. (Follow up adj (study or studies)).ti,ab.
21. (observational adj (study or studies)).ti,ab.
22. Longitudinal.ti,ab.
23. Retrospective.ti,ab.
24. Cross sectional.ti,ab.
25. Cross-sectional studies/
26. 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25
27. 13 and 26
28. exp Wound Healing/
29. (wound* adj3 heal*).ti,ab.
30. 28 or 29
31. 27 and 30
32. limit 27 to ed=19460101-20131231
33. limit 31 to ed=19460101-20131231

Search strategy: economic and health utility studies

We searched the following electronic databases:

- Ovid MEDLINE (date range searched: 1946 to 31 December 2013)
- Ovid EMBASE (date range searched: 1974 to 31 December 2013)
- EBSCO*host* CINAHL (date range searched: 1982 to 31 December 2013)
- NHS Economic Evaluation Database (date range searched: inception to 2013, Issue 12).

Date searched: 31 December 2013.

Ovid MEDLINE search strategy

1. exp Surgical Wound/
2. exp Surgical Wound Dehiscence/
3. (surg* adj5 wound*).ti,ab.
4. (surg* adj5 site*).ti,ab.
5. (surg* adj5 incision*).ti,ab.
6. (surg* adj5 dehisc*).ti,ab.
7. 1 or 2 or 3 or 4 or 5 or 6
8. (intent* or second*).ti,ab.
9. ((open* or clos*) adj5 wound*).ti,ab.
10. 8 or 9
11. 7 and 10
12. SWHSI.ti,ab.
13. 11 or 12
14. ECONOMICS/
15. "Costs and Cost Analysis"/
16. "Cost Allocation"/
17. Cost-Benefit Analysis/
18. "Cost Control"/
19. "Cost Savings"/
20. "Cost of Illness"/
21. "Cost Sharing"/
22. "Deductibles and Coinsurance"/
23. Medical Savings Accounts/
24. Health Care Costs/
25. Direct Service Costs/
26. Drug Costs/
27. Employer Health Costs/
28. Hospital Costs/
29. Health Expenditures/
30. Capital Expenditures/
31. "Value of Life"/
32. exp ECONOMICS, HOSPITAL/
33. exp Economics, Medical/
34. Economics, Nursing/
35. Economics, Pharmaceutical/
36. exp "Fees and Charges"/
37. exp BUDGETS/
38. (low adj cost).mp.
39. (high adj cost).mp.
40. (health?care adj cost$).mp.

41. (fiscal or funding or financial or finance).tw.
42. (cost adj estimate$).mp.
43. (cost adj variable).mp.
44. (unit adj cost$).mp.
45. (economic$ or pharmacoeconomic$ or price$ or pricing).tw.
46. 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 4
47. 13 and 46

Appendix 7 Patient interviews paper

McCaughan D, Sheard L, Cullum N, Dumville J, Chetter I. Patient's perceptions and experiences of living with a surgical wound healing by secondary intention: a qualitative study. *Int J Nurs Stud* 2018;**77**:29–38.[40]

Appendix 8 Nurses' and surgeons' views and experiences of SWHSIs: a qualitative study

McCaughan D, Sheard L, Dumville J, Cullum N. Nurses' and surgeons' views and experiences of surgical wounds healing by secondary intention: a qualitative study. *J Clin Nurs* 2020;**29**:2557–71.[44]

Appendix 9 Patient topic guide for qualitative interviews

- Ask for brief details about age, occupation, ethnicity, partner, children, etc., to frame the interview.
- Can you tell me a little bit about yourself and how you came to have this wound? (Explore important aspects further.)
- How has this wound impacted on your daily life?
- From answer to above question, what factors have affected you most and why? (Explore important aspects further.)
- What effect has the wound had on your relationship with your immediate family/partner/friends?
- How do you feel about the treatment you have received in connection with your wound? How could this have been improved?
- How do you feel about the interactions you have had with health-care professionals? How could this have been improved?
- Any other aspects that have not already been discussed or you would like to expand on?

Appendix 10 Health-care professional topic guide for qualitative interviews

- Could you please tell me about your clinical role in the care of patients with surgical wounds that are difficult or slow to heal?
- What are your experiences of caring for patients with wounds which are difficult or slow to heal?
  (*Probe: approximately how often do you see patients with surgical wounds which are slow to heal? Why do you think wounds do not heal or heal very slowly in some patients? What are the main issues for you as a clinician? Who looks after these patients after discharge from hospital?*)
- What are the aspects of wound management that need to be considered when choosing treatment options for patients with hard-to-heal surgical wounds?
  (*Probe: management of pain and exudates; frequency of dressing changes; availability of clinical staff with appropriate skills and training; patient needs and convenience.*)
- What would you consider to be the desirable performance characteristics of treatment options?
  (*Probe: symptom management; wound cleaning/debridement; signs of healing and sustainability; patient acceptability; cost-effectiveness.*)
- What kinds of outcomes might be achieved for patients with surgical wounds that are difficult to heal, and how might these vary for different types of wounds and patient subgroups?
- From your perspective as a health-care professional, what are the challenges of looking after a patient with a surgical wound that is difficult to heal?
  (*Probe: patient adherence to treatment; dealing with patients' feelings about their wound; own feelings as a health-care professional when wound is not healing.*)
- Are there any other aspects that have not already been discussed or that you would like to expand on?

Appendix 11 Analysis of data using the framework approach

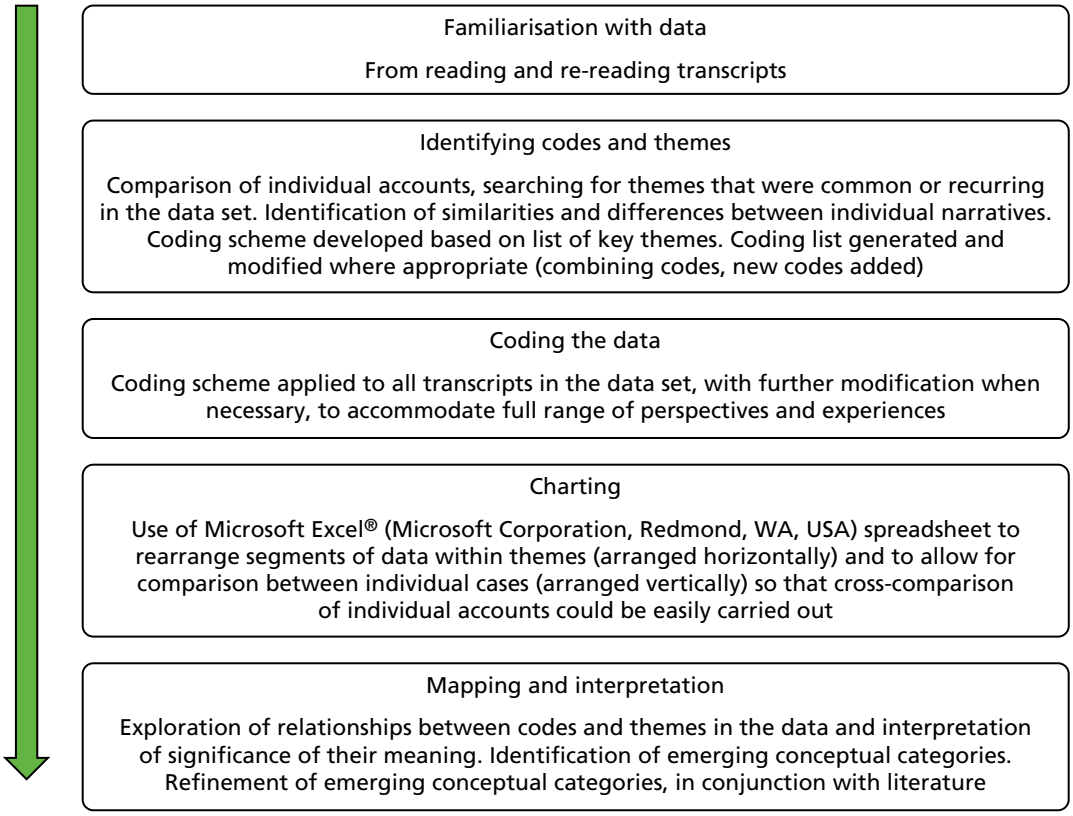


Illustration of thematic analysis of the data set

Recurrent themes identified to constitute framework for analysis, including:

- initial reactions to the open surgical wound healing by secondary intention
- perceptions of wound healing
- expressions of hope for healing
- impact of wound symptoms on daily life
- psychosocial impacts of open surgical wound and mental health
- driving and transport
- employment, finances, state benefits
- impact of open surgical wound on relationships with others and social activities
- views of different treatments for open surgical wounds
- views of NHS service provision related to care of the open surgical wound, including shortfalls in care delivery
- systematic application of coding framework to transcriptions and identification of 'negative' cases
- development of 'higher-level' themes, for example patients' perceptions of changing family roles; shifting sense of self/modified self-image; coping/not coping with feelings of social isolation
- interpretation of 'higher-level' themes, linked to theoretical perspectives in the literature, for example concepts of 'biographical disruption' (Bury[94]) and 'loss of self' (Charmaz[95])

Appendix 12 Pilot feasibility randomised controlled trial: protocol paper

Arundel C, Buckley H, Clarke E, Cullum N, Dixon S, Dumville J, *et al.* Negative pressure wound therapy versus usual care for surgical wounds healing by secondary intention (SWHSI trial): study protocol for a randomised controlled pilot trial. *Trials* 2016;**17**:535.[56]

Appendix 13 Pilot feasibility randomised controlled trial: results paper

Arundel C, Fairhurst C, Corbacho-Martin B, Buckley H, Clarke E, Cullum N, *et al.* Pilot feasibility randomized clinical trial of negative-pressure wound therapy versus usual care in patients with surgical wounds healing by secondary intention. *BJS Open* 2018;**2**:99–111.[57]

Appendix 14 Pilot feasibility randomised controlled trial: nurse participation in the SWHSI pilot feasibility trial

Long J, Meethan K, Arundel C, Clarke E, Firth A, Sylvester M, Chetter I. Exploring feedback from research nurses in relation to the design and conduct of a randomised controlled trial of wound care treatments: a sequential, dependent, mixed-methods study. *J Tissue Viability* 2020; in press.[96]

Appendix 15 Pilot and feasibility randomised controlled trial: wound pain (text message) by treatment group and time point

		Treatment group		
Time point	Weekly text message pain scores	NPWT ($N = 10$)	Usual care ($N = 10$)	Total ($N = 20$)
Week 1	*n* received/*n* sent (%)	6/13 (46.2)	9/13 (69.2)	15/26 (57.7)
	Mean (SD)	5.0 (1.9)	3.3 (3.4)	4.0 (3.0)
	Median (minimum, maximum)	5 (3, 8)	4 (0, 8)	5 (0, 8)
Week 2	*n* received/*n* sent (%)	10/13 (76.9)	9/12 (75.0)	19/25 (76.0)
	Mean (SD)	4.9 (3.2)	3.0 (3.0)	4.0 (3.2)
	Median (minimum, maximum)	6 (0, 9)	3 (0, 9)	3 (0, 9)
Week 3	*n* received/*n* sent (%)	9/12 (75.0)	8/10 (80.0)	17/22 (77.3)
	Mean (SD)	3.4 (2.8)	2.6 (3.0)	3.1 (2.8)
	Median (minimum, maximum)	3 (0, 8)	1.5 (0, 7)	2 (0, 8)
Week 4	*n* received/*n* sent (%)	9/11 (81.8)	9/9 (100.0)	18/20 (90.0)
	Mean (SD)	3.9 (3.0)	2.2 (2.4)	3.1 (2.8)
	Median (minimum, maximum)	3 (0, 8)	1 (0, 6)	3 (0, 8)
Week 5	*n* received/*n* sent (%)	10/11 (90.9)	6/8 (75.0)	16/19 (84.2)
	Mean (SD)	3.6 (3.2)	2.2 (2.5)	3.1 (3.0)
	Median (minimum, maximum)	2.5 (0, 9)	1.5 (0, 7)	2 (0, 9)
Week 6	*n* received/*n* sent (%)	9/11 (81.8)	7/8 (87.5)	16/19 (84.2)
	Mean (SD)	2.6 (3.5)	2.7 (2.9)	2.6 (3.1)
	Median (minimum, maximum)	0 (0, 8)	1 (0, 8)	1 (0, 8)
Week 7	*n* received/*n* sent (%)	7/8 (87.5)	7/7 (100.0)	14/15 (93.3)
	Mean (SD)	3.6 (3.9)	2.1 (2.7)	2.9 (3.3)
	Median (minimum, maximum)	2 (0, 8)	1 (0, 6)	1 (0, 8)
Week 8	*n* received/*n* sent (%)	6/7 (85.7)	5/7 (71.4)	11/14 (78.6)
	Mean (SD)	3.7 (3.5)	1.4 (2.1)	2.6 (3.0)
	Median (minimum, maximum)	3.5 (0, 8)	1 (0, 5)	1 (0, 8)
Week 9	*n* received/*n* sent (%)	5/7 (71.4)	7/7 (100.0)	12/14 (85.7)
	Mean (SD)	2.8 (2.6)	1.4 (1.9)	2.0 (2.2)
	Median (minimum, maximum)	2 (0, 6)	1 (0, 5)	1 (0, 6)
Week 10	*n* received/*n* sent (%)	5/7 (71.4)	6/6 (100.0)	11/13 (84.6)
	Mean (SD)	3.0 (2.1)	1.2 (1.6)	2.0 (0.2)
	Median (minimum, maximum)	3 (0, 5)	0.5 (0, 4)	2 (0, 5)
Week 11	*n* received/*n* sent (%)	5/5 (100.0)	7/7 (100.0)	12/12 (100.0)
	Mean (SD)	3.2 (2.4)	0.9 (1.2)	1.8 (2.1)
	Median (minimum, maximum)	3 (0, 6)	0 (0, 3)	1.5 (0, 6)
Week 12	*n* received/*n* sent (%)	5/5 (100.0)	6/6 (100.0)	11/11 (100.0)
	Mean (SD)	2.4 (2.4)	1.0 (1.5)	1.6 (2.0)
	Median (minimum, maximum)	1 (0, 5)	0.5 (0, 4)	1 (0, 5)

Appendix 16 Pilot feasibility randomised controlled trial: physical and mental composite scale scores derived from the Short Form questionnaire-12 items by treatment group and time point

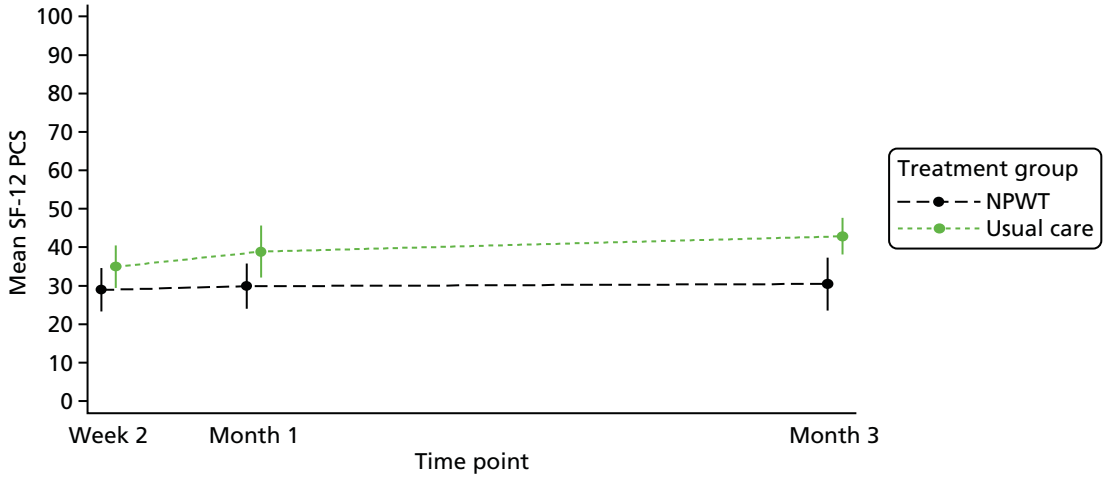


FIGURE 7 Physical composite scale scores derived from the SF-12 by randomised group across time.

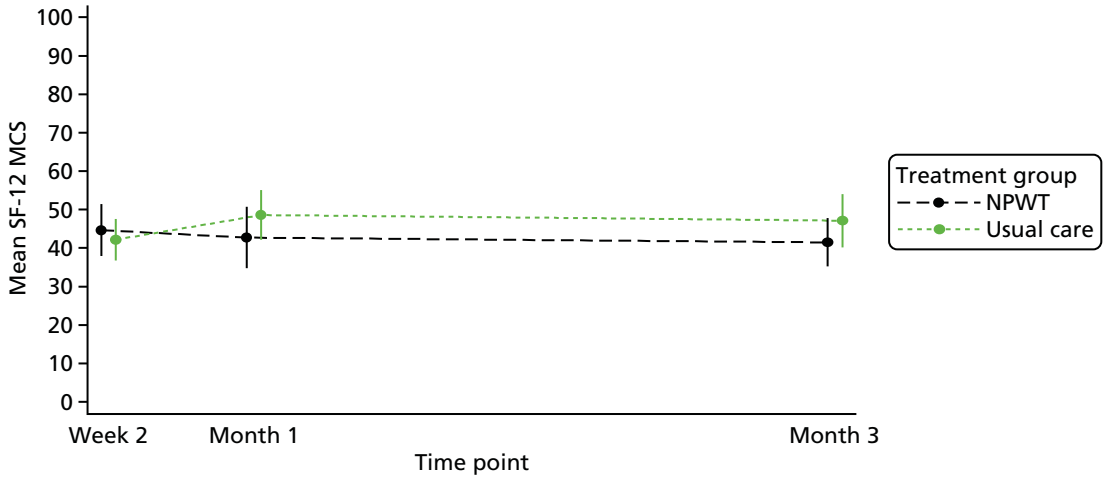


FIGURE 8 Mental composite scale scores derived from the SF-12 by randomised group across time.

Appendix 17 Unit costs of health-care services

Item	Unit of measurement	Unit cost (£)	Additional notes	Source
Hospital outpatient (doctor)	Per clinic visit	131.99	Based on average of total outpatient attendances	Department of Health and Social Care[61]
Hospital outpatient (nurse)	Per clinic visit	70.87		Department of Health and Social Care[61]
Day case	Per admission	720.78	Based on average of total day-case attendances	Department of Health and Social Care[61]
GP visit at general practice	Per patient contact (surgery), lasting 11.7 minutes	44.00		Curtis and Burns[62]
GP visit at home	Per home visit (11.4 minutes) plus 12 minutes of travel time	88.92		Curtis and Burns[62]
Nurse visit at general practice	Per 15.5-minute appointment (based on £43.00 per hour)	11.11		Curtis and Burns[62]
Nurse visit at home	Per home visit (lasting 25 minutes) plus 12 minutes of travel time	23.33	Based on average of most commonly reported	Department of Health and Social Care;[61] Curtis and Burns[62]
Inpatient admission	Per night	359.13	Based on elective inpatient excess bed-days	Curtis and Burns[62]

Appendix 18 Completion and missingness of EQ-5D questionnaires

	Completed EQ-5D, *n* (%)		Missing EQ-5D (≥ 1 dimension missing), *n* (%)	
Time point	NPWT (*N* = 19)	Usual care (*N* = 21)	NPWT (*N* = 19)	Usual care (*N* = 21)
Baseline	15 (78.9)	21 (100.0)	4 (21.1)	0 (0.0)
3 months	14 (73.7)	15 (71.4)	5 (26.3)	6 (28.6)

Appendix 19 Proportion reporting EQ-5D-3L levels 1–3 by dimension, treatment group and time point

		Time point							
		Baseline				3 months			
		NPWT[b]		Usual care[c]		NPWT[b]		Usual care[c]	
EQ-5D scale	Health state severity[a]	*n*	%	*n*	%	*n*	%	*n*	%
Mobility	No problems	5	31.25	6	28.57	3	20.00	6	40.00
	Some problems	8	50.00	14	66.67	12	80.00	9	60.00
	Unable/extreme problems	3	18.75	1	4.76	0	0.00	0	0.00
	Number reporting any problems	11	68.75	15	71.43	12	80	9	60.00
Self-care	No problems	9	56.25	17	80.95	8	53.33	11	73.33
	Some problems	7	43.75	4	19.05	7	46.67	4	26.67
	Unable/extreme problems	0	0.00	0	0.00	0	0.00	0	0.00
	Number reporting any problems	7	43.75	4	19.05	7	46.7	4	26.67
Usual activities	No problems	3	18.75	6	28.57	2	13.33	8	53.33
	Some problems	4	25.00	11	52.38	10	66.67	6	40.00
	Unable/extreme problems	9	56.25	4	19.05	3	20.0	1	6.67
	Number reporting any problems	13	81.25	15	71.43	13	86.7	7	46.67
Pain	No problems	4	25.00	5	23.81	2	13.33	10	66.67
	Some problems	7	43.75	13	61.90	10	66.67	5	33.33
	Unable/extreme problems	5	31.25	3	14.29	3	20.0	0	0.00
	Number reporting any problems	12	75	16	76.19	13	86.7	5	33.33
Anxiety	No problems	11	68.75	14	66.67	9	60.00	12	80.00
	Some problems	4	25.00	5	23.81	5	33.33	2	13.33
	Unable/extreme problems	1	6.25	2	9.52	1	6.67	1	6.67
	Number reporting any problems	5	31.25	7	33.33	6	40	3	20.00

a Level 1, no problems; level 2, some problems; level 3, unable/extreme problems.
b NPWT: percentages calculated according to valid observations (baseline = 16, 3 months = 14).
c Usual care: percentages calculated according to valid observations (baseline = 21, 3 months = 15).

EME
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