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Pressure-relieving devices for preventing heel pressure ulcers (Protocol)

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[Intervention Protocol]

Pressure-relieving devices for preventing heel pressure ulcers

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ABSTRACT

This is the protocol for a review and there is no abstract. The objectives are as follows:

To determine the effects of pressure-relieving devices in preventing heel pressure ulcers.

BACKGROUND

Description of the condition

Pressure ulcers (also known as pressure sores, bed sores or decubitus ulcers) are defined as "a localized injury to the skin and/or underlying tissue usually over a bony prominence, as a result of pressure, or pressure in combination with shear" (EPUAP 2009; NPUAP 2009). Pressure ulcer classification systems provide a method by which the depth and severity of the injury can be described and documented (Appendix 1). Pressure ulcers have traditionally been categorised according to severity, from a category I pressure ulcer (non-blanching erythema (redness) of intact skin) up to category IV (full thickness tissue loss to bone or muscle). However, recently two additional categories have been defined - 'unstageable/unclassified' and 'suspected deep tissue injury' (EPUAP 2009; NPUAP 2009). As pressure ulcers are categorised according to depth of the wound, these categories are used when the depth of the wound is unknown. The 'unstageable' category describes wounds in which slough or necrosis (loose or dead tissue) obscures the wound bed. 'Suspected deep tissue injury' describes wounds in which it is suspected that there is deeper damage, such as when bruising or a blood blister is present. Although these additional categories were initially described for use in the USA, they have started to be used and investigated worldwide (EPUAP 2009; Gefan 2008).

It has been estimated that the mean cost of treating a pressure ulcer varies from GBP 1, 214 (Category 1) to GBP 14,108 (Category 4) (Dealey 2012), and the total cost in the UK is GBP 1.4 to 2.1 billion annually (4% of total NHS expenditure) (Bennett 2004). A more recent estimate of the annual costs in the United States is USD 9.1 to 11.6 billion (AHRQ 2011). The majority of the costs are due to nursing time, and more severe pressure ulcers have higher costs that relate to higher complication rates (e.g. infections or longer hospital stay). As well as having a financial cost, pressure ulcers have a massive impact upon health-related quality of life; their presence and treatment have been found to affect people's lives emotionally, mentally, physically and socially (Gorecki 2009; Spilsbury 2007).

It is theorised that when pressure ulcers develop, they start internally at the bone and progress outwards; this is because experimental and theoretical models have indicated that internal pressures near a bony prominence are three to five times higher than

those experienced in the skin when under pressure (Gefan 2008; Le 1984). The heel and the sacrum are frequently reported as being the most common sites for pressure ulcers to develop (Amlung 2001; Barczak 1997; Whittington 2000), which is probably because these are areas where there is little subcutaneous tissue over the bones to provide padding to offset the forces of pressure or shear, or both.

Why is the heel such a high risk area?

The heel has a thickened dermis and a large fatty pad to the plantar aspect, which is well adapted to absorb shock from the calcaneum when walking and running. However, the posterior heel has a smaller surface area, little subcutaneous (tissue) volume, and no muscle to distribute pressure and provide cushioning over the bone. This leads to higher pressures being exerted directly over the bone when a person is in a supine, or seated position, with the heels on a foot stool. Therefore people who have reduced mobility, or who spend extended periods supine (e.g. patients in acute and long-term care facilities), have an increased risk for heel pressure ulcer development.

The skin over the posterior heel is supplied with oxygen by small branches from the calcaneal and peroneal arteries; the small size of the blood vessels in this area makes the skin more susceptible to ischaemia (lack of oxygen) when under prolonged pressure (Cichowitz 2009). Conditions that affect the circulation of the lower limb, such as peripheral vascular disease, also make the heel more susceptible to ischaemia as they reduce blood flow to the lower limb. Although circulatory conditions are commonly associated with older age, they can be present in younger people such as those with diabetes or hypertension, or smokers (Vogt 1992). Other circulatory problems, such as chronic venous disease and heart failure, can increase the risk of developing a heel pressure ulcer, as they lead to an increase in pedal oedema (swelling of the feet due to fluid accumulation), which impairs the delivery of oxygen and nutrients to the tissues, and also the disposal of metabolic waste products (Ryan 1969). Oedema also increases the weight of the limb, which, in turn, increases normal resting pressures.

When there is an acute reduction in the circulating volume of blood, subcutaneous tissue is one of the first tissues in which vasoconstriction (muscular narrowing of blood vessels) occurs, and the last to regain normal perfusion once the circulating volume has been restored (Gottrup 1987). This makes the feet and heels very susceptible to ischaemia during an acute illness, as the sympathetic nervous system and some medications preserve the body's organs through increasing the central circulating volume available to them, while decreasing the peripheral circulating volume.

Shear forces are a common problem in the acute and long-term care population due to poor positioning in beds or chairs, which can lead to the patient sliding downwards. Shear forces are also exerted when patients use their heel as a pivot point to reposition themselves. Friction can also cause an increased risk in heel pressure ulceration during poorly-conducted moving and handling of patients, or when patients are agitated or have tremors that can lead to their heels rubbing against bed sheets.

Peripheral neuropathy (reduced or altered ability to sense, in this case in the feet) is one of many complications of diabetes, resulting in significant morbidity and mortality (Callaghan 2012). Although neuropathy is most common amongst diabetics, it is also associated with other conditions such as alcoholism, stroke, demyelinating diseases such as multiple sclerosis, and conditions such as Guillain-Barré syndrome, which can have quite a rapid onset (White 2004). Peripheral neuropathy can lead to an increased risk of heel pressure ulcers, as people with neuropathy are unaware of pain and pressure, and so do not respond to them.

Description of the intervention

There are a number of different ways through which the extent and duration of pressure can be reduced, or removed, at the heel. This can be done through changing a person's position, using equipment that reduces pressure at the heel - or completely removes the pressure at the heel - or a combination of these methods. The equipment available includes whole body devices (e.g. mattresses) and devices specific to the foot (e.g. heel cups, booties or splints). Mattresses and mattress overlays tend to come in two types - alternating pressure (AP) and constant low pressure (CLP). CLP mattresses include foam mattresses and overlays, low air-loss mattresses, air-fluidised bead beds and air overlays.

Heel-specific off-loading can include simple methods such as use of pillows, wedges or other aids to lift the heels off the bed, as well as specific splints, heel troughs or other medical devices that completely remove pressure from the heel.

Heel-specific CLP devices include foam or gel foot protectors or heel cups, air-filled foot protectors and sheepskin products.

Heel-specific low friction devices include dressings or booties designed to reduce friction and shear at the heel.

How the intervention might work

Risk of ulceration is thought to be related to both the amount of pressure on the skin, and the duration for which it is applied. High pressures for a short time do not cause harm, similarly low pressures for a long time are considered safe. The two approaches to reducing risk tend to work by either reducing the amount of pressure on the body, or the duration of the applied pressure. Whole body devices (mattresses or mattress overlays) generally fall into one of two categories - CLP or AP. CLP devices are thought to work by reducing the magnitude of the applied pressure by distributing the body weight over a larger surface area (as pressure is related both to the force applied, and to the area over which it is spread; mathematically, Pressure = Force/Area). AP devices reduce

the duration of pressure by alternately inflating and deflating air-filled cells in a mattress over a set cyclical period.
Heel-specific devices also tend to fall into one of three categories - CLP devices, off-loading devices or low friction devices. CLP heel devices (e.g. a gel or foam heel cup or bootie) are designed either to reduce the magnitude of the applied pressure by spreading it over a larger area, or reduce the effects of the forces of friction or shear, or both. Off-loading devices are designed to remove the pressure of the 'at-risk' body site completely. This could be through using a pillow or wedge under the calf to leave the foot suspended above the mattress, or through supporting the foot or calf in a splint or trough, thereby leaving no pressure on the heel. Low friction devices consist of dressings or booties that do not reduce the magnitude of pressure at the heel, but are used to reduce risk of pressure ulcer development through reducing the forces of friction and shear. There are no heel-specific AP devices, although the heel section of some mattresses may alternate and work in this manner.

Why it is important to do this review

There are a number of different devices available that aim to prevent heel pressure ulcers. However, there appears to be a lack of evidence-based guidance in this area to assist practitioners in deciding which device or pressure-relieving method should be used specifically to reduce pressure ulcer incidence at the heel. This review will help to identify whether any device helps reduce the incidence, or prevents deterioration, of pressure ulcers that develop on the heel; and particularly, whether there is a device that could be considered to be the most effective in prevention of heel pressure ulcers in terms of incidence, health-related quality of life and cost.

OBJECTIVES

To determine the effects of pressure-relieving devices in preventing heel pressure ulcers.

METHODS

Criteria for considering studies for this review

Types of studies

All randomised controlled trials (RCTs) that compare the effects of pressure-relieving devices on the incidence of development of new heel pressure ulcers. RCTs focusing specifically on pressure-relieving devices in the prevention of diabetic foot ulcers will be included if heel ulcer data can be identified separately. Similarly, RCTs that compare the effects of pressure-relieving devices non-specific to the heel (e.g. mattresses) will be included if the heel ulcer data can be identified separately.

Types of participants

People of any age in any care setting without a pre-existing category II (or worse) heel pressure ulcer who are deemed to be at risk of developing a heel pressure ulcer. Participants' level of risk should be assessed using a recognised pressure ulcer risk assessment tool.

Types of interventions

Any device or intervention designed either to off-load pressure or reduce pressure at the heel. These could be used alone or in combination.

Total body AP devices

- Alternating air-filled overlays.
- Alternating air-filled mattress replacements.

Total body CLP devices

- Foam mattresses.
- Foam overlays.
- Low air-loss mattresses.
- Air overlays.
- Air-fluidised bead beds.

Heel-specific off-loading devices

- Pillows, wedges and other aids positioned under the legs to redistribute pressure.
- Heel troughs.
- Splints or other medical devices.

Heel-specific CLP devices

- Foam foot protectors or heel cups.
- Gel foot protectors or heel cups.
- Sheepskin overlays or booties.
- Air-filled foot protectors.

Any of the above mentioned interventions can be compared with each other, with no intervention or with standard care. Treatment arms will differ only in the pressure-relief intervention used; local wound care (which is usually used in combination with pressure relief) should not differ systematically across treatment arms within a trial.

Types of outcome measures

Primary outcomes

- Heel pressure ulcer incidence (the number of people who develop a new heel pressure ulcer of any category, or the number of new heel pressure ulcers that develop).
- Stage of any new pressure ulcer (grading system should be specified).
- Deterioration of pre-existing category 1 pressure ulcer.

Secondary outcomes

- Time to heel pressure ulcer development (including time to development of each grade of pressure ulcer).
- Cost of the intervention.
- Acceptability of the intervention from the perspective of the patient, or care-giver with respect to patient comfort.
- Durability/longevity of the devices (e.g. single-patient use/ frequency of replacement).
- Any adverse events.
- Proxy measures (e.g. interface pressures), but pressure ulcer incidence must be the primary outcome for the study.
- Quality of life as measured by a validated scale (e.g. SF-36).
- Pressure ulcer incidence to other body sites that could be attributed to the device in question.

Search methods for identification of studies

Electronic searches

We will search the following electronic databases to find reports of relevant RCTs:

- the Cochrane Wounds Group Specialised Register;
- the Cochrane Central Register of Controlled Trials (CENTRAL) (latest issue);
- Ovid MEDLINE (1946 to present);
- Ovid EMBASE (1974 to present); and
- EBSCO CINAHL (1982 to present)

The following search strategy will be used in the Cochrane Central Register of Controlled Trials (CENTRAL):
#1 MeSH descriptor: [Beds] explode all trees
#2 (bed or beds):ti,ab,kw
#3 (mattress* or cushion* or pillow*):ti,ab,kw
#4 (“foam” or cutfoam or overlay*):ti,ab,kw
#5 (“pad” or “pads” or padding):ti,ab,kw
#6 (“gel” or “gels”):ti,ab,kw
#7 (pressure next relief*):ti,ab,kw
#8 (pressure next device*):ti,ab,kw
#9 (pressure next redistribution*):ti,ab,kw
#10 (low next pressure next support*):ti,ab,kw
#11 ((constant or alternat*) next pressure*):ti,ab,kw
#12 ((air or water) next suspension*):ti,ab,kw
#13 (sheepskin* or (sheep next skin*)):ti,ab,kw
#14 “foot waffle”:ti,ab,kw
#15 (air next bag*):ti,ab,kw
#16 (elevat* near/2 device*):ti,ab,kw
#17 “static air”:ti,ab,kw
#18 MeSH descriptor: [Shoes] explode all trees
#19 (“shoe” or “shoes” or “boot” or “boots” or booties or cup or cups):ti,ab,kw
#20 (footwear or “foot wear”):ti,ab,kw
#21 MeSH descriptor: [Orthotic Devices] explode all trees
#22 (orthotic next (device* or therapy)):ti,ab,kw
#23 (orthos* or insole*):ti,ab,kw
#24 ((contact or walk*) near/1 (“cast” or “casts”)):ti,ab,kw
#25 (aircast or scotchcast):ti,ab,kw
#26 ((foot or feet) near/2 pressure):ti,ab,kw
#27 ((foot or feet) near/2 protect*):ti,ab,kw
#28 ((foot or feet) near/2 device*):ti,ab,kw
#29 (heel* near/2 pressure*):ti,ab,kw
#30 (heel* near/2 protect*):ti,ab,kw
#31 (heel* near/2 device*):ti,ab,kw
#32 (heel* near/2 (lift* or float* or splint* or glove* or suspension or elevat*)):ti,ab,kw
#33 (trough* near/2 (leg* or “foot” or “feet” or heel*)):ti,ab,kw
#34 #1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19 or #20 or #21 or #22 or #23 or #24 or #25 or #26 or #27 or #28 or #29 or #30 or #31 or #32 or #33
#35 MeSH descriptor: [Pressure Ulcer] explode all trees
#36 pressure next (ulcer* or sore* or injur*):ti,ab,kw
#37 decubitus next (ulcer* or sore* or injur*):ti,ab,kw
#38 (bed next sore*) or bedsore:ti,ab,kw
#39 #35 or #36 or #37 or #38
#40 #34 and #39
This search strategy will be adapted accordingly for Ovid MEDLINE, Ovid EMBASE and EBSCO CINAHL. The Ovid MEDLINE search will be combined with the Cochrane Highly Sensitive Search Strategy for identifying randomised trials in MEDLINE: sensitivity- and precision maximizing version (2008 revision) (Lefebvre 2011). We will combine the EMBASE search with the Ovid EMBASE filter developed by the UK Cochrane Centre (Lefebvre 2011). We will combine the CINAHL searches with the trial filters developed by the Scottish Intercollegiate Guidelines Network (SIGN 2013). No restrictions will be made on the basis of date or language of publication.
We will search the following clinical trials registries:

- EU Clinical Trials Register (https://www.clinicaltrialsregister.eu/index.html)
- ClinicalTrials.gov (http://www.clinicaltrials.gov/)
- WHO International Clinical Trials Registry Platform

(ICTRP) (http://www.who.int/ictrp/en/)

Searching other resources

We will search the bibliographies of all retrieved and relevant publications identified by these strategies for further studies. We will contact experts in the field and ask if they have been involved in, or know of, any studies relevant to this review. We will also contact the manufacturers of devices used in the prevention of heel pressure ulcers and ask for information relevant to this review (e.g. Frontier Medical Group, DM Systems, Posey, Covidien, Sundance Solutions, Smith & Nephew, Spenco).

Data collection and analysis

Selection of studies

Independently, two review authors will assess the titles and abstracts of studies identified by the search strategy against the eligibility criteria for inclusion in the review. We will obtain full versions of potentially relevant studies, and, independently, the two review authors will screen these against the inclusion criteria. Any differences in opinion will be referred to a third author for a decision or discussion until consensus is met.

A 'Preferred Reporting Items of Systematic reviews and Meta-Analyses' (PRISMA) flowchart will be completed to demonstrate the number of citations retrieved through each search method and the number excluded at each stage (Liberati 2009). For the sake of transparency, we will publish a list of studies for which we retrieved full trial reports that subsequently were excluded from the review, and state the reasons for their exclusion.

Data extraction and management

Two of the review authors will extract data from eligible studies independently using a data extraction sheet. Specifically, we will extract the following information:

- author, title, date of study and source;
- participant inclusion/exclusion criteria;
- patient characteristics (e.g. age, sex, diagnosis, comorbidity, baseline risk, details of existing ulcers);
- care setting;
- study design details;
- description of interventions;
- description of any co-interventions;
- duration of intervention (e.g. mean length of time on the support surface or wearing a heel-specific device over a 24-hour period) and length of time intervention took place (e.g. 2 weeks or until discharge);
- sample size calculation and sample size;
- method of randomisation;
- number of participants randomised into each arm;
- allocation concealment;
- blinding (of the patient/outcome assessor);
- outcome measures;
- length of follow-up;
- drop out rates and loss to follow-up;
- results;
- length of hospital stay;
- intention-to-treat analysis;
- conclusions, as reported by the study authors.

If there is any disagreement during the extraction process, this will be resolved by consensus. We will attempt to contact the study authors to obtain any missing details.

Assessment of risk of bias in included studies

Independently, two review authors will assess each included study using the Cochrane Collaboration tool for assessing risk of bias (Higgins 2011a), and a 'Risk of bias' table will be completed for each eligible study. This tool addresses seven specific domains, namely sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessors, incomplete outcome data, selective outcome reporting and other issues (e.g. extreme baseline imbalance). We will assess blinding and completeness of outcome data for each outcome separately (see Appendix 2 for details of the criteria on which the judgment will be based). We will classify trials as being at high risk of bias if they are rated 'high' for any of three key criteria, namely; randomisation sequence, allocation concealment and blinded outcome assessment. Where there is a high risk of bias in any of these key domains, we will endeavour to contact the trial authors, and ask open-ended questions about the design and conduct of the study.

Measures of treatment effect

Where possible, all outcomes will be reported using 95% confidence intervals (CI). For dichotomous outcomes we will calculate risk ratios (RR). For continuous outcomes, where the outcome measures are measured using the same scale, we will calculate mean difference (MD). Standardised mean difference (SMD) will be used as a summary statistic in meta-analysis when studies assess the same outcome, but measure it in a variety of ways (Deeks 2011). Time-to-event outcomes (i.e. time to ulceration) can be measured using the appropriate analytical method, as long as the individual time points are known for all participants (Deeks 2011). If hazard ratios are reported, these will be extracted, as they can be included in a forest plot or meta-analysis.

Unit of analysis issues

In this review the trial participant will be the unit of analysis; the level at which randomisation occurs will be taken into account.

If the heel is the unit of analysis and each heel receives the same intervention then we will identify whether the trial accounted for clustering in the analysis. If each heel receives a different intervention and the treatments were subject to adequate randomisation, then carry-over of treatment effect should be considered. If no data regarding this are reported in the study, then the authors will be contacted to see if they performed an analysis of the carry-over effect.

For cluster-randomised trials the participant will be adjusted for in the cluster as the unit of analysis. We will adjust sample sizes using the methods described in the *Cochrane Handbook for Systematic Reviews of Interventions* (Deeks 2011), using an estimate of the intra-cluster correlation coefficient (ICC) derived either from the trial, if possible, or from a similar trial.

Dealing with missing data

When data relevant to this review are missing, we will contact the study authors and request them. If we cannot access this information, for binary outcomes we will assume a best case/worst case scenario for participants with a missing outcome. For continuous outcomes we will perform an available-case analysis, based on the number of participants for whom the outcome data is known. If standard deviations (SD) are missing, but standard errors (SE) are available, the SD can be calculated (Higgins 2011b).

Assessment of heterogeneity

We will assess clinical heterogeneity by examining potentially influential characteristics e.g. types of participants or groups, or both; interventions and their duration; and the outcomes of each study. If appropriate, and if there is sufficient homogeneity, we will pool data for meta-analysis using RevMan 5.2 (Revman 2012).

We will assess statistical heterogeneity using the I^2 test (Higgins 2011c), which examines the percentage of total variation across studies due to heterogeneity rather than chance. Studies considered to be sufficiently similar will be pooled; a fixed-effect model will be used for low to moderate levels of heterogeneity (I^2 between 0% up to 50%), and a random-effects model will be used in the presence of substantial statistical heterogeneity (I^2 between 50% and 75%). Studies will not be pooled where there is considerable heterogeneity (I^2 greater than 75%) (Higgins 2011c).

Assessment of reporting biases

If 10 or more studies are included for meta-analysis, visual asymmetry of funnel plots will be used to assess any potential reporting or publication bias (Sterne 2011).The study protocols will be consulted in order to identify outcome reporting bias.

Data synthesis

The method used to synthesise studies will depend on the quality, design, and degree of heterogeneity of the studies. If there is high variability in the clinical characteristics, methodology, treatment effect or statistical heterogeneity, it may be inappropriate to perform a meta-analysis. Where studies are clinically similar and the outcome measures comparable, we will enter quantitative data into RevMan 5.2 (Revman 2012), and analyse the data using the RevMan analysis software. For statistically significant effects, where appropriate, we will calculate number needed to treat to benefit (NNTB) or number needed to treat to harm (NNTH) from the risk difference (RD) (Deeks 2011). For dichotomous outcomes, we will calculate RR plus 95% CI. For continuous outcomes, we will extract the mean and SD and calculate the MD plus 95% CI. If scales of measurement differ across trials, we will calculate the SMD with its 95% CI. For cluster-randomised trials, if possible, we will extract: the number of clusters randomised to each group, or the mean size of each cluster, or both; an estimate of the intra-class correlation coefficient (ICC); and the outcome data disregarding the cluster design (i.e. proportion of individuals who develop a pressure ulcer during the study period).

We will combine studies using a narrative overview in instances where statistical synthesis of data from more than one study is not possible or considered inappropriate. We will also comment on clinical relevance, where appropriate.

Subgroup analysis and investigation of heterogeneity

If sufficient data are available we will undertake the following subgroup analyses:

- type of setting (community, inpatient, outpatient);
- participants with/without diabetes;
- presence/absence of peripheral vascular disease;
- presence of pressure ulcer at baseline.

Sensitivity analysis

We will perform a sensitivity analysis to assess whether the findings are robust to the method used to obtain them by comparing the results of two or more meta-analyses using different assumptions (Higgins 2011b). Trials that are assessed as having a low risk of bias in all key domains, namely, adequate generation of the randomisation sequence, adequate allocation concealment and blinding of outcome assessor, for the estimates of treatment effect will be included in the initial meta-analysis. Trials deemed to be at high risk or unknown risk of bias will be included in a subsequent meta-analysis.

'Summary of findings' table

The main results of the review will be presented in 'Summary of findings' tables. These will provide key information concerning

the quality of evidence, the magnitude of effect of the interventions examined, and the sum of available data on the main outcomes (Schünemann 2011a). The 'Summary of findings' tables will also include an overall grading of the evidence related to each of the main outcomes, using the GRADE approach (Schünemann 2011b).

We plan to present the following outcomes in the 'Summary of findings' tables:

- heel pressure ulcer incidence;
- costs;
- time to pressure ulcer development;
- quality of life.

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* *Indicates the major publication for the study*

APPENDICES

Appendix 1. International NPUAP-EPUAP Pressure Ulcer Classification System

Category/Stage I: Non-blanchable redness of intact skin

Intact skin with non-blanchable erythema (redness) of a localised area usually over a bony prominence. Discoloration of the skin, warmth, oedema, hardness or pain may also be present. Darkly pigmented skin may not have visible blanching.***Further description:*** the area may be painful, firm, soft, warmer or cooler than adjacent tissue. Category/Stage I may be difficult to detect in individuals with dark skin tones. May indicate "at risk" persons.

Category/Stage II: Partial thickness skin loss or blister

Partial thickness loss of dermis presenting as a shallow open ulcer with a red/pink wound bed, without slough. May also present as an intact or open/ruptured serum-filled or sero-sanguinous filled blister. ***Further description:*** presents as a shiny or dry shallow ulcer without slough or bruising. This category/stage should not be used to describe skin tears, tape burns, incontinence-associated dermatitis, maceration (skin breakdown) or excoriation (skin lost to scratching).

Category/Stage III: Full thickness skin loss (fat visible)

Full thickness tissue loss. Subcutaneous fat may be visible, but bone, tendon or muscle are not exposed. Some slough may be present. May include undermining and tunnelling. ***Further description:*** the depth of a Category/Stage III pressure ulcer varies according to anatomical location. The bridge of the nose, ear, occiput (back of the head) and malleolus (e.g. protuberance of ankle joint) do not have (adipose) subcutaneous tissue and Category/Stage III ulcers can be shallow. In contrast, areas of significant adiposity can develop extremely deep Category/Stage III pressure ulcers. Bone/tendon is not visible or directly palpable.

Category/Stage IV: Full thickness tissue loss (muscle/bone visible)

Full thickness tissue loss with exposed bone, tendon or muscle. Slough or eschar may be present. Often include undermining and tunnelling. ***Further description:*** the depth of a Category/Stage IV pressure ulcer varies according to anatomical location. The bridge of the nose, ear, occiput and malleolus do not have (adipose) subcutaneous tissue and these ulcers can be shallow. Category/Stage IV ulcers can extend into muscle and/or supporting structures (e.g. fascia, tendon or joint capsule) making osteomyelitis (infection of bone) or osteitis (inflammation of bone) likely to occur. Exposed bone/muscle is visible or directly palpable.

Additional Categories for the USA

Unstageable/Unclassified: Full thickness skin or tissue loss - depth unknown

Full thickness tissue loss in which the actual depth of the ulcer is completely obscured by slough (yellow, tan, grey, green or brown) or eschar (tan, brown or black), or both, in the wound bed. ***Further description:*** until enough slough or eschar, or both, are removed to expose the base of the wound, the true depth cannot be determined; but it will be either a Category/Stage III or IV. Stable (dry, adherent, intact without erythema or fluctuance (indication of presence of pus)) eschar on the heels serves as "the body's natural (biological) cover" and should not be removed.

Suspected Deep Tissue Injury - depth unknown

Purple or maroon localised area of discoloured intact skin or blood-filled blister due to damage of underlying soft tissue from pressure or shear, or both. ***Further description:*** the area may be preceded by tissue that is painful, firm, mushy, boggy, warmer or cooler than adjacent tissue. Deep tissue injury may be difficult to detect in individuals with dark skin tones. Evolution may include a thin blister over a dark wound bed. The wound may further evolve and become covered by thin eschar. Evolution may be rapid, exposing additional layers of tissue even with treatment.

Appendix 2. Risk of bias criteria

1. Was the allocation sequence randomly generated?

Low risk of bias

The investigators describe a random component in the sequence generation process such as: referring to a random number table; using a computer random number generator; coin tossing; shuffling cards or envelopes; throwing dice; drawing of lots.

High risk of bias

The investigators describe a non-random component in the sequence generation process. Usually, the description would involve some systematic, non-random approach, for example: sequence generated by odd or even date of birth; sequence generated by some rule based on date (or day) of admission; sequence generated by some rule based on hospital or clinic record number.

Unclear

Insufficient information about the sequence generation process provided to permit judgement of low or high risk of bias.

2. Was the treatment allocation adequately concealed?

Low risk of bias

Participants and investigators enrolling participants could not foresee assignment because one of the following, or an equivalent method, was used to conceal allocation: central allocation (including telephone, web-based and pharmacy-controlled randomisation); sequentially-numbered drug containers of identical appearance; sequentially-numbered, opaque, sealed envelopes.

High risk of bias

Participants or investigators enrolling participants could possibly foresee assignments and thus introduce selection bias, such as allocation based on: using an open random allocation schedule (e.g. a list of random numbers); assignment envelopes were used without appropriate safeguards (e.g. if envelopes were unsealed or nonopaque or not sequentially-numbered); alternation or rotation; date of birth; case record number; any other explicitly unconcealed procedure.

Unclear

Insufficient information available to permit judgement of low or high risk of bias. This is usually the case if the method of concealment is not described or not described in sufficient detail to allow a definite judgement, for example if the use of assignment envelopes is described, but it remains unclear whether envelopes were sequentially-numbered, opaque and sealed.

3. Blinding - was knowledge of the allocated interventions adequately prevented during the study? (Participants and personnel) and (Outcome assessors)

Low risk of bias

Any one of the following.

- No blinding, but the review authors judge that the outcome and the outcome measurement are not likely to be influenced by lack of blinding.
- Blinding of participants and key study personnel ensured, and unlikely that the blinding could have been broken.
- Either participants or some key study personnel were not blinded, but outcome assessment was blinded and the non-blinding of others unlikely to introduce bias.

High risk of bias

Any one of the following.

- No blinding or incomplete blinding, and the outcome or outcome measurement is likely to be influenced by lack of blinding.
- Blinding of key study participants and personnel attempted, but likely that the blinding could have been broken.
- Either participants or some key study personnel were not blinded, and the non-blinding of others likely to introduce bias.

Unclear

Either of the following.

- Insufficient information provided to permit judgement of low or high risk of bias.
- The study did not address this outcome.

4. Were incomplete outcome data adequately addressed?

Low risk of bias

Any one of the following.

- No missing outcome data.
- Reasons for missing outcome data unlikely to be related to true outcome (for survival data, censoring unlikely to be introducing bias).
- Missing outcome data balanced in numbers across intervention groups, with similar reasons for missing data across groups.
- For dichotomous outcome data, the proportion of missing outcomes compared with observed event risk is not enough to have a clinically relevant impact on the intervention effect estimate.
- For continuous outcome data, plausible effect size (difference in means or standardised difference in means) among missing outcomes is not enough to have a clinically relevant impact on observed effect size.
- Missing data have been imputed using appropriate methods.

High risk of bias

Any one of the following.

- Reason for missing outcome data likely to be related to true outcome, with either imbalance in numbers or reasons for missing data across intervention groups.
- For dichotomous outcome data, the proportion of missing outcomes compared with observed event risk is enough to induce clinically relevant bias in intervention effect estimate.
- For continuous outcome data, plausible effect size (difference in means or standardised difference in means) among missing outcomes is enough to induce clinically relevant bias in observed effect size.
- 'As-treated' analysis done with substantial departure of the intervention received from that assigned at randomisation.
- Potentially inappropriate application of simple imputation.

Unclear

Either of the following.

- Insufficient reporting of attrition/exclusions to permit judgement of low or high risk of bias (e.g. number randomised not stated, no reasons for missing data provided).
- The study did not address this outcome.

5. Are reports of the study free of suggestion of selective outcome reporting?

Low risk of bias

Either of the following.

- The study protocol is available and all of the study's pre-specified (primary and secondary) outcomes that are of interest in the review have been reported in the pre-specified way.
- The study protocol is not available but it is clear that the published reports include all expected outcomes, including those that were pre-specified (convincing text of this nature may be uncommon).

High risk of bias

Any one of the following.

- Not all of the study's pre-specified primary outcomes have been reported.
- One or more primary outcomes is reported using measurements, analysis methods or subsets of the data (e.g. sub scales) that were not pre-specified.
- One or more reported primary outcomes were not pre-specified (unless clear justification for their reporting is provided, such as an unexpected adverse effect).
- One or more outcomes of interest in the review are reported incompletely so that they cannot be entered in a meta-analysis.
- The study report fails to include results for a key outcome that would be expected to have been reported for such a study.

Unclear

Insufficient information to permit judgement of low or high risk of bias. It is likely that the majority of studies will fall into this category.

6. Other sources of potential bias

Low risk of bias

The study appears to be free of other sources of bias.

High risk of bias

There is at least one important risk of bias. For example, the study:

- had a potential source of bias related to the specific study design used; or
- had extreme baseline imbalance; or
- has been claimed to have been fraudulent; or
- had some other problem.

Unclear

There may be a risk of bias, but there is either:

- insufficient information to assess whether an important risk of bias exists; or
- insufficient rationale or evidence that an identified problem will introduce bias.

CONTRIBUTIONS OF AUTHORS

CG developed, wrote and edited the protocol, made an intellectual contribution and approved the final version of the protocol prior to submission.

EAN and EM edited the protocol, made an intellectual contribution and approved the final version of the protocol prior to submission.

JN made an intellectual contribution to the development of the protocol.

Contributions of editorial base:

Nicky Cullum: advised on methodology, interpretation and protocol content.
Julie Bruce, Editor: approved the final protocol prior to submission.
Sally Bell-Syer: coordinated the editorial process. Advised on methodology, interpretation and content. Edited the protocol.
Ruth Foxlee: designed the search strategy and edited the search methods section.

DECLARATIONS OF INTEREST

Clare E Greenwood: in receipt of a Smith and Nephew / Leeds Teaching Hospitals Charitable Trustees Grant which funds a part time PhD, this systematic review will form a part of that PhD.

E Andrea Nelson: nothing to declare

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Elizabeth McGinnis: nothing to declare

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