

Pressure Ulcer Treatment Strategies

A Systematic Comparative Effectiveness Review

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Background: Pressure ulcers affect as many as 3 million Americans and are major sources of morbidity, mortality, and health care costs.

Purpose: To summarize evidence comparing the effectiveness and safety of treatment strategies for adults with pressure ulcers.

Data Sources: MEDLINE, EMBASE, CINAHL, Evidence-Based Medicine Reviews, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, Database of Abstracts of Reviews of Effects, and Health Technology Assessment Database for English- or foreign-language studies; reference lists; gray literature; and individual product packets from manufacturers (January 1985 to October 2012).

Study Selection: Randomized trials and comparative observational studies of treatments for pressure ulcers in adults and noncomparative intervention series ($n > 50$) for surgical interventions and evaluation of harms.

Data Extraction: Data were extracted and evaluated for accuracy of the extraction, quality of included studies, and strength of evidence.

Data Synthesis: 174 studies met inclusion criteria and 92 evaluated complete wound healing. In comparison with standard care, pla-

cebo, or sham interventions, moderate-strength evidence showed that air-fluidized beds (5 studies [$n = 908$]; high consistency), protein-containing nutritional supplements (12 studies [$n = 562$]; high consistency), radiant heat dressings (4 studies [$n = 160$]; moderate consistency), and electrical stimulation (9 studies [$n = 397$]; moderate consistency) improved healing of pressure ulcers. Low-strength evidence showed that alternating-pressure surfaces, hydrocolloid dressings, platelet-derived growth factor, and light therapy improved healing of pressure ulcers. The evidence about harms was limited.

Limitation: Applicability of results is limited by study quality, heterogeneity in methods and outcomes, and inadequate duration to assess complete wound healing.

Conclusion: Moderate-strength evidence shows that healing of pressure ulcers in adults is improved with the use of air-fluidized beds, protein supplementation, radiant heat dressings, and electrical stimulation.

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Pressure ulcers affect 3 million adults in the United States. Healing rates, which are dependent on comorbid conditions, clinical interventions, and ulcer severity, vary. Ulcer severity is assessed using various staging or grading systems, but the National Pressure Ulcer Advisory Panel staging system is most commonly used (Figure 1) (1). Ulcers can range from stage I with intact skin to stage IV with full-thickness tissue loss and exposed bone, tendon, or muscle. They can also be described as unstageable when the base of a full-thickness ulcer is covered with slough or as suspected deep-tissue injury when the skin is intact but the underlying tissue has evidence of damage. Comorbid conditions predisposing pressure ulcer development and affecting ulcer healing include those affecting patient mobility (such as spinal cord injury), wound environments (such as incontinence), and wound healing (such as diabetes and vascular disease). Delayed healing can add to the length of hospitalization, impede return to full functioning (2), and require long-term care. Cost estimates for pressure ulcer treatment range between \$37 800 and \$70 000 per ulcer, with total annual costs in the United States as high as \$11 billion (1, 3).

Pressure ulcer treatment involves various approaches, including interventions to treat the conditions that lead to pressure ulcers (support surfaces and nutritional support), interventions to protect and promote healing of the ulcer

(wound dressings; topical applications; and various adjunctive therapies, such as electrical stimulation, light therapy, and vacuum-assisted devices), and surgical repair of the ulcer (1, 3). Treatments for pressure ulcers have been described and evaluated with varying degrees of rigor and completeness (3, 4) with continued uncertainty around the best treatment options. The purpose of this review is to examine the comparative effectiveness and harms of therapies and approaches to treating pressure ulcers (5). Common terms used in this article are defined in the **Glossary**.

METHODS

Scope

We followed a standard protocol for systematic reviews and developed an analytic framework with input from key informants (clinicians, wound care researchers,

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Glossary

- Air-fluidized beds:* Beds filled with small beads through which air is forced to create a fluidlike surface and redistribute pressure.
- Alternating-pressure surfaces:* Beds with cells or sections of various sizes and patterns that inflate and deflate in cycles to change the distribution of pressure.
- Cutaneous flap:* Soft tissue harvested from skin and placed over the open wound.
- Debriding enzymes (collagenase):* Agents used to remove necrotic tissue.
- Dextranomer paste:* A polymeric paste that absorbs wound exudates.
- Electrical stimulation therapy:* Direct electric current delivered through the wound bed using surface electrodes.
- Electromagnetic therapy:* Delivery of energy composed of an electric field and a magnetic field without directly contacting the skin surface.
- Faciocutaneous flaps:* Soft tissue harvested from fascia and placed over the open wound.
- Hydrocolloid dressings:* Adhesive wafers that absorb wound fluid and form a gelatinous mass that conforms to the wound, creating a protective and moist environment.
- Hydrotherapy:* Whirlpool or pulsed lavage for wound cleansing.
- Hyperbaric oxygen therapy:* A chamber in which the pressure is 2.5 times greater than normal, which allows the blood to carry more oxygen.
- Laser therapy:* Light therapy treatment using a low-level laser.
- Light therapy:* Delivery of energy from the infrared, visible (wavelength, 380 to 760 nm), and ultraviolet spectrums to the wound surface.
- Low-air-loss beds:* Beds that have a flow of air designed to regulate heat and humidity and may also adjust pressure.
- Myocutaneous flaps:* Soft tissue harvested from muscle and placed over the open wound.
- Negative-pressure wound therapy:* Devices that provide a vacuum seal to a wound (which produces a negative pressure, causing the wound to contract and increasing the blood flow while maintaining a moist environment).
- Nutritional supplementation:* Enteral or oral nutritional support with protein-containing nutritional supplements (including mixtures of protein, carbohydrates, lipids, and various micronutrients) or micronutrient-containing supplements (vitamin C or zinc).
- Phenytol solution:* A topical application of diphenylhydantoin intended to promote skin healing.
- Platelet-derived growth factor therapy:* A biologic therapy using proteins that regulate cell growth and division.
- Radiant heat dressings:* Noncontact dressings attached to a heating element that provides warmth to increase capillary blood flow and resistance to infection.
- Shock wave therapy:* Pulses of energy applied using a specially constructed device.
- Therapeutic ultrasound:* Transmission of low-frequency sound waves through soft tissue.

and patient advocates) to answer the following key questions: In adults with pressure ulcers, what is the comparative effectiveness of treatment strategies for improved health outcomes, including but not limited to complete wound healing, healing time, reduced wound size, pain, and prevention of serious complications of infection? What are the harms of treatments for pressure ulcers? See **Figure 2** for more details.

We also attempted to discern whether the balance of benefits and harms of treatment options varied according to characteristics of the pressure ulcer, patient, or setting in which care was delivered. We met regularly throughout the review with members of a technical expert panel, some of whom served as key informants during the development phase, to oversee the clinical applicability, content completeness, and methodological rigor of the review process.

The population comprises adults with pressure ulcers. Interventions include support surfaces; nutritional supplements; local wound applications (including wound dressings, topical therapies, and biological agents); surgical procedures; and various adjunctive therapies with comparators of standard wound care, placebo, or sham therapy. In some cases, alternative treatment options were compared. At the recommendation of our technical expert panel, complete wound healing was considered the most clinically important outcome, but we also included other measures of wound improvement, such as reduction in ulcer size or rate of change over time, pain, and prevention of serious complications. Harms of therapy included but were not limited to pain, dermatologic complications, bleeding, and infection.

Data Sources and Searches

We searched for relevant English- and foreign-language studies and systematic reviews in MEDLINE, EMBASE, CINAHL, Evidence-Based Medicine Reviews, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, Database of Abstracts of Reviews of Effects, Health Technology Assessment Database, gray literature, scientific information packets, and reference lists. Given the technological advancement in treatment interventions, we restricted our search to January 1985 to October 2012 to find studies of current relevance.

Study Selection

We included randomized trials and comparative observational studies of treatments for pressure ulcers in adults. We included noncomparative intervention series ($n > 50$) for surgical interventions and evaluation of harms. Exclusion criteria were wrong population (children; adolescents; and patients with non-pressure-related ulcers, including but not limited to venous ulcers and diabetic foot ulcers), studies of interventions without comparators, hospice care settings unless complete wound healing was an outcome measured, and case reports.

At least 2 investigators independently evaluated each study to determine inclusion eligibility. Disagreement was settled by consensus or adjudication by a senior investigator when consensus could not be reached.

Data Extraction and Quality Assessment

From the included studies, details of the patient population, study design, analysis, follow-up, and results were extracted by a team member and reviewed for accuracy and completeness by an investigator. For comparability across studies, when possible, ulcer stage or grade was translated to the corresponding stage as defined by the National Pressure Ulcer Advisory Panel (**Appendix Table 1**, available at www.annals.org). Investigators rated the quality (risk of bias) of the individual studies and strength of the body of evidence, and results were reviewed by at least 1 other investigator for accuracy, with disagreements being settled by consensus (6–8). We used an approach adapted from the Agency for Healthcare Research and Quality (AHRQ)

Methods Guide for Effectiveness and Comparative Effectiveness Reviews (9) for determining the strength of evidence as “high,” “moderate,” “low,” or “insufficient” on the basis of the design, quantity, size, and quality (risk of bias) of studies, consistency across studies, precision of estimates and directness of evidence.

Data Synthesis and Analysis

Data were synthesized qualitatively with attention to characteristics, such as ulcer grade and location, patient characteristics and settings, and risk of bias of individual studies.

We conducted meta-analyses in selected instances for comparisons examining the outcome of complete wound healing where the number, quality, and homogeneity of studies permitted. We chose to limit meta-analysis to the outcome of complete wound healing because this was the principal health outcome of interest and because of the wide variability in the measurement of other outcomes, including reduction in wound size. When a meta-analysis was conducted, we used relative risk as the effect measure. We assessed the presence of statistical heterogeneity among the studies using standard chi-square tests and the magnitude of heterogeneity using the I^2 statistic (10). We used random-effects models to account for variation among studies (11) and fixed-effects Mantel–Haenszel models when variation among studies was estimated to be zero. Sensitivity analysis was conducted to assess the effect of quality on combined estimates, and meta-regression was

conducted to assess the association of effect measure with study duration. All quantitative analyses were done using STATA, version 11.0 (StataCorp, College Station, Texas).

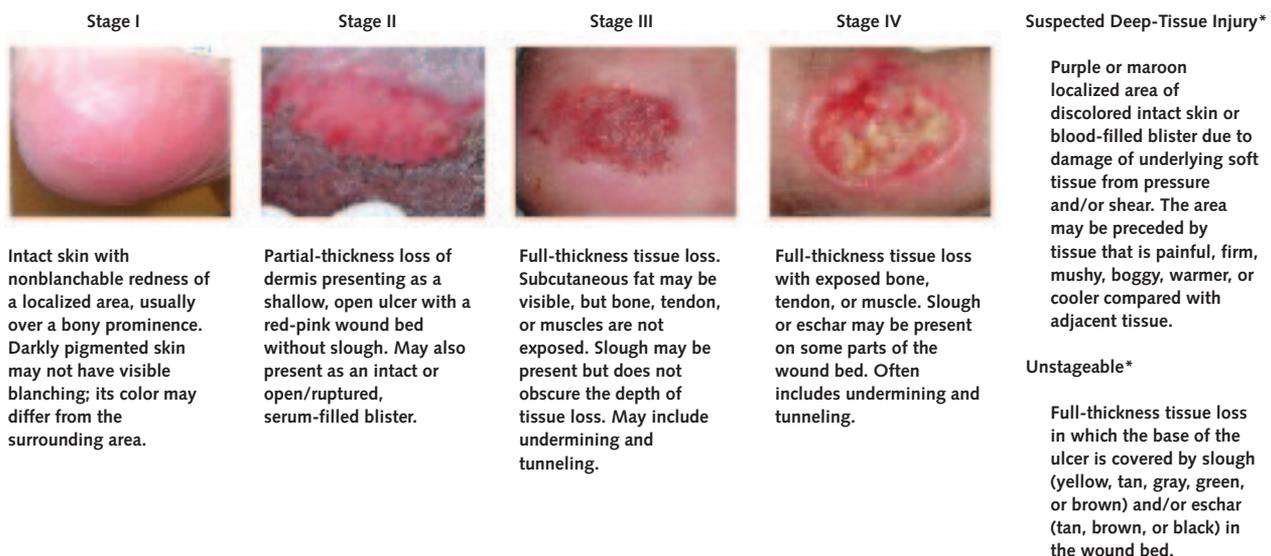
Role of the Funding Source

This research was funded by AHRQ. The draft report was reviewed by content experts, AHRQ program officers, and collaborative partners. Investigators worked with AHRQ staff to develop and refine the scope, analytic framework, and key questions; resolve issues arising during the project; and review the final report to ensure methodological standards for systematic reviews were met. The complete report (5), including the list of included and excluded studies, can be found at www.effectivehealthcare.ahrq.gov. The AHRQ had no role in study selection, quality assessment, synthesis, or development of conclusions. The investigators are solely responsible for the content and the decision to submit the manuscript for publication.

RESULTS

The results of the search and study selection are shown in **Appendix Figure 1** (available at www.annals.org). We reviewed 7149 abstracts and titles and 1846 full-text articles; we found 174 studies (182 full-text articles) that met our inclusion criteria. Gray literature was assessed but did not provide additional results. Study quality was generally poor, sample sizes were small, and follow-up was frequently too short to assess complete wound healing.

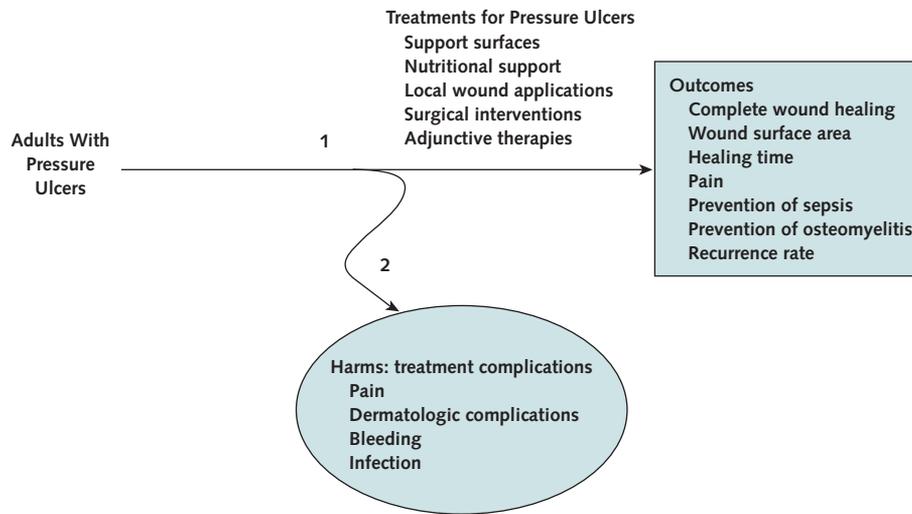
Figure 1. National Pressure Ulcer Advisory Panel pressure ulcer stages.



Pressure ulcer stages I to IV and the 2 additional categories of suspected deep-tissue injury and unstageable are defined. National Pressure Ulcer Advisory Panel copyright; photos used with permission. National Pressure Ulcer Advisory Panel and European Pressure Ulcer Advisory Panel. Pressure Ulcer Prevention and Treatment: Clinical Practice Guideline. Washington, DC: National Pressure Ulcer Advisory Panel; 2009.

* Not pictured.

Figure 2. Analytic framework of pressure ulcer treatment strategies.



Key Question 1: In adults with pressure ulcers, what is the comparative effectiveness of treatment strategies for improved health outcomes, including but not limited to complete wound healing, healing time, reduced wound surface area, pain, and prevention of serious complications of infection?

- a. Does the comparative effectiveness of treatment strategies differ according to features of the pressure ulcers, such as anatomical site or severity at baseline?
- b. Does the comparative effectiveness of treatment strategies differ according to patient characteristics, including but not limited to age; race or ethnicity; body weight; specific medical comorbid conditions; and known risk factors for pressure ulcers, such as functional ability, nutritional status, or incontinence?
- c. Does the comparative effectiveness of treatment strategies differ according to patient care settings, such as home, nursing facility, or hospital, or according to features of patient care settings, including but not limited to nurse–patient staffing ratio, staff education and training in wound care, the use of wound care teams, and home caregiver support and training?

Key Question 2: What are the harms of treatments for pressure ulcers?

- a. Do the harms of treatment strategies differ according to features of the pressure ulcers, such as anatomical site or severity at baseline?
- b. Do the harms of treatment strategies differ according to patient characteristics, including age; race or ethnicity; body weight; specific medical comorbid conditions; and known risk factors for pressure ulcers, such as functional ability, nutritional status, or incontinence?
- c. Do the harms of treatment strategies differ according to patient care settings, such as home, nursing facility, or hospital, or according to features of patient care settings, including but not limited to nurse–patient staffing ratio, staff education and training in wound care, the use of wound care teams, and home caregiver support and training?

From reference 5.

Effectiveness of Therapies Used to Treat Pressure Ulcers

The overall findings and strength of the evidence are summarized in the Table and Appendix Table 2 (available at www.annals.org), and the risk-of-bias assessments for individual studies are summarized in the Supplement (available at www.annals.org). We found data on the outcomes of complete wound healing and wound improvement, including reduction in wound size, rate of change over time, or change in ulcer stage, but not on outcomes of pain and prevention of serious complications. Most studies enrolled older hospital patients and long-term care residents with stage II to IV pressure ulcers, although some studies enrolled younger, neurologically impaired adults. When available, we reported on whether the effectiveness of interventions varied according to characteristics of the

pressure ulcer, patient, or setting in which care was delivered, but in general, few studies conducted subgroup analysis and data were insufficient to draw any conclusions in these subgroups.

Support Surfaces

We found 24 studies (21 trials and 3 observational studies) that provided evidence on various support surfaces, including air-fluidized beds, alternating-pressure beds and chair cushions, and low-air-loss beds. Of these, 4 were rated good-quality, 10 as fair-quality, and 10 as poor-quality. Eight studies evaluated the outcome of complete wound healing (12–19). No differences were found in complete wound healing when comparing types of support

Table. Summary of Evidence of Benefits and Harms of Pressure Ulcer Treatment Strategies*

Intervention	Strength of Evidence† and Summary of Results for Wound Healing	Studies, Participants, and Study Duration for Wound Healing Analysis	Strength of Evidence for Harms‡	Studies and Participants for Harms Analysis
Support surface				
AF beds vs. other surfaces§ (ulcer stage II, III, or IV and unstageable)	Moderate Reduction in wound size: superior	5 studies (n = 908) Duration: 4 d–36 wk	Insufficient Unclear harms for AF beds (rare or minor harms reported)	7 studies (for all support interventions) (n = 526)
AP beds comparison of brands/forms (ulcer stage II, III, or IV)	Moderate Complete wound healing: similar Reduction in wound size: similar	4 studies (n = 369) Duration: 4 wk–discharge, healing, or death	Insufficient Unclear harms for AP beds, comparison of brands (rare or minor harms reported)	
AP beds vs. other surfaces (ulcer stage I, II, III, or IV)	Low Reduction in wound size: similar	4 studies (n = 368) Duration: 2 wk–3 mo	Insufficient Unclear harms for AP beds vs. other surfaces (rare or minor harms reported)	
LAL beds vs. other surfaces (ulcer stage I, II, III, or IV)	Low Reduction in wound size: similar	5 studies (n = 329) Duration: 1 wk–discharge, healing, or death	Insufficient Unclear harms for LAL beds (rare or minor harms reported)	
Nutrition				
Protein-containing nutritional supplements vs. standard diets or placebo (ulcer stage I, II, III, or IV)	Moderate Rate of reduction in wound size: superior	12 studies (n = 562) Duration: 7 d–10 mo	Insufficient Unclear harms of nutritional supplementation	7 studies (n = 448)
Vitamin C vs. placebo (ulcer stage II, III, or IV)	Low Rate of wound healing: similar	1 study (n = 88) Duration: 30 d–12 wk	Insufficient Unclear harms of vitamin C supplementation	2 studies (n = 135)
Local wound applications				
Hydrocolloid dressings vs. conventional care (ulcer stage I, II, III, or IV)	Low Reduction in wound size: superior	10 studies (n = 560) Duration: 3–12 wk	Moderate Hydrocolloid (rate of harms, 0%–16%): skin reactions (inflammation, erythema), maceration, pain, wound deterioration, and overgranulation	4 studies (n = 218)
Hydrocolloid dressings vs. foam dressings (ulcer stage II, III, or IV)	Moderate Complete wound healing: equivalent	8 studies (n = 508) Duration: 2–16 wk	Moderate Foam dressings (rate of harms, 0%–30%): bleeding, overgranulation, wound deterioration, maceration, tissue damage	4 studies (n = 230)
Radiant heat vs. other dressings (ulcer stage III or IV)	Moderate Complete wound healing: similar Rate of reduction in wound size: superior	4 studies (n = 160) Duration: 4–12 wk	Insufficient Unclear harms for radiant heat dressings	1 study (n = 50)
Dextranomer paste vs. wound dressings (ulcer stage I, II, III, or IV)	Low Reduction in wound size: inferior	2 studies (n = 227) Duration: 3–8 wk	Low Dextranomer (rate of harms, 22%): minor infection, bleeding, overgranulation, and skin irritation	1 study (n = 92)
Topical collagen vs. hydrocolloid dressings or standard care (ulcer stage II, III, or IV)	Low Reduction in wound size: similar	3 studies (n = 169) Duration: 2–8 wk	Insufficient Unclear harms for topical collagen	2 studies (n = 145)
PDGF vs. placebo (ulcer stage III or IV)	Low Reduction in wound size: similar	4 studies (n = 209) Duration: 4–16 wk	Insufficient Unclear harms for PDGF	5 studies (n = 322)
Adjunctive therapy				
Electrical stimulation vs. sham (ulcer stage II, III, or IV)	Moderate Complete wound healing: similar Rate of reduction in wound size: superior	6 studies (n = 243) Duration: 4–6 wk 9 studies (n = 397) Duration: 3–16 wk	Low Local skin irritation	3 studies (n = 146)
Electromagnetic therapy vs. sham (ulcer stage II, III, or IV)	Low Rate of reduction in wound size: similar	4 studies (n = 112) Duration: 2–12 wk	Insufficient Unclear harms for electromagnetic therapy	1 study (n = 30)
Therapeutic ultrasound vs. sham or standard care (ulcer stage II, III, or IV)	Low Complete wound healing: similar Reduction in wound size: similar	3 studies (n = 148) Duration: 2–13 wk	Insufficient Unclear harms for therapeutic ultrasound	3 studies (n = 101)

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Table—Continued

Intervention	Strength of Evidence† and Summary of Results for Wound Healing	Studies, Participants, and Study Duration for Wound Healing Analysis	Strength of Evidence for Harms‡	Studies and Participants for Harms Analysis
NPWT vs. standard care or topical gel (ulcer stage III or IV)	Low Reduction in wound size: similar	3 studies (n = 138) Duration: 4–6 wk	Insufficient Unclear harms for NPWT	2 studies (n = 77)
Light therapy vs. sham or standard care (ulcer stage II, III, or IV)	Low Complete wound healing: similar	2 studies (n = 317) Duration: 12 wk	Low No clinically important harm reported	4 studies (n = 327)
Light therapy vs. sham or standard care (ulcer stage I, II, III, or IV)	Low Reduction in wound size: superior	5 studies (n = 481) Duration: 2–12 wk	Low No clinically important harm reported	4 studies (n = 327)
Laser therapy vs. sham or standard care (ulcer stage II, III, or IV)	Low Reduction in wound size: similar	3 studies (n = 137) Duration: 5–6 wk	Low No clinically important harm reported	4 studies (n = 137)
Surgery				
Cutaneous vs. fasciocutaneous vs. myocutaneous flaps (ulcer stage III or IV)	Insufficient Inconsistent results because of heterogeneity in patient populations and surgical procedures	4 studies (n = 560) Duration: 11 mo–20 y	Low Reoperation because of recurrence or flap failure: 12%–24%	2 studies (n = 255)

AF = air-fluidized; AP = alternating-pressure; LAL = low-air-loss; NPWT = negative-pressure wound therapy; PDGF = platelet-derived growth factor.

* Results are for findings with moderate or low strength of evidence. Additional key questions are addressed in the full report (5).

† Key question 1: In adults with pressure ulcers, what is the comparative effectiveness of treatment strategies for improved health outcomes, including but not limited to complete wound healing, healing time, reduced wound surface area, pain, and prevention of serious complications of infection?

‡ Key question 2: What are the harms of treatments for pressure ulcers?

§ AF beds were compared with standard beds or multiple surfaces that were not well-defined.

surfaces. We found moderate-strength evidence that wound improvement (including rate of reduction in wound size and ulcer stage) was superior with air-fluidized beds, although they were most often compared with standard hospital beds rather than other advanced support surfaces. This was based on 5 studies with highly consistent results (20–24). Healing was similar between alternating-pressure mattresses and other support surfaces (19, 25–27) (low-strength evidence), and different types of alternating-pressure mattresses provided similar benefit (moderate-strength evidence) (12, 13, 28–31). Evidence about the effectiveness of alternating-pressure seat cushions was insufficient because only 2 studies with very different populations were identified (32, 33). We found low-strength evidence that low-air-loss beds are similar to foam surfaces or foam mattresses (4 studies) (15, 17, 33, 34), and wound healing did not differ when comparing low-air-loss beds with low-air-loss overlays (1 study) (35). Most studies of support surfaces were older and compared these surfaces with standard care that may not be considered high-quality care today.

Nutrition

We found 16 studies (11 trials and 5 observational studies) that addressed nutritional support, including protein-containing nutritional supplementation and specific nutrient supplementation with vitamins or minerals, such as ascorbic acid (vitamin C) or zinc. Three trials were rated good-quality (36–38), 2 were fair-quality (39, 40),

and 6 were poor-quality (41–46). Four observational studies were rated fair-quality (47–50), and 1 was poor-quality (51). Eight studies considered the outcome of complete wound healing (36, 38–42, 46, 48).

Although the formulations varied greatly, most of the 12 studies of protein supplementation found greater reduction in ulcer size with supplementation than without, but not more complete wound healing. Because of the small number of head-to-head trials, the existing evidence base does not clarify whether any specific type of protein supplementation is superior to others. Low-strength evidence indicated no benefits in wound healing with vitamin C based on 1 good-quality study (n = 88) (37). Evidence about zinc supplementation was insufficient to draw conclusions (49).

Local Wound Applications

We identified 89 original studies that examined the effectiveness of local wound applications for pressure ulcers in 7115 patients. Seventy-six of the original studies were clinical trials. Of these, 11 were rated good-quality, 20 were fair-quality, and 45 were poor-quality. Sample sizes ranged from 10 to 168 patients. There were 13 observational studies. One cohort study was rated fair-quality, and the other observational studies were poor-quality. Fifty-nine studies addressed the outcome of complete wound healing (52–111). No differences were found in complete wound healing when comparing types of local wound applications.

We found 10 studies (1 good-quality [52], 2 fair-quality [53, 54], and 7 poor-quality [55–59, 112, 113]) that compared hydrocolloid with gauze dressings and provided low-strength evidence indicating greater reduction in wound size with hydrocolloid dressings. Statistical heterogeneity precluded quantitative pooling of results across these studies. Complete wound healing was equivalent with hydrocolloid and foam dressings (pooled relative risk, 1.12 [95% CI, 0.88 to 1.41]; $I^2 = 16.4\%$; $P = 0.301$) (8 studies; moderate-strength evidence) (72–79). Radiant heat dressings produced more rapid reduction in wound size than other dressings based on moderately consistent results from 2 good-quality and 2 fair-quality trials, but there was no evidence of benefit in terms of complete wound healing (pooled relative risk, 1.23 [CI, 0.70 to 2.14]; $I^2 = 0.0\%$; $P = 0.916$) (83–86). Evidence about the comparative effectiveness of other dressing types was insufficient.

The most commonly evaluated topical therapies were debriding enzymes (primarily collagenase), phenytoin solution, dextranomer paste, and collagen applications. Low-strength evidence showed that dextranomer is less effective than other wound dressings based on 1 good-quality trial (114) and 1 poor-quality trial (115). Evidence about enzymes and phenytoin was inconsistent and insufficient to draw conclusions. Collagen applications did not seem to provide wound-healing benefit compared with standard care, based on low-strength evidence from 1 good-quality (116) and 2 poor-quality (95, 117) trials. The most commonly evaluated biological agent was platelet-derived growth factor, for which 1 fair-quality (110) and 3 poor-quality (103, 107, 118, 119) studies provided low-strength evidence of benefit compared with placebo in promoting healing of severe (stage III or IV) ulcers. Evidence about the effectiveness of other biological agents was insufficient.

Surgery

Surgical interventions for pressure ulcers identified in studies that met our inclusion criteria were primarily surgical flaps (most commonly myocutaneous and fasciocutaneous flaps). One poor-quality trial (120) and 5 fair-quality intervention series (121–125), including 1094 pressure ulcers in 647 patients, provided evidence on the effectiveness of surgical techniques to treat stage III or IV pressure ulcers. We found low-strength evidence for a lower rate of ulcer recurrence with sacral ulcers than ischial ulcers, a higher rate of recurrent ulcer among patients with spinal cord injuries than among others, and greater wound dehiscence rates with surgeries in which bone was removed. Because of heterogeneity in patient populations and surgical procedures, there was insufficient evidence that 1 approach to closure of stage III or IV pressure ulcers was superior to another.

Adjunctive Therapies

Thirty-four trials (3 good-quality, 29 fair-quality, and 2 poor-quality) and 5 observational studies (2 fair-quality and 3 poor-quality) that evaluated adjunctive therapies met our inclusion criteria. Adjunctive therapies identified in our review included electrical stimulation, electromagnetic therapy, therapeutic ultrasound, negative-pressure wound therapy, hydrotherapy, light therapy, and laser therapy. Evidence about other adjunctive therapies—including vibration, shock wave, and hyperbaric oxygen—was limited to small, single studies that provided insufficient evidence for comparative effectiveness conclusions. Seventeen studies addressed the outcome of complete wound healing (126–142). Moderately consistent results from 1 good-quality (126) and 8 fair-quality (127–131, 143–145) trials showed that electrical stimulation improved healing rates (moderate-strength evidence) but evidence about the effect of electrical stimulation on complete wound healing was insufficient because of heterogeneous findings across studies.

Low-strength evidence showed that light therapies provided benefit in terms of reduced wound size but not complete wound healing (139, 140, 146–148). There was also low-strength evidence that electromagnetic therapy (132, 133, 149, 150), therapeutic ultrasound (135–137), negative-pressure wound therapy (138, 151, 152), and laser therapy (137, 142, 153) were no different from sham treatment or standard care in wound-healing outcomes. There was insufficient evidence to draw conclusions about hydrotherapy (152, 154).

Harms of Therapies Used to Treat Pressure Ulcers

Support Surfaces

The reported harms of support surface options were minimal, although harms were infrequently and inconsistently reported in studies of this option.

Nutrition

There was insufficient evidence to adequately describe the harms of nutritional supplementation in this patient population.

Local Wound Applications

Moderate-strength evidence from 36 studies showed that the most common harms of wound dressings and topical agents were dermatologic complications, including irritation, inflammation, and maceration. However, variability across studies precluded an estimate of adverse events for specific dressings or topical therapies, and evidence was insufficient to determine whether certain types of dressings or topical therapies were more likely to cause these complications than others. Few harms were reported with biological agents, but the evidence about the harms of these agents was insufficient to reach conclusions about adverse event rates.

Surgery

We found low-strength evidence that more adverse events occur with surgery for ischial ulcers than for sacral or trochanteric ulcers (121, 122). Surgical flap failures requiring reoperation ranged from 12% to 24% (121, 124).

Adjunctive Therapies

Low-strength evidence showed that the most common adverse effect of electrical stimulation was local skin irritation and that harms were more common in frail elderly populations than in younger populations (126–128). There was insufficient evidence to evaluate the harms of electromagnetic therapy, therapeutic ultrasound, negative-pressure wound therapy, and hydrotherapy. Light (139, 140, 146–148) and laser (137, 141, 142, 153) therapy were not associated with substantial adverse events on the basis of low-strength evidence.

There was insufficient evidence to draw any other conclusions about the effectiveness or harms of interventions based on features of the pressure ulcers, characteristics of the patient, or features of the patient care setting.

DISCUSSION

We identified 174 studies that addressed the comparative effectiveness and harms of pressure ulcer treatment and found moderate-strength evidence that air-fluidized beds, protein-containing nutritional supplements, radiant heat dressings, and electrical stimulation improved healing of pressure ulcers. Alternating-pressure surfaces, platelet-derived growth factor, hydrocolloid dressings, and light therapy may also improve healing, although the evidence was more limited and of low strength. Dermatologic reaction was noted with several local wound applications and adjunctive therapies, but in general evidence about the harms of treatments was limited.

Our review expands on previous systematic reviews by including observational studies, surgical interventions, and evaluation of harms of treatment and by extending the search to October 2012 (4). Our findings are qualitatively similar to those of other studies, with the exception of the benefit of air-fluidized surfaces and lack of evidence of benefit with electromagnetic therapy. Because the most comprehensive systematic review was published in 2008, 4 additional studies on air-fluidized surfaces were available and led to our finding of moderate-strength evidence that air-fluidized beds were more effective than other surfaces, primarily standard hospital beds, in reducing wound size. Few trials compared air-fluidized beds with other advanced support surfaces, precluding strong conclusions about comparative effectiveness. Our findings were consistent with a recent update on support surfaces by the Cochrane Collaboration (155, 156). The Cochrane review also reported some benefit from the use of sheepskins, but this finding was based on a study excluded from our review because it was published in 1964. The authors of this review con-

cluded, as we did, that the evidence base was weak, with small studies that had serious methodological limitations. Our finding of no significant wound improvement with electromagnetic therapy is also consistent with a previous Cochrane review (157) but inconsistent with others that commented on a trend toward an improved healing rate (4, 158, 159). The clinical significance of this trend remains unknown.

The applicability of our findings to real-world clinical settings is supported by the broad representation of patients with pressure ulcers cared for in various settings with interventions representing most of the therapeutic methods commonly used. However, several other features limit applicability of this review. These include the frequent use of the surrogate outcome of reduction in wound size rather than complete wound healing and that, in practice, the treatment of pressure ulcers is typically multimodal and often involves the sequential use of different therapies. Most studies were of poor- to fair-quality; small; underpowered to detect statistically significant differences; and highly variable in patient populations, ulcer characteristics (for example, anatomical site, duration, and stage), interventions (even within a given intervention category, such as different types of foam dressings), and comparators (especially in implementation of standard, or usual, care), which limited our ability to combine or compare results across studies. Studies of surgery are also limited in that most were observational and conducted in 1 center or a few centers at most. Because surgical technique and quality are often operator- or site-dependent and outcomes are influenced by local practices, staffing, and other features of the environment, it is difficult to generalize our findings for surgical interventions.

Implications for clinical and policy decision making are difficult to generate from our review, given the limitations in applicability, potential influence of selective reporting and publication bias, and lack of high-strength evidence, with most of our findings being based on low-strength or insufficient evidence. Future studies are needed with larger sample sizes, more rigorous adherence to methodological standards, information about cointerventions, standardization of comparators, and longer follow-up to allow for clinically meaningful outcome measures, including complete wound healing. Similarly, stratification of findings by patient characteristics (for example, comorbid conditions and ulcer stage) would help determine the applicability of different interventions for specific patients and situations. It is particularly important for future studies to report findings according to ulcer stage because the rate of healing, conditions necessary to promote healing, and treatment choices may differ for partial- and full-thickness ulcers.

We found limited evidence for better wound healing with air-fluidized beds, protein supplementation, radiant heat dressings, and electrical stimulation than with standard care, placebo, or sham interventions. However, the

benefit seen in all cases was reduction in wound size or better healing rates rather than completely healed wounds. In addition, there was low-strength or insufficient evidence about treatment harms, and the balance of benefits versus costs and harms for pressure ulcer therapies remains unclear. Advancing pressure ulcer care will require more rigorous study to solidify the evidence base for this widely used, and needed, set of treatments.

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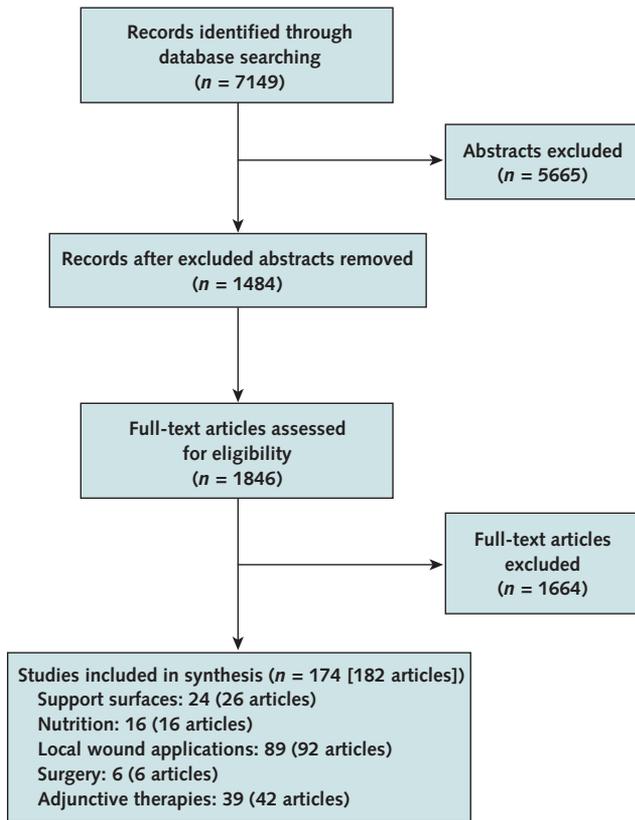
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Appendix Table 1. Stages of Pressure Ulcer Equivalency

NPUAP Stage	Description	Yatony-Kirk	Description	Shea	Description	DeLisa, Mikulic	Description	Torrance	Description
I	Intact skin with nonblanchable redness of a localized area, usually over a bony prominence. Darkly pigmented skin may not have visible blanching; its color may differ from the surrounding area.	I	Red area. Present >30 min but <24 h Present >24 h	NA	No equivalent	I	Pressure sore is an acute inflammatory response involving the epidermis. An irregular, ill-defined area of soft-tissue erythema accompanies by induration and heat persists for >24 h. The epidermis remains intact, and the ulcer is reversible.	I	Persistent erythema of the skin
II	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 blister.	II	Epidermis or dermis ulcerated with no subcutaneous fat observed	I	Limited to epidermis exposing dermis	II	Pressure sore is a break-in or blistering of the epidermis surrounded by erythema and induration. Potentially, it also is reversible.	II	Blister formation or superficial subcutaneous ulcer
III	Full-thickness tissue loss. Subcutaneous fat may be visible, but bone, tendon, or muscle are not exposed. Slough may be present but does not obscure the depth of tissue loss. May include undermining and tunneling.	III	Subcutaneous fat observed, no muscle observed	II, III	Full-thickness of dermis to junction of subcutaneous fat obliterated, limited by deep fascia undermining of skin	III	Pressure ulcer is an inflammatory fibroblastic response extending through the dermis to the junction with subcutaneous fat. Clinically presents as an irregular, shallow ulcer that has subcutaneous fat at its base and is surrounded by erythema, induration, and heat.	III	Deep subcutaneous ulceration progress through the dermis
IV	Full-thickness tissue loss with exposed bone, tendon, or muscle. Slough or eschar may be present on some parts of the wound bed. Often include undermining and tunneling.	IV to V	Muscle or fascia seen, but no bone observed Bone observed, but no involvement of joint space	IV	Bone at the base of ulceration	IV: muscle V: exposed bone	Pressure ulcer extends through the full thickness of skin into the deep fascia or muscle. Its draining, necrotic base is often foul-smelling, and undermining of the surface tissues may be excessive. Pressure ulcer penetrates the underlying bone, causing osteomyelitis. It has no anatomical limit and is surrounded by erythema and induration. Clinically, it presents as an extensive ulcer with exposed bone, joint, muscle, or fascia at its base.	IV	The lesion extends into the subcutaneous fat. Small vessel thrombosis and infection compound fat necrosis. Underlying muscle is swollen and inflamed and undergoes pathologic changes. The relatively avascular deep fascia temporarily impedes downward progress but promotes lateral extension, causing undermining of the skin. Epidermal thickening creates a distinct ulcer margin, but inflammation, fibrosis, and retraction distort the deeper areas of the sore.
NA	NA	VI	Involvement of joint space	V	Closed large cavity through a small sinus	NA	NA	V	Infective necrosis penetrates the deep fascia, and muscle destruction progresses rapidly. The wound spreads along fascial plane and involves the bursae, joints, and body cavities. Osteomyelitis easily develops. Multiple sores may communicate, resulting in massive areas of tissue destruction.
Suspected deep-tissue injury	Purple or maroon localized area of discolored intact skin or blood-filled blister due to damage of underlying soft tissue from pressure or shear. The area may be preceded by tissue found to be painful, firm, mushy, boggy, warmer, or cooler compared with adjacent tissue.	NA	NA	NA	NA	NA	NA	NA	NA
Unstageable	Full-thickness tissue loss in which the base of the ulcer is covered by slough (yellow, tan, gray, green, or brown) and/or eschar (tan, brown, or black) in the wound bed.	NA	NA	NA	NA	NA	NA	NA	NA

NA = not applicable; NPUAP = National Pressure Ulcer Advisory Panel.

Appendix Figure 1. Summary of evidence search and selection.



Full-text articles that were reviewed include additional studies identified through other sources, hand-searches of reference lists, peer review and public comment, scientific information packets, and gray literature searches. Quality-of-life outcomes and results related to histologic outcomes are in the full report (5) but not included in this article.

Appendix Table 2. Summary of Evidence of Differences of Intervention Effectiveness*

Intervention	Strength of Evidence for Comparative Effectiveness	Studies and Participants for Comparative Effectiveness Analysis	Strength of Evidence for Harms	Studies and Participants for Harms Analysis
Features of pressure ulcers†				
Surgery				
Anatomical site	Low Sacral pressure ulcers have lower recurrence rates after surgery than ischial pressure ulcers	4 studies (<i>n</i> = 560)	None reported	None reported
Severity at baseline	None reported	None reported	Low More harms with ischial vs. sacral and trochanteric surgical repairs Low Wound dehiscence is more common if bone is removed at time of surgical procedure	2 studies (<i>n</i> = 376) 1 study (<i>n</i> = 148)
Adjunctive				
Electrical stimulation vs. sham (ulcer stage II, III, or IV)	Low Rate of reduction in wound size: similar	5 studies (<i>n</i> = 197)	None reported	None reported
Patient characteristics‡				
Surgery				
Neurologic status (stage III or IV)	Low Recurrence rate: greater in patients with spinal cord injuries vs. other patients with pressure ulcers	1 study (<i>n</i> = 158)	None reported	None reported
Adjunctive				
Neurologic status	Low Rate of reduction in wound size: similar vs. other patients with pressure ulcers	4 studies (<i>n</i> = 138)	None reported	None reported
Patient care settings§				
Adjunctive				
Hospital vs. rehabilitation center	Low Electrical stimulation produced similar results in a hospital vs. rehabilitation center	9 studies (<i>n</i> = 397)	None reported	None reported

* Results are for findings with moderate or low strength of evidence. Additional key questions are addressed in the full report (5).

† Key questions 1a and 2a: Such features as anatomical site or severity of ulcer at baseline.

‡ Key questions 1b and 2b: Patient characteristics, including but not limited to age; race or ethnicity; body weight; specific medical comorbid conditions; and known risk factors for pressure ulcers, such as functional ability, nutritional status, or incontinence.

§ Key questions 1c and 2c: Patient care settings, such as home, nursing facility, or hospital, or according to features of patient care settings, including but not limited to nurse-patient staffing ratio, staff education and training in wound care, the use of wound care teams, and home caregiver support and training.