ClinicalEvidence

Pressure ulcers: treatment

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Madhuri Reddy

ABSTRACT

INTRODUCTION: Unrelieved pressure or friction of the skin, particularly over bony prominences, can lead to pressure ulcers in up to one third of people in hospitals or community care, and one fifth of nursing home residents. Pressure ulcers are more likely in people with reduced mobility and poor skin condition, such as older people or those with vascular disease. METHODS AND OUTCOMES: We conducted a systematic overview, aiming to answer the following clinical question: What are the effects of treatments in people with pressure ulcers? We searched: Medline, Embase, The Cochrane Library, and other important databases up to January 2014 (BMJ Clinical Evidence overviews are updated periodically; please check our website for the most up-to-date version of this overview). RESULTS: At this update, searching of electronic databases retrieved 307 studies. After deduplication and removal of conference abstracts, 203 records were screened for inclusion in the overview. Appraisal of titles and abstracts led to the exclusion of 163 studies and the further review of 40 full publications. Of the 40 full articles evaluated, seven systematic reviews and two RCTs were added at this update. We performed a GRADE evaluation for 15 PICO combinations. CONCLUSIONS: In this systematic overview, we categorised the efficacy for 15 interventions based on information about the effectiveness and safety of air-fluidised supports, alternating-pressure surfaces (including mattresses), debridement, dressings, electrotherapy, hyperbaric oxygen, low-air-loss beds, low-level laser therapy, low-tech constant-low-pressure supports, nutritional supplements, seat cushions, surgery, therapeutic ultrasound, topical negative pressure, and topical phenytoin.

QUESTIONS

INTERVENTIONS

Key points

- Unrelieved pressure or friction of the skin, particularly over bony prominences, can lead to pressure ulcers, which affect up to one third of people in hospitals or community care and one fifth of nursing home residents.

  Pressure ulcers are more likely in people with reduced mobility and poor skin condition, such as older people or those with vascular disease.

- The previous version of this overview looked at the effects of preventative interventions, as well as the treatment of pressure ulcers. At this update, we have focused on the treatment of pressure ulcers.

  We searched for evidence of effectiveness from RCTs and systematic reviews of RCTs.

  Overall, many of the RCTs we found were small and of limited quality. There was considerable variation between RCTs, and there were only limited occasions when it was possible to combine data from different trials. These factors make it difficult to draw robust conclusions from the current RCT evidence base.

- In people with pressure ulcers, air-fluidised supports may improve healing compared with standard care, although they can make it harder for people to get in and out of bed independently.

- We don't know whether healing is improved in people with pressure ulcers by use of other treatments such as one specific specialised support surface (including alternating-pressure surfaces, low-tech constant-low-pressure supports, low-air-loss beds, and specific seat cushions) over any other specific specialised support surface, one specific wound dressing over any other specific wound dressing, or with surgery, debridement, electrotherapy, ultrasound, low-level laser therapy, topical negative pressure, topical phenytoin, hyperbaric oxygen, or nutritional interventions.

- Given the importance of this condition, in terms of both morbidity and resource costs, there is a need for further high-quality trials in this field. However, the difficulties of undertaking RCTs in this field should not be underestimated.

Clinical context

GENERAL BACKGROUND

Pressure ulcers are frequently preventable but may result in increased length of hospital stay and contribute to premature death. The prevalence of pressure ulcers in hospital is about 13% to 14%. Incidence is highest in adult intensive care and general cardiac units. People with spinal cord injuries have a pressure ulcer prevalence of 20% to 30% during the first 5 years after initial injury.

FOCUS OF THE REVIEW

High-quality evidence of management strategies of pressure ulcers is limited, and frequently treatments are based on expert opinion and consensus. This overview is an evaluation of the most up to date, best designed studies available on pressure ulcer management strategies.

COMMENTS ON EVIDENCE

Well-designed studies on treatment of pressure ulcers are limited. We evaluated interventions for which they were available.

SEARCH AND APPRAISAL SUMMARY

The update literature search for this review was carried out from the date of the last search, June 2010, to January 2014. A back search from 1966 was performed for the new options added to the scope at this update. For more information on the electronic databases searched and criteria applied during assessment of studies for potential relevance to the overview, please see the Methods section. Searching of electronic databases retrieved 307 studies. After deduplication and removal of conference abstracts, 203 records were screened for inclusion in the overview. Appraisal of titles and abstracts led to the exclusion of 163 studies and the further review of 40 full publications. Of the 40 full articles evaluated, seven systematic reviews and two RCTs were added at this update.

DEFINITION	Pressure ulcers (also known as pressure sores, bed sores, and decubitus ulcers) may present as persistently hyperaemic, blistered, broken, or necrotic skin, and may extend to underlying structures, including muscle and bone. Pressure ulcers are usually graded on a scale of 1 to 4, with a higher grade indicating greater ulcer severity, as well as unstageable and suspected deep tissue injury (sDTI). [1]
INCIDENCE/ PREVALENCE	Reported prevalence rates range from 5% to 32% for hospital populations, 4% to 33% for community-care populations, and 5% to 21% for nursing-home populations. [2]
AETIOLOGY/ RISK FACTORS	Pressure ulcers are caused by unrelieved pressure, shear, or friction. They are most common below the waist and at bony prominences, such as the sacrum, heels, and hips. They occur in all healthcare settings. Increased age, reduced mobility, impaired nutrition, vascular disease, faecal incontinence, and skin condition at baseline consistently emerge as risk factors. [3] [4] However, the relative importance of these and other factors is uncertain.
PROGNOSIS	There are few data on prognosis of untreated pressure ulcers. The presence of pressure ulcers has been associated with a two- to four-fold increased risk of death in older people and people in intensive care. [5] [6] However, pressure ulcers are a marker for underlying disease severity and other comorbidities, rather than an independent predictor of mortality. [5]
AIMS OF INTERVENTION	To heal existing pressure ulcers and improve quality of life, with minimal adverse effects of treatment.
OUTCOMES	**Healing rates** (rate of change of area and volume, time to heal, severity of pressure ulcers); **adverse effects**.
METHODS	**Search strategy** *BMJ Clinical Evidence* search and appraisal date January 2014. Databases used to identify studies for this systematic overview include: Medline 1966 to January 2014, Embase 1980 to January 2014, The Cochrane Database of Systematic Reviews 2014, issue 1 (1966 to date of issue), the Database of Abstracts of Reviews of Effects (DARE), and the Health Technology Assessment (HTA) database. **Inclusion criteria** Study design criteria for inclusion in this systematic overview were systematic reviews and RCTs published in English, with any level of blinding (including open trials), and containing any number of individuals with any level of loss to follow-up. There was no minimum length of follow-up. We reviewed all RCTs that used objective clinical outcome measures. For many trials, we could not be sure that the size of pressure ulcers was distributed evenly between groups at baseline. Unequal distribution of wound size at baseline would have an

impact on all measures of wound healing. Ideally, studies of treatment should stratify randomisation by initial wound area and include enough participants to ensure even distribution of baseline wound size. A further difficulty in assessing the trials of pressure ulcer treatment is that it can be difficult to determine from reports whether an RCT of a new device, e.g., a mattress, is sufficiently similar to be assessed with previously described mattresses or whether it constitutes a new device. It can therefore be difficult to combine data from RCTs and assess overall effects of treatment options. *BMJ Clinical Evidence* does not necessarily report every study found (e.g., every systematic review). Rather, we report the most recent, relevant and comprehensive studies identified through an agreed process involving our evidence team, editorial team, and expert contributors. **Evidence evaluation** A systematic literature search was conducted by our evidence team, who then assessed titles and abstracts, and finally selected articles for full text appraisal against inclusion and exclusion criteria agreed *a priori* with our expert contributor. In consultation with the expert contributor, studies were selected for inclusion and all data relevant to this overview extracted into the benefits and harms section of the overview. In addition, information that did not meet our predefined criteria for inclusion in the benefits and harms section may have been reported in the 'Further information on studies' or 'Comment' section (see below). **Adverse effects** All serious adverse effects, or those adverse effects reported as statistically significant, were included in the harms section of the overview. Pre-specified adverse effects identified as being clinically important were also reported, even if the results were not statistically significant. Although *BMJ Clinical Evidence* presents data on selected adverse effects reported in included studies, it is not meant to be, and cannot be, a comprehensive list of all adverse effects, contraindications, or interactions of included drugs or interventions. A reliable national or local drug database must be consulted for this information. **Comment and Clinical guide sections** In the Comment section of each intervention, our expert contributors may have provided additional comment and analysis of the evidence, which may include additional studies (over and above those identified via our systematic search) by way of background data or supporting information. As *BMJ Clinical Evidence* does not systematically search for studies reported in the Comment section, we cannot guarantee the completeness of the studies listed there or the robustness of methods. Our expert contributors add clinical context and interpretation to the Clinical guide sections where appropriate. **Structural changes this update** At this update, we have removed the following previously reported question: What are the effects of preventative interventions in people at risk of developing pressure ulcers? **Data and quality** To aid readability of the numerical data in our overviews, we round many percentages to the nearest whole number. Readers should be aware of this when relating percentages to summary statistics such as relative risks (RRs) and odds ratios (ORs). *BMJ Clinical Evidence* does not report all methodological details of included studies. Rather, it reports by exception any methodological issue or more general issue that may affect the weight a reader may put on an individual study, or the generalisability of the result. These issues may be reflected in the overall GRADE analysis. We have performed a GRADE evaluation of the quality of evidence for interventions included in this review (see table, p 24). The categorisation of the quality of the evidence (high, moderate, low, or very low) reflects the quality of evidence available for our chosen outcomes in our defined populations of interest. These categorisations are not necessarily a reflection of the overall methodological quality of any individual study, because the Clinical Evidence population and outcome of choice may represent only a small subset of the total outcomes reported, and population included, in any individual trial. For further details of how we perform the GRADE evaluation and the scoring system we use, please see our website (www.clinicalevidence.com).

QUESTION What are the effects of treatments in people with pressure ulcers?

OPTION AIR-FLUIDISED SUPPORT

- For GRADE evaluation of interventions for Pressure ulcers: treatment, see table, p 24 .
- In people with pressure ulcers, air-fluidised supports may improve healing compared with standard care, although they can make it harder for people to get in and out of bed independently.
- However, evidence was weak and came from two small RCTs (40 people; 72 people).

Benefits and harms

Air-fluidised supports versus standard care:

We found four systematic reviews (search dates 2000; [7] 2008; [8] 2011; [9] and 2012 [10]). The first systematic review (3 RCTs, 202 people) compared air-fluidised supports with standard care. [7] The second systematic review, which had different inclusion criteria, included only one RCT identified by the first review and had further detail on this RCT. [8] The third [9] and fourth [10] systematic reviews evaluated various support surfaces for pressure ulcers, and between them identified 21 RCTs that assessed ulcer healing. [9] [10] Both reviews identified the same three RCTs as the first review comparing air-fluidised supports with standard/conventional care. [9] [10] The third review reported that

none of the RCTs measured variability around the outcome measures, and that pooling of data was not possible. None of the reviews pooled data, and so we have reported data for individual RCTs as reported in the reviews.

Healing rates

Air-fluidised supports compared with standard care Air-fluidised supports may be more effective than standard care (standard care, alternating-pressure mattress covered in foam) at healing established pressure ulcers (as measured by change in wound surface area) in people in hospital, although we don't know about people being cared for at home (low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Healing rates					
[7] [9] Systematic review	40 male hospital patients with grade 2 or 3 pressure ulcers expected to stay in hospital for at least 15 days Data from 1 RCT	**Median change in total ulcer surface area , mean 15 days** with air-fluidised support with standard care Absolute results not reported Data from RCT [11]	P = 0.05	○○○	air-fluidised support
[7] [9] Systematic review	97 people being cared for at home with grade 3 or 4 ulcers Data from 1 RCT	**Median change in total ulcer surface area , 36 weeks** with air-fluidised support with standard care Absolute results not reported	RR 1.23 95% CI 0.84 to 1.86 This RCT had a 13% withdrawal rate and did not perform an intention-to-treat analysis	⟷	Not significant
[8] [9] Systematic review	72 people, 65 people completed study, aged >18 years, acute care, grade 1 to 4 ulcers Data from 1 RCT	**Median change in wound surface area** –1.2 cm^2 with air-fluidised mattress +0.5 cm^2 with alternating-pressure mattress covered in foam Data from RCT [12]	95% CI for difference –9.2 cm^2 to –0.6 cm^2 P = 0.01	○○○	air-fluidised mattress

Adverse effects

No data from the following reference on this outcome. [7] [8] [9] [10]

Further information on studies

[7] [9] The three RCTs reported from these two systematic reviews had a combined population of 202 people. One RCT (65 people), which reported that air-fluidised therapy was effective in people with pressure ulcers as measured by a change in median surface area, had a higher drop-out rate in the group allocated air-fluidised therapy. [12] Another RCT (40 men) that reported benefit from air-fluidised therapy was of low quality. [11]

Comment: People are unable to move in and out of bed independently when they use air-fluidised beds, and this limits the number of people for whom they are suitable.

OPTION ALTERNATING-PRESSURE SURFACES

- For GRADE evaluation of interventions for Pressure ulcers: treatment, see table, p 24 .

- We don't know whether healing is improved in people with pressure ulcers by use of alternating-pressure surfaces compared with standard care.

Benefits and harms

Alternating-pressure surfaces versus standard care or constant-low-pressure devices:

We found three systematic reviews (search dates 2008; [8] 2011; [9] and 2012 [10]) that all identified the same single RCT [13] comparing alternating-pressure mattress with fluid overlay mattress.

Healing rates

Alternating-pressure surfaces compared with standard care or constant-low-pressure devices We don't know whether alternating-pressure surfaces are more effective than fluid mattress overlays at improving the proportion of people with improvement in pressure ulcers (very low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Healing rates					
[9] Systematic review	199 people, mean age 80 years, acute care, grade 1–4 ulcers Data from 1 RCT	**Proportion of people with improvement in pressure ulcers** 60/83 (72%) with alternating-pressure mattress 56/75 (75%) with fluid mattress overlay Participants could request additional turning, and this co-intervention could influence healing rates	RR 0.97 95% CI 0.80 to 1.17 P = 0.74	⟷	Not significant

Adverse effects

No data from the following reference on this outcome. [8] [9] [10]

Comment: People often have difficulty moving in bed independently on alternating-pressure mattresses. [14]

OPTION DEBRIDEMENT

- For GRADE evaluation of interventions for Pressure ulcers: treatment, see table, p 24 .
- We found no clinically important results from RCTs about the effects of debridement compared with no debridement in the treatment of people with pressure ulcers.

Benefits and harms

Debridement versus no debridement or different debriding agents versus each other:

We found two systematic reviews (search dates 1998; [15] and 2008 [8]), which did not pool data.The first systematic review found no RCTs comparing debridement with no debridement. [15] It identified 32 RCTs comparing different debriding agents such as dextranomer paste, but the studies were small, included a range of wounds, and few comparisons were undertaken in more than one RCT. The review concluded that there was insufficient evidence to promote the use of any particular debriding agent over another. The second systematic review categorised dressings by their primary purpose (e.g., debriding, hydrating, etc.) and only included RCTs that calculated wound size, used evaluation tools that incorporated these measurements, or used complete wound healing as end points. [8] The review identified three RCTs that it categorised as comparing different debriding agents with each other.

Healing rates

Debriding agents compared with no debridement or different debriding agents compared with each other We don't know whether any one debriding agent is consistently more effective than the other debriding agents at healing pressure ulcers. We found no RCTs directly comparing debridement with no debridement (very low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Healing rates					
[8] Systematic review	28 people (26 people completed the study) Data from 1 RCT	**Reduction in wound surface** with collagenase with papain-urea-chlorophyllin copper Absolute results not reported	Reported as not significant P value not reported	⟷	Not significant
[8] Systematic review	135 people (78 people completed the study) Data from 1 RCT	**Reduction in wound surface** with collagenase with fibrinolysin or deoxyribonuclease Absolute results not reported	P = 0.12	⟷	Not significant
[8] Systematic review	102 people (63 people completed the study) Data from 1 RCT	**Reduction in wound surface** with collagenase daily with collagenase every 2 days Absolute results not reported	P = 0.64	⟷	Not significant

Adverse effects

No data from the following reference on this outcome. [8] [15]

Further information on studies

[8] The review also found further RCTs comparing debriding agents with a variety of agents (including hydrating agents, absorbent agents, moist saline gauze, and sugar and egg white). Overall, the review concluded that no debriding agent was consistently superior to other dressings for wound healing.

Comment: None.

OPTION DRESSINGS (HYDROCOLLOID AND NON-HYDROCOLLOID) VERSUS EACH OTHER

- For GRADE evaluation of interventions for Pressure ulcers: treatment, see table, p 24 .
- We don't know which type of dressing is better for treating pressure ulcers.

Benefits and harms

Hydrocolloid dressings versus gauze soaked in saline, hypochlorite, or povidone iodine:

We found three systematic reviews (search dates 1997; [16] 2008; [8] and 2012 [10]) assessing dressings or topical agents for pressure ulcers. The second review did not pool data. [8] It found seven RCTs (32–94 people; 2 RCTs included in the first review) comparing hydrocolloid dressings with moist saline gauze (6 RCTs) or moist povidone-iodine gauze (1 RCT), four of which found no significant difference between groups, while two found a significant benefit with hydrocolloid versus moist saline gauze (see Further information on studies). The third review [10] identified seven RCTs that compared hydrocolloid with gauze dressings, all of which were included in the earlier systematic

reviews. [8] [16] The review noted that statistical heterogeneity precluded pooling of results. The authors concluded that the studies provided low-strength evidence of a greater reduction in wound size with hydrocolloid dressings.

Healing rates

Hydrocolloid dressings compared with gauze soaked in saline, hypochlorite, or povidone iodine We don't know whether hydrocolloid dressings are more effective than gauze soaked in saline, hypochlorite, or povidone iodine at healing pressure ulcers as we found insufficient evidence to draw robust conclusions (low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Healing rates					
[16] Systematic review	People 5 RCTs in this analysis	**Healing rate , up to 75 days** 102/205 (50%) with hydrocolloid dressings 59/191 (31%) with standard dressings Standard dressings included gauze soaked in saline, hypochlorite, or povidone iodine Overall, RCTs were small and of poor quality, and the significance of the meta-analysis in the first review was sensitive to the method of calculation (see Further information on studies)	OR 2.57 95% CI 1.58 to 4.18 This result should be interpreted with caution (see Further information on studies)	●●○	hydrocolloid dressings

Adverse effects

No data from the following reference on this outcome. [8] [10] [16]

Hydrocolloid dressings versus non-hydrocolloid dressings other than gauze soaked in saline, hypochlorite, or povidone iodine:

We found one systematic review (search date 2008), which compared hydrocolloid dressings with other dressings. [8] The review did not pool data. Overall, the review concluded that no one dressing was consistently superior to the alternatives. [8]

Healing rates

Hydrocolloid dressings compared with non-hydrocolloid dressings other than gauze soaked in saline, hypochlorite, or povidone iodine We don't know whether hydrocolloid dressings are more effective than non-hydrocolloid dressings other than gauze soaked in saline, hypochlorite, or povidone iodine at healing pressure ulcers (low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Healing rates					
[8] Systematic review	Number of people unclear 8 RCTs in this analysis	**Wound healing** with hydrocolloid dressings with other types of dressing Absolute results not reported Other types of dressing included: debriding dressings (3 RCTs), hydrating dressings (6 RCTs), absorbent dressings (1 RCT), and other specific dressings (5 RCTs)	Reported as not significant P value not reported	⟷	Not significant

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
		Many of the RCTs were of poor methodological quality			

Adverse effects

No data from the following reference on this outcome. [8]

Hydrocolloid dressings versus topical phenytoin:

See option on Topical phenytoin, p 20 .

Dressings other than hydrocolloid versus each other:

We found one systematic review (search date 2008), which compared dressings other than hydrocolloid with each other. [8] The review categorised dressings by their primary purpose (e.g., debriding, hydrating, absorbent, etc.) and only included studies that calculated wound size, used evaluation tools that incorporated these measurements, or used complete wound healing as end points. Overall, the review found no clear evidence that any one dressing was consistently superior to any other dressing (no further data reported; see Further information on studies for details of RCTs). [8]

Adverse effects

No data from the following reference on this outcome. [8]

Further information on studies

[8] The review included RCTs comparing different debriding dressings (3 RCTs), debriding versus absorbent dressings (1 RCT), absorbent dressings versus each other (2 RCTs), absorbent versus other specific dressings (3 RCTs), hydrating versus absorbent dressings (2 RCTs), hydrating versus antimicrobial dressings (1 RCT), hydrating versus other specific dressings (3 RCTs), antimicrobial versus other specific dressings (4 RCTs), and other specific dressings versus other specific dressings (13 RCTs). Many of the RCTs were of poor methodological quality (CLEAR NPT criteria [maximum 6]: 24 RCTs scored 2 or less), were small (20 RCTs included 40 people or less), and many had large differences between the number randomised and those who completed the study.

[8] *Hydrocolloid dressings versus gauze soaked in saline, hypochlorite, or povidone iodine* Of the seven RCTs, four RCTs found no significant difference between groups in wound healing. One RCT (94 people) with weak methods did not report a statistical analysis between groups. Two RCTs (first RCT: 83 people; second RCT: 32 people [12 people completed]) found a significant benefit with hydrocolloid versus moist saline gauze. One of these RCTs (32 people) had weak methods (CLEAR NPT criteria [maximum 6]: RCT score 1). The remaining RCT had baseline differences between groups in ulcer size. Although these differences were not statistically significant, they may have biased the results against standard dressings.

[16] *Hydrocolloid dressings versus gauze soaked in saline, hypochlorite, or povidone iodine* Given the large absolute risks of events in this review, a relative risk would be a preferable outcome measure for results. [17] If the meta-analysis is re-worked using relative risk instead of odds ratio, the result is no longer significant (Cullum N, 2004; personal communication).

Comment: None.

OPTION ELECTROTHERAPY

- For GRADE evaluation of interventions for Pressure ulcers: treatment, see table, p 24 .
- We don't know whether electrotherapy improves healing in people with pressure ulcers.

Benefits and harms

Electrotherapy versus sham electrotherapy or standard treatment:

We found four systematic reviews (search dates 2000; [7] 2008; [8] 2011; [18] and 2012 [10]) and one subsequent RCT. [19] Between them, the reviews identified 11 RCTs evaluating the effects of electrotherapy on healing of pressure ulcers. [7] [8] [10] [18] Here, we report data from the RCTs that met *BMJ Clinical Evidence* reporting criteria. There was consensus across the reviews that the RCTs identified were of generally low quality.

Healing rates

Electrotherapy compared with sham electrotherapy or standard treatment We don't know whether electrotherapy is more effective than sham electrotherapy or standard care at healing pressure ulcers as we found insufficient evidence to draw robust conclusions (low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Healing rates					
[7] Systematic review	Number of people unclear 2 RCTs in this analysis	**Healing rates , 3–5 weeks** with electrotherapy with sham treatment Absolute results not reported These RCTs were small and had important weaknesses in their methods; results should, therefore, be interpreted with caution	RR 7.92 95% CI 2.40 to 26.30	●●●	electrotherapy
[20] RCT	49 people In review [7]	**Percentage area of pressure ulcer healed , 4 weeks** 50% with electrotherapy 23% with sham treatment These RCTs were small and had important weaknesses in their methods; results should, therefore, be interpreted with caution	P = 0.04	○○○	electrotherapy
[8] Systematic review	7 people Data from 1 RCT	**Reduction in wound surface area** 22% with interrupted direct current 3% with placebo-interrupted direct current The RCT was too small to draw reliable conclusions	P value not reported		
[21] RCT	63 people In review [8]	**Proportion of people completely healed , 8 weeks** 5/35 (14%) with electrotherapy 3/28 (11%) with sham treatment	P = 0.39	⟷	Not significant
[21] RCT	63 people In review [8]	**Proportion of people completely healed , 12 weeks** 9/35 (26%) with electrotherapy 10/28 (36%) with sham treatment	P = 0.28	⟷	Not significant

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
[21] RCT	63 people In review [8]	**Mean time to complete healing** 63 days with electrotherapy 90 days with sham treatment	P = 0.16	⟷	Not significant
[22] RCT	34 people with spinal cord injury, grade 2 to 4 ulcers, average age 50 years In review [10]	**Mean decrease in percentage wound surface area , 3 months** 70% with high-voltage pulsed current plus standard care 36% with standard care	P = 0.048 Borderline significance	◌◌◌	high-voltage pulsed current plus standard care
[19] RCT	57 people with stage 2 and stage 3 pressure ulcers	**Mean decrease in wound surface area , 6 weeks** 89% with electrical stimulation plus standard care 44% with standard care alone Absolute numbers not reported 50 people in this analysis	P <0.001	◌◌◌	electrical stimulation plus standard care

Adverse effects

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Adverse effects					
[21] RCT	63 people In review [8]	**Adverse effects** with electrotherapy with sham treatment Absolute results not reported	2 people in the electrotherapy group had hypergranulation of the ulcer; and 2 had local irritation (2/35 [6%] for either outcome), possibly as a result of concomitant use of topical sulfadiazine cream		
[22] RCT	34 people	**Adverse effects** with electrotherapy plus standard care with standard care alone Absolute results not reported	The RCT noted that adverse effects were minor and rare, the most common with electrotherapy plus standard care was red, raised, itchy skin under the large dispersive electrode, which was attributed to contact dermatitis		
[19] RCT	57 people with stage 2 and stage 3 pressure ulcers	**Adverse effects** with electrical stimulation plus standard care with standard care alone Absolute results not reported	The RCT noted that there were no adverse effects with electrical stimulation		

No data from the following reference on this outcome. [7] [8] [10] [18]

Comment: None.

OPTION HYPERBARIC OXYGEN THERAPY New

- For GRADE evaluation of interventions for Pressure ulcers: treatment, see table, p 24 .
- We don't know whether hyperbaric oxygen therapy improves healing of pressure ulcers as we found no RCTs.

Benefits and harms

Hyperbaric oxygen therapy versus standard care or non-hyperbaric oxygen therapy:

We found five systematic reviews. [8] [10] [23] [24] [25] Two reviews were of treatment for pressure ulcers (search dates 2008; [8] and 2012 [10]) and three were of hyperbaric oxygen therapy for the management of chronic wounds (search dates 2002; [23] 2003; [24] and 2012 [25]). None of the reviews identified any RCTs examining the effects of hyperbaric oxygen therapy in people with pressure ulcers.

Comment: None.

OPTION LOW-AIR-LOSS BEDS

- For GRADE evaluation of interventions for Pressure ulcers: treatment, see table, p 24 .
- We don't know whether low-air-loss beds improve healing in people with pressure ulcers compared with standard beds or standard care.

Benefits and harms

Low-air-loss beds versus standard beds or standard care:

We found four systematic reviews (search dates 2000; [7] 2008; [8] 2011; [9] and 2012 [10]). All four reviews identified the same three RCTs comparing low-air-loss beds with standard beds or standard care in the treatment of pressure ulcers. [26] [27] [28] The first review synthesised data for two RCTs, the results of which are presented here. [7] One RCT did not fulfil our inclusion criteria. Data for a fourth RCT identified by two reviews are reported separately. [8] [9] There was consensus across the reviews that the quality of the RCTs was low, and that there was insufficient evidence to suggest that low-air-loss mattresses are more effective than other interventions for the treatment of pressure ulcers.

Healing rates

Low-air-loss beds compared with standard beds or standard care We don't know whether low-air-loss beds are more effective than convoluted foam or air and foam mattress at increasing pressure ulcer healing (very low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Healing rates					
[7] Systematic review	People 2 RCTs in this analysis	**Healing rate** with low-air-loss beds with convoluted foam Absolute results not reported 133 people included in this analysis	RR 1.25 95% CI 0.84 to 1.86 The meta-analysis may have been underpowered to detect a clinically important difference between groups	⟷	Not significant
[8] [9] Systematic review	20 people, age range 36–100 years, acute and long-term care, grade 3 or 4 ulcers Data from 1 RCT	**Mean rate of wound closure , per week** 5% with low-air-loss mattress 9% with air and foam mattress	P value not reported It was reported that data were insufficient to calculate the difference in mean rates of ulcer healing between the 2 interventions It was unclear how many ulcers achieved healing		

Adverse effects

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Adverse effects					
[29] RCT	Number of participants unclear In review [7]	**Hypothermia** with low-air-loss hydrotherapy beds with standard care Absolute results not reported	Hypothermia was found in a small number of people who used low-air-loss hydrotherapy beds (no further data reported by review)		

No data from the following reference on this outcome. [8] [9] [10]

Comment: None.

OPTION LOW-LEVEL LASER TREATMENT

- For GRADE evaluation of interventions for Pressure ulcers: treatment, see table, p 24 .
- We don't know whether low-level laser therapy improves healing in people with pressure ulcers compared with standard care.

Benefits and harms

Low-level laser treatment versus standard care or sham treatment:

We found one systematic review (search date 2008), which included RCTs that calculated wound size with wound volume or surface area, used evaluation tools that included these measurements, or used complete wound healing as an end point. [8] The review included two RCTs.

Healing rates

Low-level laser treatment compared with standard care/sham treatment We don't know whether laser treatment is more effective than standard care at increasing pressure ulcer healing (low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Healing rates					
[8] Systematic review	86 people (79 people completed study), age range 49–100 years, long-term care, grade 3 ulcers Data from 1 RCT	**Reduction in wound surface area** with low-level laser with standard care Absolute results not reported	P = 0.23	⟷	Not significant
[8] Systematic review	35 people (25 people completed study), age range 8–65 years, rehabilitation, grade 2–4 ulcers Data from 1 RCT	**Time to complete wound healing** 2.45 weeks with laser plus moist saline gauze 1.78 weeks with saline gauze alone	P = 0.33	⟷	Not significant

Adverse effects

No data from the following reference on this outcome. [8]

Low-level laser treatment versus ultrasound plus ultraviolet light:

See option on Therapeutic ultrasound, p 17 .

Comment: None.

OPTION LOW-TECH CONSTANT-LOW-PRESSURE SUPPORTS

- For GRADE evaluation of interventions for Pressure ulcers: treatment, see table, p 24 .
- We don't know whether low-tech constant-low-pressure supports improve healing in people with pressure ulcers compared with standard care.

Benefits and harms

Low-tech constant-low-pressure supports versus standard care:

We found no RCTs.

Low-tech constant-low-pressure supports versus each other:

We found four systematic reviews (search dates 2000; [7] 2008; [8] 2011; [9] and 2012 [10]), which identified the same RCT.

Healing rates

Low-tech constant-low-pressure supports compared with each other We don't know whether a layered-foam replacement mattress is more effective than a water mattress at increasing healing of pressure ulcers at 4 weeks in older people in a nursing home (low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Healing rates					
[8] [9] Systematic review	120 older people with pressure ulcers in a nursing home, 101 completed study, grade 3 or 4 Data from 1 RCT	**Complete ulcer healing , 4 weeks** 27/60 (45%) with water mattress 29/60 (48%) with layered-foam replacement mattress	RR 0.93 95% CI 0.63 to 1.37	⟷	Not significant

Adverse effects

No data from the following reference on this outcome. [7] [8] [9] [10]

Comment: None.

OPTION NUTRITIONAL SUPPLEMENTS (VITAMIN A, VITAMIN C, VITAMIN E, ARGININE, PROTEIN, ZINC, AND TOTAL CALORIE)

- For GRADE evaluation of interventions for Pressure ulcers: treatment, see table, p 24 .
- We don't know whether nutritional interventions improve healing compared with placebo or standard care in people with pressure ulcers.

Benefits and harms

Nutritional supplements versus placebo (including low dose) or standard care:

We found three systematic reviews (search dates 2002; [30] 2008; [8] and 2012 [10]). In total, the reviews identified 13 RCTs evaluating the effects of various nutritional supplements (ascorbic acid, protein supplementation, zinc, and arginine-enriched mixed nutritional supplements) on healing of pressure ulcers. [30] [8] [10] Not one of the RCTs was included in all three reviews. None of the reviews pooled data, so results are reported for individual RCTs meeting *BMJ Clinical Evidence* reporting criteria.

Healing rates

Nutritional supplements compared with placebo (including low dose) or standard care We don't know whether nutritional supplements are more effective than placebo or standard care at increasing healing of pressure ulcers (very low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Healing rates					
[30] Systematic review	88 people with pressure ulcers in nursing homes or hospital, some of whom were receiving ultrasound treatment for their pressure ulcers Data from 1 RCT	**Ulcer healing , 84 days** 17/43 (39%) with ascorbic acid (1000 mg daily) 22/45 (49%) with ascorbic acid (20 mg daily)	RR 0.81 95% CI 0.50 to 1.30	⟷	Not significant
[30] Systematic review	20 people with pressure ulcers having surgery Data from 1 RCT	**Ulcer healing , 4 weeks** with ascorbic acid (1000 mg daily) with placebo Absolute results not reported	RR 2.00 95% CI 0.68 to 5.85	⟷	Not significant
[30] Systematic review	12 institutionalised people being fed through a tube Data from 1 RCT	**Ulcer healing , 8 weeks** with very high-protein diet with high-protein diet Absolute results not reported	RR 0.11 95% CI 0.01 to 1.70	⟷	Not significant
[8] Systematic review	20 people with pressure ulcers having surgery Data from 1 RCT	**Mean reduction in would surface , 1 month** 84% with ascorbic acid 1000 mg daily 43% with placebo	P <0.005	○○○	ascorbic acid
[31] RCT **3-armed trial**	16 people with stage 2 or 3 pressure ulcers	**Mean score Pressure Ulcer Scale for Healing (PUSH) , 3 weeks** 7 with diet A	Diet C *v* Diet A and B: P <0.05 This study randomised only 16 people between the 3 groups and did not report the proportion of participants with complete healing	○○○	Diet C

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
	In review [8] [10]	6 with diet B 2.6 with diet C Diet A: standard hospital diet Diet B: standard hospital diet plus a daily supplement of 500 kcal, protein 18 g, vitamin C 72 mg, and zinc 7.5 g Diet C: a standard hospital diet plus 500 kcal, protein 21 g, vitamin C 500 mg, zinc 30 mg, and arginine 9 g PUSH score range 0 (completely healed) to 17 (greatest severity)			
[32] RCT	89 people resident in long-term care facilities with stage 2, 3, or 4 pressure ulcers In review [8] [10]	**PUSH , 8 weeks** 3.55 with concentrated, fortified, collagen protein hydrolysate supplement 3.22 with placebo Treatment administered orally or via feeding tubes PUSH score range 0 (completely healed) to 17 (greatest severity)	P <0.05 However, these results should be interpreted with caution, as groups were imbalanced at baseline (mean PUSH scores at baseline: 9.11 in people taking supplements *v* 6.07 in people taking placebo) and results were not based on an intention-to-treat analysis	○○○	concentrated, fortified, collagen protein hydrolysate supplement
[8] Systematic review	95 people (80 completed study), age range 22 to 102 years, acute care, grade 1 to 4 ulcers, trial duration 1 week Data from 1 RCT	**Adjusted mean change in ulcer size on wound surface area** 2.70 with standard care plus standard diet 2.76 with consistent wound care 2.60 with controlled nutritional support 2.34 with consistent wound care plus controlled nutritional support 4-armed trial Units of measurement not reported	Reported as not significant for any comparison P value not reported	⟷	Not significant
[33] RCT	30 people, aged 65 years or older, recent onset (<1-month history) grade 2–4 ulcers, orally or tube fed In review [10]	**PUSH change from baseline , 12 weeks** 6.1 with disease-specific nutrition treatment 3.3 with standard diet Disease-specific nutrition treatment (standard diet plus oral supplement or specific enteral formula enriched with protein, arginine, zinc, and vitamin C) PUSH scale 0 to 17	P <0.05 Analysis was not by intention to treat (2 people were excluded), only people with recent pressure ulcers were included in the trial, and people who were tube fed or fed orally were not analysed separately	○○○	disease-specific nutrition treatment

Adverse effects

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Adverse effects					
[32] RCT	Number of people unclear In review [8] [10]	**Adverse effects** with nutritional supplements	11/44 (25%) people discontinued treatment because of adverse effects (2 with hip fracture due to fall; 3 because of changes in re-		

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
		with placebo	nal laboratory values; 4 with nausea or distension; 2 died), but the RCT did not report data for each group separately, except to say that 1 person in each group died from causes unrelated to treatment		

No data from the following reference on this outcome. [8] [30] [33]

Further information on studies

[30] Many of the RCTs were small and may have lacked power to detect clinically important differences between treatments. The fourth included RCT (14 people) identified by the first review was a crossover RCT that did not report results before the crossover period, and had a high withdrawal rate.

[8] This review included three RCTs included in the first review and four further RCTs. Many of the RCTs were small and may have lacked power to detect clinically important differences between treatments. The third included RCT (36 people, age range 72–91 years, 2 weeks' trial duration) identified by the second review compared standard hospital diet, standard diet plus high protein, and standard diet plus high protein plus arginine, zinc, and antioxidants. The RCT was of poor methodological quality and data on Pressure Score Status Tool scores were not available.

[10] This review included four RCTs not included in the first or second review. [8] [30] The authors of the review noted that most of the RCTs identified were of poor quality. The authors went on to comment that the evidence base on nutritional supplementation is largest for the effects of protein supplementation on healing of pressure ulcers. Most studies found a greater reduction in ulcer size with protein supplementation. However, the authors noted that there was considerable variation in the protein formulations used varied across studies and it is unclear whether any one type of protein supplementation is more effective than another.

Comment: None.

OPTION SEAT CUSHIONS

- For GRADE evaluation of interventions for Pressure ulcers: treatment, see table, p 24 .
- We don't know whether seat cushions improve healing in people with pressure ulcers.

Benefits and harms

Seat cushions versus each other or standard care:

We found four systematic reviews (search dates 2000; [7] 2008; [8] 2011; [9] and 2012 [10]), which all identified the same small RCT. [34]

Healing rates

Seat cushions compared with each other or standard care We don't know whether a cushion with dry flotation and an alternating-pressure cushion differ in effectiveness at increasing complete pressure ulcer healing (very low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Healing rates					
[9] Systematic review	28 people Data from 1 RCT	**Complete healing** with cushion with dry flotation	RR 0.47 95% CI 0.14 to 1.56	⟷	Not significant

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
		with alternating-pressure cushion Absolute results not reported			

Adverse effects

No data from the following reference on this outcome. [7] [8] [9] [10]

Comment: None.

OPTION SURGERY

- For GRADE evaluation of interventions for Pressure ulcers: treatment, see table, p 24 .
- We found no direct information from RCTs about surgery in the treatment of pressure ulcers.

Benefits and harms

Surgery versus no surgery/other interventions:

We found one systematic review (search date 2012) that identified no RCTs of surgical treatments for pressure ulcers. [10]

Comment: None.

OPTION THERAPEUTIC ULTRASOUND

- For GRADE evaluation of interventions for Pressure ulcers: treatment, see table, p 24 .
- We don't know whether ultrasound improves healing of pressure ulcers compared with sham ultrasound.

Benefits and harms

Ultrasound versus sham ultrasound:

We found two systematic reviews (search date 2008; [35] and 2012 [10]). Both reviews identified the same three RCTs. The first review reported that all three RCTs were small (40 people; 18 people; 88 people), allocation concealment was not stated in two RCTs, and an intention-to-treat analysis was not performed in two RCTs. All three RCTs used blinded outcomes assessments. [35] The second review also reported that the evidence from the RCTs was of low strength. [10] The second review did not report the results from the studies in detail and did not perform a meta-analysis. The authors of this review commented that healing was similar across RCTs. For this reason, we report results from the first review.

Healing rates

Ultrasound compared with sham ultrasound We don't know whether therapeutic ultrasound is more effective than sham ultrasound at increasing the number of sores healed (very low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Healing rates					
[35] Systematic review	People 2 RCTs in this analysis	**Number of sores healed** with therapeutic ultrasound with sham ultrasound Absolute results not reported 1 included RCT assessed outcomes at 12 weeks; the other RCT did not report the timing of outcome assessment	RR 0.97 95% CI 0.65 to 1.45	⟷	Not significant

Adverse effects

No data from the following reference on this outcome. [10] [35]

Ultrasound plus ultraviolet light versus standard care or versus laser treatment:

We found one systematic review (search date 2008, 3 RCTs). [35] The review reported that all three RCTs were small (40 people; 18 people; 88 people), allocation concealment was not stated in two RCTs, and an intention-to-treat analysis was not performed in two RCTs. All three RCTs used blinded outcomes assessments.

Healing rates

Ultrasound plus ultraviolet light compared with standard care or laser treatment We don't know whether ultrasound plus ultraviolet light is more effective than standard care or laser treatment at increasing the number of sores healed at 12 weeks. (very low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Healing rates					
[35] Systematic review	20 people Data from 1 RCT	**Number of sores healed , 12 weeks** 6/6 (100%) with ultrasound plus UV 5/6 (83%) with standard care 3-armed trial; the remaining arm assessed laser treatment	RR 1.18 95% CI 0.76 to 1.83 The RCT was underpowered to detect clinically important differences between groups	⟷	Not significant
[35] Systematic review	20 people Data from 1 RCT	**Number of sores healed , 12 weeks** 6/6 (100%) with ultrasound plus UV 4/6 (67%) with laser treatment 3-armed trial; the remaining arm assessed standard care	RR 1.44 95% CI 0.80 to 2.60 The RCT was underpowered to detect clinically important differences between groups	⟷	Not significant

Adverse effects

No data from the following reference on this outcome. [35]

Comment: None.

OPTION TOPICAL NEGATIVE PRESSURE

- For GRADE evaluation of interventions for Pressure ulcers: treatment, see table, p 24 .
- We don't know whether topical negative pressure improves healing of pressure ulcers.

Benefits and harms

Topical negative pressure versus control:

We found five systematic reviews (search dates 2007; [36] [37] 2008; [8] 2010; [38] and 2012 [10]), which examined the effects of topical negative pressure. One review [37] identified five RCTs, one review of topical negative pressure for treating chronic wounds [36] identified seven RCTs, and another review of topical negative pressure for wound healing [38] identified three RCTs, which were already included in the first review. However, some RCTs included in the reviews included people with chronic wounds other than pressure ulcers and did not report outcomes for pressure ulcers separately. We have not reported these RCTs further. All five reviews identified the same two RCTs, which were solely in people with pressure ulcers. Both RCTs were of poor methodological quality (CLEAR NPT criteria [maximum 6]; first RCT, score 0; second RCT, score 2). [8] We found one additional RCT that compared topical negative pressure with dressing soaked with sodium hypochlorite 0.25% solution in people with chronic wounds. [39] The RCT reported results separately for a small group of people with spinal cord injury and pressure ulcers.

Healing rates

Topical negative pressure compared with control We don't know whether topical negative pressure is more effective than gauze soaked in Ringer's solution, dressings soaked in sodium hypochlorite 0.25% solution, or a regimen of three gel products at increasing healing of pressure ulcers (very low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Healing rates					
[10] [36] [37] [38] Systematic review	22 people Data from 1 RCT There were differences between groups at baseline (the mean age of people receiving topical negative pressure was 41.7 years compared with 54.4 years in people receiving gauze soaked in Ringer's solution)	**Mean time to reach 50% reduction in initial wound volume** 11 days with topical negative pressure 28 days with gauze soaked in Ringer's solution	Mean difference –1.00 days 95% CI –0.82 days to +6.21 days P = 0.9	⟷	Not significant
[8] [10] [36] [38] Systematic review	35 people Data from 1 RCT	**Wound surface reduction** 52% with topical negative pressure 42% with regimen of three gel products Absolute numbers not reported 3 gel products included: papain-urea debridement ointment, cadexomer iodine, papain-urea-chlorophyllin-copper ointment There were differences between groups in wound size at baseline	P = 0.46	⟷	Not significant

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
[39] RCT	12 people (16 wounds) aged 18 years or older with a spinal cord injury and pressure ulcers	**Median time to 50% reduction in ulcer volume** 2 weeks with topical negative pressure 3 weeks with control (dressing soaked with sodium hypochlorite 0.25% solution; dressing changed 2–3 times per day) 16 wounds in this analysis All wounds were surgically debrided before commencement of treatment	P = 0.001 The RCT randomised by people while the analysis was by wounds	○○○	topical negative pressure

Adverse effects

No data from the following reference on this outcome. [8] [10] [36] [37] [38] [39]

Further information on studies

[39] The RCT enrolled 24 people with either difficult-to-heal surgical wounds or with a spinal cord injury and pressure ulcers. Within each baseline group by type of wound, people were randomised to topical negative pressure or control (sodium hypochlorite 0.25% solution). Baseline characteristics were reported for the overall population rather than by the type of wound at baseline. This small RCT was open label in design, and the method of randomisation was unclear.

Comment: None.

OPTION TOPICAL PHENYTOIN

- For GRADE evaluation of interventions for Pressure ulcers: treatment, see table, p 24 .
- We don't know whether topical phenytoin improves healing of pressure ulcers.

Benefits and harms

Topical phenytoin versus control/standard treatment/hydrocolloid dressings:

We found one systematic review (search date 2008), which found three RCTs. [8]

Healing rates

Topical phenytoin compared with control/hydrocolloid/standard treatment We don't know whether topical phenytoin ointment is more effective than control (hydrocolloid dressings or antibiotic ointment or standard dressings or normal saline) at increasing pressure ulcer healing (very low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Healing rates					
[40] RCT	48 people In review [8]	**Mean time to healing** 35.3 days with topical phenytoin suspension (100 mg capsule in 5 mL saline)	P <0.005	○○○	topical phenytoin suspension

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
		51.8 days with hydrocolloid dressings or antibiotic ointment No data that showed baseline equivalence for wound size were presented			
[41] RCT **3-armed trial**	83 people In review [8]	**Complete ulcer healing** 11/28 (39%) with topical phenytoin 20/28 (71%) with hydrocolloid dressings The remaining arm assessed standard dressings In this RCT there were important between-group differences at baseline for ulcer size (mean size: 5 cm^2 with topical phenytoin *v* 7 cm^2 with hydrocolloid dressings *v* 10 cm^2 with standard dressings; P >0.10); although these difference were not significant, they are likely to have biased the results against standard dressings	ARR 32% 95% CI 7.4% to 56.7%	○○○	hydrocolloid dressings
[41] RCT **3-armed trial**	83 people In review [8]	**Complete ulcer healing** 11/28 (39%) with topical phenytoin 8/27 (30%) with standard dressings The remaining arm assessed hydrocolloid dressings In this RCT there were important between-group differences at baseline for ulcer size (mean size: 5 cm^2 with topical phenytoin *v* 7 cm^2 with hydrocolloid dressings *v* 10 cm^2 with standard dressings; P >0.10); although these difference were not significant, they are likely to have biased the results against standard dressings	P value not reported		
[8] Systematic review	28 people, mean age 31–34 years, rehabilitation, trial duration 2 weeks, grade 2 ulcers Data from 1 RCT	**Mean reduction in Pressure Ulcer Scale for Healing (PUSH) scores , 2 weeks** 19.53 with phenytoin solution 11.39 with normal saline	P = 0.26	⟷	Not significant

Adverse effects

No data from the following reference on this outcome. [8] [40] [41]

Comment: **Clinical guide**
Topical phenytoin is an experimental treatment rarely used in current clinical practice.

GLOSSARY

Air-fluidised supports Membranes that cover a layer of particles that are fluidised by having air forced through them. The airflow can be turned off, which makes the surface solid again, to allow the person to be moved. People find it difficult to get in and out of these beds independently; therefore, they are usually reserved for people who spend most of the day in bed.

Alternating-pressure surfaces Mattresses or overlays made of one or two layers of parallel air sacs. Alternate sacs are inflated and deflated, which provides alternating pressure and release for each area of skin.

Dextranomer paste Anhydrous, porous beads 0.1 mm to 0.3 mm in diameter. These beads are hydrophilic and absorb and adsorb exudate, wound debris, and bacteria, depending on particle size.

Electrotherapy The application of electrical fields by placing electrodes near a wound. Treatments include pulsed electromagnetic therapy, low-intensity direct current, negative-polarity and positive-polarity electrotherapy, and alternating-polarity electrotherapy.

Low-air-loss beds Mattresses that consist of inflatable upright sacs of semipermeable fabric. Inflation of the sacs increases the area of contact between the individual and the support surface and reduces the pressure on the skin. People find it difficult to get in and out of these beds independently; therefore, they are usually reserved for people who spend most of the day in bed.

Low-air-loss hydrotherapy bed A mattress that consists of cushions covered by a permeable, fast-drying filter sheet, through which air is circulated. The bed also contains a urine-collecting device.

Low-quality evidence Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

Therapeutic ultrasound The application of ultrasound to a wound with a transducer and water-based gel. The power of ultrasound waves used in wound healing is low to avoid heating the tissues.

Topical negative pressure Negative pressure (suction) applied to a wound through an open-cell dressing (e.g., foam or felt).

Very low-quality evidence Any estimate of effect is very uncertain.

SUBSTANTIVE CHANGES

Hyperbaric oxygen therapy New option. Five systematic reviews added. [8] [10] [23] [24] [25] Categorised as 'unknown effectiveness'.

Air-fluidised support Two systematic reviews added. [9] [10] Categorisation unchanged (likely to be beneficial).

Alternating-pressure surfaces Two systematic reviews added. [9] [10] Categorisation unchanged (unknown effectiveness).

Dressings (hydrocolloid and non-hydrocolloid) versus each other One systematic review added. [10] Categorisation unchanged (unknown effectiveness).

Electrotherapy Two systematic reviews added [10] [18] and one subsequent RCT [19] Categorisation unchanged (unknown effectiveness).

Low-air-loss beds Two systematic reviews added. [9] [10] Categorisation unchanged (unknown effectiveness).

Low-tech constant-low-pressure supports Two systematic reviews added. [9] [10] Categorisation unchanged (unknown effectiveness).

Nutritional supplements (vitamin A, Vitamin C, vitamin E, arginine, protein, zinc, and total calorie) One systematic review added. [10] Categorisation unchanged (unknown effectiveness).

Seat cushions Two systematic reviews added. [9] [10] Categorisation unchanged (unknown effectiveness).

Surgery One systematic review added. [10] Categorisation unchanged (unknown effectiveness).

Therapeutic ultrasound One systematic review added. [10] Categorisation unchanged (unknown effectiveness).

Topical negative pressure Two systematic reviews added [10] [38] and one additional RCT. [39] Categorisation unchanged (unknown effectiveness).

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Madhuri Reddy
Associate Professor of Medicine
Geriatric Medicine
University of California at San Francisco
San Francisco, California
US

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Disclaimer

GRADE **Evaluation of interventions for Pressure ulcers: treatment.**

Important outcomes					Healing rates				
Studies (Participants)	Outcome	Comparison	Type of evidence	Quality	Consistency	Directness	Effect size	GRADE	Comment
What are the effects of treatments in people with pressure ulcers?									
3 (202) [7] [8] [9] [10]	Healing rates	Air-fluidised supports versus standard care	4	–2	0	0	0	Low	Quality points deducted for weak methods and incomplete reporting of results
1 (158) [9]	Healing rates	Alternating-pressure surfaces versus standard care or constant-low-pressure devices	4	–2	0	–1	0	Very low	Quality points deducted for sparse data and poor study completion rate; directness point deducted for implementation of additional turning, which could confound results
at least 3 (unclear) [8] [15]	Healing rates	Debridement versus no debridement or different debriding agents versus each other	4	–3	0	0	0	Very low	Quality points deducted for incomplete reporting of results, weak methods, and poor trial completion
5 (396) [16]	Healing rates	Hydrocolloid dressings versus gauze soaked in saline, hypochlorite, or povidone iodine	4	–1	0	–1	0	Low	Quality point deducted for weak methods; directness point deducted for significance of meta-analysis result being sensitive to the method of calculation
8 (unclear) [8]	Healing rates	Hydrocolloid dressings versus non-hydrocolloid dressings other than gauze soaked in saline, hypochlorite, or povidone iodine	4	–2	0	0	0	Low	Quality points deducted for weak methods and incomplete reporting of results
at least 6 (211) [7] [8] [10] [19]	Healing rates	Electrotherapy versus sham electrotherapy or standard treatment	4	–2	0	0	0	Low	Quality points deducted for weak methods and incomplete reporting of results
3 (153) [7] [8] [9]	Healing rates	Low-air-loss beds versus standard beds or standard care	4	–2	0	–1	0	Very low	Quality points deducted for sparse data and incomplete reporting of results; directness point deducted for no statistical analysis between groups for 1 analysis
2 (104) [8]	Healing rates	Low-level laser treatment versus standard care or sham treatment	4	–2	0	0	0	Low	Quality points deducted for sparse data and incomplete reporting of results
1 (120) [9]	Healing rates	Low-tech constant-low-pressure supports versus each other	4	–2	0	0	0	Low	Quality points deducted for sparse data and incomplete reporting of results
9 (400) [8] [10] [30]	Healing rates	Nutritional supplements versus placebo (including low dose) or standard care	4	–2	0	–1	0	Very low	Quality points deducted for weak methods and incomplete reporting of results; directness point deducted for no intention-to-treat analysis in some trials
1 (28) [9]	Healing rates	Seat cushions versus each other or standard care	4	–3	0	0	0	Very low	Quality points deducted for sparse data, incomplete reporting of results, and weak methods
2 (128) [35]	Healing rates	Ultrasound versus sham ultrasound	4	–3	0	0	0	Very low	Quality points deducted for sparse data, weak methods, and incomplete reporting of results

Important outcomes					Healing rates				
Studies (Participants)	Outcome	Comparison	Type of evidence	Quality	Consistency	Directness	Effect size	GRADE	Comment
1 (18) [35]	Healing rates	Ultrasound plus ultraviolet light versus standard care or versus laser treatment	4	–3	0	0	0	Very low	Quality points deducted for sparse data, weak methods, and small number of events (3 failures in total in trial)
3 (69) [8] [36] [37] [39]	Healing rates	Topical negative pressure versus control	4	–3	0	–1	0	Very low	Quality points deducted for sparse data, weak methods, analysis by wounds rather than people randomised (1 RCT), and differences between groups at baseline; directness point deducted for variation in control intervention
3 (159) [8]	Healing rates	Topical phenytoin versus control/standard treatment/hydrocolloid dressings	4	–2	0	–1	0	Very low	Quality points deducted for sparse data and weak methods; directness point deducted for baseline differences

We initially allocate 4 points to evidence from RCTs, and 2 points to evidence from observational studies. To attain the final GRADE score for a given comparison, points are deducted or added from this initial score based on preset criteria relating to the categories of quality, directness, consistency, and effect size. Quality: based on issues affecting methodological rigour (e.g., incomplete reporting of results, quasi-randomisation, sparse data [<200 people in the analysis]). Consistency: based on similarity of results across studies. Directness: based on generalisability of population or outcomes. Effect size: based on magnitude of effect as measured by statistics such as relative risk, odds ratio, or hazard ratio.