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Alginate dressings for treating pressure ulcers

Review

Intervention

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Abstract

English

Background

Pressure ulcers, also known as bedsores, decubitus ulcers and pressure injuries, are localised areas of injury to the skin or the underlying tissue, or both. Dressings are widely used to treat pressure ulcers and there are many options to choose from including alginate dressings. A clear and current overview of current evidence is required to facilitate decision-making regarding dressing use for the treatment of pressure ulcers. This review is part of a suite of Cochrane reviews investigating the use of dressings in the treatment of pressure ulcers. Each review will focus on a particular dressing type.

Objectives

To assess the effects of alginate dressings for treating pressure ulcers in any care setting.

Search methods

For this review, in April 2015 we searched the following databases the Cochrane Wounds Group Specialised Register; The Cochrane Central Register of Controlled Trials (CENTRAL)

(*The Cochrane Library*); Ovid MEDLINE; Ovid MEDLINE (In-Process & Other Non-Indexed Citations); Ovid EMBASE; and EBSCO CINAHL. There were no restrictions based on language or date of publication.

Selection criteria

Published or unpublished randomised controlled trials (RCTs) comparing the effects of alginate with alternative wound dressings or no dressing in the treatment of pressure ulcers (stage II or above).

Data collection and analysis

Two review authors independently performed study selection, risk of bias assessment and data extraction.

Main results

We included six studies (336 participants) in this review; all studies had two arms. The included studies compared alginate dressings with six other interventions that included: hydrocolloid dressings, silver containing alginate dressings, and radiant heat therapy. Each of the six comparisons included just one study and these had limited participant numbers and short follow-up times. All the evidence was of low or very low quality. Where data were available there was no evidence of a difference between alginate dressings and alternative treatments in terms of complete wound healing or adverse events.

Authors' conclusions

The relative effects of alginate dressings compared with alternative treatments are unclear. The existing trials are small, of short duration and at risk of bias. Decision makers may wish to consider aspects such as cost of dressings and the wound management properties offered by each dressing type, for example, exudate management.

Plain language summary

English

Alginate dressings for treating pressure ulcers

What are pressure ulcers, and who is at risk?

Pressure ulcers, also known as bedsores, decubitus ulcers and pressure injuries, are wounds involving the skin and sometimes the tissue that lies underneath. Pressure ulcers can be painful, may become infected, and so affect people's quality of life. People at risk of developing pressure ulcers include those with spinal cord injuries, and those who are immobile or who have limited mobility - such as elderly people and people who are ill as a result of short-term or long-term medical conditions.

In 2004 the total annual cost of treating pressure ulcers in the UK was estimated as being GBP 1.4 to 2.1 billion, which was equivalent to 4% of the total National Health Service expenditure. People with pressure ulcers have longer stays in hospital, and this increases hospital costs. Figures from the USA for 2006 suggest that half a million hospital stays had

'pressure ulcer' noted as a diagnosis; the total hospital costs of these stays was USD 11 billion.

Why use alginate dressings to treat pressure ulcers?

Dressings are one treatment option for pressure ulcers. There are many types of dressings that can be used; these can vary considerably in cost. Alginate dressings are a type that is highly absorbant and so can absorb the fluid (exudate) that is produced by some ulcers.

What we found

In June 2014 we searched for as many relevant studies as we could find that had a robust design (randomised controlled trials) and compared alginate dressings with other treatments for pressure ulcers. We found 6 studies involving a total of 336 participants. Alginates have been compared with hydrocolloid dressings, another type of alginate dressing, dextranomer paste dressing, silver-alginate dressing, silver-zinc sulfadiazine cream and treatment with a radiant heat system in these studies. There was no evidence from these studies to suggest that alginate wound dressings are more effective at healing pressure ulcers than other types of dressings or skin surface (topical) treatments, or other interventions.

Generally, the studies we found did not have many participants and the results were often inconclusive. Some study reports did not provide information about how they were conducted and it was difficult to tell whether the results presented were likely to be true. More research of better quality is needed to find out if alginate dressings are better at healing pressure ulcers than other types of dressings or other treatments. This review is part of a suite of reviews investigating dressings for the treatment of pressure ulcers

This plain language summary is up-to-date as of June 2014.

Summary of findings (Explanation)

Summary of findings for the main comparison. Alginate dressing followed by hydrocolloid dressing compared with hydrocolloid dressing alone

Comparison 1: Alginate dressing followed by hydrocolloid dressing compared with hydrocolloid dressing alone
Patient or population: patients with pressure ulcers **Settings:** **Intervention:** alginate dressing **Comparison:** hydrocolloid dressing
[1] Outcome is indirect for ulcer healing [2]Very short follow up time [3]Very wide confidence intervals and low event rate [4] Wide confidence intervals [5] Belmin 2002

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Hydrocolloid dressing	Alginate/hydrocolloid dressing				
Change in wound size Follow up: mean 8 weeks	The mean reduction in ulcer size (compared to baseline) was 42.5%	The mean reduction in ulcer size (compared to baseline) was 69.1% Ulcers in the intervention group had reduced,on average, by 26.5 percentage points more (compared to baseline measure) (10.6 to 42.4)	n/a	110 (1 study)[5]	⊕⊖⊖⊖ **very low** [1,2]	
Wound infection Follow-up: mean 8 weeks			**RR 2.79** (0.12 to 67.10)	110 (1 study)[5]	⊕⊖⊖⊖ **very low** [,2,3]	
Adverse events Follow-up: mean 8 weeks	**94 per 1000**	**106 per 1000** (34 to 325)	**RR 1.12** (0.36 to 3.44)	110 (1 study)[5]	⊕⊕⊖⊖ **low** [3,4]	

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI)
CI: confidence interval; **RR:** risk ratio

GRADE Working Group grades of evidence
High quality: further research is very unlikely to change our confidence in the estimate of effect
Moderate quality: further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate
Low quality: 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
Very low quality: we are very uncertain about the estimate

[1] Outcome is indirect for ulcer healing
[2] Very short follow up time
[3] Very wide confidence intervals and low event rate
[4] Wide confidence intervals
[5] Belmin 2002

Summary of findings 2 Comparison between different alginates

Summary of findings 2. Comparison between different alginates

Comparison 2: Comparison between different alginates

Patient or population: patients with pressure ulcers
Settings:
Intervention: alginate dressings
Comparison: different brand of alginate dressing

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Different brand of alginate dressing	Alginate dressings				
Complete wound healing Follow-up: mean 8 weeks	Study population 83 per 1000 Moderate	125 per 1000 (14 to 1000)	**RR 1.50** (0.17 to 12.94)	36 (1 study)[4]	⊕⊖⊖⊖ **very low** [1,2,3]	
Adverse events Follow-up: mean 8 weeks	Study population 250 per 1000 Moderate	125 per 1000 (30 to 530)	**RR 0.50** (0.12 to 2.12)	36 (1 study)[4]	⊕⊖⊖⊖ **very low** [1,2,3]	

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI)
CI: confidence interval; **RR:** risk ratio

GRADE Working Group grades of evidence
High quality: further research is very unlikely to change our confidence in the estimate of effect
Moderate quality: further research is likely to have an important impact on our confidence in the

[1] Estimate informed by just one study that was deemed to be at high risk of bias for attrition and selective reporting bias
[2] Short follow-up time
[3] Wide confidence intervals - imprecise estimate. Fewer than 100 participants
[4] Brown-Etris 1997

estimate of effect and may change the estimate
Low quality: 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
Very low quality: we are very uncertain about the estimate

[1] Estimate informed by just one study that was deemed to be at high risk of bias for attrition and selective reporting bias
[2] Short follow-up time
[3] Wide confidence intervals - imprecise estimate. Fewer than 100 participants
[4] Brown-Etris 1997

Summary of findings 3 Alginate compared with dextranomer paste

Summary of findings 3. Alginate compared with dextranomer paste

Comparison 3: Alginate compared with dextranomer paste						
Patient or population: patients with pressure ulcers **Settings:** **Intervention:** alginate dressing **Comparison:** dextranomer paste dressing						
Outcomes	**Illustrative comparative risks* (95% CI)**		**Relative effect (95% CI)**	**No of participants (studies)**	**Quality of the evidence (GRADE)**	**Comments**
	Assumed risk	**Corresponding risk**				
	Dextranomer paste dressing	**Alginate dressing**				
Wound infection Follow-up: mean 8 weeks	**Study population**		**RR 0.96** (0.14 to 6.51)	92 (1 study)[4]	⊕⊖⊖⊖ **very low** [1,2]	
	44 per 1000	**43 per 1000** (6 to 289)				
	Moderate					
Adverse events Follow-up:	**Study population**		**RR 0.38** (0.13 to 1.13)	92 (1 study)[4]	⊕⊖⊖⊖ **very low** [1,3]	
	222 per 1000					

[1] Short follow-up time
[2] Limited number of events and wide confidence intervals - very imprecise estimate. Also fewer than 100 participants
[3] Wide confidence intervals and fewer than 100 participants
[4] Sayag 1996

mean 8 weeks		**84 per 1000** (29 to 251)				
	Moderate					

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI)
CI: confidence interval; **RR:** risk ratio

GRADE Working Group grades of evidence
High quality: further research is very unlikely to change our confidence in the estimate of effect
Moderate quality: further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate
Low quality: 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
Very low quality: we are very uncertain about the estimate

[1] Short follow-up time
[2] Limited number of events and wide confidence intervals - very imprecise estimate. Also fewer than 100 participants
[3] Wide confidence intervals and fewer than 100 participants
[4] Sayag 1996

Summary of findings 4 Silver-alginate compared with plain alginate

Summary of findings 4. Silver-alginate compared with plain alginate

Silver-alginate compared with plain alginate

Patient or population: patients with pressure ulcers
Settings:
Intervention: silver-alginate dressing
Comparison: alginate dressing

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Alginate dressing	silver-alginatedressing				

[1] Indirectness of outcome
[2] Wide confidence intervals, short follow-up time and fewer than 100 participants. Very imprecise estimate
[3] Meaume 2005

Change in wound size Follow up: mean 4 weeks	The mean reduction in ulcer size (compared to baseline) was 13.9%	The mean reduction in ulcer size (compared to baseline) was 31.6% Ulcers in the intervention group had reduced,on average, by 17.7 percentage points more (compared to baseline measure) (-13.07 to 48.5)	n/a	110 (1 study)[3]	⊕⊖⊖⊖ **very low** [1,2]
Wound infection Follow-up: mean 4 weeks	The mean wound infection score in the control groups was **115.3**	The mean wound infection score in the intervention groups was **33.50 lower** (82.71 lower to 15.71 higher)		28 (1 study)[3]	⊕⊖⊖⊖ **very low** [2]

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI)
CI: confidence interval

GRADE Working Group grades of evidence
High quality: further research is very unlikely to change our confidence in the estimate of effect
Moderate quality: further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate
Low quality: 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
Very low quality: we are very uncertain about the estimate

[1] Indirectness of outcome
[2] Wide confidence intervals, short follow-up time and fewer than 100 participants. Very imprecise estimate
[3] Meaume 2005

Summary of findings 5 Alginate compared with radiant heat system

Summary of findings 5. Alginate compared with radiant heat system

Comparison 6: Alginate compared with radiant heat system

[1] Comparison informed by a single study deemed to be at high risk of attrition bias
[2] Short follow-up time
[3] Indirectness of outcome
[4] Wide confidence intervals - imprecise estimate. Fewer than 100 participants in study
[5] Price 2000

Patient or population: patients with pressure ulcers
Settings:
Intervention: alginate dressing
Comparison: radiant heat system

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk Radiant heat system	Corresponding risk Alginate dressing				
Change in wound size Follow up: mean 4 weeks	The mean reduction in ulcer size (compared to baseline) was 54.6%	The mean reduction in ulcer size (compared to baseline) was 22.8% Ulcers in the intervention group had reduced,on average, by 31.8 percentage points less (compared to baseline measure) (-65.10 to 1.50)	n/a	110[5] (1 study)	⊕⊖⊖⊖ **very low** [1,2,3]	
Adverse event (pain) Follow-up: mean 6 weeks	The mean adverse event (pain) in the control groups was **21.4**	The mean adverse event (pain) in the intervention groups was **0.70 higher** (10.70 lower to 12.10 higher)		50 (1 study)[5]	⊕⊖⊖⊖ **very low** [1,2,4]	

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI)
CI: confidence interval

GRADE Working Group grades of evidence
High quality: further research is very unlikely to change our confidence in the estimate of effect
Moderate quality: further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate
Low quality: 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
Very low quality: we are very uncertain about the estimate

[1] Comparison informed by a single study deemed to be at high risk of attrition bias
[2] Short follow-up time
[3] Indirectness of outcome
[4] Wide confidence intervals - imprecise estimate. Fewer than 100 participants in study
[5] Price 2000

Background

Description of the condition

Pressure ulcers, also known as bedsores, decubitus ulcers and pressure injuries, are localised areas of injury to the skin or the underlying tissue, or both. They often occur in areas with a bony prominence such as the sacrum (base of the spine) and the heel (Vanderwee 2007), and are caused by external forces such as pressure, or shear, or a combination of both (EPUAP-NPUAP 2009).

Populations at risk of pressure ulceration include those with spinal cord injuries (Gefen 2014), and those immobilised or with limited mobility, such as elderly people and people with acute or chronic conditions that might limit movement or bodily sensation, or both (Allman 1997; Bergstrom 1998; Berlowitz 1990; Berlowitz 1997; Brandeis 1994). Incontinence can also increase risk of ulceration by producing a detrimental environment for the skin (Brandeis 1994). Impaired nutritional status may increase risk as well (Allman 1997; Donini 2005), however, evidence for the effectiveness of nutritional intake interventions for preventing or treating pressure ulcers is currently limited (Langer 2003; Smith 2013).

Normal movements relieve the pressure over bony prominences when people engage in regular, often subconscious, shifts in position when sitting or lying. These movements, that are triggered by a reduction in oxygen levels at pressure points and possible discomfort, distribute pressure from contact at the surface, thus reducing the compression of soft tissue against bone (Gebhardt 2002). People with limited autonomous movement or conditions that dull body sensation, or both (as described above), are at risk of failing to achieve adequate pressure relief. Prolonged exposure of an area of the body to pressure or compression can interrupt the local blood circulation and trigger a cascade of biochemical changes that may lead to tissue damage and ulceration. Immobility can also lead to increased damage from shear and friction, for example, when people are pulled into position in chairs and beds.

Pressure ulcers vary in severity. One of the most widely recognised systems for categorising pressure ulcers is that of the National Pressure Ulcer Advisory Panel, which is summarised below (NPUAP 2009).

- **Category/Stage I - non-blanchable erythema:** "Intact skin with non-blanchable redness of a localised area usually over a bony prominence. Darkly pigmented skin may not have visible blanching; its colour may differ from the surrounding area. The area may be painful, firm, soft, warmer or cooler as compared with adjacent tissue. Category I may be difficult to detect in individuals with dark skin tones. May indicate 'at risk' persons."
- **Category/Stage II - partial thickness:** "Partial thickness loss of dermis presenting as a shallow open ulcer with a red pink wound bed, without slough. May also present as an intact or open/ruptured serum-filled or sero-sanguinous filled blister. Presents as a shiny or dry shallow ulcer without slough or bruising (bruising indicates deep tissue injury). This category should not be used to describe skin tears, tape burns, incontinence associated dermatitis, maceration or excoriation."

- **Category/Stage III - full thickness skin loss:** "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 tunnelling. The depth of a category/stage III pressure ulcer varies by anatomical location. The bridge of the nose, ear, occiput and malleolus do not have (adipose) subcutaneous tissue and Category/Stage III ulcers can be shallow. In contrast, areas of significant adiposity can develop extremely deep category/stage III pressure ulcers. Bone/tendon is not visible or directly palpable."
- **Category/Stage IV - full thickness tissue loss:** "Full thickness tissue loss with exposed bone, tendon or muscle. Slough or eschar may be present. Often includes undermining and tunnelling. The depth of a category/stage IV pressure ulcer varies by anatomical location. The bridge of the nose, ear, occiput and malleolus do not have (adipose) subcutaneous tissue and these ulcers can be shallow. Category/Stage IV ulcers can extend into muscle and/or supporting structures (e.g., fascia, tendon or joint capsule) making osteomyelitis or osteitis likely to occur. Exposed bone/muscle is visible or directly palpable."

Pressure ulcers are relatively common, but complex, wounds. Prevalence estimates vary according to the population assessed, the data collection methods used and decisions made about whether stage I pressure ulcers should be included (as there is no active wound at this stage, but patients are 'at risk'). A large survey of hospital patients undertaken in several European countries returned a pressure ulcer prevalence (stage II and above) of 10.5% (Vanderwee 2007). In 2009, an estimate for pressure ulcer prevalence (stage II and above) across acute-care, long-term care and rehabilitation settings in the USA was 9.0%, with prevalence highest in long-term acute-care settings (26%) (VanGilder 2009). In the UK, national pressure ulcer data are collected across community and acute settings - although data collection is not yet universal - as part of the National Health Service (NHS) Safety Thermometer initiative (Power 2012). Five per cent of patients across these settings were estimated to have a pressure ulcer in January 2014 (National Safety Thermometer Data 2014).

We note that all prevalence figures quoted above are for populations currently receiving medical care. The point prevalence of pressure ulceration in the total adult population was recently estimated in a cross-sectional survey undertaken in Leeds, in the UK. Of the total adult population of 751,485, the point prevalence of pressure ulceration was 0.31 per 1000 (Hall 2014). Pressure ulcer prevalence estimates specifically for community settings have reported rates of 0.77 per 1000 adults in a UK urban area (Stevenson 2013).

Pressure ulcers have a large impact on those affected; they can be painful and may become seriously infected or malodorous. It has been shown that - after adjustment for age, sex and co-morbidities - people with pressure ulcers have lower health-related quality of life than those without pressure ulcers (Essex 2009). The financial cost of treating ulcers in the UK was recently estimated as between GBP 1214 for a stage I ulcer and GBP 14,108 for a stage IV ulcer (Dealey 2012). In 2004 the total annual cost of treating pressure ulcers in the UK was estimated as GBP 1.4 to 2.1 billion, which was equivalent to 4% of the total NHS expenditure (Bennett 2004). Pressure ulcers have been shown to increase length of hospital stay and associated hospital costs (Allman 1999). Figures from the USA suggest that 'pressure ulcer'

was noted as a diagnosis for half a million hospital stays in 2006; for adults, the total hospital cost for these stays was USD 11 billion (Russo 2008). Costs to the Australian healthcare system for treating pressure ulceration have been estimated at AUD 285 million per annum (Graves 2005).

Description of the intervention

Two main strategies are used in the treatment of pressure ulcers, namely, relief of pressure - commonly using specialist support surfaces (McInnes 2011) - alongside management of the wound environment using wound dressings. Other general strategies include providing patient education, managing pain, optimising circulation/perfusion, optimising nutrition, performing surgical wound closure and treating clinical infection (AWMA 2012; EPUAP-NPUAP 2009).

Dressings are widely used in wound care, with the aim of protecting the wound while promoting healing. Classification of dressings usually depends on the key material used in their construction. Several attributes of an ideal wound dressing have been described (e.g. BNF 2013), including:

- the ability of the dressing to absorb and contain exudate without leakage or strike-through;
- lack of particulate contaminants left in the wound by the dressing;
- thermal insulation;
- permeability to water but not to bacteria;
- avoidance of wound trauma on dressing removal;
- frequency with which the dressing needs to be changed;
- provision of pain relief; and
- comfort.

Alginate dressings are the focus of this review; their properties are described below. As alginate dressings are likely to be compared with one of the many alternative wound dressings available, a description of potential comparators, based on the British National Formulary structure (BNF 2013), is also provided. Dressings are listed below by their generic names and, when possible, with examples of corresponding trade names and manufacturers. Dressing names, manufacturers and distributors may vary between countries.

Basic wound contact dressings

- **Low-adherence dressings and wound contact materials:** these are usually cotton pads that are placed in direct contact with the wound. Examples include paraffin gauze dressing, BP 1993 and Xeroform (Covidien) dressing - a non-adherent petrolatum blend with 3% bismuth tribromophenate on fine mesh gauze. The addition of paraffin and similar substances is largely to stop the dressing from sticking to the wound.

- **Absorbent dressings:** these can be applied directly to the wound or used as secondary absorbent layers in the management of heavily exuding wounds. Examples include Primapore (Smith & Nephew), Mepore (Mölnlycke) and absorbent cotton gauze (BP 1988).

Advanced wound dressings

- **Alginate dressings:** these are highly absorbent and come in the form of calcium-alginate or calcium sodium alginate, and they can be combined with collagen. The alginate forms a gel when in contact with the wound surface, which can be lifted off at dressing removal or rinsed away with sterile saline. Bonding to a secondary viscose pad increases absorbency. Examples include Curasorb (Covidien), SeaSorb (Coloplast) and Sorbsan (Unomedical).
- **Foam dressings:** these dressings normally contain hydrophilic polyurethane foam and are designed to absorb wound exudate and maintain a moist wound surface. They are produced in a variety of versions: Some foam dressings include additional absorbent materials, such as viscose and acrylate fibres or particles of superabsorbent polyacrylate; others are silicone-coated for non-traumatic removal. Examples include Allevyn (Smith & Nephew), Biatain (Coloplast) and Tegaderm Foam (3M).
- **Hydrogel dressings:** these consist of cross-linked insoluble polymers (i.e. starch or carboxymethylcellulose) and up to 96% water. They are designed to absorb wound exudate or to rehydrate a wound, depending on wound moisture levels. They are supplied as flat sheets, as an amorphous hydrogel or as beads. Examples include ActiformCool (Activa) and Aquaflo (Covidien).
- **Films - permeable film and membrane dressings:** these dressings are permeable to water vapour and oxygen but not to water or micro-organisms. Examples includeTegaderm (3M) and Opsite (Smith & Nephew).
- **Soft polymer dressings:** these dressings are moderately absorbent and are composed of a soft silicone polymer held in a non-adherent layer. Examples include Mepitel (Mölnlycke) and Urgotul (Urgo).
- **Hydrocolloid dressings:** these occlusive dressings are usually composed of a hydrocolloid matrix bonded onto a vapour-permeable film or foam backing. This matrix forms a gel that provides a moist environment when in contact with the wound surface. Examples include GranuFLEX (ConvaTec) and NU DERM (Systagenix). Fibrous alternatives have been developed that resemble alginates, are not occlusive and are more absorbent than standard hydrocolloid dressings. An example is Aquacel (ConvaTec).
- **Capillary action dressings:** these consist of an absorbent core of hydrophilic fibres held between two low-adherent contact layers. Examples include Advadraw (Advancis) and Vacutx (Protex).

- **Odour absorbent dressings:** these dressings contain charcoal and are used to absorb wound odour, often in conjunction with a secondary dressing to improve absorbency. An example is CarboFLEX (ConvaTec).

Antimicrobial dressings

- **Honey-impregnated dressings:** these dressings contain medical-grade honey, which is thought to have antimicrobial and anti-inflammatory properties and can be used for acute or chronic wounds. Examples include Medihoney (Medihoney) and Activon Tulle (Advancis).
- **Iodine-impregnated dressings:** these dressings release free iodine, which is thought to act as a wound antiseptic, when exposed to wound exudate. Examples include Iodoflex (Smith & Nephew) and Iodozyme (Insense).
- **Silver-impregnated dressings:** these dressings are used to treat infected wounds, as silver ions are thought to have antimicrobial properties. Silver versions of most dressing types are available (e.g. silver foam, silver hydrocolloid). Examples include Acticoat (Smith & Nephew) and Urgosorb Silver (Urgo).
- **Other antimicrobial dressings:** these dressings are composed of a gauze or low-adherent dressing impregnated with an ointment thought to have antimicrobial properties. Examples include chlorhexidine gauze dressing (Smith & Nephew) and Cutimed Sorbact (BSN Medical).

Specialist dressings

- **Protease-modulating matrix dressings:** these dressings are designed to alter the activity of proteolytic enzymes in chronic wounds. Examples include Promogran (Systagenix) and Sorbion (H & R).

The diversity of dressings available to health professionals (including variations within each type) can make evidence-informed decision making challenging. Furthermore, whilst dressings may be viewed as 'inert' and cheap products, increasingly they are being formulated with an 'active' ingredient (e.g. silver) or with other antimicrobial products. With increasingly sophisticated technology applied to wound care, practitioners need to know how effective these - often expensive - dressings are compared with more traditional, usually less costly, options. Data on the current use of dressings for the treatment of pressure ulcers are limited, although older studies have shown wide variation in practice and wound (wound type) care knowledge (Pieper 1995).

How the intervention might work

Animal experiments conducted over 40 years ago suggest that acute wounds heal more quickly when their surfaces are kept moist rather than left to dry and scab (Winter 1962; Winter 1963a; Winter 1963b). A moist environment is thought to provide optimal conditions for the cells involved in the healing process, as well as allowing autolytic debridement

(removal of dead tissue by natural processes), which is thought to be an important part of the healing pathway (Cardinal 2009). The desire to maintain a moist wound environment is a key driver for the use of wound dressings. Wound dressings vary in their level of absorbency, so that a very wet wound can be treated with an absorbent dressing (such as a foam dressing) to draw excess moisture away and avoid skin damage, whilst a drier wound can be treated with a more occlusive dressing to maintain a moist environment. Alginate dressings contain sodium, or sodium and calcium, salts of alginic acid. These alginate salts are highly hydrophilic and can absorb large volumes of wound exudate.

Why it is important to do this review

Pressure ulcers are a relatively common complex type of wound that have a negative impact on people's lives and incur high costs for health services. Dressings are widely used as treatment for pressure ulcers, and understanding the existing evidence base and potential uncertainty around the clinical efficacy and cost-effectiveness of different dressing types is important for decision making in this area.

An influential international guideline recommends that a dressing which keeps the wound bed moist should be used; this recommendation was classed as level C evidence that is "supported by indirect evidence (e.g., studies in normal human subjects, humans with other types of chronic wounds, animal models) and/or expert opinion" (EPUAP-NPUAP 2009). The same guidelines suggest that alginate dressings are used to treat pressure ulcers in various scenarios, mainly for the treatment of moderately or heavily exuding ulcers, but these recommendations are based on limited evidence (EPUAP-NPUAP 2009).

Two notable systematic reviews of treatments for pressure ulcers have included trials of dressings (Reddy 2008; Smith 2013). Reddy 2008 included five trials of alginates in people with pressure ulcers. These studies were included as part of a much larger review that assessed many pressure ulcer treatments. The report stated, "No single dressing was consistently superior to other dressings in the trials of pressure ulcers we examined"; however, because of the breadth of the review, detailed examination of effect estimates and quantification of uncertainty around the alginate trials was difficult. One included study reported that a calcium-alginate dressing showed statistically significant improvement in pressure ulcer healing compared with dextranomer paste (with healing measured as mean wound surface area reduction per week). The search for trials for inclusion in the Reddy review was conducted in 2008. The more recent review seems to include dressing interventions but does not mention alginates specifically (Smith 2013). We conclude that up-to-date and transparent information on evidence for the use of alginate dressings to treat pressure ulcers is required.

This review is part of a suite of Cochrane reviews investigating the use of dressings in the treatment of pressure ulcers . Each review will focus on a particular dressing type. These reviews will be summarised in an overview of reviews that will draw together all existing Cochrane review evidence regarding the use of dressings to treat pressure ulcers.

Objectives

To assess the effects of alginate dressings on pressure ulcer healing in any care setting.

Methods

Criteria for considering studies for this review

Types of studies

We included published and unpublished randomised controlled trials (RCTs), including cluster RCTs (that could include studies in which multiple wounds on the same participant were treated with the allocated treatment and outcome data were collected and analysed for each wound), irrespective of the language of report. We included RCTs reported only as abstracts when the available data were sufficient for reasonable data extraction either from the abstract itself or from the study authors. We included cross-over trials only if outcome data were available from the end of the first treatment period before the cross-over. We excluded studies that used quasi-randomisation methods.

Types of participants

We included studies that recruited adults with a diagnosis of pressure ulcer (stage II or above) managed in any care setting. We excluded studies involving participants with stage I ulcers. We accepted study authors' definitions of what they classed as stage II or above, unless it was clear that they included wounds with unbroken skin. We included studies that recruited participants with stage II or higher pressure ulcers alongside people with other types of chronic wounds (e.g. leg or foot ulcers, or both) if the results for people with relevant pressure ulcers were presented separately (or were available from the study authors). Similarly, when a trial included both stage I and more advanced stages of pressure ulcers, we included it in the review only if data on the stage II and above ulcers were reported separately or available on request from study authors.

Types of interventions

The primary intervention was alginate wound dressings (BNF 2013). We included any RCT in which the use of a specific alginate dressing was the only systematic difference between treatment groups. We anticipated that probable comparisons would include different types of alginate dressings compared with each other; alginate dressings compared with other dressing types; and alginate dressings compared with other interventions (possibly non-dressing treatments, e.g. topical treatments).

Types of outcome measures

Primary outcomes

The primary outcome for this review was complete wound healing.

We note that, because wound healing is a subjective outcome, it can be at high risk of measurement bias when outcome assessment is not blinded. For this review, we regarded the following measures as providing the most relevant and rigorous measures of outcome.

- Time to complete wound healing (correctly analysed using censored data and preferably adjusted for prognostic co-variates such as baseline size). We

considered mean or median time to healing without survival analysis as a valid outcome only if reports specified that all wounds healed (i.e. if the trial authors regarded time to healing as a continuous measure, as there is no censoring).

- Proportion of ulcers healed during follow-up (frequency of complete healing).

When both time to healing and proportion of ulcers healed were reported, we planned to present all data in a summary outcome table for reference purposes, but would focus on reporting the 'best' healing outcome available. We considered time to healing (correctly analysed) to be the best outcome. We anticipated presenting data for the latest time point available - unless an earlier time point was clearly the primary focus of the study, in which case data from multiple time points were extracted. We accepted authors' definitions of what constituted a healed wound.

When time to healing was analysed as a continuous measure, but it was not clear whether all wounds healed, or when change or rate of change in wound size was reported without adjustment for baseline size, we documented the use of the outcome in the study, but did not plan to summarize or use the data in any meta-analysis.

Secondary outcomes

- Change (and rate of change) in wound size, with adjustment for baseline size (we attempted to contact study authors to request adjusted means when these were not presented). When change or rate of change in wound size was reported without adjustment for baseline size, use of the outcome in the study was documented but not summarised or used in any meta-analysis.
- Health-related quality of life/health status (measured using a standardised generic questionnaire such as EQ-5D (standardised instrument used to measure health outcomes), Short Form (SF)-36, SF-12 or SF-6 or wound-specific questionnaires such as the Cardiff Wound Impact Schedule). We did not include ad hoc measures of quality of life that were not likely to be validated and would not be common to multiple trials.
- Wound infection (we used the definition of infection used by the study authors rather than specifying a definition of infection here).
- Other adverse events, including pain associated with the ulcer or experienced at dressing change (measured using survey/questionnaire/data capture process or visual analogue scale), when a clear method for the collection of adverse event data was provided.
- Resource use (including measurements of resource use, such as mean number of dressing changes, number of nurse visits, length of hospital stay and whether reoperation/intervention was provided).
- Cost (allocated to resource use).
- Wound recurrence.

For all outcomes we reported outcome measures at the latest time point available (assumed to be length of follow-up if not specified) and the time point specified in the methods as being of primary interest (if this was different from latest time point available).

Search methods for identification of studies

Electronic searches

We searched the following electronic databases:

- Cochrane Wounds Group Specialised Register (searched 14 April 2015);
- The Cochrane Central Register of Controlled Trials (CENTRAL; The *Cochrane Library* 2015, Issue 3);
- The Database of Abstracts of Reviews of Effects (DARE; The *Cochrane Library* 2014, Issue 2);
- The Health Technology Assessment Database (HTA; The *Cochrane Library* 2014, Issue 2);
- The NHS Economic Evaluation Database (NHS EED; The *Cochrane Library* 2014, Issue 2);
- Ovid MEDLINE (1946 to June Week 2 2014);Ovid MEDLINE (In-Process & Other Non-Indexed Citations, 13 April 2015);
- Ovid EMBASE (1974 to 13 April 2015);
- EBSCO CINAHL (1982 to 13 April 2015).

We used the following search strategy in the Cochrane Central Register of Controlled Trials (CENTRAL):

#1 MeSH descriptor: [Occlusive Dressings] explode all trees
#2 MeSH descriptor: [Biological Dressings] explode all trees
#3 MeSH descriptor: [Alginates] explode all trees
#4 MeSH descriptor: [Hydrogels] explode all trees
#5 MeSH descriptor: [Silver] explode all trees
#6 MeSH descriptor: [Silver Sulfadiazine] explode all trees
#7 MeSH descriptor: [Honey] explode all trees
#8 MeSH descriptor: [Bandages, Hydrocolloid] explode all trees
#9 (dressing* or alginate* or hydrogel* or hydrocolloid* or "foam" or "bead" or "film" or "films" or tulle or gauze or non-adherent or "non adherent" or silver* or honey or matrix):ti,ab,kw
#10 #1 or #2 or #3 or #4 or #5 or #6 or #7 or #9
#11 MeSH descriptor: [Pressure Ulcer] explode all trees
#12 (pressure next (ulcer* or sore* or injur*)):ti,ab,kw
#13 (decubitus next (ulcer* or sore*)):ti,ab,kw
#14 ((bed next sore*) or bedsore):ti,ab,kw

#15 #11 or #12 or #13 or #14
#16 #10 and #15

We combined the Ovid MEDLINE search with the Cochrane Highly Sensitive Search Strategy for identifying randomised trials in MEDLINE: sensitivity- and precision-maximising version (2008 revision; **Lefebvre 2011**). We combined the EMBASE search with the Ovid EMBASE filter developed by the UK Cochrane Centre (**Lefebvre 2011**). We combined the CINAHL searches with the trial filters developed by the Scottish Intercollegiate Guidelines Network (**SIGN 2011**). The search strategies for Ovid MEDLINE, Ovid EMBASE and EBSCO CINAHL can be found in Appendix 1. No restrictions with respect to language, date of publication or study setting were applied.

We also searched the following clinical trials registries.

- ClinicalTrials.gov (http://www.clinicaltrials.gov/).
- World Health Organization (WHO) International Clinical Trials Registry Platform (http://apps.who.int/trialsearch/Default.aspx).
- EU Clinical Trials Register (https://www.clinicaltrialsregister.eu/).

Searching other resources

We contacted corresponding authors of trials and manufacturers and distributors of wound dressings. We searched the US Food and Drug Administration briefing documents used in the licensing of wound dressings. We tried to identify other potentially eligible trials or ancillary publications by searching the reference lists of retrieved included trials, as well as relevant systematic reviews, meta-analyses and health technology assessment reports.

Data collection and analysis

Selection of studies

Independently, two review authors assessed the titles and abstracts of the citations retrieved by the searches for relevance. After this initial assessment, we obtained full-text copies of all studies believed to be potentially relevant. Independently, two review authors checked the full papers for eligibility; disagreements were resolved by discussion, and, when required, the input of a third review author. When the eligibility of a study was unclear, we attempted to contact study authors to ask for clarification. We recorded all reasons for exclusion of studies that we obtained as full copies. We completed a PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flow chart to summarize this process (**Liberati 2009**).

We obtained all relevant publications when studies have been reported more than once. Whilst the study was included only once in the review, all reports were examined to ensure the maximal extraction of relevant data.

Data extraction and management

We extracted and summarised details of the eligible studies. Two review authors extracted data independently and resolved disagreements by discussion, drawing on a third review author when required. When data were missing from reports, we attempted to contact the

study authors to obtain this information. When a study with more than two intervention arms was included, data were extracted only from intervention and control groups that meet the eligibility criteria of the review.

We extracted the following data when possible on those trial arms that were relevant to the review.

- Country of origin.
- Type/grade/category of pressure ulcer.
- Location of pressure ulcer.
- Unit of randomisation and analysis (e.g. participant with single wound, participant with multiple wounds).
- Trial design (e.g. parallel, cluster).
- Care setting.
- Number of participants randomly assigned to each trial arm.
- Eligibility criteria and key baseline participant data.
- Details of treatment regimen received by each group.
- Duration of treatment.
- Details of any co-interventions provided.
- Primary and secondary outcome(s) (with definitions).
- Outcome data for primary and secondary outcomes (by group).
- Duration of follow-up.
- Number of withdrawals (by group).
- Publication status of study.
- Source of funding for trial.

Assessment of risk of bias in included studies

Independently, two review authors assessed the included studies that performed individual randomisation using the Cochrane tool for assessing risk of bias (**Higgins 2011a**). This tool addresses six specific domains: sequence generation, allocation concealment, blinding, incomplete data, selective outcome reporting and other issues (Appendix 2). We assessed blinded outcome assessment and completeness of outcome data for each outcome separately where required. We present the risk of bias assessment using two 'Risk of bias' summary figures; one providing a summary of bias for each item across all studies, and the second providing a cross-tabulation of each trial for all risk of bias items. For trials using cluster randomisation, we assessed the risk of bias using the following domains: recruitment bias, baseline imbalance, loss of clusters, incorrect analysis and comparability with individually randomised trials (**Higgins 2011b**; Appendix 3).

Measures of treatment effect

For dichotomous outcomes, the risk ratio (RR) was calculated with 95% confidence intervals (CIs). For continuous outcome data, we used the mean difference (MD) with 95% CIs for trials that used the same assessment scale. When trials used different assessment scales, we used the standardised mean difference (SMD) with 95% CIs. Time-to-event data (e.g. time-to-complete wound healing) were reported as hazard ratios (HRs) when possible, in accordance with the methods described in the *Cochrane Handbook f or Systematic Reviews of Interventions* (Deeks 2011). If studies reporting time-to-event data (e.g. time to healing) did not report a hazard ratio, then, when feasible, we planned to estimate this using other reported outcomes, such as numbers of events, through the application of available statistical methods (Tierney 2007).

Unit of analysis issues

Where studies randomised at the participant level and measured outcomes at the wound level, for example for wound healing, and the number of wounds appeared to be equal to the number of participants, we treated the participant as the unit of analysis.

We had anticipated a possible unit of analysis issue if individual participants with multiple wounds were randomised, the allocated treatment used on the multiple wounds per participant (or perhaps only on some participants) and then data were presented and analysed by wound not person. This is a type of clustered data and presents a unit of analysis error which inflates precision. In cases where included studies contained some or all clustered data we planned to report this alongside whether data had been (incorrectly) treated as independent. We recorded this as part of the risk of bias assessment. We did not plan to undertake further calculation to adjust for clustering.

Dealing with missing data

It is common to have data missing from trial reports. Excluding participants from the analysis post randomisation or ignoring participants who are lost to follow-up compromises the randomisation and potentially introduces bias into the trial. If it was thought that study authors might be able to provide some missing data, we planned to contact them; however, we anticipated that data would often remain missing because of loss to follow-up. In individual studies, when data on the proportion of ulcers healed were presented, we planned to assume that any randomly assigned participants who were not included in an analysis had an unhealed wound at the end of the follow-up period (i.e. they were considered in the denominator but not in the numerator). When a trial did not specify participant group numbers before dropout, we presented only complete case data.

Assessment of heterogeneity

We considered clinical heterogeneity (i.e. the degree to which RCTs vary in terms of participant, intervention and outcome characteristics) and, where possible, statistical heterogeneity. We assessed statistical heterogeneity using the Chi^2 test (a significance level of P less than 0.10 was considered to indicate statistically significant heterogeneity) in conjunction with the I^2 measure (Higgins 2003). I^2 examines the percentage of total variation across RCTs that is due to heterogeneity rather than to chance (Higgins 2003). We

considered that I^2 values of 40% or less indicated a low level of heterogeneity, and values of 75% or more indicated very high heterogeneity (Higgins 2011c).

Assessment of reporting biases

Reporting biases arise when dissemination of research findings is influenced by the nature and direction of results. Publication bias is one of a number of possible causes of 'small-study effects', that is, a tendency for estimates of the intervention effect to be more beneficial in smaller RCTs. Funnel plots allow a visual assessment of whether small-study effects may be present in a meta-analysis. A funnel plot is a simple scatter plot of the intervention effect estimates from individual RCTs against some measure of the size or precision of each trial (Sterne 2011). We planned to present funnel plots for meta-analyses comprising 10 or more RCTs using RevMan 5.3.

Data synthesis

Details of included studies were combined in a narrative review according to comparators. In terms of meta-analytical approach, in the presence of clinical heterogeneity (review author judgement) or evidence of statistical heterogeneity, or both, we planned to use the random-effects model. We anticipated using a fixed-effect approach only when clinical heterogeneity was thought to be minimal and statistical heterogeneity was estimated as non-statistically significant for the Chi^2 value and 0% for the I^2 assessment (Kontopantelis 2012).

For dichotomous outcomes, we planned to present the summary estimate as a risk ratio (RR) with 95% CI. When continuous outcomes were measured in the same way across studies, we planned to present a pooled mean difference (MD) with 95% CI. We planned to pool standardised mean difference (SMD) estimates when studies had measured the same outcome using different methods. We planned to present pooled data using forest plots. For time-to-event data, we planned to plot (and, if appropriate, pool) estimates of HRs and 95% CIs as presented in the study reports using the generic inverse variance method in RevMan 5.3. Where possible, pooled estimates of treatment effect were obtained by using RevMan (RevMan 2012).

'Summary of findings' tables

We planned to present the main results of the review in 'Summary of findings' tables. These tables present key information concerning the quality of the evidence, the magnitude of the effects of the interventions examined and the sum of available data for the main outcomes (Schunemann 2011a). The 'Summary of findings' tables also include an overall grading of the evidence related to each of the main outcomes using the GRADE (Grades of Recommendation, Assessment, Development and Evaluation) approach. The GRADE approach defines the quality of a body of evidence as the extent to which one can be confident that an estimate of effect or association is close to the true quantity of specific interest. The quality of a body of evidence involves consideration of within-trial risk of bias (methodological quality), directness of evidence, heterogeneity, precision of effect estimates and risk of publication bias (Schunemann 2011b). We planned to present the following outcomes in the 'Summary of findings' tables.

- Time to complete ulcer healing when analysed using appropriate survival analysis methods.

- Proportion of ulcers completely healing during the trial period.
- Change in wound area
- Adverse events.

Subgroup analysis and investigation of heterogeneity

When possible, we planned to perform a subgroup analysis to explore the influence of the following factor on effect sizes.

- Ulcer category: when possible, we anticipated assessing whether there were differences in effect sizes for stage II pressure ulcers and for the more severe stage III and stage IV pressure ulcers.

Sensitivity analysis

When possible, we planned to perform sensitivity analyses to explore the influence of the following factor on effect sizes.

- Risk of bias: we planned to assess the influence of removing from meta-analyses studies classed as having high and unclear risk of bias. We would include only studies that were assessed as having low risk of bias in all key domains, namely, adequate generation of the randomisation sequence, adequate allocation concealment and blinding of outcome assessor, for the estimates of treatment effect.

Results

Description of studies

See Characteristics of included studies; Characteristics of excluded studies

Results of the search

The search generated 621 records: we obtained 29 of these records, pertaining to 25 different studies (Figure 1). We are not aware of any relevant on-going studies (registers checked 26 July 2014). We located no new studies by searching reference lists as any relevant studies had been identified in the electronic searching. One study is on-going and this has been detailed here: Characteristics of ongoing studies

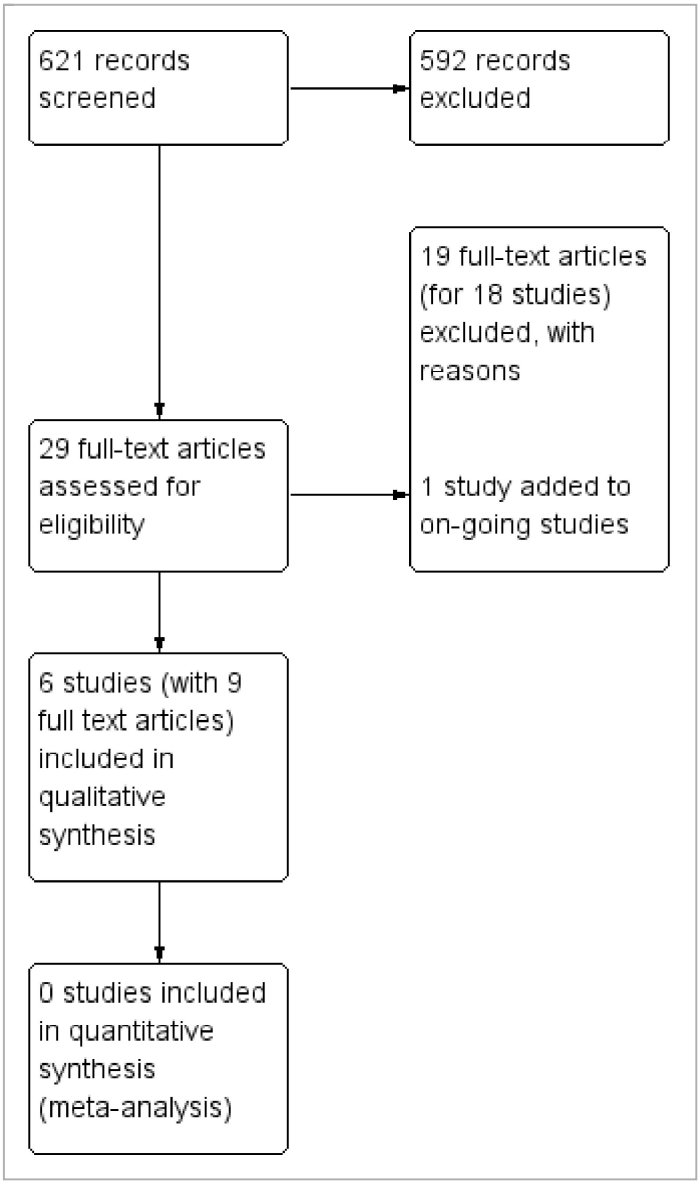

Figure 1.

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Study flow diagram.

Included studies

This review included six studies (**Belmin 2002**; **Brown-Etris 1997**; **Chuangsuwanich 2013**; **Meaume 2005**; **Price 2000**; **Sayag 1996**), which together contained 336 participants. All included studies had two arms. Three studies were conducted in France (**Belmin 2002**; **Meaume 2005**; **Sayag 1996**); one in the USA (**Brown-Etris 1997**); one in Thailand (**Chuangsuwanich 2013**), and one in the UK (**Price 2000**). Five studies had duration of follow up of eight weeks or less and the follow-up time in one study was not clear but was thought to be eight weeks (**Brown-Etris 1997**; see Table 1):

Table 1. Summary of studies

Study ID	Group A	Group B	Group C	Follow-up time	Complete healing data reported?
Belmin 2002	Calcium-alginate dressings (UrgoSorb, Urgo, France) for the first 4 weeks, and then hydrocolloid dressings (Aloplaque HP, Urgo, France) for the next four weeks (n = 57)	Hydrocolloid dressing (Duoderm E, Convatec-Bristol Myers Squibb) on the target ulcer for 8 weeks (n = 53)	n/a	8 weeks	No
Brown-Etris 1997	Collagen-alginate dressing (Fibracol, Johnson & Johnson; n = 24)	Calcium-alginate dressing (Kaltostat Convatec; n = 12)	n/a	Not clear	Yes
Chuangsuwanich 2013	Silver-alginate dressing (Askina Calgitrol Ag; B Braun Hospicare Ltd., Collooney, Co. Sligo, Ireland; n = 10, 15 wounds)	Silver-zinc sulfadiazine cream (prepared in-house; n=10, 13 wounds)	n/a	8 weeks	No
Meaume 2005	Silver-alginate dressing (Silvercel; n = 13)	Calcium-alginate dressing (Algosteril; n = 15).	n/a	4 weeks	No
Price 2000	Alginate dressing (choice of alginate dressing decided by centres; n = 25)	Radiant heat system (Warm-up, Augustine Medical Inc, USA; n = 25)	n/a	6 weeks	Yes
Sayag 1996	Calcium-alginate dressings (Algosteril; n = 47)	Dextranomer paste dressing (Debrisan; n = 45)	n/a	8 weeks	No

- four weeks (Meaume 2005);
- six weeks (Price 2000);
- eight weeks (Belmin 2002; Chuangsuwanich 2013; Sayag 1996);
- not clear (Brown-Etris 1997).

The following types of alginate dressing were evaluated: calcium-alginate dressings (Belmin 2002; Brown-Etris 1997; Meaume 2005; Sayag 1996); collagen-alginate dressings (Brown-Etris 1997); silver-alginate dressings (Chuangsuwanich 2013; Meaume 2005), and a mixed alginate dressings group (Price 2000; also see Table 1). In this review we consider all non-silver-alginate dressings to be a single group called 'alginate dressings' and silver-containing alginate dressings to be another separate group called 'silver-alginate dressings'.

The included studies made the six different treatment comparisons listed below:

- alginate dressing compared with hydrocolloid dressing (Belmin 2002);
- alginate dressing compared with a different alginate dressing (Brown-Etris 1997);
- alginate dressing compared with dextranomer paste dressing (Sayag 1996);
- silver-alginate dressing compared with alginate dressing (Meaume 2005);
- silver-alginate dressing compared with silver-zinc sulfadiazine cream (Chuangsuwanich 2013);
- alginate dressing compared with radiant heat system (Price 2000).

Excluded studies

In total 18 studies were excluded from the review for the following reasons (see Characteristics of excluded studies):

- nine studies did not evaluate an alginate dressing (Bito 2012; Brod 1990; Kurzuk-Howard 1985; Manzanero-Lopez 2004; Meaume 2003; Moody 1993; Oleske 1986; Perez 2000; Torra i Bou 1999);
- two studies did not report a relevant outcome (study authors were contacted where possible to request further information if available; Llewellyn 1996; Hock 1996);
- three studies were not RCTs (Parnell 2005; Saydak 1990; Weheida 1991);
- we could not confirm whether one study was an RCT (Sanchez 2002);
- one study included a mixed wound population and separate pressure ulcer data were not available (Beele 2010);
- the grade of included ulcers was not clear in one study (Trial 2010);
- use of alginate dressing was not the only systematic difference between trial groups in one study (Chirwa 2010).

Risk of bias in included studies

See Figure 2; Figure 3

Figure 2.

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Risk of bias summary: review authors' judgements about each risk of bias item for each included study.

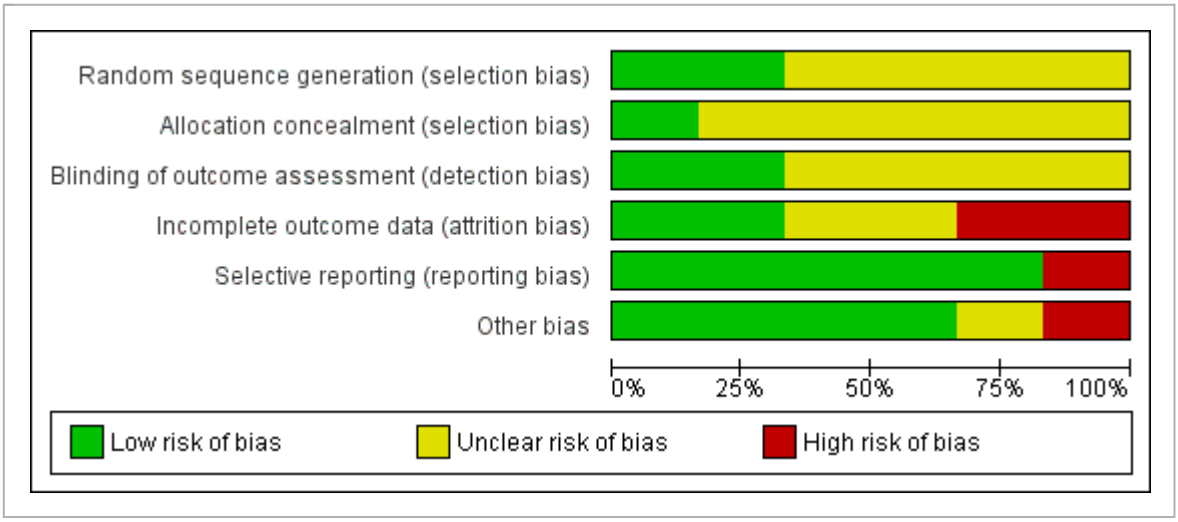

Figure 3.

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Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.

Allocation

Random sequence generation

Two studies were classed as being at low risk of bias for random sequence generation (Meaume 2005; Price 2000). There was appropriate use of computer-generated randomisation schedules in Price 2000, and Meaume 2005 used randomisation lists. The remaining four studies did not provide information about generation of randomisation sequence and were classed as being at unclear risk of bias.

Allocation concealment

We classed one study as being at low risk of bias for this domain as it used sequentially numbered, sealed envelopes (Sayag 1996). All other studies were classed as being at unclear risk of bias for this domain.

Blinding

We judged Chuangsuwanich 2013 and Price 2000 to be at low risk of bias for outcome assessment of reported outcomes relevant to this review. The remaining studies we judged to be at unclear risk of bias.

Incomplete outcome data

We deemed two studies to be at high risk of bias for incomplete outcome data (Brown-Etris 1997; Price 2000). Brown-Etris 1997 presented an interim analysis on 36 participants from a possible 80 enrolled. Price 2000 seemed to have made eight post-randomisation exclusions

(58 participants randomised and 50 included in the analysis). The remaining studies we judged to be at low or unclear risk of bias for this domain.

Selective reporting

One study was judged to be at high risk of bias for selective reporting. **Brown-Etris 1997** presented limited information in its report but did suggest that time to event data were collected but these were not presented in the study report. We classed the remaining studies as being at low risk of bias based on the reports available for this review. We obtained no protocols.

Other potential sources of bias

Chuangsuwanich 2013 had potential unit of analysis issues as some of the enrolled participants had more than one wound, and it seemed that data were presented at wound level rather than participant level. All other studies were considered to be at low risk of bias for this domain except **Brown-Etris 1997**, which was deemed to be at unclear risk of bias due to the limited information available.

Effects of interventions

See: **Summary of findings for the main comparison** Alginate dressing followed by hydrocolloid dressing compared with hydrocolloid dressing alone; **Summary of findings 2** Comparison between different alginates; **Summary of findings 3** Alginate compared with dextranomer paste; **Summary of findings 4** Silver-alginate compared with plain alginate; **Summary of findings 5** Alginate compared with radiant heat system

See Table 2 for extracted outcome data.

Table 2. Outcome table

Study	Comparison	Length of follow-up	Time to healing data	% Ulcer healed	Change in ulcer size	Healtl relate qualit life
Belmin 2002	**Group A:** calcium-alginate dressings for 4 weeks followed by hydrocolloid for 4 weeks (n = 57) **Group B:** hydrocolloid dressings (n = 53)	8 weeks	**Not reported**	**Not reported**	**% reduction in area compared with baseline** Adjusted Group A: 69.1% (SD 33.9); Group B: 42.6% (SD 49.1)	**Not** repor

Brown-Etris 1997	Group A: collagen-alginate dressing (n = 24) Group B: calcium sodium alginate dressing (n = 12)	8 weeks	**Not reported**	**Proportion healed** Group A: fully healed = 3/24 (12.5%); Group B: 1/12 (8.3%)	**Non-adjusted:reduction in wound size** Group A: 17/24 (70.3%); Group B 5/12 (41.7%)	**Not repor**
Chuangsuwanich 2013	Group A: silver-alginate dressing (n = 10, 15 wounds) Group B: silver-zinc sulfadiazine cream (n = 10, 13 wounds)	8 weeks	**Not reported**	**Not reported**	**% reduction in wound area** Group A: 44.27%; Group B: 51.07%	**Not repor**
Meaume 2005	Group A: silver-releasing hydroalginate dressing (n= 15) Group B: calcium-alginate dressing (n = 13)	4 weeks	**Not reported**	**Not reported for pressures ulcers only**	**% reduction in area compared with baseline** Adjusted Group A: -31.6% (SD 38.1); Group B: -13.9% (SD 50.3)	**Not repor**
Price 2000	Group A: alginate dressing (n = 25) Group B: radiant heat dressing (n = 25)	6 weeks	**Not reported**	Group A: 2/25 (8.0%); Group B: 3/25 (12%)	**% reduction in area compared with baseline** Adjusted Group A: -22.8% (SD 75.0); Group B -54.6% (SD 39.9)	**Not repor**

Sayag 1996	Group A: calcium-alginate dressings (n = 47) Group B: dextranomer paste dressing (n = 45)	8 weeks	Not reported	Not reported	**Mean change per week Not adjusted.** Group A 2.39cm² (SD 3.24) Group B 0.27cm² (SD 0.27)	Not repor

Comparison 1: alginate dressing followed by hydrocolloid dressing compared with hydrocolloid dressing alone (1 trial; 110 participants)

One study compared use of an alginate dressing for four weeks followed by a hydrocolloid dressing for four weeks with use of a hydrocolloid dressing alone (Belmin 2002). The study had an eight-week follow-up and was classed variously as being at unclear or low risk of bias across the six domains assessed. The study population was people 65 years or older with a pressure ulcer involving subcutaneous tissue and no evidence of wound infection.

Primary outcome: complete wound healing

The Belmin 2002 trial did not report complete wound healing.

Secondary outcome: change in wound size (proportion reduction in area compared with baseline)

Belmin 2002 reported a greater reduction in the mean percentage wound area with the alginate-hydrocolloid (69.1% reduction (standard deviation (SD) 33.9) in the alginate-hydrocolloid group compared with 42.6% reduction (SD 49.1) in the hydrocolloid: MD 26.50 (95% CI 10.62 to 42.38). *Very low quality of evidence due to indirectness of outcome and imprecision.*

Secondary outcome: wound infection

There was only one infection reported in the study (no definition of how wound infection was defined was provided) and it is therefore unclear whether there is a difference between these dressing regimens in the risk of infection: RR 2.79 (95% CI 0.12 to 67.10). V *ery low quality of evidence due to imprecision.*

Secondary outcome: adverse events

The study definition of an adverse event included all participants who experienced an adverse event and included the wound infection figures reported above. There was no evidence of a difference in the number of participants with adverse events in the alginate-hydrocolloid group 10.5% (6/57) compared with the hydrocolloid group 9.4%% (5/53) although there is high uncertainty (imprecision) around the estimate: RR 1.12 (95% CI 0.36 to 3.44). *Low quality of evidence due to imprecision.*

Secondary outcomes: resource use

There was on average almost one more dressing removal per week with the alginate-hydrocolloid than the hydrocolloid alone (3.8 removals per week (SD 1.6) in the alginate-hydrocolloid group vs. 2.9 (SD 1.0) in the hydrocolloid group: MD 0.90 (95% CI 0.41 to 1.39).

Secondary outcomes: health-related quality of life, costs, wound recurrence

Not reported.

Summary: alginate-hydrocolloid compared with hydrocolloid alone

Available data reported evidence of a mean percentage reduction in ulcer area over the eight-week period and reduced number of dressing changes favouring treatment with an alginate-hydrocolloid dressing sequence over hydrocolloid alone. There was no evidence of a difference in other outcomes. *Low or very low quality of evidence due to indirectness and/or imprecision* - Summary of findings for the main comparison.

Comparison 2: comparison between different alginates (1 trial; 36 participants)

One study compared a collagen-alginate dressing with a calcium-alginate dressing in people with pressure ulcers of stage II to IV (**Brown-Etris 1997**). The duration of follow-up was unclear but may have been eight weeks. The study was classed as being at high risk of attrition bias and reporting bias.

Primary outcome: complete wound healing (proportion of wounds healed)

There was no evidence of a difference in the number of completely healed wounds in groups treated with alternative alginate dressings; 12.5% (3/24) compared with 8.3% (1/12): RR 1.50 (95% CI 0.17 to 12.94). The small size of this study means we cannot be confident that there is no difference. *Very low quality of evidence due to risk of bias and imprecision.*

Secondary outcomes: adverse events (wound deterioration)

There was no evidence of a difference in the number of wounds that deteriorated (no further details provided) with the different alternative alginate dressings:12.5% with collagen-alginate (3/24) compared with 25% (3/12) with calcium alginate: RR 0.50 (95% CI 0.12 to 2.12). Again we cannot be confident that there is no difference due to the small sample size. As it was unclear whether participants had multiple wound deterioration events recorded there may be a unit of analysis error. *Very low quality of evidence due to risk of bias and imprecision.*

Secondary outcomes: change in wound size, health related quality of life, wound infection, resource use, costs, wound recurrence

The **Brown-Etris 1997** trial did not report on these outcomes.

Summary: comparison between different alginates

The limited data available suggest no evidence of a difference in the number of pressure ulcers that healed or deteriorated when treated with alternative alginate dressings. The quality of evidence was very low - Summary of findings 2.

Comparison 3: alginate compared with dextranomer paste (1 trial; 92 participants)

One study compared an alginate dressing with dextranomer paste (Sayag 1996). The study had an eight-week follow-up and was classed as being at low or unclear risk of bias across the domains assessed. The study population had stage III or IV pressure ulcers.

Primary outcome: complete wound healing

Sayag 1996 did not report on complete wound healing.

Secondary outcomes: wound infection

There was no evidence of a difference in the number of wound infections requiring systemic antibiotic treatment with the alginate dressing4.3% (2/47), compared with the dextranomer paste 4.4% (2/45): RR 0.96 (95% CI 0.14 to 6.51). However, only four participants had wound infections so the estimate is uncertain (i.e. imprecise). *Very low quality of evidence due to imprecision.*

Secondary outcomes: adverse events

There was no evidence of a difference in the total number of participants having at least one adverse event between the alginate group, 8.0% (4/47) and the dextranomer paste group (22.2%) (10/45): RR 0.38 (95% CI 0.13 to 1.13). *Very low quality of evidence due to imprecision.*

Secondary outcomes: resource use (mean number of dressing changes per week)

There was no evidence of a difference in the mean number of dressing changes per week between the treatments. The alginate group had a mean of 4.28 (SD 1.49) dressings per week compared with 4.52 (SD 1.42) in the dextranomer group: MD -0.24 (95% CI -0.80 to 0.32).

Secondary outcomes: change in wound size, health-related quality of life, costs, wound recurrence

Sayag 1996 did not report on these outcomes.

Summary: alginate dressing compared with dextranomer paste

The limited data suggest no evidence of a difference in the number of adverse events or mean number of dressing changes between alginate dressings and dextranomer paste. The quality of evidence was very low - Summary of findings 3 .

Comparison 4: silver-alginate compared with plain alginate (1 trial, 28 participants)

One study compared a silver-alginate dressing with a plain alginate dressing (Meaume 2005). The study had a short follow-up period of four weeks and all participants had stage III or IV ulcers and at least two symptoms of wound infection.

Primary outcomes: complete wound healing

Meaume 2005 did not report on complete wound healing.

Secondary outcomes: change in wound size (proportional reduction in area compared with baseline)

There was no evidence of a difference in the proportional reduction in wound size between the silver-alginate dressing group (31.6%; SD 38.1), and the alginate group (13.9%; SD 50.3)*:* mean difference 17.70% (95% CI -13.07 to 48.47). There is wide variation around the estimates and the resulting mean difference estimate is imprecise. V *ery low quality of evidence due to indirectness of outcome and imprecision.*

Secondary outcomes: wound infection (modified ASEPSIS index score)

Meaume 2005 used a modified version of the ASEPSIS scoring system to quantify postoperative wound infections. Higher scores were worse, but the cut-point used to define the presence of infection for this modified scale was not reported. The mean mASPEPSIS score in the silver-alginate dressing group was 81.8 (SD 45.1) and 115.3 (SD 80.2) in the alginate group : mean difference: -33.50, (95% CI -82.71 to 15.71). *Very low quality evidence due to imprecision.*

Secondary outcomes: adverse events ,health-related quality of life, resource use, costs, wound recurrence

Meaume 2005 did not report on these outcomes.

Summary: silver-alginate compared with plain alginate

There was no evidence of a difference in effects on pressure ulcer area or infection over 4 weeks between silver-alginate and plain alginate dressings. Evidence was of very low quality - Summary of findings 4.

Comparison 5: silver-alginate compared with silver-zinc sulfadiazine cream (1 trial, 20 participants)

One study, Chuangsuwanich 2013, compared a silver-alginate dressing with a silver-zinc sulfadiazine cream in people with stage III or IV pressure ulcers. The study recruited a total of 20 participants with 28 wounds and the data appear to be presented at the wound rather than participant level (i.e., a unit of analysis error); for this reason the study was classed as being at high risk of bias.

Primary outcome: complete wound healing

Chuangsuwanich 2013 did not report on complete wound healing.

Secondary outcomes: change in wound size (proportion reduction in wound area)

There was a mean percentage reduction in ulcer area of 44% in the silver-alginate dressing group and 51% in the silver-zinc sulfadiazine cream group, but standard deviation or standard error were not reported and we did not obtain them.

Secondary outcomes: resource use (mean dressing cost)

The study reported average dressing costs of USD 377 in the silver-alginate dressing group and USD 468 in the silver-zinc sulfadiazine group. The trialists did not report any details of variation around these estimates.

Secondary outcomes: wound infection, adverse events, health-related quality of life, costs, wound recurrence.

Chuangsuwanich 2013 did not report on these outcomes.

Summary: silver-alginate dressing compared with silver-zinc sulfadiazine cream

It is unclear whether there is a difference in the effects of silver-alginate dressings and silver-zinc sulfadiazine on change in ulcer area. Data could not be analysed fully so viewed as very low quality.

Comparison 6: alginate compared with radiant heat system (1 study, 50 participants)

Price 2000 compared an alginate dressing with a radiant heat system in people with stage III and IV non-infected pressure ulcers. The study had a six-week follow-up periodThe study was classed as being at high risk of bias, as it seems that there was post-randomisation exclusion of participants.

Primary outcome: complete wound healing

Price 2000 did not report on complete wound healing.

Secondary outcomes: change in wound size (proportion reduction in wound area)

There was no evidence of a difference between the groups in mean reduction in ulcer area however this comparison is underpowered and a real difference cannot be ruled out. Mean reduction in area was 22.8% (SD 75.0) in the alginate dressing group and 54.6% (SD 39.9) in the radiant heat system group: mean difference -31.80 (95% CI -65.10 to 1.50). V *ery low quality of evidence due to indirectness of outcome and imprecision.*

Secondary outcomes: adverse events (pain - assumed to be wound related)

At six weeks, there was no evidence of a difference in mean pain score between groups. The mean pain score in the alginate dressing group was 17.2 (SD 19.7), and 16.5 (SD 21.4) in the radiant heat group *:* MD 0.70, (95% CI -10.70 to 12.10). V *ery low quality of evidence due to imprecision.*

Secondary outcomes: wound infection, health-related quality of life, resource use, costs, wound recurrence

Price 2000 did not report these outcomes.

Summary: alginate dressings compared with radiant heat system

It is unclear whether alginate dressings and a radiant heat system have differential effects on change in pressure ulcer area or any other outcome. Evidence was of very low quality - Summary of findings 5

Discussion

Summary of main results

This review includes all available RCT evidence evaluating alginate dressings to treat pressure ulcers and this amounts to six studies with a total of 336 participants. The studies compared alginate dressings with six alternative treatments: a hydrocolloid dressing; another alginate dressing; silver-alginate dressing; dextranomer paste dressing; a silver-zinc sulfadiazine cream and a radiant heat treatment. In two comparisons the alginate dressing assessed was a silver dressing (silver-alginate dressing compared with alginate dressing, and silver-alginate dressing compared with silver-zinc sulfadiazine cream). Overall the body of literature was very limited: each comparison was only informed by one study, each was small and underpowered to detect differential treatment effects, should they exist. We also note that there may be comparisons that are important to decision makers for which trials have not been conducted.

The primary outcome for this review was complete wound healing, though only one included study reported this outcome. Brown-Etris 1997 compared two non silver-alginate dressings and reported the data on proportion of wounds healed. There was no evidence of a difference in the number of ulcers healed between groups. The study was small and underpowered and the GRADE assessment classed the estimate from this evidence as being of very low quality.

In terms of secondary outcomes, change in wound size (adjusted for baseline size) was presented in four studies - all reporting percentage reduction in area compared with baseline (Belmin 2002; Chuangsuwanich 2013; Meaume 2005; Price 2000). Only one study (Belmin 2002), that compared a alginate dressing with a hydrocolloid dressing, reported a statistically significant reduction in ulcer area in the alginate group.

Belmin 2002 also reported a small but statistically significant difference in the mean number of dressing changes in the sequential use of an alginate dressing compared with use of

hydrocolloid alone. There was no evidence of a difference in any other secondary outcomes reported including adverse events and wound infection. All GRADE assessments showed that adverse events and wound infection estimates that were presented were of low or very low quality.

Quality of the evidence

Limitations of design and implementation

RCTs need to be adequately powered so that they are able to detect treatment effects of a specified size if they exist. This means that sample size calculations should be used to help estimate the number of people recruited to a trial. Additionally trials should have an adequate follow-up period so that there is enough time in which important outcome events, such as complete wound healing, can occur. The trials included in this study were all small and their follow-up periods were generally short. This resulted in an evidence base with almost no complete healing data: generally the relevant outcome data that were reported were underpowered and imprecise, with wide confidence intervals.

All studies included study in this review were at a high or unclear risk of bias. In general studies did not follow good practice for conduct and reporting guidelines, for example CONSORT (Schulz 2010). Key areas of good practice are the robust generation of a randomisation sequence, for example one that is computer-generated, robust allocation concealment, for example by use of a telephone randomisation service, and blinded outcome assessment where possible. All this information should be clearly stated in the study report, as all trial authors should anticipate the inclusion of their trials in systematic reviews. Additionally studies should report clearly how they planned to collect adverse event data and how this process was standardised for both treatment arms. In terms of analysis, where possible, data from all participants should be included, that is, an intention-to-treat analysis should be conducted and measures of variation such as the standard deviation or standard error should be presented around measures where appropriate. Steps should be taken as far as is possible while conducting trials to prevent missing data .

Where possible studies should also use validated scales to measure outcomes. The use of unvalidated scales, including those that have been modified in an ad hoc way, can limit the value of collected data, as it can be difficult to interpret and to synthesis across studies.

Potential biases in the review process

The review considered as much evidence as it was possible to obtain, including studies that were not published in English-language journals. It is possible that there may be unpublished data that we have not been able to access. There is a potential for publication bias, however, this is likely to be a limited issue in this review given the large number of negative findings that have been published.

Agreements and disagreements with other studies or reviews

No other reviews have presented data on alginate dressings as transparently as they are presented here. Our findings do generally agree with the conclusion of a large review that looked at several treatments for pressure ulcers and concluded that, "No single dressing was

consistently superior to other dressings in the trials of pressure ulcers we examined" (Reddy 2008). In relation to dressings, the recent National Institue of Health and Clinical Effectiveness (NICE) Pressue Ulcer Guidelines state that "a dressing for adults that promotes a warm, moist wound healing environment to treat grade 2, 3 and 4 pressure ulcers" should be considered (NICE 2014). Also that gauze dressings should not be offered to treat a pressure ulcer in adults. The NICE review includes all studies included here and we included three studies that were not in the NICE guidelines (Brown-Etris 1997; Chuangsuwanich 2013; Price 2000).

Authors' conclusions

Implications for practice

A comprehensive review of current evidence did not evidence of differential effects of alginates and alternative wound treatments on the outcomes that matter for pressure ulcers (including healing). Practitioners may therefore elect to consider other characteristics such as costs and symptom management properties when choosing between alternatives.

Implications for research

Currently there is no evidence of a difference in ulcer healing between alginate-dressed ulcers and those treated with the other dressings and the topical treatment that have been evaluated. In terms of dressing choice, any investment in future research must maximise its value to decision-makers. Given the large number of dressing options, the design of future trials should be driven by high priority questions from patients and other decision makers. It is also important for research to ensure that the outcomes that are collected in research studies are those that matter to patients, carers and health professionals. Where trials are conducted, good practice guidelines must be followed in their design, implementation and reporting. Further reviews are being conducted to synthesise evidence regarding the effect of other dressings on the treatment of pressure ulcers. It would then be useful to conduct further evidence synthesis (overviews of reviews, network meta-analysis or both) to aid decision-making about the choice of dressings for pressure ulcers across all dressing options.

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Data and analyses

Download statistical data

This review has no analyses.

Appendices

Appendix 1. Searches

Database: Ovid MEDLINE(R) 1946 to June Week 2 2014 search strategy

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1 exp Bandages/ (19252)
2 exp Alginates/ (7152)
3 exp Hydrogels/ (10269)
4 exp Silver/ (14286)
5 exp Silver Sulfadiazine/ (780)
6 exp Honey/ (2346)
7 (dressing* or pad or pads or gauze or tulle or film or bead or foam* or non-adherent or non adherent or hydrocolloid* or alginat* or hydrogel* or silver* or honey* or matrix).tw. (384187)
8 or/1-7 (403527)
9 exp Pressure Ulcer/ (9730)
10 (pressure adj (ulcer* or sore* or injur*)).tw. (6721)
11 (decubitus adj (ulcer* or sore*)).tw. (1538)
12 (bedsore* or bed sore*).tw. (512)
13 or/9-12 (11789)
14 8 and 13 (1312)
15 randomized controlled trial.pt. (375822)
16 controlled clinical trial.pt. (88506)
17 randomi?ed.ab. (328137)
18 placebo.ab. (146697)
19 clinical trials as topic.sh. (170410)
20 randomly.ab. (194380)

21 trial.ti. (118324)
22 or/15-21 (880230)
23 exp animals/ not humans.sh. (3951750)
24 22 not 23 (809272)
25 14 and 24 (245)

Database: EMBASE 1974 to 2014 June 20 search strategy

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1 exp hydrogel dressing/ or exp occlusive dressing/ or exp wound dressing/ (9624)
2 exp hydrogel/ (17690)
3 exp silver/ (26644)
4 exp sulfadiazine silver/ (2989)
5 exp sulfathiazole silver/ (19)
6 exp honey/ (4013)
7 (dressing* or pad or pads or gauze or tulle or film or bead or foam* or non-adherent or non adherent or hydrocolloid* or alginat* or hydrogel* or silver* or honey* or matrix).tw. (514123)
8 exp alginic acid/ (12790)
9 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 (538309)
10 exp decubitus/ (15266)
11 (pressure adj (ulcer* or sore* or injur*)).tw. (8643)
12 (decubitus adj (ulcer* or sore*)).tw. (1863)
13 (bedsore* or bed sore*).tw. (798)
14 10 or 11 or 12 or 13 (17265)
15 9 and 14 (1691)
16 Randomized controlled trials/ (53514)
17 Single-Blind Method/ (18404)
18 Double-Blind Method/ (116267)
19 Crossover Procedure/ (39225)
20 (random$ or factorial$ or crossover$ or cross over$ or cross-over$ or placebo$ or assign$ or allocat$ or volunteer$).ti,ab. (1337859)
21 (doubl$ adj blind$).ti,ab. (147331)
22 (singl$ adj blind$).ti,ab. (14565)
23 or/16-22 (1406033)
24 exp animals/ or exp invertebrate/ or animal experiment/ or animal model/ or animal tissue/ or animal cell/ or nonhuman/ (20358792)
25 human/ or human cell/ (14828728)
26 and/24-25 (14782050)
27 24 not 26 (5576742)
28 23 not 27 (1214106)
29 15 and 28 (278)

CINAHL search strategy 24 June 2014

S26 S13 AND S25
S25 S14 or S15 or S16 or S17 or S18 or S19 or S20 or S21 or S22 or S23 or S24

S24 MH "Quantitative Studies"
S23 TI placebo* or AB placebo*
S22 MH "Placebos"
S21 TI random* allocat* or AB random* allocat*
S20 MH "Random Assignment"
S19 TI randomi?ed control* trial* or AB randomi?ed control* trial*
S18 AB (singl* or doubl* or trebl* or tripl*) and AB (blind* or mask*)
S17 TI (singl* or doubl* or trebl* or tripl*) and TI (blind* or mask*)
S16 TI clinic* N1 trial* or AB clinic* N1 trial*
S15 PT Clinical trial
S14 MH "Clinical Trials+"
S13 S7 AND S12
S12 S8 OR S9 OR S10 OR S11
S11 TI decubitus or AB decubitus
S10 (bed sore* or bedsore*) or AB (bed sore* or bedsore*)
S9 TI (pressure ulcer* or pressure sore*) or AB (pressure ulcer* or pressure sore*)
S8 (MH "Pressure Ulcer+")
S7 S1 or S2 or S3 or S4 or S5 or S6
S6 TI (dressing* or alginate* or hydrogel* or hydrocolloid* or foam or bead or film or films or tulle or gauze or non-adherent or non adherent or honey or silver* or matrix) or AB (dressing* or alginate* or hydrogel* or hydrocolloid* or foam or bead or film or films or tulle or gauze or non-adherent or non adherent or honey or silver* or matrix)
S5 (MH "Honey")
S4 (MH "Silver")
S3 (MH "Silver Sulfadiazine")
S2 (MH "Alginates")
S1 (MH "Bandages and Dressings+")

Appendix 2. Risk of bias assessment (individually randomised controlled trials)

1. Was the allocation sequence randomly generated?

Low risk of bias

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

High risk of bias

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

Unclear

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

2. Was the treatment allocation adequately concealed?

Low risk of bias

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

High risk of bias

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

Unclear

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

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

Low risk of bias

Any one of the following.

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

High risk of bias

Any one of the following.

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

Unclear

Either of the following.

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

4. Were incomplete outcome data adequately addressed?

Low risk of bias

Any one of the following.

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

High risk of bias

Any one of the following.

- Reason for missing outcome data likely to be related to true outcome, with imbalance in numbers or reasons for missing data across intervention groups.

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

Unclear

Either of the following.

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

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

Low risk of bias

Either of the following.

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

High risk of bias

Any one of the following.

- Not all of the study's prespecified primary outcomes have been reported.
- One or more primary outcomes are reported using measurements, analysis methods or subsets of the data (e.g. subscales) that were not prespecified.
- One or more reported primary outcomes were not prespecified (unless clear justification for their reporting is provided, such as an unexpected adverse effect).
- One or more outcomes of interest in the review are reported incompletely so that they cannot be entered in a meta-analysis.

- The study report fails to include results for a key outcome that would be expected to have been reported for such a study.

Unclear

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

6. Other sources of potential bias

Low risk of bias

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

High risk of bias

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

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

Unclear

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

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

Appendix 3. Risk of bias assessment (cluster randomised controlled trials)

In cluster randomised trials, particular biases to consider include recruitment bias; baseline imbalance; loss of clusters; incorrect analysis; and comparability with individually randomised trials.

- Recruitment bias can occur when individuals are recruited to the trial after the clusters have been randomly assigned, as knowledge of whether each cluster is an 'intervention' or 'control' cluster could affect the types of participants recruited.
- Cluster randomised trials often randomly assigned all clusters at once, so lack of concealment of an allocation sequence should not usually be an issue. However, because small numbers of clusters are randomly assigned, there is a possibility of chance baseline imbalance between randomly assigned groups, in terms of the clusters or the individuals. Although not a form of bias as such, the risk of baseline differences can be reduced by using stratified or pair-matched randomisation of clusters. Reporting of the baseline comparability of clusters, or statistical

adjustment for baseline characteristics, can help reduce concern about the effects of baseline imbalance.

- Occasionally, complete clusters are lost from a trial and have to be omitted from the analysis. Just as for missing outcome data in individually randomised trials, this may lead to bias. In addition, missing outcomes for individuals within clusters may lead to risk of bias in cluster randomised trials.
- Many cluster randomised trials are analysed by incorrect statistical methods, without taking the clustering into account. Such analyses create a 'unit of analysis error' and produce overly precise results (the standard error of the estimated intervention effect is too small) and P values that are too small. They do not lead to biased estimates of effect. However, if they remain uncorrected, they will receive too much weight in a meta-analysis.
- In a meta-analysis including both cluster and individually randomised trials, or including cluster randomised trials with different types of clusters, possible differences between the intervention effects estimated need to be considered. For example, in a vaccine trial of infectious diseases, a vaccine applied to all individuals in a community would be expected to be more effective than vaccine applied to only half of the people. Another example is provided by a Cochrane review of hip protectors (Hahn 2005). The cluster trials showed a large positive effect, whereas individually randomised trials did not show clear benefit. One possibility is that there was a 'herd effect' in the cluster randomised trials (which were often performed in nursing homes, where compliance with using the protectors may have been enhanced). In general, such 'contamination' would lead to underestimates of effect. Thus, if an intervention effect is still demonstrated despite contamination in those trials that were not cluster randomised, a confident conclusion about the presence of an effect can be drawn. However, the size of the effect is likely to be underestimated. Contamination and 'herd effects' may be different for different types of clusters.

Contributions of authors

Jo Dumville developed the review and co-ordinated its development, completed the first draft of the review , co-ordinated edits of subsequent drafts, made an intellectual contribution, approved the final version before submission and is the guarantor of the protocol.
Nikki Stubbs completed the first draft of the review and made an intellectual contribution to and approved the final version of the review before submission.
Samantha Keogh completed the first draft of the review and made an intellectual contribution to and approved the final version of the review before submission.
Rachel Walker completed the first draft of the review and made an intellectual contribution to and approved the final version of the review before submission.
Matthew Fortnam commented on the review draft and approved the final version of the review before submission.

Zhenmi Liu commented on the review draft and approved the final version of the review before submission.

Contributions of the editorial base

Nicky Cullum: advised on methodology, interpretation and content; and edited the review and approved the review for submission.
Sally Bell-Syer: co-ordinated the editorial process; advised on methodology, interpretation and content; and edited the review.
Amanda Briant: ran the searches.

Declarations of interest

Jo C Dumville: nothing to declare.
Samantha Keogh: nothing to declare.
Nikki Stubbs has received funding from pharmaceutical companies to support training and education events in the NHS where she works and payments have been received by the author for non product-related educational sessions. These have been unrelated to the subject matter of the systematic review and have never been in support or in pursuit of the promotion of products.
Rachel Walker: is currently employed by the National Health and Medical Research Council's Centre of Research Excellence in Nursing (NCREN), Griffith University Australia. Skin integrity including pressure ulcers is a research focus of NCREN.
Matthew Fortnam: nothing to declare.
Zhenmi Liu: nothing to declare

This protocol/review is part of a suite of reviews investigating the use of individual dressing types in the treatment of pressure ulcers. The first review in this suite was developed by co-author Samantha Keogh. The objective of undertaking these reviews is to use them in an overview which draws together all existing Cochrane review evidence regarding the use of dressing treatments for pressure ulcers to guide clinician decision-making.

Sources of support

Internal sources

- The National Institute for Health Research (NIHR) is the sole funder of the Cochrane Wounds Review Group, UK.
- School of Nursing, Midwifery and Social Work. University of Manchester, UK.

External sources

- NIHR Cochrane Programme Grant Project: 13/89/08 - High Priority Cochrane Reviews in Wound Prevention and Treatment, UK.

Differences between protocol and review

Change in wound size was assessed as an outcome in summary of finding assessment. Unit of analysis text changed.

Characteristics of studies

Characteristics of included studies [ordered by study ID]

Belmin 2002

Methods	A multicentre, parallel, randomised controlled trail of with 110 participants Conducted in France Follow-up was 8 weeks
Participants	Participants were recruited from 20 geriatric hospital wards Inclusion criteria listed: aged 65 years and older; having at least 1 pressure ulcer that passed through the subcutaneous tissue; pressure ulcer must be on sacrum, elsewhere on the pelvic girdle, or on the heel; pressure ulcer must have surface area less than 50 cm^2 with granulation tissue not covering more than 50% of the ulcer surface; and no evidence of local infection Exclusion criteria listed: serum albumin below 25 g/L, concurrent treatment with radiotherapy, cytotoxic drugs or corticosteroids; or if surgical or palliative care was needed
Interventions	Group A: calcium-alginate dressings (UrgoSorb, Urgo, France) for the first 4 weeks, and then hydrocolloid dressings (Aloplaque HP, Urgo, France) for the next 4 weeks (n = 57) Group B = hydrocolloid dressing (Duoderm E,Convatec-Bristol Myers Squibb) on the target ulcer for 8 weeks (n = 53)
Outcomes	Primary outcomes None reported Secondary outcomes Change in ulcer area (adjusted) Wound infection Adverse event (local adverse events; pain at dressing removal)

	Resource use (number of dressing removals per week)
Notes	Study confirmed that only 1 ulcer per participant was considered in the study Funding source: not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quotation: "Each patient was randomized to one of the two treatment strategies. The randomization was balanced by center and by blocks of four patients" Comment: not clear how random sequence was generated
Allocation concealment (selection bias)	Unclear risk	Quotation: "Each patient was randomized to one of the two treatment strategies. The randomization was balanced by center and by blocks of four patients" Comment: not clear whether allocation to treatment was concealed
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quotation: "For each tracing, the surface area was measured in triplicate by an independent investigator unaware of treatment allocation, using a digitilization table and computer program (AutoCAD), and the mean value was included in the analysis" Comment: adequate evidence of blinding out outcome measure for change in area Other outcomes: Quotation: "Because the appearance and use of the hydrocolloid and alginate dressings were very different, it was not possible to conduct the trial under blinded conditions" Comment: personnel not blinded to intervention during study
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	No direct quotation addressing this aspect Comment: data appear to be presented for all participants
Selective reporting (reporting bias)	Low risk	Comment: based on the paper only, protocol not obtained
Other bias	Low risk	No unit of analysis issue confirmed

Brown-Etris 1997

Methods	Prospective, parallel, randomised control trial of 36 participants Conducted in USA Used unequal randomisation (2:1 ratio) Duration of follow-up unclear
Participants	Participants recruited from 2 centres in the USA Inclusion criteria listed: stage II, III, IV pressure ulcers Exclusion criteria: not specified
Interventions	Group A: collagen-alginate dressing (Fibracol, Johnson & Johnson; n = 24) Group B: calcium-sodium alginate dressing (Kaltostat Convatec; n = 12)
Outcomes	Primary outcome Proportion healed Secondary outcomes Change in area (not adjusted) Adverse events (wound deterioration)
Notes	Abstract only. The abstract reported that 116 participants were enrolled and data from 80 participants were 'considered evaluable'. The interim analysis then presented data on 36 participants. Trial progress was not clear from available text. The report stated that the duration of the study was 8 weeks, but it is not clear how long people were followed up for Funding source: not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quotation: " . . . participants were stratified before randomization according to pressure ulcer location and size" Comment: no indication of how randomisation was achieved
	Unclear risk	

Allocation concealment (selection bias)		Quotation: " . . . participants were stratified before randomization according to pressure ulcer location and size" Comment: no indication of how randomisation was achieved or if allocation was concealed to investigators
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quotation: "A complete wound assessment, tracing and photography were completed weekly. The dressing change frequency was dependent on exudate level and was recorded" Comment: not clear if those assessing wounds were blinded to the intervention. The study was described as open but it is not clear if this related to outcome assessment also
Incomplete outcome data (attrition bias) All outcomes	High risk	No direct quotation addressing this aspect Comment: the abstract reported that 116 participants were enrolled and data from 80 participants were 'considered evaluable'. The interim analysis then presented data on 36 participants. Trial progress was not clear from available text
Selective reporting (reporting bias)	High risk	No direct quotation addressing this aspect Comment: limited information on which to judge, but the abstract notes that time-to-event data were collected and these were not presented. Generally, outcome data from only a selected group of the trial population seem to have been presented
Other bias	Unclear risk	None noted but limited information available

Chuangsuwanich 2013

Methods	2-arm RCT Single-centred, undertaken in Thailand Duration of follow-up was maximum of 8 weeks
Participants	20 participants with 28 wounds Inclusion criteria listed: people suffering from pressure ulcer(s) in the sacral or trochanteric area; pressure ulcers of grades ranging from III to IV according to the NPUAP pressure ulcer staging system; co-operation of the patient or her/his relatives who could complete the consent form and have regular weekly visits according to the study protocol; aged > 20 years Exclusion criteria listed: pressure ulcers with necrotic tissue that could not be managed with adequate debridement; pressure ulcers with clinical evidence of apparent infection, e.g. ulcers surrounded by an advancing, indurated red border, warm or tender, with purulent exudate, or accompanied by a bad odour; patients with a known history of hypersensitivity to any part of the drugs or products used in this study including calcium-alginate, polyurethane foam, or

	silver derivatives; patients with a known history of hypersensitivity to sulfa derivatives; patients with a history of glucose-6-phosphate dehydrogenase deficiency
Interventions	Group A: silver-alginate dressing (Askina Calgitrol Ag; B Braun Hospicare Ltd., Collooney, Co. Sligo, Ireland; n = 10, 15 wounds), changed every 3 days until completion of the study Group B: silver-zinc sulfadiazine cream (prepared in-house; n = 10, 13 wounds), changed once a day with dry gauze placed as an outer dressing Co-intervention: the wounds were debrided as necessary to remove all necrotic tissue
Outcomes	Primary outcome None reported Secondary outcomes Change in wound area (mean % change in wound size at study end; reduction in wound size by subject over time) Cost of treatment (average of overall cost of treatment which included including the dressing change workload, gauze, and silver-zinc cream; debridement cost including the workload, surgical instruments, and procedural charge and the product costs
Notes	Funding source: notes that a product used in this study was donated by B Braun. Paper also notes that, "No potential conflict of interest relevant to this article was reported." Unit of analysis issues

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quotation: "The enrolled patients were randomly divided into two groups by drawing from a sealed envelope for each group." Comment: method of generation of random schedule reported. It was not clear whether envelopes were sequentially numbered to ensure random sequence was maintained
	Unclear risk	No direct quote addressed this aspect

Allocation concealment (selection bias)		Comment: not stated how the allocation was conducted
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quotation: "After the wound was cleansed by nurse, it was examined and scored by an independent operator, plastic surgeon, who was blinded to the dressing protocol. The wound was measured and evaluated for changes in the wound size, grade, tissue characteristics, and amount of exudate. The photography of the wound bed was recorded." Comment: the process described and an indication of blinding in assessment of the outcomes
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: clear from the study how many participants withdraw and the reasons. Analysis was performed on 20 of the 22 randomised participants.
Selective reporting (reporting bias)	Low risk	Comment: based on the paper only, protocol not obtained
Other bias	High risk	Some of enrolled participants had more than one wound – unit of analysis issues

Meaume 2005

Methods	2-arm RCT Conducted in France; 13 centres, geriatric departments Follow-up was 4 weeks
Participants	99 participants (101 randomised and 2 post-randomisation exclusions), 28 of whom had pressure ulcers and the remaining study population had venous leg ulcers. Only information relevant to the pressure ulcer population are presented Relevant inclusion criteria listed: hospitalised adult patients or patients who could be seen every day for 14 days by the investigators; a grade III-IV (NPUAP system) pressure ulcer located on the ischium, sacrum, trochanter or heel; at least 50% of the wound covered in yellow slough, discoloured or friable granulation tissue, pocketing or undermining at the base of the wound or foul odour. Also in the investigator's opinion no clear signs of infection requiring the use of systemic antibiotics or lymphangitis and/or fever present but at least 2 of the following criteria were required: continuous pain; erythema; oedema; heat; moderate to high levels of serous exudate Exclusion criteria listed: people who had received systemic antibiotics during the previous 5 days for any reason. Those with a very poor life expectancy or with a clinical condition that might interfere with wound healing. People who had received topical chemical debridement within the previous 7 days

Interventions	Group A: silver-releasing hydroalginate dressing (Silvercel; n = 13) Group B: calcium-alginate dressing (Algosteril; n = 15)
Outcomes	Primary outcome Not reported for pressure ulcers specifically Secondary outcomes Change in wound area (adjusted) Wound infection (mASEPSIS index score)
Notes	Study randomised those with pressure ulcers and venous leg ulcer. Only data from pressure ulcers are presented Funding source: study was funded by a grant from Johnson and Johnson Wound Management

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Quotation: "Two *a priori* randomisation lists were prepared and balanced by blocks of six: one list was venous leg ulcers and one list for pressure ulcers (stratification). Each participating centre was provided with at least one block for each type of wound" Comment: evidence of appropriate randomisation method
Allocation concealment (selection bias)	Unclear risk	Quotation: "Two *a priori* randomisation lists were prepared and balanced by blocks of six: one list was venous leg ulcers and one list for pressure ulcers (stratification). Each participating centre was provided with at least one block for each type of wound" Comment: unclear as to how allocation to treatment was concealed from personnel
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote "The mASEPSIS scoring system, a well-validated tool, was developed to quantify postoperative wound infections and evaluate the effectiveness of antibiotics prophylaxis prior to cardiac surgery. The modified ASEPSIS Index prolongs ASEPSIS use over 14 days without changing its scoring rate" Comment: unclear if investigators using the mASEPSIS scoring system were blinded to intervention.
Incomplete outcome data	Low risk	No direct quotation to inform here: all those with pressure ulcers seem to have been included in an intention-to-treat analysis

(attrition bias) All outcomes		Comment: adequate evidence to award low risk judgement
Selective reporting (reporting bias)	Low risk	Quotation: "The primary endpoint was the mASEPSIS index score obtained in the first two weeks of treatment" Comment: outcome fully described in results analysis, therefore low risk judgement given
Other bias	Low risk	None noted

Price 2000

Methods	2-arm RCT Conducted in single UK centre 6 weeks follow-up
Participants	58 participants were randomised - only 50 were included in the analysis Inclusion criteria listed: stage III and stage IV dermal non-infected ulcers Exclusion criteria listed: those with existing dermatitis, a history of sensitivity to adhesive products, or taking oral corticosteroids
Interventions	Group A: alginate dressing (choice of alginate dressing decided by centres; n = 25) Group B: radiant heat system (Warm-up, Augustine Medical Inc, USA; n = 25)
Outcomes	Primary outcome Complete wound healing (proportion ulcers healed) Secondary outcomes Change in ulcer size (proportion reduction in area relative to baseline; adjusted) Adverse events (pain scores)
Notes	Funding source: not reported
Risk of bias	

Bias	**Authors' judgement**	**Support for judgement**

Random sequence generation (selection bias)	Low risk	Quotation: "Randomisation was achieved using a computer-generated list" Comment: adequate evidence to award a low risk judgement
Allocation concealment (selection bias)	Unclear risk	Quotation: " . . . allocation [was] concealed in opaque envelopes; once a subject was recruited the next envelope was opened" Comment: not clear the envelopes were sequential and/or that they were opened by an independent person
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quotation: "Subject demographics and detailed medical and wound histories were recorded, and weekly assessments carried out by one of two research nurses who had been blinded to the study treatment, and included: Wound dimensions (length, breadth, depth); acetate tracings; assessment of subjective rating of wound pain, using a visual analogue scale; recording of condition of surrounding skin, using 'yes/no' tick boxes to note presence of healthy, fragile, dry, macerated, oedematous, inflamed, or sweating skin."
Incomplete outcome data (attrition bias) All outcomes	High risk	Quotation: "Fifty-eight patients were enrolled to ensure that 50 were evaluable for the primary outcomes of the study: evaluable was defined as inclusion up to week 3 of the intervention. Of the eight patients lost, seven had been allocated the experimental group and one to the control group. Three died within two weeks of recruitment, three experienced a general deterioration in their condition within one week, one and asked to withdraw. Apart from the device-related incident (an allergic reaction to the adhesive), no other withdrawal was related heat therapy" Comment: evidence of post-randomisation exclusion
Selective reporting (reporting bias)	Low risk	No direct quotations, but all outcomes (healing rates, temperature, skin condition and pain) were fully reported in the results
Other bias	Low risk	None noted

Sayag 1996

Methods	2-arm RCT Participants recruited from 20 centres, 17 of which were elderly care centres and 3 of which were dermatology centres The study authors are based in France - it seems likely that this is where the study was conducted, but this was not stated explicitly Follow-up for a maximum of 8 weeks

mASEPSIS: modified ASEPSIS

[a] **Abbreviation** RCT: randomised controlled trial

Participants	92 participants Inclusion criteria listed: 60 years of age or more; being a hospital in-patient for at least 8 weeks; having a Grade III or IV pressure ulcer (Yarkony's classification) with a surface area between 5 cm^2 and 100 cm^2 Exclusion criteria listed: patients with ulcers where more than half of the total ulcer area comprised granulation tissue; those who had pressure ulcers covered by necrotic plaques or with active infection. Those suffering with end-stage renal failure, presenting with end-stage arteriopathy of the lower limbs, or being treated with radiotherapy or cytotoxic drugs
Interventions	Group A: calcium-alginate dressings (Algosteril; n = 47) Group B: dextranomer paste dressing (Debrisan; n = 45) In both groups, sterile gauze was applied as a secondary dressing
Outcomes	Primary outcomes None reported Secondary outcomes Change in ulcer size (unadjusted - mean change per week) Wound infection (local infection requiring antibiotics) Adverse events (local adverse events) Resource use (mean number of dressing changes per week)
Notes	Funding source: study was funded by Les Laboratoires Brothier

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quotation: "Six sealed numbered envelopes containing the allocated treatments were given to each centre. Written consent was obtained from the patient or the patient's legal representative (in accordance with French clinical trial legislation) and treatment was then decided by allocating the envelope with the lowest number to each patient entering the study"

mASEPSIS: modified ASEPSIS

[a] **Abbreviation** RCT: randomised controlled trial

		Comment: evidence of allocation concealment, however not entirely clear how random sequence was generated
Allocation concealment (selection bias)	Low risk	Quotation: "Six sealed numbered envelopes containing the allocated treatments were given to each centre. Written consent was obtained from the patient or the patient's legal representative (in accordance with French clinical trial legislation) and treatment was then decided by allocating the envelope with the lowest number to each patient entering the study" Comment: evidence of sufficient allocation concealment
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quotation: "The study steering committee requested that two independent experts in microbiology undertake a blind assessment of the two laboratory reports for each patient. This comprised a blind review of the bacteriological raw data contained in each report for each patient on days 1 and 15." Comment: no other information for outcomes reported in this review
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Quotation: "During the eight-week study, treatment was stopped prematurely in 10 out of the 47 patients in the alginate group (21%) and in 22 of the 45 (49%) in the dextranomer group" Comment: it seems that all participants randomised were included in the analysis, although this is not completely clear as numbers of participant for whom data are available were not clearly presented in the results section
Selective reporting (reporting bias)	Low risk	All outcomes were reported as described in the methodology
Other bias	Low risk	None noted

mASEPSIS: modified ASEPSIS
[a] **Abbreviation** RCT: randomised controlled trial

Characteristics of excluded studies [ordered by study ID]

Study	Reason for exclusion
Beele 2010	The study population included a mixed wound population and separate pressure ulcer data were not available
Bito 2012	The study did not evaluate an alginate dressing
Brod 1990	The study did not evaluate an alginate dressing

Study	Reason for exclusion
Chirwa 2010	Use of alginate dressing was not the only systematic difference between trial groups
Hock 1996	The study did not report a relevant outcome (study authors were contacted where possible to request further information if available)
Kurzuk-Howard 1985	The study did not evaluate an alginate dressing
Llewellyn 1996	The study did not report a relevant outcome (study authors were contacted where possible to request further information if available)
Manzanero-Lopez 2004	The study did not evaluate an alginate dressing
Meaume 2003	The study did not evaluate an alginate dressing
Moody 1993	The study did not evaluate an alginate dressing
Oleske 1986	The study did not evaluate an alginate dressing
Parnell 2005	The study was not a randomised controlled trial
Perez 2000	The study did not evaluate an alginate dressing
Sanchez 2002	Could not confirm whether this was a randomised controlled trial
Saydak 1990	The study was not a randomised controlled trial
Torra i Bou 1999	The study did not evaluate an alginate dressing
Trial 2010	Grade of included ulcers not clear
Weheida 1991	The study was not a randomised controlled trial

Characteristics of ongoing studies [ordered by study ID]

Guillen-Sola 2013

Trial name or title	A multi-center, randomized, clinical trial comparing adhesive polyurethane foam dressing and adhesive hydrocolloid dressing in patients with grade II pressure ulcers in primary care and nursing homes
Methods	Randomised controlled trial
Participants	Planning to recruit 820 participants from primary health care and home care centres

Interventions	Adhesive polyurethane foam
Outcomes	Percentage of wounds healed after 8 weeks
Starting date	ISRCTN record shows starting date of 30/09/2012 and end date of 30/09/2015
Contact information	M Guillen-Sola: mguillen@ibsalut.caib.es
Notes	

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