Surgical Management of Pressure Ulcers: The SIPS Study

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Details of Sponsor

Research & Innovation
University Hospitals Bristol NHS Foundation Trust
Education & Research Centre, Level 3
Upper Maudlin Street
Bristol, BS2 8AE
Tel: 0117 342 0233
Email: research@uhbristol.nhs.uk

Chief Investigators & Research Team Contact Details

Co-Chief Investigator and Professor of Health Services Research
Professor Barnaby Reeves
Bristol Trials Centre (Bristol Royal Infirmary Hub), University of Bristol
Bristol Royal Infirmary
Bristol, BS2 8HW

Tel: 0117 342 3143
Email: barney.reeves@bristol.ac.uk

Co-Chief Investigator and Professor of Applied Health Research
Dr Jo Dumville
Division of Nursing, Midwifery & Social Work
Faculty of Biology, Medicine and Health
University of Manchester
Room 5.318: Jean McFarlane Building,
Oxford Road, Manchester, M13 9PL

Tel: 0161 306 7830 Mobile: 07763 187 130
Email: jo.dumville@manchester.ac.uk

Research Fellow & Co-Applicant
Dr Ross Atkinson
Division of Nursing, Midwifery & Social Work
Faculty of Biology, Medicine and Health
University of Manchester
Room 5.332, Jean McFarlane Building,
Oxford Road, Manchester M13 9PL

Tel: 0161 306 7661 Mobile: 07737 996 255
Email: ross.atkinson@manchester.ac.uk

Advanced Nurse Practitioner in Tissue Viability & Co-Applicant
Ms Louise O'Connor
Manchester University NHS Foundation Trust
Oxford Road
Manchester
M13 9WL

Tel: 0161 701 7114 / 0161 291 2746
Email: Louise.OConnor2@mft.nhs.uk

Senior Research Fellow & Co-Applicant
Dr Maria Pufulete
Bristol Trials Centre (Bristol Royal Infirmary Hub), University of Bristol
Bristol Royal Infirmary
Bristol, BS2 8HW

Tel: 0117 342 4195
Email: maria.pufulete@bristol.ac.uk

Professor of Nursing & Co-Applicant
Professor Nicky Cullum
Division of Nursing, Midwifery & Social Work
Faculty of Biology, Medicine and Health
University of Manchester
Jean McFarlane Building, Oxford Road,
Manchester, M13 9PL
Tel: 0161 306 7779
Email: nicky.cullum@manchester.ac.uk

Senior Clinical Lecturer & Co-Applicant
Dr Jason Kin Fai Wong
Blond McIndoe Laboratories
Faculty of Medical and Human Sciences
Room 3.100, Stopford Building
Oxford Road, Manchester
M13 9PT
Tel:
Email: jason.k.wong@manchester.ac.uk

Lecturer in Community Nursing & Co-Applicant
Dr Una Adderley
School of Healthcare
Faculty of Medicine and Health
Baines Building
University of Leeds, Leeds, LS2 9JT
Tel:0113 343 123
Email: una.adderley@yhahsn.com

Research Fellow & Co- Applicant
Dr Jess Harris
Bristol Trials Centre (Bristol Royal Infirmary Hub), University of Bristol
Bristol Royal Infirmary
Bristol, BS2 8HW

Tel: 0117 342 2624
Email: jessica.harris@bristol.ac.uk

GP, Reader, NIHR Post-Doctoral Fellow & Co-Applicant
Dr Matthew Ridd
Population Health Sciences, University of Bristol
Office 1.06, Canynge Hall,
39 Whatley Road, Bristol BS8 2PS

Tel: 0117 331 4557
Email: m.ridd@bristol.ac.uk

Patient and Public Representative & Co-Applicant
Mr James Johnson

Tel:
Email: blueredblue83@gmail.com

Consultant Hand & Plastic Surgeon, NIHR Postdoctoral Fellow & Co-Applicant
Mr Jeremy Rodrigues, Stoke Mandeville Hospital & Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences
Mandeville Road, Bucks HP21 8AL
Email: j.n.rodrigues@doctors.org.uk

Study Manager
Miss Madeleine Clout
Bristol Trials Centre (Bristol Royal Infirmary Hub), University of Bristol
Bristol Royal Infirmary
Bristol, BS2 8HW

Tel: 0117 342 2526
Email: madeleine.clout@bristol.ac.uk

Study Manager
Dr Abby O'Connell
Bristol Trials Centre (Bristol Royal Infirmary Hub), University of Bristol
Bristol Royal Infirmary
Bristol, BS2 8HW

Tel: 0117 342 2987
Email: abby.oconnell@bristol.ac.uk

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Glossary / abbreviations

APC	Admitted Patient Care
BAPRAS	British Association of Plastic, Reconstructive and Aesthetic Surgeons
BOA	British Orthopaedic Association
CB	Commissioning brief
CI	Chief Investigator
CPRD	Clinical Practice Research Datalink
CTEU	Clinical Trials and Evaluation Unit
EPUAP	European pressure ulcer advisory panel
GP	General Practitioner
HES	Hospital Episode Statistics
HRQoL	Health Related Quality of Life
ICD-10	International Classification of Diseases
IQR	Interquartile range
ISAC	Independent Scientific Advisory Committees
NHS	National Health Service
NICE	National Institute for Health and Care Excellence
NIHR	National Institute for Health Research
NRES	National Research Ethics Service
ONS	Office for National Statistics
OPCS	Office of Population Censuses and Surveys
PICO	Problem, Intervention, Comparison and Outcome
PPI	Patient and Public Involvement
QNI	Queen's Nursing Institute
RCN DN	Royal College of Nursing District Nurses
RCT	Randomised controlled trial
SMG	Study Management Group
TVN	Tissue Viability Nurse
UK	United Kingdom
UTS	Up-To-Standard
WS	Workstream

1. Study summary

Being immobile for too long can lead to discomfort, for example pins and needles or pain. These sensations prompt us to move and this avoids poor blood flow which can lead to pressure ulcers (sometimes called bed sores). Pressure ulcers mainly affect older people confined to a bed or chair. However, younger or seriously ill patients with limited movement, for example due to a spinal injury, can be affected.

Pressure ulcers are a serious problem for patients and their carers. They range in severity from red skin (Stage 1) to deep wounds through muscle to bone (Stage 4). Pressure ulcers have a major impact on quality of life; they may heal slowly and become infected, and can increase the risk of dying in older people. They are also a costly problem for the National Health Service (NHS). People with pressure ulcers are usually treated in the community but may need hospital care. Common treatments for pressure ulcers include pressure relief, dressings and encouraging movement and change of position. Surgery can be used to try and close deep pressure ulcers but in the United Kingdom (UK) this treatment is not common. Finding out whether surgery works as a treatment is very important to people affected by pressure ulcers. Currently, it is not clear which patients with pressure ulcers may benefit from an operation and which of the different ways of doing the surgery seems best.

The SIPS study aims to find out more about how best to conduct research in this area, by undertaking three pieces of work.

Firstly, the study will survey the opinions and experiences of doctors, nurses and patients about the range of ways in which people with deep pressure ulcers are treated. These surveys ask respondents to describe whether refer for or carry out surgery, if so, on which patients and what other treatments they use. Alongside these surveys, we will review literature about the effectiveness of surgery to treat pressure ulcers and about the impact of severe pressure ulcers on patients' health-related quality of life.

Secondly, the study will analyse data collected routinely in the NHS over a period of 8 years. The study will describe the care that has been provided in England to patients with severe pressure ulcers, the kinds of patients who have been treated in different ways and examine how care is different in different places. To inform whether surgical treatments should be more widely available, the study will identify patients who were similar when admitted to hospital with a severe pressure ulcer and compare health outcomes (such as going back to hospital and death) among those who did and did not have surgery.

Thirdly, the study will hold meetings with experienced healthcare professionals and patients to review the survey findings and the data analyses. The study will use an established method to reach agreement about which treatments are appropriate and for whom. These steps are vital to ensure relevant future research.

This study will be carried out by an experienced multi-disciplinary team of surgeons, tissue viability nurses, statisticians, researchers and patient representatives. We expect it will take two years to complete. The results will be made publicly available to inform the future care of patients with severe pressure ulcers.

2. Background

2.1 Overview of severe pressure ulcers: description, care and definition

Pressure ulcers are primarily caused by prolonged pressure on the skin, and usually effect people confined to bed or who sits in a chair or wheelchair for a long period of time. Pressure ulcers are most common on bony parts of the body, such as the heels and hips. Early symptoms include discoloured skin (stage I), but the pressure ulcer can turn into an open wound which may reach the muscle and bone (stage IV). Treatment of pressure ulcers depends on how serious they are. Initial treatments may include wound dressings, moving position regularly or specially designed cushions. However, surgical debridement can be required and in some cases surgery to remove damaged tissue and close the wound.

Studying the ways in which severe pressure ulcers are managed is challenging because the care pathway spans community- and hospital-based care. In the UK most people with or at risk of pressure ulcers are managed in the community by nurses (community nursing teams or care home staff, although some patients will receive care from a practice nurse), often with the General Practitioner (GP) acting as a conduit between community and secondary care. Since most pressure damage occurs in patients with limited mobility, most patients receive care in their own homes (which includes care homes).

Pressure ulcer prevention in at risk populations seen as a key objective in most Trusts and nurses should: undertake initial and ongoing patient-level pressure ulcer risk assessment; provide pressure ulcer prevention interventions including education and pressure relief through repositioning and the use of pressure relieving equipment; and manage existing pressure damage.[1] When pressure ulcers occur, community-based treatment will depend on the severity of wounding. Open, superficial pressure ulcers (stage II) may be managed using dressings only but more severe pressure damage (stage III and IV) may be referred to specialist tissue viability nurses (TVNs) for advice and treatments such as negative pressure wound therapy. Despite the existence of the National Institute for Health and Care Excellence (NICE) Pressure Ulcer Care clinical guidelines,[1] local pressure ulcer treatment pathways are heterogenous and there is variation in practice.[2]

Tissue viability services are led by senior specialist nurses with advanced knowledge and skills, in both community and acute settings. TVNs are often responsible for the provision of advanced clinical care, the development of care pathways, and provision of education both within their own organisation and to other external organisations such as nursing homes.

The National Institute for Health Research (NIHR) put out a commissioning brief (CB) for primary research to evaluate surgical interventions for stage III and IV pressure ulcers. This brief called for a randomised controlled trial (RCT) to evaluate the effectiveness of surgical management compared to usual care for stage II and IV pressure ulcers that are not healing with conservative treatment. However, there has been little research in this area. The study team found that it was not possible to define the surgical procedures that require evaluation, the comparator group or the patient groups to be studied. A lack of information on the patient populations who currently have surgery and those who may be eligible also causes difficulties when scoping potential sites and calculating the number of potential study participants.

The study team set out to create a project which could define these unknown parameters, and so allow for an RCT to be designed in response to the CB. The first stage was to define a severe pressure ulcer. A key feature of the definition of stage III and IV pressure ulcers is that they are "full skin thickness." Some ulcers are full skin thickness but are unstageable because the features required to distinguish stage III from stage IV are not discernible.[3] These three kinds of pressure ulcer are coded as L89.2, L89.3 and L89.9 in the World Health Organisation's implementation of the International Classification of Diseases diagnosis codes version 10 (ICD-10).[4] Exploration of a sample of anonymised Hospital Episode Statistics (HES) data showed that surgical reconstruction occurred as often in patients diagnosed as having an unstageable pressure ulcer (L89.9) as in all patients diagnosed as having stage III and stage IV pressure ulcers (L89.2 and L89.3). Therefore, the study team believe that any pressure ulcer with one of these three codes is relevant to the CB.

2.2 Surgical reconstruction of severe pressure ulcers

Surgical reconstruction is an expensive intervention; it is potentially cost-effective providing that patients recover uneventfully and do not experience a recurrence. When studying specific patient groups who may be appropriate to undergo surgical interventions for severe pressure ulcers, as per the CB, knowledge of perceived indications for, and barriers to, surgical reconstruction are critical. Full skin thickness pressure ulcers are widely considered to represent a failure of skin care to prevent them and, therefore, understanding the circumstances in which such ulcers arise is an important aspect of the evaluation of the suitability of a patient for surgical reconstruction.

Studying surgical management of severe pressure ulcers in the UK context is challenging because surgical reconstruction is very rarely carried out. Preliminary analyses using the HES data extract obtained from the University of Bristol showed that, over two years, 81,383 patients were recorded as having had an index hospital admission in England which included an ICD-10 coded diagnosis of a severe pressure ulcer. Of these, only 165 patients also had an ICD-10 code for a reconstructive surgery during the admission.

The CB specifies that one element of the research should be an "efficient cohort study to identify priorities for future research." To do this, the study team aim to characterise the current care pathway across community and secondary care. We propose two retrospective cohort studies assembled from routine sources (HES and Clinical Practice Research Datalink (CPRD) Gold) as the most efficient cohort design. Assembling the retrospective HES cohort from routine data for England will also allow us to present data for all patients who have had their pressure ulcers managed surgically over a defined time frame, as well as understanding current practices in relevant settings.

Patients with severe pressure ulcers have restricted mobility, which may be the result of age and/or frailty, or neurological damage which limits movements. Surgery will likely only be considered in those well enough to cope, where the procedure will be successful and in those who will gain medium to longer term benefit from it. Key factors which might the influence the decision to offer surgery are life expectancy, general physical health and an agreed post-operative prevention plan which will stop a healed ulcer recurring. We were not able to find any specific data which explicitly discusses who should have reconstructive surgery. Many retrospective cohort studies are undertaken in those with spinal cord injury [5, 6] but reconstructive surgery is also done in other populations and underpinning or defining features

are unclear. These observational studies do not show a differential outcome for different types of surgery but provide only very low certainty evidence.

Some small surgical case reviews have look at risk factors for postoperative complications. [7-11] Various factors were reported to be associated with post-operative complications (mainly dehiscence and recurrence), including: ulcer size, history of previous surgery, systemic biomarkers such as creatinine, chronic conditions such as coronary heart disease and body mass index (but not in all studies).

2.3 Uncertainties and gaps in current knowledge

There is a dearth of evidence around the evaluation of surgical interventions for stage III and IV pressure ulcers. A Cochrane review on reconstructive surgery for pressure ulcers [12] concluded that: "*Currently there is no randomised evidence that supports or refutes the role of reconstructive surgery in pressure ulcer management*." NICE guidance on pressure ulcers makes no recommendations about surgical management.[1] Other guidelines recommend obtaining "a surgical consultation for possible operative repair in individuals with stage III or IV pressure ulcers that are not closing with conservative treatment".[3] This recommendation does not specify specific operations or indicate the patients likely to benefit and is based on indirect evidence or expert opinion.

There is no published data from the UK describing the number of people having reconstructive surgery, and published international cohort studies look at numbers of people in a single facility [5, 13-15].

Exploration of HES Admitted Patient Care (APC) data showed that patients who had reconstructive surgery were about 20 years younger and had fewer comorbidities than those who did not. Diagnoses in addition to the pressure ulcer showed that about half had paraplegia, tetraplegia, spinal injuries or sequelae of a transport accident. These differences were also apparent between patients who had reconstructive surgery and those who had debridement only. Reconstructive surgery was carried out in 55 of 267 hospitals (20.5%) admitting index patients; in 24 months, only two performed >10 procedures and 26 did only 1. This work also found that, prior to 2012, a single ICD-10 code L89.X was used to denote any pressure ulcer.

Exploration of CPRD showed that referrals to "district nurse service" were most common (3,045 instances in 913 patients with an incident pressure ulcer). Referrals to podiatrists were second most common (682 instances in 367 patients). Referrals to TVNs were less common (286 instances in 133 patients); this was expected since such referrals are for treatment advice rather than treatment *per se*, i.e. for patients with challenging wounds.

3. Rationale

The research is important because severe pressure ulcers have a significant chronicity and cause serious problems for patients, their carers and the NHS.[16] Severe pressure ulcers have a substantial impact on Health Related Quality of Life (HRQoL) and are associated with higher care costs.[3, 17-19] The personnel and resources which are required for the ongoing effective management of these ulcers is impacting not only on NHS healthcare providers but also carers and families. The research is also important because of uncertainty about the patients in whom

reconstructive surgery to repair a pressure ulcer is effective in the short, medium and long-term, and the surgical techniques that should be used.[12] HES data show that this surgery is carried out rarely and in a minority of acute hospitals. A package of care involving surgery may be cost-effective and may need to be considered for more patients.

Several research studies have explored and quantified the additional impact of pressure-related injury on HRQoL, over and above existing health issues. A 2009 systematic review identified and synthesised 10 qualitative and 21 quantitative studies exploring the impact of pressure ulceration on HRQoL in older patients.[3] The review identified themes which were consistently reported across studies, particularly the physical impact of ulceration (pain), psychological effects and negative impact on social activities. Additional studies including younger participants or published since the 2009 review echo these themes and reinforce the independent impact of pressure ulcers on HRQoL.[20-23] One study further demonstrates that SF-36 scores in those with pressure ulcers compared with age and condition matched controls are significantly lower in terms of poorer physical functioning, role limitations due to physical problems, and vitality.[21] Patients with complex wounds including pressure ulcers have reported that healing is the most important outcome to them. Getting rid of the wound, getting it closed and moving on, were all common sentiments in interviews with 33 such patients (8 of whom had pressure ulcers).[24] People who had ulceration also reported, qualitatively, that healing of the ulcer did enhance HRQoL, for example by eliminating the need for bed rest and allowing a return to 'normality'.[16]

This evidence shows the established link between pressure ulceration and negative HRQoL. However, there is very limited information about how surgical reconstruction impacts on HRQoL in the short, medium and long term. Surgical reconstruction of pressure ulcers is rarely carried out in the UK and the specific impact of this surgery on people with severe ulcers has not been investigated in detail. In interviews with people who had previously had ulceration,[25] small numbers of patients variously reported surgery as successful or invasive, requiring long hospital stays with ulcers recurring. Recurrence is a key issue in those at risk of ulceration, since when healing occurs the risk factors for ulceration often remain. People's access to and experience of surgery for ulceration are likely to be nested in wider issues around future prevention activity; all these aspects of care and behaviour are linked to self-reported HRQoL.

4. Aims and objectives

The aim of the SIPS study is to clarify the Population, Intervention, Comparator and Outcome (PICO) elements needed to be defined a future RCT of reconstructive surgery for severe pressure ulcers. We define reconstructive surgery as any surgical procedure that leads to epithelial closure of the wound, typically distant or local flaps of skin and muscle/fascia.

We have designed a study with three workstreams to address uncertainties in the "PIC" elements of a future potential PICO research question about the effectiveness and cost-effectiveness of reconstructive surgery.

Workstream 1 will include literature reviews and a survey of surgeons and nurses who manage patients with severe pressure ulcers in either secondary care or community settings.

The objectives of Workstream 1 are to:

1. Systematically review evidence about: (a) the effectiveness of reconstructive surgery for treating pressure ulcers[12]; (b) the impact of pressure ulceration on HRQoL.
2. Carry out comprehensive on-line surveys with relevant healthcare professions to:
    - Describe the characteristics of patients in the UK currently being referred for a surgical opinion about surgical reconstruction;
    - Describe variation in the operations and postoperative care currently being provided;
    - Describe variation in usual care provided before initiation of a surgical referral.

Workstream 2 comprises retrospective cohort studies assembled from routinely collected data sources (HES and CPRD Gold). The CPRD cohort will include data about the care pathway for patients with incident pressure ulcers, from diagnosis and management in primary care to (for a minority) secondary care and, potentially, reconstructive surgery (consultations, diagnoses, interventions and referrals both within primary care, e.g. to nursing teams, and to secondary care). The HES cohort will include information on 'index' inpatient admissions assigned an ICD-10 code for a severe pressure ulcer, and subsequent HES activity (inpatient admissions and outpatient clinic attendances).

The objectives of Workstream 2 are to:

3. Describe in the CPRD cohort patients with incident severe pressure ulcers and their entire care pathways, e.g. usual management in the community, management by TVNs, admission to hospital and subsequent care.
4. Describe in the HES cohort patients with a diagnosis of severe pressure ulcer at the time of hospital admission, their care pathways after admission and frequencies of health outcomes.
5. Compare in the HES cohort outcomes in matched groups of patients who were similar on admission and who did/did not have a surgical reconstruction operation.
6. Explore in the matched groups subgroup interactions with reconstructive surgery that may influence outcomes, e.g. comorbidities, previous hospital admission without surgery.

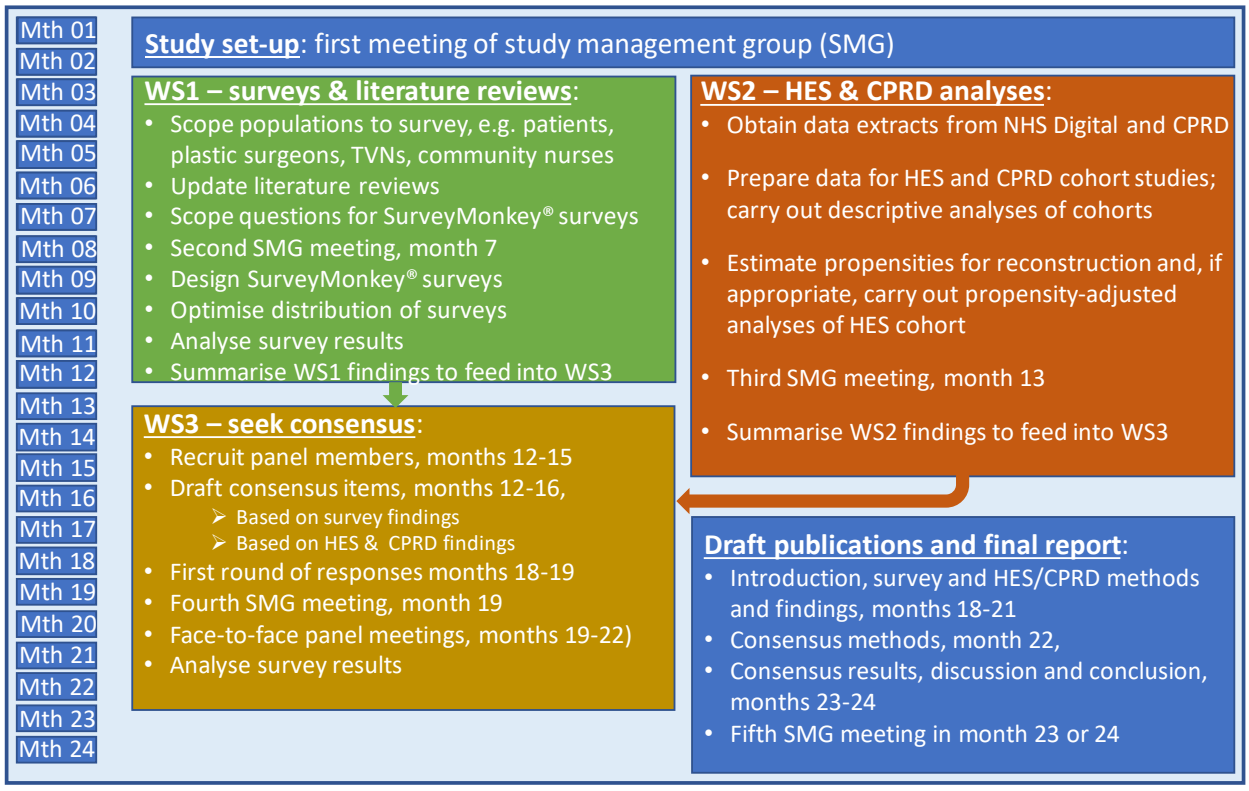
Workstream 3 is a formal consensus process, separately among health professionals and patients and carers, to make recommendations about which treatments are appropriate for whom and when. The objective of Workstream 3 is to:

7. Seek consensus about which treatments and management strategies are appropriate for whom and when, given findings from workstreams 1 and 2.

5. Plan of Investigation

5.1 Study schema

Figure 1: Study schema



Abbreviations: Mth – month; PPI – patient and public involvement; SSC- study steering committee; HES – hospital episode statistics; CPRD – Clinical Practice Research Datalink; TVN – tissue viability nurses/networks.

Abbreviations: CPRD – Clinical Practice Research Datalink; HES – Hospital Episode Statistics; Mth – month; SMG – Study management group; TVN – tissue viability nurses/networks; WS – workstream

5.2 Study design

5.2.1 Workstream 1: literature reviews, interviews and surveys

Workstream 1 focuses on gathering information from professionals and patients, updating previous systematic reviews and carrying out surveys among relevant professional groups of the management of severe pressure ulcers currently being provided across the NHS. The outcomes will be evidence from the reviews and respondents' answers to survey questions.

5.2.1.1 Systematic reviews

Two topics will be reviewed:

a) the effectiveness of reconstructive surgery for treating pressure ulcers;
b) the impact of pressure ulceration on HRQoL

With respect to (a), the previous Cochrane systematic review on reconstructive surgery [12] will be updated. The previous review found no RCTs and we will extend eligibility to include:

- quasi-randomised controlled trials (studies using a system of quasi-randomisation for participant allocation);
- non-randomised studies with a clearly reported mechanism of group formation, clearly defined inclusion criteria and defined methods of ascertainment of eligible patients and their recruitment. These studies could use any data source which, over time, follows the trajectory of relevant participants receiving different methods of treatment to assess how alternative strategies may impact on outcomes. Relevant participants are defined as those with a pressure ulcer occurring within a defined period prior to study recruitment.

Single cohorts [Altman reference], where all participants are given the same type of surgery, and cross-sectional and case-control studies will be excluded. Despite widening eligibility, there is still a high risk of the review being "empty."

Full details are available in the review protocol. In brief, the key elements of the review questions are:
Population: Adults with a diagnosis of a pressure ulcer (stage II, III, IV or unstageable) managed in any care setting. We will exclude studies with mixed wound populations; that is studies that do not restrict inclusion to pressure ulcers only.
Intervention: Reconstructive surgery for pressure ulceration. Likely comparisons are surgery compared to no surgery and different types of surgery compared with each other. Surgical wound debridement will be considered as a co-intervention, i.e. we will not consider surgical debridement alone as a type of reconstructive surgery.
Eligible studies: RCTs and non-RCTs, as described above.
Outcomes: Primary outcomes are complete wound healing (as either a time to event or proportion of wounds completely healed), wound dehiscence and wound recurrence. Secondary outcomes are HRQoL, wound infection, cost-effectiveness and incidence of a new ulcer (separate to wound recurrence as this refers to an ulcer in a different area to the index ulcer).

Standard Cochrane Wounds search methods will be applied: risk of bias assessment using the RoB 2.0 or ROBINS-I tools[26, 27]; assessment of heterogeneity; synthesis of relative treatment effects including meta-analyses where justified and feasible; presentation of summary of findings tables and GRADE assessment of included evidence for pre-specified outcomes. Sub-group analysis for ulcer stage and type of surgery will be explored.

With respect to (b), we aim to assess quantitatively the effect of a pressure ulcer (stage 2 or more severe) on HRQoL, taking care to distinguish as far as possible between the effect of the pressure ulcer and the effects of other comorbidities. Making this distinction requires evidence about changes in HRQoL over time, i.e. longitudinal cohort studies (including RCTs). These studies are most likely to provide relevant information, by measuring HRQoL on multiple occasions, ideally with pressure ulcer status changing between measurements in a proportion of the people included in the study. Studies can measure healing (starting with a population of

people all of whom had a pressure ulcer, with the ulcer healing in a proportion of participants during follow-up) or prevention (starting with a population of people without a pressure ulcer but at risk of developing one, with an ulcer developing in a proportion during follow-up). Hence, RCTs of either ulcer prevention or treatment could be eligible. Eligible studies must also measure HRQoL using one or more validated HRQoL instruments.

Full details are available in the review protocol. In brief, the key elements of the review questions are:
Population: Adults with a diagnosis of a pressure ulcer (stage II, III, IV or unstageable) or at risk of developing a pressure ulcer managed in any care setting. We will exclude studies with mixed wound populations; that is studies that do not restrict inclusion to pressure ulcers only.
Eligible studies: Longitudinal cohort studies, including RCTs, which measure HRQoL using a validated instrument on two or more occasions.
Exposure: Change in pressure ulcer status between HRQoL measurements.
Outcomes: Validated generic HRQoL instruments are: SF-36[28]; SF-12[29]; SF-6; EQ-5D[30]; Nottingham Health Profile[31]; Sickness Impact Profile[32] and the World Health Organization Quality of Life Scale[33]. Studies using a validated disease-specific instrument are also eligible; the only such instrument that we are aware of is the PurPOSE PUQOL tool.[34]
Standard Cochrane Wounds search, study selection and data extraction methods will be applied.

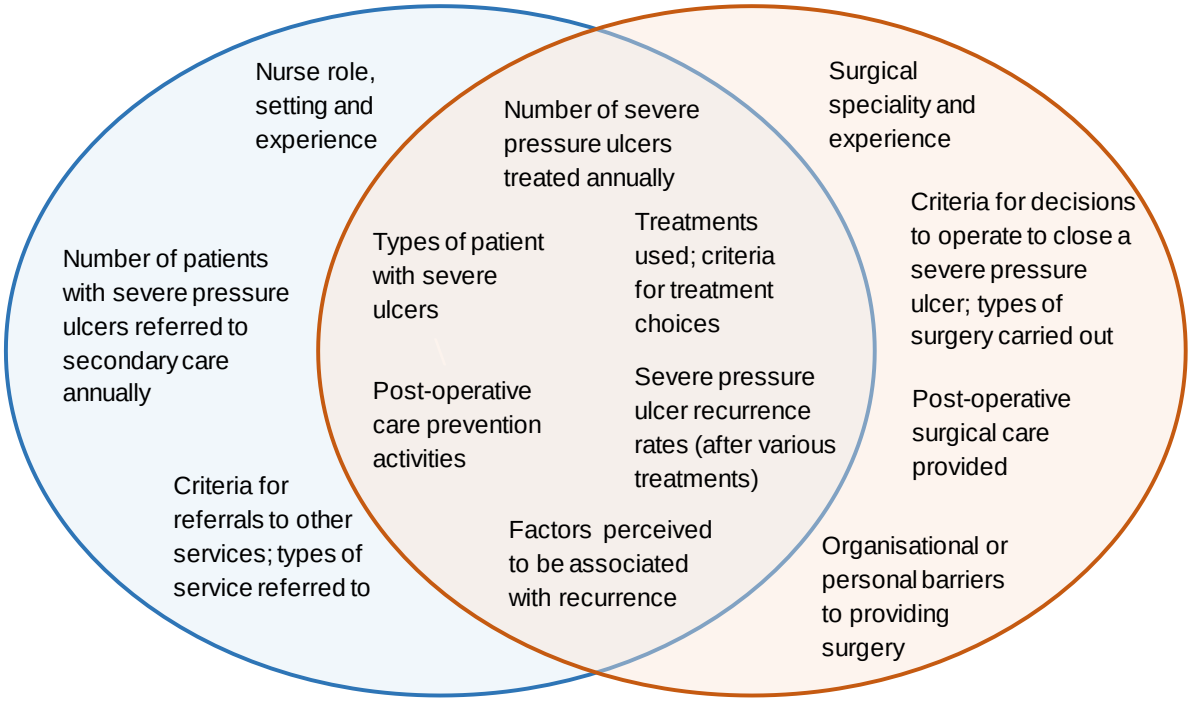
5.2.1.2 Surveys among relevant professional groups of the management of severe pressure ulcers currently being provided across the NHS

We will design on-line surveys using SurveyMonkey. We will survey surgeons, nurses and general practitioners separately, i.e. surveys with varying items relevant to their roles in the care pathway. The survey for nurses will be relevant to nurses working in different settings or across settings (community or hospital), and with varying degrees of specialism with respect to the management of pressure ulcers (e.g. community nurses, TVNs, specialist secondary care nurses), applying filter questions to ensure items presented focus on issues that are most pertinent to the respondent's role.

Surgeons will be contacted through their professional bodies, e.g. British Association of Plastic, Reconstructive and Aesthetic Surgeons (BAPRAS) and the British Orthopaedic Association (BOA). Distribution lists for nursing groups may be more difficult to identify but we expect to have support from the Tissue Viability Society (which covers community and acute sectors) and the TVN2gether group, which has a wide membership. To engage community nurses, we will approach the Queen's Nursing Institute (QNI) and Royal College of Nursing District Nurses (RCN DN) Forum (https://www.rcn.org.uk/get-involved/forums/district-nursing-forum DN Forum). We will also use social media to distribute links to the survey. We aim to distribute the survey for surgeons to plastic surgeons and orthopaedic surgeons because these are the specialties under which most surgical reconstructions were coded in the anonymised HES datasets.

The key topics on which data will be collected are summarised in Figure 2. We will collect data from community-based nurses on the care they provide to patients with severe pressure ulcers, their ability to refer these patients to secondary care and to a surgeon specifically and how they make referral decisions. We will ask surgeons about the operations they perform, barriers and facilitators that drive individual decisions to operate and institutional capacity for surgery in this patient population, and personal views on reconstructive surgery for pressure ulcers.

Figure 2: Topics for items for Workstream 1 surveys about the types of people with severe pressure ulcers treated by nurses and surgeons, and how referral and treatment decisions are made



5.2.2 Workstream 2: efficient cohort studies of the management of severe pressure ulcers

Workstream 2 comprises quantitative analyses of two retrospective cohorts assembled from routinely collected data: (i) a HES cohort (HES data from secondary care linked with mortality data) and (ii) a CPRD cohort (CPRD Gold (primary care data) linked with HES including mortality). Both cohorts are needed because CPRD covers only 7% of the English population; the CPRD cohort alone would capture <50 patients having reconstructive surgery.

5.2.2.1 HES cohort design and target population

We will request data for index admissions with a severe pressure ulcer (ICD-10 codes L89.2, L89.3, L89.9) or any pressure ulcer (L89.X) during a period of 8 years (01/04/2011-31/03/2019), linked with other HES APC and outpatient episodes and mortality data (to 31/03/2019). The target population for the HES cohort is: patients >=18 years of age in England admitted to hospital, with an ICD-10 diagnosis code for a severe pressure ulcer.

5.2.2.2 CPRD cohort design and target population

The request for CPRD-Gold data linked to HES and mortality data is limited to 10,000 individuals (with unlimited records per individual). Preliminary interrogation of CPRD-Gold indicated that there are ≈1,100 incident pressure ulcers (i.e. with no pressure ulcer recorded in the previous 12 months) per year recorded in CPRD, eligible for linkage to HES and mortality data. Therefore, we expect to request data for patients with an index record with a Read code

indicating an incident pressure ulcer (Table 1) during a period of eight (01/04/2011-31/03/2019) or nine years (01/04/2010-31/03/2019), subject to the limit of 10,000 individuals. All CPRD records, HES APC and outpatient episodes, and mortality data will be linked in this cohort (to 31/03/2019). The target population for the CPRD cohort is: patients >=18 years of age in England registered with a general practice with up-to-standard (UTS) registration and contributing data to CPRD, with a Read code indicating an incident pressure ulcer. No exclusions will be applied.

Table 1: Read codes to identify patients with an incident pressure ulcer

Medical code	Read code	Description
3928	M271.00	Non-pressure ulcer lower limb
4929	M270.13	Pressure sore
6862	M270.00	Decubitus (pressure) ulcer
11786	Z174P00	Pressure sore care
14995	M270.11	Bed sore
15505	39C0.00	Pressure sore
17592	39C..00	Pressure sore index value
17790	Z1B3.00	Dressing of pressure sore
28380	Z9K5.00	Pressure sore prevention
28814	ZRqY.00	UK consensus classification of pressure sores 1994
35329	ZQ39.12	Pressure ulcer assessment
36995	39C4.00	Waterlow pressure sore risk score
38996	ZQ39.00	Pressure sore assessment
44641	39C1.00	Superficial pressure sore
46050	ZQ52.00	Pressure sore risk assessment
49654	ZQ39.13	Bed sore assessment
55220	ZQ39.11	Decubitus ulcer assessment
55382	39C2.00	Deep pressure sore
56610	ZRrL.00	Waterlow pressure sore risk score
63243	39C3.00	Pressure sore -deep + superfic
95113	39C6.00	Maelor pressure ulcer risk assessment score
95886	39C5.00	Medley pressure sore risk score
100638	39CA.00	EPUAP (European pressure ulcer advisory panel) grade 4 ulcer
100778	39C7.00	EPUAP (European pressure ulcer advisory panel) grade 1 ulcer
100864	39C9.00	EPUAP (European pressure ulcer advisory panel) grade 3 ulcer
101006	39C8.00	EPUAP (European pressure ulcer advisory panel) grade 2 ulcer
101713	M270200	Community hospital acquired pressure ulcer
102230	M270100	Nursing home acquired pressure ulcer
102923	M270300	Hospice acquired pressure ulcer
103207	M270000	Hospital acquired pressure ulcer
103311	38Dr.00	EPUAP (Euro pressure ulc advisry panl) classification system
104552	M270z00	Decubitus ulcer and pressure area NOS
104850	M270400	Stage I decubitus ulcer and pressure area
105150	M270500	Stage II decubitus ulcer
106686	M270600	Stage III decubitus ulcer
106902	M270700	Stage IV decubitus ulcer
108537	M270.14	Decubitus ulcer and pressure area

5.2.2.3 Study setting

Pressure ulcer management in primary (CPRD cohort) and secondary NHS care (CPRD and HES cohorts).

5.2.2.4 Health technologies being assessed

Each cohort will allow the assessment of a variety of health technologies.

The HES cohort will assess reconstructive surgery operations coded with a variety of Office of Population Censuses and Surveys (OPCS)-4 codes. These codes are; distant flap of skin and muscle (S17), distant flap of skin and fascia (S18), distant pedicle flap of skin (S19), other distant flap of skin (S20), hair bearing flap of skin (S21), sensory flap of skin (S22), flap operations to relax contracture of skin (S23), local flap of skin and muscle (S24), local flap of skin and fascia (S25), local subcutaneous pedicle flap of skin (S26) and other local flap of skin (S27).

Surgical debridement (OPCS code S57.1) will also be described but is not the focus of the study. Usual care interventions are not coded in HES data, with some exceptions e.g. negative pressure therapy (OPCS code S57.7 Dressing of skin using vacuum assisted closure device NEC). Such interventions will also be described.

The CPRD cohort will assess usual care, including but not limited to: referrals to secondary care (identified from linked HES episode); referrals and discharges from specified forms of care within primary care (Table 2), dressing of ulcer/wound (Table 3) and negative wound pressure therapy.

5.2.2.5 Outcomes

Each cohort will allow the description of a number of outcomes.

In the HES cohort, the outcomes described will be: type of surgical reconstruction (OPCS code); duration of index admission; time to first subsequent admission with a pressure-ulcer related diagnosis; rate of subsequent admissions with a pressure-ulcer related diagnosis; repeat surgical reconstruction and type of reconstruction; and mortality.

Although the study does not include an economic evaluation, an important output will be a description of the primary and secondary care resources used in managing severe pressure ulcers. These data would be expected to inform any future study.

In the CPRD cohort, the outcomes described will be: frequencies of specific Read codes; referral to and discharge from community/district nursing team, generating periods of community nursing care and durations; referral to tissue viability services; admission to hospital with a pressure ulcer diagnosis, and duration of admissions related to a pressure ulcer; admission to hospital for surgical reconstruction of a pressure ulcer; and mortality.

Table 2: Read codes to identify referrals and discharges within primary care

Medical code	Read code	Description
Referral to tissue viability services		
22485	9N2m.00	Seen by tissue viability nurse
25762	8HHD.00	Referral to tissue viability nurse specialist
104199	38C5.00	Tissue viability assessment
108190	8T0J.00	Referral to tissue viability service
Referral to / discharge by community nurse		
9988	ZL23.11	Under care of community nurse
12487	ZLA3.11	Seen by community nurse
26438	ZL63.11	Referral to community nurse
85246	9N2y.00	Seen by community nurse for older people
86017	8Hl3.00	Referral to community nurse for older people
12415	ZLD8.00	Discharge by community nurse
Referral to / discharge by district nurse		
3529	9NFA.00	District nurse visit
6535	8H72.00	Refer to district nurse
11495	ZL63211	Refer to district nurse
11188	8HW1.00	Referral by district nurse
32042	03FG.00	District nurse
36890	9NFH.00	District nurse initial visit
11243	66S5.00	Shared care: district nurse/GP
12092	ZL23300	Under care of district nurse
17845	9N24.00	Seen by district nurse
18592	9NFJ.00	District nurse follow up
18968	671A.00	Discussed with district nurse
40802	9NFE.00	First annual visit by district nurse
63301	66SA.00	Shared care: practice nurse & district nurse
106669	9NNg200	Under care of district nurse
108211	9NFa.00	Home visit request by district nurse
18072	13GA.00	District nurse involv. stopped
36900	ZLD8300	Discharge by district nurse
105318	8HgP.00	Discharge by district nurse
Referral to / discharge by podiatrist		
7992	9N2Q.00	Seen by podiatrist
9647	9NN0.00	Under care of podiatrist
10090	ZL83.00	Referral to podiatrist
30691	ZL44211	Under care of hospital podiatrist
32614	ZL83111	Referral to community podiatrist
38841	ZL44100	Under care of community-based podiatrist
40620	ZL44111	Under care of community podiatrist
40892	ZL83200	Referral to hospital-based podiatrist
41262	ZL83211	Referral to hospital podiatrist

42276	ZL83100	Referral to community-based podiatrist
47319	ZL44200	Under care of hospital-based podiatrist
56717	9N2P.11	Seen by podiatrist
94317	8HVd.00	Private referral to podiatrist
43483	ZLDG.00	Discharge by podiatrist
59370	ZLDG200	Discharge by hospital-based podiatrist
59374	ZLDG211	Discharge by hospital
60610	ZLDG111	Discharge by community podiatrist
96639	ZLDG100	Discharge by community-based podiatrist

Table 3: Read codes to identify dressing of ulcer/wound

Medical code	Read code	Description
6654	81H1.00	Dressing of ulcer
15506	7G2E500	Dressing of skin ulcer NEC
22204	Z1B2300	Dressing of skin ulcer
17790	Z1B3.00	Dressing of pressure sore
96	81H..00	Dressing of wound
28848	81Hy.00	Other wound dressing
19364	81HZ.00	Wound dressing NOS
110388	8Cy..00	Wound dressing requested by community nursing team
101142	8C6..00	Wound dressing requested by accident and emergency service

5.2.2.6 Sample size considerations

Based on the anonymised HES extracts, HES cohort A should comprise about 120,000 index hospital admissions, including about 220 in which surgical reconstruction operations were carried out and about 3,900 in which surgical debridement without reconstruction was carried out. There are also likely to be about 170 subsequent admissions in which operations were carried out over 2 years of follow-up. Usual care for patients not having surgery will be characterised precisely.

We expect the CPRD cohort to comprise about 10,000 incident pressure ulcers. Severe pressure ulcers in the community are mainly managed conservatively; few are admitted to hospital and CPRD only covers 7% of the English population. These data will be summarised descriptively, Outcome frequencies (healing, infection, referrals to community nursing teams, TVNs and secondary care) will be estimated precisely, given this sample size. We expect to be able to follow very few incident ulcers through to surgical reconstruction.

5.2.2.7 Data management and analyses

HES data will be formatted to identify inpatient admissions for continuous periods of care. The index admission will be the first admission with a severe pressure ulcer diagnosis code.

Patients' age, sex and comorbidities and other diagnoses on admission will be described.[35] Comparisons between hospitalised patients with a severe pressure ulcer who did and did not

have reconstructive surgery will be confounded; the risk of bias from confounding was identified in our preliminary discussions with surgeon members of the team.

Our approach will be as follows:

a. Identify important confounding domains from the surveys of health professionals (Workstream 1).[27]
b. Classify important confounding domains according to whether we can / cannot characterise them from variables, or patterns of variables (e.g. comorbidities or activity profiles) in the available HES data.
c. Summarise descriptively the characteristics of eligible patients on index admission, including variables identified as characterising important confounding domains.
d. Describe standardised differences between the characteristics of groups of eligible patients;[36, 37] subsequent steps e-i are conditional on point estimates of standardised differences being <0.2 for variables characterising important confounding domains.
e. Fit multivariable models to estimate the propensity for having reconstructive surgery.
f. Plot distributions of propensity by groups of patients who did and did not have reconstructive surgery.
g. Optimise the choice of propensity-adjustment method according to the results of d- f, without reference to the distribution of outcomes in the groups.[38, 39]
h. Fit regression models, adjusting for propensity.
i. Interpret the findings of the propensity-adjusted models taking into account information from steps a-e (above).

Details of the propensity-adjusted analyses will be described in a statistical analysis plan. If feasible, we will also explore potential subgroup interactions with reconstructive surgery that may influence outcomes, e.g. in relation to comorbidities, previous hospital admission without surgery.

In the CPRD cohort, patients with incident pressure ulcers will be identified by Read codes. GP data will identify major comorbidities and pressure ulcer management provided. A small number will have hospital admissions, identified through linkage with HES data.

Patients' age, sex and comorbidities on diagnosis of a severe pressure ulcer will be described, together with details of their subsequent care in both primary and secondary care settings. We envisage that the expected, very small number of patients in the cohort having surgical reconstruction will prevent any comparisons with patients not having surgery.

5.2.3 Workstream 3: consensus groups to identify who should have surgical management and when

We will use a formal consensus method to elicit the views of health professionals and patients about which treatments and management strategies are appropriate for whom and when. Currently, we propose to use a method based on the modified nominal group technique.[40-42] The appropriateness of using this method will be reviewed as evidence from workstreams 1 and 2 emerges. We propose to recruit participants to four groups, two each of health professionals and patients. The decision to hold a separate consensus process for professionals and patients/carers is based on previous experience, which showed that it is difficult to bridge the gap relating to content knowledge and use of technical language between professionals and patients to allow a truly equitable contribution from both types of stakeholders.[43]

The consensus process will be structured to yield consensus about the primary output specified in the CB, namely identification of patient groups and interventions requiring primary research to determine effectiveness. The process will construct a set of recommendations about which treatments are appropriate for whom and when.

We will compile statements describing uncertainties about (a) the population that may benefit from an operation, (b) the operations that should be considered and (c) what should constitute usual care (range of treatment and duration before referral for a surgical opinion). These statements will be informed by the updated systematic review, survey responses of the multiple professions managing severe pressure ulcers and phenomenological interviews with patients (Workstream 1) and the findings from the retrospective cohort studies (Workstream 2).

We will provide summaries of the findings of Workstreams 1 and 2 (in suitable language format for patients and carers) and the statements to panel members before consensus meetings. Panel members (up to 12 per panel meeting) will respond to statements in private before the meeting; we envisage that statements will be presented on paper or electronically with supporting information, 9-point Likert scales (1 indicating “completely disagree” and 9 “completely agree”) and space for free text comments. Panel members will then attend a face-to-face meeting, discuss in turn anonymised aggregate responses to the first survey for each statement and then independently rate the statement again. Criteria for consensus will be: a median score of response ≥7 and interquartile range (IQR) of 6–9 in support of a statement; a median score of ≤3 and IQR of 1–4 in disagreement with a statement. The outputs of the consensus meetings will be descriptions of statements for which there is consensus among panel members about the populations that may benefit from an operation, the operations that should be considered and what should constitute usual care.

6. Study management

The study will be managed by the Bristol Trials Centre, Clinical Trials and Evaluation Unit (CTEU). The CTEU is an UK Clinical Research Collaboration registered Clinical Trials Unit. The CTEU will prepare all the study documentation, carry out administrative tasks, carry out study analyses in collaboration with other investigators and assist in preparation of study outputs.

6.1 Day-to-day management

The study will be managed by a study management group (SMG). The SMG will convene every 6 months, face-to-face or by teleconference, to review progress; there will also be monthly teleconference updates. The SMG includes the full range of expertise that the study team may need to draw on. The SMG will be chaired by the Chief Investigator (CI) and will include all members of the named research team.

6.2 Study Steering Committee, and Data Monitoring and Safety Committee

In agreement with the study funder, there will not be a Study Steering Committee or Data Monitoring and Safety Committee convened for this study. The study will be overseen by the co-applicants, who will form the SMG. There is no safety issue, since the study comprises retrospective cohort studies and consensus groups.

7. Safety reporting

This study does not require patients to undergo any additional investigations or to participate actively in any way. Therefore, it is not possible for clinical adverse events to be attributed to study specific procedures

8. Ethical considerations

8.1 Review by an NHS Research Ethics Committee

Considerations of scientific merit and benefit to patients are considered through applications to the Independent Scientific Advisory Committees (ISACs) of NHS Digital and CPRD. NHS Digital and CPRD have approval from a National Research Ethics Service (NRES) Committee for all observational research using anonymised HES and CPRD data approved by ISACs. Any requests for amendments will be submitted directly to NHS Digital or CPRD.

8.2 Risks and anticipated benefits

This is an observational study that will not change patients' standard care. There are therefore no risks resulting from the study to patient safety, or direct patient benefits.

The main benefit to society is the provision of high-quality evidence to address this important area of clinical uncertainty, and to provide information to allow for a randomised controlled trial of surgical reconstruction in severe pressure ulcers.

9. Research governance

This study will be conducted in accordance with GCP guidelines and the Research Governance Framework for Health and Social Care.

9.1 Sponsor approval

Any amendments to the study documents must be approved by the sponsor. The Sponsor's Finance Office will have oversight of the financial expenditure and reporting on the project. They will work with the Chief Investigator to ensure relevant financial milestones are achieved.

9.2 NHS approval

NHS Trust approval is not required as there is no participant involvement in this study.

9.3 Monitoring by sponsor

The study will be monitored and audited in accordance with the Sponsor's policy, which is consistent with the Research Governance Framework and the Medicines for Human Use (Clinical Trials) Regulations 2004. All study related documents will be made available on request for monitoring and audit by Bristol Trials Centre, CTEU and for inspection by other licensing bodies.

10. Data protection and participant confidentiality

10.1 Data protection

Data will be collected and retained in accordance with the European Union General Data Protection Regulation 2018.

10.2 Data handling, storage and sharing

10.2.1 Data handling

There will be no data collection from sites and so a study database is not required.

Extracted data from NHS Digital and CPRD will be received and processed in accordance with the specific Data Sharing Agreements.

10.2.2 Data storage

This is an observational study which requires no paper consent forms or case report forms. Any study documentation will be retained in a secure location during the conduct of the study and for 5 years after the end of the study.

Extracted data from NHS Digital and CPRD will be kept in accordance with the specific Data Sharing Agreements.

10.2.3 Data sharing

We anticipate that data from Workstreams 1 and 3 will be published in sufficient detail to avoid any need to share the raw data (i.e. data extracted from studies included in the reviews and responses of survey participants). If this is not the case, data will not be made available for sharing until after publication of the main results of the study. Thereafter, data will be made available for secondary research (without identifiable information about survey/consensus participants), conditional on assurance from the secondary researcher that the proposed use of the data is compliant with the Medical Research Council Policy on Data Preservation and Sharing regarding scientific quality, ethical requirements and value for money. A minimum requirement with respect to scientific quality will be a publicly available pre-specified protocol describing the purpose, methods and analysis of the secondary research, e.g. a protocol for a Cochrane systematic review.

Data from Workstream 2 will not be available for sharing because the licences under which the data will be obtained prohibit sharing.

11. Dissemination of findings

Some co-applicants are contributing to NHS England's National Wound Care Strategy, which will provide a key avenue to communicate findings. We will report findings at conferences and in high-impact general journals. We will impact on clinical practice by engaging with professional bodies; study collaborators have strong links with organisations including the Tissue Viability Society and NICE.

We will ensure members of our Patient and Public Involvement (PPI) forum are actively involved in carrying out activities relating to dissemination and public engagement. Opportunities such as talks to local groups and other events will be considered on a case by case basis. A lay summary of the research and its findings will be written and added to collaborator University websites and relevant blogs. To maximise visibility and accessibility of the material, we will use Google metrics to ensure our wording on the relevant site means the web page is located high in the returned list from a Google search. We also have close links with local Trusts and will aim to distribute the summary locally at relevant patient events in addition to online content.

To support further engagement work we will liaise with experienced colleagues at the NIHR Manchester Biomedical Research Centre and Public Programmes at Manchester University NHS Foundation Trust to undertake a range of engagement activities at public events including the Manchester Science Festival. These activities will raise the profile of pressure ulcers and research to improve their management.

We will link with existing networks at the University of Manchester to ensure our findings are presented locally to both academics, clinicians and members of the public, for example the Manchester Institute for Collaborative Research on Ageing, seminars for which are regularly well-attended by each of these groups.

We will publish relevant journal articles and attend at least one key conference. We will also draft media-friendly articles for relevant trade journals such as the Nursing Times and Nursing Standard. We will summarise the work using widely accessed, research-focused resources such as The Conversation and Kudos. We will also contact the NIHR Dissemination Centre to ask for advice where there are specific findings we want to publicise. Publications will be supported by targeted social media activity, especially through Twitter, using current accounts that link to a wide range of relevant stakeholder groups to ensure wide dissemination alongside a study specific account. Where required, press releases and media support will be provided.

12. Funding

The SIPS Study team, which includes researchers at the Bristol Trials Centre, CTEU, University of Manchester, University of Leeds, University of Bristol and University of Oxford, collaborated in designing the study and securing funding. The SIPS study is funded by the NIHR Health Technology Assessment programme (Reference number NIHR127850).

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14. Amendments to protocol

Amendment number (i.e. REC amendment number)	Previous version	Previous date	New version	New date	Brief summary of change	Date of ethical approval (or NA if non-substantial)

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