Hydrogel dressings for treating pressure ulcers

Jo C Dumville [1,✉], Nikki Stubbs [2], Samantha J Keogh [3], Rachel M Walker [3], Zhenmi Liu [1]

Abstract

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 different dressing options including hydrogel dressings. A clear and current overview of the current evidence is required to facilitate decision-making regarding dressing use for the treatment of pressure ulcers.

Objectives

To assess the effects of hydrogel dressings on the healing of pressure ulcers in any care setting.

Search methods

We searched the following databases: the Cochrane Wounds Group Specialised Register (searched 19 June 2014); The Cochrane Central Register of Controlled Trials (CENTRAL; 2014, Issue 5); Ovid MEDLINE (1946 to June Week 2 2014); Ovid MEDLINE (In-Process & Other Non-Indexed Citations, 23 June 2014); Ovid EMBASE (1974 to 20 June 2014); and EBSCO CINAHL (1982 to 18 June 2014). There were no restrictions based on language or date of publication.

Selection criteria

Published or unpublished randomised controlled trials (RCTs) comparing the effects of hydrogel dressings with alternative wound dressings or no dressing in the treatment of pressure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 eleven studies (523 participants) in this review. Ten studies had two arms and one had three arms that were all relevant to this review. Three studies compared a hydrogel dressing with a basic wound contact dressing; three studies compared a hydrogel dressing with a hydrocolloid dressing; three studies compared a hydrogel dressing with another hydrogel dressing; one study compared a hydrogel dressing with a foam dressing; one study compared a hydrogel dressing with a dextranomer paste dressing and one study compared a hydrogel dressing with a topical treatment (collagenase). Limited data were available for analyses in this review: we conducted no meta-analyses. Where data were available there was no evidence of a difference between hydrogel and alternative treatments in terms of complete wound healing or adverse events. One small study reported that using hydrogel dressings was, on average, less costly than hydrocolloid dressings, but this estimate was imprecise and its methodology was not clear. All included studies were small, had short follow-up times and were at unclear risk of bias.

Authors' conclusions

It is not clear if hydrogel dressings are more or less effective than other treatments in healing pressure ulcers or if different hydrogels have different effects, Most trials in this field are very small and poorly reported so that risk of bias is unclear.

Plain language summary

Hydrogel dressings for treating pressure ulcers

Background

Pressure ulcers, also known as bedsores, decubitus ulcers and pressure injuries, are areas of injury to the skin or the underlying tissue, or both. Pressure ulcers can be painful, may become infected, and affect quality of life. Those at risk of pressure ulcers include those with spinal cord injuries and people who are immobile or who have limited mobility such as some elderly people and people with acute or chronic 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 NHS expenditure. Pressure ulcers have been shown to increase length of hospital stay and the associated hospital costs. 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 costs of these stays was USD 11 billion.

Dressings are one treatment option for pressure ulcers. There are many types of dressings that can be used; these can vary considerably in cost. Hydrogel dressings are one type of available dressing. Hydrogel dressings contain a large amount of water that keeps ulcers moist rather than letting them become dry. Moist wounds are thought to heal more quickly than dry wounds. In this study we investigated whether there is any evidence that pressure ulcers treated with hydrogel dressings heal more quickly than those treated with other types of dressings or skin surface (topical) treatments.

What we found

In June 2014 we searched for as many relevant medical studies as we could find that had a robust design (randomised controlled trials) that had compared hydrogel dressings with other treatments for pressure ulcers. We found 11 studies involving a total of 539 participants. From the results of these studies we could not tell whether hydrogel wound dressings heal pressure ulcers more quickly or slowly than other types of dressing or topical treatments.

Generally, the studies we found were small and the results inconclusive. Some studies lacked information about how they were conducted and it was difficult to tell whether the results presented were robust. More research of better quality is needed before it can be determined whether hydrogel dressings are better or worse at healing pressure ulcers than other types of dressings or topical treatments.

Summary of findings

Summary of findings for the main comparison. Hydrogel dressings compared with basic wound contact dressings for pressure ulcers.

Hydrogel dressings compared with basic wound contact dressings for pressure ulcers
Patient or population: people with pressure ulcers **Settings:** **Intervention:** hydrogel dressings **Comparison: b** wound contact dressings

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Basic wound contact dressings	Hydrogel dressings				
Proportion of ulcers completely healed Follow-up: mean 10 weeks	**Study population**		**RR 0.97** (0.56 to 1.68)	30 (1 study)	⨁⊖⊖⊖ **very low**[1,2]	
	643 per 1000	**624 per 1000** (360 to 1000)				
	Moderate					
Adverse event data (wound infection and pain during treatment) Follow-up: mean 10 weeks	**Study population**		Not estimable	0 (3 studies)	See comment	It is not clear th adverse event d were systematic collected the sa way for both tri groups. Availabl data was very limited and was analysed
	See comment	See comment				
	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 the estimate of effect **Moderate quality:** further research is likely to have an important impact on our confidence i the estimate of effect and may change the estimate **Low quality:** further research is very likely to have an importa impact on our confidence in the estimate of effect and is likely to change the estimate **Very low quality:** we are ve uncertain about the estimate

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[1] 95% CIs ranged from 0.56 to 1.68

[2] 11 participants (27%) failed to complete the study - data excluded from the analyses. High risk of attrition bias

Summary of findings 2. Hydrogel dressings compared with hydrocolloid dressings for pressure ulcers.

Hydrogel dressings compared with hydrocolloid dressings for pressure ulcers						
Patient or population: people with pressure ulcers **Settings:** **Intervention:** hydrogel dressings **Comparison:** hydrocolloid dressings						
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 dressings	**Hydrogel dressings**				
Proportion of ulcers completely healed Follow-up: mean 8 weeks	**Study population**		**RR 1.00** (0.22 to 4.56)	10 (1 study)	⨁⨁⊖⊖ **low**[1]	One further st had outcome d for this compa but it could no analysed
	400 per 1000	**400 per 1000** (88 to 1000)				
	Moderate					
Adverse events	**Study population**		Not estimable	10 (1 study)	See comment	It was not clea how these dat
	See comment	See comment				were collected whether all ev were reported
	Moderate					data have not analysed furth
*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						
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[1] 95% CIs were 0.22 to 4.56. The single study that contributed data to this outcome for this comparison had only 10 people in it

Summary of findings 3. Hydrogel dressings compared with hydrogel dressings for pressure ulcers.

Hydrogel dressings compared with hydrogel dressings for pressure ulcers						
Patient or population: people with pressure ulcers **Settings:** **Intervention:** hydrogel dressings **Comparison:** hydrogel dressings						
Outcomes	**Illustrative comparative risks* (95% CI)**		**Relative effect (95% CI)**	**No of participants (studies)**	**Quality of the evidence (GRADE)**	**Comm**
	Assumed risk	**Corresponding risk**				
	Hydrogel dressings	**Hydrogel dressings**				
Proportion of ulcers completely healed (not reported)						No dat
Adverse events (wound infection) Follow-up: mean 4 weeks	**Study population**		**RR 0.13** (0.01 to 2.44)	50 (1 study)	⊕⊕⊖⊖ **low**[1]	
	125 per 1000	**16 per 1000** (1 to 305)				
	Moderate					
Adverse events (wound-related pain) Follow-up: mean 4 weeks	**Study population**		**RR 1.92** (0.01 to 2.44)	47 (1 study)	⊕⊕⊖⊖ **low**[1]	
	217 per 1000	**417 per 1000** (2 to 530)				
	Moderate					
	Study population					

Adverse events (pain on dressing removal) Follow-up: mean 4 weeks	**650 per 1000**	**774 per 1000** (520 to 1000)	**RR 1.19** (0.80 to 1.76)	42 (1 study)	⨁⨁⊖⊖ **low**[1]	
	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

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[1] 95% CIs from 0.80 to 1.76. Small and underpowered study with only 4 weeks follow-up

Summary of findings 4. Hydrogel dressings compared with foam dressing for pressure ulcers.

Hydrogel dressing compared with foam dressings for pressure ulcers						
Patient or population: people with pressure ulcers **Settings:** **Intervention:** hydrogel dressing **Comparison:** foam 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**				
	Foam	**Hydrogel**				
Proportion of ulcers completely healed Follow-up: mean 8 weeks			Not estimable	34 (1)	See comment	Limited data reported at wo rather than participant leve Unit of analysis issues

Adverse events (not reported)						

*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

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Summary of findings 5. Hydrogel dressings compared with dextranomer paste dressings for pressure ulcers.

Hydrogel dressings compared with dextranomer paste dressings for pressure ulcers						
Patient or population: people with pressure ulcers **Settings:** **Intervention:** hydrogel dressings **Comparison: d**extranomer paste dressings						
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	**Hydrogel dressings**				
Proportion of ulcers completely healed (not reported)						No data
Adverse event data Follow-up: mean 3 weeks	**Study population**		Not estimable	135 (1 study)	See comment	It was not clear h these data were collected and whether all event were reported. Th data have not bee analysed further
	See comment	See comment				
	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

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Summary of findings 6. Hydrogel dressings compared with collagenase for pressure ulcers.

Hydrogel dressings compared with collagenase for pressure ulcers						
Patient or population: people with pressure ulcers **Settings:** **Intervention:** hydrogel dressings **Comparison:** collagenase						
Outcomes	**Illustrative comparative risks* (95% CI)**		**Relative effect (95% CI)**	**No of participants (studies)**	**Quality of the evidence (GRADE)**	**Comments**
	Assumed risk	**Corresponding risk**				
	Collagenase	**Hydrogel dressings**				
Proportion of ulcers completely healed Follow-up: mean 84 days	**Study population**		Not estimable	27 (1)	See comment	Only a sub-group those randomised were followed to healing. This sub-group was not considered to be randomised
	See comment	See comment				
	Moderate					
Adverse events (not reported)						No data

*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

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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 heel (Vanderwee 2007), and are caused by external forces such as pressure, or shear, or a combination of both (EPUAP-NPUAP 2014).

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

Mobility produces relief from pressure within the body through regular, often subconscious, shifts in positions when sitting or lying. These movements, 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). Populations 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 localized 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 to 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 [dead tissue]. 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 [damage through the skin being wet] or excoriation [damage through scratching/abrasion or burns]."

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 [back of the head] and malleolus [ankle] 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 [scabbing] 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 [bone infection] or osteitis [inflammation of bone] likely to occur. Exposed bone/muscle is visible or directly palpable."

Pressure ulcers are relatively common wounds that can be complex to manage and heal. Prevalence estimates vary according to the population being assessed, the data collection methods used and decisions about whether or not stage I pressure ulcers should be included (since there is no active wound at this stage, but patients are 'at risk' and have early tissue damage). 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, a USA estimate for pressure ulcer prevalence (stage II and above) across acute-care, long-term care and rehabilitation settings 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 the prevalence figures quoted above are for at-risk populations currently receiving medical care. The point prevalence of pressure ulceration in the total adult population was recently estimated using a cross-sectional survey undertaken in Leeds, UK. Of the total adult population of 751,485 the point prevalence of pressure ulceration per 1000 was 0.31 (Hall 2014). UK 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; the ulcers can be painful, discharge exudate and may become seriously infected. It has been shown that - after adjustment for age, sex and co-morbidities - people with pressure ulcers have a 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 being between GBP 1214 for a stage I ulcer, to 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 being 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 the 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 costs of 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

There are two main strategies in the treatment of pressure ulcers, namely relief of pressure, usually through the use of pressure relieving beds, mattresses and cushions ("support surfaces") (McInnes 2011), alongside management of the wound environment using wound dressings. Other general strategies include patient education, pain management, optimising circulation/perfusion, optimising nutrition, surgical wound closure and the treatment of clinical infection (AWMA 2012; EPUAP-NPUAP 2014).

Dressings are widely used in wound care, with the aim of protecting the wound and 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 (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 and but not bacteria;
- avoidance of wound trauma on dressing removal;
- frequency with which the dressing needs to be changed;
- provision of pain relief; and
- comfort.

Hydrogel dressings are the focus of this review; their properties are described below. As hydrogel dressings are likely to be evaluated against one of the many 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, where possible, with examples of corresponding trade names and manufacturers. Dressing names, manufacturers and distributors may vary between countries.

1. 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.
- **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).

2. Advanced wound dressings

- **Alginate dressings:** these are highly absorbent and come in the form of calcium alginate or calcium sodium alginate, and 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:** normally these dressings contain hydrophilic polyurethane foam and are designed to absorb wound exudate and maintain a moist wound surface. These 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; while some are silicone-coated for non-traumatic removal. Examples include: Allevyn (Smith & Nephew), Biatain (Coloplast) and Tegaderm (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 rehydrate a wound, depending on the wound moisture levels. They are supplied as either flat sheets, 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 composed of a soft silicone polymer held in a non-adherent layer. Examples include: Mepitel (Mölnlycke) and Urgotul (Urgo).
- **Hydrocolloid dressings:** these are occlusive dressings 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 that are more absorbant than standard hydrocolloid dressings. Examples include: 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. Examples include: CarboFLEX (ConvaTec).

3. Anti-microbial 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 etc). 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).

4. Specialist dressings

- **Protease-modulating matrix dressings:** these dressings 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 other anti-microbial products. With increasingly sophisticated technology being applied to wound care, practitioners need to know how effective these alternative dressings are compared with more traditional, and usually less costly, options. There are limited data about the current use of dressings for the treatment of pressure ulcers 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 suggested 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. Different 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. Hydrogels are insoluble polymers that can bind a relatively large volume of water that can then be 'donated' to wounds to maintain a moist environment. Furthermore, if the hydrogel polymer matrix is not fully hydrated, it can absorb some wound exudate and help to optimise the moisture level of the wound. When hydrogel material is manufactured in the form of a fixed structure via cross-linking of the polymers it is considered to be a hydrogel sheet dressing.

Why it is important to do this review

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

A key international guideline recommends that a dressing should be chosen "that keeps the wound bed moist", this recommendation was classed as being 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 2014). The same guidelines suggests that hydrogel dressings are used to treat pressure ulcers in various scenarios, but these recommendations are based on limited evidence (EPUAP-NPUAP 2014).

Two notable systematic reviews of treatments for pressure ulcers have included trials of dressings (Reddy 2008; Smith 2013). Reddy 2008 (search date 2008) included eight trials of hydrogel dressings in people with pressure ulcers. These studies were included as part of a much larger review that

reviewed multiple interventions for treating pressure ulcers. The report stated that "No single dressing was consistently superior to other dressings in the trials of pressure ulcers we examined", however, because of the breath of the review, detailed examination of the effect estimates and quantifying uncertainty around the hydrogel trials was difficult. The more recent review seems to include dressing interventions but does not mention hydrogels specifically (Smith 2013). We conclude that up-to-date and transparent information on the evidence for the use of hydrogel 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 hydrogel dressings for healing pressure ulcers in any care setting.

Methods

Criteria for considering studies for this review

Types of studies

Published and unpublished randomised controlled trials (RCTs), including cluster RCTs (which could include studies where multiple wounds on the same participant were treated with the allocated treatment and outcome data were collected and analysed for each wound) were eligible for inclusion, irrespective of language of report. RCTs reported only as abstracts were eligible for inclusion only where there was sufficient data available for reasonable data extraction either from the abstract itself or from the study authors. Cross-over trials were eligible if outcome data were available from the end of the first treatment period prior to cross-over. Studies using quasi-randomisation were excluded.

Types of participants

RCTs that recruited adults with a diagnosis of pressure ulcer (stage II or above) managed in any care setting were eligible for inclusion. We excluded 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. Studies that recruited participants with ulcers of stage II or higher alongside people with other types of chronic wound (e.g. leg or foot ulcers, or both) were included if the results for people with relevant pressure ulcers were presented separately (or available from the study authors). Similarly, where a trial included both stage I and more advanced staged pressure ulcers, the study was only included if data on ulcers of stage II and above were reported separately or available on request from study authors.

Types of interventions

The primary intervention was hydrogel wound dressings (BNF 2013). Any RCT where the use of a specific hydrogel dressing was the only systematic difference between treatment groups was eligible for inclusion. We anticipated comparisons could include: different types of hydrogel dressings compared with each other; hydrogel dressings compared with other dressing types; and hydrogel dressings compared with other interventions (possibly non-dressing treatments e.g. topical treatments).

Types of outcome measures

We list primary and secondary outcomes below. Decisions regarding study selection were not based on whether measured outcome data were reported in a 'usable' way, nor on the absence of the primary outcome if other relevant outcomes were reported.

Primary outcomes

The primary outcome for this review was complete wound healing.

We note that, since wound healing is a subjective outcome, it can be at high risk of measurement bias when outcome assessment is not blinded and so we focused on this in our risk of bias assessment. For this review we regarded the following 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 covariates such as baseline size). We only considered mean or median time to healing without survival analysis as a valid outcome 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).

Where both time to healing and proportion of ulcers healed were reported, we presented all data in a summary outcome table for reference purposes, but focused on reporting the 'best' healing outcome available. We considered time to healing to be the best outcome. We presented data for the latest time point available unless there was an earlier time point that 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.

Secondary outcomes

- Change (and rate of change) in wound size, with adjustment for baseline size (we contacted study authors to request adjusted means when not presented). Where change or rate of change in wound size was reported without adjustment for baseline size we documented use of the outcome in the study, but did not extract data, summarize or use the data in any meta-analysis.
- Participant health-related quality of life/health status (measured using a standardised generic questionnaire such as EQ-5D, 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 (with infection as defined by the study authors).
- 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), where a clear methodology for the collection of adverse event data was provided.
- Resource use (including measurements of resource use such as number of dressing changes, nurse visits, length of hospital stay and re-operation/intervention).
- Cost (allocated to resource use).

- Wound recurrence.

Search methods for identification of studies

Electronic searches

We searched the following electronic databases:

- Cochrane Wounds Group Specialised Register (searched 19 June 2014);
- The Cochrane Central Register of Controlled Trials (CENTRAL *The Cochrane Library*; 2014, Issue 5);
- The Database of Abstracts of Reviews of Effects (DARE; 2014, Issue 2);
- The Health Technology Assessment Database (HTA; Issue 2);
- The NHS Economic Evaluation Database (NHS EED; 2014, Issue 2);
- Ovid MEDLINE (1946 to June Week 2 2014);
- Ovid MEDLINE (In-Process & Other Non-Indexed Citations, 23 June 2014);
- Ovid EMBASE (1974 to 20 June 2014);
- EBSCO CINAHL (1982 to 18 June 2014).

We searched the Cochrane Central Register of Controlled Trials (CENTRAL) using the following exploded MeSH headings and keywords:

#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

The search strategy was adapted to search Ovid MEDLINE, Ovid EMBASE and EBSCO CINAHL (Appendix 1). 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). There were no restrictions with respect to language, date of publication or study setting.

We also searched the following clinical trials registries:

- ClinicalTrials,gov (http://www.clinicaltrials.gov/);
- 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 the manufacturers and distributors of wound dressings. We searched the US Food and Drug Administration briefing documents used in the licensing of wound dressings. We searched for 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 felt to be potentially relevant. Independently, two review authors checked the full papers for eligibility; disagreements were resolved by discussion and, where required, the input of a third review author. Where 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 for which we obtained full copies. We completed a PRISMA flowchart to summarise this process (Liberati 2009).

We obtained all relevant publications when studies were 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 where required. Where data were missing from reports, we attempted to contact the study authors to obtain this information. Where a study was included with more than two intervention arms, data were extracted only from intervention and control groups that met the review's eligibility criteria.

We extracted the following data, where possible from those trial arms that are relevant to the review:

- country of origin;
- type/grade/category of pressure ulcer;
- location of pressure ulcer;
- unit of randomisation and analysis, e.g. single wound, patient, or multiple wounds on the same patient;
- trial design, e.g. parallel; cluster;
- care setting;
- number of participants randomised 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;
- 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; and,
- source of funding for trial.

Assessment of risk of bias in included studies

Independently, two review authors assessed the included studies that had individual randomisation using the Cochrane Collaboration 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. 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 by all of the risk of bias items. For trials using cluster randomisation we planned to assess 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 we calculated the risk ratio (RR) with 95% confidence intervals (CI). For continuous outcome data we planned to use mean differences (MD) with 95% CIs for trials that used the same assessment scale. When trials used different assessment scales, we planned to use the standardised mean difference (SMD) with 95% CIs. We anticipated reporting time-to-event data (e.g. time-to-complete wound healing) as hazard ratios (HR) where possible in accordance with the methods described in the *Cochrane Handbook* for *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, where feasible, we planned to estimate this using other reported outcomes, such as the numbers of events, through the application of available statistical methods (Tierney 2007).

Unit of analysis issues

Unit of analysis issues may arise with studies that include participants with multiple wounds that are treated with the same intervention, and report outcomes for each wound, or with studies in which multiple assessments of an outcome are presented for participants. We recorded whether trials presented outcomes in relation to a wound, a limb (e.g. foot or leg), a participant, or as multiple wounds on the same participant. For wound healing, unless otherwise stated, where the number of wounds appeared to equal the number of participants, we treated the participant as the unit of analysis.

Where a cluster trial has been conducted and correctly analysed, effect estimates and their standard errors may be meta-analysed using the generic inverse-variance method in Review Manager (RevMan 2014). We also recorded occasions when multiple wounds on a participant were

(incorrectly) treated in the included study as being independent of each other, rather than having within-patient analysis methods applied. This was be recorded as part of the 'Risk of bias' assessment.

Where a cluster-randomised trial was conducted, but incorrectly analysed at the individual rather than the cluster level, we planned to approximate the correct analyses if possible following Chapter 16 of the *Cochrane Handbook for Systematic Reviews of Interventions* using information on (Higgins 2011b):

- the number of clusters (or groups) randomised to each intervention group; or the average (mean) size of each cluster;
- the outcome data, ignoring the cluster design for the total number of individuals (for example, number or proportion of individuals with events, or means and standard deviations); and,
- an estimate of the intracluster (or intraclass) correlation coefficient (ICC).

Dealing with missing data

It is common to have data missing from trial reports. Excluding participants post-randomisation from the analysis, or ignoring those participants who are lost to follow-up, compromises the randomisation and potentially introduces bias into the trial. If we thought that study authors might be able to provide some missing data then we contacted them. In individual studies, where data on the proportion of ulcers healed were presented, we assumed that randomised participants 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 the numerator). Where a trial did not specify participant group numbers prior to drop-out, we presented only complete case data. For time-to-healing analysis using survival analysis methods, drop-outs should be accounted for as censored data. Hence all participants will contribute to the analysis. We acknowledge that such analysis assumes that drop-outs are missing at random. We present data for area change of ulcer, and for all secondary outcomes, as a complete case analysis.

Assessment of heterogeneity

We considered clinical heterogeneity (that is the degree to which RCTs vary in terms of participant, intervention and outcome characteristics) and 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 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 the 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 trial size or precision (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 narrative review according to comparators. Both clinical and statistical heterogeneity were explored. We had planned to pool data using meta-analysis (conducted using RevMan 5.3), that is, where studies appeared similar in terms of intervention, study duration and outcome assessment and data type, however, no data were meta-analysed in this review. Had we pooled data, in the absence of clinical heterogeneity and in the presence of statistical heterogeneity (I^2 value over 50%), we planned to use a random-effects model, however, we did not anticipate pooling studies where heterogeneity was very high (I^2 value over 75%). Where there was no evidence of clinical or statistical heterogeneity we would have used a fixed-effect model.

For dichotomous outcomes we presented the summary estimate as a risk ratio (RR) with 95% CI. Where continuous outcomes were measured in the same way across studies, we would have presented a pooled mean difference (MD) with 95% CI. We planned to pool standardised mean difference (SMD) estimates where studies had measured the same outcome using different methods. 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.

'Summary of findings' tables

We 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 the available data for the main outcomes (Schunemann 2011a). The 'Summary of findings' tables also include an overall grading of the evidence relating 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 (in the protocol) to present the following outcomes in the 'Summary of findings' tables:

- time to complete ulcer healing, where analysed, using appropriate survival analysis methods;
- proportion of ulcers completely healing during the trial period; and,
- adverse events.

Subgroup analysis and investigation of heterogeneity

We planned to perform a sub-group analysis to explore the influence of the following factor on effect sizes:

- ulcer category: where possible assessed whether there are differences in effect sizes for stage II pressure ulcers and the more severe stage III and IV pressure ulcers

Sensitivity analysis

We planned to perform the following sensitivity analyses in order to explore the influence of the following factor on effect sizes:

- risk of bias: we planned to assess the influence of removing studies classed as being at high and unclear risk of bias from meta-analyses. We would only include studies that were assessed as having a low risk of bias in all key domains, namely adequate generation of the

randomisation sequence, adequate allocation concealment and blinding of outcome assessor, for the estimates of treatment effect.

Elements of this methods section are based on the standard Cochrane Wounds Protocol Template.

Results

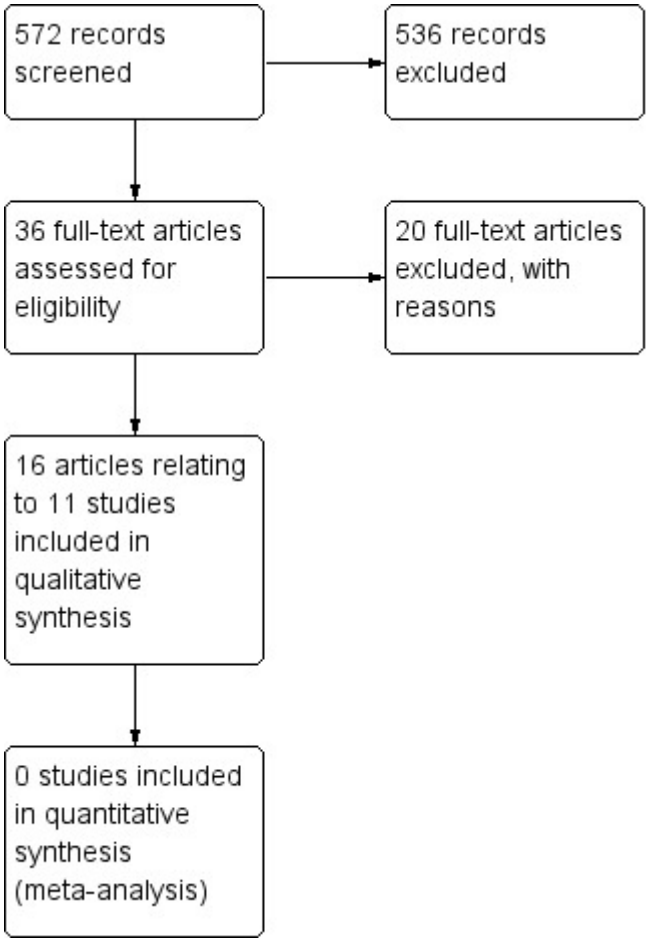
Description of studies

See Characteristics of included studies; Characteristics of excluded studies

Results of the search

The search generated 572 records: we retrieved 36 of these records, pertaining to 31 different studies, for consideration for inclusion (Figure 1). We are not aware of any relevant on-going studies (registers checked 24 July 2014). We located no new studies from searching reference lists, as the relevant studies had been identified through the electronic searching.

1.



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Study flow diagram

Included studies

Eleven studies were included in this review (Bale 1998a; Bale 1998b; Colin 1996; Darkovich 1990; Matzen 1998; Milne 2012; Motta 1999; Mulder 1993; Sopata 2002; Thomas 1998; Young

1996): see Characteristics of included studies as well as a summary tables Table 7 and Table 8 for more details.

1. Summary of studies.

Study ID	Group A	Group B	Group C	Duration of follow-up	Complete healing data
Bale 1998a	Hydrogel dressing (Sterigel®) n = 26	Hydrogel dressing (no further details) n = 24	n/a	4 weeks	No
Bale 1998b	Hydrogel dressing (Comfeel Purilon® gel) n = 12	Hydrogel dressing (Intrasite®) n = 11	n/a	4 weeks	No
Colin 1996	Hydrogel dressing (Intrasite® gel) n = 67	Dextranomer paste dressing (Debrisan® Paste) n = 68	n/a	3 weeks	No
Darkovich 1990	Hydrogel dressing n = not clear; 35 stage II ulcers	Hydrocolloid dressing (DuoDERM®) n = not clear; 36 stage II ulcers	n/a	60 days (approximately 9 weeks)	Yes – per wo and not participant
Matzen 1998	Hydrogel dressing n = 17	Conventional treatment (wet saline compresses) n = 15	n/a	12 weeks	Yes
Milne 2012	Hydrogel dressing (SoloSite Gel) n = 14	Collagenase (Santyl ointment) n = 13	n/a	84 days	Yes (only for set of randomised participants
Motta 1999	Hydrogel dressing (AcryDerm®, Wound Dressing/ Flexigel®) n = 5	Hydrocolloid dressing (DuoDerm®) n = 5	n/a	8 weeks	Yes
Mulder 1993	Hydrogel dressing (Clearsite®) n = 23	Hydrocolloid dressing (DuoDerm®) n = 23	Saline solution-moistened dressing n = 21	8 weeks	No

Sopata 2002	Hydrogel dressing (Aquagel) n = 17 participants with 20 ulcers	Foam dressing (Lyofoam/polyurethane foam dressing (Seton)) n = 17 participants with 18 wounds	n/a	weeks	Yes
Thomas 1998	Hydrogel dressing (Carrasyn® gel Wound Dressing) n = 16 (complete case analysis number at randomisation not reported)	Saline dressing n = 14 (complete case analysis number at randomisation not reported)	n/a	10 weeks	Yes
Young 1996	Hydrogel dressing (NU-GEL®) n = 34	Hydrogel dressing (Intrasite® gel) n = 31	n/a	6 weeks	Yes

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n/a; not applicable

2. Study outcomes.

Study	**Comparison**	**Length of follow-up**	**Time to healing data**	**% Ulcer healed**	**Mean change in ulcer size**	**I**
Bale 1998a	Group A (n = 26): amorphous hydrogel (Sterigel) Group B (n = 24): established hydrogel	4 weeks	Not reported	Not reported	Not reported	

Bale 1998b	Group A (n = 12 hydrogel, Comfeel Purilon gel (Coloplast) Group B (n = 11): hydrogel, Intrasite gel (Smith & Nephew)	4 weeks	Not reported	Not reported	Not reported	
Colin 1996	Group A (n = 67): amorphous hydrogel (Intrasite Gel) Group B (n = 68): dextranomer paste dressing (Debrisan Paste)	3 weeks	Not reported	Not reported	**Median reduction in wound area at 21 days (range):** Group A: 35% (-185 to 91) **Group B:** 7% (-340 to 98)	

Darkovich 1990	Group A (n = 41, 62 ulcers): biofilm hydrogel (BF Goodrich Company) Group B (n = 49, 67 ulcers): hydrocolloid dressing (DuoDERM, ConvaTec/Bristol-Myers)	Approximately 9 week	Not reported	**Read from graph by review authors:** Group A: 32% Group B: 16%	**% reduction in wound area (compared to baseline), adjusted:** Group A: 64% Group B: 34%	
Matzen 1998	Group A (n = 17): amorphous hydrocolloid (hydrogel, Coloplast A/S, Denmark) Group B (n = 15): conventional treatment (wet saline compresses)	12 weeks	Not reported	Not reported	**Adjusted Mean relative volume (from initial 100%):** Group A: 26% (SD 20) Group B: 64% (SD 16)	
Milne 2012	Group A (n = 14): hydrogel dressings (SoloSite Gel, Smith & Nephew,Largo, FL) Group B (n = 13): collagenase (Santyl Ointment, Healthpoint, LTD, Fort Worth, TX	Maximum 84 days	Mean time to healing reported for sub-group of participants.	Reported that 3 participants healed in Group A and 9 in Group B. However since only a sub-group of those randomised (those debrided by day 42) were followed to healing (4 in Group A and 11 in Group B) these data are not presented further	Not reported	

Motta 1999	Group A (n = 5**):** hydrogel dressing (AcryDerm®, Wound Dressing, AcryMed Portland, Ore, now known as Flexigel Smith & Nephew, Largo, FL) Group B (n = 5): hydrocolloid dressing (DuoDERM CGF, ConvaTec, Skillman, NJ)	8 weeks	Not reported	**Completely healed:** Group A: 2/5 Group B: 2/5	**Adjusted** Not reported **Non-adjusted** (calculated by review authors from data in paper) Group A: 0.15 (SD 0.21) Group B: 0.35 (SD 0.43)	
Mulder 1993	Group A (n = 23): Clearsite hydrogel Group B (n = 23): DuoDERM hydrocolloid Group C (n = 21): standard (saline solution-moistened dressing)	8 weeks	Not reported	Not reported	**Adjusted** **Mean % reduction per week in wound size:** Group A (n = 20) 8.0% (SD 14.8) Group B (n = 21) 3.3% (SD 32.7) Group C (n = 20) 5.1% (SD 14.8)	
Sopata 2002	Group A: hydrogel dressing (Aquagel; n = 17 participants with 20 wounds) Group B foam dressing (Lyofoam/polyurethane	8 weeks	Not reported	**Numbers completely healed** Group A: 15 ulcers	Unadjusted data on rate of wound healing per day (cm^2/day) reported	

	foam dressing (Seton); n = 17 participants with 18 wounds)			Group B: 15 ulcers	in paper. Not extracted
Thomas 1998	Group A: amorphous hydrogel dressing, (Carrasyn Gel Wound Dressing, Carrington Laboratories, Inc, Irving, TX) Group B: saline dressing	10 weeks	**Mean time-to-healing data** presented only for healed wounds. Not extracted	**Numbers completely healed*** Group A: 10/16 Group B: 9/14 **Denominator only for complete case analysis as figures for numbers randomised not presented*	Not reported
Young 1996	Group A (n = 34): NU-GEL hydrogel with alginate (Johnson & Johnson Medical) Group B (n = 31): amorphous hydrogel, (IntraSite gel, Smith & Nephew)	6 weeks	Not reported	Not reported	**Mean % reduction per day (compared to baseline mm^2 per day):** Group A: 1.46 (no SD reported) Group B 0.96 (no SD reported)

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Collectively the included studies contained 523 participants relevant to this review. This figure was calculated using available data, however, Darkovich 1990 had potential unit of analysis issues because some participants entered the study with more than one wound and outcome data were presented at the wound rather than participant level. From the study report we were unable to determine the number of participants to whom the relevant pressure ulcer data pertained. So, in order to include the Darkovich 1990 figures when calculating the total number of participants we assumed one wound per person.

Ten of the included studies had two comparison groups and one had three groups (Mulder 1993). Three of the studies were conducted in the UK (Bale 1998a; Bale 1998b; Young 1996), five were conducted in the USA (Darkovich 1990; Motta 1999; Milne 2012; Mulder 1993; Thomas 1998), one was conducted in Denmark (Matzen 1998), one was conducted in Poland (Sopata 2002), and one was reported as being multi-national with no further details provided (Colin 1996).

All included studies had relatively short follow-up times ranging from three weeks to 12 weeks (Colin 1996; Matzen 1998 respectively). Included studies also had small sample sizes with the smallest having 10 participants (Motta 1999), and the largest 143 participants (information is presented on

135 of these 143 participants; Colin 1996). The median size of each group, for the 10 studies that had clear data concerning the number of participants, was 17 participants.

The included studies evaluated six comparisons:

- Hydrogel dressings compared with basic wound contact dressings (including saline gauze; Matzen 1998; Mulder 1993; Thomas 1998).
- Hydrogel dressings compared with hydrocolloid dressings (Darkovich 1990; Motta 1999; Mulder 1993).
- One brand of hydrogel dressing compared with another brand of hydrogel dressing (Bale 1998a; Bale 1998b; Young 1996).
- Hydrogel dressings compared with foam dressings (Sopata 2002).
- Hydrogel dressings compared with dextranomer paste dressings (Colin 1996).
- Hydrogel dressings compared with a topical application of collagenase (Milne 2012).

Three studies reported complete wound healing (Milne 2012; Motta 1999; Thomas 1998), and one study reported this outcome but at the wound level, that is, participants could have more than one wound (Darkovich 1990).

Excluded studies

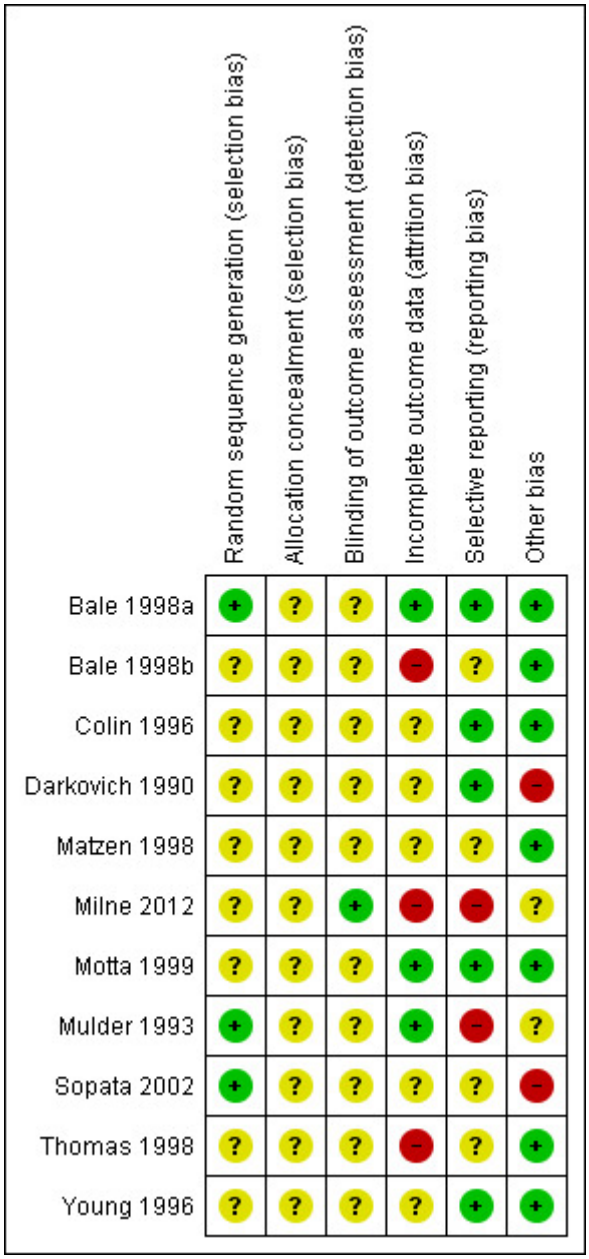
In total 20 studies were excluded from the review; we have listed reasons for exclusion below.

- Ten studies did not evaluate a hydrogel dressing (Banks 1994; Bito 2012; Brod 1990; Kurzuk-Howard 1985; Manzanero 2004; Meaume 2003; Moody 1994; Oleske 1986; Perez 2000; Torra i Bou 1999b).
- Three studies did not report a relevant outcome (study authors were contacted where possible to request further information if available; Fear 1992; Peschardt 1997; Torra i Bou 1999a).
- Four studies were not randomised controlled trials (Flanagan 1995; Parnell 2005; Sadyak 1990; Weheida 1991).
- The study population in one study included stage I pressure ulcers (we attempted to contact study authors to request data on stage II ulcers only; Kaya 2005).
- In two studies use of a hydrogel dressing was not the only systematic difference between trial groups (Lum 1996; Small 2002).

Risk of bias in included studies

We classed studies as being at an overall high risk of bias if one of the following domains was deemed to be at a high risk of bias: generation of randomisation sequence, allocation concealment, or blinded outcome assessment. On the basis of this approach, we deemed no included studies to be at a high risk of bias (Figure 2; Figure 3).

2.



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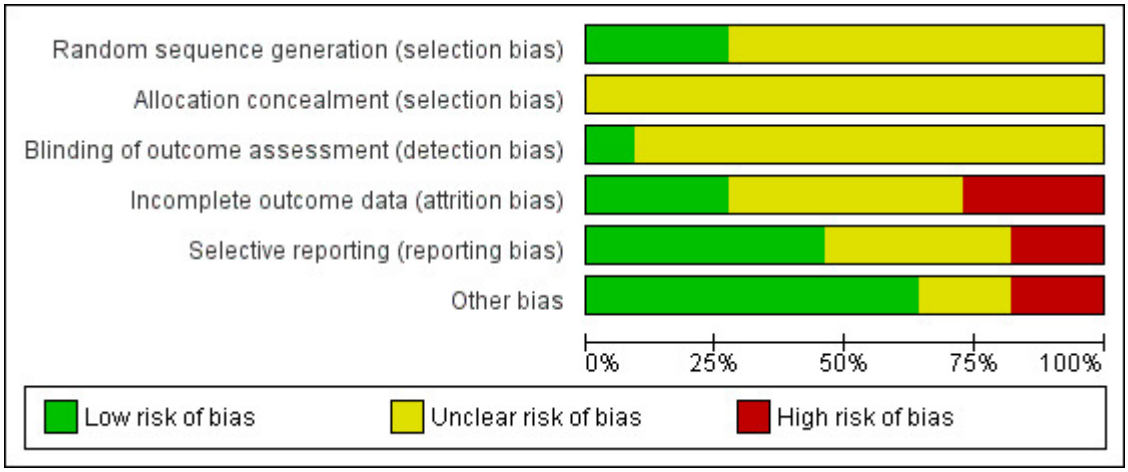
Risk of bias summary: review authors' judgements about each risk of bias item for each included study

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

We classed three studies as being at low risk of bias for the generation of randomisation sequence (Bale 1998a; Mulder 1993; Sopata 2002), as they reported use of a computer-generated number list randomisation schedule. We classed the remaining eight studies as being at unclear risk of bias for this domain, as no information regarding generation of the randomisation sequence was available for assessment.

We classed all 11 studies as being at unclear risk of bias for the domain of allocation concealment, as no information regarding allocation of the randomisation sequence was reported.

Blinding

We classed 10 studies as being at unclear risk of bias for blinding, as there was no indication that blinded outcome assessments were conducted for any outcomes relevant to the review. One study reported performing blinded outcome assessment for wound healing parameters (Milne 2012).

Incomplete outcome data

We deemed three studies to be at high risk of bias for the domain of incomplete outcome data (Bale 1998b; Milne 2012; Thomas 1998). Bale 1998b was presented as an interim analysis; Milne 2012 presented outcome data for only those randomised participants whose wound(s) had been debrided by the mid-point of study follow-up, and Thomas 1998 appeared to exclude data from 27% of those randomised. We considered four studies to be at a low risk of bias for this domain (Bale 1998a; Motta 1999; Mulder 1993; Sopata 2002), and the remaining four studies to be at an unclear risk of bias (Colin 1996; Darkovich 1990; Matzen 1998; Young 1996).

Selective reporting

Two studies were considered to be at high risk of bias for the domain of selective reporting (Milne 2012; Mulder 1993). Milne 2012 reported outcome data for only a specific group of those randomised. Mulder 1993 described outcome data that were not reported in the study results. Six studies were deemed to be at a low risk of bias for this domain (Bale 1998a; Colin 1996; Darkovich 1990; Motta 1999; Sopata 2002; Young 1996), and three at an unclear risk of bias (Bale 1998b; Matzen 1998; Thomas 1998).

Other potential sources of bias

We considered Darkovich 1990 to be at a high risk of bias as there were possible unit of analysis issues. The study reports that 90 participants with 129 ulcers were randomised (some were stage I ulcers) ; data were then presented at the ulcer level. We also deemed Sopata 2002 to be at a high risk of bias due to unit of analysis issues, as the trialists had recruited participants with multiple wounds and presented complete healing data at the wound rather than participant level. It was not possible to assess unit of analysis issues for one study (Mulder 1993). We deemed the remaining studies to be at a low risk of bias for other potential sources of bias.

Effects of interventions

See: Table 1; Table 2; Table 3; Table 4; Table 5; Table 6

Dressing compared with dressing

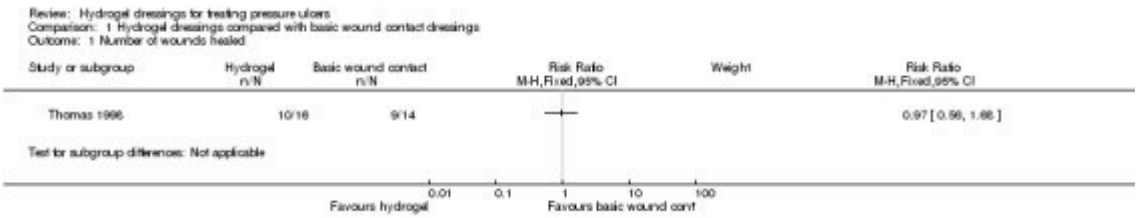
Comparison 1: hydrogel dressings compared with basic wound contact dressings (3 trials; 106 participants)

Three studies compared hydrogel dressings with basic wound contact dressings (Matzen 1998; Mulder 1993; Thomas 1998). The trials used three different brands of hydrogel (Table 7), and the basic wound contact treatments were described as: wet saline compress (Matzen 1998); saline solution-moistened dressing (Mulder 1993); and saline dressing (Thomas 1998). The follow-up periods of the studies were 12 weeks (Matzen 1998), 10 weeks (Thomas 1998), and eight weeks (Mulder 1993). We classed both Mulder 1993 and Thomas 1998 as being at a high risk of bias for one domain (reporting bias for the former and attrition bias for the latter). All studies were small in terms of participant numbers and events observed.

Primary outcome: complete wound healing (proportion of ulcers healed during follow-up)

One study presented data on complete wound healing (Thomas 1998). We can only present complete case data here as the number of participants randomised to each trial group prior to loss to follow-up was not reported. There was no evidence of a difference in the number of ulcers healed in the hydrogel-dressed group (63%: 10/16) compared with the basic wound contact-dressed group (64%: 9/14): RR 0.97 (95% CI 0.56 to 1.68; Analysis 1.1). The analysis provides low precision due to the small sample size, so there could be an effect in either direction (or none).This study was classed as being at high risk of attrition bias due to the apparent exclusion of participants from the analysis.

1.1. Analysis.



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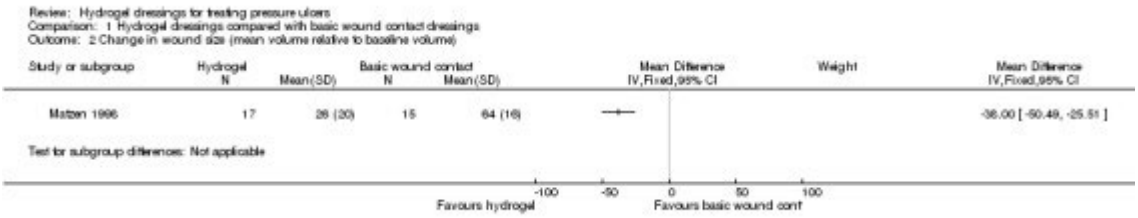
Comparison 1 Hydrogel dressings compared with basic wound contact dressings, Outcome 1 Number of wounds healed.

Secondary outcome: change in wound size

Matzen 1998 reported that the basic wound contact dressing group had a mean relative wound volume that was 64% of baseline volume (standard deviation (SD) 16) compared with the hydrogel-dressed group which had a mean relative wound volume that was 26% of baseline volume (SD 20). There was a statistically significant difference in the mean difference of -38% in favour of hydrogel (95% CI -50.49 to -25.51; Analysis 1.2).

1.2. Analysis.



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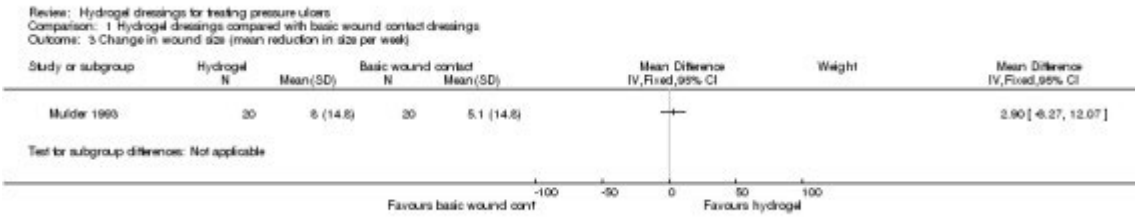
Comparison 1 Hydrogel dressings compared with basic wound contact dressings, Outcome 2 Change in wound size (mean volume relative to baseline volume).

Mulder 1993 reported the mean percentage reduction per week in wound size for each group. This was 5.1% (SD 14.8) in the basic wound contact dressing group and 8.0% (SD 14.8) for the hydrogel dressing group: mean difference 2.9%, (95% CI -6.27 to 12.07; Analysis 1.3).

1.3. Analysis.



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Comparison 1 Hydrogel dressings compared with basic wound contact dressings, Outcome 3 Change in wound size (mean reduction in size per week).

Secondary outcome: wound infection

Matzen 1998 reported that six participants in the basic wound contact dressing group developed necrotic tissue with infection. No information about the hydrogel dressing group was presented. It is not clear if adverse event data were recorded systematically for both groups.

Secondary outcome: other adverse events

Matzen 1998 measured pain during treatment on a scale from 1 to 4. The median score and associated range for both groups was the same: median 2 (range 1 to 3).

Mulder 1993 reported limited adverse event data (summarised in Table 8). It was not clear how these data were collected and whether all events were reported. The extracted data are not considered further.

Summary: hydrogel dressings compared with basic wound contact dressings (3 trials; 106 participants)

The relative effects of hydrogel dressings and basic wound contact dressings are unclear as there are very few comparative data available. The trials included are small, report very limited outcome data and are at an unclear or high risk of bias. One small study reported a greater mean reduction in ulcer size in the hydrogel group compared with the basic wound contact dressing group.

Comparison 2: hydrogel dressings compared with hydrocolloid dressings (3 trials; unable to calculate number of participants)

Three studies compared hydrogel dressings with hydrocolloid dressings (Darkovich 1990; Motta 1999; Mulder 1993). The trials included two different named brands of hydrogel dressing and an unspecific hydrogel dressing - all three studies used the same hydrocolloid dressing as a comparator (Table 7). The follow-up times for the studies were nine weeks (Darkovich 1990); and eight weeks (Motta 1999; Mulder 1993). Darkovich 1990 was classed as being at a high risk of bias due to unit of analyses issues. Mulder 1993 was classed as being at a high risk of reporting bias.

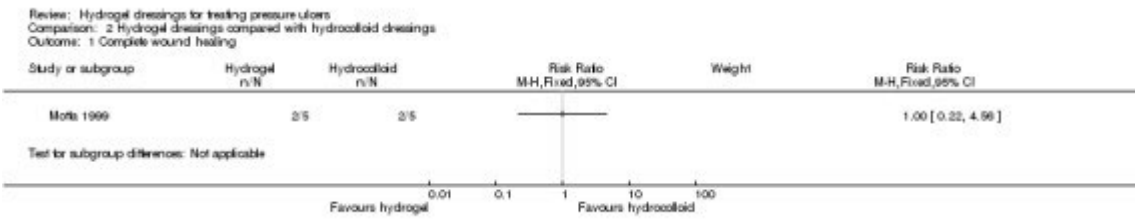
Primary outcome: complete wound healing (proportion of ulcers healed during follow-up)

Two of the three studies presented data on complete wound healing.

A graph presented by Darkovich 1990 reported that 32% of stage II pressure ulcers were healed in the hydrogel dressing group compared with 16% in the hydrocolloid dressing group. However, this trial recruited participants with more than one ulcer wound and data were presented at the wound level rather than at participant level. Additionally the study does not report how many people with a stage II ulcer were randomised, so, while we report the percentage data here, we do not have access to the figures used to calculate these. We were unable to contact the study authors to clarify these issues, and as a result of these issues, the data from this trial are not considered further here.

Motta 1999 reported that 40% (2/5) of participants in the hydrogel dressing group had a healed ulcer and 40% (2/5) in the hydrocolloid dressing group also had a healed ulcer: RR 1.00, (95% CI 0.22 to 4.56; Analysis 2.1). This study was very small and underpowered; there was high imprecision so the result is compatible with both increased and decreased healing with hydrogel dressings relative to hydrocolloid dressings.

2.1. Analysis.



Open in a new tab

Comparison 2 Hydrogel dressings compared with hydrocolloid dressings, Outcome 1 Complete wound healing.

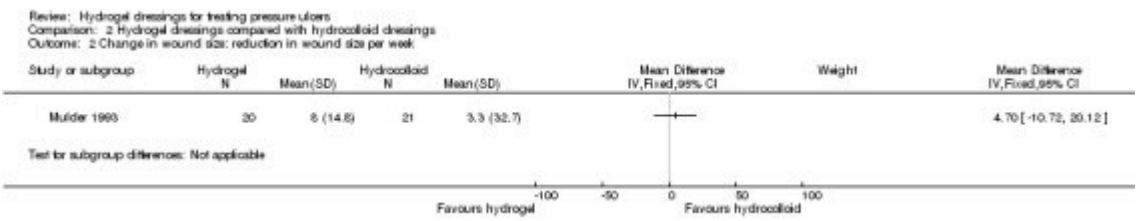
Secondary outcome: change in wound size

Two of the three studies present data on adjusted change in wound size.

Darkovich 1990 reported a 64% reduction in wound area (compared to baseline) in the hydrogel dressing group and a reduction of 34% in the hydrocolloid dressing group. The data limitations (the number of participants with a stage II pressure ulcer was not reported) as well as the lack of data on variation around the point estimate precluded further analysis. It is known that this trial has unit of analyses issues so these data should be treated with caution.

Mulder 1993: reported a mean 8% (SD 14.8) per week reduction in wound size (compared to baseline) in the hydrogel dressing group and a 3.3% (SD 32.7) per week reduction for the hydrocolloid dressing group: mean difference (MD) 4.70, (95% CI -10.72 to 20.12; Analysis 2.2).

2.2. Analysis.



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Comparison 2 Hydrogel dressings compared with hydrocolloid dressings, Outcome 2 Change in wound size: reduction in wound size per week.

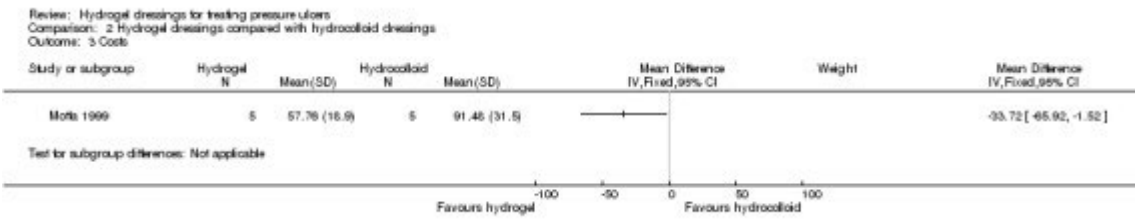
Secondary outcome: other adverse events

Mulder 1993 report limited adverse event data (summarised in Table 8). It was not clear how these data were collected and whether all events were reported. The reported data were considered to be limited and so are not considered further in this review.

Secondary outcome: costs

Motta 1999 reported a mean cost of treatment of USD 57.76 (SD 18.9) in the hydrogel dressing group and USD 91.48 (SD 31.5) in the hydrocolloid dressing group: mean difference (favouring hydrogel) USD -33.72 (95% CI -65.92 to -1.52; Analysis 2.3). These costs were reported to include the number of dressings used per participant multiplied by the unit cost of the dressing plus the cost of labour time per dressing. Whilst this is a statistically significant difference, there is huge imprecision around the treatment estimate with 95% CIs suggesting that the difference could be as large as USD 66 or as small as USD 1.5. Additionally these cost data alone are of limited value in the absence good evidence regarding any potential harms or benefits that the dressings may cause.

2.3. Analysis.



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Comparison 2 Hydrogel dressings compared with hydrocolloid dressings, Outcome 3 Costs.

Summary: hydrogel dressings compared with hydrocolloid dressings (3 trials; number of participants unknown)

The relative effects of hydrogels and hydrocolloids for the healing of pressure ulcers are unclear due to the lack of good quality comparative data. The three included trials were small, with short follow-up periods, were at an unclear of bias and reported limited outcome data. One study reported lower mean participant costs with hydrogel.

Comparison 3: one brand of hydrogel dressings compared with another hydrogel dressing (3 trials; 138 participants)

Three studies compared one brand of hydrogel dressing with another brand (Bale 1998a; Bale 1998b; Young 1996). The follow-up times were four weeks (Bale 1998a; Bale 1998b), and six weeks (Young 1996). We classed Bale 1998b as being at a high risk of attrition bias.

Primary outcome: complete wound healing (proportion of ulcers healed during follow-up)

None of the three studies included in this comparison reported on complete wound healing.

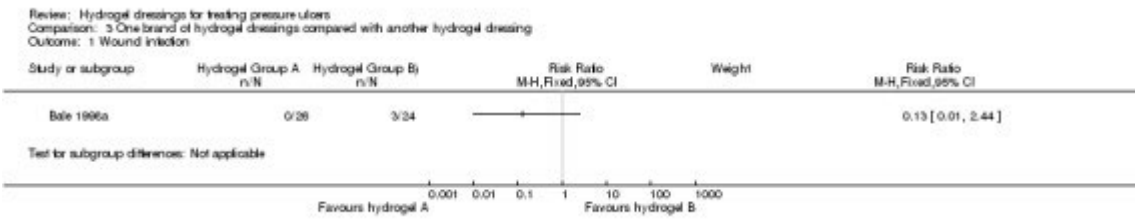
Secondary outcome: change in ulcer size

Young 1996 reported mean proportion reduction per day in wound size (compared to baseline) (see Table 8). No information regarding variation around the mean figures (e.g. SD) were presented, so we have not considered the data further.

Secondary outcome: wound infection

Bale 1998a reported no cases of wound infection (0/26) in one hydrogel dressing group and 12.5% (3/24) in the other hydrogel dressing group: RR 0.13, (95% CI 0.01 to 2.44; Analysis 3.1).

3.1. Analysis.



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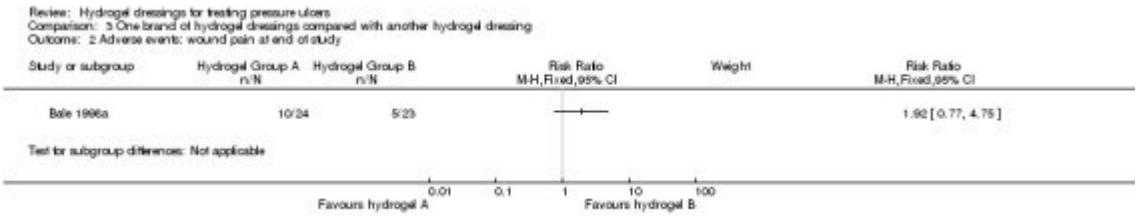
Comparison 3 One brand of hydrogel dressings compared with another hydrogel dressing, Outcome 1 Wound infection.

Secondary outcome: other adverse events

Bale 1998a reported that 41.6% (10/24) of the participants in one hydrogel dressing group reported no wound-related pain at study end compared with 21.7% (5/23) in the other hydrogel group: RR 1.92 (95% CI 0.77 to 4.75; Analysis 3.2).

3.2. Analysis.

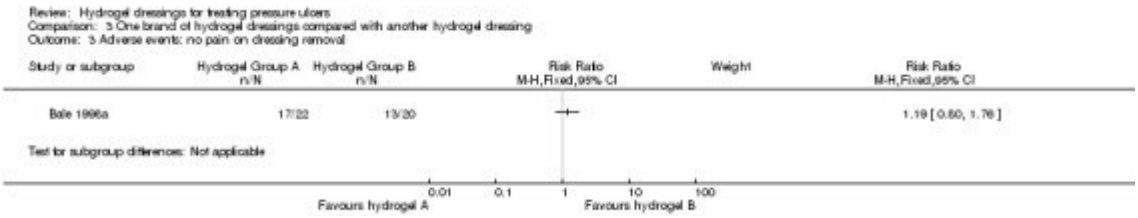


Open in a new tab

Comparison 3 One brand of hydrogel dressings compared with another hydrogel dressing, Outcome 2 Adverse events: wound pain at end of study.

Bale 1998a reported that 77% of participants (17/22) in hydrogel Group A had no pain on dressing removal compared with 65% (13/20) in hydrogel Group B: RR 1.19 (95% CI 0.80 to 1.76; Analysis 3.3).

3.3. Analysis.



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Comparison 3 One brand of hydrogel dressings compared with another hydrogel dressing, Outcome 3 Adverse events: no pain on dressing removal.

Bale 1998b reported a median pain score on dressing application using a 1 to 4 scale (it was not clear whether this is a validated measure). The median for both groups was 1 (range 1 to 3; Table 8).

Young 1996 reported no treatment-related adverse events in either group during the study.

Secondary outcome: resource use

Young 1996 reported mean dressing wear times for each hydrogel group (Table 8). No information regarding variation around the mean figures (e.g. SD) were presented, so we have not considered the data further.

Summary: one brand of hydrogel dressings compared with another hydrogel dressing (3 trials; 138 participants)

There are very few comparative data available to assess the relative treatment effects of different hydrogel dressings. Included trials are small, have short follow-up periods are at unclear of bias and report limited outcome data with no study reporting data on complete wound healing. Based on this current evidence base there is no evidence of a difference between hydrogel dressings in terms of adverse events, but available information is very limited.

Comparison 4: hydrogel dressings compared with foam dressings (1 trial; 34 participants with 38 wounds)

One study compared a hydrogel dressing with a foam dressing (Sopata 2002; Table 7), it had an eight-week follow-up and we classed it as being at a high risk of bias due to unit of analysis issues.

Primary outcome: complete wound healing (proportion of ulcers healed during follow-up)

Fifteen pressure ulcers were reported as healed in both the hydrogel dressing group and the hydrocolloid dressing group. However, the trialists recruited participants with more than one ulcer and presented data at the wound level rather than at participant level. Presenting data at the ulcer level means that 75% (15/20) of ulcers healed in the hydrogel group compared with 83% (15/18) in the foam dressing group. However, because of the unit of analysis issues with this analysis and a lack of further information, we have not considered the data further here.

No other outcomes were reported.

Summary: hydrogel dressings compared with foam dressings (1 trial; 34 participants with 38 wounds)

There were no clear data available for this comparison.

Comparison 5: hydrogel dressings compared with dextranomer paste dressings (1 trial; 135 participants)

One study compared a hydrogel dressing with dextranomer paste dressing (Colin 1996). This trial was at unclear risk of bias (Figure 2) and had a three-week follow-up.

Primary outcome: complete wound healing (proportion of ulcers healed during follow-up)

The one study included in this comparison did not report on complete wound healing.

Secondary outcome: change in ulcer size

Colin 1996 reported mean proportion reduction in wound area at 21 days (compared to baseline) (Table 8). Only range data and no information regarding variation around the mean figures (e.g. SD) were presented, so we did not consider the data further.

Secondary outcome - adverse events:

Colin 1996 reported limited adverse events. The information has been extracted in Table 8 but is not considered further.

Summary: hydrogel dressings compared with dextranomer paste dressings

There was one study that compared hydrogel dressings with dextranomer paste dressings. The study was small, had a short follow-up time, was at unclear of bias and reported limited outcome data. There was little data that could contribute usefully to this review.

Dressing compared with topical treatment

Comparison 6: hydrogel dressings compared with collagenase (1 trial; 27 participants)

One small study with 84-day follow-up compared a hydrogel dressing with collagenase (Milne 2012). We classed the study as being at a high risk of attrition bias, as only wounds debrided by day 42 were followed for the remaining follow-up period. Thus of the 14 participants randomised to hydrogel dressings, only four had been debrided at this point and were followed up to healing. Eleven of the 13 randomised to collagenase had been debrided and were followed up for healing. Thus for outcomes following debridement these data are highly compromised and could be considered non-randomised.

Primary outcome: complete wound healing (proportion of ulcers healed during follow-up)

Milne 2012 reported that three participants healed in the hydrogel group (14 participants) compared with nine in the collagenase group (13 participants). However only a sub-group of those randomised were followed up to this point for this outcome, so these data must be interpreted with caution.

Summary: hydrogel dressings compared with collagenase (1 trial; 27 participants)

Only one study compared hydrogel dressings with collagenase; it was small, at a high risk of attrition bias and presented very limited data.

'Summary of findings' tables

We planned to present an overview; synthesis of the volume and quality of the evidence is presented in 'Summary of findings' table for each of the dressing comparisons for following outcomes:

- time to complete ulcer healing where the data were analysed using appropriate survival analysis methods;
- proportion of ulcers completely healing during the trial period; and,
- adverse events.

Due to limitations in the reported data, we were only able to include estimates of complete healing and adverse events as detailed below.

Comparison 1: hydrogel dressings compared with basic wound contact dressings: *proportion of ulcers completely healed and adverse event data (*Table 1). **Comparison 2:** hydrogel dressings compared with hydrocolloid dressings: *proportion of ulcers completely healed and adverse event data (*Table 2. **Comparison 3:** One hydrogel dressing compared with another hydrogel dressing: *adverse event data (*Table 3). **Comparion 4:** hydrogel dressings compared with foam dressings: *proportion of ulcers completely healed (*Table 4). **Comparison 5:** hydrogel dressings compared with dextranomer paste dressing: *adverse event data (*Table 5). **Comparison 6:** hydrogel dressings compared with collagenase: *proportion of ulcers completely healed (*Table 6).

Discussion

Summary of main results

This review includes all available RCT evidence evaluating hydrogel dressings to treat pressure ulcers. The review includes 11 studies with a total of 523 participants that were relevant to the review. The studies compared hydrogel dressings with six different comparator treatments: basic wound contact dressings; hydrocolloid dressings; other hydrogel dressings; foam dressings; dextranomer paste dressings and a collagenase topical application. Overall the evidence found was limited: included studies were small and therefore statistically underpowered to detect treatment differences, should they exist. The volume and quality of reported data were also limited. For example the primary outcome for this review was complete wound healing, and data concerning the proportion of wounds healed were presented in five studies (Darkovich 1990; Milne 2012; Motta 1999; Sopata 2002; Thomas 1998). In Darkovich 1990 it was not clear how many participants had stage II pressure ulcers so the data had limited usability. Sopata 2002 also had unit of analysis issues. In Milne 2012 healing data were only presented for a sub-set of those randomised, so again we did not deem analysis of these data to be appropriate. From the remaining available data there was no evidence of a difference in numbers of healed wounds for the hydrogel dressing groups and either the basic wound contact dressings or hydrocolloid dressings.

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 for important outcome events, such as complete wound healing, to occur.The trials included in this study were all small and their follow-up periods were generally short which limited the number of healing events that took place and ruled out assessment of other potentially important outcomes such as recurrence. This resulted in an evidence base that is underpowered and can only report imprecise findings with wide confidence intervals.

All studies included study in this review were of high or unclear risk of bias. In general, the studies did not follow good practice, as laid out in conduct and reporting guidelines e.g. CONSORT (Schulz 2010). Key areas of good practice are: the robust generation of a randomisation sequence, for example, computer-generated randomisation; robust allocation concealment, for example the use of a telephone randomisation service; and, where possible, blinded outcome assessment. 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 plan to collect adverse events data and how this process will be standardised for both/all 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 SD or standard error should be presented around measures where appropriate. Steps should be taken during trial conduct to prevent missing data, as far as is possible.

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 hydrogel gel 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).The NICE review included all the studies included here, but this review includes three additional studies that were not included in the NICE review (Bale 1998a; Bale 1998b; Young 1996).

Authors' conclusions

Implications for practice.

A comprehensive review of current evidence did not find reliable evidence that hydrogel dressings either increase or decrease the healing pressure ulcers compared with other dressings. Practitioners

may therefore elect to consider other characteristics such as costs and symptom management properties when choosing between dressings.

Implications for research.

Currently there is no evidence of a difference in ulcer healing between hydrogel dressings and the other dressings and topical treatments 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 the questions of high priority to 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.

Acknowledgements

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Appendices

Appendix 1. Searches

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

---------- 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

---------- 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. Assessment of risk of bias (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; coin tossing; shuffling cards or envelopes; throwing dice; drawing of lots.

High risk of bias

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

Unclear

Insufficient information about the sequence generation process provided to permit 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 not sequentially-numbered); alternation or rotation; date of birth; case record number; any other explicitly unconcealed procedure.

Unclear

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

3. Blinding - was knowledge of the allocated interventions adequately prevented during the study?

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 was 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 was likely to introduce bias.

Unclear

Either of the following.

- Insufficient information provided 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 was 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 was not enough to have a clinically relevant impact on observed effect size.
- Missing data have been imputed using appropriate methods.

High risk of bias

Any one of the following.

- Reason for missing outcome data likely to be related to true outcome, with either imbalance in numbers or reasons for missing data across intervention groups.
- For dichotomous outcome data, the proportion of missing outcomes compared with observed event risk was 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 was 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 a judgement of low or high risk of bias (e.g. number randomised not stated, no reasons for missing data provided).
- The study did not address this outcome.

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

Low risk of bias

Either of the following.

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

High risk of bias

Any one of the following.

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

Unclear

Insufficient information provided 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. Assessment of risk of bias (cluster randomised controlled trials)

Types of bias in cluster-randomised 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.

1. Recruitment bias

Recruitment bias can occur when individuals are recruited to the trial after the clusters have been randomised, as knowledge about whether each cluster is an 'intervention' or 'control' cluster could affect the types of participants recruited.

2. Baseline imbalance

Cluster-randomised trials often randomise 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 randomised, there is a possibility of chance baseline imbalance between the randomised groups, in terms of either the clusters or the individuals. Although this is 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.

3. Loss of clusters

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 also lead to a risk of bias in cluster-randomised trials.

4. Incorrect analysis

Many cluster-randomised trials are analysed by incorrect statistical methods, that do not take the clustering into account. Such analyses create a 'unit of analysis error' and produce over-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, but if they remain uncorrected, they will receive too much weight in a meta-analysis.

5. Comparability with individually randomised trials

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 being 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 if the vaccine was 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 any 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 cluster.

Appendix 4. Glossary

amorphous	Lacking a clear shape or structure
autonomous	Of own free will
excoriation	Surface injury to the skin such as abrasions
exudate	Fluid that leaks out of a wound
hydrogel dressing	Water-based jelly-like substance, used to maintain the moisture at the surface of a wound
maceration	Softening and breakdown of skin due to exposure to moisture
non-blanchable	When an area of skin that is red is pressed the redness remains – as opposite to wh is blanchable and all redness disappears on pressing
occlusive	In the context of a dressing – something that is air-tight and water-tight
osteitis	Broad term for an infection of the bone
osteomyelitis	Inflammation in the marrow of a bone, can occur as a complication of infected pres ulcers
sero-sanguinous	Consists of serum and blood
shearing (in the context of pressure ulceration)	When a part of the body moves but the skin covering the area does not move with but remains static
slough	Dead cellular material at the surface of a wound
undermining and tunnelling	Tissue damage that extends below the surface of a wound and that can be out of c site of the wound surface: can sometimes involve deep tissues

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Data and analyses

Comparison 1. Hydrogel dressings compared with basic wound contact dressings.

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect s
1 Number of wounds healed	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtota only
2 Change in wound size (mean volume relative to baseline volume)	1		Mean Difference (IV, Fixed, 95% CI)	Subtota only
3 Change in wound size (mean reduction in size per week)	1		Mean Difference (IV, Fixed, 95% CI)	Subtota only

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Comparison 2. Hydrogel dressings compared with hydrocolloid dressings.

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect si
1 Complete wound healing	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtota only
2 Change in wound size: reduction in wound size per week	1		Mean Difference (IV, Fixed, 95% CI)	Subtota only
3 Costs	1		Mean Difference (IV, Fixed, 95% CI)	Subtota only

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Comparison 3. One brand of hydrogel dressings compared with another hydrogel dressing.

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect siz
1 Wound infection	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotal only
2 Adverse events: wound pain at end of study	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotal only
3 Adverse events: no pain on dressing removal	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotal only

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Characteristics of studies

Characteristics of included studies [ordered by study ID]

Bale 1998a.

Methods	Multi-centred, 2-arm RCT Undertaken in the UK Duration of follow up was maximum of 4 weeks (or until wound debridement)
Participants	50 participants Inclusion criteria listed: patients with necrotic pressure sores Exclusion criteria listed: patients with wounds greater than 8cm in diameter; patients with disease resulting in immunosuppression; women who were pregnant or nursing mothers; patients participating in any other clinical trial less than one month prior to this study or were already participating in this trial
Interventions	Group A: hydrogel (Sterigel®) manufactured from corn bran and composed of 2% w/w hemicellulose matrix and 20% propylene glycol (humectant and preservative) in purified water (n = 26) Group B: hydrogel (no further details; n = 24) Co-intervention: in both groups a low-adherent dressing (Telfa) and a semipermeable film (Tegaderm) were used as the secondary dressings. The hydrogel dressings were replaced in each group
Outcomes	Primary outcome: • none reported Secondary outcomes: • wound infection • adverse events (wound pain and pain on dressing removal)
Notes	Funding source: Seton Healthcare Study author confirmed that no further study data were available

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Quotation: "*Randomisation was by allocating the next sequential number from a computer-generated random number list*." Comment: method of generation of random schedule reported

Allocation concealment (selection bias)	Unclear risk	Quotation: no direct quotation Comment: not stated how allocated was concealed
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	**Wound infection and pain outcomes** Quotations: "*at each assessment, the nurse who was not blind to the tria* "*Photographs and tracings were also taken at each assessment.*" "*The photographs were sent for computerised wound analysis, undertaken by independent assessor who was blind to the treatment groups*." Comment: whilst outcomes not assessed in this review (e.g. wound debridement) were blinded it is likely that infection and adverse event assessment were not
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quotation: "*Two patients in Group A withdrew . . . which were unrelated the study. Three patients in Group B were withdrawn because they devel a wound infection.*" Comment: from the data presented, the analyses seem to be missing da two participants in each group
Selective reporting (reporting bias)	Low risk	Comment: outcomes pre-specified in the methods section were reporte results. This conclusion is based on the paper only, as protocol not obtai
Other bias	Low risk	No evidence that more than one wound per participant was analysed – r unit of analysis issues

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Bale 1998b.

Methods	2-arm RCT Undertaken in the UK Duration of follow up 4 weeks
Participants	23 participants Inclusion criteria listed: a pressure sore of grades 2, 3, and 4 with yellow/black necrosis an sloughy tissue covering the wound bed; availability for the maximum study period (up to 2 days); aged 18 years or over Exclusion criteria listed: a grade 1 sore; known hypersensitivity to any dressing materials to used in the study; uncontrolled diabetes mellitus; clinical signs of wound infection; receive cytotoxic therapy with the preceding 6 months; active vasculitis or any other reason at the investigator's discretion
Interventions	Group A: hydrogel, (Comfeel Purilon® gel: Coloplast; n = 12) Group B: hydrogel, (Intrasite® gel: Smith & Nephew; n = 11) Co-intervention: both gels were applied with the same secondary dressing regime – Comfe Ulcer Plus dressing. The dressing procedure involved removal of the old dressing, rinsing w isotonic saline solution, re-application of the gel dressing, and covering with Comfeel Ulcer dressing. Appropriate pressure-relieving equipment was used whenever possible. All

	participants had some form of pressure relief on entry into the study. Dressing changes occurred on a daily basis
Outcomes	Primary outcome: • none Secondary outcome: • adverse events (pain on dressing application)
Notes	Reported as an interim analysis of first 23 participants in a study with planned sample size 50 Funding source: not reported Study author confirmed that no further study data were available

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quotation: "*this is a prospective, randomized, controlled clinical trial. Patients . . . randomly allocated to . . .* " Comment: method of generation of random schedule not reported
Allocation concealment (selection bias)	Unclear risk	Comment: not stated
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quotation: "*Assessments by the study nurse . . .* " Comment: no mention of blinding in study report
Incomplete outcome data (attrition bias) All outcomes	High risk	Quotation: "*An interim analysis of the results for the first 23 patients is presented*." Comment: the presentation of data and the methods outlined suggest th data analysis was done considering only the first 23 participants. No justification was presented for this interim analysis
Selective reporting (reporting bias)	Unclear risk	Comment: outcomes pre-specified in the methods section were reported results. This conclusion is based on the paper only, as protocol not obtai
Other bias	Low risk	Comment: none noted

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Colin 1996.

Methods	2-arm parallel RCT Described as multi-national (no further details) Follow-up was 3 weeks
Participants	143 participants randomised, but 8 were excluded from analysis, and data for 135 participants was presented. It is not clear how the 143 were split into groups, so the information for 135 are presented here Inclusion criteria listed: sloughy pressure sores Excluded criteria listed: none reported Only stated "*strict inclusion and exclusion criteria*." Limited information
Interventions	Group A: hydrogel (Intrasite® gel; n = 67) Group B: dextranomer paste (Debrisan® Paste; n = 68) Co-intervention: in both groups a non-occlusive absorbent dressing (Melolin) was us as a secondary dressing
Outcomes	Primary outcome: • none reported Secondary outcome: • adverse events (including pain on dressing application and removal)
Notes	Funding source: not reported

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quotation: "*the patients were randomly allocated to two treatment groups.*" Comment: method of generation of random schedule not reported
Allocation concealment (selection bias)	Unclear risk	Comment: not stated
Blinding of outcome assessment (detection bias) L SEP All outcomes	Unclear risk	**All outcomes** Quotation: "*a formal wound assessment and an evaluation of dressi characteristics was performed every seven days. Photographs of eac sore were taken at the initial and final assessment.*"

		Comment: not clear who assessed the wounds or the pictures and whether this assessment was blinded
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Quotation: "*A total of 143 patients were recruited to the clinical stud but 8 patients provided no on-treatment efficacy data and were therefore excluded from intention-to-treat . . . .*" Comment: 8 participants not included in analysis: not clear to which groups these 8 participants belonged
Selective reporting (reporting bias)	Low risk	Comment: outcomes pre-specified in the methods section were reported in results. This conclusion is based on the paper only, as protocol not obtained
Other bias	Low risk	Quotation "*Where a patient presented with more than one pressure sore, only the largest sore was assessed*" Comment: no unit of analysis issue apparent

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Darkovich 1990.

Methods	2-arm RCT Multi-centred in acute care and nursing homes, undertaken in USA Duration of follow up 60 days
Participants	90 participants (129 ulcers – of these 71 ulcers were reported as stage II – not clear in how many participants) Inclusion criteria listed: people with stage I (ulceration or skin breakdown limited to superf epidermal and dermal layer); stage II (ulceration extending through the dermis but not thro adipose tissue); blood sugar level < 180 mg/dl; improved nutritional status; no known infec sinus tracts or fistulae in the wound Excluded criteria listed: people with venous stasis ulcers or diabetic ulcers, or receiving radiation therapy Only data regarding stage II ulcers was extracted
Interventions	Group A: hydrogel (BF Goodrich Company; n = not clear, 35 stage II ulcers) Group B: hydrocolloid dressing (DuoDERM, ConvaTec/Bristol-Myers; n = not clear, 36 stage ulcers) Co-intervention: initially the wound was cleansed with a 50/50 solution of 3% hydrogen peroxide and normal saline, rinsed with normal saline, and patted dry. Excessively oily skin around the wound was wiped with isopropyl alcohol or a standard skin preparation. Pressu reducing air mattresses (GaymarSof.Care®) were used for all participants. Dressing changed average every 3 to 4 days; wounds were cleansed with normal saline at each dressing chan
Outcomes	Primary outcome:

	• compete wound healing (numbers completely healed) Secondary outcome: • change in wound area (% area healed)
Notes	Data reported for stage I and II wounds separately. Data for stage II ulcers only presented h Funding source: not reported Data reported at the wound and not participant level. Not clear how many people were included in the analyses

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quotation: "*. . . control in a clinical trial . . .* " Comment: method of generation of random schedule not reported
Allocation concealment (selection bias)	Unclear risk	Quotation: "*Participants in the study were selected by clinicians or the patient care staff*." Comment: insufficient information on which to make a judgement
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quotation: "*the investigators were ET nurse/registered nurse . . .* " Comment: insufficient information on which to make a judgement
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Comment: unclear what data were included in analyses, as no informat on number of participants was given in results figures
Selective reporting (reporting bias)	Low risk	Comment: outcomes pre-specified in the methods section were reporte results. This conclusion is based on the paper only, as protocol not obta
Other bias	High risk	Comment: data reported at the wound rather than participant level. Ur analyses issues

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Matzen 1998.

Methods	2-arm RCT Multi-centred in home environment, undertaken in Denmark Duration of follow up 12 weeks
Participants	32 participants Inclusion criteria listed: people with stage 3 or 4 non-infected pressure sores located in sacral or trochanteric areas Excluded criteria listed: people with diseases or taking drugs known to impair healing
Interventions	Group A: hydrogel (Coloplast A/S, Denmark; n = 17) Group B: conventional treatment (wet saline compresses; n = 15) Co-intervention: all participants received initial surgical debridement in the outpatient clinic. All sores were dressed with Comfeel Transparent Dressing (Coloplast A/S, Denma All sores were cleaned and changed daily
Outcomes	Primary outcome: • complete wound healing (% ulcers healed) Secondary outcomes: • change in wound area (Mean % change in wound volume at study end) • wound infection (not defined) • adverse events (pain during treatment)
Notes	Funding source: not reported

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quotation: "*A randomised controlled study was carried out . . . the patie were randomised to be treated with either hydrogel or wet saline compresses.*" Comment: method of generation of randomisation schedule not reporte
Allocation concealment (selection bias)	Unclear risk	Comment: not stated

Blinding of outcome assessment (detection bias) [SEP] All outcomes	Unclear risk	**All outcomes** Quotation: "*Once a week the healing was estimated by the same investigator.*" Comment: insufficient information to judge. No other information provi for other outcomes
Incomplete outcome data (attrition bias) [SEP] All outcomes	Unclear risk	Quotation: "*The data of all the patients are included in the results . . .* " Comment: in total 20 participants were withdrawn (from the total of 32 is equivalent to 62.5%). Though the report states that "*the data of all patients are included*", it is unclear from the study report what data wer included in the analysis
Selective reporting (reporting bias)	Unclear risk	Comment: infection outcome presented for one group but not the othe Participants were also noted as being followed to healing within the foll up time, but healing data were not presented
Other bias	Low risk	No evidence of unit of analysis issues

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Milne 2012.

Methods	2-arm RCT Multi-centred in a long-term care setting environment, undertaken in USA Duration of follow-up: pressure ulcers from time of necrotic tissue removal up to 84 days fr initial enrolment
Participants	27 participants Inclusion criteria listed: aged over 18 years; 85% necrotic nonviable tissue on a pressure ulc between 1 cm^2 and 64 cm^2; hydrogel or collagenase dressing naive on study pressure ulcer; current use of parenteral or oral antibiotics, except for urinary tract suppressive therapy; haemoglobin A1C (HbA1c) < 7.9%; currently receiving adequate pressure redistribution to t affected area via such devices as a Group 2 or Group 3 specialty bed and a static air wheelc cushion, if out of bed and/or an offloading device if the pressure ulcer was located on the lo extremity; compliance with nutritional interventions per registered dietician; no allergies to collagenase or hydrogel; no allergies to semi-occlusive secondary dressing; written informe consent Exclusion criteria listed: steroid use > 5 mg daily; inability to co-operate with offloading recommendations; ankle-brachial index < 0 .85 if the pressure ulcer was located on the low extremity; presence of callus requiring sharp or surgical debridement within 3 days prior to enrolment; medical instability as deemed by the investigator; pregnancy; participation in another clinical trial or wound dressing evaluation in the 30 days prior to enrolment
Interventions	Group A: hydrogel dressing (SoloSite Gel, Smith & Nephew,Largo, FL; n = 14) Group B: collagenase (Santyl Onitment, Healthpoint, LTD, Fort Worth, TX; n = 13) Co-intervention: each dressing change consisted of the following: normal saline irrigation w device providing 4-15 psi (Irri-Max, Weston, FL) followed by application of the assigned

	therapeutic agent, "*nickel thick*," to the entire wound bed. In the presence of wound depth, after application of the assigned agent, the wound was then filled to the depth equal to tha the surrounding wound tissue with gauze dampened with normal saline, so that there was excess moisture noted when pressure from the clinician's hand was applied. The wound wa then covered with a semi-occlusive dressing (CoverSite, Smith and Nephew,Largo, FL). Dress changes occurred on a daily basis and as needed if the dressing integrity was lost due to dislodgement or incontinence
Outcomes	Primary outcome: • percentage of wounds that underwent epithelialisation (deemed to mean complete wound healing) Secondary outcome: • none
Notes	Funding source: not reported Study was reported as being in 2 phases. The review authors extracted it as 1 trial since randomisation only occurred once at the start of the study. Phase 2 of the trial followed onl those participants that had been debrided; because of this, we deemed the outcome data collection following debridement to be at a high risk of bias since only a sub-group of those randomised were followed up - see below Study authors confirmed that stage 1 pressure ulcers were excluded

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quotation: "*Randomization occurred after informed consent was obtained to reduce selection bias*." Comment: method of generation of random schedule not reported
Allocation concealment (selection bias)	Unclear risk	Comment: method of allocation not reported
Blinding of outcome assessment (detection bias) All outcomes	Low risk	**Wound healing** Quotation: "*Wound photos were evaluated for wound healing parameters us calibrated digital wound measurement software (Pictzar, Biovisual Technolog Elmwood Park, NJ) by 2 designated investigators blinded to randomization*." Comment: investigators enrolling participants could not foresee assignment to blindness of randomisation

Incomplete outcome data (attrition bias) SEP All outcomes	High risk	Comment: only a sub-group of those randomised were followed up to healin Only wounds debrided by day 42 were followed for the remaining follow-up period. Of the 14 participants randomised to hydrogel, 4 were debrided and were followed up to healing. Of the 13 randomised to the comparator treatn 11 were debrided and were followed up for healing. For the wound healing outcome of interest here there is very high level of participants lost to follow and it is difficult to present these outcome data meaningfully
Selective reporting (reporting bias)	High risk	Comment: data only reported for a sub-set of patients randomised
Other bias	Unclear risk	Comment: baseline difference in mean wound size with 12.29 cm^2 in the collagenase group and 7.9 cm^2 in the hydrogel group

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Motta 1999.

Methods	2-arm RCT Home healthcare setting, undertaken in USA Duration of follow up 8 weeks
Participants	10 participants Inclusion criteria listed: people with stage II or III pressure ulcers; understood and executed informed consent agreement Exclusion criteria listed: underlying medical condition such as long-term use of steroids or uncontrolled diabetes
Interventions	Group A: hydrogel (AcryDerm®, Wound Dressing, AcryMed Portland, Ore also known as Flexigel® Smith & Nephew, (Largo, Fla, n = 5) Group B: hydrocolloid dressing (DuoDERM® CGF, ConvaTec, Skillman, NJ; n = 5) Co-intervention: treatment was initiated by customary wound preparation procedures including light debridement, cleansing, and sterile saline irrigation, as required. The wound care dressings used in the study were obtained through normal wound care distribution channels and applied according to the manufacturer's recommendations, and were change on an "as needed basis" but not less than once weekly
Outcomes	Primary outcome: • complete wound healing (% ulcers healed) Secondary outcomes: • reduction in wound size

	• cost of treatment (mean cost of total treatment – including dressing and nursing c
Notes	Funding source: this study was funded by an educational grant from AcryMed Portland, Or

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quotation: "*A total of 10 home healthcare patients . . . were enrolled ar randomized for wound treatment using either . . . all of whom were randomly assigned to either . . .*" Comment: method of generation of random schedule not reported
Allocation concealment (selection bias)	Unclear risk	Comment: not reported
Blinding of outcome assessment (detection bias) SEP All outcomes	Unclear risk	Comment: no mention of blinding in study report
Incomplete outcome data (attrition bias) SEP All outcomes	Low risk	Comment: all data reported; no dropouts
Selective reporting (reporting bias)	Low risk	Comment: outcomes pre-specified in the methods section were reporte results. This conclusion is based on the paper only, as protocol not obta
Other bias	Low risk	No evidence that more than 1 wound per participants was analysed – n unit of analysis issues

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Mulder 1993.

Methods	3-arm RCT Multi-centred (3 independent sites) undertaken in USA Duration of follow up 8 weeks
Participants	67 participants Inclusion criteria listed: a stage II or III pressure ulcer no smaller than 1.5 cm x 0 .5 cm with maximum size of 10 cm x 10 cm; at least 18 years of age; had signed an informed consent statement; and a life expectancy of at least 2 months Exclusion criteria listed: stage IV wounds or those with tendon, bone, capsule, or fascia exposure; pregnant women; receiving chemotherapy; documented wound infection; extens

	undermining (> 1.0 cm) of the ulcer; testing positive for human immunodeficiency virus (HI taking > 10 mg of corticosteroids per day
Interventions	Group A: hydrogel (Clearsite® New Dimensions in Medicine, Dayton, Ohio; n = 23) Group B: hydrocolloid dressing (DuoDerm® ConvaTec/Bristol Myers-Squibb, Princeton, NJ; n 23) Group C: saline solution-moistened dressing (n = 21) Co-intervention: dressings were changed 3 times a day for saline solution-moistened gauze twice a week for the hydrocolloid dressing and the hydrogel dressing Appropriate instructions were given to the patients or the caregiver on changing dressings. When patients could not change their own dressings, assistance was provided by the clinica research nurse
Outcomes	Primary outcome: • none reported Secondary outcomes: • change in wound area (mean % reduction per week in wound size) • adverse events (adverse events and pain on dressing removal)
Notes	Funding source: not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quotation: "*The study was designed as a prospective, randomized, controlled three-arm parallel evaluation. Treatment groups were randomized in a 1 :1 :1 ratio by a computer generated randomization scheme*". Comment: the investigators described a random component in the sequence generation process, using a computer random number generator
Allocation concealment (selection bias)	Unclear risk	Comment: not reported
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	**All outcomes** Quotation: "*Wounds were photographed and treatment effect was assessed weekly. The perimeter of the target wounds was also traced weekly onto a pl sheet with a permanent marker. All tracings were measured with a VIASprogram*." "*Wound and dressing evaluations were done by the primary c*

		investigator.The same investigator performed the evaluations for each patien throughout the study whenever possible. A pre-trial conference was used to standardize observations between evaluators." Comment: process described, but no indication of blinding in assessment of outcomes
Incomplete outcome data (attrition bias) SEP All outcomes	Low risk	Comment: Table 6 presents mean and median percent reduction per week b treatment modality; there seem to be 6 participants (9%) in total missing fro the analyses
Selective reporting (reporting bias)	High risk	Quotation: after dressing removal, a scale was used to rate ease of removal, associated with removal, presence of dressing material remnant, and, if pres ease of removal of remnant Also stated that trialists measured wound healing (healing defined as comple (100%) wound re-epithelialisation) Comment: data described in methods not reported in results
Other bias	Unclear risk	No details given to allow review authors to judge whether participants had > wound followed, or whether this lack of independence was into account in t analysis

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Sopata 2002.

Methods	2 arm RCT Single centred, undertaken in Poland 8 week follow-up period
Participants	34 participants with 38 wounds Inclusion criteria listed: people with grade II or III pressure ulcers; patients with advanced cancer; life expectancy more than 8 weeks. Exclusion criteria listed: poor general condition, with very low levels of haemoglob 7 mmol/l) and albumin (< 2.5 g/dl); use of drugs such as corticosteroids that could affect wound healing
Interventions	Group A: hydrogel dressing (Aquagel; n = 17 participants with 20 wounds) Group B: foam dressing (Lyofoam/polyurethane foam dressing (Seton); n = 17 participants with 18 wounds) Study report noted that dressings were changed according to clinical need
Outcomes	Primary outcome: • complete wound healing (% ulcers healed)

	Secondary outcome: • none
Notes	Unit of analysis issues, as some participants had > 1 ulcer and data were presente the wound rather than participant level

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Quotation: "*Patients were randomly assigned using a computer numbering system*" Comment: adequate method
Allocation concealment (selection bias)	Unclear risk	Coment: not reported
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Coment: not reported
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Comment: none noted
Selective reporting (reporting bias)	Unclear risk	Comment: outcomes pre-specified in the methods section were reported in results. This conclusion is based on the paper only, as protocol not obtained
Other bias	High risk	Comment: unit of analysis issues, as some participants had > 1 ul and data were presented at the wound rather than participant le

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Thomas 1998.

Methods	2-arm randomised controlled trial Multi-centred, undertaken in USA Duration of follow-up 10 weeks
Participants	41 participants Inclusion criteria listed: people of either sex; aged 18 or older; with a sta III or IV pressure ulcer with an area ≥ 1.0 cm^2 Exclusion criteria listed: ulcers resulting from venous or arterial insufficiency or other non-pressure etiology (e.g. vasculitis or diabetic ulcer); wounds with sinus tracts and/or

	undermining > 1 cm; clinically infected wounds; concomitant use of other topical mediatio the study ulcer or concomitant systemic steroid therapy was not allowed; severe generaliz medical condition and estimated survival of < 6 months; HIV-positive; currently abusing alc or drugs; pregnant; breast-feeding; not on acceptable means of contraception; had a curre diagnosis of cancer; or receiving chemotherapy
Interventions	Group A: hydrogel dressing (Carrasyn® Gel Wound Dressing, Carrington Laboratories, Inc, Irving, TX) Group B: saline dressing 41 participants were randomised but it is noted that 11 failed to complete and were exclu from the analysis. Information regarding the number of participants at randomisation was provided. Of the 30 participants included in the analysis, 16 were included in Group A and Group B Co-intervention: the study ulcer was treated with a 1/3 inch layer of either the acemannan hydrogel or a sterile non woven saline-soaked gauze, then covered with a dry sterile non-woven gauze and held in place with a thick gauze dressing. Dressing changed daily by patie until the next follow-up; during the follow-up, wounds were cleansed with saline and gentl mechanical wiping with gauze
Outcomes	Primary outcome: • complete wound healing (numbers and rates of completely healed; mean time-to-healing) Secondary outcome: • none reported
Notes	Funding source: a grant from Carrington Laboratories, Inc, Irving, TX

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quotation: "*a randomized, controlled trial*." Comment: method of generation of random schedule not reported
Allocation concealment (selection bias)	Unclear risk	Quotation: "*Subjects were recruited from skilled nursing facilities and ho health care agencies*." Comment: insufficient information on which to base judgement

Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	**All outcomes** Quotation: "*at each visit, the study parameters were recorded and the wound photographed . . . "* Comment: insufficient information on which to base judgements for all outcomes
Incomplete outcome data (attrition bias) All outcomes	High risk	Quotation: "*11 patients (27%) failed to complete the study . . . no deaths were attributed to the study treatment.*" "*Statistical analysis was perfor on the remaining 30 subjects*." Comment: data excluded from the analyses
Selective reporting (reporting bias)	Unclear risk	Comment: outcomes pre-specified in the methods section were reporte results. This conclusion is based on the paper only, as protocol not obtai
Other bias	Low risk	No evidence of unit of analysis issues, but report does not specifically no that 1 wound per person was followed and there was limited informatio

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Young 1996.

Methods	2-arm RCT Multi-centred (both hospital and community-treated patients), undertaken in the UK Duration of follow-up 6 weeks
Participants	65 participants Inclusion criteria listed: people with grade 2, 3 or 4 pressure sores on any area of the body with any amount of wound exudate and any amount of slough or necrotic tissue Exclusion criteria listed: pressure sores > 10 cm x 10 cm or that were clinically infected; pe receiving any treatment that may have delayed wound healing and those whose dressing needed changing more than twice a day due to contamination (e.g. urine/faeces)
Interventions	Group A: hydrogel (NU-GEL®, Johnson & Johnson Medical; n = 34) Group B: hydrogel (IntraSite® gel, Smith & Nephew; n = 31) Co-intervention: after dispensing the study gel onto the wound, a secondary dressing of Release Non-Adherent Absorbent Dressing (Johnson & Johnson Medical) was applied, follo by a protective/retaining material if necessary. The frequency of redressing was determine the amount of exudate, but it was advised that dressings be left in place for up to 3 days. I necessary, mechanical debridement of devitalised tissue was permitted. Gel and wound assessments were made at each dressing change during the study period
Outcomes	Primary outcome: • None

	Secondary outcomes: • change in wound size • adverse events
Notes	Funding source: not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quotation: "*This paper describes a multi-centre, prospective, randomiz study . . . "* Comment: method of generation of random schedule not reported
Allocation concealment (selection bias)	Unclear risk	Comment: not stated
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quotation: "*wound assessments were made at each dressing change during the study period*." Comment: no mention of blinding in study report
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Comment: not stated
Selective reporting (reporting bias)	Low risk	Comment: outcomes pre-specified in the methods section were report in results. This conclusion is based on the paper only, as protocol not obtained
Other bias	Low risk	No evidence of unit of analysis issues, but report does not specifically that 1 wound per person was followed and there was limited informat

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Abbreviations

RCT; randomised controlled trial w/w; weight to weight

Characteristics of excluded studies [ordered by study ID]

Study	Reason for exclusion
Banks 1994	Study did not evaluate a hydrogel dressing
Bito 2012	Study did not evaluate a hydrogel dressing
Brod 1990	Study did not evaluate a hydrogel dressing
Fear 1992	No relevant outcome reported - author contacted
Flanagan 1995	Study was not an RCT. Also did not evaluate a hydrogel dressing
Kaya 2005	Study population included people with stage I pressure ulcers - authors contacted to see if data stage II and above available
Kurzuk-Howard 1985	Study did not evaluate a hydrogel dressing
Lum 1996	Use of a hydrogel dressing was not the only systematic difference between trial groups
Manzanero 2004	Study did not evaluate a hydrogel dressing
Meaume 2003	Study did not evaluate a hydrogel dressing
Moody 1994	Study did not evaluate a hydrogel dressing
Oleske 1986	Study did not evaluate a hydrogel dressing
Parnell 2005	Study was not a randomised controlled trial.
Perez 2000	Study did not evaluate a hydrogel dressing
Peschardt 1997	No relevant outcome reported - author contacted
Sadyak 1990	Study was not an RCT
Small 2002	Use of a hydrogel dressing was not the only systematic difference between trial groups
Torra i Bou 1999a	No relevant outcome reported - author contacted
Torra i Bou 1999b	Study did not evaluate a hydrogel dressing
Weheida 1991	Study was not an RCT

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Abbreviation

RCT; randomised controlled trial

Contributions of authors

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

Contributions of editorial base:

Nicky Cullum: edited the protocol and review; advised on methodology, interpretation and protocol content. Approved the final review prior to submission. Sally Bell-Syer: coordinated the editorial process. Advised on methodology, interpretation and content. Edited the protocol and the review. Amanda Briant: designed the search strategy and edited the search methods section and ran the searches for the review.

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Declarations of interest

Jo C Dumville: nothing to declare. Nikki Stubbs: funding from pharmaceutical companies supports training and education events in the service 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. Samantha J Keogh: nothing to declare. Rachel M 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. Zhenmi Liu: nothing to declare.

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