Surgical Management of Pressure Ulcers: The SIPS Study

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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 and Aurum) 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.[17-20] 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.[19] 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.[21-24] 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.[22] 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).[25] 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,[26] 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, CPRD Gold and CPRD Aurum). 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.

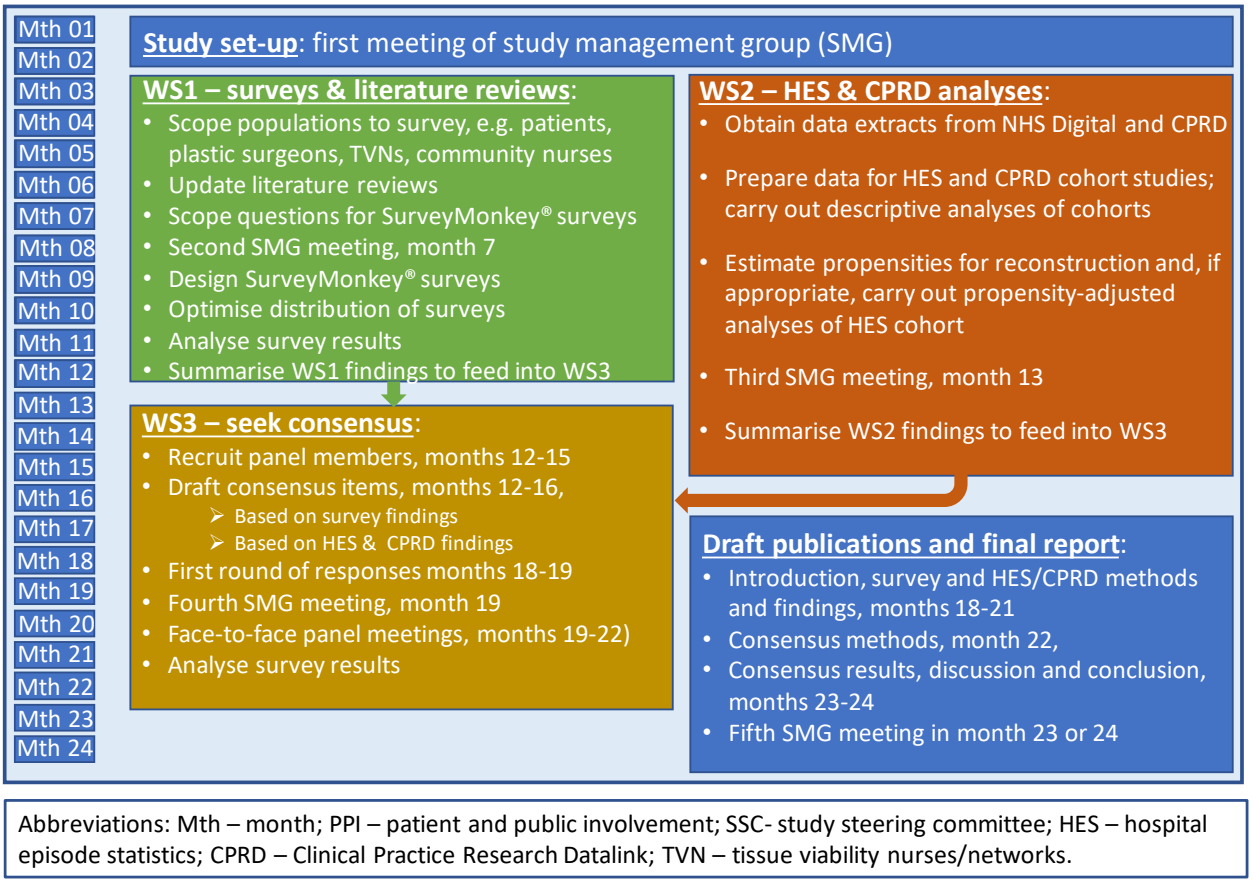
Workstream 3 is a formal consensus process, separately among health professionals and patients and carers, to make recommendations about which treatments are appropriate for whom and when. The objective of Workstream 3 is to:

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,[27] 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 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[28, 29]; 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 in studies with rigorous comparator groups so we will focus on 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: 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[30]; SF-12[31]; SF-6; EQ-5D[32]; Nottingham Health Profile[33]; Sickness Impact Profile[34] and the World Health Organization Quality of Life Scale[35]. Studies using a validated disease-specific instrument are also eligible; the only such instrument that we are aware of is the PurPOSE PUQOL tool.[36]
Standard Cochrane Wounds search, study selection and data extraction methods will be applied.

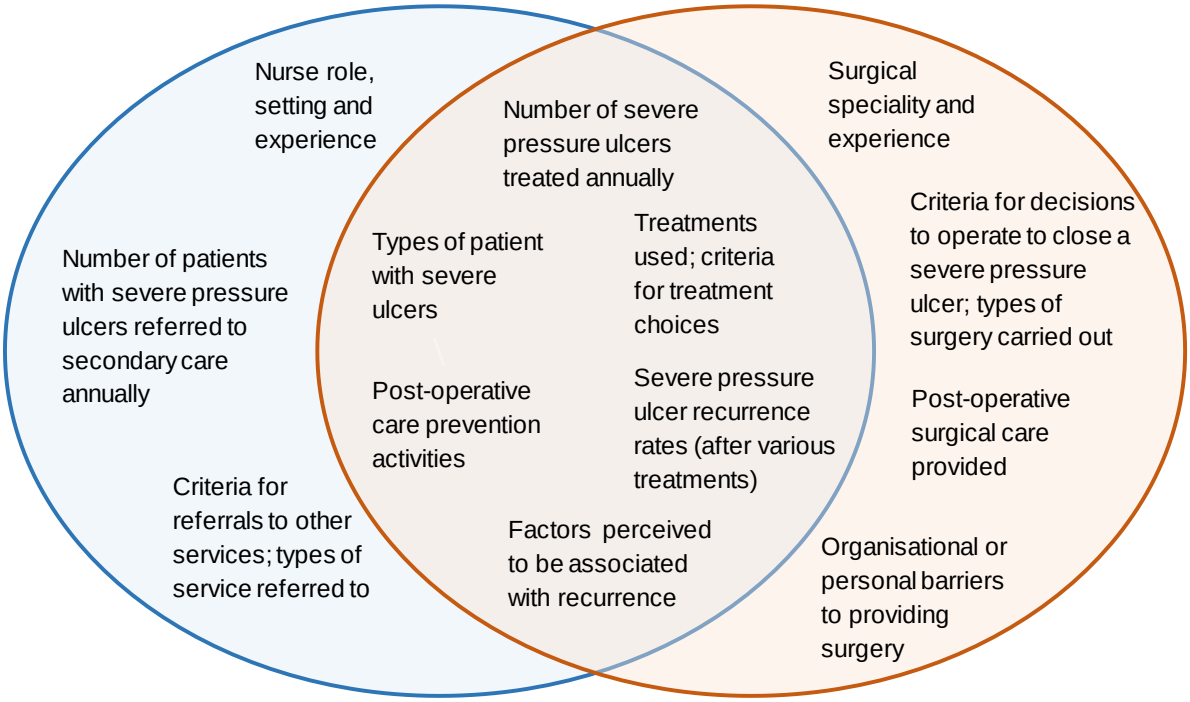
5.2.1.2 Surveys among relevant professional groups of the management of severe pressure ulcers currently being provided across the NHS

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 and CPRD Aurum (primary care data) linked with HES including mortality). Both cohorts are needed because CPRD covers around 22% 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

We will request data from CPRD-Gold and CPRD-Aurum linked to HES and mortality data. We will request data for patients with an index record with a Read or SNOMED code indicating an incident pressure ulcer (Table 1 and Table 2) during a period of 11 years (01/04/2008-31/03/2019). 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 or SNOMED 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
45784	388T.00	Braden assessment scale
103311	38Dr.00	EPUAP (Euro pressure ulc advisry panl) classification system
17592	39C..00	Pressure sore index value
15505	39C0.00	Pressure sore
44641	39C1.00	Superficial pressure sore
55382	39C2.00	Deep pressure sore
63243	39C3.00	Pressure sore -deep + superfic
36995	39C4.00	Waterlow pressure sore risk score
95886	39C5.00	Medley pressure sore risk score
95113	39C6.00	Maelor pressure ulcer risk assessment score
109961	39C6.11	Maelor score
100778	39C7.00	EPUAP (European pressure ulcer advisory panel) grade 1 ulcer
101006	39C8.00	EPUAP (European pressure ulcer advisory panel) grade 2 ulcer
100864	39C9.00	EPUAP (European pressure ulcer advisory panel) grade 3 ulcer
100638	39CA.00	EPUAP (European pressure ulcer advisory panel) grade 4 ulcer
6862	M270.00	Decubitus (pressure) ulcer
14995	M270.11	Bed sore
4929	M270.13	Pressure sore
108537	M270.14	Decubitus ulcer and pressure area
103207	M270000	Hospital acquired pressure ulcer
102230	M270100	Nursing home acquired pressure ulcer
101713	M270200	Community hospital acquired pressure ulcer
102923	M270300	Hospice acquired pressure ulcer
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
104552	M270z00	Decubitus ulcer and pressure area NOS
3928	M271.00	Non-pressure ulcer lower limb
11786	Z174P00	Pressure sore care
17790	Z1B3.00	Dressing of pressure sore
28380	Z9K5.00	Pressure sore prevention
38996	ZQ39.00	Pressure sore assessment
55220	ZQ39.11	Decubitus ulcer assessment
35329	ZQ39.12	Pressure ulcer assessment
49654	ZQ39.13	Bed sore assessment
46050	ZQ52.00	Pressure sore risk assessment
107400	ZRai.00	Norton score
28814	ZRqY.00	UK consensus classification of pressure sores 1994

56610	ZRrL.00	Waterlow pressure sore risk score

Table 2: SNOMED codes to identify patients with an incident pressure ulcer

medcodeid	term	cleansedreadcode
6446501000006116	Assess pressure sore care	
6446491000006112	Assess pressure ulcer care	
1787140012	Bed sore	M270.11
2474687014	Braden assessment scale	388T.00
7277351000006113	Braden pressure ulcer risk score	
1647761000000119	Community hospital acquired pressure ulcer	M270200
608941000006119	Decubitus (pressure) ulcer	M270.00
1816831000006112	Decubitus ulcer and pressure area	M270.14
1816881000006113	Decubitus ulcer and pressure area NOS	M270z00
3257651000006111	Decubitus ulcer prevention education	
889551000006113	Decubitus/pressure ulcer	M270.99
4590631000006116	Deep and superficial pressure sore	
4590621000006119	Deep and superficial pressure ulcer	
926391000006116	Deep pressure sore	
256983018	Deep pressure sore	39C2.00
4590601000006112	Deep pressure ulcer	
904401000006116	Dressing of pressure sore	
4936821000006118	Dressing of pressure ulcer	
1752401000006112	EPUAP (Euro pressure ulc advisry panl) classification system	38Dr.00
7261641000006116	EPUAP (European pressure ulcer advisory panel) classification	
741781000000112	EPUAP (European pressure ulcer advisory panel) grade 1 ulcer	39C7.00
741801000000113	EPUAP (European pressure ulcer advisory panel) grade 2 ulcer	39C8.00
741821000000116	EPUAP (European pressure ulcer advisory panel) grade 3 ulcer	39C9.00
741841000000111	EPUAP (European pressure ulcer advisory panel) grade 4 ulcer	39CA.00
8123031000006119	European pressure ulcer advisory panel grade 1 ulcer	
8123051000006114	European pressure ulcer advisory panel grade 2 ulcer	
8123071000006116	European pressure ulcer advisory panel grade 3 ulcer	
8123091000006115	European pressure ulcer advisory panel grade 4 ulcer	
2986711011	History of pressure ulcer	
1647781000000111	Hospice acquired pressure ulcer	M270300
1647721000000110	Hospital acquired pressure ulcer	M270000
515331000000119	Maelor pressure ulcer risk assessment score	39C6.00
515341000000111	Maelor score	39C6.11

medcodeid	term	cleansedreadcode
2160104011	Medley pressure sore risk score	39C5.00
6763851000006113	Medley pressure ulcer risk score	
399941017	Non-pressure ulcer lower limb	M271.00
2617509017	Nonstageable pressure ulcer	
1647741000000115	Nursing home acquired pressure ulcer	M270100
8061081000006118	Observation of Waterlow pressure sore risk score	
2003741000006116	Preliminary pressure ulcer risk assessment	
1779199011	Pressure sore	M270.13
926371000006117	Pressure sore	
208311000006115	Pressure sore	39C0.00
926401000006119	Pressure sore - deep + superfic	
208331000006114	Pressure sore -deep + superfic	39C3.00
1938931000006117	Pressure sore associated with indwelling urinary catheter	
926361000006112	Pressure sore index value	
256980015	Pressure sore index value	39C..00
4949191000006119	Pressure sore prevention	
4949201000006116	Pressure sore protection	
994521000006110	Pressure ulcer	
1992981000006111	Pressure ulcer acquired in own home	
1480104019	Pressure ulcer care assessment	
2003861000006110	Pressure ulcer clinical pathway protocol followed	
2003761000006117	Pressure ulcer clinical pathway protocol not followed	
4590561000006112	Pressure ulcer index value	
2987070016	Pressure ulcer prevention	
2988929017	Pressure ulcer prevention education	
4949211000006118	Pressure ulcer protection	
2014921000006112	Pressure ulcer risk assessment not required	
2015161000006119	Pressure ulcer risk assessment required	
2016551000006119	Pressure ulcer self management plan	
1776931000006113	Reason for referral: Pressure Ulcer	
2008461000006117	SSKIN pressure ulcer prevention care bundle	
2015761000006115	SSKIN pressure ulcer prevention care bundle - Incont/moisture	
2015741000006119	SSKIN pressure ulcer prevention care bundle - Keep moving	
2015751000006117	SSKIN pressure ulcer prevention care bundle - Nutrition	
2015721000006114	SSKIN pressure ulcer prevention care bundle - Skin inspection	
2015731000006112	SSKIN pressure ulcer prevention care bundle - Surface	
1816841000006119	Stage I decubitus ulcer and pressure area	M270400
1816851000006117	Stage II decubitus ulcer	M270500
1816861000006115	Stage III decubitus ulcer	M270600
1816871000006110	Stage IV decubitus ulcer	M270700

medcodeid	term	cleansedreadcode
256982011	Superficial pressure sore	39C1.00
926381000006119	Superficial pressure sore	
4590581000006119	Superficial pressure ulcer	
6974601000006113	Unstageable pressure ulcer	
415946011	Waterlow pressure sore risk score	39C4.00
2015171000006114	Waterlow pressure sore risk score completed	
907451000006114	[RFC] At risk of developing pressure sores	
908861000006110	[RFC] Pressure sore	
910541000006110	[RFC] Pressure sore prevention	
907211000006112	[RFC] Pressure sores	

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 3), dressing of ulcer/wound (Table 4) 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 and SNOMED 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 3: 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 4: 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 75,000 incident pressure ulcers. Severe pressure ulcers in the community are mainly managed conservatively and few are admitted to hospital. CPRD Gold covers around 5% of the English population and CPRD Aurum around 17%, giving approximately 22% coverage overall. 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.[37] 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).[29]
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;[38, 39] 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.[40, 41]
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 or SNOMED 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, 43] 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.[44]

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)
N/A	1.0	28 February 2020	2.0	4th November 2020	Added CPRD-Aurum details and updated CPRD details, amended systematic review outcomes, updated various contact details, added systematic review protocols and draft SAP as appendices, minor wording changes throughout	N/A

15. Appendix 1: Systematic Review 1 Protocol

Exploring effectiveness evidence for reconstructive surgery for treating pressure ulcers

Background

Pressure ulcers, also known as bedsores, decubitus ulcers and pressure injuries, are localised areas of ischaemic injury to the skin and/or underlying tissue. They are caused by prolonged external mechanical forces such as pressure or shear beyond the normal physiological constraints [1]. These forces are higher adjacent to an underlying bony prominence such as the sacrum, ischium, trochanter and heel [2], which is where pressure ulcers tend to occur. Populations at greatest risk include non-ambulatory individuals and people with limited mobility or tactile sensation [3−7].

Pressure ulcers vary in severity. One of the most widely recognised systems for categorising pressure ulcers is that of the National Pressure Ulcer Advisory Panel, which is summarised below [8].

- Stage 1: intact skin with a localised area of non-blanchable erythema.
- Stage 2: partial-thickness skin loss with exposed dermis.
- Stage 3: full-thickness loss of skin in which adipose tissue is visible.
- Stage 4: full-thickness skin and tissue loss with exposed or directly palpable fascia, muscle, tendon, ligament, cartilage or bone in the ulcer.
- Unstageable pressure injury: full-thickness skin and tissue loss that is obscured by slough or eschar so that the severity of injury cannot be confirmed.
- A deep tissue pressure injury: local injury of persistent non-blanchable deep red, maroon, purple discolouration or epidermal separation revealing a dark wound bed or blood-filled blister.

Prevalence estimates vary according to the population being assessed, the data collection methods used and decisions about whether or not Stage I pressure ulcers should be included (since there is no active wound at this stage, but patients are 'at risk'). A large survey of hospital patients undertaken in several European countries returned a pressure ulcer prevalence (Stage II and above) of 10.5% [2]. In the UK, national pressure ulcer data are collected across community and acute settings - although data collection is not yet universal - as part of the National Health Service (NHS) Safety Thermometer initiative [9]. Five per cent of patients across these settings were estimated to have a pressure ulcer in January 2014 [10].

All the prevalence figures quoted above are for populations currently receiving medical care. The point prevalence of pressure ulceration in the total population was recently estimated using a cross-sectional survey undertaken in Leeds, UK. Of the total adult population of 751,485, the point prevalence of pressure ulceration was 0.31 per 1000 [11]. A community-specific pressure ulcer prevalence estimate in the UK reported a prevalence of 0.77 per 1000 adults in a UK urban area [12].

Surgical intervention for pressure ulcers is reserved for the most severe ulcers. In theory, if the pressure is removed and nutrition optimised [13,14], most ulcers should heal. It has been suggested in the literature that surgery is only considered after failure of conservative measures and usually reserved for Stage III and IV ulcers [15].Other factors in addition to the choice of surgical reconstruction may contribute to successful outcome: treatment

adherence, quality of local tissues, aetiological factors, patient co-morbidities, education status and motivation [16].

This review focuses on evidence about the effectiveness of surgical reconstruction of pressure ulcers, where surgical reconstruction is defined as any surgical procedure which aims, at the end of the procedure, to achieve a closed wound with skin coverage. Many surgical procedures start with thorough debridement to achieve a wound surface of healthy bleeding tissue. Debridement may be part of a surgical reconstruction process but, as it does not aim to achieve wound closure alone, is not considered as an intervention in this review.

Reconstructive surgical methods that may be used include the following [17]:

Primary wound closure: involves direct surgical advancement of the wound edges either directly or in layers to close the wound [18].

Skin grafting: involves harvesting a thin piece of skin that is surgically removed from a donor area to replace skin in the defect or denuded area. Skin grafts are occasionally used to treat pressure ulceration when all precipitating factors for pressure ulcer formation have been removed. They are used to facilitate quick wound cover and subsequently to accelerate wound healing [19].

Local random pattern flap: this reconstructive method involves surgically moving the local tissues around the wound, based on a random pattern of blood supply, into the wound defect [20].

Regional flap including:

- muscle or musculocutaneous flap; this surgical approach involves moving whole or part of a named muscle based on a defined blood supply with or without a skin island to provide cover to the wound [21];
- fascial or fasciocutaneous flap; this surgical approach involves moving a surgically defined fascial based island of tissue with its intact blood supply with or without skin to cover the wound [22];
- perforator flap; this is a refinement of the previous musculocutaneous or fasciocutaneous flap approach whereby the specific perforating blood vessels are identified in the flap and dissected to allow either greater movement or less muscle sacrifice as well as separation of components to each flap [23].

Free flap: this surgical approach involves raising a defined island of tissue with an artery and vein that is surgically detached and moved to the site of the wound where other local arteries or veins of similar size are identified and then the vessels are surgically anastomosed to re-establish blood flow to the island of tissue [24].

Tissue expansion: this surgical approach involves a gradual increment and recruitment of tissue surrounding a pressure ulcer. It is performed by expanding the skin with a tissue expander, which is inserted into a subcutaneous pocket near the ulcer and slowly expanded at a defined rate with saline. Once the skin and soft tissues are expanded to a volume capable of covering the pressure ulcer, the expander is removed and the tissues are inset to cover the wound. Another method is to apply slow skin traction over the wound with an incremental traction dressing, which works on the same principle of gradual mechanical traction on skin, promoting tissue creep [25]. Eventually the extra skin recruited can be used to close the wound.

All of the above approaches can be performed as a one-stage procedure, or as part of a multistage procedure to increase the likelihood of the tissue surviving manipulation, reduce the overall surgical impact on the patient or to ensure that all infected or aggravating factors are minimised. This is particularly important as the skin quality around pressure ulcers is usually sub-optimal.

This systematic review aims to assess the effects of reconstructive surgery for healing pressure ulcers (Stage 2 or above), comparing any methods of reconstructive surgery (i.e. primary wound closure, skin grafting and surgery involving flap closure or tissue expansion) with no surgery or comparing alternative forms of reconstructive surgery, irrespective of the care setting in which care is provided.

Methods

Study inclusion criteria

Types of study

We have mapped the design features of eligible studies in Table 1 following the taxonomy of Reeves et al 2017 [26].

Was the intervention/comparator	Review eligibility Criteria	Rationale
Allocated to (provided for/ administered to/chosen by) individuals?	Eligible	We will include studies where individuals are allocated into groups.
Allocated to (provided for/administered to/chosen by) clusters of individuals?	Not eligible	This feature describes studies which, by design, allocate to clusters e.g. clustered randomised controlled trials and most controlled before and after studies. Such studies are not eligible for this review.
Clustered in the way it was provided (by practitioner or organizational unit)?	Eligible	This feature distinguishes studies with intrinsic clustering from studies which allocate to clusters by design (described above). Intrinsic clustering could arise at the surgeon, unit or hospital level. Studies with potential intrinsic clustering will be included with the clustering mechanism described where possible alongside any approaches undertaken to mitigate for the non-independent nature of these data.
Were outcome data available:		
After intervention/comparator only (same individuals)?	Eligible for specific outcomes	Eligible for all outcomes
Before (once) AND after intervention/comparator (same individuals)?	Eligible for specific outcomes	Eligible for all outcomes
Before (once) AND after intervention/comparator (not all same individuals)?	Not eligible	This is a defining feature of controlled-before and after studies which, here, are considered clustered by nature and not eligible for this review.

Multiple times before AND multiple times after intervention/comparator (same individuals)?	Eligible for specific outcomes	Eligible for following outcomes: Health related quality of life
Multiple times before AND multiple times after intervention/comparator (not all same individuals)?	Not eligible	This is a defining feature of interrupted time series designs which are clustered by nature and not eligible for this review.
Was the intervention effect estimated by		
Change over time (same individuals at different time points)?	Eligible for specific outcomes	Eligible for following outcomes: Health related quality of life
Change over time (not all same individuals at different time points)?	Not Eligible	This is a defining feature of controlled-before and after studies and studies with an interrupted time series design which are considered clustered by nature and not eligible for this review.
Difference or ratio between groups (of individuals or clusters receiving either intervention or comparator)?	Eligible for specific outcomes	Eligible for following outcomes: Wound healing, health related quality of life and wound recurrence
Did the researchers aim to control for confounding (design or analysis)		
Using methods that control in principle for any confounding?	Eligible	
Using methods that control in principle for time-invariant unobserved confounding?	Eligible	
Using methods that control only for confounding by observed covariates?	Eligible	
No attempt to control for confounding	**Ineligible**	
Were groups of individuals or clusters formed by		
Randomization?	Eligible	
Quasi-randomization?	Eligible	
Explicit rule for allocation based on a threshold for a variable measured on a continuous or ordinal scale or boundary (in conjunction with identifying the variable dimension, below)?	Eligible	
Some other action of researchers?	Eligible in specific cases	We will include studies with group allocation based on researcher action where (a) there is a clear definition description of the researcher/investigator and (b) where the mechanism or decision rules which informed allocation are clearly described in the study report.
Time differences?	Not Eligible	This is a defining feature of controlled-before and after studies, studies with an interrupted time series design which are considered clustered by nature in this context, or uncontrolled studies in which outcomes are measured before and after intervention/comparator. Studies of these kinds are not eligible for this review.

Location differences?	Not Eligible	This is a defining feature of controlled-before and after studies which are considered clustered by nature in this context and not eligible for this review.
Health care decision makers/ practitioners?	Eligible	
Participants' preferences?	Eligible	
Policy maker	Not Eligible	Allocation at policy level generally a feature of clustered design. In this context considered to have poor control for confounding with associated causal inference at very high risk of bias. Studies with this mechanism of allocation are not eligible for this review.
On the basis of outcome?	Not Eligible	Defining feature of a case-control study which are not eligible for this review.
Some other process? (specify)	Not Eligible	
Were the following features of the study carried out after the study was designed		
Characterization of individuals/ clusters before intervention?	Eligible	
Actions/choices leading to an individual/cluster becoming a member of a group?	Eligible	
Assessment of outcomes?	Eligible	
Were the following variables measured before intervention: (answer "yes" to more than one item, if applicable)		
Potential confounders?	Eligible	
Outcome variable(s)?	Eligible	

Table 1: Eligibility of non-randomised studies defined by specific design features (Reeves et al 2017) [26].

To summarise, these criteria mean that (i) randomised controlled trials will be included, as will (ii) quasi-randomised controlled trials (studies using a system of quasi-randomisation for participant allocation); (iii) non-randomised studies with clearly reported mechanism of group formation, described methods of ascertainment of eligible participants and their recruitment and clear adjustment for cofounding in the analysis. 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. We will not include single cohorts where all participants are given the same type of surgery. Cross-sectional and case-control studies will also not be included.

Types of participants

We will include studies that recruited adults with a diagnosis of a pressure ulcer (any stage) managed in any care setting. We will accept study authors' definitions of stages. We expect studies to have recruited almost entirely people with Stage 3 or 4 pressure ulcers because surgical reconstruction would rarely be carried out for less severe pressure ulcers. We plan to exclude studies with mixed wound populations at baseline, that is studies that did not restrict inclusion to people with a pressure ulcer, e.g. which may have included participants with other types of wounds such as venous leg or diabetic foot ulcers.

Types of interventions

The primary intervention is reconstructive surgery for pressure ulceration (where reconstructive surgery is defined as a surgical procedure that aims to achieve, a closed wound with skin coverage). We anticipate likely comparisons will include surgery (i.e. primary wound closure, skin grafting and surgery involving flap closure or tissue expansion) compared with no surgery and different types of surgery compared with each other.

Whilst studies investigating the effects of surgical debridement alone on pressure ulceration are excluded as they do not aim to achieve wound closure, reconstructive surgery will often include wound debridement. In this context we consider debridement as a co-intervention. So a study of pressure ulcer debridement (no surgical reconstruction) compared with conservative care (no reconstruction) would be excluded. A study of surgical reconstruction compared with conservative care and debridement would be included, with some debridement presumed in the reconstruction arm. We will extract information on debridement and all other reported co-interventions described and these will also be considered in the risk of bias assessment.

Outcomes

Primary outcomes

The primary outcome for this review is wound breakdown, after surgical reconstruction.

Wound breakdown: We broadly define this outcome as measuring whether an open wound recurs, or has never healed by the time of assessment, at broadly the same site as that being treated in the study. We will accept study authors' definitions of wound breakdown and will record how breakdown is defined with respect to time since surgery, anticipating that some definitions will be short-term and some longer term (could be considered as recurrence of a healed wound rather than breakdown of a healing surgical wounds soon after surgery).

Secondary outcomes

Secondary outcomes are as follows:

- Health-related quality of life: we will include quality of life where it is reported using a validated scale such as the SF-36 or EQ-5D or a validated disease-specific questionnaire such as the Cardiff Wound Impact Schedule. We will not include ad hoc measures of quality of life that are unvalidated or were not common to multiple trials;
- Wound infection: we will accept study authors' definitions of wound infection;
- Mean costs reported per group or the mean difference between groups
- Incident secondary ulcer: a second pressure ulcer that developed in a different area during the follow-up period.

If a study is otherwise eligible (i.e. correct study design, population and intervention/comparator) but does not report a listed outcome then we will contact the study authors where possible to establish whether an outcome of interest was measured but not reported.

We will report outcome measures at the latest time point available for a study (assumed to be length of follow-up if not specified) and the time point specified in the methods of the included study as being of primary interest (if this is different from latest time point available). For all outcomes we plan to categorise the timing of assessment of outcomes as follows:

- less than one week to eight weeks as short-term;
- from eight weeks to 16 weeks as medium-term;
- and more than 16 weeks as long-term.

Search methods for identification of studies

We will search the following electronic databases: The Cochrane Wounds Specialised Register; The Cochrane Central Register of Controlled Trials (CENTRAL); Ovid MEDLINE; Ovid MEDLINE (In-Process & Other Non-Indexed Citations); Embase; EBSCO CINAHL Plus. See Appendix 1 for search strategy examples.

There are no restrictions with respect to language, date of publication or study setting. Citations will be de-duplicated as part of the search process so identical records included more than once will be removed prior to screening.

We will aim to identify other potentially eligible trials or ancillary publications by searching the reference lists of included studies as well as relevant systematic reviews, meta-analyses and health technology assessment reports.

Study selection

Two review authors will independently assessed the titles and abstracts of the citations retrieved by the searches for relevance. After the initial assessment, we will obtain full-text copies of all study reports considered to be potentially relevant. Two review authors will independently check the full papers for eligibility. We will resolve disagreements by discussion and, where required, consult the input of a third review author. We will record all reasons for exclusion of studies for which we have obtained full copies. We will complete a PRISMA flowchart to summarise this process. Where studies have been reported in multiple publications/reports we will obtain all the available publications. Whilst a study will only be included once in the review, we will extract data from all reports to ensure maximal relevant data were obtained.

Data extraction and management

We will extract and summarise details of the eligible studies using a data extraction sheet. Two review authors will extract data independently and resolve disagreements by discussion, drawing on a third review author where required. Where key data are missing from reports, we plan to contact the study authors to obtain this information. Where a study with more than two intervention arms is included, we will only extract data from intervention and control groups that meet the eligibility criteria. We will extract the following details. Study descriptors, participant eligibility criteria, baseline age, sex, ulcer area and duration, number of people with spinal cord injury, number of people with a recurrence ulcer, number of people with single or multiple ulcers at time of surgery. Intervention and co-intervention details, description of follow-up, outcome data and analytical approaches used, missing data with reasons for missingness where noted.

Assessment of risk of bias in included studies

Two review authors will independently assess included studies using the Cochrane approach for assessing risk of bias as detailed in the Cochrane Handbook for Systematic Reviews of Interventions. For RCTs we will use the Risk of Bias 2 (RoB2) tool.[27] To assess cohort studies we will use the ROBINS-1 tool.[28] ROBINS-I requires pre-specification of potential confounding domains and co-interventions to allow assessment of

risk of bias in light of how these elements are present and dealt with for each study−outcome dyad.

Confounding by indication will be a risk in non-randomised studies: we consider key potential confounding domains for studies in this review to be: participant's age; life expectancy; health status (e.g. fitness for surgery); and ulcer area and duration at baseline.

Also important to assess is the allocation of co-interventions within study groups: differential use of these may impact on relative estimates if the co-interventions are independently associated with outcomes. Where possible we will assess for differential use of the following discretionary co-interventions by group: support surfaces, repositioning regimens and negative pressure wound therapy. Debridement may be a co-intervention used in conjunction with reconstructive surgery or used as a treatment in its own right; this will be recorded and considered for each comparison as relevant.

Measures of treatment effect

RCTs

For dichotomous outcomes we will calculate the risk ratio (RR) with 95% confidence intervals (CI). For continuously distributed outcome data we will use the mean difference (MD) with 95% CIs, where trials used the same or a similar assessment scale. If trials use different assessment scales, we plan to use the standardised mean difference (SMD) with 95% CIs.

We will report correctly analysed time-to-event data (e.g. time to wound breakdown) as hazard ratios (HR) where possible in accordance with the methods described in the Cochrane Handbook for Systematic Reviews of Interventions [26]. If studies reporting time-to-event data (e.g. time to healing) do not report a hazard ratio, then, where feasible, we will estimate this using other reported outcomes, such as the numbers of events, through the application of available statistical methods.

Non-randomised study designs

If available, we will extract unadjusted and adjusted treatment effects, recording (as part of ROBINS-I) the confounding domains which are controlled for. Where multiple adjusted treatment effects are reported we will choose the one that is judged to control best for the pre-specified important confounding domains. The rationale for this decision will be recorded.

Data synthesis

We will synthesise included data narratively and also using meta-analysis where applicable. Comparisons will be structured according to type of comparator and then by outcomes ordered by duration of follow-up period. Treatment effects will be synthesised, where appropriate (see below), using the inverse variance method.

We will consider clinical and methodological heterogeneity and undertake pooling when studies appear appropriately similar in terms of participants, support surfaces, and outcome type.

By default, we will meta-analyse RCTs and non-randomised studies separately. Unadjusted non-randomised treatment effects will not be included in any synthesis, since they will (by definition) be scored as being at critical risk of bias. We will only meta-analyse non-randomised studies which are judged to be at low or moderate risk of bias and are considered to be homogenous in terms of study design features.

If included studies support one or more meta-analyses, we anticipate using random-effects models to estimate an underlying average treatment effect from studies. We will exercise caution when meta-analysed data are at risk of small study effects because a random-effects model may be unsuitable. In such instances, or where there are other reasons to question the choice of a random-effects model, we will assess the impact of the approach using sensitivity analyses to compare results from alternate models.

Suitable meta-analysis methods are those based on estimates and standard errors, particularly the generic inverse-variance model. We will perform meta-analyses largely using Review Manager 5.3 (Review Manager 2014) and using *Stata: Release 14* (StataCorp. 2015) or R (R Core Team, 2019) where necessary. We will present data using forest plots where possible.

Sub Group analyses

We will investigate heterogeneity using the methods described in Section 10.10 of the Cochrane Handbook for Systematic Reviews of Interventions [29]. We will perform subgroup analyses/ meta-regression to determine whether the size of treatment effects is influenced by the following three study-level characteristics:

- Risk of bias (binary: low vs unclear or high risk of bias in one or more domain);
- Ulcer stage
- Type of surgery

We will not perform subgroup analysis/ meta-regression when the number of studies included in the meta-analysis is not reasonable (e.g., fewer than 10).

Assessing the certainty of evidence and "Summary of findings" tables

We will present an overall grading of the certainty of the evidence associated with each of the following outcomes assessed using the principle of the Grading of Recommendations Assessment, Development and Evaluation (GRADE).[30]

- Wound breakdown
- Health-related quality of life

The GRADE approach defines the certainty of a body of evidence as the extent to which one can be confident that an estimate of effect or association is close to the true quantity of specific interest.

We will present a separate “Summary of findings” table for each relevant comparison-outcome pair evaluated in this review.

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15.1 Appendix 1: Searches

For logistical reasons these were run as separate searches rather than combined searches.
All run 23rd April 2019

RCT Searches
Cochrane Wounds Specialised Register
1 MESH DESCRIPTOR Surgical Procedures, Operative EXPLODE ALL AND INREGISTER
2 MESH DESCRIPTOR Surgical Flaps EXPLODE ALL AND INREGISTER
3 (surger* or surgical*) AND INREGISTER
4 (primary near3 closure*) AND INREGISTER
5 (skin near3 (graft* or transplant*)) AND INREGISTER
6 ((surg* or reconstruct* or random or region* or muscle or musculocutaneous or fascial* or fasciocutaneous* or perforat* or free) near2 flap*) AND INREGISTER
7 "tissue expansion" AND INREGISTER
8 #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 AND INREGISTER
9 MESH DESCRIPTOR Pressure Ulcer EXPLODE ALL AND INREGISTER
10 (pressure NEXT (ulcer* or sore* or injur*)) AND INREGISTER
11 (decubitus NEXT (ulcer* or sore*)) AND INREGISTER
12 ((bedsore* or bed sore*)) AND INREGISTER
13 #9 OR #10 OR #11 OR #12 AND INREGISTER
14 #8 AND #13 AND INREGISTER

The Cochrane Central Register of Controlled Clinical Trials (CENTRAL)

#1 MeSH descriptor: [Surgical Procedures, Operative] explode all trees

#2 MeSH descriptor: [Surgical Flaps] explode all trees

#3 (surger* or surgical*) .ti,ab,kw

#4 (primary near/3 closure*):ti,ab,kw

#5 (skin near/3 (graft* or transplant*)):ti,ab,kw

#6 ((surg* or reconstruct* or random or region* or muscle or musculocutaneous or fascial* or fasciocutaneous* or perforat* or free) near/2 flap*):ti,ab,kw

#7 "tissue expansion":ti,ab,kw

#8 {or #1-#7}

#9 MeSH descriptor: [Pressure Ulcer] explode all trees

#10 (pressure next (ulcer* or sore* or injur*)):ti,ab,kw

#11 (decubitus next (ulcer* or sore*)):ti,ab,kw

#12 ((bed next sore*) or bedsore*):ti,ab,kw

#13 {National Institute for Health Research, #9-`#12-`#12}

#14 (#8 and #13) in Trials

Ovid MEDLINE

1 exp surgical procedures, operative/
2 exp Surgical Flaps/
3 (surger* or surgical*).ti,ab.
4 (primary adj3 closure*).ti,ab.
5 (skin adj3 (graft* or transplant*)).ti,ab.
6 ((surg* or reconstruct* or random or region* or muscle or musculocutaneous or fascial* or fasciocutaneous* or perforat* or free) adj2 flap*).ti,ab.
7 tissue expansion.ti,ab.
8 or/1-7
9 exp Pressure Ulcer/
10 (pressure adj (ulcer* or sore* or injur*)).tw.
11 (decubitus adj (ulcer* or sore*)).tw.
12 (bedsore* or bed sore*).tw.
13 or/9-12
14 and/8,13
15 randomized controlled trial.pt.
16 controlled clinical trial.pt.
17 randomi?ed.ab.
18 placebo.ab.
19 clinical trials as topic.sh.
20 randomly.ab.
21 trial.ti.
22 or/15-21
23 exp animals/ not humans.sh.
24 22 not 23
25 14 and 24

Ovid Embase

1 exp surgical technique/
2 exp skin graft/
3 exp tissue flap/
4 exp tissue expansion/
5 (surger* or surgical*).ti,ab.
6 (primary adj3 closure*).ti,ab.
7 (skin adj3 (graft* or transplant*)).ti,ab.

8 ((surg* or reconstruct* or random or region* or muscle or musculocutaneous or fascial* or fasciocutaneous* or perforat* or free) adj2 flap*).ti,ab.
9 tissue expansion.ti,ab.
10 or/1-9
11 exp decubitus/
12 (pressure adj (ulcer* or sore* or injur*)).tw.
13 (decubitus adj (ulcer* or sore*)).tw.
14 (bedsore* or bed sore*).tw.
15 or/11-14
16 10 and 15
17 Randomized controlled trials/
18 Single-Blind Method/
19 Double-Blind Method/
20 Crossover Procedure/
21 (random* or factorial* or crossover* or cross over* or cross-over* or placebo* or assign* or allocat* or volunteer*).ti,ab.
22 (doubl* adj blind*).ti,ab.
23 (singl* adj blind*).ti,ab.
24 or/17-23
25 exp animals/ or exp invertebrate/ or animal experiment/ or animal model/ or animal tissue/ or animal cell/ or nonhuman/
26 human/ or human cell/
27 and/25-26
28 25 not 27
29 24 not 28
30 16 and 29

EBSCO CINAHL Plus

S27	S13 AND S26
S26	S14 OR S15 OR S16 OR S17 OR S18 OR S19 OR S20 OR S21 OR S22 OR S23 OR S24 OR S25
S25	TI allocat* random* or AB allocat* random*
S24	MH "Quantitative Studies"
S23	TI placebo* or AB placebo*

S22	MH "Placebos"
S21	TI random* allocat* or AB random* allocat*
S20	MH "Random Assignment"
S19	TI randomi?ed control* trial* or AB randomi?ed control* trial*
S18	AB (singl* or doubl* or trebl* or tripl*) and AB (blind* or mask*)
S17	TI (singl* or doubl* or trebl* or tripl*) and TI (blind* or mask*)
S16	TI clinic* N1 trial* or AB clinic* N1 trial*
S15	PT Clinical trial
S14	MH "Clinical Trials+"
S13	S7 AND S12
S12	S8 OR S9 OR S10 OR S11
S11	TI decubitus or AB decubitus
S10	TI (bed sore* or bedsore*) or AB (bed sore* or bedsore*)

S9	TI (pressure ulcer* or pressure sore*) or AB (pressure ulcer* or pressure sore*)
S8	(MH "Pressure Ulcer+")
S7	S1 OR S2 OR S3 OR S4 OR S5 OR S6
S6	TI tissue expansion OR AB tissue expansion
S5	TI ((surg* or reconstruct* or random or region* or muscle or musculocutaneous or fascial* or fasciocutaneous* or perforat* or free) N2 flap*) OR AB ((surg* or random or region* or muscle or musculocutaneous or fascial* or fasciocutaneous* or perforat* or free) N2 flap*)
S4	TI (skin N3 (graft* or transplant*)) or AB (skin N3 (graft* or transplant*))
S3	TI (primary N3 closure*) OR AB (primary N3 closure*)
S2	TI surger* or surgical* OR AB surger* or surgical*
S1	(MH "Surgery, Operative+")

US National Institutes of Health Ongoing Trials Register (ClinicalTrials.gov)

Surgery OR reconstruction OR flap OR graft OR transplant | Pressure Ulcer
Surgery OR reconstruction OR flap OR graft OR transplant | Pressure Injury
Surgery OR reconstruction OR flap OR graft OR transplant | Pressure Ulcers Stage II
Surgery OR reconstruction OR flap OR graft OR transplant | Pressure Ulcers Stage III
Surgery OR reconstruction OR flap OR graft OR transplant | Pressure Ulcer, Stage IV

World Health Organization International Clinical Trials Registry Platform
(surgery OR reconstruction OR flap OR graft OR transplant) [Intervention]
AND pressure ulcer [Title]

(surgery OR reconstruction OR flap OR graft OR transplant) [Intervention]
AND pressure ulcer [Condition]

(surgery OR reconstruction OR flap OR graft OR transplant)[Intervention]
AND Pressure sore [Title]

(surgery OR reconstruction OR flap OR graft OR transplant)[Intervention]
AND Pressure sore [Condition]

(surgery OR reconstruction OR flap OR graft OR transplant)[Intervention]
AND decubitus [Condition]

(surgery OR reconstruction OR flap OR graft OR transplant) [Intervention]
AND bed sore [Condition]

Non-Randomised Study Searches

MEDLINE

1 exp surgical procedures, operative/
2 exp Surgical Flaps/
3 (surger* or surgical*).ti.
4 (primary adj3 closure*).ti,ab.
5 (skin adj3 (graft* or transplant*)).ti,ab.
6 ((surg* or reconstruct* or random or region* or muscle or musculocutaneous or fascial* or fasciocutaneous* or perforat* or free) adj2 flap*).ti,ab.
7 tissue expansion.ti,ab.
8 or/1-7
9 exp Pressure Ulcer/
10 (pressure adj (ulcer* or sore* or injur*)).ti,kw.
11 (decubitus adj (ulcer* or sore*)).ti,kw.
12 (bedsore* or bed sore*).ti,kw.
13 or/9-12
14 and/8,13
15 exp cohort studies/
16 cohort$.tw.
17 controlled clinical trial.pt.
18 epidemiologic studies/
19 or/15-18
20 14 and 19

Embase 1974

1 exp surgical technique/
2 exp skin graft/
3 exp tissue flap/
4 exp tissue expansion/
5 (surger* or surgical*).ti.
6 (primary adj3 closure*).ti,ab.

7 (skin adj3 (graft* or transplant*)).ti,ab.
8 ((surg* or reconstruct* or random or region* or muscle or musculocutaneous or fascial* or fasciocutaneous* or perforat* or free) adj2 flap*).ti,ab.
9 tissue expansion.ti,ab.
10 or/1-9
11 exp decubitus/
12 (pressure adj (ulcer* or sore* or injur*)).ti,kw.
13 (decubitus adj (ulcer* or sore*)).ti,kw.
14 (bedsore* or bed sore*).ti,kw.
15 or/11-14
16 10 and 15
17 exp cohort analysis/
18 exp longitudinal study/
19 exp prospective study/
20 exp follow up/
21 cohort$.tw.
22 or/17-21
23 16 and 22

CINAHLPlus

S18 S13 AND S17
S17 S14 OR S15 OR S16
S16 TI longitudinal or AB longitudinal
S15 TI cohort* or AB cohort*
S14 (MH "Prospective Studies+")
S13 S7 AND S12
S12 S8 OR S9 OR S10 OR S11
S11 TI decubitus or AB decubitus
S10 TI (bed sore* or bedsore*) or AB (bed sore* or bedsore*)
S9 TI (pressure ulcer* or pressure sore*) or AB (pressure ulcer* or pressure sore*)
S8 (MH "Pressure Ulcer+")
S7 S1 OR S2 OR S3 OR S4 OR S5 OR S6
S6 TI tissue expansion OR AB tissue expansion
S5 TI ((surg* or reconstruct* or random or region* or muscle or musculocutaneous or fascial* or fasciocutaneous* or perforat* or free) N2 flap*) OR AB ((surg* or random or region* or muscle or musculocutaneous or fascial* or fasciocutaneous* or perforat* or free) N2 flap*)
S4 TI (skin N3 (graft* or transplant*)) or AB (skin N3 (graft* or transplant*))
S3 TI (primary N3 closure*) OR AB (primary N3 closure*)
S2 TI (surger* or surgical*)
S1 (MH "Surgery, Operative+")

Database(s): Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Daily and Versions(R) 1946 to 23/04/2019
Search Strategy:

#	Searches	Results
1	exp surgical procedures, operative/	

2 exp Surgical Flaps/
3 (surger* or surgical*).ti,ab.
4 (primary adj3 closure*).ti,ab.
5 (skin adj3 (graft* or transplant*)).ti,ab.
6 ((surg* or reconstruct* or random or region* or muscle or musculocutaneous or fascial* or fasciocutaneous* or perforat* or free) adj2 flap*).ti,ab.
7 tissue expansion.ti,ab.
8 or/1-7
9 exp Pressure Ulcer/
10 (pressure adj (ulcer* or sore* or injur*)).tw.
11 (decubitus adj (ulcer* or sore*)).tw.
12 (bedsore* or bed sore*).tw.
13 or/9-12
14 and/8,13
15 controlled clinical trial.pt.
16 14 and 15

Database(s): Embase 1974 to 23/04/2019

Search Strategy:

Searches Results
1 exp surgical technique/
2 exp skin graft/
3 exp tissue flap/
4 exp tissue expansion/
5 (surger* or surgical*).ti,ab.
6 (primary adj3 closure*).ti,ab.
7 (skin adj3 (graft* or transplant*)).ti,ab.
8 ((surg* or reconstruct* or random or region* or muscle or musculocutaneous or fascial* or fasciocutaneous* or perforat* or free) adj2 flap*).ti,ab.
9 tissue expansion.ti,ab.
10 or/1-9
11 exp decubitus/
12 (pressure adj (ulcer* or sore* or injur*)).tw.
13 (decubitus adj (ulcer* or sore*)).tw.
14 (bedsore* or bed sore*).tw.
15 or/11-14
16 10 and 15
17 Controlled clinical study/
18 16 and 17

CINAHLPlus 1937 to 23/04/2019

S15 S13 AND S14
S14 PT clinical trial

S13 S7 AND S12
S12 S8 OR S9 OR S10 OR S11
S11 TI decubitus or AB decubitus
S10 TI (bed sore* or bedsore*) or AB (bed sore* or bedsore*)
S9 TI (pressure ulcer* or pressure sore*) or AB (pressure ulcer* or pressure sore*)
S8 (MH "Pressure Ulcer+")
S7 S1 OR S2 OR S3 OR S4 OR S5 OR S6
S6 TI tissue expansion OR AB tissue expansion
S5 TI ((surg* or reconstruct* or random or region* or muscle or musculocutaneous or fascial* or fasciocutaneous* or perforat* or free) N2 flap*) OR AB ((surg* or random or region* or muscle or musculocutaneous or fascial* or fasciocutaneous* or perforat* or free) N2 flap*)
S4 TI (skin N3 (graft* or transplant*)) or AB (skin N3 (graft* or transplant*))
S3 TI (primary N3 closure*) OR AB (primary N3 closure*)
S2 TI surger* or surgical* OR AB surger* or surgical*
S1 (MH "Surgery, Operative+")

16. Appendix 2: Systematic Review 2 Protocol

Measuring health related quality of life in people with pressure ulcers: a systematic review.

Background

Pressure ulcers, also known as bedsores, decubitus ulcers and pressure injuries, are localised areas of ischaemic injury to the skin and/or underlying tissue. They are caused by prolonged external mechanical forces such as pressure or shear beyond the normal physiological constraints [1]. These forces are higher adjacent to an underlying bony prominence such as the sacrum, ischium, trochanter and heel [2], which is where pressure sores tend to occur. Populations at greatest risk include non-ambulatory individuals and people with limited mobility or tactile sensation [3−7].

Pressure ulcers vary in severity. One of the most widely recognised systems for categorising pressure ulcers is that of the National Pressure Ulcer Advisory Panel, which is summarised below [8].

- Stage 1: intact skin with a localised area of non-blanchable erythema.
- Stage 2: partial-thickness skin loss with exposed dermis.
- Stage 3: full-thickness loss of skin in which adipose tissue is visible.
- Stage 4: full-thickness skin and tissue loss with exposed or directly palpable fascia, muscle, tendon, ligament, cartilage or bone in the ulcer.
- Unstageable pressure injury: full-thickness skin and tissue loss that is obscured by slough or eschar so that the severity of injury cannot be confirmed.
- A deep tissue pressure injury: local injury of persistent non-blanchable deep red, maroon, purple discolouration or epidermal separation revealing a dark wound bed or blood-filled blister.

Prevalence estimates vary according to the population being assessed, the data collection methods used and decisions about whether or not Stage I pressure ulcers were included (since there is no active wound at this stage, but patients are 'at risk'). A large survey of hospital patients undertaken in several European countries returned a pressure ulcer prevalence (Stage II and above) of 10.5% [2]. In the UK, national pressure ulcer data are collected across community and acute settings - although data collection is not yet universal - as part of the National Health Service (NHS) Safety Thermometer initiative [9]. Five per cent of patients across these settings were estimated to have a pressure ulcer in January 2014 [10].

All the prevalence figures quoted above are for populations currently receiving medical care. The point prevalence of pressure ulceration in the total population was recently estimated using a cross-sectional survey across health and care services in Leeds, UK. Of the total adult population of 751,485, the point prevalence of pressure ulceration was 0.31 per 1000 [11]. UK pressure ulcer prevalence estimates specifically for community settings have reported rates of 0.77 per 1000 adults in a UK urban area [12].

Health related quality of life is a multi-dimensional concept focused on how health/ill-health and associated treatments impact on experiences of daily living and well-being. A review of qualitative and quantitative literature on the impact of pressure ulcers on health related quality of life (13; Gorecki 2009) identified 31 studies (21 quantitative studies and 10 qualitative.) Using a content analysis approach the review identified 11 health-related quality of life themes considered to be impacted by pressure ulceration. These include social impact; physical impact and limitations; psychological impact; impact of symptoms and impact on general health and consequences. The research for the review alongside interviews with 30 people with pressure ulcers led to the development of a conceptual framework for health-related quality of life in pressure ulcers containing four domains: symptoms, physical functioning; psychological well-being and social functioning [14]. These domains have been used to develop a recently validated health-related quality of life tool specifically for pressure ulceration called the PU-QOL tool [14].

To date no review has systematically reviewed quantitative findings of the impact of pressure ulcers on health-related quality of life and how this changes over time. This is not a straightforward task because people with pressure ulcers are likely to have other health conditions that also impact on their health-related quality of life. Because of the need to control for these factors we have focused this review on data from randomised controlled trials.

Objective

The aim of this review is to assess the impact of pressure ulceration on health-related quality of life over time when measured using validated tools. Specifically we will explore whether increasing or decreasing, average, levels of ulceration is associated with a change in HRQOL outcomes.

Types of study

Eligible studies: We will include randomised controlled trials which report one or more health related quality of life score measured using a validated instrument (see 'outcome' below for instruments which satisfy this criterion) in (i) individuals with pressure ulcers or (ii) on populations at risk of developing pressure ulcers. We will exclude the following study types

- Studies comparing forms of wound assessment e.g. agreement/reproducibility/diagnostic studies
- Pilot studies
- Split wound or split body studies

Types of participants

We will include adults (defined here as 18 years or older) with (i) a diagnosis of a pressure ulcer (Stage II, III, IV or Unstageable) managed in any care setting or (ii) at risk of pressure ulcer development.

We will exclude studies with the following participants:

- Populations with a range of wound types (not exclusively a pressure ulcer population)
- Intensive care Unit populations and non-responsive population (e.g. those in comas)
- Healthy volunteer study populations
- Animal studies

Outcome

The outcome data for this review are those collected via validated multi-dimensional measure of health related quality of life. Eligible generic measures considered are: SF-36; SF-12; SF-6; EQ-5D; Nottingham Health Profile; Sickness Impact Profile and the World Health Organization Quality of Life Scale. Validated disease specific tools are eligible; at this stage the only eligible tool we are aware of is the PurPOSE PUQOL tool.

Search methods for identification of studies

We will search the following electronic databases: The Cochrane Wounds Specialised Register; The Cochrane Central Register of Controlled Trials (CENTRAL); Ovid MEDLINE; Ovid MEDLINE (In-Process & Other Non-Indexed Citations); Ovid Embase; EBSCO CINAHL Plus. See Appendix 1 for further search details.

There are no restrictions with respect to language, date of publication or study setting. Citations will be de-duplicated as part of the search process so identical records included more than once will be removed prior to screening. We will aim to identify other potentially eligible studies or ancillary publications by searching the reference lists of retrieved included studies as well as relevant systematic reviews, meta-analyses and health technology assessment reports.

Study selection

Two review authors will independently assess the titles and abstracts of the citations retrieved by the searches for relevance. After the initial assessment, we will obtain full-text copies of all studies considered to be potentially relevant. Two review authors will independently check the full papers for eligibility. We will resolve disagreements by discussion and, if required, discuss with a third review author. We will record all reasons for exclusion of studies for which we have obtained full copies. We will complete a PRISMA flowchart to summarise this process. Where studies have been reported in multiple publications/reports we will obtain all the available publications. Whilst a study will only be included once in the review, we will extract data from all reports to ensure as many relevant data as possible are obtained.

Data extraction and management

We will extract and summarise details of the eligible studies using a data extraction sheet. Two review authors will extract data independently and resolve disagreements by discussion, drawing on a third review author where required. Where data are missing from reports, we plan to contact the study authors to obtain this information.

We will extract data on the following where reported: study type; participant age; co-morbidities; included pressure ulcers grades (and methods used for assessment); time points assessed; health related quality of life measure used and associated outcome data reported at specific time points; method of analyses reported; wound healing data.

Assessment of risk of bias in included studies

Two review authors will independently assess included studies using the Cochrane approach for assessing risk of bias as detailed in the Cochrane Handbook for Systematic Reviews of Interventions. For RCTs we will use the Risk of Bias 2 (RoB2) tool.[15]

Data synthesis

Study-level data will be presented narratively in terms of the study type; study population; health related quality of life measure and outcome data. We anticipate that most data will be presented as mean values with standard deviation. We will consider follow-up times as 8 weeks or less as short term; medium term follow-up as more than 8 weeks to 24 weeks and long term follow-up as more than 24 weeks. Where data are presented as multi-level model data (i.e. repeated health-related quality of life measures in an individual over time) we will present summary data where this has been calculated in the study. Otherwise we will present mean values from the latest time point possible. Where possible we will present follow-up health related quality of life data alongside proportion of wounds healed data or of incidence ulcers for reference. Where possible we will present adjusted data.

Where appropriate in terms of clinical and methodological heterogeneity we will consider pooling change in HRQOL data stratified by % increase or decrease in ulcer outcomes. We anticipate using a random effects model for meta-analyses, with statistical heterogeneity assessed using the tau^2 and I^2 measures alongside other judgements.

We will perform meta-analyses largely using Review Manager 5.3 (Review Manager 2014) and using Stata: Release 14 (StataCorp. 2015) or R (R Core Team, 2019) where necessary. We will present data using forest plots where possible.

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16.1 Appendix 1: Searches

CENTRAL: We undertook a broad search using the MeSH term pressure ulcer to identify all potentially relevant trials for manual screening. This was supplemented with more detailed searches of Medline, Embase and Cihnal as detailed below.

Database(s): Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Daily and Versions(R) 1946 to April 14, 2020
Search Strategy:

#	Searches	Results
1	exp Pressure Ulcer/	12192
2	(pressure adj (ulcer* or sore* or injur*)).tw.	10845
3	(decubitus adj (ulcer* or sore*)).tw.	1778
4	(bedsore* or (bed adj sore*)).tw.	694
5	or/1-4	16640
6	exp "Quality of Life"/	190705
7	"quality of life".mp.	337263
8	(HRQoL or HRQL).mp.	19512
9	exp "Activities of Daily Living"/	100477
10	(activities of daily life or daily living activities or ADL).mp.	12142
11	exp Health Status/	331741
12	exp Self Concept/	108394
13	exp Patient Reported Outcome Measures/	5373
14	exp Social Adjustment/	23195
15	exp pain measurement/	84924
16	health status.mp.	151221
17	(self-concept or self concept or social-concept or social concept).mp.	57772
18	(wellness or wellbeing or well-being).mp.	97538
19	(functional adj ability).mp.	4841
20	good health.mp.	8489
21	healthiness.mp.	649
22	(social adj (adjustment* or function* or impact)).mp.	39133
23	(physical adj (limit* or funct* or impact)).mp.	27048
24	(psychological adj (well being or well-being or funct*)).mp.	12882
25	symptom*.mp.	1137626
26	(pain adj3 measur*).mp.	94703
27	((measuring or measurement) adj5 "quality of life").mp.	5371
28	or/6-27	1869287
29	(sf-36 or "short form-36").mp.	20209
30	(SF-12 or "short-form-12").mp.	5485
31	(SF-6 or "short form-6").mp.	572
32	(EQ-5D or EQ-5D-3L or EQ-5D-5L or EQ-5D-Y).mp.	7877
33	(PU-QOL or PurPOSE PUQOL).mp.	8
34	nottingham health profile.mp.	1150
35	sickness impact profile.mp.	7878
36	world health organi?ation quality of life scale.mp.	168
37	or/29-36	40670
38	5 and 28 and 37	36

39	randomized controlled trial.pt.	503989
40	controlled clinical trial.pt.	93621
41	randomi?ed.ab.	569923
42	placebo.ab.	206885
43	clinical trials as topic.sh.	190776
44	randomly.ab.	331233
45	trial.ti.	216625
46	or/39-45	1317613
47	exp animals/ not humans.sh.	4690854
48	46 not 47	1213961
49	38 and 48	7

Database(s): Embase 1974 to 2020 April 14
Search Strategy:

#	Searches	Results
1	exp decubitus/	20462
2	(pressure adj (ulcer* or sore* or injur*)).tw.	13245
3	(decubitus adj (ulcer* or sore*)).tw.	1993
4	(bedsore* or (bed adj sore*)).tw.	1008
5	or/1-4	24069
6	exp "quality of life"/	481647
7	quality of life.mp.	582847
8	(HRQoL or HRQL).mp.	32039
9	exp daily life activity/	87772
10	(activities of daily life or daily living activities or ADL).mp.	22207
11	exp health status/	234271
12	exp self concept/	190951
13	exp patient-reported outcome/	21244
14	exp social adaptation/	118970
15	exp pain measurement/	15271
16	health status.mp.	158982
17	(self-concept or self concept or social-concept or social concept).mp.	89518
18	(wellness or wellbeing or well-being).mp.	150776
19	(functional adj ability).mp.	7125
20	good health.mp.	11267
21	healthiness.mp.	857
22	(social adj (adjustment* or function* or impact)).mp.	28112
23	(physical adj (limit* or funct* or impact)).mp.	41147
24	(psychological adj (well being or well-being or funct*)).mp.	28800
25	symptom*.mp.	1795443
26	(pain adj3 measur*).mp.	31985
27	((measuring or measurement) adj5 "quality of life").mp.	5380
28	or/6-27	2863740
29	(sf-36 or "short form-36").mp.	33672
30	(SF-12 or "short-form-12").mp.	10463
31	(SF-6 or "short form-6").mp.	352
32	(EQ-5D or EQ-5D-3L or EQ-5D-5L or EQ-5D-Y).mp.	15209
33	(PU-QOL or PurPOSE PUQOL).mp.	6
34	nottingham health profile.mp.	1624
35	sickness impact profile.mp.	3294
36	world health organi?ation quality of life scale.mp.	266
37	or/29-36	61792
38	5 and 28 and 37	69
39	Randomized controlled trials/	177179
40	Single-Blind Method/	36555
41	Double-Blind Method/	147019
42	Crossover Procedure/	62794
43	(random* or factorial* or crossover* or cross over* or cross-over* or placebo* or assign* or allocat* or volunteer*).ti,ab.	2188926
44	(doubl* adj blind*).ti,ab.	208109

45 (singl* adj blind*).ti,ab. 24692
46 or/39-45 2321485
47 exp animals/ or exp invertebrate/ or animal experiment/ or animal model/ or animal tissue/ or animal cell/ or nonhuman/ 27217453
48 human/ or human cell/ 20738870
49 and/47-48 20676205
50 47 not 49 6541248
51 46 not 50 2031907
52 38 and 51 14

S62	S38 AND S61
S61	S60 NOT S59
S60	S39 OR S40 OR S41 OR S42 OR S43 OR S44 OR S45 OR S46 OR S47 OR S48 OR S49 OR S50 OR S51 OR S52 OR S53
S59	S57 NOT S58
S58	MH (human)
S57	S54 OR S55 OR S56
S56	TI (animal model*)
S55	MH (animal studies)
S54	MH animals+
S53	AB (cluster W3 RCT)
S52	MH (crossover design) OR MH (comparative studies)
S51	AB (control W5 group)
S50	PT (randomized controlled trial)
S49	MH (placebos)
S48	MH (sample size) AND AB (assigned OR allocated OR control)
S47	TI (trial)
S46	AB (random*)
S45	TI (randomised OR randomized)
S44	MH cluster sample
S43	MH pretest-posttest design
S42	MH random assignment
S41	MH single-blind studies
S40	MH double-blind studies
S39	MH randomized controlled trials

S38	S5 AND S28 AND S37
S37	S29 OR S30 OR S31 OR S32 OR S33 OR S34 OR S35 OR S36
S36	world health organi?ation quality of life scale
S35	sickness impact profile
S34	nottingham health profile
S33	(PU-QOL or PurPOSE PUQOL)
S32	(EQ-5D or EQ-5D-3L or EQ-5D-5L or EQ-5D-Y)
S31	(SF-6 or "short form-6")
S30	(SF-12 or "short-form-12")
S29	(sf-36 or "short form-36")
S28	(S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16 OR S17 OR S18 OR S19 OR S20 OR S21 OR S22 OR S23 OR S24 OR S25 OR S26 OR S27)
S27	((measuring or measurement) N5 "quality of life")
S26	(pain N3 measur*)
S25	symptom*
S24	(psychological N1 (well being or well-being or funct*))
S23	(physical N1 (limit* or funct* or impact))
S22	(social N1 (adjustment* or function* or impact))
S21	healthiness
S20	good health
S19	(functional N1 ability)
S18	(wellness or wellbeing or well-being)
S17	(self-concept or self concept or social-concept or social concept)

S16	health status
S15	(MH "Pain Measurement")
S14	(MH "Social Adjustment")
S13	(MH "Patient-Reported Outcomes")
S12	(MH "Self Concept+")
S11	(MH "Health Status+")
S10	(activities of daily life or daily living activities or ADL)
S9	(MH "Activities of Daily Living+")
S8	(HRQoL or HRQL)
S7	quality of life
S6	(MH "Quality of Life+")
S5	S1 OR S2 OR S3 OR S4
S4	(bedsore* or (bed N1 sore*))
S3	(decubitus N1 (ulcer* or sore*))
S2	(pressure N1 (ulcer* or sore* or injur*))
S1	(MH "Pressure Ulcer+")

17. Appendix 3: Draft Data Analysis Plan 1 (HES Data)

Data analysis plan 1: HES data

Aim and objectives

1. To describe the patients with a diagnosis of severe pressure ulcer on hospital admission, their care pathways after admission and frequencies of health outcomes.
2. To compare health outcomes in matched groups of patients who were similar on admission and who did/did not have a surgical reconstruction operation.
3. To explore subgroup interactions in the matched groups with reconstructive surgery that may influence outcomes, e.g. comorbidities, previous hospital admission without surgery.

Data sources

HES extracts of admitted patient care (APC) and outpatient (OP) care datasets will be used. We will request data for adult patients and an index admission of 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 to 31/03/2019), linked with all other HES APC and outpatient episodes and mortality data (01/04/2011 to 31/03/2019).

L89.2 Stage III decubitus ulcer; L89.3 Stage IV decubitus ulcer; L89.9 Decubitus ulcer and pressure area, unspecified; L89.X is a code used prior to 2012 and is a "catch all" code for decubitus ulcer

Data management

Within HES APC the data are provided as episodes; these are single periods of care under one consultant. These are then combined to create a spell which is a patient's stay in that hospital. This could be one or many episodes. Standard data formatting processes will be used to combine these spells into continuous inpatient spells (CIPS) which are periods of care within the NHS, regardless of any transfers which may take place.

Definitions and derivations

Diagnosis and procedure codes for pressure ulcers

HES APC data record both diagnoses using ICD-10 codes, and procedures using OPCS-4 codes.

	ICD-10 diagnosis codes	OPCS procedure codes
Severe pressure ulcer	– L89.2 Stage III decubitus ulcer – L89.3 Stage IV decubitus ulcer – L89.9 Decubitus ulcer and pressure area, unspecified – L89.X is a code used prior to 2012 and is a "catch all" code for decubitus ulcer	
Reconstructive surgery operations		– S17 distant flap of skin and muscle – S18 distant flap of skin and fascia – S19 distant pedicle flap of skin – S20 other distant flap of skin – S21 hair bearing flap of skin – S22 sensory flap of skin – S23 flap operations to relax contracture of skin – S24 local flap of skin and muscle – S25 local flap of skin and fascia – S26 local subcutaneous pedicle flap of skin
Surgical debridement		– S57.1 Debridement of skin NEC
Usual care interventions		– S57.7 Dressing of skin using vacuum assisted closure device NEC

Index admission

The index admission will be the first admission with a severe pressure ulcer diagnosis code. The index event will be defined as the start of the first episode that records the severe pressure ulcer code, since exact dates of diagnosis are not available within HES.

Patient characteristics

Patients' age, sex and other diagnoses on admission will be described using the data recorded at the time of admission.

Important confounding domains will be identified from the surveys of health professionals in Workstream 1. These confounding domains are likely to cover comorbidities including common chronic diseases (e.g. cardiovascular diseases, diabetes, chronic pulmonary diseases, renal diseases and neurodegenerative disorders), complicating conditions (e.g. anaemia, infectious diseases and disability) and previous admissions with pressure ulcers. These will be assessed by reviewing all diagnoses recorded in admissions in the year prior to and including the index admission, except for previous admissions for pressure ulcers which will only be reviewed in admissions prior to the index admission. As diagnosis codes will be used to identify these comorbidities, we will assume that absence of evidence will reflect a patient being free of that condition, although we will assess how many patients have no admissions in the previous year as these patients may have comorbidities recorded as missing. Lists of appropriate diagnosis codes will be drawn up using several resources, including those used in previous studies, per-reviewed publications and those stored in code repositories such as ClinicalCodes.org hosted by the University of Manchester. All code lists will be reviewed by a clinician.

Eligibility criteria

Patients aged >=18 years in England admitted to hospital, with an ICD-10 diagnosis code for a severe pressure ulcer.

Outcomes

The following outcomes will be described:

- Type of surgical reconstruction using OPCS codes above
- Duration of index admission defined as the number of days between the admission and discharge for the CIPS including the index event
- Time to first subsequent admission with a pressure ulcer related diagnosis defined as the number of days to the next CIPS where a severe pressure ulcer is recorded. As before, the date of this subsequent pressure ulcer will be defined at the start date of the first episode within that CIPS where the pressure ulcer is recorded. The time between the index event and any subsequent event will be reviewed to try to understand whether the subsequent admission relates to a new pressure ulcer or the same one as in the index admission.
- Rate of subsequent admissions with a pressure ulcer related diagnosis defined as the number of CIPS after the index admission where a pressure ulcer diagnosis is recorded, divided by the amount of time.
- Repeat surgical reconstruction and type of reconstruction defined by reviewing further reconstructions that are recorded in CIPS after the index admission.
- Mortality using the linked mortality dataset.

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 using the APC and OP data. These data would be expected to inform any future study.

Statistical analysis

Propensity scores

Comparisons between hospitalised patients with a severe pressure ulcer who did and did not have reconstructive surgery ("eligible patients") will be confounded; the risk of bias from confounding was identified in our preliminary discussions with surgeon members of the team. As a first step we will calculate standardised mean differences (SMDs) for all confounders according to surgical reconstruction or not, those with SMD below 0.2 will be considered important.

Secondly, we will calculate propensity scores (propensity for having reconstructive surgery) and review removing tails of the resulting propensity score distributions. The propensity scores will be calculated using the comorbidities identified in Workstream 1, probably using a stepwise process to select the key confounders, and the tails of the distributions will be those untreated subjects who are never treated, and those treated subjects who are always treated. Reviewing the overlap of these propensity scores according to whether reconstructive surgery was used or not will aid this process.

Statistical modelling

Regression models using relevant outcomes identified in section 4.5 will be built, adjusting for both important confounders and propensity scores. If it is feasible, we will explore potential subgroup interactions reconstructive surgery and factors that may influence outcomes, e.g. in relation to comorbidities or previous hospital admission without surgery.

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