APPENDIX 14 to WHiTE Platform Master Protocol

World Hip Trauma Evaluation 14

Pressure ulcer prevention 3: A randomised clinical trial assessing early heel specific adjunct devices for heel pressure ulcer prevention in people with a fractured hip (PRESSURE 3).

This appendix must be read with the accompanying WHiTE Platform Master Protocol. This appendix describes only the additional details relevant to the conduct of this particular randomised comparison within the context of the overarching master protocol.

This comparison is funded by the National Institute for Health Research (NIHR) Health technology Assessment Programme (NIHR134839). The views expressed are those of the author(s) and not necessarily those of the NIHR or the Department of Health and Social Care.

FUNDED BY

NIHR | National Institute for Health and Care Research

World Hip Trauma Evaluation Appendix 14 - Pressure Ulcer Prevention 3: A randomised clinical trial assessing early heel specific adjunct devices for heel pressure ulcer prevention in people with a fractured hip (PRESSURE 3).

Short title: WHiTE14-PRESSURE 3

NIHR HTA Ref: NIHR134839

ISRCTN: ISRCTN10696770

Date and Version No: V2.0 05 Aug 2024

Lead Investigators: Professor Matthew Costa (Lead Investigator), University of Oxford

Professor Jane Nixon (Co-Lead Investigator), Leeds Institute Health Sciences, University of Leeds

Investigators: Associate Professor Susan Dutton, University of Oxford (Retired)

Prof Stavros Petrou, University of Oxford

Dr Clare Greenwood, Leeds Teaching Hospitals NHS Trust

Dr Elizabeth McGinnis, University of Leeds

Dr Juul Achten, University of Oxford

Dr Duncan Appelbe, University of Oxford

Dr Isabelle Smith, University of Leeds

Mrs Delia Muir, University of Leeds

Mr Richard Grant, Public and Patient Involvement

Funder: National Institute for Health and Care Research (NIHR) Health Technology Assessment Programme

We declare no conflicts of interest.

TABLE OF CONTENTS

1 APPENDIX AMENDMENT HISTORY

Amendment No.	Protocol Appendix Version No.	Date issued	Author(s) of changes	Details of Changes made
AM 22 (SA09)	2.0	05Aug2024	Kate Herbert	Update to inclusion criteria - patients to be randomised within 4 days of diagnosis. In line with this, the randomisaed intervention will now be initiated within 4 days of diagnosis rather than within 2 days of randomisation – the overall window from diagnosis to initiation of intervention remains the same. Addition of Pilot phase of the comparison. Other minor typographical changes. Staffing updates.

2 KEY CONTACTS

Comparison Lead Investigators	Lead: Professor Matthew Costa Matthew.Costa@ndorms.ox.ac.uk Oxford Trauma and Emergency Care, Kadoorie Centre, University of Oxford, Ox9 3DU Co-Lead: Professor Jane Nixon J.E. Nixon@leeds.ac.uk Tel: 01133431488 Leeds Institute Health Science, University of Leeds, LS2 9JT
Comparison Manager	Ms Kate Herbert white14-pressure3@ndorms.ox.ac.uk
Funder(s)	National Institute for Health and Care Research, NIHR Coordinating Centre, University of Southampton, Alpha House, Enterprise Road, Southampton SO16 7NS
Senior Statistician	Sofia Massa, octru-stats@ndorms.ox.ac.uk
Committees	**Comparison Management Group** Matthew Costa Jane Nixon Juul Achten Duncan Appelbe Susan Dutton (retired) Nicholas Peckham Isabelle Smith Richard Grant Elizabeth McGinnis Clare Greenwood Amrita Athwal Kate Herbert Sofia Massa Asma Saleh May Ee Png

3 LAY SUMMARY

Every year around 70,000 people in the UK break their hip. Hip fractures can take a long time to recover from and can lead to a range of complications associated with reduced mobility, including pressure ulcers.

Pressure ulcers (PU) are caused by sitting/lying in one position or being unable to move a part of the body. They cause pain, discomfort, and distress to patients, leading to reduced quality of life and sometimes death. They range in seriousness: Category 1 is a reddened area; Category 2 is a blister/skin loss and Categories 3 and 4 are deep wounds.

People with a hip fracture are at high risk of heel PU development due to difficulty moving their affected leg and use of the opposite heel when pushing themselves up/moving in bed. Factors which lead to hip fractures are also risks for PU development, for example frailty. If PUs develop on the heel of a person with a hip fracture, they cause added problems as they take a long time to heal (often months) reducing mobility, affecting the shoes they can wear and increasing their time to start walking again. This project is about the prevention of heel PUs in patients with hip fractures.

Usual care for PU prevention includes specialist mattresses, electric powered bedframes and repositioning in bed.

PRESSURE 3 will compare usual care alone with usual care plus one of two types of specialist heel equipment:

a) Heel off-loading devices ensuring no contact with the heel. They include foam troughs and boots which are applied to the legs

b) Constant low pressure (CLP) devices which are softer than a mattress and so reduce the pressure at the heel. They include pads made of foam or gel and are laid on top of the bedsheet.

Both types of specialist equipment are currently used as standard for specific patient groups in the NHS, but are not routinely used for patients with a hip fracture.

We will study 3102 patients with a hip fracture from at least 30 NHS hospitals. Participants will have a 1 in 3 chance of getting the off-loading device, the low-pressure device or usual care as decided by a computer. To make the study results relevant to all NHS patients with hip fracture we will include patients who can provide consent and patients who may be confused with the agreement of their next of kin or patients who may be confused with the agreement of a consultee (someone who is acting in the best interest of the patient, either a healthcare professional or someone who has a close personal relationship with the patient).

Patients who agree to take part in this research will have their heels assessed twice weekly until they leave hospital. The study will compare the number of participants who develop a heel pressure ulcer. At 4 months, we will ask the participants to complete a simple questionnaire by telephone, email, or post to tell us about their recovery after leaving hospital.

This randomised comparison has been developed by a team of patient representatives, clinical experts in trauma orthopaedics and pressure ulcers study management specialists, experienced statisticians, and health economists. The Oxford Clinical Trials Research Unit, based at the University of Oxford, will assure the quality of the comparison. A monitoring committee of patient representatives and independent experts will oversee the progress and conduct of the comparison.

4 PRESSURE 3 SYNOPSIS

Comparison title	World Hip Trauma Evaluation 14 – Pressure Ulcer Prevention 3; A randomised clinical trial assessing early heel specific adjunct devices for heel pressure ulcer prevention in people with a fractured hip.			
Short title	WHiTE14-PRESSURE 3			
Registration	The comparison has been registered with the current controlled trials database under reference number; ISRCTN10696770			
Funder	NIHR HTA Programme			
Design	Pragmatic, multi-centre, randomised, three-arm parallel group comparison with embedded economic evaluation.			
Participants	Adults, aged 60 years and over, admitted with a hip fracture within previous 4 days that in the opinion of the treating clinical team may benefit from surgical treatment. Patients who lack capacity may be entered into the comparison under a pre-specified representative agreement process.			
Sample Size	3102			
Comparison Duration	36 months			
Anticipated Recruitment period	21 months			
	PRESSURE 3 Objectives	**Instruments**	**Time-Points**	
			Part of Platform common outcome set	**Pressure 3 specific**
Primary	To compare the incidence of new Category ≥2 heel PUs between the treatment groups	International Classification Scale (EPUAP/ NPIAP/PPPIA)	N/A	Baseline, twice weekly until index hospital discharge or 30 days, whichever is soonest
Secondary	To compare the incidence of new Category 1 heel PUs between the treatment groups	International Classification Scale (EPUAP/NPIAP/PPPIA)	N/A	Baseline, twice weekly until index hospital discharge or 30 days, whichever is soonest
	To compare the overall incidence of new Category ≥1 heel PUs between treatment groups	International Classification Scale (EPUAP/NPIAP/PPPIA)	N/A	Baseline, twice weekly until index hospital discharge or 30 days, whichever is soonest
	To compare the progression of Category ≥1 heel PUs to a higher Category between treatment groups	International Classification Scale (EPUAP/NPIAP/PPPIA)	N/A	Baseline, twice weekly until index hospital discharge or 30 days, whichever is soonest
	To compare the proportion of resolved heel PUs	Bespoke participant questionnaire	N/A	4 months post-diagnosis of a hip fracture

	between treatment groups			
	To determine the comparative cost-effectiveness between treatment groups	EQ-5D-5L, bespoke participant resource use CRF and medical records	Baseline and 4 months post-diagnosis of a hip fracture	N/A
	To compare health related quality of life between the treatment groups	EQ-5D-5L	Baseline and 4 months post-diagnosis of a hip fracture	N/A
	To compare mortality risk between the treatment groups	Death notification CRF	As required up to 4 months post-diagnosis of a hip fracture	N/A
	To compare mobility between the treatment groups	modified New Mobility Score	Baseline and 4 months post-diagnosis of a hip fracture	N/A
	To compare residential status between the treatment groups	NHFD – residential status questions	Baseline and 4 months post-diagnosis of a hip fracture	N/A
	To compare risk and pattern of complications between treatment groups	Bespoke complications CRF	Up to 4 months post-diagnosis of a hip fracture	Twice weekly until index hospital discharge or 30 days, whichever is soonest
	To quantify and value healthcare resource use from a NHS and personal social services perspective	Bespoke participant resource use CRF and medical records	Baseline and 4 months post-diagnosis of a hip fracture	N/A
Intervention 1	**Standard Care plus Constant Low Pressure Devices for up to 30 days or index hospital discharge (whichever is sooner)** including foam and gel pads will be used which distribute pressure over a larger surface area and reduce the magnitude of the applied pressure by increasing the overall contact area. Products will be identified and specified for use in this comparison			
Intervention 2	**Standard Care plus Heel Off-loading Devices for up to 30 days or index hospital discharge (whichever is sooner)** including heel lift/suspension boots will be used to completely eliminate heel pressure. Products which maintain the heel in a completely pressure free state (i.e. no contact with the mattress) will be identified as eligible for use in this comparison			
Comparator	**Standard Care** In this pragmatic randomised comparison, any interventions prescribed for the prevention of PUs to participants in the standard care group will be at the discretion of the attending clinical team. Records will be made of the type of mattress and additional heel adjuvant devices each participant has been assigned pre randomisation.			

5 ABBREVIATIONS

AE	Adverse Event
CACE	Complier Average Causal Effect
CLP	Constant Low Pressure
CMG	Comparison Management Group
CRF	Case Report Form
EPUAP	European Pressure Ulcer Advisory Panel
EQ-5D-5L	EuroQol 5 Dimension 5 Level
HTA	Health Technology Assessment
ITT	Intention to Treat
ISRCTN	International Standard Randomised Controlled Trial Number
NHFD	National Hip Fracture Database
NHS	National Health Service
NICE	National Institute for Health and Care Excellence
NIHR	National Institute for Health and Care Research
NRLS	National Reporting and Learning System
NPIAP	National Pressure Injury Advisory Panel
PPPIA	Pan Pacific Pressure Injury Alliance
PU	Pressure Ulcer
QALY	Quality Adjusted Life Year
REC	Research Ethics Committee
sDTI	suspected Deep Tissue Injury
SAE	Serious Adverse Event
WHiTE	World Hip Trauma Evaluation

6 BACKGROUND AND RATIONALE

6.1 What is the clinical problem being addressed?

Worldwide there are 1.3 million hip fractures/year, including nearly 70,000 in the UK[1-3], with a projected increase to >6 million worldwide by 2050.[4] The global cost of hip fracture has been estimated at 1.75 million disability adjusted life years lost annually and accounts for 1.4% of total healthcare expenditure, which does not include the substantial cost of informal care in the community.[1,3,5] Patients have a 1 year mortality rate of 25% and experience a permanent reduction in their health-related quality of life similar to having a stroke.[6] Patients with hip fracture, who are frail before their injury and take a long time to regain their normal activities afterwards, are vulnerable to a range of complications associated with their reduced mobility, including pressure ulcers (PUs).

PUs are localised areas of damage to skin and underlying tissue as a result of mechanical load in the form of pressure, shear, and friction. The international classification from the National Pressure Injury Advisory Panel (NPIAP), European Pressure Ulcer Advisory Panel (EPUAP) and Pan Pacific Pressure Injury Alliance (PPPIA) is as follows: Category 1 (non blanching erythma); Category 2 (superficial blister/skin loss); Category 3/4 severe cavity wounds exposing fat, muscle and bone; Unstagable (unable to assess the severity of the injury, usually due to presence of non-viable tissue) and; suspected Deep Tissue Injury (sDTI)[7]. Other skin changes of intact skin are also referred to as 'altered skin' and 'vulnerable skin' and have been classified for research as Category A.[8,9] Category 2 PUs are reportable to the National Reporting and Learning System (NRLS)[10] and Category 3/4 PUs are reportable as 'serious incidents' on the Strategic Executive Information System.[11]

PUs are painful to patients[12-14] and confer major burden and impact on people's quality of life[15] due to prolonged bedrest, symptoms (pain, smell, exudate), frequent redressing visits, delayed discharge, nursing home care and hospitalisation for surgery/severe infection.[16,17] Hospital prevalence studies identify ~10% of patients as having one or more Category ≥2 Pus.[12,18,19] Adverse event reporting to the NRLS indicates ~0.5% of all hospital admissions develop a new Category ≥2 PU, with incidence rates of 7.8-25.2% reported in high-risk populations. Economic costs associated with PUs are estimated at 4% of NHS expenditure (£1.4-£2.1 billion; 2000 prices).[20] Effective prevention strategies targeting PUs have the potential to generate downstream cost savings and meet the cost-effectiveness criteria of health technology assessment agencies.[21]

Patients with a hip fracture are particularly prone to the development of PUs due to immobility of the affected limb, overuse of the contralateral limb/heel when pushing up the bed to self-repositioning creating repetitive pressure/shear/frictional forces. The high proportion of patients who lack capacity, exacerbating the impact of underlying risk factors associated with older age and frailty.

This randomised comparison is focused upon the prevention of Category ≥2 heel PUs in patients with hip fracture.

6.2 How does the existing literature support this proposal?

In the literature, Category ≥2 PU incidence rates of 9.6% up to as high as 31.6%[22-24] have been reported in patients following hip fracture. PUs that develop on the heel account for a quarter of Category ≥2 PUs.[9,22,24,25] Heel specific prevention is important because heel PUs:

a) are more likely to deteriorate to severe PUs than those elsewhere on the body[9,12,13,24,25]

b) take longer to heal compared to PUs elsewhere on the body[16,26-28]

c) less than 50% heal within 18 months/prior to death/amputation[16]

A systematic review/meta-analysis was undertaken (original search to September 2019 plus ISRCTN registered trial available August 2020 and updated June 2021)[29,30] to identify trials with heel specific devices and heel level data:

Off-loading vs standard care: 3 trials (including 1 RCT of patients with hip fracture) – significant difference in heel PUs reported for both Category ≥1 (3 trials, 18/258 vs 60/234; RR 0.20, 95%CI 0.05-0.80, low quality)[24,31,32] and Category ≥2 (2 trials, 0/223 vs 10/199; RR 0.08, 95%CI 0.01-0.67, medium quality).[24,31]

Constant Low Pressure (CLP) vs standard care: no eligible trials.

Off-loading vs CLP: 1 trial – non-significant differences reported for Category ≥1 heel Pus (9/163 (off-loading) vs 3/77 (CLP); RR 1.42, 95% CI 0.4-5.7, very-low quality).[33]

Whilst results suggest that off-loading may be effective at reducing heel Pus, the included studies reported issues with device compliance.[24,31] One study (n=239) used a structured questionnaire to elicit patient experience of the Heel Lift Suspension Boot and reported that whilst 59% patients reported the boots as comfortable overall, patients reported that the off-loading devices interfered with sleep (32%) and affected movement in bed (41%); reasons for non-concordance included weight and bulk of the boot (36%), heat (31%) and discomfort (24%).[24]

In light of reported patient acceptability and compliance issues we have undertaken a mixed methods realist evaluation,[34] collated standard care data in PRESSURE 2, a mattress trial that involved high risk patients[9] and had a consultation meeting with Tissue Viability Nurse Specialists.

Key findings:

off-loading devices are perceived to be more effective/useful when patients are completely immobile and confined to bed and a trip hazard when patients start to rehabilitate and mobilise;

CLP foam pads were observed to be in use for prevention and easier to keep in place, having less impact upon movement in bed.

Neither off-loading devices or CLP devices are in common use for prevention of heel PUs, with PRESSURE 2 observing their use in 10% of a high risk patient population, and off-loading devices are generally initiated for treatment of Category ≥2 heel PUs rather than prevention.[34]

6.3 Need for this comparison

In people with a hip fracture the development of a heel PU is particularly problematic for rehabilitation and their ability to engage with physiotherapy and resume walking is severely impacted. The presence of a heel PU causes heel pain and there is a risk of PU deterioration when they start wearing shoes which are needed forweight bearing and walking again. This in turn leads to prolonged dependence and serious adverse sequela including delayed hospital discharge, and residential/ nursing home care.

Off-loading devices may be effective at reducing heel PUs but there are issues relating to clinical utility. CLP devices have clinical utility, but their effectiveness as an adjunct to standard care is not known. Whilst available in the NHS, the use of heel specific devices for prevention is not common even in high-risk patient populations. This randomised comparison will provide definitive evidence on clinical and cost effectiveness of both Off-loading and CLP devices in the prevention of heel PUs. We expect the results from this research to inform both the NICE PU prevention guideline (CG179) and NICE hip fracture guideline (CG124) at their scheduled updates in 2025/2026.

7 OBJECTIVES AND OUTCOME MEASURES

Notes on the specific timeframes used throughout this comparison - as no official record is made in the medical notes of date and time of diagnosis, date and time of presentation to the recruitment centre will be used in lieu of this. Time between presentation and diagnosis is between 1 and 2 hours. The majority of participants will be discharged from their acute episode hospital setting within the first 30-days after diagnosis of a hip fracture. A small proportion of participants will have extended stays beyond this point. For the former group, primary assessments will be made until the day of discharge. For those participants who remain in the acute episode hospital setting for longer than 30 days, no further primary assessments will be made after 30 days.

7.1 Primary objective

To compare the incidence of new Category ≥2 heel PUs from diagnosis of a hip fracture to index hospital discharge or 30 days whichever is soonest between *Standard Care plus early initiation of a Heel Off-loading Device*, *Standard Care plus early initiation of a CLP Device* and *Standard Care alone* in patients aged 60 and over with a hip fracture which in the opinion of the treating clinical team may benefit from surgical treatment.

7.2 Secondary objectives

1. To compare the incidence of new Category 1 heel PUs from diagnosis of a hip fracture to index hospital discharge or 30 days whichever is soonest between treatment groups in participants with normal or Category A skin status on the heel(s) at randomisation.
2. To compare the overall incidence of new Category ≥1 heel PUs from diagnosis of a hip fracture to index hospital discharge or 30 days whichever is soonest between treatment groups in participants with normal or Category A skin status on the heel(s) at randomisation.
3. To compare the progression of Category ≥1 heel PUs to a higher Category from diagnosis of a hip fracture to index hospital discharge or 30 days whichever is soonest between treatment groups.
4. To compare the proportion of resolved heel PUs at 4 months post-diagnosis of a hip fracture between treatment groups in participants with a Category ≥1 heel PU at their final pre-discharge/30 day in-hospital skin status assessment.
5. To quantify the comparative cost effectiveness of the trial treatments up to 4 months post-diagnosis of a hip fracture.

7.3 Outcome Measures

The common outcome data described in the Platform Master Protocol at baseline and 4 months post-diagnosis of a hip fracture will be collected and augmented with additional data collection pre-

randomisation, at baseline, up to index hospital discharge or 30 days whichever is soonest and at 4 months post-diagnosis of a hip fracture as per section 9.7.1. Additional outcomes specific for this randomised comparison are:

7.3.1 In-hospital skin status assessment for heel pressure ulcers

This skin status assessment will be used to inform the primary objective (incidence of Category ≥2 heel PUs) as well as three secondary objectives (incidence of Category 1 heel PUs, incidence of Category ≥1 heel PUs and progression of any PU to a higher category).

Skin status assessments of the heels will be undertaken using the international classification scale (EPUAP/ NPIAP/PPPIA)[7] by a trained member of the local research team. These will take place pre-randomisation and twice weekly from randomisation until index hospital discharge or 30 days, whichever is soonest (where a week is defined as any 7 day period from baseline, with no assessments made on two consecutive days). The pre-randomisation assessment will be used to determine the skin status stratification factor and as the baseline assessment. If the participant has a bandage and/or dressing in situ, the local research team will consult with ward staff and participants to complete the skin assessment during standard care bandage and/or dressing change in order to complete the skin status assessment.

Skin status will be reported as follows:

- '0' will be recorded to indicate that skin has been assessed and is normal
- 'A' will be recorded where there is an alteration to intact skin, for example discolouration, dry skin
- The presence of a pressure ulcer will be recorded as per international classification[7] Category 1-4, U, or suspected Deep Tissue Injury (sDTI).

7.3.2 Complications during in-hospital stay

A site-reported complication form (see section 10.1) will be completed during the participant's in-hospital stay or to 30 days whichever is soonest. Completion will be performed at the time of skin status assesments as per 7.3.1. Reports will be made of any falls requiring medical intervention, device-related complications and any Category ≥2 PU development on any other major anatomical sites at risk (buttocks, sacrum, ankles and elbows).

7.3.3 4 month post-diagnosis of hip fracture participant-reported heel skin status

At the 4-months post-diagnosis of a hip fracture follow-up, participants who had a Category ≥1 heel PU at their final skin status assessment as per section 7.3.1, will be asked to report if they have a wound/PU or dressing/bandage on their affected heel. If no wound/PU or dressing/bandage is indicated, the heel PU will be classed as 'resolved'. Where patients do not have capacity, those procedures laid down in Section 11.4 of the Platform Master Protocol will apply.

8 DESIGN

8.1 Concept

PRESSURE 3 is a pragmatic three-arm randomised comparison with embedded economic evaluation assessing the clinical and cost effectiveness of early initiation of heel off-loading devices and CLP devices on prevention of pressure ulcer development. This will be embedded within the overarching WHiTE

Platform. Randomisation will be on a 1:1:1 basis to *standard care*, *standard care plus off-loading*, and *standard care plus CLP*, stratified by recruitment centre, consent type (individual vs consultee), heel skin status at randomisation (0 or A vs Category 1 PU or suspected deep tissue injury).[7]

This will be a two-phased comparison. Phase 1 (internal pilot) will confirm the expected rate of recruitment in 6 UK hospitals. Phase 2 (main phase) will extend the randomised comparison to approximately 30 UK hospitals.

8.1.1 Internal Pilot

The pilot will take place at a minimum of 6 recruitment centres over a period of six months. The aim of this initial phase will be to determine the number of eligible and recruited patients in the recruitment centres and optimising trial procedures and data collection systems over the course of six months.

Screening will be recorded by each recruitment centre to determine the number of patients assessed for eligibility and reasons for any exclusion. The number of eligible and recruited patients, and the number of patients who decline consent or withdraw will be recorded. The Platform Oversight Committees (POC) will review recruitment during the feasibility phase in order to make a recommendation regarding continued progress of the comparison against the specified stop/go criteria (see section 11.4). If the comparison is stopped after the pilot phase, then all comparison participants will be followed up as per protocol. If the comparison continues into the main phase, participants from the internal pilot will be included in the final analysis.

8.1.2 Main phase

During the main comparison phase, patients will be recruited from approximately 24 additional centres, bringing the minimum number of recruitment centres to 30 across the UK.

Participants will be allocated on a 1:1:1 basis to *standard care*, *standard care plus off-loading*, and *standard care plus CLP*. Both types of specialist equipment are currently used as standard for specific patient groups in the NHS, but are not routinely used for patients with a hip fracture. Clinical teams across the NHS are very familiar with both treatments.

Assessments will include all those described in the Master protocol, augmented with additional data relevant to this specific randomised comparison. In summary:

Baseline demographic data will be collected as per the requirements in the master protocol (see section 12.2). Along with key pressure ulcer risk factors and a skin assessment. A skin assessment and adherence check will also be completed twice weekly until discharge or 30 days whichever is soonest. When the patient is discharged from hospital, the local research team will check the participant medical records for any early complications.

In addition to the data being collected at 4 months post-diagnosis of a hip fracture to satisfy the platform outcomes (see master protocol), a PRESSURE 3 specific skin status questionnaire will be completed.

9 COMPARISON PROCEDURES

A comparison flow chart is shown in Annex A.

9.1 PARTICIPANT IDENTIFICATION

9.1.1 Comparison participants

A subset of patients in the overarching WHiTE Platform will be eligible for this randomised comparison.

9.1.2 Inclusion criteria

In addition to the inclusion stated in the overarching Platform Master Protocol:

- adults aged 60 years and older with a hip fracture,

the patient is eligible if ALL of the following apply:

- randomisation occurs within 4 days of diagnosis of a hip fracture
- in the opinion of the treating clinical team the patient may benefit from surgical treatment

9.1.3 Exclusion criteria

In addition to the exclusion criteria stated in the overarching Platform Master Protocol:

- previous participation in the same randomised comparison
- a second hip fracture (other side) while the patient is still enrolled in the Platform following their first hip fracture,

the patient is not eligible if ANY of the following apply:

- a heel off-loading or CLP device has been assigned prior to randomisation
- there is an existing Category 2-4 or Unstageable PU on either heel or 'not applicable' on both heels (ie no evaluable heel sites)
- there is a contra-indication to the interventions e.g. allergy to device material

Patients can be included if only one heel is available for evaluation – amputation of one leg, having a plaster cast or boot applied to one leg or having one heel that cannot be evaluated is not classed as an exclusion. The use of pillows is, in this context, not classed as heel-off loading or CLP and their use at time of consent discussion is not an exclusion criteria. Patients can be included if a heel has Category A /Cat 1 PU or sDTI.

9.2 Screening

Potentially eligible patients will be identified at each recruitment centre and approached for recruitment prior to their surgical treatment where possible. As part of our inclusive approach, patients who lack capacity may be entered into the comparison under the WHiTE Platform pre-specified consultee agreement process.

Screening logs will be kept at each recruitment centre to determine number of eligible and recruited patients, and the number who decline consent or withdraw. Standard Platform screening data will be augmented with information regarding absence or presence of ≥2 heel PUs. Screening data will be reviewed each month by the Comparison Management Group (CMG) to assess whether representative

samples of patients are being approached and to ensure no bias occurs in any of the centres with regards inclusion/ exclusion of specific groups of patients.

9.3 Consent

Patients will be presumed to have capacity unless established otherwise and the default will be to seek prospective individual consent from every patient. Where patients do not have capacity, those procedures laid down in Section 11.4 of the Platform Master Protocol will apply.

With regards to these provisions, the randomised comparison described in this appendix is **not** a clinical trial of an investigational medicinal product.

9.4 Randomisation

Randomisation will be on a 1:1:1 basis to *standard care*, *standard care plus heel off-loading* and *standard care plus CLP*, stratified by recruitment centre, consent type (individual vs consultee), skin status at randomisation (Skin Status 'Category 0/A' vs Skin Status 'Category 1 or suspected deep tissue injury') via a secure, 24-hour, web-based randomisation system using a minimisation algorithm (including a small number to seed the algorithm and a random element) ensuring allocation concealment to the point of randomisation.

Stratification by centre will balance centre specific effects, including differences in routine care pathways. Consent type will be used as a surrogate for the patient's mental capacity at the time of enrolment into the randomised comparison. Lack of capacity has been identified as a risk factor for the development of Category 2 PUs. Additionally, having a pre-existing skin change increases a patient risk for the development of Category 2 PUs.[9]

Consent and randomisation will be performed as soon as possible after admission to hospital to maximise the number of eligible patients and enable early initiation of the allocated intervention.

9.5 Blinding

It is not possible to blind participants, the clinical team or the clinical research nurse/registered healthcare professional to the intervention. This poses a risk to internal validity. Blinded assessments will be performed to mitigate some of this risk.

Blinded assessments of the primary outcome will be conducted on a subset of participants in six recruitment centres during the first six months of recruitment: following removal of any adjuvant device, a paired outcome assessment will be undertaken simultaneously but with no communication between the unblinded trained member of the local research team and a delegated blinded independent assessor (one of the following: one of the two clinical coordinators in the management team (co-applicants Greenwood and McGinnis), an independent research nurse or a member of the local Tissue Viability Nurse team). The blinded assessment will be undertaken on approximately 4-8 participants at each site. The CMG will perform a timely review of the blinded assessments for each recruitment centre, with additional training being recommended to sites if deemed necessary. Additional recruitment centres will undergo blinded assessments if deemed appropriate by the CMG or oversight committee.

9.6 Description of the randomised treatments

9.6.1 Standard Care

In this pragmatic randomised comparison, any interventions prescribed for the prevention of PUs to participants in the standard care group will be at the discretion of the attending clinical team. From our previous multi-centre research, it is anticipated that standard care of high-risk patients, such as those with hip fracture will include: the provision of high specification foam mattresses or specialised air mattress (on a 50:50 basis); an electric profiling bed; repositioning more frequently than 3 hourly and non trial heel adjuvant devices (pillows at heel, prevention dressings) (approximately 10%),[9,14] but this may vary per centre. A record will be kept of the type of mattress and additional heel adjuvant devices each participant has been assigned pre randomisation as part of standard care.

9.6.2 Interventions

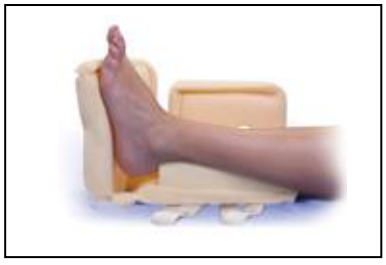
The two technologies being assessed in this comparison against standard care alone are early initiation (within 4 days of diagnosis of a hip fracture) of heel specific PU prevention adjunct devices used in bed in addition to any standard care mattress.

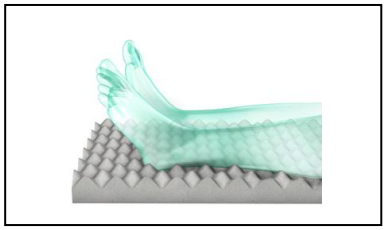
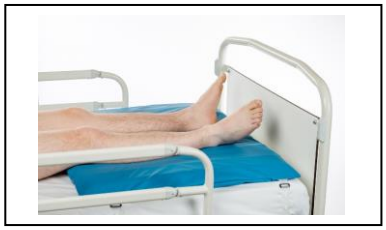
All participants allocated to one of the technologies under investigation will receive standard care as per local practice. In addition, they will receive the allocated adjunct device as soon as possible after randomisation. **The intervention period will be defined as from randomisation to index hospital discharge or 30 days whichever is soonest.**

Using a pragmatic approach, we will allow each hospital to use its existing supply chain for PU prevention devices. A list of comparison-approved, off-loading heel lift/suspension boots and CLP foam and gel pad devices (examples in *Figure 1*) will be provided to the participating WHiTE centres. Following randomisation, a member of the local team will initiate the device intervention (as allocated) from ward/hospital supplies.

1. **Heel Off-loading Devices** including heel lift/suspension boots will be used to completely eliminate heel pressure. Products which maintain the heel in a completely pressure free state (i.e., no contact with the mattress) will be identified and specified for comparison use (see *Figure 1* illustrating three examples).
2. **Constant Low Pressure Devices** including foam and gel pads will be used which distribute pressure over a larger surface area and reduce the magnitude of the applied pressure by increasing the overall contact area (see
3. Figure *1* Examples of Offloading and Constant Low Pressure Devices*Figure 1* illustrating three examples)

Figure 1 Examples of Offloading and Constant Low Pressure Devices

Offloading Devices		
		

Inflatable/air filled offloading device	Padded/Foam heel offloading device	Orthotic Device
Constant Low Pressure Devices		
		
Gel sheet/pad	Eggcrate foam heel sheet/ utility pad	Inflatable heel sheet/pad

Compliance with initiation of the allocated treatment (or no allocation for the standard care group) will be defined as the participant receiving the allocated intervention on at least one heel within 4 days of diagnosis of a hip fracture. A record will be made of reasons for non-compliance within the 4-day window.

Adherence will be assessed twice weekly at the time of the skin status assessment. For all randomised participants, it will be reported whether any device, and if so, what type of device has been used whilst the participant was in/on the bed since the last skin status assessment. For those participants that were deemed 'compliant' with randomisation as per the above definition and continue to use the allocated intervention, the frequency of use (some of the time, most of the time, all of the time) (if applicable) between skin assessments will also be recorded. This adherence assessment will be based on direct observation, information obtained from the participant's healthcare records and through consultation with participants and ward staff. Information will be collected on reasons for non-adherence to the randomised allocation. Participants will only have the device available to them during their index hopsital stay.

9.7 Assessments

9.7.1 Schedule of WHiTE14-PRESSURE 3 specific assessments

The overall schedule of assessments, including the common outcome set as per the Platform Master Protocol (greyed out) and the additional outcomes measured for this comparison, and methods for data collection are described in Table 1 **Error! Reference source not found.**below:

Table 1 Schedule of assessments, instruments and means of collection

Time Point	Data	Source	Setting
Contact 1 Pre-randomisation	i) Skin status assessment ii) Type of mattress and additional heel adjuvant devices	Clinical Assessment	Acute inpatient

Contact 2 Baseline (collected immediately post-randomisation)	i) Demographics ii) Key pressure ulcer risk factors [8] iii) Injury details *Pre-injury (obtained retrospectively):* iv) EQ-5D-5L v) Residential status vi) Mobility vii) Resource use	Participant or consultee questionnaire & medical record	Acute inpatient - face to face; medical record review
Contact 3 ≤4 days post-diagnosis	i) Compliance with initiation of treatment	Clinical Assessment, medical records, observation, consultation with participant/ consultee and ward staff	Acute inpatient - face to face; medical record review
Contact 4-11 Twice weekly up to index hospital discharge or 30 days whichever is soonest	i) Skin status assessment ii) Adherence iii) Complications	Clinical Assessment, medical records, observation, consultation with participant/ consultee and ward staff	Acute inpatient - face to face; medical record review
Contact 12 4 months post-diagnosis of a hip fracture	i) Skin status^ ii) EQ-5D-5L iii) Mobility iv) Residential status v) Mortality vi) Complications vii) Resource use	Medical records, participant/consultee questionnaire	Telephone, online or postal

^ Skin status questions will only be included for those participants, who, at their final in-hospital skin status assessment, were diagnosed with a Category ≥1 heel PU.
Greyed out information indicates data collection as per Master Protocol.

9.8 Definition of End of Comparison

The end of comparison is the point at which the follow up of the last participant has been completed, all the data has been entered and all queries have been resolved. The last direct data collection from participants or consultee will be at 6 months (4 months plus an additional 2 for chasing up missing/incomplete data). The Sponsor and main Research Ethics Committee (REC) will be notified in writing within 15 days if the comparison has been concluded or terminated early.

10 SAFETY REPORTING

Safety reporting related to the **fracture and surgical procedure** for each participant will begin from the time of consent and will end when the participant has reached their final follow up time point as per Section 15 of the Platform Master Protocol. Due to the nature of the interventions, safety reporting related to the **interventions** will begin once the intervention has been initiated, and end after the intervention period (ie until index hospital discharge or 30 days whichever is soonest). Investigators will follow up serious adverse events (SAEs) until resolved or participation in the study is complete.

Adverse events that do not meet the definition of SAEs and unrelated SAEs are not required to be reported, as a result of the randomised comparison being classed as 'low risk' (as per the comparison specific risk assesment) and well-established safety profile of the interventions being investigated.

All unexpected SAEs are to be reported according to the guidelines specified in section 15 of the Platform Master Protocol.

10.1 Related and expected Serious Adverse Events

See Platform Master Protocol for details of SAEs that are expected and related to the *fracture and surgical procedure*.

The following SAEs are expected and related to the *interventions* and will be reported as complications, during the intervention period only, on bespoke site-reported Case Report Forms (CRFs):

- Incidence of new Category ≥2 PU on any other area of the body than the heel
- Falls requiring medical intervention
- Device related complications that fullfill the criteria for a SAE (eg achilles tendon trauma or foot drop)

11 STATISTICS & ANALYSES

11.1 Sample size determination

There are two primary hypotheses to be tested with regards the incidence of new Category≥2 heel PUs in patients diagnosed with a hip fracture:

i) Offloading device plus standard care vs standard care alone, and
ii) CLP device plus standard care vs standard care alone

The comparison is designed using a shared control group (standard care), therefore in order to preserve the family wise error rate of 5%, an adjustment for multiplicity using Bonferroni, a conservative adjustment method, has been made. The two primary hypothesis tests will therefore be tested using 2.5% (2-sided) significance. Assuming an incidence of 5 % of new Category ≥2 heel PUs in the standard of care arm, a 3% reduction in the incidence to 2%, is considered to be the minimally clinically relevant difference.

Therefore, 2790 participants (930 participants per group) are required to detect this difference with 90% power and a 2.5% (2-sided) significance level. Since the primary outcome measure will be collected on the ward before discharge, we anticipate minimal loss to follow-up for the primary outcome but have allowed for 10% loss to follow-up, taking the overall target sample size to 3102 (1034 per group).

11.2 Analysis populations

The intent-to-treat (ITT) population includes all randomised participants in their intervention group, regardless of whether they received their allocated intervention.

Note: participants who withdraw from the comparison between randomisation and the development of a new Category ≥2 heel PUs to index hospital discharge will provide data up to the point of withdrawal.

The per protocol population will include all participants who received their allocated intervention within 4 days of diagnosis of a hip fracture (as per 9.6.2). Those participants with major deviations from the protocol, which will be fully described in the Statistical Analysis Plan, will be excluded from these analysis.

11.3 The level of statistical significance

Statistical significance will be assessed at 2.5% for two-sided tests and 97.5% confidence intervals will be reported to take account of the two comparisons we are undertaking for all outcomes. All p-values will be reported to 3 decimal places.

11.4 Decision Points

A total of 3102 participants will be randomised across approximately 30 recruitment centres. We will exploit the efficiencies available from nesting this within the Platform. This Platform has been built based upon the experiences of the WHiTE Cohort Study, which has successfully delivered three hip fracture trials[35–37] and three further trials are currently underway (ISRCTN92825709, 18393176, 15606075). The comparison processes are streamlined and harmonised with those of the Platform so that we should be able to achieve 65% recruitment of eligible patients and 90% follow-up of available participants (those alive and not withdrawn) at the primary outcome time-point.

During the 6 months internal pilot phase, we expect to recruit 180-240 participants from the 6 pilot recruitment centres. The POC will monitor recruitment during the feasibility phase and make a recommendation with regards continued progress of the comparison against the specified stop/go criteria. If recruitment is below 180 participants, we will consider stopping the comparison for feasibility reasons, if between 180 and 240 participants we will review the recruitment processes and implement the committees' recommendations. In the event that recruitment is lower than anticipated we have a network of 120 hospitals in addition to these 6 that have previously worked with us on multicentre trials.

If the comparison is stopped, then all comparison participants will be followed up as per protocol. If the comparison continues into the main phase, participants from the internal pilot will be included in the final analysis.

Following the pilot phase, approximately 24 additional recruitment centres will be involved with recruitment. Those participants recruited during the pilot phase will be included in the final sample.

The internal pilot progression criteria are:

Progression Criteria	Red	Amber	Green
Trial recruitment % complete	<75%	75%	100%
Number of sites opened	<4	4-5	≥6
Recruitment rate/ site/ month	<6 Participants	6-7 Participants	≥8 Participants
Total number of participants recruited	<180	180-239	≥240
Allocation compliance	<60%	60-79%	≥80%

11.5 Statistical Analysis

The primary outcome, the incidence of new Category ≥2 heel PUs from diagnosis of a hip fracture to index hospital discharge (or 30 days whichever is soonest) will be analysed on the basis of intention-to-

treat, using multi-variable logistic regression adjusting for the stratification factors: site, consent type and skin status at baseline.

Proportions of new Category≥2 heel PUs will be reported for each group and for the two principal comparisons: heel offloading device plus standard care versus standard care alone and CLP device plus standard care versus standard care. Absolute differences and odds ratios together with 97.5% confidence intervals will be reported. Supporting analyses of the primary outcome will be undertaken adjusting for additional prognostic factors using the same methods as described above. Further supporting complier average causal effect (CACE) analysis will be undertaken to take into account compliance to the interventions where compliance is defined as initiation of intervention within four days of diagnosis of a hip fracture. Information regarding use of and adherence to the interventions will also be reported.

Time to development of a new Category ≥2 heel PU will also be explored using time-to-event methodology. Continuous time multi-state models of heel PU onset and progression will be used to provide deeper insight into the effect of the interventions on PU progression.[38]

Analysis of secondary outcomes (incidence of new Category 1 heel PUs, incidence of new Category ≥1 heel PU, Category≥1 heel PU progression and the EQ-5D-5L utility and VAS scores) will be undertaken using multi-variable logistic or linear regression adjusting for stratification factors as appropriate. Safety outcomes, including SAEs, complications, mobility, residential status, and incidence of death will be reported descriptively.

11.6 Health economic analysis

An economic evaluation conducted from the recommended NHS and personal social services perspective[39] will be embedded within the randomised comparison design. The costs of the treatment options, including the heel off-loading devices, constant low-pressure devices and adjunct devices, will be based on estimates of resource inputs, including staff inputs and consumables, captured daily by the comparison case report forms. Broader resource utilisation will be captured through two principal sources:

(1) routine hospital data collection systems and

(2) participants/carer questionnaires administered 4 months post-diagnosis of hip fracture.

Unit costs for health and social care resources will largely be derived from local and national sources and estimated in line with best practice. Responses to the EQ-5D-5L at each assessment point will be converted into utility scores, for the purposes of quality-adjusted life year (QALY) estimation, using recommended algorithms.[40] The cost-effectiveness of the treatment options will be expressed in terms of incremental cost per QALY gained. Bivariate regression of costs and QALYs, with multiple imputation of missing data, will be conducted to generate within-trial estimates of incremental cost-effectiveness associated with the treatment options. Sensitivity analyses will be undertaken to assess the impact of areas of uncertainty surrounding components of the economic evaluation. The sensitivity analyses will include re-estimation of cost-effectiveness based on cases with complete data, and re-estimation of cost-effectiveness assuming a wider societal perspective. Cost-effectiveness acceptability curves will show the probability of cost-effectiveness of each the treatment options evaluated at alternative cost-effectiveness thresholds. If economic outcomes are non-convergent within the comparison follow-up

period, then extrapolation of cost-effectiveness through decision-analytic modelling will be considered, drawing upon the best available information from the literature to supplement the comparison data. The economic assessment methods will adhere to the recommendations of the National Institute for Health and Care Excellence (NICE) Reference Case.[39]

12 DISSEMINATION POLICY

The protocol, statistical analysis plan and health economics analysis plan will be published in open-access journals prior to the completion of the recruitment and follow-up phase of the randomised comparison, respectively. The clinical results and economic evaluation will be submitted to high quality peer-reviewed journals for publication.

Slide decks of the results will be made available to all principal investigators to be used for local and regional meetings. Distribution of randomised comparison outcomes at a local level will ensure a wide distribution amongst the large clinical teams that take responsibility for the care of hip fracture patients.

Results will further be presented at national (Orthopaedic Trauma Society meeting, Tissue Viability Society) and international meetings (Fragility Fracture Network annual meeting, European Pressure Ulcer Advisory Panel annual meeting).

As well as a written lay summary, a lay dissemination animated video will be prepared. We anticipate to use this on social media but also to be played in hospital/GP waiting areas to inform the public.

A dedicated website, which will be open to all participants and their carers will have up to date information on progress of the randomised comparison. However, as we are aware of the specific challenges that the comparison population, who are elderly (average age 84 years) and often frail, might face in accessing this information in a digital format, where possible we can also provide updates through postal newsletters.

13 REFERENCES

1. Johnell O, Kanis JA. An estimate of the worldwide prevalence, mortality and disability associated with hip fracture. *Osteoporos Int* 2004; **15**(11): 897-902.
2. Physicians RCo. National Hip Fracture Database annual report 2019. 2020. https://www.nhfd.co.uk/20/hipfractureR.nsf/docs/reports2020 (accessed 31/08/2021).
3. National Falls Prevention Coordination G. Falls and fracture consensus statement. London: Public Health England; 2017.
4. Cooper C, Campion G, Melton LJ, 3rd. Hip fractures in the elderly: a world-wide projection. *Osteoporos Int* 1992; **2**(6): 285-9.
5. Williamson S, Landeiro F, McConnell T, et al. Costs of fragility hip fractures globally: a systematic review and meta-regression analysis. *Osteoporosis International* 2017; **28**(10): 2791-800.
6. Sullivan PW, Slejko JF, Sculpher MJ, Ghushchyan V. Catalogue of EQ-5D Scores for the United Kingdom. *Medical Decision Making* 2011; **31**(6): 800-4.
7. National Pressure Ulcer Advisory Panel, European Pressure Ulcer Advisory Panel , Pan Pacific Pressure Injury Alliance. Prevention and Treatment of Pressure Ulcers: Clinical Practice Guideline. In: Haesler E, editor. Osborne Park, Western Australia: Osborne Park; 2019.
8. Coleman S, Gorecki C, Nelson EA, et al. Patient risk factors for pressure ulcer development: systematic review. *Int J Nurs Stud* 2013; **50**(7): 974-1003.
9. Nixon J, Brown S, Smith IL, et al. Comparing alternating pressure mattresses and high-specification foam mattresses to prevent pressure ulcers in high-risk patients: the PRESSURE 2 RCT. *Health Technol Assess* 2019; **23**(52): 1-176.
10. NPSA. Seven steps to patient safety: full reference guide. 2004. https://www.publichealth.hscni.net/sites/default/files/directorates/files/Seven%20steps%20to%20safety.pdf (accessed 31/08/21).
11. NHS England. Serious Incident Framework. 2015. https://www.england.nhs.uk/wp-content/uploads/2015/04/serious-incidnt-framwrk-upd.pdf (accessed 23/06/2022).
12. Briggs M, Collinson M, Wilson L, et al. The prevalence of pain at pressure areas and pressure ulcers in hospitalised patients. *BMC Nursing* 2013; **12**(1): 19.
13. McGinnis E, Briggs M, Collinson M, et al. Pressure ulcer related pain in community populations: a prevalence survey. *BMC Nursing* 2014; **13**(1): 16.
14. Smith IL, Brown S, McGinnis E, et al. Exploring the role of pain as an early predictor of category 2 pressure ulcers: a prospective cohort study. *BMJ Open* 2017; **7**(1): e013623.
15. Gorecki C, Brown JM, Nelson EA, et al. Impact of pressure ulcers on quality of life in older patients: a systematic review. *Journal of the American Geriatrics Society* 2009; **57**(7): 1175-83.
16. McGinnis E, Greenwood DC, Nelson EA, Nixon J. A prospective cohort study of prognostic factors for the healing of heel pressure ulcers. *Age and ageing* 2014; **43**(2): 267-71.
17. Horn SD, Bender SA, Bergstrom N, et al. Description of the National Pressure Ulcer Long-Term Care Study. *Journal of the American Geriatrics Society* 2002; **50**(11): 1816-25.
18. Clark M, Semple MJ, Ivins N, Mahoney K, Harding K. National audit of pressure ulcers and incontinence-associated dermatitis in hospitals across Wales: a cross-sectional study. *BMJ Open* 2017; **7**(8): e015616.
19. Smith IL, Nixon J, Brown S, Wilson L, Coleman S. Pressure ulcer and wounds reporting in NHS hospitals in England part 1: Audit of monitoring systems. *Journal of Tissue Viability* 2016; **25**(1): 3-15.
20. Bennett G, Dealey C, Posnett J. The cost of pressure ulcers in the UK. *Age and ageing* 2004; **33**(3): 230-5.
21. Legood R, McInnes E. Pressure ulcers: guideline development and economic modelling. *Journal of advanced nursing* 2005; **50**(3): 307-14.
22. Baumgarten M, Margolis DJ, Orwig DL, et al. Pressure ulcers in elderly patients with hip fracture across the continuum of care. *Journal of the American Geriatrics Society (JAGS)* 2009; **57**(5): 863-70.

23. Chiari P, Forni C, Guberti M, Gazineo D, Ronzoni S, D'Alessandro FJPo. Predictive factors for pressure ulcers in an older adult population hospitalized for hip fractures: a prognostic cohort study. PLoS One. 2017; **12**(1): e0169909.
24. Donnelly J, Winder J, Kernohan WG, Stevenson M. An RCT to determine the effect of a heel elevation device in pressure ulcer prevention post-hip fracture. *Journal of Wound Care* 2011; **20**(7): 309-18.
25. Smith IL, Brown S, McGinnis E, et al. Exploring the role of pain as an early predictor of category 2 pressure ulcers: a prospective cohort study. BMJ Open. 2017; **7**(1): e013623.
26. Bergstrom N, Horn SD, Rapp M, et al. Preventing pressure ulcers: A multisite randomized controlled trial in nursing homes. Ontario Health Technology Assessment Series. 2014; **14**(11): 1-32.
27. Gardner SE, Frantz RA, Bergquist S, Shin CD. A prospective study of the pressure ulcer scale for healing (PUSH). *The journals of gerontology Series A, Biological sciences and medical sciences* 2005; **60**(1): 93-7.
28. Nixon J, Cranny G, Iglesias C, et al. Randomised, controlled trial of alternating pressure mattresses compared with alternating pressure overlays for the prevention of pressure ulcers: PRESSURE (pressure relieving support surfaces) trial. BMJ (Clinical research ed.). 2006; **332**(7555): 1413.
29. Greenwood C, Nelson EA, Nixon JE, E. M. Comparative effectiveness of medical devices for the prevention of heel pressure ulcers: a systematic review. 2019. https://www.crd.york.ac.uk/PROSPERO/display_record.php?RecordID=152949 (accessed 27.01.20).
30. Greenwood CE, Nelson EA, Nixon J, E., Vargas-Palacios A, McGinnis E. Comparative Effectiveness of Heel Specific Medical Devices for the Prevention of Heel pressure Ulcers: a Systematic Review. Journal of Tissue Viability; 2022; 31(4), 579–592
31. Baath C, Engstrom M, Gunningberg L, Muntlin Athlin A. Prevention of heel pressure ulcers among older patients--from ambulance care to hospital discharge: A multi-centre randomized controlled trial. *Applied nursing research : ANR* 2016; **30**: 170-5.
32. Cadue JF, Karolewicz S, Tardy C, Barrault C, Robert R, Pourrat O. Prevention of heel pressure sores with a foam body-support device. A randomized controlled trial in a medical intensive care unit. [French]. *Presse Medicale* 2008; **37**(1 I): 30-6.
33. Gilcreast DM, Warren JB, Yoder LH, Clark JJ, Wilson JA, Mays MZ. Research comparing three heel ulcer-prevention devices. *Journal of Wound, Ostomy and Continence Nursing* 2005; **32**(2): 112-20.
34. Greenwood C. An exploration of the use of devices for the prevention of heel pressure ulcers in secondary care: A realist evaluation. White Rose eTheses online: University of Leeds; 2020.
35. Griffin XL, Parsons N, Achten J, Costa ML. A randomised feasibility study comparing total hip arthroplasty with and without dual mobility acetabular component in the treatment of displaced intracapsular fractures of the proximal femur the warwick hip trauma evaluation two : White two. *Bone Jt J* 2016; **98**-**B**: 1431–5.
36. Masters JPM, Achten J, Cook J, Dritsaki M, Sansom L, Costa ML. Randomised controlled feasibility trial of standard wound management versus negative-pressure wound therapy in the treatment of adult patients having surgical incisions for hip fractures. *BMJ Open* 2018; **8**. DOI:10.1136/bmjopen-2017-020632.
37. Sims AL, Parsons N, Achten J, Griffin XL, Costa ML, Reed MR. A randomized controlled trial comparing the Thompson hemiarthroplasty with the Exeter polished tapered stem and Unitrax modular head in the treatment of displaced intracapsular fractures of the hip. *Bone Jt J* 2018; **100B**: 352–60.
38. Smith IL, Nixon JE, Sharples L. Power and sample size for multistate model analysis of longitudinal discrete outcomes in disease prevention trials. *Stat Med* 2021; **40**(8): 1960-71.
39. National Institute for Health and Care Excellence. Guide to the methods of technology appraisal 2013. 2013. https://www.nice.org.uk/process/pmg9/chapter/foreword (accessed 30.04.21).
40. van Hout B, Janssen MF, Feng Y-S, et al. Interim Scoring for the EQ-5D-5L: Mapping the EQ-5D-5L to EQ-5D-3L Value Sets. *JVAL* 2012; **15**(5): 708-15.

14 ANNEX A: FLOW CHART