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Dressings and topical agents for preventing pressure ulcers (Review)

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[Intervention Review]

Dressings and topical agents for preventing pressure ulcers

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ABSTRACT

Background

Pressure ulcers, which are localised injury to the skin, or underlying tissue or both, occur when people are unable to reposition themselves to relieve pressure on bony prominences. Pressure ulcers are often difficult to heal, painful and impact negatively on the individual's quality of life. The cost implications of pressure ulcer treatment are considerable, compounding the challenges in providing cost effective, efficient health services. Efforts to prevent the development of pressure ulcers have focused on nutritional support, pressure redistributing devices, turning regimes and the application of various topical agents and dressings designed to maintain healthy skin, relieve pressure and prevent shearing forces. Although products aimed at preventing pressure ulcers are widely used, it remains unclear which, if any, of these approaches are effective in preventing the development of pressure ulcers.

Objectives

To evaluate the effects of dressings and topical agents on the prevention of pressure ulcers, in people of any age without existing pressure ulcers, but considered to be at risk of developing a pressure ulcer, in any healthcare setting.

Search methods

In February 2013 we searched the following electronic databases to identify reports of relevant randomised clinical trials (RCTs): the Cochrane Wounds Group Specialised Register; the Cochrane Central Register of Controlled Trials (CENTRAL) (*The Cochrane Library*); Database of Abstracts of Reviews of Effects (*The Cochrane Library*); Ovid MEDLINE; Ovid MEDLINE (In-Process & Other Non-Indexed Citations); Ovid EMBASE; and EBSCO CINAHL.

Selection criteria

We included RCTs evaluating the use of dressings, topical agents, or topical agents with dressings, compared with a different dressing, topical agent, or combined topical agent and dressing, or no intervention or standard care, with the aim of preventing the development of a pressure ulcer.

Data collection and analysis

We assessed trials for their appropriateness for inclusion and for their risk of bias. This was done by two review authors working independently, using pre-determined inclusion and quality criteria.

Main results

Five trials (940 participants) of unclear or high risk of bias compared a topical agent with a placebo. Four of these trials randomised by individual and one by cluster. When results from the five trials were combined, the risk ratio (RR) was 0.78 (95% CI 0.47 to 1.31; P value 0.35) indicating no overall beneficial effect of the topical agents. When the cluster randomised trial was omitted from the analysis, use of topical agents reduced the pressure ulcer incidence by 36%; RR 0.64 (95% CI 0.49 to 0.83; P value 0.0008).

Four trials (561 participants), all of which were of high or unclear risk of bias, showed that dressings applied over bony prominences reduced pressure ulcer incidence; RR 0.21 (95% CI 0.09 to 0.51; P value 0.0006).

Authors' conclusions

There is insufficient evidence from RCTs to support or refute the use of topical agents applied over bony prominences to prevent pressure ulcers. Although the incidence of pressure ulcers was reduced when dressings were used to protect the skin, results were compromised by the low quality of the included trials. These trials contained substantial risk of bias and clinical heterogeneity (variations in populations and interventions); consequently, results should be interpreted as inconclusive. Further well designed trials addressing important clinical, quality of life and economic outcomes are justified, based on the incidence of the problem and the high costs associated with pressure ulcer management.

PLAIN LANGUAGE SUMMARY

Dressings or topical agents for preventing pressure ulcers

Pressure ulcers, sometimes known as bedsores or pressure sores, commonly occur in people who cannot, or find it difficult to, move themselves. Pressure ulcers are hard to heal, so it is important to try to prevent them from occurring in the first place. Various cream and lotions (topical agents) have been used for this purpose; the idea is that pressure ulcers are less likely to occur when the skin is healthy and nourished. A number of different types of dressings are also used to protect the skin from damage. We reviewed studies that compared topical agents or dressings with other methods for preventing pressure ulcers. We found nine trials that investigated these that included 1501 people. These showed that the evidence concerning the use of topical agents or dressings for preventing pressure ulcers is not clear. The reason why the evidence is not clear is because the quality of trials was low and most had manufacturer sponsorship, which introduces potential biases, such as overestimating the effectiveness of the product. Consequently, further trials are needed to confirm results of this review.

SUMMARY OF FINDINGS FOR THE MAIN COMPARISON [Explanation]

Topical agent versus placebo combined studies for preventing pressure ulcers

Patient or population: Patients at risk of developing pressure ulcers
Settings: Hospitals
Intervention: Topical agent versus placebo

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Control	Topical agent versus placebo				
Pressure ulcer incidence Observation Follow-up: 3 to 24 weeks	**Study population**		**RR 0.78** (0.47 to 1.31)	940 (5 studies)	⊕◯◯◯ **very low**[1,2,3,4]	
	251 per 1000	**195 per 1000** (118 to 328)				
	Moderate					
	313 per 1000	**244 per 1000** (147 to 410)				

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

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

[1] Limited information provided for generation of allocation sequence, allocation concealment and outcome evaluation. Three of the five trials had incomplete reporting and the majority received manufacturer sponsorship

[2] There were variations in both the intervention products and the control products. Different measures (some unvalidated) were used to assess the stage of the pressure ulcer

[3] Most of the participants were geriatric patients in hospitals and nursing homes. Other groups at high risk (such as those unable to reposition and intensive care patients) were not represented

[4] Confidence intervals were wide due to small sample sizes

BACKGROUND

Description of the condition

A pressure ulcer is defined as localised injury to the skin, underlying tissue or both, usually over a bony prominence, as a result of pressure, or pressure in combination with shear. A number of contributing or confounding factors are also associated with pressure ulcers; the significance of these factors has yet to be elucidated (EPUAP/NPUAP 2009). Prevalence rates range from 8.8% to 53.2% (Gallagher 2008; Moore 2012) and incidence rates vary from 7% to 71.6% (Moore 2011; Scott 2006; Whittington 2004). Pressure ulcers are generally staged 1, 2, 3 and 4, according to the depth of tissue damage, with grade 1 being the least severe and grade 4 indicating full-scale tissue destruction (Moore 2005) (Appendix 1). The most common anatomical sites for pressure ulcers to occur are the sacrum and the heels, and the majority are stage 1 or stage 2 in severity (Gallagher 2008; Gethin 2005; Moore 2000; Moore 2011).

Pressure ulcers occur in people who do not have the ability to reposition themselves in order to relieve pressure on bony prominences. This ability is often diminished in the very old, the malnourished and those with an acute illness (Wann-Hansson 2008). It is important to note, however, that although pressure ulcers often occur in older individuals, other populations, such as those with spinal cord injury and hospital patients exposed to prolonged periods of immobility (for example during long surgical procedures) also have high pressure ulcer incidence (Gallagher 2008; Sheerin 2005). Certain patients, with stage 1 pressure ulcers, are also at increased risk of the pressure ulcer progressing to a stage 4 (Vanderwee 2009). For example, individuals with hypotension, contractures, or a history of cerebral vascular accident, tend to develop more serious pressure ulcers despite standard preventive measures (Vanderwee 2009). Thus, a clear focus on the adoption of targeted prevention strategies is important at the outset, so that the individual is not exposed to pressure ulcers in the first instance (Sullivan 2013; Vanderwee 2009).

Pressure ulcers impact negatively on an individual's quality of life. Indeed, the emotional, physical, mental and social domains of life are all profoundly affected (Spilsbury 2007). Pain is described as one of the most significant problems for individuals with pressure ulcers (Spilsbury 2007). Importantly, many of the treatment regimens adopted exacerbate these adverse effects (Hopkins 2006). Thus, it is important to consider the impact of prevention and treatment strategies on the individual, and to choose those that will reduce discomfort and enhance rehabilitation wherever possible (Gorecki 2009). Pressure ulcers are also associated with increased mortality (Kroger 2008). Whether this relates to the fact that pressure ulcers occur in a population that is for the most part debilitated, with a high incidence of co-morbidities, or whether it relates to the presence of a pressure ulcer alone, remains unclear (Brown 2003; Tarnowski 2013; Thomas 1996). However, a recent cohort study suggests an almost two-fold increase in death among those with pressure ulcers when compared to their matched counterparts who do not have pressure ulcers (Landi 2007).

Pressure ulcers impose a significant financial burden on healthcare systems, indeed Dealey 2012 suggests that the total annual cost for pressure ulcer management in the UK is GBP 1.4 to 2.1 billion annually, or 4% of the total UK healthcare expenditure. In Australia, the mean hospital costs for pressure ulcers are estimated at AUD 296.05 million (Graves 2005a). In the United States, hospital costs for adults with a diagnosis of pressure ulcers totaled USD 11.0 billion in 2006 (Russo 2006). That pressure ulcers are an expensive problem has also been reported in the Netherlands where they have been found to be the third most costly issue for healthcare services. (Haalboom 2000). This is not due to the cost of medication or surgical interventions, but due to prolonged hospitalisation and the intensive nursing care required. Indeed, pressure ulcers are associated with significantly higher mean unadjusted hospital costs per episode of care. (USD 37,288 versus USD 13,924, P value 0.0001) (Allman 1999).

The exact mechanisms by which externally applied mechanical forces (pressure and shear) result in pressure ulcer development are not clearly understood (Stekelenburg 2007). Pressure is equal to force divided by area, the same amount of force applied to a small area, when compared to a bigger area, will result in greater pressure (O'Callaghan 2007). Shear is the mechanical stress acting parallel to a plane of interest, such as is seen when a person sits up in bed and then begins to slide down the bed, with his/her skin remaining in the same place because it sticks to the bed linen (Collier 2006). It is postulated that, in the presence of prolonged pressure and shear forces, there are four mechanisms within three functional units that lead to pressure ulcer development. The functional units are the capillaries, the interstitial (between cells) spaces and the cells (Nixon 2005). The mechanisms are local ischaemia (lack of oxygen) Kosiak 1959, reperfusion injury (injury to cells caused by the restoration of blood supply to tissues) (Tsuji 2005), impaired interstitial (between cells) fluid flow, and lymphatic drainage (Reddy 1981) and sustained deformity of cells (Stekelenburg 2007). These mechanisms, alone or combined, reduce the oxygen and nutrient supply to cells, impair the removal of waste products following cell metabolism, leading to cell damage and inevitable tissue destruction. It is important to note, however, that none of the process described will have any relevance unless the individual is exposed to sustained external mechanical forces. Therefore, as pressure/shear are the causative factors, reducing the amount and duration of pressure/shear will decrease the likelihood of pressure ulcer development.

Description of the intervention

Pressure ulcer prevention is now an expanding industry and involves a range of interventions, such as nutritional care (Langer 2003), skin care, use of pressure redistribution surfaces (McInnes

2011), and repositioning (Moore 2011). Selection of an appropriate topical therapy (i.e. those applied to the skin) is also believed to contribute to pressure ulcer prevention strategies, and such therapies are widely used within the clinical setting (Butcher 2009), in combination with other preventive strategies.

A topical agent is a cream or an ointment that is applied directly to the skin (Reddy 2006). Whereas a dressing is a therapeutic or protective material applied to a wound to promote healing, it may also be used to protect the skin from damage (Butcher 2009). Dressings are classified into groups depending on their characteristics (Moore 2006).

For the purposes of pressure ulcer prevention, the types of dressings used are primarily those that afford protection to the skin, such as:

- semi-permeable film dressings (a thin polyurethane membrane coated with a layer of an acrylic adhesive);
- hydrocolloid dressings (a dressing containing a dispersion of gelatin, pectin and carboxy-methylcellulose together with other polymers and adhesives forming a flexible wafer); or
- foam dressings (an open cell, hydrophobic, polyurethane foam sheet) (Dressings.org 2010).

Topical agents may be used in isolation, but are more likely to be impregnated in dressings, or used in combination with dressings.

How the intervention might work

The EPUAP/NPUAP 2009 guidelines suggest that use of film dressings may help to protect the skin against the adverse effects of friction, furthermore, they suggest that use of foam dressings may protect parts of the body at risk of shear injury. It has also been suggested that the application of topical agents directly to the skin will protect against the adverse affects of friction (Reddy 2006). Both friction and shear are included as risk factors for pressure ulcer development in the Braden pressure ulcer risk assessment scale (Bergstrom 1987). However, the recent EPUAP/NPUAP pressure ulcer prevention and management guidelines have removed friction from their definition of a pressure ulcer (EPUAP/NPUAP 2009), suggesting that although friction forces contribute to tissue damage, they are not a contributory factor in pressure ulcer development (EPUAP/NPUAP 2009). Nonetheless, the International Review 2010 argues that because friction and shear are closely linked, friction should be discussed in the context of pressure ulcer development (and thus pressure ulcer prevention). One hypothesis upon which the use of dressings/topical agents for the prevention of pressure ulcers is based, relates to their role in the reduction of friction forces (Butcher 2009). Furthermore, Lahmann 2011 identified that friction was a causative factor in the development of superficial wounds resembling grade 1 and 2 pressure ulcers, whereas, pressure and shear were responsible for the development of deeper ulcers (grades 3 and 4). Earlier work by Kottner 2009 supports this argument, in classifying ulcers as superficial - predominantly caused by friction, or deep - predominantly caused by pressure. Therefore, there is debate regarding the relative contribution of friction to the development of pressure ulcers, nonetheless, friction does contribute to tissue damage, which in itself is problematic for patients and carers, and this is where topical agents and dressings may play a role.

Why it is important to do this review

The use of dressings for preventing pressure ulcers is discussed in the literature and in international pressure ulcer prevention guidelines. To date, the level of evidence to support these recommendations has not been systematically assessed (Butcher 2009). The use of adjunct therapies (for example, dressings, creams, or lotions) as part of prevention strategies adds to the overall costs, therefore it is important to explore whether use of these therapies provides potential benefit to patients (Moore 2008).

OBJECTIVES

To evaluate the effects of dressings and topical agents for preventing pressure ulcers, in people of any age without existing pressure ulcers, but considered to be at risk of developing a pressure ulcer, in any care setting.

METHODS

Criteria for considering studies for this review

Types of studies

Studies that randomise individuals (randomised controlled trials (RCTs)) or that randomise by groups (cluster-RCTs), were eligible for inclusion.

Types of participants

People of any age, both adults and children, without a pressure ulcer, but considered to be at risk of developing a pressure ulcer, in any care setting.

Types of interventions

The primary intervention was any wound dressing or topical agent applied to the skin at any frequency with the aim of preventing the development of a pressure ulcer. We included RCTs comparing the use of dressings, topical agents, or topical agents with dressings, compared with a different dressing, topical agent, combined

topical agent and dressing, no intervention or standard care or any other intervention as a comparator, with the aim of preventing the development of a pressure ulcer.

Types of outcome measures

Primary outcomes

Pressure ulcer incidence (the proportion of people developing any new pressure ulcer(s) of any grade). For the purpose of this review a pressure ulcer was defined as a localised injury to the skin, underlying tissue or both, usually over a bony prominence, as a result of pressure, or pressure in combination with shear. This review included all grades of pressure ulcer damage, following the definition of the EPUAP/NPUAP (EPUAP/NPUAP 2009). We accepted the definition of the method of assessment of pressure ulcer damage as outlined by trial authors.

Secondary outcomes

- Stage of any new pressure ulcer(s).
- Time to ulcer development.
- Costs of interventions.
- Quality of life as measured by a validated scale.
- Pain at dressing change, measured using a validated scale.
- Acceptability of the intervention (or satisfaction) with respect to patient comfort.
- Adverse events.
- Length of hospital stay.

Search methods for identification of studies

Electronic searches

In February 2013 we searched the following electronic databases for RCTs or cluster-RCTs which evaluated the use of dressings or topical agents for the prevention of pressure ulcers:

- The Cochrane Wounds Group Specialised Register (searched 21 February 2013);
- The Cochrane Central Register of Controlled Trials (CENTRAL) (*The Cochrane Library* 2013, Issue 1);
- Ovid MEDLINE (2005 to February Week 2 2013);
- Ovid MEDLINE (In-Process & Other Non-Indexed Citations, February 20, 2013);
- Ovid EMBASE (2005 to 2013 Week 07);
- EBSCO CINAHL (2005 to 15 February 2013).

We used the following search strategy in the Cochrane Central Register of Controlled Trials (CENTRAL):
#1 MeSH descriptor: [Biological Dressings] explode all trees 61
#2 MeSH descriptor: [Occlusive Dressings] explode all trees 435
#3 MeSH descriptor: [Hydrogels] explode all trees 211
#4 MeSH descriptor: [Alginates] explode all trees 170
#5 dressing*:ti,ab,kw 2468
#6 (hydrocolloid* or alginate* or hydrogel* or foam or bead or film or films or tulle or gauze or non-adherent or non adherent):ti,ab,kw 4780
#7 MeSH descriptor: [Anti-Bacterial Agents] explode all trees 8199
#8 MeSH descriptor: [Administration, Topical] explode all trees 11774
#9 #7 and #8 449
#10 (topical near/2 antibiotic*):ti,ab 274
#11 MeSH descriptor: [Anti-Infective Agents, Local] explode all trees 1473
#12 MeSH descriptor: [Anti-Inflammatory Agents] explode all trees 10106
#13 MeSH descriptor: [Glucocorticoids] explode all trees 3075
#14 #12 or #13 12314
#15 #8 and #14 1724
#16 (topical near/2 (steroid* or corticosteroid* or glucocorticoid*)):ti,ab,kw 1314
#17 MeSH descriptor: [Estrogens] explode all trees 1247
#18 #8 and #17 122
#19 (topical near/2 (oestrogen or estrogen)):ti,ab,kw 29
#20 MeSH descriptor: [Enzymes] explode all trees 21699
#21 #8 and #20 353
#22 (topical near/2 enzym*):ti,ab,kw 4
#23 MeSH descriptor: [Growth Substances] explode all trees 2398
#24 #8 and #23 38
#25 (topical near/2 growth factor*):ti,ab,kw 13
#26 MeSH descriptor: [Collagen] explode all trees 1645
#27 #8 and #26 70
#28 (topical near/2 collagen):ti,ab,kw 14
#29 (topical near/2 silver):ti,ab 16
#30 MeSH descriptor: [Ointments] explode all trees 1588
#31 (ointment* or lotion* or cream*):ti,ab,kw 6662
#32 MeSH descriptor: [Honey] explode all trees 80
#33 honey.ti,ab,kw 5
#34 (topical next (agent* or preparation* or therap* or treatment*)):ti,ab,kw 1778
#35 (#1 or #2 or #3 or #4 or #5 or #6 or #9 or #10 or #11 or #15 or #16 or #18 or #19 or #21 or #22 or #24 or #25 or #27 or #28 or #29 or #30 or #31 or #32 or #33 or #34) 17393
#36 MeSH descriptor: [Pressure Ulcer] explode all trees 495
#37 pressure next (ulcer* or sore*):ti,ab,kw 872
#38 decubitus next (ulcer* or sore*):ti,ab,kw 89
#39 (bed next sore*) or bedsore*:ti,ab,kw 48
#40 (#36 or #37 or #38 or #39) 935
#41 #35 and #40 293
The search strategies for Ovid MEDLINE, Ovid EMBASE and EBSCO CINAHL can be found in Appendix 2. 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 2010). There were no restrictions with respect to language, date of publication or study setting .

We searched the following clinical trials registries on June 4 2012:

- Clinical Trials.gov
- Internationsl Clinical Trials Registry Platfom (ICTRP)

Searching other resources

We searched the bibliographies of all retrieved and relevant publications identified by these strategies for further studies. We contacted manufacturers of dressings (n = 15) used in the prevention of pressure ulcers, as identified in the British National Formulary (BNF 2011), and experts in the field to ask for information relevant to this review.

Data collection and analysis

Selection of studies

Two review authors independently assessed titles and, where available, abstracts of the studies identified by the search strategy against the eligibility criteria for inclusion in the review. We obtained full versions of potentially relevant studies and the two review authors independently screened these against the inclusion criteria. Any differences in opinion were resolved by discussion and, where necessary, reference to the Cochrane Wounds Group editorial base.

Data extraction and management

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

- author, title, source;
- date of study, study's geographical location;
- care setting;
- inclusion/exclusion criteria;
- patient characteristics;
- balance of groups at baseline;
- study design details;
- method of randomisation;
- allocation concealment;
- sample size calculation and sample size;
- intervention details, concurrent interventions;
- type of dressing and frequency of dressing change;
- use of additional dressing materials;
- patient length of hospital stay;
- outcome measures;
- blinding (of the patient/outcome assessor);
- length of follow-up;
- loss to follow-up;
- results;
- intention-to-treat analysis; and
- conclusions as reported by the study authors.

Any differences in opinion were resolved by discussion and, where necessary, with reference to the Cochrane Wounds Group editorial base. If data were missing from reports, we attempted to contact study authors to obtain the missing information.

Assessment of risk of bias in included studies

Two review authors independently assessed the included studies using the Cochrane Collaboration tool for assessing risk of bias (Higgins 2011a). This tool addresses six specific domains: namely, sequence generation, allocation concealment, blinding, incomplete outcome data, selective outcome reporting and other issues (e.g. extreme baseline imbalance) see Appendix 3 for details of criteria on which the judgement were based. We assessed blinding and completeness of outcome data for each outcome separately.

Measures of treatment effect

For dichotomous outcomes, we calculated risk ratio (RR) plus 95% confidence intervals (CI). If continuous outcomes had been reported, we would have calculated mean difference (MD) plus 95% confidence intervals. We would also have analysed time-to-event data (e.g. time to ulceration) as survival data, using the appropriate analytical method (as per the *Cochrane Handbook for Systematic Reviews of Interventions* version 5) (Deeks 2011). If time-to-event data had been incorrectly presented as continuous data, we would have presented the data in a narrative format in the review.

Summary of findings tables

To assess the overall body of evidence, we developed two Summary of findings tables (one for each comparison - topical agents and dressings), using GRADE profiler^{TM}. The quality of the body of evidence was assessed against five principle domains 1) limitations in design and implementation; 2) indirectness of evidence or generalisability of findings; 3) inconsistency of results - for example unexplained heterogeneity and inconsistent findings; 4) imprecision of results where confidence intervals are wide; and 5) other potential biases, for example publication bias or high manufacturer involvement (Schunemann 2011) .

Unit of analysis issues

There was one unit of analysis issue and one potential unit of analysis issue. In the (Houwing 2008) trial, a cluster design was

used and data was analysed as though allocation was by individual. In the Nakagami 2007 trial, patients acted as their own controls. That is, the intervention dressing was randomly applied to the left or right greater trochanter and, although there was a potential for a unit of analysis issue with the design, this did not occur as no pressure ulcers occurred in either group.

Dealing with missing data

If there was evidence of missing data, we contacted the trial authors to request the information. Where trial authors could not provide missing data, we assessed the risk of bias of the missing data and decided if the missing data were of 'low' or 'high' risk of bias according to our risk of bias criteria (Higgins 2011a). Or, if data were considered to be missing at random, we analysed the available information. Where outcome data were missing, we used an available-case analysis, based on the numbers of participants for whom outcome data were known.

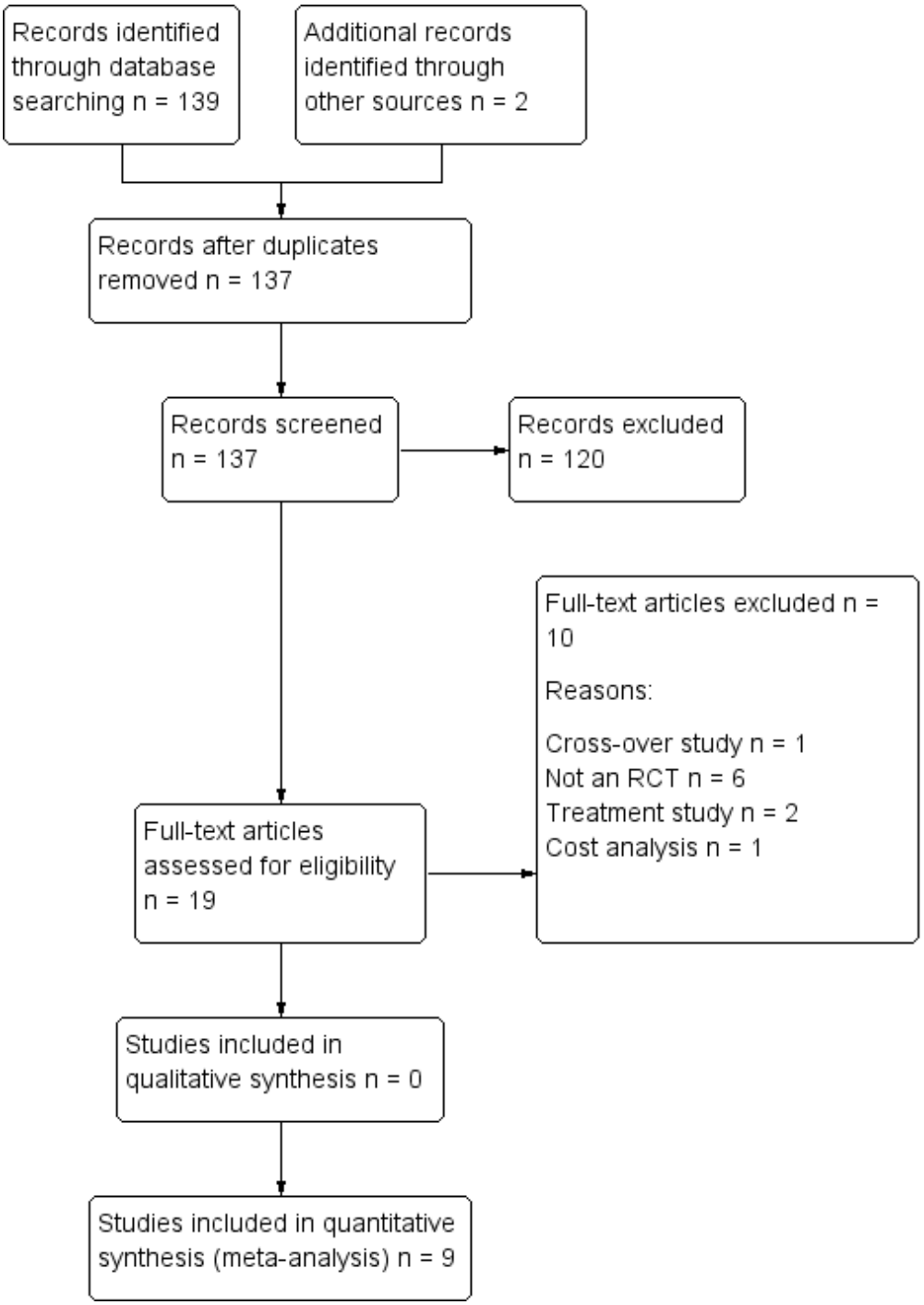
Assessment of heterogeneity

We explored clinical heterogeneity by examining potentially influential factors, e.g. type of topical agent or dressing, care setting or participant characteristics, such as level of mobility. We assessed statistical heterogeneity using the I^2 statistic (Higgins 2003). This examines the percentage of total variation across studies due to clinical and/or methodological heterogeneity rather than to chance. Values of I^2 over 75% indicate a high level of heterogeneity.

Assessment of reporting biases

We completed a 'Risk of bias' table for each eligible study and presented an assessment of risk of bias using a 'Risk of bias' summary figure (Figure 1) which presents the judgements in a cross-tabulation. This display of internal validity indicates the weight the reader may give to the results of each study.

Figure 1. Study flow diagram.



Data synthesis

We conducted a structured narrative summary of the studies reviewed. We entered quantitative data into RevMan 5 (RevMan 2011), and conducted analyses using RevMan software. For dichotomous outcomes, we calculated risk ratio (RR) plus 95% CI. We carried out statistical pooling on groups of studies that were considered to be sufficiently similar. Where heterogeneity was absent or low (I^2 = 0% to 25%) we used a fixed-effect model; if there was evidence of heterogeneity (I^2 more than 25%), we used a random-effects model. If heterogeneity was very high (I^2 over 75%) we did not pool the data (Higgins 2003). We included the cluster randomised controlled trial (Houwing 2008) in the data synthesis, even though the study was analysed as if the randomisation was performed on individuals rather than clusters. To explore the effect of this approach, we conducted separate analyses with and without the cluster trial.

Subgroup analysis and investigation of heterogeneity

If sufficient data had been available we would have undertake the following subgroup analysis:

- type of setting (community, hospital, inpatient, outpatient).

However, all studies were conducted in hospital settings.

Sensitivity analysis

We were to have performed a sensitivity analysis by excluding studies at high risk of bias. In this sensitivity analysis, we would have only included 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. However, no studies met these criteria.

RESULTS

Description of studies

Results of the search

The search yielded a total of 139 citations and two further papers were identified when JW contacted 15 dressings manufacturers enquiring about further potential papers. Both review authors examined the abstracts of all papers independently to assess for potential relevance. After excluding duplicates, 19 trials appeared to meet the inclusion criteria and full texts were retrieved. A further 10 trials were subsequently excluded; reasons for their exclusion are shown in Figure 1 and are detailed in the Characteristics of excluded studies.

Included studies

See the Characteristics of included studies table.

Nine trials with a total of 1501 participants were included in the review (Green 1974; Han 2011; Houwing 2008; Kalowes 2012; Nakagami 2007; Qiuli 2010; Smith 1985; Torra i Bou 2005; Van Der Cammen 1987), one of which was a cluster RCT (Houwing 2008). Contact was attempted with seven investigators to seek additional information. We were unable to locate Green 1974, no response was received from the authors of Han 2011, Qiuli 2010, Torra i Bou 2005 or Van Der Cammen 1987, but Houwing 2008 and Kalowes 2012 responded and provided answers to several questions.

Participants

The mean age of participants in seven of the trials varied between 67.5 and 86 years (Green 1974; Houwing 2008; Kalowes 2012; Nakagami 2007; Van Der Cammen 1987; Smith 2010; Torra i Bou 2009). In a trial of spinal injury patients, the mean age was 56 years (Han 2011). The participants in the Qiuli 2010 study were aged between 55 and 80 years.

Three of the trials were conducted in the UK (Green 1974; Smith 2010; Van Der Cammen 1987), one in China (Han 2011), two in Japan (Nakagami 2007; Qiuli 2010), one in Spain (Torra i Bou 2009), one in the Netherlands (Houwing 2008), and one in the USA (Kalowes 2012).

An inclusion criterion for four trials was that the individuals were at high risk of pressure ulcer development according to the Braden pressure ulcer risk assessment scale (Bergstrom 1987; Houwing 2008; Kalowes 2012; Nakagami 2007; Torra i Bou 2009). For one trial the individuals had a Norton pressure sore risk-assessment scale score of between five and 14 (meaning high or very high risk) (Norton 1975; Van Der Cammen 1987), and for a further trial the participants had a Waterlow score of 18-23 (meaning high or very high risk) (Qiuli 2010; Waterlow 1985). For the remaining trials other non-validated risk assessment methods were used. For example Green 1974 used what was defined as a 'clinical risk score', Smith 2010 included 'patients with intact skin' and it was unclear what criteria were used for the Han 2011 trial.

Four studies included elderly hospital or nursing home patients (Green 1974; Houwing 2008; Nakagami 2007; Smith 1985); one included internal medicine patients at high risk of pressure injury (Torra i Bou 2005). Participants in the Han 2011 trial were admitted with a posterior spinal injury; in the Van Der Cammen

1987 trial participants were hospitalised and chair-bound; participants in the Kalowes 2012 trial were nursed in a medical/surgical/trauma intensive care unit or a cardiac intensive care unit, and the participants in the Qiuli 2010 trial were nursed in a neurosurgical department.

Interventions

See "Additional tables; Table 1' for the composition of the topical agents and dressings.

Topical applications

In the Green 1974 study the intervention was a lotion described as "active", containing hexachlorophane 0.5%, saturated hydrocarbons (squalene (Cosbiol 3%) and glyoxyle diureide), allantoin 0.2%, antioxidants, lanolin, fatty acids, fatty acid esters, fatty alcohols, preservatives and distilled water. For the control group, a lotion described as "inert" containing lanolin, fatty acids, fatty acid esters, fatty alcohols, preservatives, distilled water and mineral oils, was applied. The lotions were applied manually to pressure areas (sacral, trochanteric, heel and shoulder and other areas, as indicated). Excess friction was avoided. The participants' skin was inspected every two hours, and, if the participant was incontinent, the skin was washed with soap and water, then dried, and the relevant lotion applied. In the absence of incontinence, routine washing and reapplication of lotion was carried out every six hours.
In the Smith 1985 study the topical application for the intervention group was Conotrane, which contains silicone cream, 20% dimethicone 350 and a broad spectrum antiseptic (0.05% hydrargaphen). For the control group the topical application was described as a bland cream known as Unguentum. For both groups, as part of the routine skin care regimen, the skin of the participants was washed when required, with water, then dried thoroughly and the ointment applied.
In the Houwing 2008 study the topical application for the intervention group was massage using a "DMSO-cream." The DMSO-cream consisted of 5% dimethyl sulfoxide in Vaseline-cetomacrogol cream; participants also had a 30^{o} position change every six hours. For the placebo group the topical application was a three-minute massage of the buttock, heel, and ankle regions with an indifferent cream (Vaseline-cetomacrogol), combined with a 30^{o} position change every six hours for four weeks. For the control group, no topical application was applied, but the participants had a 30^{o} position change every six hours for four weeks.
In the Torra i Bou 2005 study the topical application for the intervention group was Mepentol, a hyperoxygenated fatty acid compound consisting of oleic acid, palmitic acid, stearic acid, palmitoleic acid, linoleic acid, gamma linoleic acid, arachidonic acid, and eicosenoic acid. For the control group, the topical application was a compound consisting of trisostearin (99.4%) and perfume (0.6%). In both groups, the topical application was applied twice daily to at least three areas of the body, sacrum, trochanter and heels.
Finally, in the Van Der Cammen 1987 study the topical application was Prevasore, which contains hexyl nicotinate, zinc stearate, isopropyl myristate, Dimethicone 350, cetrimide and glycol. For the control group the topical application was Dermalex which contains hexachlorophane, squalene and allantoin. In both groups, the participants' buttocks and sacral areas were washed and dried and the topical application was applied at least twice daily and again after changing, if the individual was wet or soiled.
In all of the studies using topical applications, no additional dressings were applied, the topical application was applied to the skin and the skin was then left bare.

Dressings

In the Han 2011 study the intervention was a polyurethane film and foam dressing (Hang' huier transparent strip and foam dressing). This was applied to the pressure areas of the participants during surgery. The control group did not have any dressings applied.
In the Nakagami 2007 study, the intervention was a dressing, known as PPD (pressure ulcer preventive dressing). This consists of a skin adhesive layer (hydrocolloid) containing an intercellular lipid-ceramide, a support layer (urethane film) and an outer layer of multi-filament nylon fibres. The dressing was applied to either the right or left greater trochanter (depending on randomisation) of the participant. The dressing was replaced weekly. No dressing was applied in the control arm of the study.
In the Qiuli 2010 study the intervention was a soft silicone, self-adherent, bordered foam dressing applied to the integral skin site of pressed bone protuberance. The frequency of dressing changes was not mentioned in the paper. For the control group, massage of the site of bone protuberance was undertaken at each patient-turning episode (two- to three-hourly). The duration of massage was not mentioned in the paper. Both groups were nursed on air cushion mattresses and repositioned every two to three hours.
In the final study of Kalowes 2012, the intervention was a soft silicone, self-adherent, bordered foam dressing applied to the subjects' sacrum. The dressing was changed every three days, or as needed. No dressing was applied to the skin of the control group participants. Both groups were nursed according to the SKIN bundle (**S**urface, **K**eep turning, **I**ncontinence and **N**utrition) (Gibbons 2006).

Outcomes

All the studies included the development of a pressure ulcer as their primary outcome.Two used the validated scale of EPUAP 1999 (Houwing 2008; Nakagami 2007). Han 2011 reported use of an international measurement for pressure ulcers titled "WCET"; Green 1974 used a five-point scale; Smith 1985 used the classification of Barbarel 1977; while Van Der Cammen 1987 used a

five-point scale; finally, Torra i Bou 2005, Qiuli 2010 and Kalowes 2012 did not identify the classification system used.

Ethics and consent

No information about ethics approval or participant consent was provided by Green 1974, Han 2011, Kalowes 2012, Qiuli 2010 or Van Der Cammen 1987. Although Smith 1985 had ethics approval, it was not reported whether participants consented. Information on ethics and consent for the remaining studies was not available (Houwing 2008; Nakagami 2007; Torra i Bou 2005).

Funding

Seven of the nine trials reported receiving support from the manufacturers of the interventional product (Green 1974; Han 2011; Kalowes 2012; Nakagami 2007; Smith 1985; Torra i Bou 2005; Van Der Cammen 1987). Sponsorship for the Houwing 2008 study came from ZonMw (Ministry of Health, Welfare and Sport and the Netherlands Organisation for Scientific Research). Qiuli 2010 did not state whether sponsorship was received. In the Nakagami 2007 trial, investigators were involved in developing the dressing used in the study. The corresponding author in the Van Der Cammen 1987 trial was an employee of the company producing the intervention product.

Excluded studies

We excluded a total of 10 studies. Six studies were not RCTs (Callaghan 1998; Declaire 1997; Garcia Fernandez 2005; Hsu 2011; Huang 2009; Smith 2010); one was a cross-over study (Duimel-Peeters 2007); one was a cost analysis from an unpublished study with limited information (Torra i Bou 2009); and two considered interventions for treating pressure ulcers rather than preventing them (Kuisma 1987; Stoker 1990). See the Characteristics of excluded studies table for details.

Risk of bias in included studies

See Figure 2 for the summary of the risk of bias and Figure 3 for the graph of the risk of bias of the included studies. Several studies had inadequate reporting, which limited our assessment of potential bias (see Figure 2; and Figure 3).

Figure 2. Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.

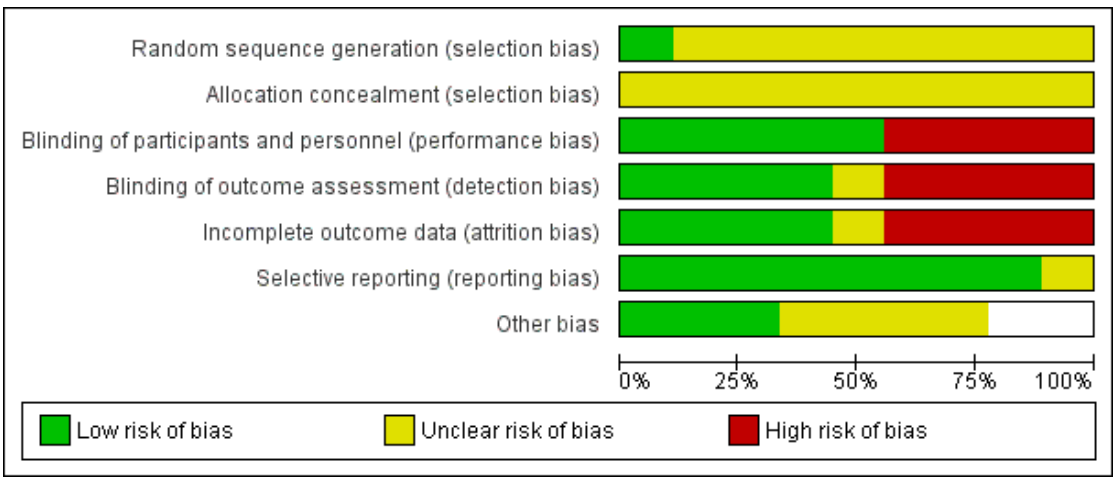
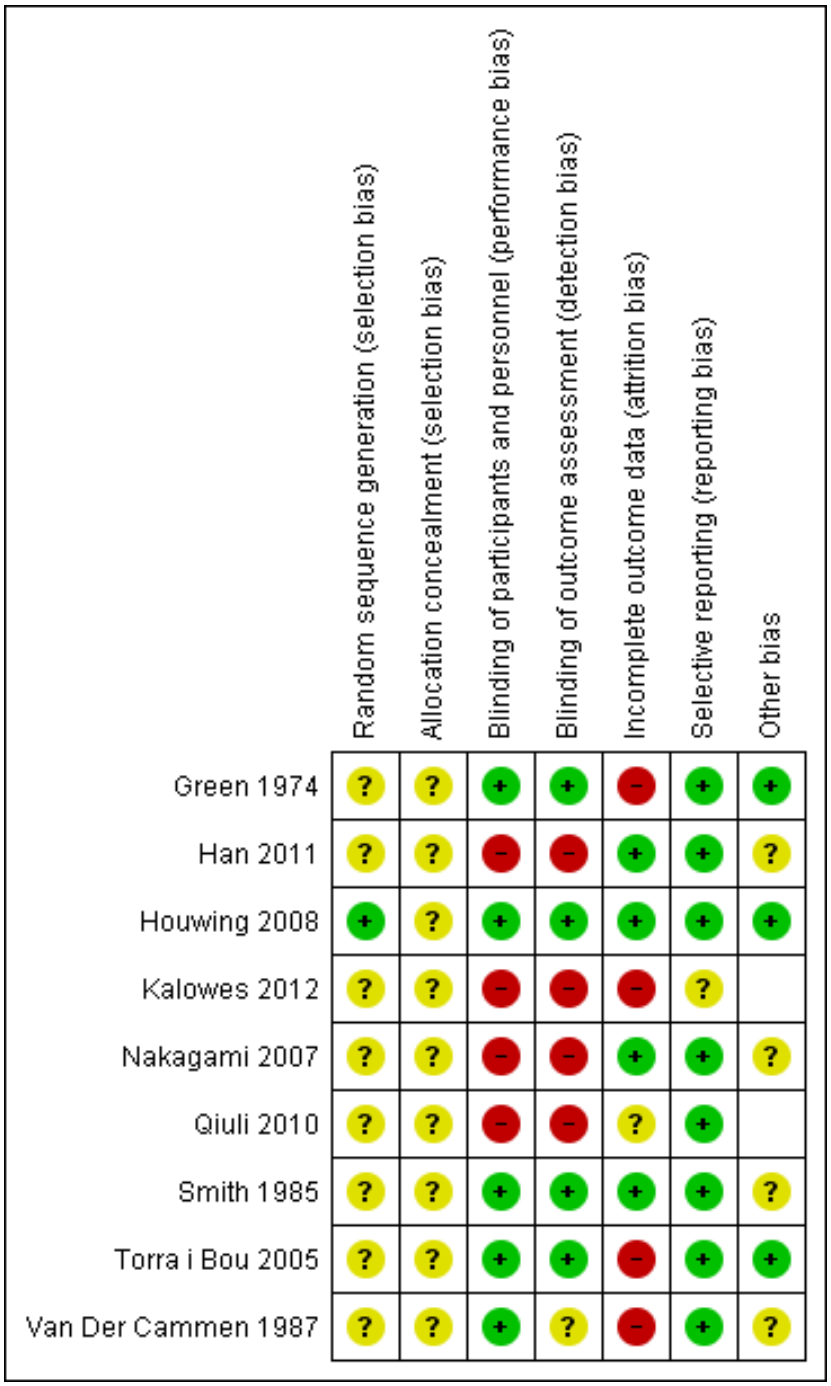


Figure 3. Risk of bias summary: review authors' judgements about each risk of bias item for each included study.



Allocation

Random sequence generation

Methods used for generating the allocation sequence were unclear in all but one of the trials (Houwing 2008).

Allocation concealment

Methods used for concealing the group allocation were unclear in all trials.

Blinding

All of the 'topical agent' trials were blinded to investigators, patients and outcome assessors (Green 1974; Houwing 2008; Smith 1985; Torra i Bou 2005; Van Der Cammen 1987). Difference in the appearance of dressings in the remaining trials made blinding impossible (Han 2011; Kalowes 2012; Nakagami 2007; Qiuli 2010).

Incomplete outcome data

Outcome data reporting was judged to be complete in five trials (Han 2011; Houwing 2008; Nakagami 2007; Qiuli 2010; Smith 1985). In the remaining four studies (Green 1974; Kalowes 2012; Torra i Bou 2005; Van Der Cammen 1987), 9% to 48% of those recruited were excluded from the analysis, so the studies were judged to be at high risk of bias.

Selective reporting

All of the trials provided information on the outcomes identified in their trial methods, so were considered to be at low risk of reporting bias. None of the trials had registered their protocol on a trials registry database.

Other potential sources of bias

In the Smith 1985 study, 33% more participants in the placebo group were incontinent for urine, and 25% more were incontinent for faeces, than in the treatment group and this was not adjusted for in the analysis. We had only limited information about the methods used in the Han 2011 study, and data from a conference presentation to interpret for the Kalowes 2012 study. It is possible that there may have been biases about which we were unaware. Finally in the Nakagami 2007 and Van Der Cammen 1987 studies, the investigators were part of the group that developed the intervention products, so introducing a potential for bias, for example, overestimating the treatment effect.

Effects of interventions

See: **Summary of findings for the main comparison** Topical agent compared with placebo for preventing pressure ulcers; **Summary of findings 2** Dressing compared with no dressing combined studies for preventing pressure ulcers

See Summary of findings for the main comparison and Summary of findings 2 for a summary of main outcomes.

All of the studies reported data for our primary outcome; pressure ulcer incidence. Five trials investigated the effects of topical agents and four trials the effects of dressings. In line with these differences, we used two comparisons, one for topical applications and one for dressings regardless of dressing type. It was not possible to combine numerical data for our secondary outcomes, so these results are presented in narrative form.

How the results are presented and what the terms mean

Results for dichotomous variables are presented as risk ratios (RR) with 95% CI. Risk ratio is the ratio of the risk of the event of interest (e.g. pressure ulcers developed) in the experimental group divided by the risk of this event in the control group and indicates the chances of pressure ulcer development for people in the experimental group compared with the control group (Higgins 2011b). A risk ratio of one means there is no difference between two groups in terms of their risk of pressure ulcer development, whereas a risk ratio of greater than one, or of less than one, usually means that use of a specific topical agent or dressing either increases (risk ratio greater than one) or decreases (risk ratio less than one) the risk of pressure ulcer development (Higgins 2011b). As, by definition, the risk of an event occurring in the control group is 1, then the RR reduction associated with using an experimental treatment is 1-RR. The RR indicates the relative benefit of a therapy but not the actual benefit, that is, it does not take into account the number of people who would have developed a pressure ulcer anyway, without the intervention (Higgins 2011b).

Comparison 1: Topical agent compared with placebo (five trials, 940 participants)

Primary outcome

Incidence of pressure ulcers

Five trials were included in this comparison.

The study by Green 1974, with a three-week follow-up period, found a pressure ulcer incidence of 25% (n = 19/76; with erythema 17%, n = 13/76; superficial sores 7.8%, n = 6/76) in the

intervention group and a pressure ulcer incidence of 34% (n = 31/91; with erythema 13.2%, n = 12/91; superficial sores 20.8%, n = 19/91) in the control group. The intervention group were treated with an active lotion and the control were treated with an inert lotion. There was no statistically significant difference in pressure ulcer incidence between the two groups (RR 0.73, 95% CI 0.45 to 1.19; P value 0.21) (Analysis 1.1).

The study by Smith 1985, had a 24-week follow-up period, and noted a pressure ulcer incidence of 27% (n = 35/129) in the experimental group treated with Conotrane. Conversely, a pressure ulcer incidence of 36.4% (n = 47/129) was noted in the control group treated with a bland cream, known as Unguentum. The majority of pressure ulcers (87%) in both groups were described as superficial. There was no statistically significant difference in pressure ulcer incidence between the two groups (RR 0.74, 95% CI 0.52 to 1.07; P value 0.11) (Analysis 1.1).

The study by Van Der Cammen 1987, with a follow-up of three weeks, noted a pressure ulcer incidence of 1.8% (n = 1/54) in those treated with Prevasore (the intervention treatment) compared with a pressure ulcer incidence of 6.0% (n = 3/50) in those treated with Dermalex (the control treatment).There was no statistically significant difference in pressure ulcer incidence between the two groups (RR 0.31, 95% CI 0.03 to 2.87; P value 0.30) (Analysis 1.1).

The study by Torra i Bou 2005, with a follow-up of 30 days, compared an intervention of Mepentol with a placebo compound. The trial authors identified a pressure ulcer incidence of 7.3% (n = 12/164) in the intervention group, compared with a pressure ulcer incidence of 17.37% (n = 29/167) in the placebo group. There was a statistically significant difference in pressure ulcer incidence between those treated with the topical agent (Mepentol) and the placebo (RR 0.45, 95% CI 0.22 to 0.80; P value 0.008) (Analysis 1.1).

The study by Houwing 2008, with a follow-up of four weeks, explored the impact of three different regimens on the incidence of pressure ulcers. Participants were treated with either the intervention treatment of massage with a DMSO-cream combined with a six-hourly, 30^o position change; or a placebo intervention consisting of a three-minute massage with what the trial authors referred to as an indifferent cream combined with a six-hourly, 30^o position change; or a control intervention, where no creams were applied to participants' skin, but they did have a six-hourly, 30^o position change. Houwing 2008 identified a pressure ulcer incidence of 62.1% (n = 18/29) in the intervention group, 31.3% (n = 10/32) in the placebo group and 38.9% (n = 7/18) in the control group. There was no statistically significant difference in pressure ulcer incidence between the intervention and the control group (RR 1.60, 95% CI 0.84 to 3.04; P value 0.16) (Analysis 2.1). There was no statistically significant difference in pressure ulcer incidence between the placebo and control group (RR = 0.80, 95% CI 0.37 to 1.74; P value 0.58) (Analysis 3.1). There was a statistically significant difference in pressure ulcer incidence between the intervention and the placebo group (RR = 1.99, 95% CI 1.10 to 3.57; P value 0.02) (Analysis 4.1), this difference was in favour of the placebo group which meant that the intervention increased the number of pressure ulcers that developed compared to the placebo group.

Houwing 2008 used cluster randomisation and did not allow for the clustering in the analysis, so we have reported the combined results with and without this study. When results were combined with inclusion of Houwing 2008, the overall RR was 0.78 (95% CI 0.47 to 1.31; P value 0.35) indicating no overall beneficial effect of the topical agents. There was a high level of heterogeneity in this analysis (72%), which persisted when a random-effects model was used (Analysis 5.1; Figure 4). When results were combined without Houwing 2008, the level of heterogeneity was 0%, the overall RR was 0.64 (95% CI 0.49 to 0.83; P value 0.0008) (Analysis 5.2; Figure 5), showing a statistically significant beneficial effect of the topical agents, however, this should be interpreted with caution owing to the potential bias in the included trials.

Figure 4. Forest plot of comparison: Topical agent versus placebo, outcome: 5.1 Pressure ulcer incidence. (Houwing study included)

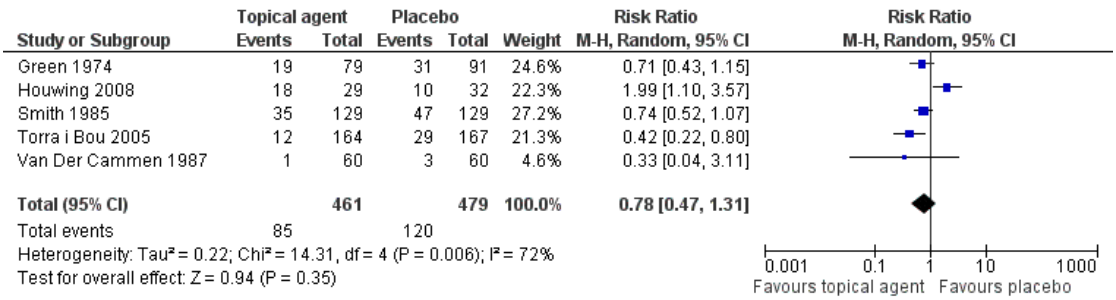
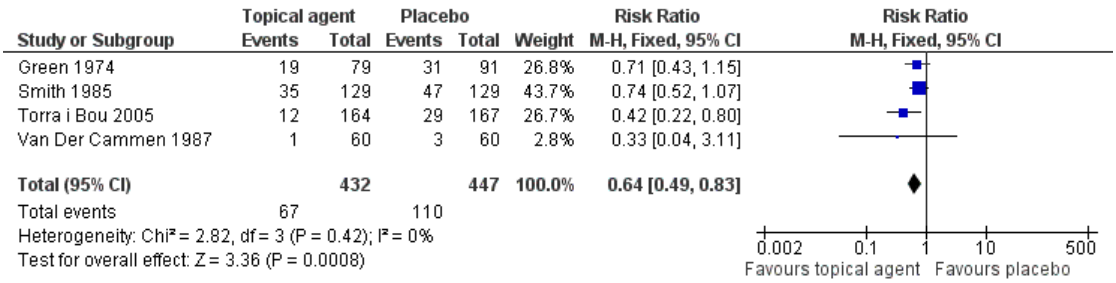


Figure 5. Forest plot of comparison: Topical agent versus placebo, outcome: 5.2 Pressure ulcer incidence. (Houwing study excluded)



Secondary outcomes

Stage of any new pressure ulcer(s)

In the Smith 1985 trial (258 participants) the group that used a silicone cream application found there was no difference in the incidence of third or fourth stage pressure ulcers compared with placebo (stage 3: intervention 5/129 (3.8%); placebo 4/129 (3.0%) and stage 4: intervention 0/129 (0.0%); placebo 1/129 (0.7%)).

Time to ulcer development

Two trials assessed time to the development of a new pressure ulcer (501 participants) (Green 1974; Torra i Bou 2005). In the Green 1974 trial, ulcers appeared approximately one day later in the intervention group than in the placebo group (intervention 9.8 days versus placebo 8.7 days (whether these are means or medians was not stated in the trial report). Kaplan-Meier survival curves, used in the Torra i Bou 2005 trial, indicated that pressure ulcer development was delayed among people in the intervention group; the reported P value was 0.0054.

Adverse events

Only Green 1974 reported data about adverse events. In their study of 170 participants, two people in the intervention arm developed erythematous eruptions of the skin where the cream had been applied. A patch test indicated hypersensitivity to the product (Dermalex™ which is an emollient based cream consisting of mainly hexachlorophane).

Cost

Costs in the Torra i Bou 2005 trial were based on the cost of the intervention product (Mepentol) only, this was reported to be approximately EUR 9.3 per month, no comparison cost data were provided.

Comparison 2: Dressing compared with no dressing (four trials, 444 participants)

Primary outcome

Incidence of pressure ulcers

Four trials were included in this comparison.

The Nakagami 2007 study had a three-week follow-up period. Participants were treated with a dressing, known as PPD, applied to either the right or the left trochanter. Particpants acted as their own controls, i.e. no dressing was applied to the opposite trochanter. No pressure ulcers developed in either group (intervention n = 0/37; control n = 0/37). This study is prone to unit of analysis error, as two sides of each patient were randomised to intervention and control however no pressure ulcers developed in either group. The trial authors reported the presence of persistent erythema in 5.5% (n = 2/37) of the intervention group and in 29.7% (n = 11/37) of the control group. We have interpreted the presence of persistent erythema as stage 1 pressure ulcer. There was a statistically significant difference in pressure ulcer incidence between the intervention and the control groups in favour of the dressing (RR 0.18, 95% CI 0.04 to 0.76; P value 0.02) (Analysis 6.1).

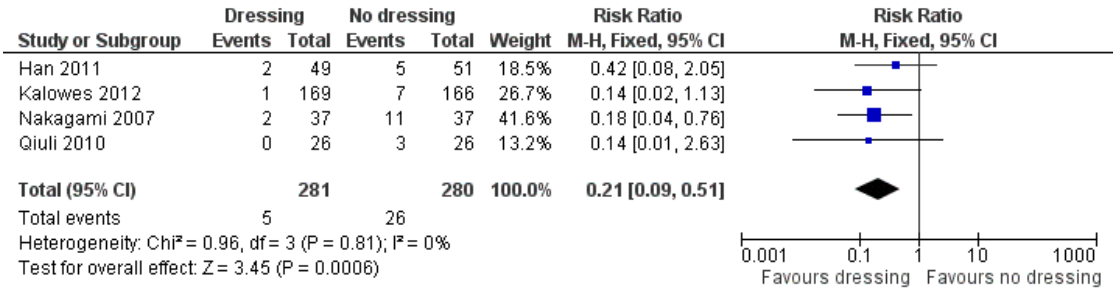
The Han 2011 study, had a 72-hour follow-up period. The intervention group, treated with Kang' huier transparent strip and foam dressing (a polyurethane film and foam dressing) had a pressure ulcer incidence of 4.1% (n = 2/29). The control group had no dressings applied and had a pressure ulcer incidence of 9.8% (n = 5/51). There was no statistically significant difference in pressure ulcer incidence between the two groups (RR 0.70, 95% CI 0.15 to 3.40; P value 0.66) (Analysis 6.1).

The Qiuli 2010 study had a seven-day follow-up period. The intervention group (n = 26), had a dressing applied at the integral skin site of pressed bone protuberance; pressure ulcer incidence in this group was zero. The control group (n = 26) had no dressing applied, but had massage on the site of bone protuberance; pressure ulcer incidence in this group was 11.5% (n = 3/26). There was no statistically significant difference in pressure ulcer incidence between the two groups (RR 0.14, 95% CI 0.01 to 2.63; P value 0.19) (Analysis 6.1).

The Kalowes 2012 study followed up participants while in the intensive care unit, where the mean length of stay was 6.5 days (range 0 to 120 days). The intervention group had a dressing applied to the skin covering the sacral area.The control group had no dressing applied. The incidence of pressure ulcers in the intervention group was 0.5% (n = 1/169), and the incidence in the control group was 4% (n = 7/166). The trial authors reported a statistically significant difference between the groups (P value 0.001), however, RevMan analysis did not replicate this and found no statistical difference between the groups (RR 0.14, 95% CI 0.02 to 1.13; P value 0.06) (Analysis 6.1).

When data were combined from these four studies (Han 2011; Kalowes 2012; Nakagami 2007; Qiuli 2010), they showed that dressings applied over bony prominences reduced the pressure ulcer incidence P value to 0.0006; RR 0.21 (95% CI 0.09 to 0.51) (Analysis 7.1; Figure 6). Although the difference was statistically significant, the studies are at high or uncertain risk of bias and firm conclusions cannot be drawn from this analysis.

Figure 6. Forest plot of comparison: Dressing versus no dressing, outcome: 7.1 Pressure ulcer incidence.



Secondary outcomes

Stage of any new pressure ulcer(s)

In the Kalowes 2012 trial (335 participants), using a dressing applied to the skin covering the sacral area, yielded no statistically significant difference in the incidence of deep tissue injury compared to the group with no dressing (deep tissue injury: intervention 1/169 (0.5%); placebo 1/166 (0.6%). The remaining six pressure ulcers occurred in the placebo group and were classified as: unstageable: 2/166 (1%) and stage 2: 4/166 (2%).

Pre-defined outcomes sought but not reported

No studies reported on quality of life, pain at dressing change, or length of hospital stay. Stage of any new pressure ulcer(s); time to ulcer development; cost and adverse events were poorly described.

ADDITIONAL SUMMARY OF FINDINGS [Explanation]

Dressing versus no dressing combined studies for preventing pressure ulcers

Patient or population: Patients at risk of developing pressure ulcers
Settings: Hospital
Intervention: Dressing versus no 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				
	Control	Dressing versus no dressing combined studies				
Pressure ulcer incidence Observation Follow-up: > 48 h to 3 weeks	Study population		RR 0.21 (0.09 to 0.51)	561 (4 studies)	⊕⊕◯◯ low[1,2,3,4]	
	93 per 1000	19 per 1000 (8 to 47)				
	Moderate					
	107 per 1000	22 per 1000 (10 to 55)				

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

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

[1] There was no description of sequence generation or allocation concealment in any of the trials. Intervention blinding was not possible. Outcome assessment was not blinded in two studies and unclear in the remaining two trials. Three of the four trials received manufacturer support

[2] Although heterogeneity was low, three types of dressings were used, the composition of each was quite different

[3] Participants in all of the trials were at very high risk of pressure ulcer development (drawn from intensive care/cardiac care units or geriatric units), so results may not be generalisable to all hospitalised patients

[4] Three of the four trials were small, with fewer than 100 participants. This resulted in wide confidence intervals around the effect size, creating uncertainty around the precision of the result.

DISCUSSION

This review identified nine trials exploring the impact of dressings (n = 4) or topical agents (n = 5) on the incidence of pressure ulcers. When the four dressings trials were combined (Han 2011; Kalowes 2012; Nakagami 2007; Qiuli 2010), dressings applied over bony prominences were found to reduce pressure ulcer incidence. However, these studies have a high, or uncertain risk of bias, thus, firm conclusions cannot be drawn from this finding. However, pooled analyses could be interpreted as indicating the potential for a likely effect given that all studies favoured the use of a dressing and the relatively narrow CI but further, independently funded trials are required to confirm these findings.

A key question to consider is whether dressings can contribute to pressure and shear force reduction, in terms of their ability to afford greater protection of bony prominences (Butcher 2009). Pressure must be present for a pressure ulcer to develop, the effect of pressure is time dependent, and the time it takes a pressure ulcer to develop will be influenced by the general condition of the individual (Moore 2012). Immobility is of significance, which makes logical sense, as people who are unable to reposition themselves in order to relieve pressure will be exposed to prolonged external mechanical forces (Moore 2012). Furthermore, when pressure is not evenly distributed, then it is the point pressure (i.e. the pressure applied on a specific area of the body) that causes damage. Additionally, the thickness and tone of the subcutaneous tissues influence the relationship between externally applied forces and corresponding interstitial pressures (Bader 1990). Thus, when a person is exposed to prolonged externally-applied mechanical forces, an aspect of pressure ulcer prevention strategies is to redistribute the force over the greatest area, thereby reducing the magnitude of pressure. The principles upon which pressure redistribution is based (apart from actually changing the person's position) are immersion and envelopment (International Review 2010). Immersion is the ability of the product to allow the person to sink into it, and envelopment refers to how well the product moulds to the shape of the body contours (for example the heel) (International Review 2010). At its essence, immersion allows for pressure to spread out over the surrounding areas, thus redistributing it rather than alleviating it (Baranoski 2008). For dressings, their relatively small size (area) means that their potential for pressure redistribution is minimal, bearing in mind that pressure is equal to force divided by area. Dressings will only play a small part in the prevention of pressure ulcers, as the key causative factor is pressure and shear, thus relief of pressure and shear is fundamental to preventing pressure ulcers. Logically, dressings cannot relieve pressure they can only contribute to dissipating pressure, although to what effect remains unclear. Indeed, dressings, which are generally relatively thin in composition and of a small size, can only have a limited role in pressure redistribution, as they cannot readily adhere to the principles of immersion and envelopment. Furthermore, consideration needs to be given to the effects that the edges of the dressing have on interface pressures (the pressures between the skin and the edge of the dressing). When data were combined from the four studies (Han 2011; Kalowes 2012; Nakagami 2007; Qiuli 2010), they showed that dressings applied over bony prominences reduced the pressure ulcer incidence, however, due to the high or uncertain risk of bias, firm conclusions cannot be drawn from this analysis.It is unlikely that the reduction in incidence relates to the pressure/shear reduction ability of the dressings, rather may relate to the ability to reduce friction forces. A further issue of concern is the role of skin assessment in pressure ulcer prevention. The EPUAP/NPUAP guidelines highlight the importance of including skin assessment as part of the overall pressure ulcer prevention strategy of the organisation (EPUAP/NPUAP 2009). Specifically, they state that staff should include a complete skin assessment as part of the risk screening of patients. In addition, the skin should be assessed regularly to determine any changes in condition, with the frequency of this assessment increased, if alteration in skin condition is noticed (EPUAP/NPUAP 2009). It is unlikely that dressings will be removed very regularly to facilitate this assessment, as to do so may cause discomfort to the patient and may be perceived as contributing to increased costs. Thus, this may reduce the practicality of dressing use for pressure ulcer prevention.

Friction is commonly referred to as the action of two objects rubbing against each other, for example a person's heel and the sheet covering the bed International Review 2010. It has been suggested that keeping the skin moisturised is important because this allows the heel, for instance, to move more freely over the sheet, and so reduces friction forces. This review included five studies that explored the effects of topical agents in pressure ulcer incidence (Green 1974; Houwing 2008; Smith 1985; Torra i Bou 2005; Van Der Cammen 1987). The Houwing 2008 trial was responsible for high heterogeneity. In that study, outcomes favoured the placebo arm, whereas all other trials favoured the intervention product. Therefore, when results were combined with Houwing 2008 included, the findings showed no overall beneficial effect of the topical agents. When results were combined without Houwing 2008, the problems with heterogeneity were removed, and the findings suggested a statistically significant beneficial effect of the topical agents. However, as Houwing 2008 was the only trial without manufacturer funding, these results should be interpreted with caution owing to the potential bias in the included trials. An alternative explanation for the heterogeneity, may be that Houwing 2008 was the only cluster RCT. A further problem with trying to understand the implications of our review of topical applications was that many of the studies were quite old and most included products that are not commercially available. None of the trials used commonly used creams, such as Sorbelene or aqueous cream as comparators, products that are widely used for moisturising the skin. Four of the studies mentioned repositioning as a key component of pressure ulcer prevention strategies within the trials (Green 1974; Houwing 2008; Torra i Bou 2005; Van Der Cammen 1987). Smith 1985 stated that the intervention was

integrated into the staffs' usual routine skin care regimens. This suggests that use of topical agents alone, may be insufficient to prevent pressure ulcers. The precise role of dressings and topical agents, therefore, remains unclear.

Summary of main results

Development of new pressure ulcers

This systematic review examined the evidence from randomised controlled trials (RCTs) that focused on the effects of interventions aimed at reducing the development of new pressure ulcers. Two categories of interventions were used, creams or topical applications applied to the skin, and dressings placed over bony prominences such as the sacrum and hips. Most of the intervention creams contained essential fatty acids because of their known role in wound healing (McCusker 2010). However, evidence of the benefit of topical applications remains inconclusive, with no clear benefit shown for topical products. Further information is required to clarify the effect of topical agents on the prevention of pressure ulcers.

In four small studies, dressings applied over bony prominences appeared to confer a slight prophylactic affect, with a 79% risk reduction in the incidence of new pressure ulcers in people assigned to the group in which a dressing was used. However, the wide confidence intervals (0.09 to 0.51) around the effect size and the high risk of bias evident all studies indicate that additional research is required to confirm these results.

Other outcomes

There was limited evidence from one study to suggest that the application of a topical agent may delay the development of a new pressure ulcer, but not prevent its occurrence (Torra i Bou 2009). As with other outcomes, this result requires further investigation before any recommendation about the effect of topical agents on timing of pressure ulcer development can be made. The review did not identify any other benefit for topical agents or dressings over a placebo topical agent or standard care.

Overall completeness and applicability of evidence

Most of the studies focused on the primary outcome, development of a new pressure ulcer, in populations of elderly hospitalised or nursing-home patients. While these groups represent many of those at risk of pressure injury, other high risk groups, such as people with paraplegia and other immobile people also require investigation (Alderden 2011). The included studies failed to provide adequate economic evaluations. Healthcare providers need such data, to be able to assess the cost/benefit implications of new interventions adequately. Only one study mentioned adverse events (Green 1974), and none provided information about other important patient-related outcomes such as quality of life or acceptability of the product.

Quality of the evidence

Limitations in study design and implementation

Risk of bias was assessed according to six components: sequence generation; allocation concealment; blinding; selective outcome reporting, incomplete follow-up and other potential biases. The methodological quality of most of the RCTs was poor, with limitations in a number of these domains (Figure 4). The Nakagami 2007 study is prone to unit of analysis error, as two sides of each patient were randomised to intervention and control.

Indirectness of evidence

The review was limited by variations in both the experimental and the control interventions. For example, the constituents of the topical applications varied between studies, as did the placebo cream, and in the trials that compared dressings with standard care, the dressings were made of different materials. Consequently, the evidence was restricted to indirect comparisons between these varied interventions. Additionally, a number of the high-risk groups were not represented within the included studies, so the evidence may be regarded as indirect for other patients (such as intensive care patients and other immobile people). Taken together, these limitations restrict confident decision making with regard to the use of topical agents and dressings to prevent the development of pressure ulcers.

Unexplained heterogeneity or inconsistency of results

We combined results of studies that investigated the effect of topical agents on the development of pressure injury, despite a high level of heterogeneity between studies (albeit within our pre-defined cut-off point for pooling data). One study was responsible for the high heterogeneity (Houwing 2008). In that study, outcomes favoured the placebo arm, whereas all other trials favoured the intervention product. The Houwing 2008 trial was the only one that did not report manufacturer support.

Imprecision of results

Confidence intervals were wide in both of the pooled outcomes indicating a high level of uncertainty around the effect size (Figure 4; Figure 6). Further research is, therefore, very likely to have an important impact on the confidence of the estimate of effect for both topical agents and dressings.

Publication bias

We feel confident that our comprehensive electronic searches identified all existing, published randomised controlled trials addressing the review question. It is theoretically possible, though unlikely, that we did not manage to locate some potentially eligible studies. In line with Cochrane policy, this review will be updated in future, and any studies identified that meet the inclusion criteria will be included at that stage.

Potential biases in the review process

We followed clearly described procedures to prevent potential bias in the review process. This included a careful literature search and the methods we used were transparent and reproducible. None of the authors has any conflict of interest. It is possible that trials published in journals that were outside our search strategy may have been missed.

Agreements and disagreements with other studies or reviews

Although there have been many systematic reviews and studies addressing treatment of pressure ulcers, there has been less attention paid to preventing their occurrence. The prevention reviews that exist have focused on other interventions, such as support surfaces (McInnes 2011), risk assessment tools (Moore 2008), and nutritional interventions (Langer 2003). One overview of pressure ulcer prevention strategies did include topical applications (Reddy 2006). Our results concur with Reddy 2006 who concluded that "The incremental benefit of specific topical agents over simple moisturizers . . . remains unclear".

AUTHORS' CONCLUSIONS

Implications for practice

Pressure ulcers are a relatively common and important complication of hospitalisation and the application of creams or other topical agents is frequently used as an intervention to prevent pressure ulcers from forming. However, there is insufficient evidence from independently funded clinical trials to support or refute the use of topical agents for this purpose.

There is also a paucity of evidence from well conducted randomised controlled trials (RCTs) about the effectiveness of dressings to prevent pressure ulcers. Although there was a reduced incidence of pressure ulcers when dressings were used to protect the skin, results were compromised by the low-quality of included trials. These trials contained substantial risk of bias (e.g. inadequate randomisation) and clinical heterogeneity (variations in populations and interventions); consequently, our results should be interpreted as inconclusive.

Implications for research

The evidence base for use of topical agents and dressings to prevent pressure ulcers is limited, despite the wide use of these interventions. Further trials are justified, based on the incidence of the problem and the high costs associated with pressure ulcer management. Future trials should be large enough to show meaningful differences; include patient-related outcomes such as product acceptability, adverse events and quality of life, and economic evaluations to assist healthcare managers to make rational decisions. Standard, validated tools should be used to measure outcomes such as pressure ulcer staging, and quality of life.

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* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Green 1974

Methods	Double blind RCT, with 3-week follow-up, method of randomisation not stated
Participants	319 geriatric participants from 6 geriatric departments in the UK
Interventions	**Topical agent trial** Group 1 (intervention): active lotion containing: hexachlorophane 0.5%, saturated hydrocarbons (squalene (Cosbiol 3%) and glyoxyle diureide), allantoin 0.2%, antioxidants, lanolin, fatty acids, fatty acid esters, fatty alcohols, preservatives and distilled water Group 2 (control): inert lotion containing: lanolin, fatty acids, fatty acid esters, fatty alcohols, preservatives, distilled water and mineral oils Lotions applied with fingers to pressure areas (sacral, trochanteric, heel and shoulder and other areas as indicated). Excess friction avoided. Skin inspected every 2 h, participant turned and changed if soiled, washed with soap and water, skin dried and lotion applied after each cleansing. In the absence of incontinence, routine washing and reapplication of lotion was carried out every 6 h Bed cradles used for all participants to keep the weight of the bedding off the feet and lower legs Participants with a score of 10 or less (clinical at risk score) were nursed on a large cell alternating pressure mattress
Outcomes	The outcome of interest was pressure ulcer incidence, noted as either erythema or superficial sores
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not stated
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding of participants and personnel (performance bias) All outcomes	Low risk	**Evidence for participants:** blinded **Comment:** quote: "The active and inert lotions were similar in appearance and texture. They were randomly dispensed in identical plastic squeeze bottles to avoid possible bias of application" **Evidence for personnel:** blinded **Comment:** quote: "The active and inert lotions were similar in appearance and tex-

Green 1974 (*Continued*)

		ture. They were randomly dispensed in identical plastic squeeze bottles to avoid possible bias of application, or other nursing procedures“
Blinding of outcome assessment (detection bias) All outcomes	Low risk	**Evidence for outcomes:** blinded **Comment:** quote: ”The active and inert lotions were similar in appearance and texture. They were randomly dispensed in identical plastic squeeze bottles to avoid possible bias of application, or other nursing procedures, and of the research nurses observations“
Incomplete outcome data (attrition bias) All outcomes	High risk	ITT not conducted, 152 participants excluded
Selective reporting (reporting bias)	Low risk	**Evidence:** pressure ulcers described as erythema or superficial in the results **Comment:** pressure ulcers of greater than grade 2 were grounds for discontinuation of trial
Other bias	Low risk	

Han 2011

Methods	RCT, follow-up 72 hours.
Participants	100 people admitted for posterior spinal surgery in Shandong, China. The study excluded people with previous skin disease, those undergoing emergency surgery, and those with operation time of < 3 h. Follow-up at 24 h and 72 h post surgery
Interventions	**Dressing trial** Intervention group: Kang' Huier transparent strip and foam dressing Control group: routine operating room protective measures
Outcomes	Pressure ulcer incidence
Notes	Authors state that the 2 pressure ulcers in the intervention group occurred outside the treated area

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	**Evidence for outcomes:** not described **Comment:** states only that participants were randomly grouped. But authors did not explain how the sequence was

Han 2011 (*Continued*)

		generated
Allocation concealment (selection bias)	Unclear risk	**Evidence for outcomes:** not described
Blinding of participants and personnel (performance bias) All outcomes	High risk	**Evidence for outcomes:** blinding impossible due to the nature of the intervention
Blinding of outcome assessment (detection bias) All outcomes	High risk	**Evidence for outcomes:** blinding impossible due to the nature of the intervention.
Incomplete outcome data (attrition bias) All outcomes	Low risk	**Comment:** 100 participants enrolled and all accounted for in the results
Selective reporting (reporting bias)	Low risk	**Evidence for outcomes:** the only outcome pre-specified was 'pressure sore'.
Other bias	Unclear risk	**Comment:** We had only the most important data interpreted. It is possible that there may have been biases about which we are unaware

Houwing 2008

Methods	Cluster RCT, 4-week follow-up, randomly assigned at ward level not at participant level. Exact method of randomisation not stated
Participants	79 participants at risk of development of pressure ulcers, in 8 nursing homes in the Netherlands
Interventions	**Topical agent trial** Group 1 (intervention): massage using a "DMSO-cream." This cream consisted of 5% dimethyl sulfoxide in Vaseline-cetomacrogol cream, combined with a 30^o position change. This procedure was repeated every 6 h for 4 weeks Group 2 (placebo): 3-minute massage of the buttock, heel, and ankle regions with an indifferent cream (Vaseline-cetomacrogol) combined with a 30^o position change. This procedure was repeated every 6 h for 4 weeks Group 3 (control): 30^o position change, repeated every 6 h for 4 weeks
Outcomes	Pressure ulcer incidence
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Throw of a dice (additional information from the author)

Houwing 2008 (*Continued*)

Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding of participants and personnel (performance bias) All outcomes	Low risk	**Evidence for participants:** stated as double blind **Comment:** stated as double blind **Evidence for personnel:** stated as double blind **Comment:** stated as double blind
Blinding of outcome assessment (detection bias) All outcomes	Low risk	**Evidence for outcomes:** blinded **Comment:** quote: "presence of a pressure ulcer confirmed by two external observers"
Incomplete outcome data (attrition bias) All outcomes	Low risk	**Evidence:** none excluded
Selective reporting (reporting bias)	Low risk	**Evidence:** outcome measure was the presence of a pressure ulcer **Comment:** this was reported by the authors
Other bias	Low risk	

Kalowes 2012

Methods	Prospective RCT
Participants	367 people nursed in a medical/surgical/trauma intensive care unit and a cardiac intensive care unit
Interventions	**Dressing trial** Group 1 (intervention): silicone foam dressing and SKIN care bundle Group 2 (control): SKIN care bundle
Outcomes	Pressure ulcer incidence
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote: "randomly assigned"
Allocation concealment (selection bias)	Unclear risk	Not stated

Kalowes 2012 (*Continued*)

Blinding of participants and personnel (performance bias) All outcomes	High risk	Not stated, but difference in the appearance of dressing makes blinding impossible
Blinding of outcome assessment (detection bias) All outcomes	High risk	Not stated
Incomplete outcome data (attrition bias) All outcomes	High risk	**Evidence:** 367 participants enrolled into the study, analysis conducted on 335 participants
Selective reporting (reporting bias)	Unclear risk	**Evidence:** outcome measure was the presence of a pressure ulcer **Comment:** this was reported by the authors

Nakagami 2007

Methods	RCT, 3-week follow-up, method of randomisation not stated
Participants	37 participants, aged ≥ 65 with a Braden score of < 15, in a 500 bed geriatric hospital in Japan
Interventions	**Dressing trial** Group 1: PPD (dressing with skin adhesive layer (hydrocolloid), a support layer (urethane film) and an outer layer of multi filament nylon fibres). Applied to either the right or the left trochanter. PPD replaced every week Group 2: participants acted as their own control, i.e. no dressing was applied to the opposite trochanter
Outcomes	Incidence of pressure ulcer Incidence of persistent erythema
Notes	Pressure ulcer classification system not clearly described

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Not stated
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding of participants and personnel (performance bias) All outcomes	High risk	**Evidence for participants:** not blinded **Comment:** quote: "impossible due to the type of intervention" **Evidence for personnel:** not blinded **Comment:** quote: "impossible due to the

Nakagami 2007 (*Continued*)

		type of intervention"
Blinding of outcome assessment (detection bias) All outcomes	High risk	**Evidence for outcomes:** not blinded **Comment:** quote: "test area outlined so that the dressing applied back to the same area"
Incomplete outcome data (attrition bias) All outcomes	Low risk	ITT conducted
Selective reporting (reporting bias)	Low risk	**Evidence:** all outcomes reported in the paper were those outlined by the authors
Other bias	Unclear risk	**Comment:** investigators were part of the group that developed the PPD

Qiuli 2010

Methods	RCT, 7-day follow-up, method of randomisation not stated
Participants	52 participants, Waterlow score18-23, in a department of neurosurgery, Harbin, China
Interventions	Intervention: mepilex dressing applied to weight-bearing bony areas Control: massage of bony areas Both groups turned 2-3 hourly and nursed on air cushion beds
Outcomes	Incidence of pressure ulcer
Notes	Pressure ulcer classification system not described

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Not stated
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not stated, but difference in the appearance of dressing makes blinding impossible
Blinding of outcome assessment (detection bias) All outcomes	High risk	Not stated

Incomplete outcome data (attrition bias) All outcomes	Unclear risk	All participants included in the final analysis
Selective reporting (reporting bias)	Low risk	**Evidence:** all outcomes reported in the paper were those outlined by the authors

Smith 1985

Methods	Double-blind RCT, 24-week follow-up, method of randomisation not stated
Participants	258 elderly continuing-care patients, UK
Interventions	**Topical agent trial** Group 1 (intervention): Conotrane (silicone cream; 20% dimethicone 350; and a broad spectrum antiseptic (0.05% hydrargaphen)), skin washed, dried and ointment applied Group 2 (control): Unguentum cream, skin washed, dried and ointment applied
Outcomes	Pressure ulcer incidence
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Not stated
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding of participants and personnel (performance bias) All outcomes	Low risk	**Evidence for participants:** no mention within the article **Comment:** quote: The placebo ointment had been suitably scented so that it was indistinguishable from the active preparation **Evidence for personnel:** no mention within the article **Comment:** quote: "The placebo ointment had been suitably scented so that it was indistinguishable from the active preparation"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	**Evidence for outcomes:** no mention within the article **Comment:** quote: "The placebo ointment had been suitably scented so that it was indistinguishable from the active preparation"

Smith 1985 (*Continued*)

Incomplete outcome data (attrition bias) All outcomes	Low risk	**Evidence:** results table 1: of 258 participants **Comment:** data presented related to those who entered the study
Selective reporting (reporting bias)	Low risk	**Evidence:** all outcomes reported in the paper were those outlined by the authors
Other bias	Unclear risk	**Comment:** one third more participants in the placebo group were incontinent of urine and one quarter more were incontinent of faeces when compared with the treatment group

Torra i Bou 2005

Methods	Multicentre double-blind RCT, randomised code in a closed envelope, 30-day follow-up
Participants	380 individuals at risk of pressure ulcers, in Spain
Interventions	**Topical agent trial** Group 1 (intervention): Mepentol, a hyperoxygenated fatty acid compound (consisting of: oleic acid, palmitic acid, stearic acid, palmitoleic acid, linoleic acid, gamma-linoleic acid, arachidonic acid, and eicosenoic acid), applied twice daily to at least 3 areas of the body, sacrum, trochanter, heels Group 2 (control): compound consisting of trisostearin (99.4%) and perfume (0.6%) applied twice daily to at least 3 areas of the body, sacrum, trochanter, heels
Outcomes	Pressure ulcer incidence Cost
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	**Comment:** did not state how the randomisation sequence was generated
Allocation concealment (selection bias)	Unclear risk	**Evidence:** coded randomisation in closed envelope **Comment:** did not state that the envelopes were opaque

Torra i Bou 2005 (*Continued*)

Blinding of participants and personnel (performance bias) All outcomes	Low risk	**Evidence for participants:** blinded **Comment:** quote: "only the coordinator had access to the packaging codes so neither the investigator nor patient knew which group a patient had been allocated to" **Evidence for personnel:** blinded **Comment:** quote: "only the coordinator had access to the packaging codes so neither the investigator nor patient knew which group a patient had been allocated to"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	**Evidence for outcomes:** blinded **Comment:** quote: "only the coordinator had access to the packaging codes so neither the investigator nor patient knew which group a patient had been allocated to"
Incomplete outcome data (attrition bias) All outcomes	High risk	**Evidence:** ITT not conducted, results presented for 167 and 164 participants and not for the original 380 enrolled
Selective reporting (reporting bias)	Low risk	**Evidence:** all outcomes reported in the paper were those outlined by the authors
Other bias	Low risk	

Van Der Cammen 1987

Methods	Double-blind RCT, method of randomisation not stated	
Participants	120 chair-bound participants, with a Norton score 5-14, from the Department of Geriatric Medicine, UK	
Interventions	Topical agent trial Group 1 (intervention): buttocks and sacral areas washed and dried, and Prevasore (Hexyl nicotinate, zinc stearate, isopropyl myristate, Dimethicone 350, cetrimide and glycol) applied at least twice daily, and after changing, if wet or soiled Group 2 (control): buttocks and sacral areas washed and dried, and Dermalex (hexachlorophane, squalene and allantoin) applied at least twice daily, and after changing, if wet or soiled	
Outcomes	Pressure ulcer incidence	
Notes	Data presented for 104 participants	
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**

Van Der Cammen 1987 (*Continued*)

Random sequence generation (selection bias)	Unclear risk	Not stated
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding of participants and personnel (performance bias) All outcomes	Low risk	**Evidence for participants:** Quote " . . . this formulation was compared, in a double blind clinical trial . . " **Evidence for personnel:** Quote " . . . this formulation was compared, in a double blind clinical trial . . . "
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	**Evidence for outcomes:** not mentioned **Comment:** although unclear, it is probable that outcome assessment was blinded, given that the trial was 'double blinded'
Incomplete outcome data (attrition bias) All outcomes	High risk	**Evidence:** ITT not conducted **Comment:** Data presented relate to the number who concluded the study excluding those withdrawn
Selective reporting (reporting bias)	Low risk	**Evidence:** All outcomes reported in the paper are those outlined by the authors
Other bias	Unclear risk	**Comment:** Corresponding author member of staff of the manufacturer of the product under investigation

Abbreviations
< = less than
≥ = more than, or equal to
h = hour(s)
ITT = intention-to-treat analysis
PPD = pressure ulcer preventative dressing
RCT = randomised controlled trial

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Callaghan 1998	Not an RCT
Declaire 1997	Not an RCT
Duimel-Peeters 2007	Cross-over trial
Garcia Fernandez 2005	Review of a previous study by Torra i Bou
Hsu 2011	Quasi-experimental
Huang 2009	Not an RCT
Kuisma 1987	Treatment intervention not prevention
Smith 2010	Not an RCT
Stoker 1990	Treatment intervention not prevention
Torra i Bou 2009	Cost analysis from an unpublished study, presented at a Pressure Ulcer Advisory Panel meeting in 2002. No abstract available

DATA AND ANALYSES

Comparison 1. Topical agent versus placebo

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Pressure ulcer incidence	4		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected

Comparison 2. Topical agent versus control (Houwing)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Pressure ulcer incidence	1	47	Risk Ratio (M-H, Fixed, 95% CI)	1.60 [0.84, 3.04]

Comparison 3. Placebo versus control (Houwing)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Pressure ulcer incidence	1	50	Risk Ratio (M-H, Fixed, 95% CI)	0.80 [0.37, 1.74]

Comparison 4. Topical agent versus placebo (Houwing)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Pressure ulcer incidence	1	61	Risk Ratio (M-H, Fixed, 95% CI)	1.99 [1.10, 3.57]

Comparison 5. Topical agent versus placebo combined studies

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Pressure ulcer incidence	5	940	Risk Ratio (M-H, Random, 95% CI)	0.78 [0.47, 1.31]
2 Pressure ulcer incidence	4	879	Risk Ratio (M-H, Fixed, 95% CI)	0.64 [0.49, 0.83]

Comparison 6. Dressing versus no dressing

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Pressure ulcer incidence	4		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected

Comparison 7. Dressing versus no dressing combined studies

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Pressure ulcer incidence	4	561	Risk Ratio (M-H, Fixed, 95% CI)	0.21 [0.09, 0.51]

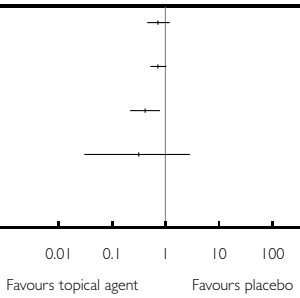
Analysis 1.1. Comparison 1 Topical agent versus placebo, Outcome 1 Pressure ulcer incidence.

Review: Dressings and topical agents for preventing pressure ulcers

Comparison: 1 Topical agent versus placebo

Outcome: 1 Pressure ulcer incidence

Study or subgroup	Topical agent n/N	Placebo n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
Green 1974	19/76	31/91		0.73 [0.45, 1.19]
Smith 1985	35/129	47/129		0.74 [0.52, 1.07]
Torra i Bou 2005	12/164	29/167		0.42 [0.22, 0.80]
Van Der Cammen 1987	1/54	3/50		0.31 [0.03, 2.87]



Analysis 2.1. Comparison 2 Topical agent versus control (Houwing), Outcome 1 Pressure ulcer incidence.

Review: Dressings and topical agents for preventing pressure ulcers

Comparison: 2 Topical agent versus control (Houwing)

Outcome: 1 Pressure ulcer incidence

Study or subgroup	Topical agent n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Houwing 2008	18/29	7/18		100.0 %	1.60 [0.84, 3.04]
Total (95% CI)	**29**	**18**		**100.0 %**	**1.60 [0.84, 3.04]**

Total events: 18 (Topical agent), 7 (Control)

Heterogeneity: not applicable

Test for overall effect: Z = 1.42 (P = 0.16)

Test for subgroup differences: Not applicable

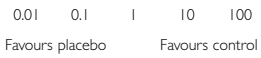
Analysis 3.1. Comparison 3 Placebo versus control (Houwing), Outcome 1 Pressure ulcer incidence.

Review: Dressings and topical agents for preventing pressure ulcers

Comparison: 3 Placebo versus control (Houwing)

Outcome: 1 Pressure ulcer incidence

Study or subgroup	Placebo n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Houwing 2008	10/32	7/18		100.0 %	0.80 [0.37, 1.74]
Total (95% CI)	**32**	**18**		**100.0 %**	**0.80 [0.37, 1.74]**
Total events: 10 (Placebo), 7 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.55 (P = 0.58)					
Test for subgroup differences: Not applicable					



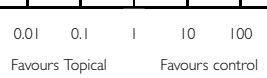
Analysis 4.1. Comparison 4 Topical agent versus placebo (Houwing), Outcome 1 Pressure ulcer incidence.

Review: Dressings and topical agents for preventing pressure ulcers

Comparison: 4 Topical agent versus placebo (Houwing)

Outcome: 1 Pressure ulcer incidence

Study or subgroup	Topical n/N	Placebo n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Houwing 2008	18/29	10/32		100.0 %	1.99 [1.10, 3.57]
Total (95% CI)	**29**	**32**		**100.0 %**	**1.99 [1.10, 3.57]**
Total events: 18 (Topical), 10 (Placebo)					
Heterogeneity: not applicable					
Test for overall effect: Z = 2.29 (P = 0.022)					
Test for subgroup differences: Not applicable					



Analysis 5.1. Comparison 5 Topical agent versus placebo combined studies, Outcome 1 Pressure ulcer incidence.

Review: Dressings and topical agents for preventing pressure ulcers

Comparison: 5 Topical agent versus placebo combined studies

Outcome: 1 Pressure ulcer incidence

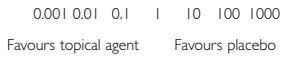
Study or subgroup	Topical agent n/N	Placebo n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Green 1974	19/79	31/91		24.6 %	0.71 [0.43, 1.15]
Houwing 2008	18/29	10/32		22.3 %	1.99 [1.10, 3.57]
Smith 1985	35/129	47/129		27.2 %	0.74 [0.52, 1.07]
Torra i Bou 2005	12/164	29/167		21.3 %	0.42 [0.22, 0.80]
Van Der Cammen 1987	1/60	3/60		4.6 %	0.33 [0.04, 3.11]
Total (95% CI)	**461**	**479**		**100.0 %**	**0.78 [0.47, 1.31]**

Total events: 85 (Topical agent), 120 (Placebo)

Heterogeneity: $Tau^2 = 0.22$; $Chi^2 = 14.31$, df = 4 (P = 0.01); $I^2 = 72\%$

Test for overall effect: Z = 0.94 (P = 0.35)

Test for subgroup differences: Not applicable



Analysis 5.2. Comparison 5 Topical agent versus placebo combined studies, Outcome 2 Pressure ulcer incidence.

Review: Dressings and topical agents for preventing pressure ulcers

Comparison: 5 Topical agent versus placebo combined studies

Outcome: 2 Pressure ulcer incidence

Study or subgroup	Topical agent n/N	Placebo n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Green 1974	19/79	31/91		26.8 %	0.71 [0.43, 1.15]
Smith 1985	35/129	47/129		43.7 %	0.74 [0.52, 1.07]
Torra i Bou 2005	12/164	29/167		26.7 %	0.42 [0.22, 0.80]
Van Der Cammen 1987	1/60	3/60		2.8 %	0.33 [0.04, 3.11]
Total (95% CI)	**432**	**447**		**100.0 %**	**0.64 [0.49, 0.83]**

Total events: 67 (Topical agent), 110 (Placebo)

Heterogeneity: $Chi^2 = 2.82$, df = 3 (P = 0.42); $I^2 = 0.0\%$

Test for overall effect: Z = 3.36 (P = 0.00078)

Test for subgroup differences: Not applicable

Analysis 6.1. Comparison 6 Dressing versus no dressing, Outcome 1 Pressure ulcer incidence.

Review: Dressings and topical agents for preventing pressure ulcers

Comparison: 6 Dressing versus no dressing

Outcome: 1 Pressure ulcer incidence

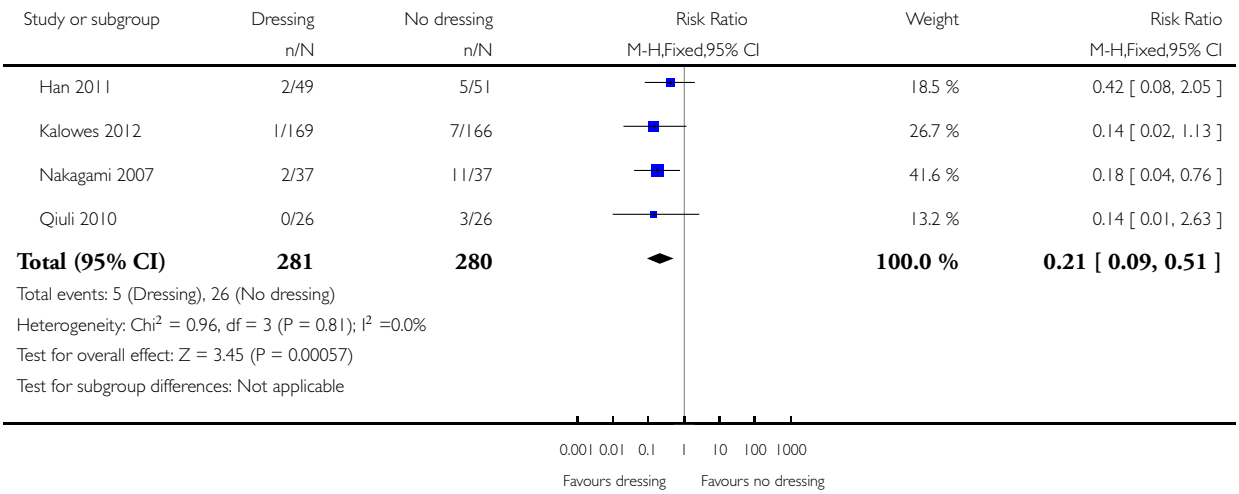
Study or subgroup	Dressing n/N	No dressing n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
Han 2011	2/29	5/51		0.70 [0.15, 3.40]
Kalowes 2012	1/169	7/166		0.14 [0.02, 1.13]
Nakagami 2007	2/37	11/37		0.18 [0.04, 0.76]
Qiuli 2010	0/26	3/26		0.14 [0.01, 2.63]

Analysis 7.1. Comparison 7 Dressing versus no dressing combined studies, Outcome 1 Pressure ulcer incidence.

Review: Dressings and topical agents for preventing pressure ulcers

Comparison: 7 Dressing versus no dressing combined studies

Outcome: 1 Pressure ulcer incidence



ADDITIONAL TABLES

Table 1. Intervention topical agents and dressings

AUTHOR YEAR	TOPICAL AGENTS	DRESSINGS
Green 1974	Dermalex™: consisting of hexachlorophane 0.5%, squalene (Cosbiol 3%), and allantoin 0.2%, lanolin, fatty acids, fatty alcohols, and antioxidants	
Han 2011		Kang' huier transparent strip and foam dressing
Houwing 2008	DMSO-cream: consisting of 5% dimethyl sulfoxide in Vaseline-cetomacrogol cream	

Table 1. Intervention topical agents and dressings (*Continued*)

Kalowes 2012		Soft silicone, self adherent, bordered foam dressing
Nakagami 2007		REMOIS PAD (designed to reduce shear forces with a low friction outer layer and containing a ceramide supplementation to improve the water-holding capacity of the skin. Ceramide is composed of sphingosine and a fatty acid)
Qiuli 2010		Soft silicone, self adherent, bordered foam dressing
Smith 1985	Conotrane: consisting of a silicone cream, 20% dimethicone 350, and a broad spectrum antiseptic (0.05% hydrargaphen)	
Torra i Bou 2005	Mepentol: a hyperoxygenated fatty acid compound consisting of oleic acid, palmitic acid, stearic acid, palmitoleic acid, linoleic acid, gamma linoleic acid, arachidonic acid, and eicosenoic acid	
Van Der Cammen 1987	Prevasore: consisting of hexyl nicotinate, zinc stearate, isopropyl myristate, Dimethicone 350, cetrimide and glycol	

APPENDICES

Appendix 1. International NPUAP-EPUAP pressure ulcer classification system for ulcer grading

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

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

Category/Stage II: partial thickness skin loss or blister

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

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

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

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

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

Appendix 2. Search strategies for Ovid MEDLINE, Ovid EMBASE and EBSCO CINAHL

Ovid Medline

1 exp Biological Dressings/ (590)
2 exp Occlusive Dressings/ (1560)
3 exp Hydrogels/ (7950)
4 exp Alginates/ (4561)
5 dressing$.ti,ab. (7994)
6 (hydrocolloid$ or alginate$ or hydrogel$ or foam or bead or film or films or tulle or gauze or non-adherent or non adherent).ti,ab. (72393)
7 exp Anti-Bacterial Agents/ (215334)
8 exp Administration, Topical/ (41359)
9 and/7-8 (2703)
10 (topical adj2 antibiotic$).ti,ab. (1112)
11 exp Antiinfective Agents, Local/ (83845)
12 exp Anti-Inflammatory Agents/ (180341)
13 exp Glucocorticoids/ (71762)
14 or/12-13 (191854)
15 8 and 14 (6251)
16 (topical adj2 (steroid$ or corticosteroid$ or glucocorticoid$)).ti,ab. (4415)
17 exp Estrogens/ (57995)
18 8 and 17 (1634)
19 (topical adj2 (oestrogen or estrogen)).ti,ab. (77)
20 exp Enzymes/ (1289849)
21 8 and 20 (2786)
22 (topical adj2 enzym$).ti,ab. (14)
23 exp Growth Substances/ (290263)
24 8 and 23 (1738)
25 (topical adj2 growth factor$).ti,ab. (55)
26 exp Collagen/ (52416)
27 8 and 26 (315)
28 (topical adj2 collagen).ti,ab. (17)
29 (topical adj2 silver).ti,ab. (62)
30 exp Honey/ (1486)
31 honey$.ti,ab. (7191)

32 exp Ointments/ (3714)
33 (ointment$ or lotion$ or cream$).ti,ab. (11253)
34 (topical adj (agent$ or preparation$ or therap$ or treatment$)).ti,ab. (5368)
35 or/1-6,9-11,15-16,18-19,21-22,24-25,27-34 (198846)
36 exp Pressure Ulcer/ (5267)
37 (pressure adj (ulcer$ or sore$)).ti,ab. (4400)
38 (decubitus adj (ulcer$ or sore$)).ti,ab. (585)
39 (bedsore$ or (bed adj sore$)).ti,ab. (245)
40 or/36-39 (6597)
41 35 and 40 (679)
42 randomized controlled trial.pt. (243536)
43 controlled clinical trial.pt. (39760)
44 randomized.ab. (198232)
45 placebo.ab. (92274)
46 clinical trials as topic.sh. (80060)
47 randomly.ab. (136251)
48 trial.ti. (73632)
49 or/42-48 (549699)
50 Animals/ (2494493)
51 Humans/ (6922271)
52 50 not 51 (1627525)
53 49 not 52 (500327)
54 41 and 53 (151)

Ovid Embase

1 exp foam dressing/ (181)
2 exp gauze dressing/ (799)
3 exp hydrocolloid dressing/ (454)
4 exp hydrogel dressing/ (147)
5 exp Wound Dressing/ (6673)
6 exp Hydrogel/ (13683)
7 exp Calcium Alginate/ (1232)
8 dressing$.ti,ab. (11539)
9 (hydrocolloid$ or alginate$ or hydrogel$ or foam or bead or film or films or tulle or gauze or non-adherent or non adherent).ti,ab. (110602)
10 exp Antibiotic Agent/ (543716)
11 exp Topical Drug Administration/ (14698)
12 and/10-11 (2182)
13 (topical adj2 antibiotic$).ti,ab. (1608)
14 exp Antiinfective Agent/ (1331673)
15 11 and 14 (5355)
16 exp Antiinflammatory Agent/ (743751)
17 exp Corticosteroid/ (401726)
18 exp Glucocorticoid/ (311297)
19 or/16-18 (830153)
20 11 and 19 (4840)
21 (topical adj2 (steroid$ or corticosteroid$ or glucocorticoid$)).ti,ab. (7159)
22 exp Estrogen/ (118910)
23 11 and 22 (207)
24 (topical adj2 (oestrogen or estrogen)).ti,ab. (149)
25 exp Enzymes/ (1821631)
26 11 and 25 (898)

27 (topical adj2 enzym$).ti,ab. (19)
28 exp Growth Factor/ (318023)
29 11 and 28 (299)
30 (topical adj2 growth factor$).ti,ab. (72)
31 exp Collagen/ (96769)
32 11 and 31 (209)
33 (topical adj2 collagen).ti,ab. (21)
34 (topical adj2 silver).ti,ab. (90)
35 exp Honey/ (2696)
36 honey$.ti,ab. (10147)
37 exp Ointments/ (4759)
38 (ointment$ or lotion$ or cream$).ti,ab. (18505)
39 (topical adj (agent$ or preparation$ or therap$ or treatment*)).ti,ab. (8287)
40 or/1-9,12-13,15,20-21,23-24,26-27,29-30,32-39 (173972)
41 exp Decubitus/ (9199)
42 (pressure adj (ulcer$ or sore$)).ti,ab. (5687)
43 (decubitus adj (ulcer$ or sore$)).ti,ab. (781)
44 (bedsore$ or (bed adj sore$)).ti,ab. (415)
45 or/41-44 (10385)
46 40 and 45 (1126)
47 exp Clinical trial/ (793074)
48 Randomized controlled trial/ (286529)
49 Randomization/ (50655)
50 Single blind procedure/ (15585)
51 Double blind procedure/ (85986)
52 Crossover procedure/ (31907)
53 Placebo/ (165507)
54 Randomi?ed controlled trial$.tw. (80377)
55 RCT.tw. (10556)
56 Random allocation.tw. (910)
57 Randomly allocated.tw. (14266)
58 Allocated randomly.tw. (1214)
59 (allocated adj2 random).tw. (264)
60 Single blind$.tw. (9677)
61 Double blind$.tw. (90376)
62 ((treble or triple) adj blind$).tw. (239)
63 Placebo$.tw. (137423)
64 Prospective study/ (200692)
65 or/47-64 (1088348)
66 Case study/ (15964)
67 Case report.tw. (167009)
68 Abstract report/ or letter/ (511635)
69 or/66-68 (690338)
70 65 not 69 (1060158)
71 animal/ (725145)
72 human/ (8645166)
73 71 not 72 (484830)
74 70 not 73 (1037853)
75 46 and 74 (309)

EBSCO CINAHL

S39 S33 and S38

S38 S34 or S35 or S36 or S37
S37 TI decubitus or AB decubitus
S36 TI (bed sore* or bedsore*) or AB (bed sore* or bedsore*)
S35 TI (pressure ulcer* or pressure sore*) or AB (pressure ulcer* or pressure sore*)
S34 (MH "Pressure Ulcer")
S33 S1 or S2 or S3 or S6 or S7 or S8 or S9 or S10 or S12 or S13 or S15 or S16 or S18 or S19 or S21 or S22 or S26 or S27 or S28 or S29 or S30 or S31 or S32
S32 TI (topical agent* or topical preparation* or topical therap* or topical treatment*) or AB (topical agent* or topical preparation* or topical therap* or topical treatment*)
S31 TI (ointment* or lotion* or cream*) or AB (ointment* or lotion* or cream*)
S30 (MH "Ointments")
S29 TI honey* or AB honey*
S28 (MH "Honey")
S27 TI topical* N2 silver* or AB topical* N2 silver*
S26 S5 and S25
S25 S23 or S24
S24 (MH "Silver Sulfadiazine")
S23 (MH "Silver")
S22 TI collagen* or AB collagen*
S21 S5 and S20
S20 (MH "Collagen")
S19 TI topical* N2 growth factor* or AB topical* N2 growth factor*
S18 (S5 and S17)
S17 (MH "Growth Substances+")
S16 TI topical* N2 enzyme* or AB topical* N2 enzyme*
S15 S5 and S14
S14 (MH "Enzymes+")
S13 TI (topical* N2 oestrogen* or topical* N2 estrogen*) or AB (topical* N2 oestrogen* or topical* N2 estrogen*)
S12 S5 and S11
S11 (MH "Estrogens+")
S10 TI (topical* N2 steroid* or topical* N2 corticosteroid* or topical* N2 glucocorticoid*) or AB (topical* N2 steroid* or topical* N2 corticosteroid* or topical* N2 glucocorticoid*)
S9 (MH "Antiinflammatory Agents, Topical+")
S8 (MH "Antiinfective Agents, Local+")
S7 TI topical* N2 antibiotic* or AB topical* N2 antibiotic*
S6 S4 and S5
S5 MH "Administration, Topical+")
S4 (MH "Antibiotics+")
S3 TI (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 AB (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*)
S2 (MH "Alginates")
S1 (MH "Bandages and Dressings+")

Appendix 3. Risk of bias criteria

1. Was the allocation sequence randomly generated?

Low risk of bias

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

High risk of bias

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

Unclear

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

2. Was the treatment allocation adequately concealed?

Low risk of bias

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

High risk of bias

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

Unclear

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

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

Low risk of bias

Any one of the following:

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

High risk of bias

Any one of the following:

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

Unclear

Any one of the following:

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

4. Were incomplete outcome data adequately addressed?

Low risk of bias

Any one of the following:

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

High risk of bias

Any one of the following:

- Reason for missing outcome data likely to be related to true outcome, with 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 enough to induce clinically relevant bias in intervention effect estimate.
- For continuous outcome data, plausible effect size (difference in means or standardised difference in means) among missing outcomes enough to induce clinically relevant bias in observed effect size.

- 'As-treated' analysis done with substantial departure of the intervention received from that assigned at randomisation.
- Potentially inappropriate application of simple imputation.

Unclear

Either of the following:

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

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

Low risk of bias

Either of the following:

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

High risk of bias

Any one of the following:

- Not all of the study's pre-specified primary outcomes have been reported.
- One or more primary outcomes is reported using measurements, analysis methods or subsets of the data (e.g. 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 to permit judgement of low or high risk of bias. It is likely that the majority of studies will fall into this category.

6. Other sources of potential bias

Low risk of bias

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

High risk of bias

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

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

Unclear

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

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

WHAT'S NEW

Last assessed as up-to-date: 1 February 2013.

Date	Event	Description
24 February 2015	Amended	Contact details updated.

CONTRIBUTIONS OF AUTHORS

Zena Moore (ZM) developed the first draft of protocol.

ZM and Joan Webser (JW) contributed to writing the published protocol and the final review.

ZM and JW independently selected studies for inclusion, assessed study quality and extracted data.

Contributions of editorial base

Nicky Cullum: edited the protocol; advised on methodology, interpretation and protocol content. Approved the final protocol prior to submission.
Liz McInnes, Editor: approved the final review prior to submission.
Sally Bell-Syer: co-ordinated the editorial process. Advised on methodology, interpretation and content and edited the protocol and review.
Ruth Foxlee: designed the search strategy and edited the search methods section.

DECLARATIONS OF INTEREST

Zena Moore, is a member of the medical advisory board of Systagenix Wound Management. She has received an honorarium for speaking at professional meetings for KCI, ConvaTec, Systagenix Wound Management, Fanin Health Care and Smith & Nephew.

Joan Webster: none

SOURCES OF SUPPORT

Internal sources

- Faculty of Nursing & Midwifery, RCSI, Ireland.

External sources

- NIHR/Department of Health (England), (Cochrane Wounds Group), UK.

INDEX TERMS

Medical Subject Headings (MeSH)

*Bandages; Administration, Cutaneous; Drug Administration Schedule; Pressure Ulcer [*prevention & control]; Randomized Controlled Trials as Topic; Skin Care [*methods]; Skin Cream [*administration & dosage; chemistry]

MeSH check words

Aged; Humans; Middle Aged