National Clinical Guideline Centre

Pressure ulcer management

The prevention and management of pressure ulcers in primary and secondary care

Clinical Guideline 179

Methods, evidence and recommendations

April 2014

Commissioned by the National Institute for Health and Clinical Excellence

Update information

Minor changes since publication

February 2019: After a surveillance review, links were added throughout to other NICE guidance that has been produced since this guideline was originally published. Some terms used in some recommendations were updated to reflect current practice. These changes can be seen in the short version of the guideline at http://www.nice.org.uk/guidance/cg179

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Contents

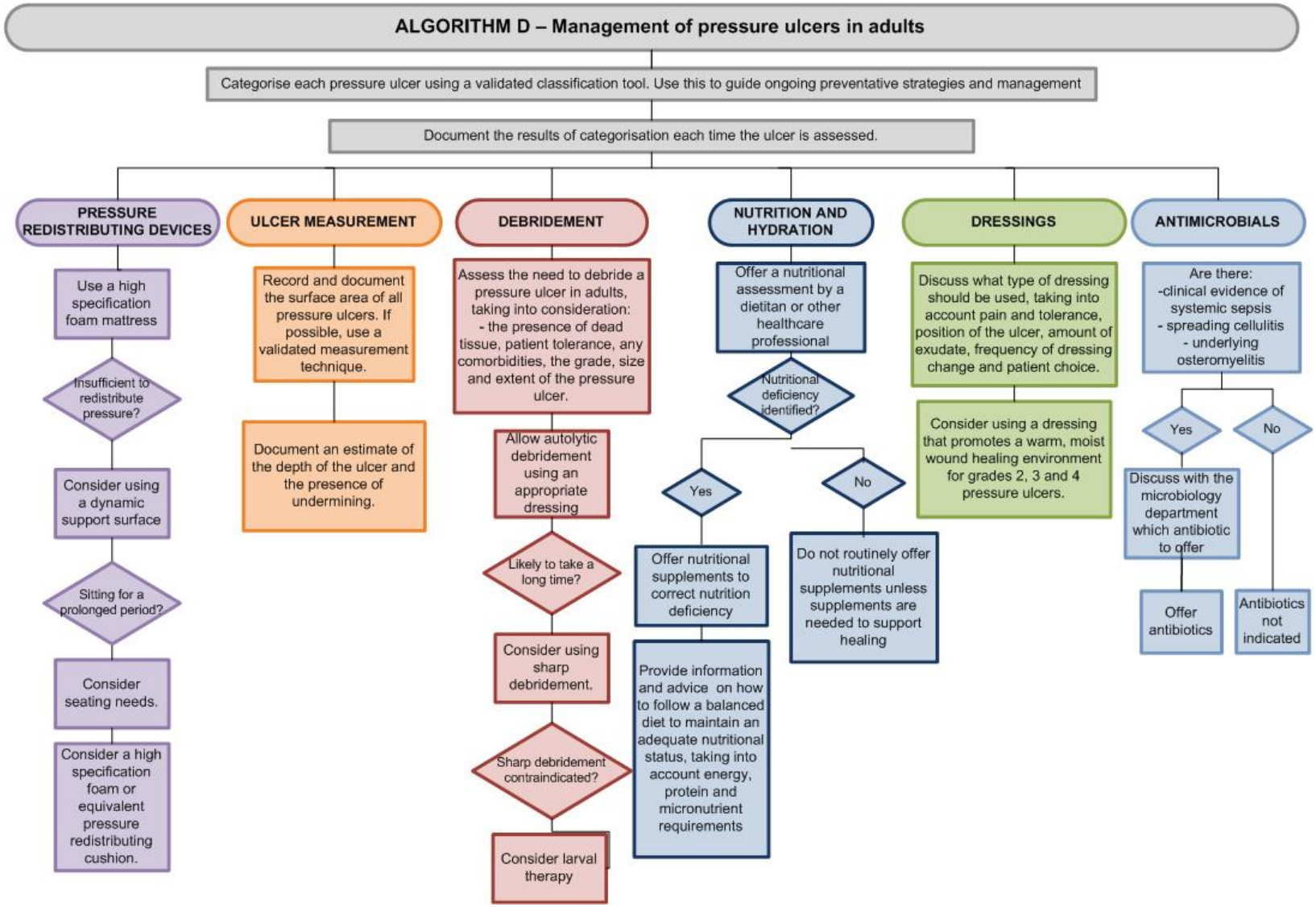
Acknowledgements, GDG membership and methods

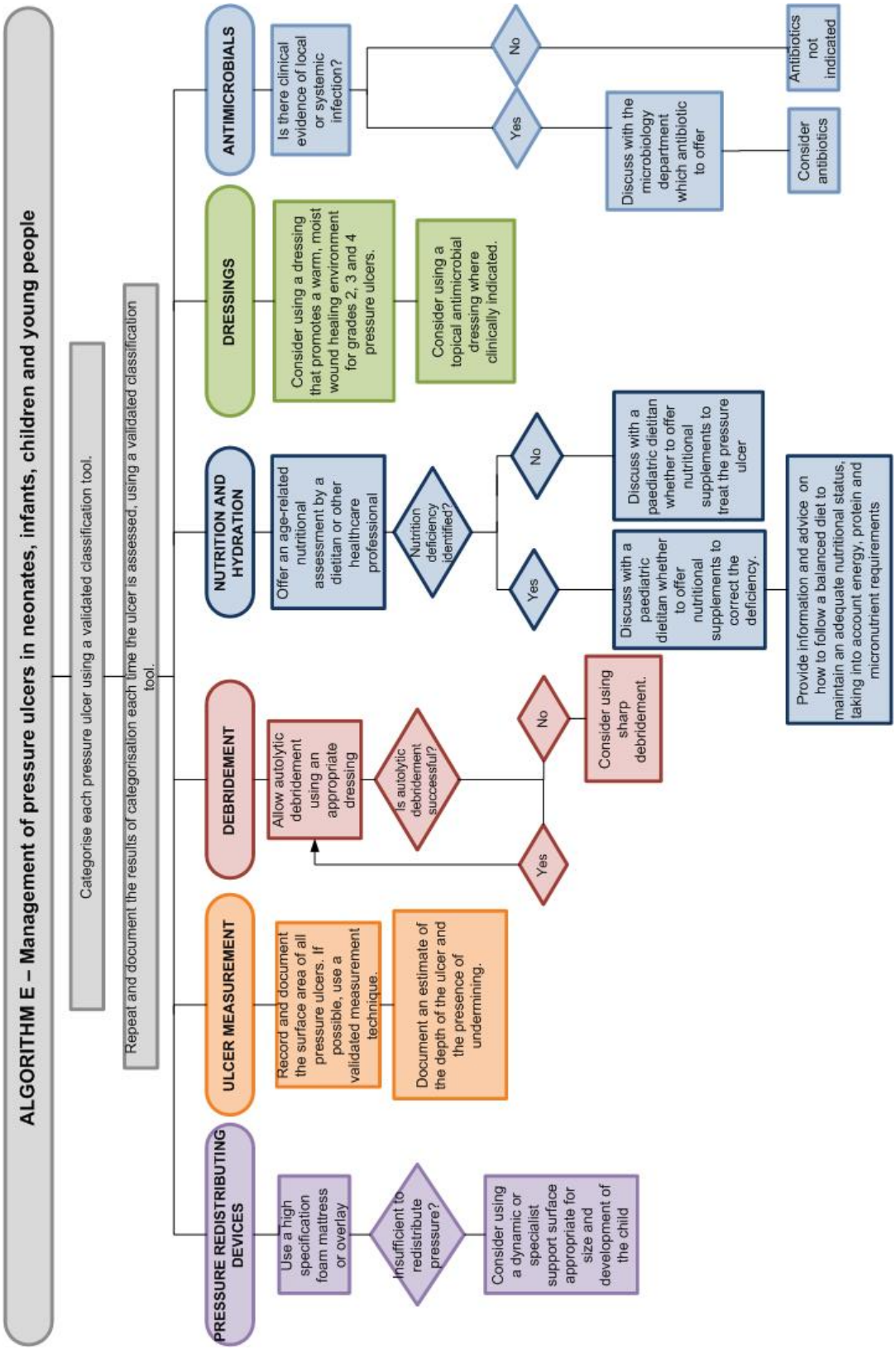
Further details on acknowledgements, GDG membership and methods used to develop this guideline can be found in part 1 of the guideline, ‘Prevention of pressure ulcers’.

1 Guideline summary

1.1 Algorithms

For algorithms on identifying pressure ulcer risk and the prevention of pressure ulcers, please see part 1, ‘Prevention of pressure ulcers’.


ALGORITHM D – Management of pressure ulcers in adults
Categorise each pressure ulcer using a validated classification tool. Use this to guide ongoing preventative strategies and management
Document the results of categorisation each time the ulcer is assessed.
PRESSURE REDISTRIBUTING DEVICES
Use a high specification foam mattress
Insufficient to redistribute pressure?
Consider using a dynamic support surface
Sitting for a prolonged period?
Consider seating needs.
Consider a high specification foam or equivalent pressure redistributing cushion.
ULCER MEASUREMENT
Record and document the surface area of all pressure ulcers. If possible, use a validated measurement technique.
Document an estimate of the depth of the ulcer and the presence of undermining.
DEBRIDEMENT
Assess the need to debride a pressure ulcer in adults, taking into consideration: - the presence of dead tissue, patient tolerance, any comorbidities, the grade, size and extent of the pressure ulcer.
Allow autolytic debridement using an appropriate dressing
Likely to take a long time?
Consider using sharp debridement.
Sharp debridement contraindicated?
Consider larval therapy
NUTRITION AND HYDRATION
Offer a nutritional assessment by a dietitan or other healthcare professional
Nutritional deficiency identified?
Yes
Offer nutritional supplements to correct nutrition deficiency
Provide information and advice on how to follow a balanced diet to maintain an adequate nutritional status, taking into account energy, protein and micronutrient requirements
No
Do not routinely offer nutritional supplements unless supplements are needed to support healing
DRESSINGS
Discuss what type of dressing should be used, taking into account pain and tolerance, position of the ulcer, amount of exudate, frequency of dressing change and patient choice.
Consider using a dressing that promotes a warm, moist wound healing environment for grades 2, 3 and 4 pressure ulcers.
ANTIMICROBIALS
Are there: -clinical evidence of systemic sepsis - spreading cellulitis - underlying osteromyelitis
Yes
Discuss with the microbiology department which antibiotic to offer
Offer antibiotics
No
Antibiotics not indicated


ALGORITHM E – Management of pressure ulcers in neonates, infants, children and young people
Categorise each pressure ulcer using a validated classification tool.
Repeat and document the results of categorisation each time the ulcer is assessed, using a validated classification tool.
PRESSURE REDISTRIBUTING DEVICES
Use a high specification foam mattress or overlay
Insufficient to redistribute pressure?
Consider using a dynamic or specialist support surface appropriate for size and development of the child
ULCER MEASUREMENT
Record and document the surface area of all pressure ulcers. If possible, use a validated measurement technique.
Document an estimate of the depth of the ulcer and the presence of undermining.
DEBRIDEMENT
Allow autolytic debridement using an appropriate dressing
Is autolytic debridement successful?
No
Consider using sharp debridement.
Yes
NUTRITION AND HYDRATION
Offer an age-related nutritional assessment by a dietitan or other healthcare professional
Nutrition deficiency identified?
No
Discuss with a paediatric dietitan whether to offer nutritional supplements to treat the pressure ulcer
Yes
Discuss with a paediatric dietitan whether to offer nutritional supplements to correct the deficiency.
Provide information and advice on how to follow a balanced diet to maintain an adequate nutritional status, taking into account energy, protein and micronutrient requirements
DRESSINGS
Consider using a dressing that promotes a warm, moist wound healing environment for grades 2, 3 and 4 pressure ulcers.
Consider using a topical antimicrobial dressing where clinically indicated.
ANTIMICROBIALS
Is there clinical evidence of local or systemic infection?
No
Antibiotics not indicated
Yes
Discuss with the microbiology department which antibiotic to offer
Consider antibiotics

1.2 Key priorities for implementation

From the full set of recommendations, the GDG selected 10 key priorities for implementation. The criteria used for selecting these recommendations are listed in detail in The guidelines manual.[131] The reasons that each of these recommendations was chosen are shown in the table linking the evidence to the recommendation in the relevant chapter.

- Carry out and document an assessment of pressure ulcer risk for adults
  - being admitted to secondary care or care homes in which NHS care is provided or
  - receiving NHS care in other settings such as primary and community care settings, and emergency departments, if they have a risk factor, for example:
    - significantly limited mobility (for example, people with a spinal cord injury)
    - significant loss of sensation
    - a previous or current pressure ulcer
    - nutritional deficiency
    - the inability to reposition themselves
    - significant cognitive impairment [1.1.2]

- Offer adults who have been assessed as being at high risk of developing a pressure ulcer a skin assessment by a trained healthcare professional (see recommendation 1.3.4). The assessment should take into account any pain or discomfort reported by the patient and the skin should be checked for:
  - skin integrity in areas of pressure
  - colour changes or discoloration[a]
  - variations in heat, firmness and moisture (for example, because of incontinence, oedema, dry or inflamed skin).[1.1.5]

- Develop and document an individualised care plan for neonates, infants, children, young people and adults who have been assessed as being at high risk of developing a pressure ulcer, taking into account:
  - the outcome of risk and skin assessment
  - the need for additional pressure relief at specific at-risk sites
  - their mobility and ability to reposition themselves
  - other comorbidities
  - patient preference.[1.3.1]

- Encourage adults who have been assessed as being at risk of developing a pressure ulcer to change their position frequently and at least every 6 hours. If they are unable to reposition themselves, offer help to do so, using appropriate equipment if needed. Document the frequency of repositioning required.[1.1.8]

- Use a high-specification foam mattress for adults who are:

[a] Healthcare professionals should be aware that non-blanching erythema may present as colour changes or discolouration, particularly in darker skin tones or types.

- admitted to secondary care
- assessed as being at high risk of developing a pressure ulcer in primary and community care settings.[1.1.13]

- Carry out and document an assessment of pressure ulcer risk for neonates, infants, children and young people:

o being admitted to secondary or tertiary care or

o receiving NHS care in other settings (such as primary and community care and emergency departments) if they have a risk factor, for example:

– significantly limited mobility (for example, people with a spinal cord injury)

– significant loss of sensation

– a previous or current pressure ulcer

– nutritional deficiency

– the inability to reposition themselves

– significant cognitive impairment. [1.2.1]

- Provide training to healthcare professionals on preventing a pressure ulcer, including:
  - who is most likely to be at risk of developing a pressure ulcer
  - how to identify pressure damage
  - what steps to take to prevent new or further pressure damage
  - who to contact for further information and for further action.[1.3.4]

- Provide further training to healthcare professionals who have contact with anyone who is assessed as being at high risk of developing a pressure ulcer. Training should include:
  - how to carry out a risk and skin assessment
  - how to reposition
  - information on pressure redistributing devices
  - discussion of pressure ulcer prevention with patients and their carers
  - details of sources of advice and support.[1.3.5]

- Discuss with adults with heel pressure ulcers and if appropriate, their carers, a strategy to offload heel pressure as part of their individualised care plan.[1.4.26]

1.3 Full list of recommendations

1. Document the surface area of all pressure ulcers in adults. If possible, use a validated measurement technique (for example, transparency tracing or a photograph).

2. Document an estimate of the depth of all pressure ulcers and the presence of undermining, but do not routinely measure the volume of a pressure ulcer.

3. Document the surface area of all pressure ulcers in neonates, infants, children and young people, preferably using a validated measurement technique (for example, transparency tracing or a photograph).

4. Document an estimate of the depth of a pressure ulcer and the presence of undermining, but do not routinely measure the volume of a pressure ulcer in neonates, infants, children and young people.

5. Categorise each pressure ulcer in adults using a validated classification tool (such as the International NPUAP-EPUAP (2009) Pressure Ulcer Classification System). Use this to guide ongoing preventative strategies and management. Repeat and document each time the ulcer is assessed.

6. Categorise each pressure ulcer in neonates, infants, children and young people at onset using a validated classification tool (such as the International NPUAP-EPUAP (2009) Pressure Ulcer Classification System) to guide ongoing preventative and management options. Repeat and document each time the ulcer is assessed.

7. Offer adults with a pressure ulcer a nutritional assessment by a dietitian or other healthcare professional with the necessary skills and competencies.

8. Offer nutritional supplements to adults with a pressure ulcer who have a nutritional deficiency.

9. Do not offer nutritional supplements to treat a pressure ulcer in adults whose nutritional intake is adequate

10. Provide information and advice to adults with a pressure ulcer and where appropriate, their family or carers, on how to follow a balanced diet to maintain an adequate nutritional status, taking into account energy, protein and micronutrient requirements

11. Do not offer subcutaneous or intravenous fluids to treat pressure ulcers in adults whose hydration status is adequate.

12. Offer an age-related nutritional assessment to neonates, infants, children and young people with a pressure ulcer. This should be performed by a paediatric dietitian or other healthcare professional with the necessary skills and competencies.

13. Discuss with a paediatric dietitian (or other healthcare professional with the necessary skills and competencies) whether to offer nutritional supplements specifically to treat pressure ulcers in neonates, infants, children and young people whose nutritinal intake is adequate.

14. Offer advice on a diet that provides adequate nutrition for growth and healing in neonates, infants, children and young people with pressure ulcers.

15. Discuss with a paediatric dietitian whether to offer nutritional supplements to correct nutritional deficiency in neonates, infants, children and young people with pressure ulcers.

16. Assess fluid balance in neonates, infants, children and young people with pressure ulcers.

17. Ensure there is adequate hydration for age, growth and healing in neonates, infants, children and young people. If there is any doubt, seek further medical advice.

18. Use high-specification foam mattresses for adults with a pressure ulcer. If this is not sufficient to redistribute pressure, consider the use of a dynamic support surface.

19. Do not use standard-specification foam mattresses for adults with a pressure ulcer.

20. Consider the seating needs of people who have a pressure ulcer who are sitting for prolonged periods.

21. Consider a high-specification foam or equivalent pressure redistributing cushion for adults who use a wheelchair or who sit for prolonged periods and who have a pressure ulcer.

22. Use a high-specification cot or bed mattress or overlay for all neonates, infants, children and young people with a pressure ulcer.

23. If pressure on the affected area cannot be adequately relieved by other means (such as repositioning), consider a dynamic support surface, appropriate to the size and weight of the child or young person with a pressure ulcer, if this can be tolerated.

24. Consider using specialist support surfaces (including dynamic support surfaces where appropriate) for neonates, infants, children and young people with pressure ulcers, taking into account their current pressure ulcer risk and mobility.

25. Tailor the support surface to the location and cause of the pressure ulcer for neonates, infants, children and young people.

26. Do not routinely offer adults negative pressure wound therapy to treat a pressure ulcer, unless it is necessary to reduce the number of dressing changes (for example, in a wound with a large amount of exudate).

27. Do not offer the following to adults to treat a pressure ulcer:

- electrotherapy
- hyperbaric oxygen therapy.

28. Do not routinely use negative pressure wound therapy to treat a pressure ulcer in neonates, infants, children and young people.

29. Do not use the following to treat a pressure ulcer in neonates, infants, children and young people:

- electrotherapy
- hyperbaric oxygen therapy.

30. Assess the need to debride a pressure ulcer in adults, taking into consideration:

- the amount of necrotic tissue
- the grade, size and extent of the pressure ulcer
- patient tolerance
- any comorbidities

31. Offer debridement to adults if identified as needed in the assessment:

- use autolytic debridement, using an appropriate dressing to support it
- consider using sharp debridement if autolytic debridement is likely to take longer and prolong healing time.

32. Do not routinely offer adults:

- larval (maggot) therapy

- enzymatic debridement.

Consider larval therapy if debridement is needed but sharp debridement is contraindicated or if there is associated vascular insufficiency.

33. Consider autolytic debridement with appropriate dressings for dead tissue in neonates, infants, children and young people. Consider sharp and surgical debridement by trained staff if autolytic debridement is unsuccessful.

34. Do not offer systemic antibiotics specifically to heal pressure ulcers in adults.

35. After a skin assessment, offer systemic antibiotics to adults with a pressure ulcer if there are any of the following:

- clinical evidence of systemic sepsis
- spreading cellulitis
- underlying osteomyelitis.

36. Discuss with the local hospital microbiology department which antibiotic to offer adults to ensure that the systemic antibiotic is effective against local strains of infection.

37. Do not offer systemic antibiotics to adults based only on positive wound cultures without clinical evidence of infection.

38. Consider systemic antibiotics for neonates, infants, children and young people with pressure ulcers with clinical evidence of local or systemic infection.

39. Discuss with a local hospital microbiology department which antibiotic to offer neonates, infants, children and young people to ensure that the chosen systemic antibiotic is effective against local strains of bacteria.

40. Do not routinely use topical antiseptics or antimicrobials to treat a pressure ulcer in adults.

41. Do not routinely use topical antiseptics or antimicrobials to treat a pressure ulcer in neonates, infants, children and young people.

42. Consider using a dressing for adults that promotes a warm, moist wound healing environment to treat grade 2, 3 and 4 pressure ulcers.

43. Discuss with adults with a pressure ulcer and, if appropriate, their family or carers, what type of dressing should be used, taking into account:

- pain and tolerance
- position of the ulcer
- amount of exudate
- frequency of dressing change

44. Do not offer gauze dressings to treat pressure ulcers in adults.

45. Do not use iodine dressings to treat pressure ulcers in neonates.

46. Consider using a dressing that promotes a warm, moist healing environment to treat grade 2, 3 and 4 pressure ulcers in neonates, infants, children and young people.

47. Consider using topical antimicrobial dressings to treat pressure ulcers where clinically indicated in neonates, infants, children and young people, for example, where there is spreading cellulitis

48. Do not offer gauze dressings to treat pressure ulcers in neonates, infants, children and young people.

49. Do not offer gauze dressings to treat pressure ulcers in neonates, infants, children and young people.

50. Discuss with adults with a heel pressure ulcer and, if appropriate, their family or carers, a strategy to offload heel pressure as part of their individualised care plan.

51. Discuss with the parents or carers of neonates and infants and with children and young people (and their parents or carers if appropriate) a strategy to offload heel pressure as part of their individualised care plan to manage their heel pressure ulcer, taking into account differences in size, mobility, pain and tolerance.

1.4 Key research recommendations

1. What is the effect of enzymatic debridement of non-viable tissue compared with sharp debridement on the rate of healing of pressure ulcers in adults?

2. Does negative pressure wound therapy (with appropriate dressing) improve the healing of pressure ulcers, compared with use of dressing alone in adults with pressure ulcers?

3. Do pressure redistributing devices reduce the development of pressure ulcers for those who are at risk of developing a pressure ulcer?

4. When repositioning a person who is at risk of developing a pressure ulcer, what is the most effective position – and optimum frequency of repositioning – to prevent a pressure ulcer developing?

5. Which pressure ulcer tools are most effective for predicting pressure ulcer risk in children?

6. In neonates, infants, children, young people and adults who have adequate nutritional status and who have a pressure ulcer, does providing further nutritional supplements improve healing of the pressure ulcer?

2 Pressure ulcer treatment

2.1 Introduction

Many pressure ulcers can be prevented but if a pressure ulcer does develop then it is imperative that it is treated promptly and effectively. Although potentially very serious, most pressure ulcers can be succesfully treated. Stage 1 pressure ulcers are usually reversible if identified promptly and most stage 2 and 3 pressure ulcers can be healed with appropriate care. Stage 4 pressure ulcers can heal but are often more problematic, with some requiring surgery to achieve healing. This guideline considers a wide range of areas such as support surfaces and adjunctive therapies, for the management of pressure ulcers.

The management of pressure ulcers requires a multidisciplinary approach for optimum management to be achieved. Usually the first requirement when a pressure ulcer develops is to remove the causal process by introducing pressure relieving strategies such as repositioning and the use of appropriate support surfaces. 'Repositioning' refers to the movement of the individual to relieve pressure, which may require assistance or can be done by the individual. The term 'support surfaces' refers to items such as mattresses or cushions on which the person is positioned. Once relief from pressure has been provided, healing needs to be stimulated by debridement, that is the removal of dead tissue. This can be achieved by various techniques including the use of various dressings or physical removal. Any other casual factors will also ideally be corrected such as nutritional deficiencies or poor blood supply and the wound will need to be cleaned and dressed to allow healing. The evidence for these factors and other therapies, including electrotherapy, negative pressure wound therapy and hyperbaric oxygen therapy are reviewed in this guideline. Consideration of ulceration caused by ischemia or neuropathy, moisture, friction and shear, venous leg ulcers, pressure ulcers caused by devices and Kennedy terminal ulcers have been excluded. Treatment strategies for pressure ulcers can potentially be both costly and complex. A multitude of devices including different mattress systems and pressure ulcer wound care products are currently used within the NHS although few have been evaluated in randomised control trials (RCTs). There is therefore a need to evaluate the evidence to decide which of the many available treatments promote the most cost-effective healing of pressure ulcers.

The management of pressure ulcers is provided in a wide range of settings such as in the community, in hospital or in residential care. Thus a range of staff are involved in the provision of patient care and patient support. In addition, it should also be recognised that the management of pressure ulcers is challenging for patients, family members and caregivers.

2.1.1 Extrapolating adults recommendations to neonates, infants, children and young people

For ease of use, the guideline and its recommendations have been divided into two sections, part 1 (prevention) and part 2 (management). Part 1 and part 2 both contain recommendations for adults and neonates, infants, children and young people, using methods outlined in Chapter 3 and 4, respectively.

It is acknowledged that the recommendations for adults and those for neonates, infants, children and young people differ. However, due to the variances in the sites where younger populations may develop pressure ulcers, the GDG chose to use the results of a Delphi consensus to develop the recommendations, rather than extrapolating from evidence in adult populations.

However, the GDG recognises that some of the recommendations developed for adults may be applicable to neonates, infants, children and young people and that healthcare professionals may wish to consider the principles of these recommendations when treating these populations.

In each 'Linking evidence to Recommendations' section, recommendations for adults can be found in yellow boxes and recommendations for neonates, infants, children and young people in pink boxes. Recommendations which are applicable for all ages can be found in blue boxes.

2.1.2 Pressure ulcers caused by devices

The GDG wished to highlight that the prevention and management of pressure ulcers caused by devices is outside the scope of the current guideline (see Appendix A).

2.1.3 Accounting for individuals' comfort

Throughout the guideline, when developing recommendations for the prevention and management of pressure ulcers, the GDG have taken into consideration the individuals' concurrent needs for sleep, pain relief, meal times and rehabilitation. The GDG felt that it was important to highlight that a balance needs to be achieved between all of these factors for those at risk of or who have developed a pressure ulcer.

3 Pressure ulcer measurement

3.1 Introduction

The measurement of pressure ulcer size can be used by healthcare professionals for recording and monitoring the progression and healing of a pressure ulcer. Recording this accurately can allow an assessment to be made as to whether a treatment is effective in promoting healing, by reducing the size of the pressure ulcer.

It is important for healthcare professionals to understand that a pressure ulcer does not ony affect the visible skin but that it also has a cavity underneath it with depth and volume. As well as the visible cavity, a cavity under the skin that cannot be directly observed (undermining) may be present. This would need to be considered in addition to any measurement of visible damage.

A variety of methods and tools are available for measuring different aspects of a pressure ulcer, for example, planimetry or photography. To be useful, the method used must be both accurate and reliable, without causing damage to the tissue, or undue pain or discomfort to the individual.

Given the potential benefits of measuring a pressure ulcer in identifying its progression to assess healing and progression the GDG were interested in investigating which tools were both reliable and accurate for measuring pressure ulcers.

3.2 Review question: What are the most reliable techniques/tools to measure the dimensions of a pressure ulcer?

One systematic review[141] looked at the performance of instruments designed for measuring the dimensions of pressure ulcers. This systematic review was included in the current evidence review and it was subsequently updated to include 1 other study (Terris 2011)[185]. Overall 13 studies were included in the evidence review.[11,26,34,48,66,70,77,107,168,169,182,185,188] Evidence from these is summarised in the clinical GRADE evidence profile below. The quality of these studies is outlined in Table 5-Table 7.

The O'Meara review[141] looked at studies of any design which reported an evaluation of a pressure ulcer measurement instrument as the main focus of the investigation. The authors did not include assessment checklists where the focus was the performance of the tool overall rather than the measurement of pressure ulcer dimensions.

Summary of included studies

Study	Population	Instruments	Outcomes (for definitions, see Table 1)
Griffin 1993[70]	Mean age 31 years in a spinal cord injury rehabilitation centre with stage 2 to 5 pressure ulcers.	Tracing from photo, digital table, and computerised planimetry; direct transparency tracing, digital tablet and computerised planimetry.	• Intra-rater reliability; agreement
Anthony 1985[11]	Minimal details of participant characteristics and settings.	Slide photo digitiser, and computerised planimetry; acetate tracing and square count.	• Intra-rater reliability; inter-rater reliability.
Schubert 1996[169]	People from a geriatric clinic, with stage 3 pressure ulcers.	Transparency tracing and digital planimetry.	• Intra-rater reliability; inter-rater reliability.
Lucas 2002[107]	Older adults in long-term care settings, Netherlands with stage 3 pressure ulcers.	Photo, transparent grid, whole and partial square count.	• Intra-rater reliability; inter-rater reliability.
Sugama 2007[182]	Older adults in long-term care settings.	Portable digital device consisting of 3 layer sterile tracing grid and digital pad (VISITRAK).	• Intra-rater reliability; inter-rater reliability • Accuracy
Frantz 1992[66]	Minimal details of participant characteristics and settings.	Stereophotogrammetry and computerised image analysis; scanned photographic images and computerised planimetry (reference standard).	• Inter-rater reliability
Buntinx 1996[34]	Older adults in geriatric department of hospital.Study included other wounds but did not separate by wound type. Pressure ulcers were the predominant wound type (21/27).	Transparent grid.	• Inter-rater reliability
Schubert 1997[168]	Minimal details of participant characteristics and settings	Transparency tracing plus: • digital planimetry (reference standard) • diameter product • whole square count • whole and partial square count • whole and residual square count.	• Accuracy.
Thomas 1990[188]	Inpatients and outpatients at a large metropolitan county hospital. Study	Slide photography, digitising tablet, and computerised planimetry; transparency tracing and digital planimetry;	• Agreement.

Study	Population	Instruments	Outcomes (for definitions, see Table 1)
	included other wounds but wound stratified by type of ulcer.	kundin device and mathematical formula.	
Cutler 1993[48]	Older adults in long-term care settings, LA, USA.	Elliptical area (direct diameter measurement); elliptical area (diameters from tracing); elliptical area (diameters from photos); tracing and computerised planimetry; photo and computerised planimetry.	• Agreement
Schubert 1996[169]	Older adults in a geriatric clinic.	Saline-gel injection into wound cavity; subsequent measurement of volume required to fill cavity.	• Intra-rater reliability; inter-rater reliability.
Berg 1990[26]	Minimal details of participant characteristics and settings.	Sterile fluid injection into cavity; subsequent measurement of volume required to fill cavity.	• Inter-rater reliability.
Hayward 1993[77]	People with pressure ulcers in an inpatient service.	Alginate mould of wound cavity with application of: water displacement (reference standard) and NMR spectroscopy.	• Accuracy
Terris 2011[185]	People with stage 3 and 4 pressure ulcers with spinal cord injuries.	14 cm disposable ruler placed adjacent to pressure ulcer to measure length and width of wound. Digital photographs taken with camera.	• Intra-rater reliability; inter-rater reliability

Table 1: Definitions of outcome measures used in this review

Outcome	Definition
Intra-rater reliability	Do 2 assessments performed by the same investigator produce the same result?
Inter-rater reliability	Do 2 or more different investigators achieve the same result?
Accuracy	The closeness of computations or estimates to the exact or true values.
Agreement	The degree to which scores or ratings are identical

Table 2: Details of statistical measures used in this review

Heading	Definition
Correlation	Extent to which 2 or more variables are associated with each other.
Co-efficients of variation	The ratio of the standard deviation of the measurements on a subject to the mean of these measurements.
Intraclass correlation coefficient	A measure of the inter-rater reliability for 2 or more raters. May also be used to assess test-retest reliability. Conceptualised as ratio of between-groups variance to total variance.
Kappa coefficient	A measure of non-random agreement between observers or measurements of the same categorical variable.
Pearons's correlation coefficient	A measure of the linear relationship between 2 variables in a sample and used as an estimate of the correlation in the whole population.

Table 3: Glossary of instruments for measuring dimensions of pressure ulcers

Instrument	Details
Tracing from photograph	Making a slide of the pressure ulcer using a camera with a macrolens and then outlining pressure ulcer margins from the projected slide image (photographic method).
Transparency tracing	Transparency method. A transparent plastic film (for example, acetate) is placed directly over the pressure ulcer and the margins are traced usually with an indelible pen.
Transparent grid	An adhesive transparent plastic film is placed over the wound (see transparency tracing) and a pre-printed transparent square grid is used along with this so the tracing can be traced onto this grid sheet with an indelible pen. The grid squares can then be counted (see square count).
Computerised/ digital planimetry/ digital tablet/slide photo digitiser	A planimeter or digitising tablet can be used to calculate the ulcer surface area from the photographs taken using slide film and a camera. An enlarged slide is then scanned by a digitiser connected to a microcomputer, the pressure ulcer is compared to the known frame and an area calculated.
Square count	After a tracing of the pressure ulcer has been made it is then laid over squared graph paper of known dimensions and the squares inside the sore boundary are counted to give an absolute value of area.
Whole square count	The number of whole squares which lie inside the tracing.
Partial square count	Each partial square was assumed to contribute on average half (50%) the area of a whole square.
Residual square count	Residual square count for each such partial square a visual estimate was made of the proportion that was inside the tracing. The sum of all proportions gave the equivalent number of whole squares.
Stereophotogrammetry	A method of applying optical triangulation to produce 3-dimensional measurements from 2 separate 2-dimensional photographs.
Kundin device and mathematical formula	A disposable, 3-dimensional, plastic-coated paper wound gauge.

Instrument	Details
NMR spectroscopy of a mould	Nuclear magnetic resonance spectrometer is a research technique that exploits the magnetic properties of certain atomic nuclei to determine physical and chemical properties of atoms or the molecules in which they are contained. It relies on the phenomenon of nuclear magnetic resonance and can provide detailed information about the structure, dynamics, reaction state, and chemical environment of molecules. It was used to make cross sectional images of the moulds which then could be made and processed with software.

Table 4: Categorisation of values into levels of acceptability[a]

Acceptability of values	**Very good/excellent**		**Fair/good**		**Poor**	
Correlation	**Excellent**		**Good**	**Fair**	**Poor**	
Intra class coefficient (ICC)[b]	0.75+		0.60 to 0.74	0.40 to 0.59	<0.40	
Kappa coefficient[c]	0.75+		0.60 to 0.74	0.40 to 0.59	<0.40	
Correlation	**Perfect**	**High**	**Moderate**		**Low**	**No correlation**
Pearson's correlation coefficient[d]	1.00	0.75+	0.25 and 0.75		<0.25	0
Intra-rater reliability % variation	**Adequate**		**Acceptable**		**Poor**	
Coefficient of variation[e]	<10%		10-20%		>20%	
Inter-rater reliability % variation	**Adequate**		**Acceptable**		**Poor**	
Coefficient of variation[f]	<20%		20-30%		>30%	

(a) These have been categorised into excellent/good/poor to provide a general idea of what the values mean in the evidence tables below.

(b) Fleiss, J. L. (1981) Statistical methods for rates and proportions. 2nd ed. (New York: John Wiley) pp. 38–46

(c) Orwin RG. Evaluating coding decisions. In: Cooper H, Hedges LV (editors). The Handbook of Research Synthesis. New York (NY): Russell Sage Foundation, 1994.

(d) As per NCGC guidance 2012.

(e) As per NCGC guidance 2012.

(f) As per NCGC guidance 2012.

3.2.1 Clinical evidence for intra-rater reliability

Table 5: Clinical evidence profile: measurement of wound diameter

Study	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	n	Tool	Statistical methods	Evaluation	Acceptability of values	Quality
Intra-rater reliability – minimal details of participant characteristics – no details of pressure ulcer site provided.											
Anthony 1985[11]	Very serious limitations [a]	No serious inconsistency	No serious indirectness	Serious imprecision[b]	N/A	4 subjects with 4 pressure ulcers	Longest diameter assessed with tape measure Shortest diameter assessed with tape measure.	Mean (range) of coefficients of variation (SD/mean %) for 3 nurses' assessment of 2 wounds x10	4.2% (2.1 – 6.8%) 7.0% (4.1-11%)	Very good/excellent Very good/excellent	Very low
Intra-rater reliability - People with spinal cord injuries with a stage 3 or 4 pressure ulcer – no details of pressure ulcer sites for the 10 pressure ulcers provided but the 15 people in the whole study pressure ulcer sites were n=2 ankle, n=8 foot and heel, n=8 ischium, n=1 knee, n=8 sacrum and buttock, n=1 thigh, n=3 trochanter.											
Terris 2011[185]	Very serious limitations [a]	No serious inconsistency	No serious indirectness	Serious imprecision[b]	Serious[c]	10 pressure ulcers (randomly selected) study included 15 participants with 31 pressure ulcers	Length assessed with ruler Width assessed with ruler Digital photographs taken	Kappa coefficient; 2 wound care nurses and a 3rd study team member for in-person assessments and to take digital photos	0.072 (p=0.02) 0.110 (p=0.009)	Poor Poor	Very low
Inter-rater reliability - minimal details of participant characteristics – no details of pressure ulcer site provided.											
Anthony 1985[11]	Very serious	No serious inconsistency	No serious indirectness	Serious imprecision[b]	N/A	4 subjects with 4	Longest diameter	Difference between	Means (cm): 1st wound	Poor	Very low

Study	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	n	Tool	Statistical methods	Evaluation	Acceptability of values	Quality
	limitations [a]					pressure ulcers; 3 observers	assessed with tape measure Shortest diameter assessed with tape measure	means for 3 nurses' assessment of 2 wounds tested using ANOVA	2.19, 7.75, 6.87 ($p<0.001$); 2nd wound 1.93, 1.76, 1.53 ($p<0.01$) Means (cm): 1st wound 1.45, 1.94, 1.82 ($p<0.001$); 2nd wound 1.30, 1.45, 1.63 ($p<0.01$)	Poor	
Inter-rater reliability – elderly adults in geriatric department of hospital – no details of pressure ulcer site provided.											
Buntinx 1996[34]	Very serious limitations [a]	No serious inconsistency	No serious indirectness	Serious [b]	Serious [c]	20 subjects, 27 wound (21 pressure ulcers, 2 leg ulcers, 3 venous leg ulcers and an amputation wound)	Longest diameter (instrument not stated) Longest diameter perpendicular to the above	Correlation coefficients (exact analysis not stated) between six raters assessing 27 wounds. Difference between means of the six raters.	Range of correlation coefficients 0.72 -0.98 p=0.93 for overall difference between means p=0.88 for overall difference	Very good/excellent	Very low

Study	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	n	Tool	Statistical methods	Evaluation	Acceptability of values	Quality
							(instrument not stated)	Correlation coefficients not reported for this wound dimension. Difference between means of six raters reported as above.	between means		
Inter-rater reliability - People with spinal cord injuries with a stage 3 or 4 pressure ulcer– pressure ulcer sites were n=2 ankle, n=8 foot and heel, n=8 ischium, n=1 knee, n=8 sacrum and buttock, n=1 thigh, n=3 trochanter.											
Terris 2011[185]	Very serious limitations[a]	No serious inconsistency	No serious indirectness	Serious limitations[b]	Serious[c]	15 subjects with 31 pressure ulcers	Length assessed with ruler Width assessed with ruler Digital photographs taken	Kappa coefficient	0.075 (p=0.003) 0.103 (<0.001)	Poor Poor	Very low

(a) The study was of low methodological quality (see table below). Anthony and Buntinx used ANOVA for inter-rater reliability but did not give full account of the methods used and they did not give estimate of all potential sources of variability. There were a small number of assessors.

(b) There were a limited number of observations.

(c) No confidence interval was given so cannot comment on imprecision.

Inter-rater reliability results were mixed. It is not possible to comment on the acceptability of the methods of analysis as there was not enough detail given.

Table 6: Clinical evidence profile: measurement of pressure ulcer depth

Study	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	n	Tool	Statistical methods	Evaluation	Acceptability of values	Quality
Intra-rater reliability – elderly participants with stage 3 pressure ulcers at geriatric clinic – pressure ulcer site n=8 sacral, n=2 trochanter, n=1 forefoot.											
Schubert 1996[169]	Very serious limitations[a]	No serious inconsistency	No serious indirectness	Serious imprecision[b]	Serious[c]	11 participants with 11 pressure ulcers	Depth at wound centre assessed with probe	Coefficient of variation generated from repeated measures ANOVA for assessment of 11 wounds (unclear whether 1 or 2 nurses involve in assessment)	Coefficient of variation 26%	Poor	Very low
Inter-rater reliability – elderly participants with stage 3 pressure ulcers at geriatric clinic – pressure ulcer site n=8 sacral, n=2 trochanter, n=1 forefoot.											
Schubert 1996[169]	Very serious limitations[a]	No serious inconsistency	No serious indirectness	Serious imprecision[b]	Serious[c]	11 participants with 11 pressure ulcers	Depth at wound center assessed with probe	Coefficient of variation generated from repeated measures ANOVA; 11 wounds measured on four separate occasions 2 nurses involved	Coefficient of variation 48%	Poor	Very low
Inter-rater reliability - minimal details of participant characteristics 5 stage 2 ulcers, 18 stage 3 ulcer and 13 stage 4 ulcer (NPUAP) – pressure ulcer site n=10 coccyx, n=10 malleolus, n=6 heel; n=4 ischial tuberosity, n=3 trochanter, n=2 lateral foot.											
Frantz 1992[66]	Serious limitations[a]	No serious inconsistency	No serious indirectness	Serious imprecision[b]	Serious[c]	36 pressure	Depth measur	Pearson's correlation	Pearson's correlation	Very good/excellent	Very low

Study	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	n	Tool	Statistical methods	Evaluation	Acceptability of values	Quality
						ulcers	ed using steroph otogra mmetry and comput erised image analysis	used for 2 raters assessing 144 steroslides (four photos of 36 ulcers taken at 2-week intervals)	0.96		
Accuracy - elderly adults with stage 3 pressure ulcers at geriatric clinic– pressure ulcer site n=8 sacral, n=2 trochanter, n=1 forefoot.											
Schubert 1996[169]	Very serious limitations[a]	No serious inconsistency	No serious indirectness	Serious imprecision [b]	Serious[c]	11 patients with 11 pressure ulcers	Probe assesse d against ratio betwee n wound volume and area (referen ce standar d)	Difference between normalised (that is relative to baseline) means for the 2methods derived from time series data for each participant.	Group mean 55% (highest value 144%)	Poor	Very low
Accuracy – minimal details of patient characteristics 5 stage 2 ulcers, 18 stage 3 ulcer and 13 stage 4 ulcers (NPUAP) – pressure ulcer site n=10 coccyx, n=10 malleolus, n=6 heel; n=4 ischial tuberosity, n=3 trochanter, n=2 lateral foot.											
Frantz 1992[66]	Serious limitations[a]	No serious inconsistency	No serious inconsistency	Serious imprecision[b]	Serious[c]	36 pressure ulcers	Depth measur ed using steroph otogra mmetry and	Pearson's correlation used for 2 raters assessing 144 steroslides	Pearson's correlation 0.96	Very good/excellent	Very low

Study	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	n	Tool	Statistical methods	Evaluation	Acceptability of values	Quality
							computerised image analysis	(four photos of 36 ulcers taken at 2-week intervals)			

(a) The study was of low/very low methodological quality (see table below).
(b) There were a limited number of observations.
(c) No confidence interval was given so cannot comment on imprecision.

Central pressure ulcer depth with a probe was not valid when it was compared to a reference standard. It is to be noted that the reference standard used may not be valid due to the assumption that pressure ulcer depth would not vary over the base of the pressure ulcer and that the walls of the pressure ulcer were steep. Intra and inter-rater reliability was more variable for the depth probe compared to measurements of other wound dimensions. Stereophotogrammetry with computerised image analysis was highly correlated for inter-rater reliability. However the Pearson's correlation coefficient does not measure association repeatability. Therefore it does not estimate any bias that may occur in measurements of 1 assessor to another.

Table 7: Clinical evidence profile: measurement of pressure ulcer surface area

Study	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	N	Tool	Statistical methods	Evaluation	Acceptability of values	Quality
Intra-rater reliability - mean age 31 years in a spinal cord injury rehabilitation centre with grade 2 to 5 ulcers, USA – pressure ulcer sites n=8 gluteal/ischial, n=12 sacral/coccygeal, n=2 trochanteric, various size 688+/-228mm^2											
Griffin 1993[70]	No serious limitations	No serious	No serious	Very serious[b,d]	N/A	20 people with 22 pressure ulcers	Tracing from photo, digital table, and computerised planimetry; Direct transparency tracing, digital tablet and computerised planimetry	ICC generated from 1-way random-effects ANOVA. One physiotherapist assessed five wounds twice with 1 hour	ICC (SE) SEM for mean of 3 measurements per wound: Instrument 1: 0.999 (0.577) 18.8mm2 Instrument 2: 0.999 (0.577)	Instrument 1: Very good/excellent Instrument 2: Very good/excellent	Low

Study	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	N	Tool	Statistical methods	Evaluation	Acceptability of values	Quality
								between measurements	25.1mm2 Mean (SE) surface area estimated from mean of 3measurements per wound (mm2) Instrument 1: 1,188.9 (626.4) Instrument 2: 18.1% (10.0-42.6%)		
Intra-rater reliability – minimal details of participant characteristics– no details of pressure ulcer site											
Anthony 1985[11]	Very serious limitations[a]	No serious inconsistency	No serious indirectness	Very serious[b,d]	N/A	4 subjects with 4 pressure ulcers	Slide photo digitiser, and computerised planimetry; Acetate tracing and square count	Mean (range) of coefficients of variation (SD/mean %) for 3 nurses' assessment of four wounds x10 on the same day	Instrument 1: 11.0% (2.8-28.2%) Instrument 2: 18.1% (10.0-42.6%)	Fair/good	Very low
Intra-rater reliability – elderly adults with stage 3 pressure ulcers– pressure ulcer site n=8 sacral, n=2 trochanter, n=1 forefoot.											
Schubert 1996[169]	Very serious limitations[a]	No serious inconsistency	No serious indirectness	Serious imprecision[b]	Serious[c]	11 people with 11 pressure ulcers	Transparency tracing and digital planimetry	Coefficient of variation generated from repeated	Coefficient of variation 2%	Very good/excellent	Very low

Study	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	N	Tool	Statistical methods	Evaluation	Acceptability of values	Quality
								measures ANOVA; 11 wounds measured on four separate occasions (number of assessors unclear)			
Intra-rater reliability - older adults in long-term care with stage 3 pressure ulcers, pressure ulcer sites were n=7 gluteal, n=7 sacrum/coccyx, n=1 greater trochanter, n=2 medial femoral epicondyle, n=3 lateral malleolus, n=10 calcaneus.											
Lucas 2002[107]	No serious limitations	No serious inconsistency	No serious indirectness	Serious imprecision[b]	Serious[c]	26 people, 30 wounds	Photo, transparent grid, and whole plus partial square count	ICC from 2-way random effects ANOVA. Two physiotherapists assessed 30 wound x2 on 2 occasions, 2 weeks apart.	ICC 0.99 for both assessors	Very good/excellent	Low
Intra-rater reliability - older adults in long-term care – pressure ulcer site n=5 sacral, n=3 trochanteric, n=1 iliac, n=1 calcaneal.											
Sugama 2007[182]	No serious limitations	No serious inconsistency	No serious indirectness	Serious imprecision[b]	Serious[c]	10 ulcers	Portable digital device consisting of 3-layer sterile tracing grid and digital pad (VISITRAK)	ICC derived from ANOVA. Four nurses assessed 10 wounds from 10 people..	ICC 0.99	Very good/excellent	Low
Inter-rater reliability – minimal details of participant characteristics– no details of pressure ulcer site provided.											
Anthony	Very serious	No serious	No serious	Serious	Seriou	4	Slide photo	Difference	Statistically	Poor	Very low

Study	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	N	Tool	Statistical methods	Evaluation	Acceptability of values	Quality
1985[11]	limitations[a]	inconsistency	indirectness	imprecision[b]	s[c]	subjects with 4 pressur e ulcers	digitiser, and computerised planimetry; Acetate tracing and square count	between means for 3nurses' assessment of 4wounds tested using ANOVA	significant differences observed between assessors for 2 out of four ulcers for instrument 1 and for 3 out of four ulcers for instrument 2 (p< 0.01 for all comparison s)		
Inter-rater reliability – elderly participants with stage 3 pressure ulcers at a geriatric clinic– pressure ulcer site n=8 sacral, n=2 trochanter, n=1 forefoot.											
Schubert 1996[169]	Very serious limitations[a]	No serious inconsistency	No serious indirectness	Serious imprecision[b]	Seriou s[c]	11 people with 11 pressur e ulcers	Transparency tracing and digital planimetry	Coefficient of variation from repeated measures ANOVA for assessment of 11 wounds by 2 nurses	Coefficient of variation 3%	Very good/excellent	Very low
Inter-rater reliability – older adults in long-term care with stage 3 pressure ulcers pressure ulcer sites were n=7 gluteal, n=7 sacrum/coccyx, n=1 greater trochanter, n=2 medial femoral epicondyle, n=3 lateral malleolus, n=10 calcaneus.											
Lucas 2002[107]	No serious limitations	No serious inconsistency	No serious inconsistency	Serious imprecision[b]	Seriou s[c]	26 people, 30 wounds	Photo, transparent grid, and whole plus partial square count	ICC from 2-way random effects ANOVA. Two physiothera	ICC 0.99	Very good/excellent	Low

Study	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	N	Tool	Statistical methods	Evaluation	Acceptability of values	Quality
								pists assessed 30 wounds x2 on2 occasions, 2 weeks apart			
Inter-rater reliability – older adults in long-term care– pressure ulcer site n=5 sacral, n=3 trochanteric, n=1 iliac, n=1 calcaneal.											
Sugama 2007[182]	No serious limitations	No serious inconsistency	No serious indirectness	Serious imprecision[b]	Serious[c]	10	Portable digital device consisting of 3-layer sterile tracing grid and digital pad (VISITRAK)	ICC derived from ANOVA. Four nurses assessed 10 wounds from 10 people.	ICC 0.99	Very good/excellent	Low
Inter-rater reliability –details of participant characteristics 5 stage 2 ulcers, 18 stage 3 ulcer and 13 stage 4 ulcer (NPUAP) – pressure ulcer site n=10 coccyx, n=10 malleolus, n=6 heel; n=4 ischial tuberosity, n=3 trochanter, n=2 lateral foot.											
Frantz 1992[66]	Serious limitations[a]	No serious inconsistency	No serious indirectness	Serious imprecision[b]	Serious[c]	36 pressure ulcers	Stereophotogrammetry and computerised image analysis;	Peasons's correlation for 2 raters assessing 144 steroslides (four photos of 36 ulcers taken at 2-week intervals	Pearson's correlation coefficient 0.98	Very good/excellent	Very low
Inter-rater reliability – elderly adults at a geriatric department of a hospital– no details of pressure ulcer site provided.											
Buntinx 1996[34]	Very serious limitations[a]	No serious inconsistency	No serious inconsistency	Serious imprecision[b]	Serious[c]	27 pressure ulcers	Transparent grid	Correlation coefficients (exact method not stated) between 6 raters	Range of correlation coefficients 0.94-0.98	Very good/excellent	Very low

Study	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	N	Tool	Statistical methods	Evaluation	Acceptability of values	Quality
								(3physicians, 3 nurses) assessing 27 wounds (20 people)			
Accuracy - minimal details of participant characteristics – no details of pressure ulcer site provided.											
Schubert 1997[168]	Very serious limitations[a]	No serious inconsistency	No serious inconsistency	No serious	Serious[c]	373 ulcers	Transparency tracing plus: Digital planimetry (reference standard) Diameter product Whole square count Whole plus partial square count Whole plus residual square count	Regression with reference area as independent variable and index measurements as dependent variables. Regression coefficients were compared with the null hypothesis using Student's t-test. One assessor measured 373 wounds	Instrument 2: average value significantly higher than reference standard (31% p<0.001 for difference between instruments) Instrument 3: significantly lower than reference standard (-13%, p<0.001) Instrument 4: mean value around 1% greater than reference standard Instrument 5: mean	N/A	Very low

Study	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	N	Tool	Statistical methods	Evaluation	Acceptability of values	Quality
									value around 1% less than reference standard		
Accuracy - older adults in long-term care – pressure ulcer sites were n=12 sacral, n=12 trochanteric, n=4 calcaneal, n=1 iliac and n=1 toe.											
Sugama 2007[182]	Serious limitations[a]	No serious inconsistency	No serious indirectness	Serious imprecision[b]	Serious[c]	30 people with 30 pressure ulcers	Portable digital device consisting of 3-layer sterile tracing grid and digital pad; Scanned photographic images and computerised planimetry (reference standard)	Correlation coefficient (exact method not stated) calculated from average of 3 measurements. Four nurses assessed 30 people with 1 wound each.	Correlation coefficient 0.99 (p<0.001)	Very good/excellent	Very low
Agreement - mean age 31 years in a spinal cord injury rehabilitation centre with grade 2 to 5 ulcers– pressure ulcer sites n=8 gluteal/ischial, n=12 sacral/coccygeal, n=2 trochanteric, various size 688+/-228mm^2.											
Griffin 1993[70]	Serious limitations[a]	No serious inconsistency	No serious indirectness	Serious imprecision[b]	Serious[c]	20 people with 22 ulcers	Tracing from photo, digital table, and computerised planimetry; Direct transparency tracing, digital tablet and computerised planimetry	Pearson's correlation 2 way mixed model ANOVA with patients and methods as main effects; 3-way mixed model ANOVA with patients,	Pearson's correlation 0.98 (p<0.0001). Two –way ANOVA: significant difference between patients (p=0.0001) but not between	Very good/excellent	Very low

Study	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	N	Tool	Statistical methods	Evaluation	Acceptability of values	Quality
								methods and days as main effects. One physiotherapist assessed 20 people with 22 wounds	methods (p=0.88) Three-way ANOVA: no significant differences between methods over time.		
Agreement - inpatients and outpatients – size ranged 15.83mm^2 to 35740mm^2 – no details of pressure ulcer site provided.											
Thomas 1990[188]	Very serious limitations[a]	No serious inconsistency	No serious indirectness	Serious imprecision[b]	Serious[c]	37 pressure ulcers	Slide photography, digitising tablet, and computerised planimetry; Transparency tracing and digital planimetry; Kundin device and mathematical formula	Assessed using Pearson's correlation and repeated measures ANOVA. Thirty-seven pressure ulcers assessed. No information about assessors.	Pearson's correlation between instruments: 1&2, 0.996; 1&3, 0.934; 2&3, 0.936; p</=0.0001 for all correlations. p=0.0001 for difference between means (instruments).	Very good/excellent	Very low
Agreement - older patients in long-term care with stage 3 or 4 pressure ulcers - size ranged from 1.2cm^2 to 61.6cm^2 – pressure ulcer sites were n=8 sacrum, n=4 coccyx, n=4 hip, n=3 heel, n=1 buttock.											
Cutler 1993[48]	Very serious limitations[a]	No serious inconsistency	No serious indirectness	Serious imprecision[b]	Serious[c]	20 people with 20 pressure ulcers	Elliptical area (direct diameter measurement); Elliptical area	Assessed using Pearson's correlation coefficient and	Pearson's correlation: between instruments: 1 & 4, 0.979; 1& 5,	Very good/excellent	Very low

Study	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	N	Tool	Statistical methods	Evaluation	Acceptability of values	Quality
							(diameters from tracing) Elliptical area (diameters from photos); Tracing and computerised planimetry; Photo and computerised planimetry.	variance components model assessing effects of people, sample (refers to duplicate tracing or photograph) and replication (refers to multiple measurements obtained from computerised planimetry.	0.971; 1& 2, 0.982; 4& 5, 0.963; 2&4, 0.991; 3&5, 0.989; p< 0.001 for all correlations except 4& 5, which was not reported. Estimates from the variance components model suggested that most of the observed variation came from participants rather than samples or replication (that is the instruments).		

(a) The study was of low/very low methodological quality (see table below).
(b) There were a limited number of observations.
(c) No confidence interval was given so cannot comment on imprecision.
(d) The confidence interval was wide.

O'Meara (2012)[141] summarised the findings by reliability, accuracy and agreement:

3.2.1.1 Reliability

Intra-rater reliability for transparency tracing from a Polaroid photo and whole plus partial square count from a grid was satisfactory. The intra-class correlation coefficient was good. Intra-rater reliability of tracing from slide photography versus direct contact transparency tracing (both with computerised planimetry) was high and showed no difference between the instruments but there were a small number of pressure ulcers assessed. A portable digital system showed that the intra-rater and inter-rater reliability was good. A transparency tracing with whole plus partial square count was adequate for inter-rater reliability. Another study assessed stereophotogrammetry and computerised image analysis and had a good Pearson's correlation coefficient.

3.2.1.2 Accuracy

One study analysed the accuracy of 4 interventions in addition to tracing onto a grid compared to a reference standard (transparency tracing and digital planimetry). Whole square count and whole plus residual square count were found to have accuracy. It was a large study but there was an inappropriate use of regression analysis to estimate accuracy. Another study compared a portable digital device to a scanned photographic image combined with computerised planimetry (reference standard). This was highly correlated but the exact statistical method was not reported so the suitability of the analysis cannot be assessed.

3.2.1.3 Agreement

Photography combined with digital planimetry, transparency tracing combined with digital planimetry and the Kundin device with a mathematical adjustment showed statistically significant differences. Another study showed that photographic tracing and direct acetate tracing (both combined with a digitising table and computerised planimetry) had no statistically significant differences. There were methodological and statistical problems in the agreement studies.

Intra-rater reliability reliability of sterile saline gel mixture to fill the pressure ulcer cavity was found to be good and inter-rater reliability fair or good in 1 study. Another study showed no statistically significant difference in the variation for inter-rater reliability for a sterile salien gel to fill the pressure ulcer cavity. An additional study reported a high Pearson's correlation for sterophotogrammetry combined with computerised image analysis by 2 assessors independently. There was a high Pearson's correlation for nuclear magnetic resonance spectroscopy of alginate mold and water displacement of the mold (reference standard) for agreement. Pearson's correlation coefficient is not appropriate for inter-rater reliability, accuracy or agreement as it only looks at association rather than bias and can give misleading results.

3.2.1.4 Overall findings

O'Meara (2012)[141] reported that most of the evaluations had methodological and/or statistical problems. The methods that may be reliable are: measuring surface area with grid tracings from photographs combined with whole plus partial square count; a portable digital pad and sterophotogrammetry combined with computerised image analysis. There may be agreement between photographic tracing and direct transparency tracing (both combined with computerised planimetry). No conclusions could be made for studies of diameter or depth and evaluations of volume measurement were of poor quality. There was little data on feasibility.

Table 8: Quality of reliability studies

Study	Are the participants representative?	Selection criteria clear?	Assessors representative?	Assessor selection criteria clear?	Time period short enough between measurements short enough?	Did all receive scheduled repetitions of measurements?	Description of execution of measurements adequate for replication?	Description of sequence of repeated measurements adequate?	Inter-rater reliability: was measurement performed without knowledge of other rater's values?	Was order of measurements random?	Were withdrawals explained?
Anthony 1985[11]	Unclear	No	Unclear	No	Yes	No	Yes	Yes	Unclear	No	No[a]
Berg 1990[26]	Unclear	No	Unclear	No	Yes	Yes	Yes	No	Yes	No	N/A
Buntinx 1996[34]	Yes	Yes	Yes	No	Unclear	Unclear	No	No	Unclear	No	No[a]
Frantz 1992[66]	Yes	Yes	Unclear	No	Yes	Yes	Yes	Yes	Yes	No	N/A
Griffin 1993[70]	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	N/A	Yes	Yes
Lucas 2002[107]	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	n/a
Schubert 1996[169]	Yes	Yes	Unclear	No	Unclear	Unclear	Yes	No	Yes	No	Yes
Sugama 2007[182]	Yes	No	Yes	No	Yes	Yes	Yes	Yes	Unclear	Yes	n/a
Terris 2011[185]	Yes	Yes	Yes	No	Yes	Unclear	Yes	Unclear	Unclear	Unclear	N/A

(a) No, not explained, but there may not have been any withdrawals.

N/A, not applicable (no withdrawals or inter-rater reliability not assessed)

3.2.2 Economic evidence (adults)

No relevant economic evaluations comparing ulcer measurement techniques were identified.

3.2.3 Clinical evidence (neonates, infants, children and young people)

No RCTs or cohort studies were identified. Recommendations were developed using a modified Delphi consensus technique. Further details can be found in Appendix N.

3.2.4 Economic evidence (neonates, infants, children and young people)

No relevant economic evaluations comparing ulcer measurement techniques were identified.

3.2.5 Evidence statements

3.2.5.1 Clinical (adults)

3.2.5.1.1 Measurement of pressure wound diameter

- One study (n=4) reported that measuring the longest diameter with a tape measure had potentially very good/excellent intra-rater reliability for measurement of pressure ulcer diameter (very low quality).
- One study (n= 4) reported that measuring the shortest diameter with a tape measure had potentially very good/excellent intra-rater reliability for measurement of pressure ulcer diameter (very low quality).
- One study (n= 15) reported that measuring the length with a ruler and using digital photographs had potentially poor intra-rater reliability for measurement of pressure ulcer diameter (very low quality).
- One study (n= 15) reported that measuring the width with a ruler and using digital photographs had potentially poor intra-rater reliability for measurement of pressure ulcer diameter (very low quality).
- One study (n=4) reported that measuring the longest diameter with a tape measure had potentially poor inter-rater reliability for measurement of pressure ulcer diameter (very low quality).
- One study (n= 4) reported that measuring the shortest diameter with a tape measure had potentially poor inter-rater reliability for measurement of pressure ulcer diameter (very low quality).
- One study (n= 15) reported that measuring the length with a ruler and using digital photographs had potentially poor inter-rater reliability for measurement of pressure ulcer diameter (very low quality).
- One study (n= 15) reported that measuring the width with a ruler and using digital photographs had potentially poor inter-rater reliability for measurement of pressure ulcer diameter (very low quality).
- One study (n=20) reported that measuring the longest diameter with an instrument that was not stated had potentially very good/excellent inter-rater reliability for measurement of pressure ulcer diameter (very low quality).
- One study (n=20) reported that measuring the longest diameter perpendicular with an instrument that was not stated had potentially very good/excellent inter-rater reliability for measurement of pressure ulcer diameter (very low quality).

3.2.5.1.2 Measurement of pressure ulcer depth

- One study (n=11) reported that measuring the depth at the center of the pressure ulcer with a probe had potentially poor intra-rater reliability for measurement of pressure ulcer depth (very low quality).
- One study (n=11) reported that measuring the depth at the center of the pressure ulcer with a probe had potentially poor inter-rater reliability for measurement of pressure ulcer depth (very low quality).
- One study (n=unknown, 36 pressure ulcers included) reported that measuring the depth using sterophotogrammetry and computerised image analysis had potentially very good/excellent inter-rater reliability for measurement of pressur ulcer depth (very low quality).
- One study (n=11) reported that measuring the depth using a probe assessed against a ratio between pressure ulcer volume and area had potentially poor accuracy for measurement of pressure ulcer depth (very low quality).
- One study (n= unknown, 36 pressure ulcers included) reported that measuring the depth using sterophotogrammetry had potentially very good/excellent accuracy for measurement of pressure ulcer depth (very low quality).

3.2.5.1.3 Measurement of wound surface area

- One study (n=20) reported that measuring the pressure ulcer surface area using tracing from photo, digital table and computerised planimetry may have had very good or excellent intra-rater reliability for measurement of pressure ulcer surface area (very low quality).
- One study (n=20) reported that measuring the pressure ulcer surface area using direct transparency tracing, digital tablet and computerised planimetry may have had very good or excellent intra-rater reliability for measurement of pressure ulcer surface area (very low quality).
- One study (n=4) reported that measuring the pressure ulcer surface area using slide photo digitiser and computerised planimetry may have had fair or good intra-rater reliability for measurement of pressure ulcer surface area (very low quality).
- One study (n=4) reported that measuring the pressure ulcer surface area using acetate tracing and square count may have had fair or good intra-rater reliability for measurement of pressure ulcer surface area (very low quality).
- One study (n=11) reported that measuring the pressure ulcer surface area using transparency tracing and digital planimetry potentially hadvery good or excellent intra-rater reliability for measurement of pressure ulcer surface area (very low quality).
- One study (n=26) reported that measuring the pressure ulcer surface area using photo, transparent grid and whole and partial square count potentially had very good or excellent intra-rater reliability for measurement of pressure ulcer surface area (very low quality).
- One study (n=10) reported that measuring the pressure ulcer surface area using a portable digital device consisting of 3-layer sterile tracing grid and digital pad potentially had very good/excellent intra-rater reliability for measurement of pressure ulcer surface area (very low quality).
- One study (n=4) reported that measuring the pressure ulcer surface area using slide photo digitiser and computerised planimetry potentially had poor inter-rater reliability for measurement of pressure ulcer surface area (very low quality).
- One study (n=4) reported that measuring the pressure ulcer surface area using acetate tracing and square count potentially had poor inter-rater reliability for measurement of pressure ulcer surface area (very low quality).
- One study (n=11) reported that measuring the pressure ulcer surface area using transparency tracing and digital planimetry potentially had very good or excellent inter-rater reliability for measurement of pressure ulcer surface area (very low quality).

- One study (n=26) reported that measuring the pressure ulcer surface area using photo, transparent grid and whole and partial square count potentially had very good or excellent inter-rater reliability for measurement of pressure ulcer surface area (very low quality).
- One study (n=10) reported that measuring the pressure ulcer surface area using a portable digital device consisting of 3-layer sterile tracing grid and digital pad potentially had very good/excellent inter-rater reliability for measurement of pressure ulcer surface area (very low quality).
- One study (n= unknown, 36 pressure ulcers included) reported that measuring the pressure ulcer surface area using a stereophotogrammetry and computerised image analysis potentially has very good or excellent inter-rater reliability for measurement of pressure ulcer surface area (very low quality).
- One study (n= unknown, 27 pressure ulcers included) reported that measuring the pressure ulcer surface area using a transparent grid potentially had very good or excellent inter-rater reliability for measurement of pressure ulcer surface area.
- One study (n= unknown, 373 pressure ulcers included) reported that measuring the pressure ulcer surface area using transparency tracing plus diameter product compared to reference standard potentially had unknown accuracy for measurement of pressure ulcer surface area (very low quality).
- One study (n=30) reported that measuring the pressure ulcer surface area using transparency tracing plus whole square count compared to reference standard potentially had unknown accuracy for measurement of pressure ulcer surface area (very low quality).
- One study (n=30) reported that measuring the pressure ulcer surface area using transparency tracing plus whole and partial square count compared to reference standard potentially had unknown accuracy for measurement of pressure ulcer surface area (very low quality).
- One study (n= 30) reported that measuring the pressure ulcer surface area using transparency tracing plus whole and residual square count compared to a reference standard potentially had unknown accuracy for measurement of pressure ulcer surface area (very low quality).
- One study (n=30) reported that measuring the pressure ulcer surface area using a portable digital devices (3-layer sterile tracing grid and digital pad compared to scanned photographic images and computerised planimetry (reference standard) potentially had very good or excellent accuracy for measurement of pressure ulcer surface area (very low quality).
- One study (n=20) reported that measuring the pressure ulcer surface area using tracing from photo, digital table and computerised planimetry compared to direct transparency tracing, digital table and computerised planimetry potentially had very good or excellent agreement for measurement of pressure ulcer surface area (very low quality).
- One study (n= unknown, 37 pressure ulcers included) reported that measuring the pressure ulcer surface area using slide photography, digitising tablet and computerised planimetry compared to transparency tracing and digital planimetry potentially had very good or excellent agreement for measurement of pressure ulcer surface area (very low quality).
- One study (n= unknown, 37 pressure ulcers included) reported that measuring the pressure ulcer surface area using transparency tracing and digital planimetry compared to a Kundin device and mathematical formula potentially hadvery good or excellent agreement for measurement of pressure ulcer surface area (very low quality).
- One study (n= unknown, 37 pressure ulcers included) reported that measuring the pressure ulcer surface area using tracing from slide photography, digitising tablet and computerised planimetry compared to a Kundin device and mathematical formula potentially had very good or excellent agreement for measurement of pressure ulcer surface area (very low quality).
- One study (n=20) reported that measuring the pressure ulcer surface area using elliptical area (direct diameter measurement) compared to tracing and computerised planimetry potentially had

very good or excellent agreement for measurement of pressure ulcer surface area (very low quality).

- One study (n=20) reported that measuring the pressure ulcer surface area using elliptical area (direct diameter measurement) compared to photo and computerised planimetry potentially had very good or excellent agreement for measurement of pressure ulcer surface area (very low quality).
- One study (n=20) reported that measuring the pressure ulcer surface area using elliptical area (direct diameter measurement) compared to elliptical area (diameters from tracing) and mathematical formula potentially had very good or excellent agreement for measurement of pressure ulcer surface area.
- One study (n=20) reported that measuring the pressure ulcer surface area using tracing and computerised planimetry compared to elliptical area (diameters from tracing) potentially had very good/excellent agreement for measurement of pressure ulcer surface area (very low quality).
- One study (n=20) reported that measuring the pressure ulcer surface area using elliptical area (diameters from tracing) compared to tracing and computerised planimetry potentially had very good or excellent agreement for measurement of pressure ulcer surface area (very low quality).
- One study (n=20) reported that measuring the pressure ulcer surface area using elliptical area (diameters from photos) compared to photo and computerised planimetry potentially had very good or excellent agreement for measurement of pressure ulcer surface area (very low quality).
- One study (n=11) reported that measuring the pressure ulcer volume using saline-gel injection into wound cavity and subsequent measurement of volume required to fill cavity potentially had very good or excellent intra-rater reliability of measurement of pressure ulcer volume (very low quality).
- One study (n=11) reported that measuring the pressure ulcer volume using saline-gel injection into wound cavity and subsequent measurement of volume required to fill cavity potentially had fair or good inter-rater reliability of measurement of pressure ulcer volume (very low quality).
- One study (n=5) reported that measuring the pressure ulcer volume using sterile fluid injection into wound cavity and subsequent measurement of volume required to fill cavity potentially had very good or excellent inter-rater reliability of measurement of pressure ulcer volume (very low quality).
- One study (n= unknown, 36 pressure ulcers included) reported that measuring the pressure ulcer volume using sterophotogrammetry and computerised image analysis potentially had very good or excellent inter-rater reliability of measurement of pressure ulcer volume (very low quality).
- One study (n=4) reported that measuring the pressure ulcer volume using alginate mold of wound cavity with application of water displacement (reference standard) compared to NMR spectroscopy potentially had very good or excellent accuracy of measurement of pressure ulcer volume (very low quality).
- One study (n=20) reported that measuring the pressure ulcer volume using mathematical adjustment applied to weight of alginate mold compared to spheroid volume from measuring wound dimensions potentially had very good or excellent accuracy of measurement of pressure ulcer volume (very low quality).

3.2.5.2 Economic (adults)

No relevant economic evaluations were identified.

3.2.5.3 Clinical (neonates, infants, children and young people)

No evidence was identified.

3.2.5.4 Economic (neonates, infants, children and young people)

No relevant economic evaluations were identified.

3.3 Recommendations and link to evidence

3.3.1 Adults

Recommendations	**1. Document the surface area of all pressure ulcers in adults. If possible, use a validated measurement technique (for example, transparency tracing or a photograph).** **2. Document an estimate of the depth of all pressure ulcers and the presence of undermining, but do not routinely measure the volume of a pressure ulcer.**
Relative values of different outcomes	The GDG considered reliability and accuracy to be the most critical outcomes to inform decision-making on measuring the dimensions of a pressure ulcer.. Other important outcomes included impact linked to healing/delayed healing, complications and severity. No data was identified on these outcomes.
Trade-off between clinical benefits and harms	The methods of pressure ulcer measurement that may be reliable included; measuring surface area with grid tracings from photographs combined with whole plus partial square count or a portable digital pad and sterophotogrammetry combined with computerised image analysis. There may be agreement between photographic tracing and direct transparency tracing (both combined with computerised planimetry). There were no conclusions made for diameter or depth. Evaluations of volume measurement were of poor quality and there was little data on feasibility. Most of the studies had problems in regards to methodology and/or statistical evaluation and thus it was hard to draw a conclusion on the best technique. It was agreed by the GDG that it was important to measure the surface area of a pressure ulcer, as this would allow the healthcare professional to confirm the progress of healing and reduction in the size of the pressure ulcer. It was felt that this was of particular importance to grade 3 to 4 pressure ulcers. The GDG therefore agreed that the surface area of all pressure ulcers should be measured, given that it was considered possible to obtain an accurate measurement, using straightforward and cost effective techniques (for example, transparent tracing or photographic planimetry). The GDG felt that obtaining and recording a quantitative assessment of healing and reduction in size was particularly important where care was being provided by multiple healthcare professionals, as this would allow for consistent reporting of changes in pressure ulcer size, and thus a reduction in healthcare professional subjectivity. Additionally, the GDG considered that the subsequent management approach offered may depend upon the results of surface area measurement. For example, additional management strategies may be needed for a person with a pressure ulcer that has increased in size. The group agreed that the technique chosen to measure the surface area should be carefully considered by the healthcare professional and may depend upon the site of the ulcer.

	The GDG did not consider the measurement of volume to be as relevant to the subsequent care provided and therefore, formal measurement of this was not recommended routinely. It was acknowledged that there were more difficulties in obtaining an accurate measurement of volume and the availability of equipment would mean that this would be difficult to achieve consistently across the NHS. However, the group felt that there were some circumstances in which the measurement of volume may be important (for example, where the presence of undermining is suspected) and therefore, a qualitative assessment of the volume of the wound to confirm healing and ulcer improvement may be useful to identify cases where formal measurement would be beneficial. The measurement of depth was not considered by the GDG to be helpful, given that the depth of a wound can vary considerably across a pressure ulcer and measurement of ulcer volume should be conducted in situations where this is considered necessary. The GDG did not consider there to be an advantage of a particular measurement technique, though it was acknowledged that there was some potential harms relating to the use of some methods of measurement. The group agreed that there may be infection control issues relating to the use of saline to obtain a measurement of pressure ulcer volume. The GDG also highlighted possible issues with patient tolerability in using a probe to ascertain pressure ulcer depth. Photographic techniques were considered to provide a method of measurement which did not require contact with the wound which may be more tolerable for the individual, although it was acknowledged that there were limitations to this technique as it was not possible to identify any undermining.
Economic considerations	No economic studies were identified that answered the review question. It was acknowledged that there may be economic implications of documenting the surface area of pressure ulcers, especially if photographic techniques are used. However the GDG felt that doing so was an important part of pressure ulcer management, and would lead to a more efficient allocation of resources, as the progress of a pressure ulcer could be accurately monitored, and management strategies allocated accordingly. The GDG therefore agreed that, when taking into account future savings and improvements in quality of life due to improved healing, the initial cost would be justified, provided that a straightforward technique could be used. Such documentation is considered current best practice, and as such, this recommendation is not expected to have a large impact on resource. In some studies highly specialised measurements were used. These were likely to be costly and unavailable within routine practise except within the research field and so are not recommended. Finally, the GDG did not think it would be cost-effective to routinely measure the volume of a pressure ulcer. The group agreed that this would have a larger impact on resources and would provide little benefit over a qualitative assessment undertaken at the time of surface area measurement.
Quality of evidence	Overall, the quality of the evidence was very low. Only the outcomes accuracy and reliability were reported. The GDG did not feel that the study by Buntinx used appropriate statistical analysis and therefore the results of this study should not be considered. The group also noted that it was not always appropriate to use the Pearson's

	correlation as a measure of accuracy.
Other considerations	Photographic techniques for the measurement of pressure ulcers may present data confidentiality considerations relating to the production and storage of digital images.

3.3.2 Neonates, infants, children and young people

Recommendations	**3. Document the surface area of all pressure ulcers in neonates, infants, children and young people, preferably using a validated measurement technique (for example, transparency tracing or a photograph).** **4. Document an estimate of the depth of a pressure ulcer and the presence of undermining, but do not routinely measure the volume of a pressure ulcer in neonates, infants, children and young people.**
Relative values of different outcomes	The GDG considered reliability and accuracy to be the most critical outcomes for making a decision on the most reliable and accurate tool to measure the dimension of a pressure ulcers. Other important outcomes included impact linked to healing/delayed healing, complications and severity. No data was identified on these outcomes.
Trade-off between clinical benefits and harms	The GDG used 3 statements from the Delphi consensus survey to develop the recommendations: 'Healthcare professionals should formally document the surface area of a pressure ulcer in neonates, infants, children and young people, using a validated quantitative technique such as planimetry.', 'Healthcare professionals should undertake a qualitative assessment of the depth and volume of pressure ulcers in neonates, infants, children and young people' and 'Healthcare professionals should not formally measure the depth and volume of a pressure ulcer in neonates, infants, children and young people.' The 2 former statements were agreed in Round 1 of the Delphi consensus survey and a recommendation was subsequently agreed to highlight the need to document surface area of the pressure ulcer, using validated techniques. The GDG felt that transparency tracing and photography were the methods of measuring the surface area of a pressure ulcer that were likely to be readily available to the greatest number of healthcare professionals and were not likely to be overly time consuming. The GDG emphasised the need to ensure that the results were documented so that the progress of the pressure ulcer could be easily assessed, particularly where care was being delivered by a team. The latter statement was amended and included in Round 2. The GDG discussed the statements on formal measurement and qualitative assessment of pressure ulcer depth and volume. Comments received during Round 1 suggested that there were benefits to the healthcare professional in knowing the depth and volume of a pressure ulcer. However there was disagreement as to which was the best method to do so. The GDG therefore agreed that the 2 statements would be merged into a single statement to reflect that an estimate of depth and volume was likely to be the most appropriate means of measuring a pressure ulcer. The statement 'Healthcare professionals should document an estimate of the depth and volume of a pressure ulcer in neonates, infants, children and young people.' was therefore included in Round 2, where it was agreed at the pre-defined consensus agreement level. The GDG discussed this statement and agreed that the volume of a pressure ulcer should not be routinely measured using formal methods, as the resource implications of carrying out this measurement were likely to be significant. Additionally, the GDG were not aware of any benefits to formally measure the volume of a pressure ulcer that could not be gained from an estimate. Additionally,

	the GDG noted that some methods used for measuring volume may be harmful to the person who has a pressure ulcer and can cause pain and discomfort, particularly in neonates, infants, children and young people. However, in line with the statement included in Round 2 of the survey, it was agreed that an estimate of volume may be useful information to note and that this should be documented in the notes. The GDG highlighted that it was also important to note the presence of any undermining, as this would not be information documented in formal measurement of ulcer surface area.
Economic considerations	It was acknowledged that there may be economic implications of documenting the surface area of pressure ulcers, especially if photographic techniques are used. However, the GDG felt that doing so was an important aspect of pressure ulcer management, and would lead to a more efficient allocation of resources, as the progress of a pressure ulcer could be accurately monitored, and management strategies allocated accordingly. The GDG therefore agreed that, when taking into account future savings and improvements in quality of life due to improved healing, the initial cost would be justified, provided that a straightforward technique could be used. Such documentation is considered current best practice, and as such, this recommendation is not expected to have a large impact on resource. Finally, the GDG did not think it would be cost-effective to routinely measure the volume of a pressure ulcer. The group agreed that this would have a larger impact on resources and would provide little benefit over a qualitative assessment undertaken at the time of surface area measurement.
Quality of evidence	No RCTs or cohort studies were identified for neonates, infants, children or young people. Formal consensus using a modified Delphi was therefore used to develop the recommendation. To inform the recommendation, the GDG used 3 statements which were included in Round 1 of the Delphi consensus survey and reached 75%, 71% and 16% consensus agreement. The latter statement was therefore included in Round 2 of the survey, where it reached 86% consensus agreement. Further details can be found in Appendix N.
Other considerations	The GDG noted that other validated methods of measuring pressure ulcers were available, for example, planimetry. The GDG highlighted that it was possible for an ulcer to increase in size during the course of healing.

4 Categorisation of pressure ulcers

4.1 Introduction

Several classification systems for categorising the severity of pressure ulcers have been proposed over the years. Early systems were for generally developed for research or audit purposes but present systems are now used within normal clinical practice as part of the provision of care, local and national prevention policies and clinical audit. Systems used a variety of terms to classify the pressure ulcer, most commonly 'category', 'stage' or 'grade'. Generally, the higher the grade of ulcer, the more severe it is considered. Although systems were originally developed to help healthcare professionals to identify the depth of tissue damage in each pressure ulcer but their use has allowed for healthcare professionals to communicate and plan the care of an individual.

As part of producing a consistent system, the NPUAP and EPUAP developed a common international definition and classification system for pressure ulcers (European Pressure Ulcer Advisory Panel and National Pressure Ulcer Advisory Panel. Treatment of pressure ulcers: Quick Reference Guide. Washington DC: National Pressure Ulcer Advisory Panel; 2009[132]) and this is embedded within clinical practice for by many healthcare professionals.

The GDG were therefore interested in identifying the most effective method means of categorising different types of pressure ulcers, using a variety of tools.

4.2 Review question: What is the best method of categorising different types of pressure ulcers?

For full details see review protocol in Appendix C.

4.2.1 Clinical evidence (adults)

Twenty three studies were included that met the protocol criteria for this clinical question. Nineteen studies[9,20-22,33,34,52,53,60,88,97,109,137,139,164,167,201,203 76] evaluated only 1 tool per study, but 4[78,150,163,210] evaluated 2 or more tools. The studies evaluating multiple tools provide the most valid comparison between different tools, as confounding is more likely if different tools are compared across the different contexts of different studies. However results from studies evaluating only 1 tool have also been included, as a crude comparison of different tools between studies is still possible. Twelve studies used photographs of pressure ulcers, and 11 used real participants (Table 9) for measurement of reliability and accuracy. Results for these have been presented together, but the use of photographs or real participants is clearly indicated, as this may have influenced results. These articles, and important definitions, are summarised in Table 9 to Table 13. Quality of outcomes is summarised in tables Table 22 andTable 23.

Summary of included studies

Table 9: Summary of studies included in the review

Study	Photographs (n)/patients (n)	Evaluators	Instruments	Outcomes
Pedley 2004[150]	Patients (n=30)	2 nurses from UK	EPAP and 2 digit Stirling	• Inter-rater reliability
Schoonhaven 2007[167]	Patients (n=128)	2 nurses from Holland	EPUAP	• Inter-rater reliability
Feuchtinger 2006[60]	Patients (n=90)	Clinical staff and research nurses (n unclear)	EPUAP	• Inter-rater reliability
Vanderwee 2007A[203]	Patients (n=unclear)	1870 nurses from Belgium	EPUAP	• Inter-rater reliability/accuracy
Kottner 2009[97]	Patients from care homes in Holland (n=684)	Number not stated. First evaluation by trained nurses. Second evaluation by specialist wound management nurses	EPUAP	• Inter-rater reliability
Vanderwee 2007[201]	Patients (n=225)	'Local co-ordinator' and 'team of nurses'. Number unknown	EPUAP	• Inter-rater reliability
Beeckman 2007[21]	Photographs (n=20)	1452 nurses from Belgium, Netherlands, UK, Sweden and Portugal.	EPUAP	• Accuracy
Beeckman 2008[20]	Photographs (n=20)	426 nurses from Belgium	EPUAP	• Accuracy
Beeckman 2010[22]	Photographs (n=20)	1217 Belgian, Dutch, British and Portuguese nurses	EPUAP	• Accuracy
Kelly 2011[88]	Photographs (n=3)	93 nurses in Norfolk	EPUAP	• Accuracy
Sarhan 2010[164]	Photographs (n=50)	10 nurses at a National Spinal Injury Centre.	EPUAP	• Accuracy

Study	Photographs (n)/patients (n)	Evaluators	Instruments	Outcomes
Defloor 2006[52]	Photographs (n=56)	559 nurses	EPUAP	• Sequential intra-rater reliability • Concurrent intra-rater reliability • Accuracy
Defloor and Schoonhaven 2004[53]	Photographs (n=56)	44 pressure ulcer experts from Belgium	EPUAP	• Inter-rater reliability • Accuracy
Nixon 2005A[139]	Patients (n=2646)	120: 1 lead research nurse, 410 research nurse and 109 ward nurses	Modified EPUAP scale	• Accuracy
Marrie 2003[109]	Patients with pressure ulcers (n=46)	Unclear, possibly 2.	NPUAP	• Inter-rater agreement
Buckley 2005[33]	Photographs (n=10)	33 home health nurses	NPUAP	• Accuracy
Hart 2010[76]	Photographs (n=18)	256 staff nurses and wound/skin care nurses	NPUAP	• Inter-rater reliability
Alvey 2012[9]	Photographs (n=5)	31 student and qualified nurses	NPUAP, with computerised clinical decision support	• Accuracy
Buntinx 1996[34]	Patients (n=20)	3 physicians and 3 nurses from Belgium	Shea	• Inter-rater reliability
Russell 2001[163]	Photographs (n=12)	97 nurses – 27 clinical nurse specialists, 21 pressure ulcer advisory panel members, 25 acute nurses and 24 community nurses.	Stirling EPUAP	• Accuracy • Precision
Healey 1995[78]	Photographs (n=10)	109 nurses	Stirling scale Torrance scale Surrey scale	• Inter-rater reliability • Ease of use
Nixon 1998[137]	Patients (n=unclear)	94 nurses from UK	Torrance	• Inter-rater reliability
Yarkony 1990[210]	Patients with pressure	10 registered	Yarkony-kirk	• Inter-rater 'correlation'

Study	Photographs (n)/patients (n)	Evaluators	Instruments	Outcomes
	ulcers (unclear) (n=10)	rehabilitation nurses	Shea	• Inter-rater 'agreement'

Table 10: Definitions of outcome measures used in this review

Outcome	Definition
Concurrent intra-rater reliability	Do 2 assessments performed by the same investigator during the same testing session produce the same result?
Sequential intra-rater reliability	Do 2 assessments performed by the same investigator during 2 testing sessions at different times produce the same result?
Inter-rater reliability	Do 2 or more different investigators achieve the same result?
Accuracy	The closeness of computations or estimates to the exact or true values (decided by an expert panel).

Table 11: Details of statistical measures used in this review

Heading	
Intraclass Correlation Coefficient	A measure of the inter-rater reliability for 2 or more raters. May also be used to assess test-retest reliability. Conceptualised as ratio of between-groups variance to total variance.
Kappa Coefficient	A measure of non-random agreement between observers or measurements of the same categorical variable
Spearman's Correlation Coefficient	A measure of the linear relationship between 2 categorical variables in a sample and used as an estimate of the correlation in the whole population.

Table 12: Glossary of instruments for categorising pressure ulcers

Instrument	Grading/staging details
NPUAP 1989	**Grade 1**: non-blanchable erythema of intact skin, the heralding lesion of pressure ulceration **Grade 2**: Partial thickness skin loss involving epidermis, dermis or both. The ulcer is superficial and presents clinically as an abrasion, blister or shallow crater **Grade 3**: Full thickness skin loss involving damage or necrosis to subcutaneous tissue that may extend down to, but not through, underlying fascia. The ulcer presents clinically as a deep crater, with or without undermining of adjacent tissue **Grade 4**: Full-thickness skin loss with extensive destruction, tissue necrosis, or damage to muscle bone or supporting structures (for example, joint capsule).
EPUAP 1989	**Grade 1**: non-blanchable erythema of intact skin. Discolouration of the skin, warmth, oedema, induration or hardness may also be used as indicators, particularly in individuals with darker skin. **Grade2**: Partial thickness skin loss involving epidermis, dermis or both. The ulcer is superficial and presents clinically as an abrasion or blister **Grade 3:** Full thickness skin loss involving damage to or necrosis of subcutaneous tissue that may extend down to, but not through, underlying fascia. **Grade 4**: Extensive destruction, tissue necrosis, or damage to muscle, bone or supporting structures with or without full thickness skin loss
NPUAP/EPUAP 2009 [European Pressure Ulcer Advisory Panel and National Pressure Ulcer Advisory Panel. Treatment of pressure ulcers: Quick Reference Guide. Washington DC: National Pressure Ulcer Advisory Panel; 2009]	**Category/Stage 1: Non-blanchable redness of intact skin** Intact skin with non-blanchable erythema of a localized area usually over a bony prominence. Discoloration 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 as compared to adjacent tissue. Category/Stage I may be difficult to detect in individuals with dark skin tones. May indicate "at risk" persons. **Category/Stage 2: 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 3: 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

Instrument	Grading/staging details
	directly palpable. **Category/Stage 4: 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 tunneling. ***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 (for example, fascia, tendon or joint capsule) making osteomyelitis or osteitis likely to occur. Exposed bone/muscle is visible or directly palpable.
Torrance [Healey F. The reliability and utility of pressure sore grading scales. Journal of Tissue Viability. 1995; 5: 111-114]	1. Blanching hyperaemia 2. Non blanching hyperaemia 3. Ulceration progresses through the dermis only 4. Lesion extends into the subcutaneous fat 5. Infective necrosis penetrates the deep fascia
Stirling [Healey F. The reliability and utility of pressure sore grading scales. Journal of Tissue Viability. 1995; 5: 111-114]	0. Normal appearance, intact skin 0.1 Healed with scarring 0.2 Tissue damage but not assessed as a pressure sore 1.1 Non blanchable erythema with increased localised heat 1.2 Blue/purple/black discolouration 2.1 blister 2.2 Abrasion 2.3 shallow ulcer without undermining of adjacent tissue 2.4 Any of these with blue/purple/black discolouration or induration 3.1 Crater, without undermining of adjacent tissue 3.2 Crater, with undermining of adjacent tissue 3.3 Sinus, the full extent of which is uncertain 3.4 Full thickness skin loss, but wound bed is covered with necrotic tissue which masks the true extent of tissue damage 4.1 Visible exposure of bone, tendon or capsule 4.2 Sinus assessed as extending to bone, tendon or capsule
Yakony-Kirk [Yarkony GM et al. Classification of pressure ulcers. Arch Dermatol 1990	1. Red area. Present longer than 30 minutes, but less than 24 hours OR present longer than 24 hours 2. Epidermis and/or dermis ulcerated with no subcutaneous fat observed

Instrument	Grading/staging details
126; 1218-1219]	3. Subcutaneous fat observed, no muscle observed 4. Muscle/fascia observed, but no bone observed 5. Bone observed, but no involvement of joint space 6. Involvement of joint space
Shea [Shea JD. Pressure sores: classification and management. Clin Orthop. Relat. Res. 1975; 112: 89-100]	1. Limited to epidermis, exposing dermis 2. Full thickness of dermis to junction of subcutaneous fat 3. Fat obliterated, limited by deep fascia undermining of skin 4. Bone at the base of ulceration 5. Closed large cavity through a small sinus

Table 13: Categorisation of values into levels of acceptability

Agreement (reliability and accuracy)	Excellent	Good	Fair	Poor
Intra class coefficient (ICC)[a]	0.75+	0.60 to 0.74	0.40 to 0.59	<0.40
Kappa coefficient[b]	0.75+	0.60 to 0.74	0.40 to 0.59	<0.40

(a) Fleiss, J. L. (1981) Statistical methods for rates and proportions. 2nd ed. (New York: John Wiley) pp. 38–46

(b) Orwin RG. Evaluating coding decisions. In: Cooper H, Hedges LV (editors). The Handbook of Research Synthesis. New York (NY): Russell Sage Foundation, 1994.

4.2.2 Clinical evidence for studies assessing more than 1 tool

Quality of evidence was generally considered low quality, but where high quality evidence was identified it has been highlighted in the following summary.

Yarkony [210] showed the Yarkony-Kirk scale had superior inter-rater reliability to the Shea scale[173] within the samples studied. However, the lack of variance data made it impossible to make inferences to the population (Table 14).

Healey [78] showed that the Torrance scale[194] had better inter-rater reliability than the 2 digit Stirling scale in the studied sample, but population inferences were again not possible. Importantly, both tools' kappa readings were classified as 'poor' (Table 15). The Stirling also appeared to be more difficult to use.

In a study with high quality outcomes, Russell and Reynolds [163] compared the EPUAP with 2 digit Stirling, using continuous measures for 'accuracy' and 'precision' (Table 16). The former was the absolute mean of all positive and negative deviations from the gold standard, whilst the latter was the absolute mean of all absolute departures from the gold standard. The 2 digit Stirling tool was significantly better for both outcomes (accuracy mean difference: 0.1 better for Stirling (95% CIs 0.04 to 0.17); precision mean difference: 0.13 better for Stirling (95% CIs: 0.09 to 0.17); see forest plots in Appendix I).

In another study with high quality outcomes, Pedley [150] also compared the EPUAP with 2 digit Stirling, in terms of inter-rater reliability (Table 19). Although the EUAP had greater reliability in terms of the sample values, with Stirling classified as 'fair' and EPUAP as ' poor', population inferences were not possible due to the lack of variance data.

Overall, despite the fact that most evidence only existed as point estimates, the Yarkony-Kirk scale seemed superior to the Shea scale. The Torrance appeared superior to Stirling, whilst the Stirling scale appeared superior to the EPUAP. Note that because of different populations in different studies, it is not possible to use indirect treatment comparisons to conclude that the Torrance scale was also superior to the EPUAP.

4.2.2.1 Evidence summaries

Table 14: Yarkony-kirk versus Shea

Study	Statistical measure	Yarkony-kirk	Shea	n	Comments	Quality
Inter-rater reliability						
Yarkony et al. 1990[210]	% agreement of staging. This represented the number of pairwise assessments that agreed on staging level.	85%	68%	Unclear. 10 registered rehabilitation nurses staging 72 pressure ulcers on unknown number of participants. Only 2 pair of raters assessed each pressure ulcer but unclear how the pairs were allocated.	**PATIENT STUDY** Standard correlation methods unsuitable for assessing reliability, as possible for measures to be perfectly correlated but not agree. Unclear how the 10 nurses made up the testing pairs. Potential for bias as 1 testing technique may have had pairs who were randomly similar and the other tool may have had pairs who were not. Only by ensuring the same pairs were used across tools can we have a useful comparison. Nurses trained and experienced with Shea, but not Yarkony.	Low

Table 15: Torrance versus 2 digit Stirling

Study	Statistical measure	Torrance	2 digit Stirling	n	Comments	Quality
Inter-rater reliability						
Healey 1995[78]	Cohen's kappa for inter-rater reliability	0.29	0.15	37 nurses graded 10* photos using Torrance; Another independent sample of 37 nurses graded the same 10* photos using 2 digit Stirling. Agreement across all raters per picture calculated for each scale, and then overall value for all photos derived for each	**PHOTOGRAPHIC STUDY** Unclear how groups were allocated, so possibility of bias – for example, through 1 group of raters being more homogenous than the other.	Low

Study	Statistical measure	Torrance	2 digit Stirling	n	Comments	Quality
				scale. *due to technical error some raters only graded 6 photos		
Ease of use						
Healey 1995[78]	Descriptive	16% found it easy to use, 35% found it difficult to use	11% found it easy to use, 57% found it difficult to use	As above	As above	NA

Table 16: EPUAP versus Stirling

Study	Statistical measure	EPUAP	Stirling	n	Comments	Quality
Accuracy (lower value indicates better accuracy)						
Russell 2001[163]	Absolute mean of all interval positive and negative differences from gold standard (decided by expert consensus)	Absolute Mean(sd) [n] 0.15(0.21)[86]	Absolute Mean(sd) [n] 0.045[a](0.21)[85]	97 nurses graded 12 photos using both scaling systems.	**PHOTOGRAPHIC STUDY** Assuming an interval scale for such an ordinal measure may be invalid. Wide range of expertise, including 27 clinical nurse specialists, 21 pressure ulcer advisory panel members, 25 acute nurses and 24 community nurses.	High
Precision (lower value indicates better precision)						
Russell 2001[163]	Mean of all interval absolute differences from gold standard (that is all taken as positive) (decided by expert consensus)	Mean(sd) [n] 0.49(0.15)[86]	Mean(sd) [n] 0.36(0.15)[85]	As above	As above	High

Study	Statistical measure	EPUAP	Stirling	n	Comments	Quality
Inter-rater reliability (higher better)						
Pedley 2004[150]	Cohen's kappa for inter-rater reliability	0.308	0.475	2 nurses evaluated 35 PUs in 30 people.	**PATIENT STUDY** Both nurses familiar with both testing scales. Low number of included nurses means we cannot be certain these results are representative of all nurses.	High

(a) The reported figure in the paper was -0.045. However, to calculate the mean difference this value was converted to an absolute value. Although it was important to include positive and negative values to derive this accuracy value, which allows for cancellation of positive and negative differences from the gold standard provided there is no systematic bias to negative or positive, the sign of the final mean was not important (and indeed would be misleading as we are simply interested in the absolute discrepancy from zero - just as an archer would be interested in a 1cm distance from the bullseye, not whether it was 1cm north or 1cm south).

4.2.2.2 Clinical evidence for studies assessing 1 tool

4.2.2.2.1 NPUAP

Two studies with low quality outcomes evaluated the inter-rater reliability of the NPUAP(1989) scale, with Marrie[109] demonstrating excellent reliability and Hart[76] showing fair reliability (Table 17).

In terms of accuracy, Buckley [33] showed a moderate agreement of 67.8% for home health nurses compared to a gold standard (Table 17), using a high quality methodology.

4.2.2.2.2 EPUAP

The EPUAP(1989) has been extensively studied (Table 18). Defloor[52] showed 'poor' concurrent and 'fair' sequential intra-rater reliability, but inter-rater reliability appears to be in the 'excellent' category [53,60,167,201,203]. However all these reliability studies were of low quality.

Accuracy appears to range from 'poor' in terms of kappa values[20,21] to very high agreement percentages in other studies[53]. It is difficult to account for these accuracy differences in terms of the characteristics of the assessors, or the use of photographs or patients, but the higher quality of methodology in the 2 former studies compared to the latter suggests this may be an important factor explaining the varying results.

4.2.2.2.3 EPUAP/NPUAP (2009)

The EPUAP/NPUAP (2009) scale has shown good inter-rater reliability in terms of very high % agreement in a low quality study[97] (Table 19).

However its accuracy appears 'moderate' [88] in terms of kappa, and % agreement figures appear modest[9,164]. Of these accuracy studies, only Sarhan [164] was high quality.

4.2.2.2.4 Torrance

A low quality study showed the Torrance scale has good inter-rater reliability in terms of % agreement [137] (Table 20).

4.2.2.2.5 Shea

A study with high quality methodology [34] showed the Shea scale appears to have only 'fair' inter-rater reliability in terms of kappa (Table 21).

4.2.2.3 Summary

In conclusion, inter-rater reliability appears good throughout the various tools that have been studied singly, with perhaps the EPUAP having the most favourable results. Overall, accuracy appears less impressive, and this is uniform across tools.

4.2.2.4 Evidence summaries

Table 17: NPUAP 1989

Study	Statistical measure	NPUAP 1989	n	Comments	Quality (see tables 15 and 16).
Inter-rater reliability					
Marrie 2003[109]	ICC	0.91 (no variance measure supplied)	Unclear but probably 2 assessors each graded ulcers in 46 participants.	**PATIENT STUDY** Poor description of assessors.	Low
Inter-rater reliability					
Hart 2006[76]	Kappa	0.56 (sd: 0.17)	256 staff nurses and wound/skin care nurses looked at 18 photographs of pressure ulcers and assigned a stage of pressure ulcer to them.	**PHOTOGRAPHIC STUDY** Highly trained raters, so may lack external validity. Provided photos with and without an accompanying verbal description, but only results pertaining to no verbal description given here. WOC certification was a factor improving inter-rater reliability: kappa was 0.66(SE 0.04) for certified versus 0.54 (SE 0.03) for non-certified nurses.	Low
Accuracy					
Buckley 2005[33]	% accuracy (percentage of raters agreeing with gold standard	Mean across all 5 pressure ulcer photos: 67.8% Photo 1 of stage IV: 39%	33 home health nurses looked at the 5 pressure ulcer photos. They then assigned a stage of pressure ulcer to them.	**PHOTOGRAPHIC STUDY** During viewing nurses were given a brief case history, read aloud. This	High

Study	Statistical measure	NPUAP 1989	n	Comments	Quality (see tables 15 and 16).
	for each photo. Gold standard decided by expert consensus)	Photo 2 if stage IV: 100% Photo of stage II: 82% Photo of PU covered with necrotic tissue: 82% Photo of PU covered with eschar: 88%		may have enhanced accuracy and thus reduced external validity.	

Table 18: EPUAP 1989

Study	Statistical measure	EPUAP 1989	n	Comments	Quality
Concurrent intra-rater reliability					
Defloor 2006[52]	Kappa	0.38 (95% CIs: 0.26-0.50)	473 nurses looked at 65 photos of pressure ulcers in 1 sitting and assigned a stage of pressure ulcer to them. There were 9 pairs of identical photos within the pack of 65, and it was on the agreement of the stage of pressure ulcer across these 9 pairs during the same session from which the concurrent intra-rater reliability measure was derived.	**PHOTOGRAPHIC STUDY** The 473 nurses were participating in a wound care conference, reducing external validity.	Low
Sequential intra-rater reliability					
Defloor 2006[52]	Kappa	0.52 (95% CIs: 0.50-0.55)	86 different nurses looked at 56 photos (no duplicates) twice with an interval of 1 month and assigned a stage of pressure ulcer to them. Agreement of the stage of	**PHOTOGRAPHIC STUDY** Expertise of these 86 nurses not clearly described.	Low

Study	Statistical measure	EPUAP 1989	n	Comments	Quality
			pressure ulcer across all 56 photos across both sessions yielded the sequential intra-rater reliability measure.		
Inter-rater reliability					
Schoonhaven 2007[167]	Kappa for inter-rater reliability	0.96	2 nurses looked at 128 people and assigned a stage of pressure ulcer to them.	**PATIENT STUDY** These were expert assessors and so results may lack external validity. Very poorly reported.	Low
Inter-rater reliability					
Vanderwee 2007[201]	Spearman's rho	0.96 ($p<0.001$)	Unknown number of nurses and 'local co-ordinator' evaluated 225 people.	**PATIENT STUDY** Poor reporting of evaluators. Inappropriate measure of reliability.	Low
Inter-rater reliability					
Vanderwee 2007A[203]	Kappa for inter-rater reliability	Researcher against nursing staff: 0.88 (95% CIs: 0.85-0.91) Study nurse against nursing staff: 0.89 (95% CIs: 0.87-0.92)	1868 nursing staff, 1 researcher and 1 study nurse assessed unknown number of people.	**PATIENT STUDY** The reliability was not between the different nurses but instead between each nurse and the researcher and/or study nurse. Hence this may be more of an accuracy than reliability study.	Low
Inter-rater reliability					
Defloor and Schoonhoven 2004	Linear weighted kappa	Inter-rater reliability linear weighted kappa between all 44	44 nursing staff looked at 56 photos and assigned a stage of	**PHOTOGRAPHIC STUDY**	Low

Study	Statistical measure	EPUAP 1989	n	Comments	Quality
		experts (excluding grading of incontinence lesions): 0.78-0.79 (researchers 0.79, staff nurses 0.78, pressure ulcer nurses 0.79)	pressure ulcer to them.	Raters described as 'experts' which may reduce external validity.	
Inter-rater reliability					
Feuchtinger 2006[60]	% agreement	Overall agreement between raters: 97.7% (767/990)	Unknown number of clinical staff and research nurses carried out 90 pairwise assessments in 90 people (with multiple pressure ulcer sites).	**PATIENT STUDY** Very unclear reporting of assessors.	Low
Accuracy					
Defloor 2006[202]	Kappa. Compared to gold standard derived from expert consensus.	0.50 (95% CIs: 0.49-0.52)	473 nurses looked at 56 photographs and assigned a stage of pressure ulcer to them and the agreement with the gold standard was evaluated.	**PHOTOGRAPHIC STUDY** The 473 nurses were participating in a wound care conference, reducing external validity. Accuracy also measured in the same way with the other cohort of 86 nurses, but results very similar so not reported.	High
Accuracy					
Nixon 2005[139]	% agreement on pressure ulcer	Overall: 78.8% (1888/2396 stagings agreed with gold standard)	Number of people not reported. Six research nurses	**PATIENT STUDY**	High

Study	Statistical measure	EPUAP 1989	n	Comments	Quality
	gradings done by 109 nurses against a gold standard (6 research nurses).	Break down of different sites: Sacrum: 76% Left buttock: 75% Right buttock: 75% Right hip: 94% Left hip: 95% Left heel: 69% Right heel: 71%	each undertook simultaneous (but independent) staging measurements with the same 109 nurses on different patients (looking at up to 4 pressure ulcer sites on each individual).	This was designated an inter-rater reliability analysis by the study authors, but because the 109 nurses are being compared to the 6 research nurses, who, in a previous analysis had excellent agreement (105/107 grade agreed) this analysis has been designated an accuracy analysis in this review.	
Accuracy					
Beeckman 2007[21]	Kappa. Compared to gold standard derived from expert consensus (12 trustees from the EPUAP).	Median (IQR) kappa: 0.29 (0.14-0.47).	1452 nurses looked at 20 photographs and assigned a stage of pressure ulcer to them. These were compared to gold standard stagings.	**PHOTOGRAPHIC STUDY** Accuracy increased by expertise: Chi square 36.2 ($p<0.001$) Best for 'expert', [kappa 0.47(0.32-0.56)] lowest for 'limited' [kappa 0.25 (0.089-0.38)].	High
Accuracy					
Beeckman 2008[20]	Kappa. Compared to gold standard derived from expert consensus (12 trustees from	Overall median (IQR) kappa: 0.24	426 nurses looked at 20 photographs and assigned a stage of pressure ulcer to them. These were compared to gold standard stagings.	**PHOTOGRAPHIC STUDY** Analysis included ulcers that were not PUs. Not possible to extricate	High

Study	Statistical measure	EPUAP 1989	n	Comments	Quality
	the PUCLAS workgroup).		Specific grade % agreement Normal skin: 92.9% Blanchable erythema: 68.7% Grade 1: 38.2% Grade 2: 29.1% Grade 3: 24.6% Grade4: 47.9%	them from overall result, but individual pressure ulcer accuracy ratings given. No clear effect for accuracy to depend on qualification: student nurses had kappa of 0.19-0.23* compared to 0.25-0.30* for qualified nurses. *2 values given as these were baseline values in an RCT (post-intervention results not relevant and so not reported).	
Accuracy					
Beeckman 2010[22]	% agreement. Compared to gold standard derived from expert consensus (12 trustees from the EPUAP).	50.0% (8266/16520 stagings accurate).	1217 nurses looked at 20 photographs and assigned a stage of pressure ulcer to them, which were compared to gold standard stagings.	**PHOTOGRAPHIC STUDY** Article results included non-pressure ulcers. Results on left are those with these non-pressure ulcer data removed by systematic reviewer. Some nurse attending a wound care conference so this may have reduced external validity.	High

Study	Statistical measure	EPUAP 1989	n	Comments	Quality
Accuracy					
Defloor and Schoonhoven 2004[53]	% agreement with gold standard provided by 9 EPUAP trustees	Accuracy for: normal skin 99.4% blanchable erythema 95.3% non-blanchable erythema 96.1% blister 86.8% superficial pressure ulcers 94.5% deep pressure ulcers 95.2% Overall: 94.55%	44 pressure ulcer 'experts' looked at 56 photographs and assigned a stage of pressure ulcer to them, which were compared to gold standard stagings.	**PHOTOGRAPHIC STUDY** Raters described as 'experts' which may reduce external validity.	Low

Table 19: EPUAP/NPUAP 2009

Study	Statistical measure	EPUAP/ NPUAP 2009	n	Comments	Quality
Accuracy					
Alvey 2012[9]	% agreement with gold standard (WOC nurse)	Overall: 64.2% (79/123) Suspected deep tissue injury: 80% (24/30) StageI: 74% (23/32) Stage III: 65% (20/31) Unstageable: 39% (12/31)	31 student and qualified nurses looked at 5 photographs and assigned a stage of pressure ulcer to them (but the stage II photograph assessments had to be excluded from analysis due to computer error).	**PHOTOGRAPHIC STUDY** The tool included computerised clinical decision support, involving drop down menus to facilitate accurate staging. Hence this may have influenced accuracy.	High
Accuracy					
Kelly and Isted 2011[88]	Kappa and % agreement compared to an	Overall: 56% (156/279) [Kappa: 0.48] Stage I: 86% Stage II: 56%	93 nurses looked at 3 photographs and assigned a stage of pressure ulcer to them.	**PHOTOGRAPHIC STUDY** Gold standard unspecified. No effect of	Low

Study	Statistical measure	EPUAP/ NPUAP 2009	n	Comments	Quality
	unspecified gold standard.	StageIII: 43% Stage IV: 89% Unstageable: 6%		seniority on accuracy: band 2-4 nurses had overall accuracy of 57% and band 5-7 nurses had overall accuracy of 55%. Chi square with Yates' correction showed no significant difference.	
Accuracy					
Sarhan 2010[164]	% agreement compared to gold standard, which was the result recorded in patient notes based on a face to face examination by a trained nursing staff member.	Overall: 85% Sacrum stage 4: 102/150 [68%] Ischium stage 3: 77/80 [96%] Foot stage 1: 20/20 [100%] Foot stage 2: 20/20 [100%] Ankle stage 1: 20/20 [100%] Ankle stage 2: 20/20 [100%] Trochanter stage 3: 35/40 [88%] Trochanter stage 4: 20/30 [67%] Hip stage 3: 34/40 [85%] Hip stage 4: 23/30 [77%] Knee stage 3: 8/10 [80%] Knee stage 4: 15/20 [75%] Back stage 1: 10/10 [100%] Back stage 2: 10/10 [100%]	10 nurses looked at 50 images of pressure ulcers and assigned a stage of pressure ulcer to them from 50 people with spinal cord injury.	**PHOTOGRAPHIC STUDY** The gold standard is suspect, as the expertise of the nurse carrying out the face to face examination was unclear. Thus this may not be a true accuracy study. If it is not a true accuracy study, it has little relevance to this review, as in this context these results only demonstrate that photographic diagnosis is a reasonable proxy for face to face diagnosis.	Low
Inter-rater reliability					
Kottner 2009[97]	%Inter-rater agreement (P_0)	2007: P_0=338/352 = 0.96 (trained nurses) 2008: P_0=318/332 = 0.96 (wound management nurses)	Unknown number of trained nurses and wound management nurses assessed 12792 participants from care	**PATIENT STUDY** Two analyses done over 2 successive years for different rater groups –	Low

Study	Statistical measure	EPUAP/ NPUAP 2009	n	Comments	Quality
			homes. Each person was assessed just once by any single pair of assessors, with a 1-3 day interval.	hence the 2 separate results for different years. The article appeared to report the results wrongly, stating that the P_0 results on left (0.96 for both years) were for the assessment of pressure ulcer / no pressure ulcer rather than of the 5 different stagings. However the tabular data in article strongly suggested that the results are for the reliability across all 5 different stagings.	

Table 20: Torrance (1983)

Study	Statistical measure	Torrance (1983)	n	Comments	Quality
Inter-rater reliability					
Nixon 1998[137]	% agreement	Pre-study: 97.8 (649/664) During study: 91.5 (779/851)	Pre-study: 94 nurses. 133 paired assessments were done on people, generating 664 paired assessments of skin sites. During-study: 171 co-assessments undertaken in recovery area and ward, generating 851 site assessments.	**PATIENT STUDY** Two reliability studies done (pre- and during-study). Unclear why this was so. Poorly reported methodology. Expertise of nurses unknown.	Low

Table 21: Shea

Study	Statistical measure	Shea	n	Comments	Quality
Inter-rater reliability					
Buntinx 1996[34]	Group kappa	0.42(95% CIs: 10-74)	3 physicians and 3 nurses performed 126 assessments on unknown number of people.	**PATIENT STUDY** Expertise of nurses unknown.	High

Table 22: Quality of reliability studies.(tThis was modified from QUADAS).

Study	Are the patients representative?	Selection criteria clear?	Assessors representative?	Assessor selection criteria clear?	Time period between measurements short enough?	Did all receive scheduled repetitions of measurements?	Description of execution of measurements adequate for replication?	Description of sequence of repeated measurements adequate?	Inter-rater reliability: was measurement performed without knowledge of other rater's values?	Was order of measurements random?	Were withdrawals explained?	Overall Quality [a]
Kottner 2009[97]	Yes	Yes, random	Unclear	No	No (1-3 days)	No	No	Yes	Yes	Unclear	No	Low
Yarkony 1990[210]	Unclear	No	Unclear	No	Yes	Yes	No	No	Yes	Unclear	NA	Low
Healey 1995[78]	NA - photos	NA - photos	Unclear	Yes	NA	Yes	Yes	Yes	Yes	Unclear	NA	Low
Marrie 2003[109]	Yes	No	Unclear	No	Unclear	Yes	Yes	Yes	Unclear	Unclear	NA	Low
Defloor 2006[52]	NA - photos	NA - photos	No	Yes	NA	Yes	Yes	Yes	NA (intra-rater)	Yes	NA	Low
Hart 2006[76]	NA - photos	NA - photos	No	Yes	NA	Yes	Yes	Yes	Yes	NA	Yes	Low
Vanderwee 2007[201]	Yes	Yes	Unclear	No	Unclear	Yes	No	No	Yes	Unclear	NA	Low
Vanderwee 2007A[203]	Unclear	Yes, random	No	No	Unclear	Yes	Yes	Yes	Yes	Unclear	NA	Low
Nixon 1998[137]	Unclear	No	Unclear	No	Unclear	Yes	Yes	Yes	Unclear	Unclear	NA	Low
Schoonhaven 2007[167]	Yes	No	No	Yes	Unclear	Yes	No	No	Unclear	Unclear	NA	Low
Buntinx 1996[34]	Yes	Yes, convenience	Unclear	Yes	Unclear	Yes	Yes	Yes	Yes	Unclear	NA	High
Pedley 2004[150]	Yes	Yes, convenience	No	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	NA	High
Defloor	NA -	NA	No	No	NA	Yes	Yes	Yes	Unclear	NA	NA	Low

Study	Are the patients representative?	Selection criteria clear?	Assessors representative?	Assessor selection criteria clear?	Time period between measurements short enough?	Did all receive scheduled repetitions of measurements?	Description of execution of measurements adequate for replication?	Description of sequence of repeated measurements adequate?	Inter-rater reliability: was measurement performed without knowledge of other rater's values?	Was order of measurements random?	Were withdrawals explained?	Overall Quality [a]
and Schoonhoven 2004[53]	photos											
Feuchtinger 2006[60]	Yes	No	Unclear	No	Unclear	Yes	No	No	Unclear	Unclear	Na	Low

*(a) *For most categories, ' yes' responses gained 1 point, but triple weighting was given to 'Inter-rater reliability: was measurement performed without knowledge of other rater's values?', and double weighting to each of 'Are the patients representative?' and 'Time period between measurements short enough?'. For photographic studies, NA was taken as a yes for 'Time period between measurements short enough?'. This was because the use of photographs would avoid any bias from long intervals between ratings. The total score was therefore out of 15. Scores of 10/15 and above were categorised as high quality and scores of 9 and below were categorised as low quality. The weightings are based on an estimate of the relative importance of the quality criteria, and the scores are designed to be roughly in line with the threshold for 'high quality' used by some researchers for the full QUADAS assessment.*

NA=not applicable

Table 23: Quality of accuracy studies. This was modified from QUADAS.

Study	Are the patients representative?	Selection criteria clear?	Assessors representative?	Assessor selection criteria clear?	If a reference standard is employed, is it likely to generate a valid measurement?	Time period between measurements short enough?	If a reference standard is employed, did the whole sample or a random selection of the sample receive verification using the reference standard?	If a reference standard is employed, did patients receive the same reference standard regardless of the index measurement result?	If a referenced standard is used, was this independent of the index measurement?	Description of execution of measurements adequate for replication?	Results for each measurement method interpreted without knowledge of the results of the other methods used?	Was order of measurements random?	Were withdrawals explained?	Overall grading[a]
Alvey 2012[9]	NA - photos	NA - photos	Unclear	Yes	Yes	NA	Whole	Yes	Yes	Yes	Yes	NA	NA	High
Nixon 2005A[139]	Yes	Yes	Yes	Yes	Yes	Yes	Whole	Yes	Yes	Yes	Unclear	NA	NA	High
Sarhan 2010[164]	NA - photos	NA - photos	Unclear	No	No	NA	Whole	Yes	Yes	Yes	Yes	NA	NA	Low
Russell 2001[163]	NA - photos	NA - photos	Yes	Yes	Yes	NA	Whole	Yes	Yes	Yes	Yes	NA	NA	High
Defloor 2006[52]	NA - photos	NA - photos	No	Yes	Yes	NA	Whole	Yes	Yes	Yes	Yes	Yes	NA	High
Beeckman 2010[22]	NA - photos	NA - photos	Yes	Yes, convenience	Yes	NA	Whole	Yes	Yes	Yes	Yes	NA	NA	High
Buckley 2005[33]	NA - photos	NA - photos	Yes	Yes, convenience	Yes	NA	Whole	Yes	Yes	Yes	Yes	NA	NA	High
Kelly 2011[88]	NA - photo	NA - photo	Yes	Yes, random	Unclear	NA	Whole	Yes	Yes	Yes	Yes	NA	NA	Low

Study	Are the patients representative?	Selection criteria clear?	Assessors representative?	Assessor selection criteria clear?	If a reference standard is employed, is it likely to generate a valid measurement?	Time period between measurements short enough?	If a reference standard is employed, did the whole sample or a random selection of the sample receive verification using the reference standard?	If a reference standard is employed, did patients receive the same reference standard regardless of the index measurement result?	If a referenced standard is used, was this independent of the index measurement?	Description of execution of measurements adequate for replication?	Results for each measurement method interpreted without knowledge of the results of the other methods used?	Was order of measurements random?	Were withdrawals explained?	Overall grading[a]
	s	s												
Beeckman 2007[21]	NA - photos	NA - photos	Yes	Yes, convenience	Yes	NA	Whole	Yes	Yes	Yes	Yes	NA	NA	High
Beeckman 2008[20]	NA - photos	NA - photos	Yes	Yes, convenience	Yes	NA	Whole	Yes	Yes	Yes	Yes	NA	NA	High
Vanderwee 2007A[203]	Unclear	Yes, random	Unclear	No	Unclear	Unclear	Whole	Yes	Yes	Yes	Yes	NA	NA	Low
Defloor and Schoonhoven 2004[53]	NA - photos	NA - photos	No	No	Yes	NA	Whole	Yes	Yes	Yes	Yes	NA	NA	Low

(a) **For most categories, ' yes' responses gained 1 point, but triple weighting was given to 'If a reference standard is employed, is it likely to generate a valid measurement?', and double weighting to each of 'Are the patients representative?' and 'Time period short enough between measurements short enough?'. For photographic studies, NA was taken as a yes for 'Time period short enough between measurements short enough?'. This was because the use of photographs would avoid any bias from long intervals between ratings. The total score was therefore out of 17. Scores of 11/17and above were categorised as high quality and scores of 10 and below were categorised as low quality. The weightings are based on an estimate of the relative importance of the quality criteria, and the scores are designed to be roughly in line with the threshold for 'high quality' (10/15) used by some researchers for the full QUADAS assessment.*

NA=not applicable

4.2.3 Economic evidence (adults)

Published literature

No relevant economic evaluations comparing ulcer measurement techniques were identified.

4.2.4 Clinical evidence (neonates, infants, children and young people)

No RCTs or cohort studies were identified. Recommendations were developed using a modified Delphi consensus technique. Further details can be found in Appendix N.

4.2.5 Economic (neonants, infants, children and young people)

No economic evidence was identified.

4.2.6 Evidence statements

4.2.6.1 Clinical (adults)

4.2.6.1.1 Accuracy

- Predominantly high quality evidence from 12 studies suggested that the accuracy of pressure ulcer categorisation was adequate in the EPUAP, NPUAP and Stirling categorisation tools. Of the 3 tools studied, EPUAP had the greatest weight of high quality evidence supporting its accuracy.

4.2.6.1.2 Intra-rater reliability

- Low quality evidence from 1 study suggested that intra-rater reliability of pressure ulcer categorisation was adequate in the EPUAP.

4.2.6.1.3 Inter-rater reliability

- Predominantly low quality evidence from 14 studies suggested that inter-rater reliability of pressure ulcer categorisation was adequate in the Yarkony-kirk, Stirling, EPUAP, NPUAP, Torrance and Shea categorisation tools. Of the 6 tools studied, EPUAP had the greatest weight of evidence supporting its inter-rater reliability.

4.2.6.2 Clinical (neonates, infants, children and young people)

- No evidence was identified.

4.2.6.3 Economic (neonates, infants, children and young people)

- No relevant economic evaluations were identified.

4.3 Recommendations and link to evidence

4.3.1 Adults

Recommendations	5. Categorise each pressure ulcer in adults using a validated classification tool (such as the International NPUAP-EPUAP (2009) Pressure Ulcer Classification System). Use this to guide ongoing preventative strategies and management. Repeat and document each time the ulcer is assessed.
Relative values of different outcomes	Accuracy of categorisation tools was regarded as a critical outcome, as it is vital if it is to be used to inform treatment as inaccurate categorisation might lead to inappropriate treatments being used. Accuracy was identified as more important than reliability, as an accurate measurement will be reliable, but it is possible to be reliable but not accurate. Therefore high accuracy encapsulates both accuracy and reliability, but high reliability can exist alongside poor accuracy. However, reliability was still regarded as important, as it is useful for allowing the comparison of pressure ulcer measurement across time. Such charting of progress is essential for making decisions on continuing, adapting or changing treatments. High intra-rater reliability is important for meaningful comparisons between categorisations made by 1 assessor on the same patient across time. High inter-rater reliability is important when comparing measurements undertaken by different assessors on the same patient over time. Ease of use of the tools was also regarded as an important outcome, as this minimises patient and assessor time.
Trade-off between clinical benefits and harms	The GDG did not consider there would be any direct harms from the use of the reviewed tools.Inaccurate or unreliable tools could be regarded as an indirect source of potential harm for the individual with the pressure ulcer. Conversely, clinical benefits are likely to arise from accurate and reliable tools, as this will lead to optimal treatment decisions and affective charting of progress. Hence a discussion of the trade-off between benefits and harms may, in this context, be conducted by discussing the relative reliability and accuracy of the different tools. Accuracy was measured only in the European Pressure Ulcer Advisory Panel (EPUAP), Stirling and National Pressure Ulcer Advisory Panel (NPUAP) categorisation tools. The EPUAP tool appeared to have superior accuracy to the NPUAP categorisation tool. In the only study investigating the accuracy of the NPUAP categorisation tool, agreement was 67.8%, while the 3 EPUAP accuracy studies that used percentage agreement as a measure showed values of 78.8%, 50% and 94.5%. The Stirling and EPUAP tools were measured together in 1 study, with Stirling having superior accuracy. However the parametric analysis measures used were inappropriate and so the validity of these results is unclear. Overall, of the 3 tools, the EPUAP tool had the most evidence suggesting adequate accuracy, thus this may be the tool conferring the most clinical benefits from high accuracy. None of the tools stood out as likely to confer any significant harm upon people as a result of poor accuracy. Intra-rater reliability was measured only in the EPUAP tool, but it was poor to fair. Inter-rater reliability was measured in the Yarkony-kirk, Stirling, EPUAP, NPUAP, Torrance and Shea tools. Again, the EPUAP tool had the most supportive evidence. Although 1 pairwise comparison showed that the Stirling tool was superior to the EPUAP tool, the kappa rating for Stirling was only ‘fair’.In stand-alone studies of the EPUAP toolan ’excellent’ kappa rating was indicated. The EPUAP may therefore be the tool conferring the most clinical benefits from its high reliability. No tool stood out as likely to confer any significant harm upon peopleas a result of poor reliability.

	The GDG were in agreement that using a categorisation tool had many benefits, such as standardising practice between healthcare professionals and organisations. The evidence was unclear and did not allow the GDG to recommend the use of a specific categorisation tool yet, they wished to provide an example of a tool to aid healthcare professionals. is As the EPUAP categorisation tool is widely used and embedded in clinical practice across the UK the GDG chose to include reference to this tool within the recommendation, acknowledging that other categorisation tools were available.
Economic considerations	Different methods of categorisation are unlikely to have different resource implications. Categorisation of a pressure ulcer is considered best practice, and is essential in order to assess preventative and management efforts effectively. Using a categorisation tool that has high reliability and accuracy could ensure appropriate treatments are implemented efficiently. Categorisation is already embedded in clinical practice therefore, no additional resources are thought to be required.
Quality of evidence	The majority of accuracy outcomes were high quality. Most of these related to studies concerning the EPUAP tool, further strengthening the conclusion that the most convincing evidence indicates it is an accurate form of categorisation. In contrast, the majority of reliability outcomes were low quality. The greater quality of the accuracy studies was partly due to their simpler methodology, as there was less scope for important methodological omissions. It was unclear in some studies which version of EPUAP was used. An important issue concerns the use of either photographs or patients in the different studies. The GDG felt that photographs were not as accurate as directly seeing the patient. However, this was taken into account when assessing the quality criterion for both accuracy and reliability. Hence further consideration of this factor when reviewing the quality of evidence would constitute double-counting.
Other considerations	The GDG felt it was important that the categorisation of pressure ulcers was used to standardise practice as it would help to monitor the severity of pressure ulcers in an environment and help inform treatment. The GDG agreed that modified versions of validated tools should not be used. The GDG highlighted that the use of a classification scale was a static measurement of a dynamic process and thus it was important to continually reassess the category of a pressure ulcer. It was agreed that classification should be repeated each time the pressure ulcer is assessed.

4.3.2 Neonates, infants, children and young people

Recommendations	**6. Categorise each pressure ulcer in neonates, infants, children and young people at onset using a validated classification tool (such as the International NPUAP-EPUAP (2009) Pressure Ulcer Classification System) to guide ongoing preventative and management options. Repeat and document each time the ulcer is assessed.**
Relative values of different outcomes	Accuracy of categorisation tools was regarded as a critical outcome, as it is vital that categorisation is accurate if it is to be used to inform treatment as inaccurate categorisation might lead to inappropriate treatments being used. Accuracy was regarded identified as more important than reliability, as an accurate measurement will also be reliable, but it is possible to be reliable but not accurate. Therefore high accuracy encapsulates both accuracy and reliability, but high reliability can exist alongside poor accuracy. However, reliability was still regarded as important, as it is

	useful for allowing the comparison of pressure ulcer measurement across time. Such charting of progress is essential for making decisions on continuing, adapting or changing treatments. High intra-rater reliability is important for meaningful comparisons between categorisations made by 1 assessor on the same patient across time. High inter-rater reliability is important when comparing measurements undertaken by different assessors on the same patient over time. Ease of use of the tools was also regarded as an important outcome, as this will minimise patient and assessor time.
Trade-off between clinical benefits and harms	The GDG used 1 statement from the Delphi consensus survey to inform the recommendation on categorisation of pressure ulcers. The statement was 'Healthcare professionals should classify all pressure ulcers in neonates, infants, children and young people using the EPUAP/NPUAP grading scheme'. The statement was agreed by the Delphi consensus panel. Further detail on the Delphi consensus survey can be found in Appendix N. The statement on categorisation was included in Round 1 of the Delphi consensus survey. Comments from the panel members emphasised that the categorisation of pressure ulcers was essential to ensure consistency and standardisation of practice. The GDG discussed the results of the survey and agreed that categorisation of pressure ulcers was appropriate and a recommendation was therefore developed to support the categorisation of all pressure ulcers. The GDG noted however, that the results of categorisation should help to guide the management of the pressure ulcer, as well as future preventative strategies. The GDG discussed how often categorisation should be repeated and agreed that a pressure ulcer should be categorised at each assessment and the results of categorisation documented. A number of comments from panel members suggested that the EPUAP categorisation tool was in widespread use across the UK and the GDG therefore chose to include reference to this tool within the recommendation, acknowledging that other categorisation tools were available.
Economic considerations	Different methods of categorisation are unlikely to have different resource implications. Categorisation of a pressure ulcer is considered best practice, and is essential in order to assess preventative and management efforts effectively in neonates, infants, children and young people.
Quality of evidence	No RCTs or cohort studies were identified for neonates, infants, children or young people. Formal consensus using a modified Delphi was therefore used to develop the recommendation. To inform the recommendation, the GDG used 1 statement which was included in Round 1 of the Delphi consensus survey and reached 84% consensus agreement. Further details can be found in Appendix N.
Other considerations	There were no other considerations.

5 Nutrition and hydration

5.1 Introduction

Nutritional factors are important in the healing process of pressure ulcers, in conjunction with other management strategies, as various nutrients have been associated with promoting pressure ulcer repair through their role in collagen formation and development of connective tissue.For example, nutrients such as protein, vitamin C and zinc have historically been considered important, due to their role in collagen formation. Other nutritional supplements considered to be potentially important are arginine, an amino acid that stimulates insulin secretion and protein formation, collagen protein and hydrolysate, which provide protein in a hydrolysed form. Adjusting intake of these components can be achieved by varying amounts in the diet but also by the use of specific supplements. Supplementation can be achieved by the use of single tablets or in combination, often as a drink. Due to the numerous compositions of nutrient drinks, they are notoriously difficult to compare with each other. One of the major factors frequently considered to impact on pressure ulcer healing is baseline nutritional status, as a poor nutritional state is generally considered to inhibit pressure ulcer healing. It is therefore important to identify those at risk of malnutrition and start treatment to improve nutritional state as well as contemplating any further needs associated with pressure ulcer repair. NICE clinical guideline 32 'Nutrition support in adults'[130] provides recommendations on screening the nutritional status of people in hospital and in the community. The GDG were therefore interested in whether recommendations for nutritional interventions would be different depending on the presence or absence of malnutrition.

The GDG were also interested in whether there was any guidance on hydration interventions that would aid the treatment of pressure ulcers.

5.2 Review question: What are the most clinically and cost-effective nutritional interventions for the treatment of pressure ulcers?

For full details see review protocol in Appendix C.

5.2.1 Clinical evidence (adults)

No randomised trials of interventions for hydration to treat pressure ulcers were found. For nutritional interventions to treat pressure ulcers, 1 Cochrane review was identified[102] which included 4 randomised trials (Taylor, 1974[183], Ter Riet, 1995[184], Chernoff, 1990[42], and Norris, 1971[140]). These randomised trials have been included in the evidence review and the Cochrane Review was updated. Ten further randomised trials were found(Desneves, 2005[54], Lee, 2006[104], Cereda, 2009[40], Van Anholt, 2010[198], Brewer, 1967[30], Benati, 2001[25] and Ohura, 2011[142], Meaume, 2009[114], Leigh, 2012[105] and Theilla, 2012[186,187]). One study (Meaume, 2009)[114] only included people with heel pressure ulcers. Benati (2001)[25] met the inclusion criteria for the review but it had incomplete outcome reporting and so it was not possible to extract any results from this paper.

The evidence from these studies is summarised in the clinical GRADE evidence profile below (Table 4). See also the study selection flow chart in Appendix D, forest plots in Appendix I, study evidence tables in Appendix G and exclusion list in Appendix J.

Most of the studies identified looked at different forms of nutritional supplementation, in addition to the standard hospital diet, versus the standard hospital diet alone. The supplements differed in their composition therefore it was not possible to meta-analyse them. Two studies were identified which

compared ascorbic acid against placebo. Although the populations differed (people in a nursing home and people who had undergone surgery) they were meta-analysed.

Studies which included pressure ulcers of all stages were analysed separately from those which included people with pressure ulcers of stages 2 and above (the classification system used is reported, where provided by the authors). Studies including participants who had an adequate nutritional status were separated from those who had a nutritional deficiency.

Summary of included studies

Study	Intervention/comparator	Population	Outcomes	Study length
Benati 2001[25]	Normal hospital diet plus an oral supplementation with an iso-calorie and iso-protein solution enriched with arginine, vitamins and trace elements with antioxidant effect versus normal hospital diet plus oral supplementation with high protein calorie solution versus normal hospital diet.	People with severe cognitive impairment and pressure ulcers. Reduced oral food intake.	• Pressure ulcer status tool (PSST)	2 weeks
Brewer 1967[30]	Oral zinc sulphate 220mgs (50mg zinc) 3 times per day versus inert substance (lactose).	People with spinal cord injuries and poorly healing pressure ulcers of various sizes, types, locations and duration (5 months to 2 years).	• Proportion of people completely healed; side effects	2-3 months
Cereda 2009[40]	Disease-specific nutritional treatment - standard hospital diet plus 400ml oral supplement (500kcal, 34g protein, 6g arginine, 500mg vitamin C, 18mg zinc) or tube fed 100ml high protein formula (20% energy from protein, enriched with arginine, zinc and vitamin C) versus standard protocol - hospital diet (16% energy from protein) without any additional supplement or tube fed standard formula energy and the infusion of appropriate volumes of a standard formula satisfied protein requirements.	Elderly residents in long-term facilities with stage 2, 3 or 4 pressure ulcers (NPUAP 2007) who were orally or tube fed.	• Reduction in pressure ulcer area reduction in Pressure Ulcer Scale for Healing (PUSH) tool score at week 12; proportion of people with complete healing; % reduction in pressure ulcer area at 12 weeks; all-cause mortality.	12 weeks
Chernoff 1990 [42]	Very high protein (25% of calories) formula versus high protein (16% of calories) formula.	Long-term tube fed institutionalised people with pressure ulcers.	• Proportion of people with complete healing; % reduction in ulcer surface area.	8 weeks
Desneves 2005[54]	Standard hospital diet plus 2 tetrapaks of a	Inpatients with stage 2,3	• Reduction in PUSH tool scores.	3 weeks

Study	Intervention/comparator	Population	Outcomes	Study length
	defined arginine-containing supplement (500kcal, 21g protein, 0g fat, 500mg vitamin C, 30mg zinc and 9g arginine) versus standard hospital diet plus 2 tetrapaks of high protein, high energy supplement (providing additional 500kcal, 18g protein, 0g fat, 72mg vitamin C and 7.5mg zinc) versus standard hospital diet.	or 4 pressure ulcer. Diagnosis: dementia (n=1), cerebrovasulcar accident (n=6), spinal cord injury (n=2), parkinson's disease (n=1), chronic cardiac failure (n=2), fractured bones (n=3), pressure ulcers (alone) (n=1).		
Lee 2006[104]	Standard diet plus concentrated, fortified, collagen protein hydrolysate supplement versus standard diet plus placebo.	Residents of long-term care facilities with pressure ulcers stage 2, 3 or 4.	• Reduction in mean PUSH tool score; % reduction in PUSH tool score.	8 weeks
Leigh 2012[105]	Hospital diet plus 4.5g arginine supplement versus hospital diet plus 9g arginine supplement.	Inpatients with category 2, 3 or 4 pressure ulcers.	• Reduction in mean PUSH tool score; Reduction in mean PUSH tool score by nutritional status; concordance.	3 weeks
Norris 1971[140]	Oral zinc sulphate (200mg) capsules 3 times per day versus placebo.	People in a hospital with chronic disease and geriatric problems with non-superficial pressure ulcers. Diagnosis: brain damage after head injury (n=1), senile dementia n=1), subdural hematoma (n=1), paraplegia (n=4), multiple sclerosis (n=2), cerebral thrombosis (n=1), poliomyelitis (n=1), quadriplegia (n=1), brain damage after cardiac	• Mean reduction in pressure ulcer volume.	12 weeks treatment then crossed over for another 12 weeks.

Study	Intervention/comparator	Population	Outcomes	Study length
		arrest (n=1), rheumatoid arthritis, amputee (n=1).		
Ohura 2011[142]	Protein, fat, carbohydrate versus same nutrition as before trial.	Tube fed people with stage 3 to 4 pressure ulcers. The majority of participants were older adults.	• Proportion of people with complete healing within 12 weeks; reduction in pressure ulcers at 12 weeks; study-related adverse events.	12 weeks
Taylor 1974[183]	Basic hospital diet plus 500mg ascorbic acid twice daily versus basic hospital diet plus placebo.	People undergoing surgery with pressure ulcers. Diagnosis fractured neck of femur n=9), rheumatoid arthritis (n=2), cerebrovascular accident (n=2), fractured pelvis (n=1), peripheral vascular disease (n=1), paraplegia (n=1), gastric ulcer (n=1), benign prostatic hypertrophy (n=1), diverticular disease (n=1), aortic aneurysm (n=1).	• % surface reduction at 1month; completely healed pressure sores; mean rates of healing (cm^2 per week); all-cause mortality.	1 month
Ter Riet 1995[184]	Ascorbic acid supplementation (500mg twice daily) as effervescent tablets versus identical placebo which contained 10mg of ascorbic acid.	People from 11 nursing homes and 1 hospital with pressure ulcers (partial thickness skin loss or worse). Most people had nutritional deficiency on admission.	• Time to complete healing; mean surface area reduction (cm^2/week and %/week); proportion of people with complete healing at 84 days; mean volume reduction (ml/week/%/week); mean healing velocity (cm/week); all-cause mortality.	12 weeks
Theilla 2012[186,187]	Enteral nutritional formula enriched in fish oil and antioxidants versus isonitrogenous	People in an intensive care unit with grade 2 or	• Increase in PUSH tool mean score.	28 days

Study	Intervention/comparator	Population	Outcomes	Study length
	nutritional formula.	higher pressure ulcers.		
Van Anholt 2010A[198]	Oral nutritional supplement 250kcal, 28.4g carbohydrates (45% energy), 20g protein (30% energy), 3g arginine, 7g fat (25% energy), 238mg vitamin A, 250mg vitamin C, 38mg vitamin E, 1.5mg carotenoids, 9mg zinc, 64ug selenium, 1.35mg copper, 200ug folic acid versus non-caloric, flavoured placebo.	Non-malnourished people at health care centres, hospitals and long-term care facilities, aged 18 to 90 years with stage 3 to 4 pressure ulcers (EPUAP).	• Reduction in pressure ulcer size per week; reduction in mean PUSH tool scores; incidence of diarrhoea, nausea and vomiting; all-cause mortality.	Maximum 8 weeks
Meaume 2009[114]	10g sachet of ornithine alpha-ketoglutarate versus 1 sachet of placebo.	Elderly people (geriatric, internal medicine, physical medicine and rehabilitation, trauma, plastic surgery, cardiology, neurology and dermatology settings) who had pressure ulcers of the heel of stage 2 or 3 (NPUAP classification).	• % reduction in pressure ulcer surface area; greater than 90% reduction by week 6; rate of complete healing (cm^2/day); all-cause mortality.	6 weeks.

Table 24: Minimal important difference for continuous outcomes – baseline values

Study	Treatment	Control
Pressure ulcer surface area - mean cm^2 baseline values and standard deviations		
Cereda 2009[40] – protein, arginine, zinc	20.15 (11.13)	20.7 (14.7)
Van Anholt 2010[199] – protein, arginine	10.5 (2.3)	11.5 (2.5)
Meaume 2009[114]– alpha ketoglutarate	8.7 (6.7)	8.2 (8.9)
Median standard deviation: 7.8 x 0.5 = 3.9 MID for pressure ulcer surface area		
Pressure ulcer scale for healing (PUSH) score - mean baseline values and standard deviations		
Cereda 2009[40] – protein, arginine, zinc	13.5 (2.2)	14.0 (2.6)
Lee 2006[104]- protein	9.11 (4.15)	6.07 (2.65)
Desneves 2005[54] – arginine	9.4 (1.2)	8.7 (1.0)
Desneves 2005[54] – protein, vitamin C, zinc	8.0 (0.5)	8.7 (1.0)
Van Anholt 2010[199] – protein, arginine	11.5 (0.7)	11.4 (0.7)
Median standard deviation: 1.1 x 0.5 = 0.55 MID for pressure ulcer surface area		

Table 25: Clinical evidence profile: 500kcal, 34g protein, 6g arginine, 500mg vitamin C, 18mg zinc and standard hospital diet versus standard hospital diet

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Supplement and standard hospital diet	Standard hospital diet	Relative (95% CI)	Absolute	Quality	Importance
Proportion with complete healing – elderly adults in long term care with stage 2, 3, 4 ulcers[i] (unclear if nutritionally deficient)[40]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	1/13 (7.7%)	0/15 (0%)	Peto OR 8.62 (0.17 to 438.7)f	80 more per 1000 (from 110 fewer to 260 more)	Very low	Critical
							-	0%		80 more per 1000 (from 110 fewer to 260 more)		
Mean % reduction in ulcer size (change scores) – elderly adults in long term care lts with stage 2, 3, 4 ulcers[i] (unclear if nutritionally deficient)[40]												
1	Randomised trial	Serious[a]	No serious inconsistency	No serious indirectness	Very serious[e]	None	72% n=13	45% n=15	-	MD 27% p=0.05	Very low	Critical
Mean reduction in ulcer size (cm^2) (change scores) – elderly adults in long term care with stage 2, 3, 4 ulcers[i](unclear if nutritionally deficient)[40]												
1	Randomised trial	Serious[a]	No serious inconsistency	No serious indirectness	Very serious[c]	Serious[g]	14.5 (s.d 8.03) n=13	8.41 (s.d 5.59) n=15	-	MD 6.09 higher (0.89 to 11.29 higher)	Very low	Critical
Mean reduction in PUSH scores (change scores) (0= complete healing, 17=greatest severity) (change scores) – elderly adults in long term care with stage 2, 3, 4 ulcers (unclear if nutritionally deficient)[40]												
1	Randomised trial	Serious[a]	No serious inconsistency	No serious indirectness	Serious[d]	Serious[h]	-6.1 (s.d 2.7) n=13	-3.3 (s.d 2.4) n=15	-	MD 2.8 lower (4.71 to 0.89 lower)	Very low	Critical
All-cause mortality - elderly long term care adults with stage 2, 3, 4 ulcers[i](unclear if nutritionally deficient)[40]												

Quality assessment							No of patients		Effect			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Supplement and standard hospital diet**	**Standard hospital diet**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
1	Randomised trial	Serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	2/15 (13.3%)	0/15 (0%)	Peto OR 7.94 (0.47 to 133.26)[f]	130 more (from 60 fewer to 330 more)	Very low	Important
							-	**0%**		-		
Proportion of people with pressure ulcers completely healed												
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate of change in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital												
-	-	-	-	-	-	-	-	-	-	-	-	-
Patient acceptability of supplements												
-	-	-	-	-	-	-	-	-	-	-	-	-
Side effects (nausea, vomiting, diarrhoea)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) Cereda (2009)[40] used a computer-generated randomisation list used but no details of allocation concealment were provided. The drop-out rate was higher than the event rate for the outcome 'proportion with complete healing'.
(b) The confidence interval crossed both MID points (0.75 to 1.25 for dichotomous data and 0.5 x SD for continuous data). Limited number of events.
(c) The confidence interval crossed both MID points (0.75 to 1.25 for dichotomous data and 0.5 x SD for continuous data).
(d) The confidence interval crossed 1 MID point (0.75 to 1.25 for dichotomous data and 0.5 x SD for continuous data).
(e) No standard deviations were given. The study used a cery small sample size.
(f) Peto-odds ratio was used as 1 arm had zero events.
(g) The Mann-Whitney U-test was used for non-homogenous distribution of variance, but log transformation was not conducted.
(h) The data was analysed using ANOVA for repeated measures but log transformation was not conducted.

(i) NPUAP 2007 classification of pressure ulcers.

Table 26: Clinical evidence profile: 250kcal, 28.4g carbohydrates, 20g protein, 3g arginine, 7g fat, vitamins, minerals and standard hospital diet versus standard hospital diet and placebo

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Nutritional supplement and standard hospital diet	Standard hospital diet and placebo	Relative (95% CI)	Absolute	Quality	Importance
Reduction in mean PUSH scores (change scores) – elderly adults with stage 3-4 ulcers (non-malnourished)[198]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[e]	None[f]	6 n=22	5.4 n=21	-	MD 0.6 p=0.011g	Very low	Critical
Rate of mean reduction in ulcer size (cm^2/week) (change scores)– elderly adults with stage 3-4 ulcers (non-malnourished) [198]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[e]	None[f]	8.4cm2/week n=22	8.75cm2/week n=21 0.15cm2/day after week 8	-	MD =0.35cm2/weekj p=0.006g	Very low	Critical
Adverse events related to the product– elderly adults with stage 3-4 ulcers (non-malnourished) [198]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	None	9/22 (40.9%)	4/21 (19%)	RR 2.15 (0.78 to 5.92)	219 more per 1000 (from 42 fewer to 937 more)	Very low	Important
							-	19.1%		220 more per 1000 (from 42 fewer to 940 more)		
Incidence of diarrhoea– elderly adults with stage 3-4 ulcers (non-malnourished)[198]												
1	Randomised	Very	No serious	No serious	Very	None	6/22	2/21	RR	177 more	Very	Important

Quality assessment							No of patients		Effect			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Nutritional supplement and standard hospital diet**	**Standard hospital diet and placebo**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
	trial	serious[a]	inconsistency	indirectness	serious[c]		(27.3%)	(9.5%)	2.86 (0.65 to 12.64)	per 1000 (from 33 fewer to 1000 more)	low	
							-	9.5%		177 more per 1000 (from 33 fewer to 1000 more)		
Incidence of nausea– elderly adults with stage 3-4 ulcers (non-malnourished)[198]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[c]	None	1/22 (4.5%)	1/21 (4.8%)	RR 0.95 (0.06 to 14.3)	2 fewer per 1000 (from 45 fewer to 633 more)	Very low	Important
							-	4.8%		2 fewer per 1000 (from 45 fewer to 638 more)		
Incidence of vomiting– elderly adults with stage 3-4 ulcers (non-malnourished)[198]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[c]	None	0/22 (0%)	1/21 (4.8%)	Peto OR 0.13 (0 to	41 fewer per 1000 (from 48 fewer to 198	Very low	Important

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Nutritional supplement and standard hospital diet	Standard hospital diet and placebo	Relative (95% CI)	Absolute	Quality	Importance
									6.51)	more)		
							-	4.8%		41 fewer per 1000 (from 48 fewer to 199 more)		
Proportion of people with pressure ulcers completely healed												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital												
-	-	-	-	-	-	-	-	-	-	-	-	-
Patient acceptability of supplements												
-	-	-	-	-	-	-	-	-	-	-	-	-
Mortality (all-cause)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) Van Anholt (2010)[198] did not provide details of allocation concealment or sequence generation, or details of the blinding of outcome assessors. Recruitment stopped early due to lack of patients fulfilling inclusion criteria. High drop-out.

(b) The confidence interval crossed 1 MID point (0.75 to 1.25 for dichotomous data and 0.5 x SD for continuous data).

(c) The confidence interval crossed both MID points (0.75 to 1.25 for dichotomous data and 0.5 x SD for continuous data). There were a limited number of events.
(d) The confidence interval crossed both MID points (0.75 to 1.25 for dichotomous data and 0.5 x SD for continuous data).
(e) No standard deviations were provided by the author. The study had a small sample size.
(f) If data did not meet the assumption of normal distribution, they were log-transformed to enhance normality before statistical analysis (for pressure ulcer size).
(g) The study reported the p value for treatment by time. The p value for treatment by time[2] (curve fits: p</=0.016 for ulcer size (cm2/week) and p</=0.033 for PUSH scores/week. A repeated-measures mixed model was used and data was adjusted for centre.
(h) EPUAP and NPUAP 2009 classification of pressure ulcers.
(i) Data estimated from graph.
(j) The mean difference was calculated from estimated graph values.

Table 27: Clinical evidence profile: 500kcal, 18g protein, 0g fat, 72mg vitamin C and 7.5mg zinc and standard hospital diet versus standard hospital diet for treating pressure ulcers

Quality assessment							No of patients		Effect			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Nutritional supplement and standard hospital diet**	**Standard hospital diet**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
PUSH scores at week 3 (0=complete healing, 17=greatest severity) (final scores) – elderly adults or people with a spinal injury, stage 2, 3 or 4 ulcers[d] (unclear if nutritionally deficient) [54]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	Serious[c]	6 (s.d 1.2) n= 5	7 (s.d 1.5) n= 6	-	MD 1 lower (2.6 lower to 0.6 higher)	Very low	Critical
Proportion of people with pressure ulcers completely healed												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate of change in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Nutritional supplement and standard hospital diet	Standard hospital diet	Relative (95% CI)	Absolute	Quality	Importance
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital												
-	-	-	-	-	-	-	-	-	-	-	-	-
Patient acceptability												
-	-	-	-	-	-	-	-	-	-	-	-	-
Side effects (nausea, vomiting, diarrhoea)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Mortality (all-cause)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) Desneves (2005)[54]:did not provide details of allocation concealment or details of blinding of participants or those administering treatment. However, outcome assessors were blinded.
(b) The confidence interval crossed both MID points (0.75 to 1.25 for dichotomous data and 0.5 x SD for continuous data).
(c) The between-group comparisons were evaluated using the Mann-Whitney U-test but no log transformations conducted.
(d) Australian Wound Management Association Clinical Practice Guidelines classification of pressure ulcers.

Table 28: Clinical evidence profile: 500kcal, 21g protein, 0g fat 500mg vitamin C, 30mg zinc and 9g arginine and standard hospital diet versus standard hospital diet

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Nutritional supplement and standard hospital diet	Standard hospital diet	Relative (95% CI)	Absolute	Quality	Importance
PUSH scores at week 3 (0=complete healing, 17=greatest severity) (final scores) – elderly adults or people with a spinal injury, stage 2, 3 or 4 ulcers[d](unclear if nutritionally deficient) [54]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	Serious[b]	2.6 (s.d 0.6) n= 5	7 (s.d 1.5) n= 6	-	MD 4.4 lower (5.71 to 3.09 lower)	Very low	Critical
Proportion of people with pressure ulcers completely healed												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate of reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital												
-	-	-	-	-	-	-	-	-	-	-	-	-
Patient acceptability of supplements												
-	-	-	-	-	-	-	-	-	-	-	-	-
Side effects (nausea, vomiting, diarrhoea)												
-	-	-	-	-	-	-	-	-	-	-	-	-

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Nutritional supplement and standard hospital diet	Standard hospital diet	Relative (95% CI)	Absolute	Quality	Importance
Mortality (all-cause)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) Desneves (2005) did not provide details of allocation concealment or details of blinding of participants or those administering treatment. However outcome assessors were blinded.
(b) The between-group comparisons were evaluated using the Mann-Whitney U-test but no log transformations conducted.
(c) Australian Wound Management Association Clinical Practice Guidelines classification of pressure ulcers.

Table 29: Clinical evidence profile: 500kcal 21g protein, 0g fat, 500mg vitamin C, 30mg zinc, 9g of arginine and standard hospital diet versus 500kcal 18g protein, 0g fat, 72mg vitamin C and 7.5mg zinc and standard hospital diet

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	500kcal 21g protein, 0g fat, 500mg vitamin C, 30mg zinc, 9g of arginine and standard hospital diet	500kcal 18g protein, 0g fat, 72mg vitamin C and 7.5mg zinc and standard hospital diet	Relative (95% CI)	Absolute	Quality	Importance
PUSH scores at week 3 (0=complete healing, 17=greatest severity) (final scores) – elderly adults or people with a spinal injury, stage 2, 3 or 4 ulcers[c] (unclear if nutritionally deficient) [54]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	Serious[b]	2.6 (s.d 0.6) n= 5	6 (s.d 1.2) n= 5	-	MD 3.4 lower (4.58 to	Very low	Critical

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	500kcal 21g protein, 0g fat, 500mg vitamin C, 30mg zinc, 9g of arginine and standard hospital diet	500kcal 18g protein, 0g fat, 72mg vitamin C and 7.5mg zinc and standard hospital diet	Relative (95% CI)	Absolute	Quality	Importance
										2.22 lower)		
Proportion of people with pressure ulcers completely healed												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate of reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital												
-	-	-	-	-	-	-	-	-	-	-	-	-
Patient acceptability of supplements												
-	-	-	-	-	-	-	-	-	-	-	-	-
Side effects (nausea, vomiting, diarrhoea)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Mortality (all-cause)												

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	500kcal 21g protein, 0g fat, 500mg vitamin C, 30mg zinc, 9g of arginine and standard hospital diet	500kcal 18g protein, 0g fat, 72mg vitamin C and 7.5mg zinc and standard hospital diet	Relative (95% CI)	Absolute	Quality	Importance
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) Desneves (2005) did not provide details of allocation concealment or blinding of participants or those administering treatment. However outcome assessors were blinded.
(b) The between-group comparisons were evaluated using the Mann-Whitney U-test but no log transformations conducted.
(c) Australian Wound Management Association Clinical Practice Guidelines classification of pressure ulcers.

Table 30: Clinical evidence profile: 4.38g protein, 2.23g fat, 15.62g carbohydrate, minerals and vitamins (per 100ml) and standard hospital diet versus standard hospital diet

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Nutritional supplement and standard hospital diet	Standard hospital diet	Relative (95% CI)	Absolute	Quality	Importance
Proportion with complete healing- majority elderly, tube-fed adults with stage 3 to 4 pressure ulcers (unclear if nutritionally deficient)[142]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	None	7/21 (33.3%)	4/29 (13.8%)	RR 2.42 (0.81 to 7.21)	196 more per 1000 (from 26 fewer to	Very low	Critical

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Nutritional supplement and standard hospital diet	Standard hospital diet	Relative (95% CI)	Absolute	Quality	Importance
										857 more)		
							-	13.8%		196 more per 1000 (from 26 fewer to 857 more)		
Mean reduction in ulcer size (cm^2)(change scores)-majority elderly, tube-fed adults with stage 3 to 4 pressure ulcers (unclear if nutritionally deficient)[142]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None[d]	1.31 (s.d 0.24) n= 21	0.32 (s.d 0.2) n= 29	-	MD 0.99 higher (0.86 to 1.12 higher)e	Low	Critical
Study-related adverse events –majority elderly, tube-fed adults with stage 3 to 4 pressure ulcers (unclear if nutritionally deficient)[142]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[c]	None	8/29 (27.6%)	5/30 (16.7%)	RR 1.66 (0.61 to 4.47)	110 more per 1000 (from 65 fewer to 578 more)	Very low	Important
							-	16.7%		110 more per 1000 (from 65 fewer to 579		

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Nutritional supplement and standard hospital diet	Standard hospital diet	Relative (95% CI)	Absolute	Quality	Importance
										more)		
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate of reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital												
-	-	-	-	-	-	-	-	-	-	-	-	-
Patient acceptability of supplements												
-	-	-	-	-	-	-	-	-	-	-	-	-
Mortality												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) Ohura (2011)[142] was an unblinded study with a high drop-out with a differential of greater than 10% between arms.
(b) The confidence interval crossed 1 MID point (0.75 to 1.25 for dichotomous data and 0.5 x SD for continuous data).
(c) The confidence interval crossed both MID points (0.75 to 1.25 for dichotomous data and 0.5 x SD for continuous data).
(d) For size of pressure ulcer, analyses were performed on log-transformed data, taking into consideration a lognormal distribution observed in the population at each time point.
(e) A graph and confidence intervals were reported in the study (which were assumed to be log-transformed) so the point estimate and 95% confidence intervals were calculated.
(f) NPUAP classification of pressure ulcers.

Table 31: Clinical evidence profile: very high protein dietary formula (92 to 150gms/day) versus high protein dietary formula (57 to 90 gms/day)

Quality assessment							No of patients		Effect			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Very high protein dietary formula (92 to 150gms/day)**	**High protein dietary formula (57 to 90 gms/day**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
Proportion with complete healing – long-term tube-fed adults with pressure ulcers (unclear if nutritionally deficient)[42]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	None	4/6 (66.7%)	0/6 (0%)	Peto OR 15.64 (1.57 to 155.75)	670 more per 1000 (from 260 more to 1070 more)	Very low	Critical
							-	0%		670 more per 1000 (from 260 more to 1070 more)		
Mean surface area reduction (%) – long-term tube-fed adults with pressure ulcers (unclear if nutritionally deficient)[42]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[c]	None	73% n=6	42% n=6	-	MD 31%	Very low	Critical
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate of reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Very high protein dietary formula (92 to 150gms/day)	High protein dietary formula (57 to 90 gms/day	Relative (95% CI)	Absolute	Quality	Importance
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital												
-	-	-	-	-	-	-	-	-	-	-	-	-
Patient acceptability of supplements												
-	-	-	-	-	-	-	-	-	-	-	-	-
Side effects (nausea, vomiting, diarrhoea)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Mortality (all-cause)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) Chernoff (1990)[42] was an abstract. No details of sequence generation, allocation concealment or blinding were reported by the authors. No details were provided on baseline differences except ulcer size – the very high protein group ranged from 1.6cm^2 to 46.4cm^2 and 1.6cm^2 to 63.8cm^2 in the high protein group.

(b) A very small sample size was used and there were a limited number of events.

(c) No standard deviations given. The study used a very small sample size.

Table 32: Clinical evidence profile: 1000mg ascorbic acid (500mg twice daily) and standard hospital diet versus standard hospital diet and placebo

Quality assessment							No of patients		Effect			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**500mg ascorbic acid and standard hospital diet**	**Standard hospital diet and placebo**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
Proportion with complete healing – people from 11 nursing homes and 1 hospital (most with nutritional deficiencies) with pressure ulcers (partial thickness skin loss or worse) and adults undergoing surgery (unclear if nutritionally deficient)[k 184]; Taylor (1974)[183]												
2	Randomised trials	Very serious[a]	Serious inconsistency[d]	No serious indirectness	Very serious[b]	None	23/53 (43.4%)e	25/55 (45.5%)e	RR 0.95 (0.62 to 1.47)	23 fewer per 1000 (from 173 fewer to 214 more)	Very low	Critical
							-	39.4%		20 fewer per 1000 (from 150 fewer to 185 more)		
Time to complete healing (better indicated by lower values) – people from 11 nursing homes and 1 hospital with pressure ulcers (partial thickness skin loss or worse) (most with nutritional deficiencies) [184]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None[f]	n= 43	n= 45	-	HR 0.78 higher (0.39 to 1.54 higher)	Very low	Critical
Mean % surface area reduction – people undergoing surgery (unclear if nutritionally deficient)[183]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	84 (s.d 2.4) n= 10	42.7 (s.d23.43) n= 10	-	MD 41.3 higher (20.51 to	Very low	Critical

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	500mg ascorbic acid and standard hospital diet	Standard hospital diet and placebo	Relative (95% CI)	Absolute	Quality	Importance
										62.09 higher)g		
Rate of mean reduction in ulcer size (cm2/week) – people from 11 nursing homes and 1 hospital with pressure ulcers (partial thickness skin loss or worse) (most with nutritional deficiencies)[184]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[c]	None	0.21 n=43	0.27 n=45	-	MD -0.06 Adjusted difference: -0.02 (95% CI -0.20 to 0.16)h	Very low	Critical
Rate of mean reduction in ulcer size (cm^2/week) – people undergoing surgery (unclear if nutritionally deficient)[183]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[l]	None	2.47 n=10	1.45 n=10	-	MD 1.02	Very low	Critical
Rate of mean reduction in volume (ml/week) – people from 11 nursing homes and 1 hospital with pressure ulcers (partial thickness skin loss or worse) (most with nutritional deficiencies)[184]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[c]	Serious[i]	0 n=43	0.20 n=45	-	MD -0.20 Adjusted difference: -0.66 (95% CI -1.44 to 0.78)f	Very low	Critical
Rate of % reduction in volume (%/week) – people from 11 nursing homes and 1 hospital with pressure ulcers (partial thickness skin loss or worse) (most with nutritional deficiencies)[184]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[c,j]	Serious[i]	-3.39 n=43	16.71 n=45	-	-20.10 Adjusted	Very low	Critical

Quality assessment							No of patients		Effect			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**500mg ascorbic acid and standard hospital diet**	**Standard hospital diet and placebo**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
										difference: 35.33 (95% CI -11.31 to 81.91)		
Rate of mean healing velocity (cm/week) – people from 11 nursing homes and 1 hospital with pressure ulcers (partial thickness skin loss or worse) (most with nutritional deficiencies) [184]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[c]	Serious[i]	0.12 n=43	0.19 n=45	-	-0.08 Adjusted difference -0.05 (95% CI -0.148 to 0.048)	Very low	Critical
All-cause mortality– people from 11 nursing homes and 1 hospital (most with nutritional deficiencies) with pressure ulcers (partial thickness skin loss or worse) and people undergoing surgery (unclear if nutritionally deficient)[184]; Taylor (1974)[183]												
2	Randomised trials	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	4/53 (7.5%)	6/55 (10.9%)	RR 0.69 (0.21 to 2.32)	34 fewer per 1000 (from 86 fewer to 144 more)	Very low	Important
							-	10.6%		33 fewer per 1000 (from 84 fewer to 140 more)		

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	500mg ascorbic acid and standard hospital diet	Standard hospital diet and placebo	Relative (95% CI)	Absolute	Quality	Importance
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital												
-	-	-	-	-	-	-	-	-	-	-	-	-
Patient acceptability of supplements												
-	-	-	-	-	-	-	-	-	-	-	-	-
Side effects												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) Ter Riet (1994)[184] did not provide details of allocation concealment. The control group had a greater number of large ulcers at baseline.There was a high drop-out rate. Taylor (1974)[183] was a quasi-randomised study using year of birth. There was inadequate allocation concealment.

(b) The confidence interval crossed both MID points (0.75 to 1.25 for dichotomous data and 0.5 x SD for continuous data).

(c) No standard deviations were given.

(d) I^2 was 56% but p value was 0.13 so this was not significant. The populations differed as 1 study included people in a nursing home and the other included people undergoing surgery.

(e) Data was extracted from graphs in the Cochrane Review by Langer.

(f) Cox proportional hazards analysis in which wound survival ratio was adjusted for differences from baseline. Kaplan-Meier wound survival curves were done for all participants, p=0.84 log rank test, 1 tailed.

(g) The standard deviation was calculated from the standard error.

(h) The 95% CI were calculated from 90% CI, which was reported by the authors.

(i) No log transformation of data and non-parametric tests were used.

(j) There were only 12 people in the intervention group and 13 people in the control group when this was measured.

(k) Ter Riet (1994)[184] state that most participants had a nutritional deficiency on admission. Taylor (1974)[183] does not mention whether participants were nutritionally deficient.

(l) No standard deviations given. The study used a small sample size.

Table 33: Clinical evidence profile: zinc sulfate versus placebo

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Zinc sulfate	Placebo	Relative (95% CI)	Absolute	Quality	Importance
Proportion with complete healing - zinc sulfate 220mg versus placebo (unclear if nutritionally deficient)[30]												
1	Randomised trial	Very serious [a]	No serious inconsistency	No serious indirectness	Very serious[b]	Serious[c]	1/6 (16.7%)	2/7 (28.6%)	RR 0.58 (0.07 to 4.95)	120 fewer per 1000 (from 266 fewer to 1000 more)	Very low	Critical
							-	28.6%		120 fewer per 1000 (from 266 fewer to 1000 more)		
Mean reduction in pressure ulcer volume (ml) - zinc sulfate 200mg 3 times per day versus placebo – people in a hospital with chronic disease and geriatric problems with non-superficial pressure ulcers (unclear if nutritionally deficient)[140]												
1	Randomised trial	Very serious [d]	No serious inconsistency	No serious indirectness	Very serious[b]	Serious[c]	10.1 (s.d 9) n= 10	6 (s.d 17.5) n= 10	-	MD 4.1 higher (8.1 lower to 16.3 higher)	Very low	Critical
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate of reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Zinc sulfate	Placebo	Relative (95% CI)	Absolute	Quality	Importance
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital												
-	-	-	-	-	-	-	-	-	-	-	-	-
Patient acceptability of supplements												
-	-	-	-	-	-	-	-	-	-	-	-	-
Side effects (nausea, vomiting, diarrhoea)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Mortality (all-cause)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) Brewer (1967)[30] did not provide details of sequence generation or unclear allocation concealment. No details of baseline values were provided.
(b) The confidence interval crossed both MID points (0.75 to 1.25 for dichotomous data and 0.5 x SD for continuous data).
(c) No log transformations and no non-parametric tests were used.
(d) Norris (1971)[140] did not provide details of sequence generation. There was a high drop-out rate.

Table 34: Clinical evidence profile: concentrated, fortified, collagen protein hydrolysate versus placebo

Quality assessment							No of patients		Effect			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Concentrated, fortified, collagen protein hydrolysate**	**Placebo**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
Mean reduction in PUSH scores (final scores) – elderly adults or people with a spinal injury, stage 2, 3, or 4 ulcers (unclear if nutritionally deficient but overweight)[104]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	Serious[e]	3.55 (s.d 4.66) n= 44	3.22 (s.d 4.11) n= 27	-	MD 0.33 higher (1.74 lower to 2.4 higher)	Very low	Critical
% reduction in PUSH tool score (change scores) – elderly adults or people with a spinal injury, stage 2, 3, or 4 ulcers (unclear if nutritionally deficient but overweight)[104]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[d]	None	60% n=44	48% n=27	-	MD 12% p<0.05	Very low	Critical
All-cause mortality– elderly adults or people with a spinal injury, stage 2, 3, or 4 ulcers (unclear if nutritionally deficient but overweight)[104]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[c]	None	1/56 (1.8%)	1/33 (3%)	RR 0.59 (0.04 to 9.11)	12 fewer per 1000 (from 29 fewer to 246 more)	Very low	Important
							-	3%		12 fewer per 1000 (from 29 fewer to 243 more)		
Proportion of people with pressure ulcers completely healed												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate of reduction in size or volume of pressure ulcers												

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Concentrated, fortified, collagen protein hydrolysate	Placebo	Relative (95% CI)	Absolute	Quality	Importance
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital												
-	-	-	-	-	-	-	-	-	-	-	-	-
Patient acceptability												
-	-	-	-	-	-	-	-	-	-	-	-	-
Side effects (nausea, vomiting, diarrhoea)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) There was inadequate sequence generation (the first participant was randomised by a flip of a coin, following participants were alternated between the 2 groups.) There was no allocation concealment. There was a high drop-out rate.

(b) The confidence interval crossed 1 MID point (0.75 to 1.25 for dichotomous data and 0.5 x SD for continuous data).

(c) The confidence interval crossed both MID points (0.75 to 1.25 for dichotomous data and 0.5 x SD for continuous data). There were a limited number of events.

(d) No standard deviations were given.

(e) ANOVA with repeated measures was used to compare pressure ulcer healing. No log transformation and no non-parametric tests were used.

(f) NPUAP 2005 classification for pressure ulcers.

Table 35: Clinical evidence profile: ornithine alpha-ketoglutarate versus placebo

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	10g Ornithine alpha-ketoglutarate	Placebo	Relative (95% CI)	Absolute	Quality	Importance
Rate of complete healing (cm^2/day) – elderly adults who had pressure ulcers of the heel of stage 2 or 3 (unclear if nutritionally deficient)[114]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	None	0.07 (s.d 0.11) n= 85	0.04 (s.d 0.08) n= 75	-	MD 0.03 higher (0 to 0.06 higher)	Very low	Critical
Mean % reduction in ulcer size – elderly adults who had pressure ulcers of the heel of stage 2 or 3 (unclear if nutritionally deficient) – log transformed data[114]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious	None[f]	59.5 (s.d 71.4) n= 85	54 (s.d 69) n= 75	-	Simple analysis: MD 5.5 higher (16.28 lower to 27.28 higher) Ancova analysis p=0.477	Very low	Critical
Mean surface area reduction (cm^2) – elderly adults who had pressure ulcers of the heel of stage 2 or 3(unclear if nutritionally deficient)[114]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious	None[f]	2.3 (s.d 4.2) n= 85	1.7 (s.d 1.7) n= 75	-	MD 0.6 higher (0.37 lower to 1.57 higher)	Very low	Critical
90% reduction by week 6– elderly adults who had pressure ulcers of the heel of stage 2 or 3(unclear if nutritionally deficient)[114]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious [c]	None	23.4% n=85	13% n=75	OR 0.49 (CI 0.16 to 14.6)e	-	Very low	Critical

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	10g Ornithine alpha-ketoglutarate	Placebo	Relative (95% CI)	Absolute	Quality	Importance
All-cause mortality – elderly adults who had pressure ulcers of the heel of stage 2 or 3 (unclear if nutritionally deficient)[114]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[c]	None	5/89 (5.6%)	3/76 (3.9%)	RR 1.42 (0.35 to 5.76)	17 more per 1000 (from 26 fewer to 188 more)	Very low	Important
							-	4%		17 more per 1000 (from 26 fewer to 190 more)		
Proportion of people with pressure ulcers completely healed												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital												
-	-	-	-	-	-	-	-	-	-	-	-	-
Patient acceptability of supplements												
-	-	-	-	-	-	-	-	-	-	-	-	-
Side effects (nausea, vomiting, diarrhoea)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Mortality												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) There was a very high drop-out in both arms. Due to problems in recruitment, the study was opened up to other centres so some centres had 2 participants and randomisation was balanced by blocks of 4. There were baseline differences. The missing data higher than event rate.
(b) The confidence interval crossed 1 MID point.
(c) The confidence interval crossed both MID points.
(d) This is the value reported by the study.
(e) This is the odds ratio reported by study.
(f) ANCOVA used. Non-parametric tests detected between-group differences (p=0.044) which were confirmed by parametric tests after log-transformation to normalise distribution (p=0.027 for group comparisons).
(g) NPUAP classification of pressure ulcers.

Table 36: Clinical evidence profile: arginine 4.5g versus arginine 9g

Quality assessment							No of patients		Effect			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Arginine 4.5g**	**Arginine 9g**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
Decrease in PUSH tool scores (better indicated by lower values) – people in hospital with pressure ulcers grade 2, 3 or 4[105]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	3.4 n=12	3.1 n=11	MD 0.30 p=0.991	Not pooled	Very low	Critical
Proportion of people with pressure ulcers completely healed												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate of reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital												
-	-	-	-	-	-	-	-	-	-	-	-	-
Patient acceptability of supplements												
-	-	-	-	-	-	-	-	-	-	-	-	-

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Arginine 4.5g	Arginine 9g	Relative (95% CI)	Absolute	Quality	Importance
Side effects (nauseas, vomiting, diarrhoea)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Mortality (all-cause)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) No details were provided of blinding of participant or healthcare professional; there was a greater than 10% differential drop-out.
(b) No standard deviations were given for between group differences. No log transformations were provided.
(c) NPUAP classification of pressure ulcers.

Table 37: Clinical evidence profile: arginine 4.5g in malnourished participants versus arginine 9g in malnourished participants

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Arginine 4.5g	Arginine 9g	Relative (95% CI)	Absolute	Quality	Importance
Decrease in PUSH tool scores (better indicated by lower values) – people in hospital with pressure ulcers grade 2, 3 or 4[105]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	0.90 n=unclear	2.9 n=unclear	MD 2	Not pooled	Very low	Critical
Proportion of people with pressure ulcers completely healed												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate of reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Arginine 4.5g	Arginine 9g	Relative (95% CI)	Absolute	Quality	Importance
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital												
-	-	-	-	-	-	-	-	-	-	-	-	-
Patient acceptability of supplements												
-	-	-	-	-	-	-	-	-	-	-	-	-
Side effects (nausea, vomiting, diarrhoea)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Mortality (all-cause)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) No details of blinding of participant or healthcare professionals were provided. There was a greater than 10% differential drop-out.
(b) No standard deviations given for between group differences were provided and the authors did not report the sample size. No log transformations were provided.
(c) NPUAP classification of pressure ulcers.

Table 38: Clinical evidence profile: arginine 4.5g in well-nourished participants versus arginine 9g in well-nourished participants

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Arginine 4.5g + well nourished	Arginine 9g + well nourished	Relative (95% CI)	Absolute	Quality	Importance
Decrease in PUSH tool scores (better indicated by lower values)- people in hospital with pressure ulcers grade 2, 3 or 4[105]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	2.7 n= unclear	3 n= unclear	MD 0.30	Not pooled	Very low	Critical
Proportion of people with pressure ulcers completely healed												

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Arginine 4.5g + well nourished	Arginine 9g + well nourished	Relative (95% CI)	Absolute	Quality	Importance
-	-	-	-	-	-	-	-	-	-	-	-	-
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate of reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital												
-	-	-	-	-	-	-	-	-	-	-	-	-
Patient acceptability of supplements												
-	-	-	-	-	-	-	-	-	-	-	-	-
Side effects												
-	-	-	-	-	-	-	-	-	-	-	-	-
Mortality (all-cause)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) No details of blinding of participants or healthcare professionals were provided. There was a greater than 10% differential drop-out.
(b) No standard deviations given for between group differences were provided and the authors did not report sample size. No log transformations were provided.
(c) NPUAP classification of pressure ulcers.

Table 39: Clinical evidence profile: nutritional formula with fish oil and macronutrients versus isocaloric control formula

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Nutritional formula with fish oil and macronutrients	Isocaloric control formula - ICU patients	Relative (95% CI)	Absolute	Quality	Importance
Increase in mean PUSH tool score (better indicated by lower values) – people in intensive care with pressure ulcers grade 2 or above[c] – unclear if nutritionally deficient[186,187]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	1.50 n= 20	0.30 n= 20	MD 1.20	Not pooled	Very low	Critical
Proportion of people with pressure ulcers completely healed												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Reduction in size or volume of pressure ulcers												
Rate of reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital												
-	-	-	-	-	-	-	-	-	-	-	-	-
Patient acceptability												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) No details of allocation concealment were provided by the authors. There was no blinding of staff in the intensive care unit, participants or the assessor of pressure ulcer severity.
(b) No standard deviations were given for between group differences. No log transformations were provided
(c) NPUAP classification of pressure ulcers.

5.2.2 Economic evidence (adults)

5.2.2.1 Published literature

One study was included with a relevant comparison.[80] This is summarised in the economic evidence profile below (Table 40). See also the study selection flow chart in Appendix D and study evidence table in Appendix H.

Table 40: Economic evidence profile: Nutritional supplement verses standard hospital diet

Study	Applicability	Limitations	Other comments	Incremental cost	Incremental effects	Cost effectiveness	Uncertainty
Hisahige 2012[80] (Japan)	Partially applicable[a]	Potentially serious limitations[b]	Economic evaluation based on single RCT plus post trial extrapolation. Comparison of nutritional supplementation to standard hospital diet in people with pressure ulcers.	-£586	-16.2 pressure ulcer days	The supplement dominates the standard hospital diet (cost saving and fewer pressure ulcer days)	Unclear.

(a) This study is set in Japan; the authors claim to reports a societal perspective, yet this does appear to align with the perspective of a Japanese healthcare provider in this case.

(b) The effectiveness estimates are based on the results of a single RCT set in Japan, rather than a systematic procedure. QALYs are reported but calculation is unclear. It is unclear how the cost-effectiveness ratios have been calculated; many of these are negative. Only these cost-effectiveness ratios are reported from the analysis of uncertainty.

5.2.2.2 Unit costs

In the absence of recent UK cost-effectiveness analysis, relevant unit costs are provided below to aid consideration of cost effectiveness. These costs represent costs per day of various supplements used in the treatment of pressure ulcers. These are the list prices, and the GDG acknowledged that the actual price paid is often much lower than those stated in the table below. The specific supplements included are illustrative only, and should not be interpreted as GDG recommendations.

Table 41: Unit cost estimates per day for nutritional supplements in a community setting

Item	Cost	Notes
Vitamin C (200mg)	£0.14	£1.31 per packet of 28 tablets. 3 tablets per day.
High protein supplements[a] (200ml)	£3.70	Fortisip extra. £1.85 per 200ml bottle. 2 bottles given per day.

(a) Such supplements also contain further potentially beneficial ingredients such as zinc and vitamin C

Source: BNF62[85], dosage based on discussion with GDG member

Total costs depend on the duration and quantity of the nutritional supplementation that is required, and will vary greatly amongst participants. Monthly costs of vitamin C and protein supplementation would be £4 and £115 respectively.

5.2.3 Clinical evidence (neonates, infants, children and young people)

No RCTs or cohort studies were identified. Recommendations were developed using a modified Delphi consensus technique. Further details can be found in Appendix N.

5.2.4 Economic evidence (neonates, infants, children and young people)

No economic evidence was identified.

5.2.5 Evidence statements

5.2.5.1 Clinical (adults)

5.2.5.1.1 Supplement of 500kcal, 34g protein, 6g arginine, 500mg vitamin C, 18mg zinc in addition to a standard hospital diet versus standard hospital diet alone

- One study (n=28) showed a supplement of 500kcal, 34g protein, 6g arginine, 500mg vitamin C, 18mg zinc in addition to a standard hospital diet may be more clinically effective than standard hospital diet alone for complete healing of pressure ulcers (very low quality).
- One study (n=28) reported a supplement of 500kcal, 34g protein, 6g arginine, 500mg vitamin C, 18mg zinc in addition to a standard hospital diet may be more clinically effective and a standard hospital diet alone for reduction in ulcer size (%). The mean for the supplement was 72% and 45% for the standard hospital diet. No estimate of precision could be derived (very low quality).
- One study (n=28) showed a supplement of 500kcal, 34g protein, 6g arginine, 500mg vitamin C, 18mg zinc in addition to a standard hospital diet may be more clinically effective than standard hospital diet alone for reduction in ulcer size (cm^2) (very low quality).
- One study (n=28) showed a supplement of 500kcal, 34g protein, 6g arginine, 500mg vitamin C, 18mg zinc in addition to a standard hospital diet is potentially more clinically effective than standard hospital diet alone for reducing mean PUSH tool scores (very low quality).
- One study (n=28) showed a standard hospital diet alone may be more clinically beneficial than a supplement of 500kcal, 34g protein, 6g arginine, 500mg vitamin C, 18mg zinc in addition to a standard hospital diet for reducing all-cause mortality (very low quality).

- No evidence was found for the following outcomes:
  - Time to complete healing (time to event data)
  - Rate of complete healing
  - Rate in change of size of ulcer
  - Pain (wound-related)
  - Time in hospital
  - Patient acceptability of supplements
  - Side effects (nausea, vomiting, diarrhoea)
  - Health-related quality of life

5.2.5.1.2 Supplement of 250kcal, 28.4g carbohydrates, 20g protein, 3g arginine, 7g fat, vitamins, minerals in addition to a standard hospital diet versus standard hospital diet and placebo

- One study (n=43) showed there may be no clinical difference between a supplement of 250kcal, 28.4g carbohydrates, 20g protein, 3g arginine, 7g fat, vitamins, minerals in addition to a standard hospital diet and a standard hospital diet and placebo for reducing mean PUSH tool score, the direction of the estimate of effect favoured the supplement. Imprecision could not be derived. (very low quality).
- One study (n=43) showed there may be no clinical difference between a supplement of 250kcal, 28.4g carbohydrates, 20g protein, 3g arginine, 7g fat, vitamins, minerals in addition to a standard hospital diet and a standard hospital diet and placebo for rate of reduction in ulcer size (cm2/week). The direction of the estimate of effect favoured the standard hospital diet and placebo. Imprecision could not be derived. (very low quality).
- One study (n=43) showed a supplement of 250kcal, 28.4g carbohydrates, 20g protein, 3g arginine, 7g fat, vitamins, minerals in addition to a standard hospital diet is potentially more clinically harmful than a standard hospital diet and placebo for adverse events related to the product (very low quality).
- One study (n=43) showed a supplement of 250kcal, 28.4g carbohydrates, 20g protein, 3g arginine, 7g fat, vitamins, minerals in addition to a standard hospital diet may be more clinically harmful than a standard hospital diet and placebo for adverse events related to the product (very low quality).
- One study (n=43) showed a supplement of 250kcal, 28.4g carbohydrates, 20g protein, 3g arginine, 7g fat, vitamins, minerals in addition to a standard hospital diet may be more clinically harmful compared to a standard hospital diet and placebo for diarrhoea (very low quality).
- One study (n=43) showed there may be no clinical difference between a supplement of 250kcal, 28.4g carbohydrates, 20g protein, 3g arginine, 7g fat, vitamins, minerals in addition to a standard hospital diet compared to a standard hospital diet and placebo for nausea. The direction of the estimate of effect favoured the supplement (very low quality).
- One study (n=43) showed there may be no clinical difference between a supplement of 250kcal, 28.4g carbohydrates, 20g protein, 3g arginine, 7g fat, vitamins, minerals in addition to a standard hospital diet compared to a standard hospital diet and placebo for vomiting. The direction of the estimate of effect favoured the supplement (very low quality).
- No evidence was found for the following outcomes:
  - Time to complete healing (time to event data)
  - Rate of complete healing
  - Reduction in size of ulcer and volume of ulcer.
  - Proportion of people completely healed
  - Pain (pressure ulcer related)
  - Time in hospital

- Patient acceptability of supplements
- Mortality (all-cause)
- Health-related quality of life

5.2.5.1.3 Supplement of 500kcal, 18g protein, 0g fat, 72mg vitamin C and 7.5mg zinc in addition to a standard hospital diet versus standard hospital diet

- One study (n=11) showed there may be no clinical difference between a supplement of 500kcal, 18g protein, 0g fat, 72mg vitamin C and 7.5mg zinc in addition to a standard hospital diet and a standard hospital diet for reducing PUSH tool scores by week 3. The direction of the estimate of effect favoured the supplement (very low quality).
- No evidence was found for the following outcomes:
  - Time to complete healing (time to event data)
  - Rate of complete healing
  - Rate in change of size of ulcer
  - Reduction in size of ulcer and volume of ulcer.
  - Proportion of people completely healed
  - Pain (pressure ulcer-related)
  - Time in hospital
  - Patient acceptability of supplements
  - Side effects (nausea, vomiting, diarrhoea)
  - Mortality (all-cause)
  - Health-related quality of life

5.2.5.1.4 Supplement of 500kcal, 21g protein, 0g fat, 500mg vitamin C, 30mg zinc and 9g arginine and standard hospital diet versus standard hospital diet

- One study (n=11) showed a clinical benefit of a supplement of 500kcal, 21g protein, 0g fat, 500mg vitamin C, 30mg zinc and 9g arginine for reducing PUSH tool scores and standard hospital diet compared to a standard hospital diet alone (very low quality).
- No evidence was found for the following outcomes:
  - Time to complete healing (time to event data)
  - Rate of complete healing
  - Rate in change of size of ulcer
  - Reduction in size of ulcer and volume of ulcer.
  - Proportion of people completely healed
  - Pain (pressure ulcerrelated)
  - Time in hospital
  - Patient acceptability of supplements
  - Side effects (nausea, vomiting, diarrhoea)
  - Mortality (all-cause)
  - Health-related quality of life

5.2.5.1.5 Supplement of 500kcal, 21g protein, 0g fat, 500mg vitamin C, 30mg zinc and 9g arginine versus supplement of 500kcal, 18g protein, 0g fat, 72mg vitamin C and 7.5mg zinc in addition to standard hospital diet

- One study (n=11) showed a clinical benefit of a supplement of 500kcal, 21g protein, 0g fat, 500mg vitamin C, 30mg zinc and 9g arginine for reducing PUSH tool scores compared to a supplement of

500kcal, 18g protein, 0g fat, 72mg vitamin C and 7.5mg zinc in addition to a standard hospital diet (very low quality).

- No evidence was found for the following outcomes:
  - Time to complete healing (time to event data)
  - Rate of complete healing
  - Rate in change of size of ulcer
  - Reduction in size of ulcer and volume of ulcer.
  - Proportion of people completely healed
  - Pain (pressure ulcer related)
  - Time in hospital
  - Patient acceptability of supplements
  - Side effects (nausea, vomiting, diarrhoea)
  - Mortality (all-cause)
  - Health-related quality of life

5.2.5.1.6 Supplement of 4.38g protein, 2.23g fat, 15.62g carbohydrate, minerals and vitamins (per 100ml) and standard hospital diet versus standard hospital diet

- One study (n=50) showed there is potentially a clinical benefit for a supplement of 4.38g protein, 2.23g fat, 15.62g carbohydrate, minerals and vitamins (per 100ml) and standard hospital diet for complete healing of pressure ulcers when compared to a standard hospital diet (very low quality).
- One study (n=50) showed there is no clinical difference between a supplement of 4.38g protein, 2.23g fat, 15.62g carbohydrate, minerals and vitamins (per 100ml) and standard hospital compared to a standard hospital diet for reducing the mean ulcer size (cm2) (low quality).
- One study (n=50) showed a supplement of 4.38g protein, 2.23g fat, 15.62g carbohydrate, minerals and vitamins (per 100ml) and standard hospital diet may be clinically harmful for study-related adverse events when compared to a standard hospital diet (very low quality).
- No evidence was found for the following outcomes:
  - Time to complete healing (time to event data)
  - Rate of complete healing
  - Rate in change of size of ulcer
  - Pain (pressure ulcer related)
  - Time in hospital
  - Patient acceptability of supplements
  - Mortality (all-cause)
  - Health-related quality of life

5.2.5.1.7 Very high protein dietary formula (92 to 150gms/day) versus high protein dietary formula (57 to 90gms/day)

- One study (n=12) showed a very high protein dietary formula (92 to 150gms/day) is potentially more clinically effective for complete healing of pressure ulcers when compared to a high protein dietary formula (57 to 90gms/day) in long-term tube-fed people (very low quality).
- One study (n=12) reported a very high protein dietary formula (92 to 150gms/day) may be more clinically effective for reducing mean surface area (%) of pressure ulcers when compared to a high protein dietary formula (57 to 90gms/day) in long-term tube-fed people. No estimate of precision could be derived (very low quality).
- No evidence was found for the following outcomes:
  - Time to complete healing (time to event data)

- Rate of complete healing
- Rate in change of size of ulcer
- Pain (pressure ulcer related)
- Time in hospital
- Patient acceptability of supplements
- Side effects (nausea, vomiting, diarrhoea)
- Mortality (all-cause)
- Health-related quality of life

5.2.5.1.8 Supplement of 1000mg ascorbic acid in addition to standard hospital diet versus hospital diet and placebo

- Two studies (n=108) showed there may be no clinical difference between a supplement of 1000mg ascorbic acid in addition to standard hospital diet and hospital diet and placebo for complete healing of pressure ulcers. The direction of estimate of effect favoured the standard hospital diet and placebo group (very low quality).
- One study (n=85) reported there may be no difference between a supplement of 1000mg ascorbic acid in addition to standard hospital diet and hospital diet and placebo for time to complete healing of pressure ulcers (very low quality).
- One study (n=20) showed a hospital diet and placebo were more clinically effective than a supplement of 1000mg ascorbic acid in addition to standard hospital diet for reducing mean surface area (%) (very low quality).
- One study (n=88) reported there is possibly no clinical difference between a supplement of 1000mg ascorbic acid in addition to standard hospital diet and hospital diet and placebo for rate of mean reduction in ulcer size (cm2/week). The direction of the estimate of effect favoured either intervention (very low quality).
- One study (n=88) reported there is possibly no clinical difference between a supplement of 1000mg ascorbic acid in addition to standard hospital diet and hospital diet and placebo for rate of mean reduction in ulcer size (%). The direction of the estimate of effect favoured either intervention (very low quality).
- One study (n=88) reported there may be no clinical difference between a supplement of 1000mg ascorbic acid in addition to standard hospital diet and hospital diet and placebo for rate of mean reduction in ulcer size (cm2/week/%). The direction of the estimate of effect favoured either intervention (very low quality).
- One study (n=88) reported there is potentially no clinical difference between a supplement of 1000mg ascorbic acid in addition to standard hospital diet and hospital diet and placebo for rate of mean reduction in ulcer volume (cm^2/week/%). The direction of the estimate of effect favoured the supplement (very low quality).
- One study (n=88) reported there is potentially no clinical difference between a supplement of 1000mg ascorbic acid in addition to standard hospital diet and hospital diet and placebo for rate of mean healing velocity. The direction of the estimate of effect favoured the supplement (very low quality).
- One study (n=88) showed there may be no clinical difference between a supplement of 1000mg ascorbic acid in addition to standard hospital diet and hospital diet and placebo for mortality. The direction of the estimate of effect favoured the supplement (very low quality).
- No evidence was found for the following outcomes:
  - Time to complete healing (time to event data)
  - Rate of complete healing
  - Pain (pressure ulcer related)

- Time in hospital
- Patient acceptability of supplements
- Side effects (nausea, vomiting, diarrhoea)
- Health-related quality of life

5.2.5.1.9 Zinc sulphate versus placebo

- One study (n=13) showed zinc sulphate may be more clinically effective for complete healing than placebo (very low quality).
- One study (n=13) showed there may be no clinical difference between zinc sulphate and placebo for mean reduction in pressure ulcer volume. The direction of the estimate of effect favoured zinc sulphate (very low quality).
- No evidence was found for the following outcomes:
  - Time to complete healing (time to event data)
  - Rate of complete healing
  - Rate in change of size of ulcer
  - Pain (pressure ulcer related)
  - Time in hospital
  - Patient acceptability of supplements
  - Side effects (nausea, vomiting, diarrhoea)
  - Mortality (all-cause)
  - Health-related quality of life

5.2.5.1.10 Supplement of concentrated, fortified, collagen protein hydrolysate versus placebo

- One study (n=71) showed there is potentially no clinical difference between a supplement of concentrated, fortified, collagen protein hydrolysate when compared to placebo for reducing PUSH tool scores. The direction of the estimate of effect favours placebo (mean) (very low quality).
- One study (n=71) showed there is potentially no clinical difference between a supplement of concentrated, fortified, collagen protein hydrolysate when compared to placebo for reducing PUSH tool scores (%). The direction of the estimate of effect favours placebo (very low quality).
- One study (n=89) showed there may be no clinical difference between a supplement of concentrated, fortified, collagen protein hydrolysate when compared to placebo for all-cause mortality. The direction of the estimate of effect favoured the placebo (very low quality).
- No evidence was found for the following outcomes:
  - Time to complete healing (time to event data)
  - Rate of complete healing
  - Rate in change of size of ulcer
  - Reduction in size of ulcer and volume of ulcer.
  - Proportion of people completely healed
  - Pain (pressure ulcer related)
  - Time in hospital
  - Patient acceptability of supplements
  - Side effects (nausea, vomiting, diarrhoea)
  - Health-related quality of life

5.2.5.1.11 Ornithine alpha-ketoglutarate versus placebo

- One study (n=160) showed there is potentially no clinical difference between ornithine alpha-ketoglutarate and placebo for rate of complete healing of heel pressure ulcers (grade 2 or 3 pressure ulcers). The direction of the estimate of effect favoured ornithine alpha-ketoglutarate (very low quality).
- One study (n=160) showed no clinical difference between ornithine alpha-ketoglutarate and placebo for mean reduction in size (% reduction). The direction of the estimate of effect favoured ornithine alpha-ketoglutarate (very low quality).
- One study (n=160) showed no clinical difference between ornithine alpha-ketoglutarate and placebo for mean reduction in size (mean surface area reduction). The direction of the estimate of effect favoured ornithine alpha-ketoglutarate (very low quality).
- One study (n=160) showed no clinical difference between ornithine alpha-ketoglutarate and placebo for 90% reduction in heel pressure ulcers. The direction of the estimate of effect favoured ornithine alpha-ketoglutarate (low quality).
- One study (n=165) showed there may be no clinical difference between ornithine alpha-ketoglutarate and placebo for mortality. The direction of the estimate of effect favoured the placebo (very low quality).
- No evidence was found for the following outcomes:
  - Time to complete healing (time to event data)
  - Rate in change of size of ulcer
  - Proportion of people completely healed
  - Pain (pressure ulcer related)
  - Time in hospital
  - Patient acceptability of supplements
  - Side effects (nausea, vomiting, diarrhoea)
  - Health-related quality of life

5.2.5.1.12 Arginine 4.5g and Arginine 9g

- One study (n=23) reported there may be no difference between arginine 4.5g and arginine 9g for reducing PUSH tool scores. The direction of estimate of effect favoured arginine 4.5g. The clinical importance is unknown (very low quality).
- One study (n=unclear) reported there may be no difference between arginine 4.5g in malnourished patient and arginine 9g in malnourished people for reducing PUSH tool scores. The direction of estimate of effect favoured arginine 9g. The clinical importance is unknown (very low quality).
- One study (n=unclear) reported there may be no difference between arginine 4.5g in non-malnourished patient and arginine 9g in non-malnourished people for reducing PUSH tool scores. The direction of estimate of effect favoured arginine 9g. The clinical importance is unknown (very low quality).
- No evidence was found for the following outcomes:
  - Time to complete healing (time to event data)
  - Rate of complete healing
  - Rate in change of size of ulcer
  - Reduction in size of ulcer and volume of ulcer.
  - Proportion of people completely healed
  - Pain (pressure ulcer related)
  - Time in hospital

- Patient acceptability of supplements
- Side effects (nausea, vomiting, diarrhoea)
- Mortality (all-cause)
- Health-related quality of life

5.2.5.1.13 Nutritional formula with fish oil versus macronutrients and an isocaloric control formula

- One study (n=40) reported there may be no difference between a nutritional formula with fish oil and macronutrients and an isocaloric control formula for increasing mean PUSH tool scores. The direction of estimate of effect favoured the isocaloric control formula. The clinical importance is unknown (very low quality).
- No evidence was found for the following outcomes:
  - Time to complete healing (time to event data)
  - Rate of complete healing
  - Rate in change of size of ulcer
  - Reduction in size of ulcer and volume of ulcer.
  - Proportion of people completely healed
  - Pain (pressure ulcer related)
  - Time in hospital
  - Patient acceptability of supplements
  - Side effects (nausea, vomiting, diarrhoea)
  - Mortality (all-cause)
  - Health-related quality of life

5.2.5.2 Economic (adults)

- One cost-effectiveness analysis from Japan found that nutritional supplementation dominates standard hospital diet in the treatment of pressure ulcers (reduced costs and fewer pressure ulcer days).This study was deemed to be partially applicable and had potentially serious limitations.

5.2.5.3 Clinical (neonates, infants, children and young people)

No evidence was identified.

5.2.5.4 Economic (neonates, infants, children and young people)

No evidence was identified.

5.3 Recommendations and link to evidence

5.3.1 Adults

Recommendations	7. **Offer adults with a pressure ulcer a nutritional assessment by a dietitian or other healthcare professional with the necessary skills and competencies.** 8. **Offer nutritional supplements to adults with a pressure ulcer who have a nutritional deficiency.** 9. **Do not offer nutritional supplements to treat a pressure ulcer in adults whose nutritional intake is adequate** 10. **Provide information and advice to adults with a pressure ulcer and where appropriate, their family or carers, on how to follow a balanced diet to maintain an adequate nutritional status, taking into account energy, protein and micronutrient requirements**
Relative values of different outcomes	The GDG identified that the proportion of people with pressure ulcers completely healed, time to complete healing, reduction in size and volume and rate of reduction in size and volume of pressure ulcers were the most critical outcomes to inform decision making. The following were considered to be important outcomes; side effects, health related quality of life, time in hospital, mortality and acceptability of treatment.
Trade-off between clinical benefits and harms	The evidence was limited. Thirteen studies were identified but each of these looked at different supplement mixes. There was no strong evidence of a change in critical or important outcomes associated with the use of nutritional supplementation. A nutritional supplement of 500 calories, 34g protein, 6g arginine, 500mg vitamin C, 18mg zinc showed some benefit for complete healing, a higher mean reduction in the size of pressure ulcer and lower mortality rate. It was unclear if the population of this study had any nutritional deficiency. A nutritional supplement of 250 calories, 28.4g carbohydrates, 20g protein, 3g arginine, 7g fat, vitamins and minerals showed no benefits, showed a clinical harm from adverse events, including a higher incidence of diarrhoea, in a non-malnourished population. A nutritional supplement of 500 calories, 18g protein, 0g fat, 72mg vitamin C and 7.5mg zinc showed no benefit in PUSH tool scores. The PUSH tool monitors the length, width, amount of exudate and tissue type of a pressure ulcer, and is a method of predicting pressure ulcer healing in an elderly or spinal injured population. It was not clear if the population of this study had any nutritional deficiency. A nutritional supplement including 500 calories, 21g protein, 0g fat, 500mg vitamin C, 30mg zinc and 9g arginine showed a lower PUSH score (with lower being more beneficial). These supplements were all in addition to the standard hospital diet and compared to the standard hospital diet. When the 2 supplements were compared there to each other there was a clinical benefit of the supplement which included 500 calories, 21g protein, 0g fat, 500mg vitamin C, 30mg zinc and 9g arginine for reduction in PUSH tool scores.

	A study of tube fed people who received 4.38g protein, 2.23g fat, 15.6g carbohydrate, minerals and vitamins per 100ml in addition to the standard hospital diet showed a higher incidence of complete healing in the supplement group. However, the group also had a higher incidence of adverse events. A very high protein formula (92 to 150gm/day) given in addition to the standard hospital diet was clinically beneficial compared to an additional high protein formula (57g to 90 g per day) in long-term tube-fed people. However, it was unclear if the population of this study had any nutritional deficiency and the GDG were concerned that the clinical benefits were dependant on the protein content of the hospital diet. The study also had a very small sample size. Two studies were meta-analysed for 1000mg ascorbic acid supplementation in addition to the standard hospital diet in a population of people whom mostly had nutritional deficiencies. No difference was found except for a higher reduction in the surface area of the pressure ulcer in the group who received nutritional supplementation. When zinc sulphate 220mg was compared to placebo in a population of people with spinal cord injuries, in whom it was unclear if there was any nutritional deficiency, there was less complete healing of pressure ulcers in the zinc sulphate group. Yet, another study of zinc sulphate 200mg 3 times per day compared to placebo (lactose) showed a higher mean reduction in pressure ulcer volume. The GDG were uncertain of the clinical benefit of this outcome, particularly as these studies had very small sample sizes. There were no differences between a concentrated, fortified, collagen protein hydrolysate nutritional supplement compared to placebo, in an overweight population with no indication of nutritional deficiency. There were no differences for ornithine alpha-ketoglutarate compared to placebo and it was unclear if the population were nutritionally deficient. There were no differences reported between arginine 4.5g and arginine 9g for reducing PUSH tool scores. The GDG considered there to be insufficient evidence to support the use of nutritional supplements for people with press The GDG developed a corresponding recommendation to highlight that people who have a pressure ulcer should receive an assessment to identify the presence of any nutritional deficiency. The GDG considered that all people who have a pressure ulcer would benefit from maintaining an adequate nutritional status and information should be provided to these groups to help encourage this.
Economic considerations	The GDG considered 1 economic analysis from Japan which found that nutritional supplementation dominated a standard hospital diet amongst tube-fed, bed-ridden people with stage 3 to 4 pressure ulcers. However it was unclear whether the paitents were nutritionally deficient. The applicability of this study is limited as the study was conducted in Japan. The GDG discussed that the correction of nutritional deficiency is best practice and is an issue of patient safety. The GDG agreed that it was important for people to be provided with adequate nutrition, as the correction of nutritional deficiency has benefits which extend far beyond the treatment of pressure ulcers. The GDG considered the UK costs of nutritional supplements and agreed that whilst the list prices documented were not negligible, the actual prices paid for nutritional

	supplements were very low especially in hospitals, and the correction of nutritional deficiency can be achieved at low cost particularly with a 'food first' approach. The GDG felt there was limited additional benefit to providing extra nutritional supplementation where nutritional status was adequate and intake was meeting any additional losses. It was felt that, given the (albeit small) costs, it would not be cost-effective to do so. The GDG discussed the resource implications of nutritional assessment by a dietician or healthcare professional with the necessary skills and competencies. It was recognised that there is an economic implication associated with healthcare professional time, but that this was necessary in order to promote the efficient use of resources; that is, it is necessary to establish an individual's nutritional status in order to plan treatment accordingly. The GDG agreed that the cost of assessing the patient would be offset by efficiencies gained through appropriate treatment strategies, leading to reduced treatment costs overall, and improvements in quality of life. The additional costs of providing information are thought to be small, and justified by potentially large gains.
Quality of evidence	Overall, the quality of evidence for the effects of nutritional supplements for the management of pressure ulcers was of low quality because of study limitations. The GDG acknowledged that evidence was often difficult to interpret as nutritional interventions are rarely used in isolation and in clinical practice, are used with appropriate dressings, repositioning and pressure redistributing devices. There was also limited information about liquid losses from the pressure ulcer that would need replacing such as levels of exudative loss. The GDG highlighted that studies of nutritional supplementation do not always consider the consumption of supplements and overall calorie intake. These recommendations were based on GDG informal consensus after reviewing the evidence for nutritional supplements.
Other considerations	The GDG clearly stated that it was important people were provided with adequate nutrition, regardless of the effectiveness of nutritional supplementation in treating pressure ulcers. However, if people did not have a nutritional deficiency then there was limited evidence for additional nutritional supplementation as long as ongoing losses in energy and protein from exudate are also met. The GDG felt that people should be offered a nutritional assessment from a qualified practitioner so that a person's nutritional status can be determined. They also noted the importance of giving peopleand carers information and advice regarding nutrition so that they can ensure they are meeting their nutritional requirements and replacing any losses from the pressure ulcer. The GDG highlighted the importance of ensuring that people who are nutritionally deficient should be provided with appropriate nutritional supplementation to provide the correct level of nutrition, in line with NICE clinical guideline 32 'Nutrition support in adults: Oral nutrition support, enteral tube feeding and parenteral nutrition[130]. Recommendations on the provision of information to patients and carers can be found in NICE clinical guideline 138 'Patient experience in adult NHS services: improving the experience of care for people using adult NHS services.'

Recommendations	11. Do not offer subcutaneous or intravenous fluids to treat pressure ulcers in adults whose hydration status is adequate.
Relative values of different outcomes	The GDG identified that the proportion of people with pressure ulcers completely healed, time to complete healing, reduction in size and volume and rate of reduction in size and volume of pressure ulcers were the most critical outcomes to inform decision making. Side effects, health related quality of life, time in hospital, mortality and acceptability of treatment were considered important outcomes.
Trade off between clinical benefits and harms	No evidence was found for hydration for the treatment of pressure ulcers. The GDG felt that if a person's hydration is adequate then they would not require a hydration strategy to alter how they are being hydrated. The GDG also considered that it was unlikely that there would be any benefits to the provision of additional fluids in people with an adequate hydration status and that it was possible that the provision of additional fluids could result in harms to the individual. The GDG noted that medical opinion should be sought by any healthcare professional that has identified a person has less than adequate hydration status.
Economic considerations	Extra resources would be required to provide additional hydration strategies to individuals with adequate hydration. Given that the GDG felt that such additional strategies were not required, it would not be cost-effective to offer these.
Quality of evidence	This recommendation was based on GDG consensus as there was no evidence found.
Other considerations	There were no other considerations.

5.3.2 Neonates, infants, children and young people

Recommendations	12. Offer an age-related nutritional assessment to neonates, infants, children and young people with a pressure ulcer. This should be performed by a paediatric dietitian or other healthcare professional with the necessary skills and competencies.
Relative values of different outcomes	The GDG identified that the proportion of people with pressure ulcers completely healed, time to complete healing, reduction in size and volume and rate of reduction in size and volume of pressure ulcers were the most critical outcomes to inform decision making.
Trade-off between clinical benefits and harms	The GDG developed the statement that 'Healthcare professionals should offer neonates, infants, children and young people with pressure ulcers a suitable age related nutritional assessment' which was accepted during round 1 of the Delphi consensus survey at a consensus level of 100%. The GDG therefore used the statement to develop a recommendation that all neonates, infants, children and young people who have developed a pressure ulcer should have a suitable age related nutritional assessment. The GDG considered that it was important for healthcare professionals to identify whether any child who has had a pressure ulcer has an adequate nutritional intake, as correction of nutritional deficiency may improve the ability of the body to heal. The GDG considered that there is likely to be significant benefits to providing a nutritional assessment to this population, in the subsequent ability to heal, as well as other related improvements associated with identifying nutritional deficiencies. The GDG felt that any resource implications of providing an assessment would be outweighed by the subsequent benefits of identifying deficiency, in terms of both pressure ulcer treatment and other related health outcomes.

	Comments received from the Delphi consensus panel provided further support for the provision of a nutritional assessment for all people who have developed a pressure ulces, highlighting that the loss of protein from the wound may result in a decreased ability to heal and suboptimal nutritional status.
Economic considerations	There may be cost-implications of offering a nutritional assessment to neonates, infants, children and young people with pressure ulcers. However, such assessment will promote efficient allocation of resources, as it will allow nutritional supplementation to be targeted towards those who require it most. The GDG agreed that the cost of assessing the patient would be offset by efficiencies gained through appropriate treatment strategies, leading to reduced treatment costs overall, and improvements in quality of life. The GDG noted that nutritional status was a crucial issue of patient safety, and would have potentially large quality of life gains which would extend far beyond the treatment of pressure ulcers.
Quality of evidence	No evidence was identified on the use of nutritional interventions or hydration strategies for the treatment of pressure ulcers (randomised trials or cohort studies) in neonates, infants, children or young people. The GDG therefore used formal consensus methods (modified Delphi consensus) to develop statements to help inform the recommendation. One statement was included in Round 1 of the Delphi consensus survey, where it reached 100% consensus agreement.
Other considerations	Members of the Delphi consensus panel highlighted that healthcare professionals should take into account weight and ethnicity when assessing nutritional status.

Recommendations	**13. Discuss with a paediatric dietitian (or other healthcare professional with the necessary skills and competencies) whether to offer nutritional supplements specifically to treat pressure ulcers in neonates, infants, children and young people whose nutritional intake is adequate.** **14. Offer advice on a diet that provides adequate nutrition for growth and healing in neonates, infants, children and young people with pressure ulcers.** **15. Discuss with a paediatric dietitian whether to offer nutritional supplements to correct nutritional deficiency in neonates, infants, children and young people with pressure ulcers.**
Relative values of different outcomes	The GDG identified that the proportion of people with pressure ulcers completely healed, time to complete healing, reduction in size and volume and rate of reduction in size and volume of pressure ulcers were the most critical outcomes to inform decision making.
Trade-off between clinical benefits and harms	The GDG developed 2 statements for inclusion in the Delphi consensus survey: 'Healthcare professionals should offer neonates, infants, children and young people with pressure ulcers, who are nutritionally deficient, correction of their nutritional deficiency' and 'Healthcare professionals should ensure that neonates, infants, children and young people with pressure ulcers have a diet that maintains adequate nutritional status, including that required for growth and wound healing'. The former statement was agreed in Round 1 of the Delphi consensus, at a consensus agreement level of 94%. The latter was also agreed in Round 1 of the Delphi consensus, at a level of 99%. The GDG agreed that for neonates, infants, children and young people who have

	pressure ulcers and who received a nutritional assessment identifing a nutritional deficiency, healthcare professionals should aim to correct the deficiency. The GDG considered that there were benefits in terms of pressure ulcer treatment and other health related outcomes to the correction of nutritional deficiency and that any harms, for example possible resource implications, were likely to be outweighed. A recommendation was therefore developed to highlight that any neonate, infant, child or young person who has a pressure ulcer should be provided with a diet which provides suitable nutrition to allow for growth and healing, as these requirements may be increased in these individuals. Qualitative responses gathered during Round 1 of the survey highlighted the importance of correcting a nutritional deficiency in conjunction with someone with appropriate expertise, namely a dietitian, with experience of working with the relevant population (either a paediatric dietitian or a dietitian with appropriate experience of working with neonates, infants, children or young people). The GDG felt that this was appropriate and that involving a paediatric dietitian was likely to be necessary as many healthcare professionals would not have relevant expertise to provide suitable nutritional supplementation. A recommendation was therefore developed to highlight that before offering correction of a nutritional deficiency in neonates, infants, children and young people with pressure ulcers, there should be a discussion with a dietitian with suitable experience of working with these populations. The GDG also discussed whether neonates, infants, children and young people with an adequate nutritional status, but who have developed a pressure ulcer, should be offered further nutritional supplementation, specifically for treatment of the pressure ulcer. The GDG felt that there should be discussed with a dietitian before providing further supplementation in this situation. A recommendation was therefore developed to reflect this.
Economic considerations	The GDG considered the UK costs of nutritional supplements and agreed that whilst the list prices documented were not negligible, the actual prices paid for nutritional supplements were very low, and correction of nutritional deficiency can be achieved at low cost. Discussion with a suitable dietician will allow the correct nutrients to be provided, and is expected to promote clinically and cost-effective treatment. The GDG discussed that ensuring neonates, infants, children and young people are offered a diet adequate nutrition for growth and healing is best practice and is an issue of patient safety. The GDG highlighted that provision of adequate nutrition has benefits which extend far beyond treatment of pressure ulcers.
Quality of evidence	No evidence was identified on the use of nutritional interventions or hydration strategies for the treatment of pressure ulcers(randomised trials or cohort studies) in neonates, infants, children or young people. The GDG therefore used formal consensus methods (modified Delphi consensus) to develop statements to help inform the recommendation. Two statements were included in Round 1 of the survey, where they reached 94% and 99% consensus agreement.
Other considerations	Panel members highlighted that some clinical conditions or situations (for example, those entering end of life care) may not benefit from the correction of nutritional deficiency and in these situations, care should be considered on a case by case basis.

Recommendations	**16. Assess fluid balance in neonates, infants, children and young people with pressure ulcers.**

	17. Ensure there is adequate hydration for age, growth and healing in neonates, infants, children and young people. If there is any doubt, seek further medical advice.
Relative values of different outcomes	The GDG identified that the proportion of people with pressure ulcers completely healed, time to complete healing, reduction in size and volume and rate of reduction in size and volume of pressure ulcers were the most critical outcomes to inform decision making.
Trade-off between clinical benefits and harms	The GDG developed 1 statement for inclusion in the Delphi consensus survey: 'Healthcare professionals should not offer hydrational supplementation to neonates, infants, children or young people at risk of developing pressure ulcers, where hydrational intake is adequate for developmental age and associated fluid losses. The statement was not agreed in Round 1 of the Delphi consensus. The GDG discussed the qualitative responses received during Round 1 and identified that there was general agreement on the principles underlying the statement. The GDG therefore amended the statement to clarify that the statement refers to any supplementation specifically for pressure ulcer prevention in those neonates, infants, children and young people who have sufficient hydration. The statement was therefore amended to 'Healthcare professionals should ensure that neonates, infants, children and young people have adequate hydration for age, growth and healing. Where there is any doubt, seek medical advice.' The statement was included in Round 2 of the Delphi consensus and was accepted by the panel. Qualitative responses received during Round 2 of the survey generally agreed that the statement highlighted that over-hydration was often considered to be a problem. Comments also noted that any assessment of fluid balance should account for any additional fluid requirements needed for wound healing. As such, the GDG discussed these issues and felt that 2 recommendations were needed, to ensure that neonates, infants, children and young people who have developed pressure ulcers are offered an assessment of fluid balance and to highlighted that anyone who has a pressure ulcer is provided with adequate hydration to account for their age, growth and healing. The GDG felt that where inadequate hydration was identified in an assessment, all healthcare professionals should seek further advice from a suitable healthcare professional, likely to be a medical doctor. The GDG therefore amended the recommendation to reflect this and did not feel that it was appropriate to develop a recommendation on the correction of any fluid deficiency.
Economic considerations	There may be cost-implications of assessing fluid balance and ensuring adequate hydration in those with pressure ulcers. However, such assessment will promote efficient allocation of resources, as it will allow hydration strategies to be targeted towards those who require them. In addition, the GDG discussed that ensuring adequate hydration for growth and healing is best practice and is an issue of patient safety, and would have potentially large quality of life gains which would extend far beyond the treatment of pressure ulcers.
Quality of evidence	No evidence was identified on the use of nutritional interventions or hydration strategies for the treatment of pressure ulcers (randomised trials or cohort studies) in neonates, infants, children or young people. The GDG therefore used formal consensus methods (modified Delphi consensus) to develop statements to help inform the recommendation. 1 statement was included in Round 1 of the Delphi consensus survey that reached 47% consensus agreement. The statement was amended and included in Round 2 of the survey, where it was agreed at a consensus level of 97%.
Other considerations	Recommendations on the use of intravenous fluids in neonates, infants, children and

	young people will be included in the NICE clinical guideline 'Intravenous fluids in children', currently in development.

6 Pressure redistributing devices

6.1 Introduction

Pressure relieving and redistributing devices are widely accepted methods of both preventing and treating pressure ulcers. A vast range of devices, including different types of mattresses, overlays, cushions and seating, are available which vary considerably in both cost and mechanism. Generally, these devices work by reducing pressure, friction or shearing forces and may be unpowered and considered 'low-tech' or 'static', or powered devices which are 'high-tech'.

The selection of device by the healthcare professional is likely to depend upon the person's mobility, the result of skin assessment, the severity and site of the pressure ulcer, weight, staff availability and skill. The choice of a pressure redistributing device by a healthcare professional should also account for a person's wishes and tolerability of the device.

It is generally accepted that these devices should be used in conjunction with other treatment strategies such as repositioning and management of the pressure ulcer (for example, by use of an appropriate dressing).

The GDG were interested in what the most clinically and cost effective pressure redistributing devices are for the management of pressure ulcers.

Recommendations on the use of pressure redistributing devices for the prevention of pressure ulcers can be found in part 1 of the guideline.

6.2 Review question: What are the most clinically and cost effective pressure redistributing devices for the management of pressure ulcers?

For full details see review protocol in Appendix D.

6.2.1 Clinical evidence (adults)

A Cochrane Review looking at support surfaces for treating pressure ulcers was retrieved from the search and this was used as the basis for our review. It included 17 randomised trials[6,29,44,51,55-57,59,73,89,123,126,136,145,161,162,180]. Two additional randomised trials were found via systematic searches and were used to update the Cochrane review.[39,108] Evidence from the RCTs are summarised in the clinical GRADE evidence profile below. See also the study selection flow chart in Appendix D, forest plots in Appendix I, study evidence tables in Appendix G and exclusion list in Appendix J.

Various types of devices were used to redistribute pressure, and for the purposes of the Cochrane review, these were categorised as 'low-tech' (non-powered), constant low pressure (CLP), high-tech and other devices.

The 'low-tech' CLP devices included:

- Standard foam mattresses
- Alternative foam mattresses or overlays
- Gel-filled mattresses or overlays
- Fibre-filled mattresses or overlays
- Air-filled mattresses or overlays
- Water-filled mattresses or overlays

- Bead-filled mattresses or overlays
- Sheepskins

The high-tech support surfaces included:

- Alternating-pressure mattresses or overlays
- Air-fluidised beds
- Low-air-loss beds

The other support surfaces included:

- Turning beds or frames
- Operating table overlays
- Wheelchair cushions

The Cochrane Review notes that this classification has since been updated by the National Pressure Ulcer Advisory Panel (EPUAP & NPUAP 2009) and will be considered in future updates of their review.

Summary of included studies

Study	Intervention/comparison	Population	Outcomes	Length of study
Allman 1987[6]	Air-fluidised therapy (CLINITRON) repositioned every 4 hours versus conventional treatment (including 2-hourly turns, heel and elbow protectors, alternating-pressure mattresses).	People undergoing surgery aged 18 or over with pressure ulcers of all stages. Graded using the Shea staging system.	• Median change in total surface area of ulcers; improvement in condition of pressure ulcer; pain response.	Mean 13 days follow-up (range 4-77 days).
Branom 2001[29]	PressureGuard CFT (constant force therapy) (non-powered mattress) versus LAL mattress.	People in hospital from long term and sub-acute care centre specialising in ventilator-dependent adults and those with extensive wound care needs. Bedridden adults with a pressure ulcer at grade 3 or 4 on trunk or pelvis (classification system not reported).	• Meeting the goals of pressure ulcer treatment as determined by medical team (including wound closure, maintenance of condition and preparation for flap). • The rate of pressure ulcer healing over 8 weeks.	8-week follow-up.
Caley 1994[38]	LAL bed (Monarch, Mediscus) versus LAL overlay.	People in acute care with existing pressure ulcers.	• Median change in pressure ulcer area	Average 24-day follow-up.
Cassino 2013[39]	Three-dimensional overlay (AIARTEX), made of 3-D macro-porous material vs dry viscoelastic polyurethane polymer overlay (AKTON)	Long-term care patients	• Complete healing; improved; unchanged/worsened; suspension due to worsening; suspension due to intolerance; mortality; comfort	12 weeks
Clark 1998[44]	ProActive 2 cushion (Pegasus) (cushion for day chairs and wheelchairs, seating automatically adjusts to an individual's weight) versus ROHO cushion (dry flotation system). All individuals had a Pegasus Airwave System in bed.	Elderly adults in 2 acute care hospitals and 2 nursing homes. Grade 2 pressure ulcers or above, classification system not reported.	• Number of pressure ulcers healed completely; rate of healing (cm^2/day); rate of healing (cm^3/day).	Average 58.6 days (ProActive and 43.73 days (ROHO).

Study	Intervention/comparison	Population	Outcomes	Length of study
Day 1993[51]	Air suspension bed (Therapulse, Kinetic concepts); foam mattress overlay (Geomatt, SpanAmerica). Wound care standardised for 2 groups.	Hospitalised adults with existing grade 2-4 pressure ulcers, graded using the NPUAP classification system.	• Mean pressure ulcer size (initial minus end) divided into grade 2 and grade 3/4 ulcers; mean comfort scores.	7-day follow-up.
Devine 1995[55]	Alternating-pressure mattress (Nimbus I) (modular, with rows of figure-of-8 shaped cells; 2 sets of cells are inflated and deflated over 10 minute cycle) versus alternating-pressure mattress (Pegasus Airwave) (double layer mattress with a 3-cell alternating cycle lasting 7.5 minutes). All participants were subject to the standard hospital protocol for wound dressing; details of this were not provided.	Elderly adults in hospital with pressure ulcers of grade 2 or above. The classification system used was not specified.	• Complete healing at 4 weeks; comfort; median rate of reduction in area (cm^2/day); withdrawal rates by group and reasons for withdrawal.	4-week follow-up.
Evans 2000[56]	Alternating-pressure mattress replacement system (APMRS) (Nimbus 3) versus alternating-pressure mattress replacement system (APMRS) for adults in hospital (P.Biwave, P.Airwave.P.Cairwave or AlphaXCell) or alternating-pressure mattress overlay (AlphaXCell or Quattro) for people in a nursing home. Turning and wound care was standardised for 2 groups.	People in a hospital or nursing home, aged over 65 years with either grade 2 or 3 pressure ulcer (classification system not reported), or grade 2 pressure ulcer and difficulty to reposition in bed, unable to tolerate 30 degree tilt, unable to move in bed, in bed for over 20 hours or 24 hours, over 108kg and bed-bound or who have undergone spinal anaesthetic.	• Absolute and relative reduction in pressure ulcer surface area; comfort.	2-week follow-up period.
Ferrell 1993[59]	LAL bed (KINAIR) versus 10cm convoluted foam overlay on top of standard foam	Older adults in an elderly nursing home with	• Rate of healing; pressure ulcer surface area was traced	Median follow-up of 33 days (LAL group)

Study	Intervention/comparison	Population	Outcomes	Length of study
	mattress .Both groups had similar co-interventions as per standard care that is mobilisation as much as possible; 2-hourly turning during waking hours; avoidance of head-of-bed elevation; avoidance of dragging people on sheets; nutritional support; infection control.	multiple medical problems, and with trunk or trochanter pressure ulcers. Grade 2 pressure ulcers or above (Shea grading system).	twice/week on plastic film and area measured using planimetry; ulcers completely healed (covered with epithelium).	and 40 days (foam mattress).
Groen 1999[73]	Foam replacement mattress (3 layers of polyurethane foam designated as comfort, load-distributing and support layers) versus Secutex water mattress (placed on top of standard hospital mattress, 3 PVC sections holding 26 litres water each, with heating element).Standard turning protocol (every 2-3 hour) for both groups.	People in a nursing home, aged over 59 years with a pressure ulcer on trunk, grade 3 (superficial cutaneous or subcutaneous necrotic) or grade 4 (deep subcutaneous necrotic). The classification system used was not reported.	• Proportion with healed pressure ulcers at 4 weeks; mean pressure ulcer severity score at 4 weeks.	4-week follow-up.
Keogh 2001[89]	Profiling bed with a pressure reducing foam mattress or cushion versus flat-based bed with a pressure relieving or redistributing mattress or cushion.	People from 2 surgical and 2 medical wards; over 18 years old; Waterlow score of 15-25; tissue damage no greater than grade 1 (EPUAP grading system).	• Proportion with healed grade 1 pressure ulcers.	5-10 days follow-up.
Makhsous 2009[108]	Wheelchair cushion equipped with an individualised cyclic pressure-relief protocol versus regular wheelchair cushions. Treatment was specific to the individual and a variety of wound care modalities applied when required (topical wound dressings eg wound gel, hydrocolloid, alginate, foam and moisture barrier) also	Wheelchair users with spinal cord injury (paraplegia or tetraplegia) with existing stage 2 or 3 pressure ulcers (classification system not specified) in the sacral and/or ischial area.	• Healing of pressure ulcers; healing rate of pressure ulcers; PUSH score improvement; % surface area healing; % PUSH score improvement.	30 days follow-up.

Study	Intervention/comparison	Population	Outcomes	Length of study
	silver antimicrobial dressings and negative pressure wound therapy.			
Mulder 1994[123]	Air suspension bed (Therapulse, Kinetic concepts) (a pulsating air suspension therapy – cushions alternatively inflate and deflate but classed as LAL rather than AP) versus convoluted foam mattress overlay. Wound care and repositioning standardised for both groups.	People in a nursing home with grade 3-4 pressure ulcers (International Association of Enterostomal Therapists staging system).	• Wound closure; pressure ulcer improvement (pressure ulcer reduced by 1 grade or more, including healed completely).	Maximum 12-weeks' follow-up or until ulcers healed, whichever came first.
Munro 1989[126]	Air-fluidised bed (Clinitron) versus standard care. The bed/mattress in the standard care group was not described. Sheepskins or gel pads were placed beneath ulcer areas. Standard care involved positioning and massage.	Males with grade 2 or 3 pressure ulcers (classification system not specified), expected to remain in hospital for at least 15 days.	• Change in mean pressure ulcer area (mm^2); individuals' perception of pain; patient satisfaction.	15-day follow-up.
Nixon 2006[136]	Alternating-pressure overlay within 24 hours of admission versus alternating-pressure mattress within 24 hours of admission.	Adults over 55 years of age, from vascular, orthopaedic, medical or care of the elderly wards with an expected length of stay at least 7 days and Braden score of 1 or 2, or an existing grade 2 pressure ulcer (grading system not specified).	• Proportion of people developing a new pressure ulcer of grade 2 or above; time to development of new pressure ulcers; proportion of participants developing a new pressure ulcer within 30 days; healing of existing pressure ulcers; patient acceptability; adverse events.	30-day follow-up.
Osterbrink 2005[145]	Repose device versus small cell versus large cell.	Participants recruited from aged care facility, acute care hospitals and home care setting, over 18 years old, with at least 1 grade 2 pressure ulcer at any bony prominence (EPUAP classification). If	• Pressure ulcer healing success; weekly changes in pressure ulcer (ulcer size, grade, wound bed, edge appearance and local treatment).	Follow-up time as long as clinical circumstances allowed. Maximum duration 42 days.

Study	Intervention/comparison	Population	Outcomes	Length of study
		recruited from hospital, must have been nursed on care of the elderly, neurological or surgical units.		
Russell 2000[160]	Two types of alternating cell mattress systems with pressure-relieving cushions: Huntleigh Nimbus 3 with Aura cushion and 4-hourly turning versus Pegasus Cairwave Therapy System with Proactive 2 seating cushion and 8-hourly turning.	Individuals from care of the elderly units with pressure ulcers of grade 2 and above (Torrance classification system). Average age 83.9 and 84.6 years in the 2 groups.	• Pressure ulcer healing: all types, and divided into heel and sacral pressure ulcers at 12 and 18 months.	18-month follow-up.
Russell 2003[162]	Alternating-pressure, multicell mattress with 10 minute cycle time (Nimbus 3) versus fluid overlay mattress (RIK static). All adults had standard 4-hourly re-positioning, but could have additional turning at the individual's request.	Adults with grade 1 or 2 pressure ulcers (EPUAP classification) admitted to hospital. Mean age 80 years. Baseline Waterlow scores 21.8 and 21.3 in groups 1 and 2 respectively and baseline Burton scores 14.6 and 14.2.	• Improved pressure ulcer response; length of hospital stay.	Length of follow-up unclear, but presumably until discharge from enrolment hospital.
Strauss 1991[180]	Home air-fluidised therapy (CLINITRON) when grade 3 or 4 prsesure ulcers present, plus the consultative and technical services of a visiting nurse specialist versus conventional or standard therapy, individual specific and prescribed (n=50), but included alternating –pressure pads, air-filled mattresses, water-filled mattresses, high density foam pads.	People: with at least 1 grade 3 or 4 pressure ulcer (Shea classification); who would probably require future hospitalisation for the pressure ulcer; with severely limited mobility; for who home air-fluidised therapy was a practical option, likely to comply, live at least 1 year; aged	• Pressure ulcers classified by blinded observers as improved; unchanged; worse; or not accessible; pressure ulcer-related hospitalisations and costs per patient; pressure ulcer-related hospital days per person.	36-week follow-up

Study	Intervention/comparison	Population	Outcomes	Length of study
		16 years or over.		

6.2.1.1 Low tech constant pressure devices

Table 42: Clinical evidence profile: water mattress overlay versus low-tech mattress

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Water mattress overlay	Low-tech mattress	Relative (95% CI)	Absolute	Quality	Importance
Proportion of people with pressure ulcers completely healed at 4 weeks – grade 3 ulcers (no classification system specified), people in a nursing home, 4-week follow-up[73]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	27/60 (45%)	29/60 (48.3%)	RR 0.93 (0.63 to 1.37)	34 fewer per 1000 (from 179 fewer to 179 more)	Very low	Critical
							-	48.3%		34 fewer per 1000 (from 179 fewer to 179 more)		
Percentage reduction in pain (change values)– grade 3 ulcers (no classification system specified), people in a nursing home, 4-week follow-up[73]												
1	Randomised trial	Very serious[a, d]	No serious inconsistency	No serious indirectness	Very serious[c]	None	35.9%	16.2%	MD 19.7% higher	-	Very low	Important
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate of reduction in size of pressure ulcers												

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Water mattress overlay	Low-tech mattress	Relative (95% CI)	Absolute	Quality	Importance
-	-	-	-	-	-	-	-	-	-	-	-	-
Reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital or NHS care												
-	-	-	-	-	-	-	-	-	-	-	-	-
Patient acceptability												
-	-	-	-	-	-	-	-	-	-	-	-	-
Side effects												
-	-	-	-	-	-	-	-	-	-	-	-	-
Mortality												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) Groen (1999) did not provide details of the randomisation method used. There was unclear allocation concealment and no blinding of outcome assessors was reported. There was insufficient reporting of incomplete outcome data and no details provided of type of analysis used. The authors report selectively and the details of the grading system used are not specified.

(b) The confidence interval crossed both MID points.

(c) There was not enough data to analyse in Revman.

(d) There were baseline differences in pain at start of trial (40% in water mattress overlay group and 20% for low-tech mattress group).–

Table 43: Clinical evidence profile: 3 dimensional macroporous overlay versus gel overlay

Quality assessment	No of patients	Effect	Quality	Importance

No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	3-D microporous overlay	Gel overlay	Relative (95% CI)	Absolute		
Proportion of people with pressure ulcers completely healed – people in long-term care - all grade of ulcers (EPUAP-NPUAP)[39]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	3/35 (8.6%)	5/37 (13.5%)	RR 0.63 (0.16 to 2.46)	50 fewer per 1000 (from 114 fewer to 197 more)	Very low	Critical
							-	13.5%		50 fewer per 1000 (from 113 fewer to 197 more)		
Mortality (all-cause) – people in long-term care - all grade of ulcers (EPUAP-NPUAP)[39]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	3/35 (8.6%)	7/37 (18.9%)	RR 0.45 (0.13 to 1.62)	104 fewer per 1000 (from 165 fewer to 117 more)	Very low	Important
							-	18.9%		104 fewer per 1000 (from 164 fewer to 117 more)		
Suspension due to worsening of pressure ulcers– people in long-term care - all grade of ulcers (EPUAP-NPUAP)[39]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[c]	None	9/35 (25.7%)	17/37 (45.9%)	RR 0.56 (0.29 to 1.09)	202 fewer per 1000 (from 326 fewer to 41 more)	Very low	Important
							-	46%		202 fewer per 1000 (from 327 fewer to 41 more)		

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	3-D microporous overlay	Gel overlay	Relative (95% CI)	Absolute	Quality	Importance
Suspension due to intolerance– people in long-term care - all grade of ulcers (EPUAP-NPUAP)[39]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	5/35 (14.3%)	2/37 (5.4%)	RR 2.64 (0.55 to 12.75)	89 more per 1000 (from 24 fewer to 635 more)	Very low	Important
								5.4%		89 more per 1000 (from 24 fewer to 635 more)		
Unchanged/worsened– people in long-term care - all grade of ulcers (EPUAP-NPUAP)[39]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[c]	None	16/35 (45.7%)	22/37 (59.5%)	RR 0.77 (0.49 to 1.2)	137 fewer per 1000 (from 303 fewer to 119 more)	Very low	Critical
							-	59.5%		137 fewer per 1000 (from 303 fewer to 119 more)		
Improved– people in long-term care - all grade of ulcers (EPUAP-NPUAP)[39]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[c]	None	16/35 (45.7%)	9/37 (24.3%)	RR 1.88 (0.96 to 3.68)	214 more per 1000 (from 10 fewer to 652 more)	Very low	Critical
							-	24.3%		214 more per 1000		

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	3-D microporous overlay	Gel overlay	Relative (95% CI)	Absolute	Quality	Importance
										(from 10 fewer to 651 more)		
Patient comfort (fair to excellent) – people in long-term care - all grade of ulcers (EPUAP-NPUAP)[39]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[c]	None	27/35 (77.1%)	19/37 (51.4%)	RR 1.5 (1.05 to 2.16)	257 more per 1000 (from 26 more to 596 more)	Very low	Important
								51.4%		257 more per 1000 (from 26 more to 596 more)		
Patient comfort (poor) – people in long-term care - all grade of ulcers (EPUAP-NPUAP)[39]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[c]	None	8/35 (22.9%)	18/37 (48.6%)	RR 0.47 (0.23 to 0.94)	258 fewer per 1000 (from 29 fewer to 375 fewer)	Very low	Important
							-	48.7%		258 fewer per 1000 (from 29 fewer to 375 fewer)		
Time to complete healing (time to event data)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate of healing (continuous data)												

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	3-D microporous overlay	Gel overlay	Relative (95% CI)	Absolute	Quality	Importance
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate of change in size of ulcer (absolute and relative) (continuous data)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Reduction in size of ulcer and volume of ulcer												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital or NHS care (continuous data)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Side effects												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life (continuous data)												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) The study was unblinded. There were baseline differences for grade of pressure ulcers, but the higher grade were in the intervention group.
(b) The confidence interval crossed both MID points.
(c) The confidence interval crossed 1 MID point.

6.2.1.2 High-tech pressure devices

Table 44: Clinical evidence profile: low-air-loss bed versus low-tech foam mattress overlay

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Low-air-loss bed	Foam mattress overlay	Relative (95% CI)	Absolute	Quality	Importance
Proportion of people with pressure ulcers completely healed - Shea grade 2 ulcers or above, people in an elderly nursing home, mean 36 days follow-up[g59]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	None	26/43 (60.5%)	19/41 (46.3%)	RR 1.3 (0.87 to 1.96)	139 more per 1000 (from 60 fewer to 445 more)	Very low	Critical
							-	46.3%		139 more per 1000 (from 60 fewer to 444 more)		
Proportion of people with pressure ulcers completely healed - International Association of Enterostomal Therapists (IAET) staging system stage 3 and 4 ulcers, people in a nursing home, 12 weeks follow-up[g123]												
1	Randomised trial	Very serious[c]	No serious inconsistency	No serious indirectness	Very serious[d]	None	5/31 (16.1%)	3/18 (16.7%)	RR 0.97 (0.26 to 3.58)	5 fewer per 1000 (from 123 fewer to 430 more)	Very low	Critical
							-	16.7%		5 fewer per 1000 (from 124 fewer to 431 more)		
Proportion of people with pressure ulcers completely healed (meta-analysed) – Shea grade 2 ulcers or above and International Association of Enterostomal Therapists staging system stage 3 and 4 ulcers – people in an elderly nursing home[123];[59]												
2	Randomised trials	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	None	31/74 (41.9%)	22/59 (37.3%)	RR 1.25 (0.84 to	93 more per 1000 (from 60	Very low	Critical

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Low-air-loss bed	Foam mattress overlay	Relative (95% CI)	Absolute	Quality	Importance
		,[c]							1.86)	fewer to 321 more)		
							-	31.5%		79 more per 1000 (from 50 fewer to 271 more)		
Pressure ulcers reduced by 1 grade or more including healed completely - International Association of Enterostomal Therapists staging system stage 3 and 4 ulcers, people in a nursing home, 12-weeks follow up[123]												
1	Randomised trial	Very serious[c]	No serious inconsistency	No serious indirectness	Very serious[d]	None	10/31 (32.3%)	5/18 (27.8%)	RR 1.16 (0.47 to 2.86)	44 more per 1000 (from 147 fewer to 517 more)	Very low	Critical
							-	27.8%		44 more per 1000 (from 147 fewer to 517 more)		
Rate of healing (mm^2/day) median (25th, 75th percentiles) - Shea grade 2 ulcers or above, people in a nursing home, mean 36 days follow-up[59]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[f]	Serious[i]	9.0 (4.0, 19.8)	2.5 (0.5 to 6.5)	p=0.0002	-	Very low	Critical
Mean change in ulcer size (final values)– NPUAP stage 2 ulcers, people in hospital, 7 days follow-up[51]												
1	Randomised trial	Very serious[e]	No serious inconsistency	No serious indirectness	Serious[b]	Serious[h]	7.3 (s.d 2.4) n= 25	5.3 (s.d 2.1) n=23	-	MD 2 higher (0.73 to 3.27 higher)	Very low	Critical
Mean change in ulcer size (final values) – NPUAP stage 3 and 4 ulcers, people in hospital, 7 days follow-up[51]												
1	Randomised	Very	No serious	No serious	No serious	Serious	37.1 (s.d 8.1)	12.4 (s.d 3.5)	-	MD 24.7	Very	Critical

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Low-air-loss bed	Foam mattress overlay	Relative (95% CI)	Absolute	Quality	Importance
	trial	serious[e]	inconsistency	indirectness		[h]	n=17	n=12		higher (20.37 to 29.03 higher)	low	
Mean comfort scores (perception of comfort) (better indicated by lower values) – NPUAP stage 2 to 4 ulcers, people in hospital, 7 days follow-up[51]												
1	Randomised trial	Very serious[e]	No serious inconsistency	No serious indirectness	No serious imprecision	None	4.1 (s.d 1.3) n=20	3.7 (s.d 1.3) n=19	T[37]=0.91 p>0.05	MD 0.4 higher (0.42 lower to 1.22 higher)	Low	Critical
Mortality - Shea grade 2 ulcers or above, people in a nursing home, mean 36 days follow-up[59]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very seriousd	None	11/43 (25.6%)	7/41 (17.1%)	RR 1.5 (0.64 to 3.49)	85 more per 1000 (from 61 fewer to 425 more)	Very low	Important
						-	-	17.1%		86 more per 1000 (from 62 fewer to 426 more)		
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital or NHS care												
-	-	-	-	-	-	-	-	-	-	-	-	-
Side effects												
-	-	-	-	-	-	-	-	-	-	-	-	-

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Low-air-loss bed	Foam mattress overlay	Relative (95% CI)	Absolute	Quality	Importance
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) Ferrell (1993) terminated at interim analysis as difference much larger than expected. There was unclear sequence generation and blinding, as well as insufficient reporting of incomplete outcome data. There was a higher drop-out than event rate for the 'proportion completely healed' outcome.

(b) The confidence interval crossed 1 MID point.

(c) Mulder (1994) did not provide details of the randomisation method and there was unclear allocation concealment and blinding. It was also unclear from which group drop-outs came from; not all of the pre-specified outcomes were reported and ulcer size was not reported at baseline.There was iInsufficient reporting of incomplete outcome data and a higher drop-out than event rate for' proportion completely healed' outcome.

(d) The confidence interval crossed both MID points.

(e) Day (1993) did not report clear methods of randomisation, allocation concealment or blinding. There was insufficient reporting of incomplete outcome data and not all of the pre-specified outcomes were analysed. The authors did not report initial ulcer sizes.

(f) There was not enough data to put in Revman.

(g) The Cochrane review did not conduct meta-analysis as the outcomes were measured in different ways. Ferrell (1993) used tracing of the epithelial border of the ulcer on plastic film and then the are measured using a polar planimeter. The wounds were assessed using the four-point Shea scale and the Sessing scale (similar to Shea scale, but was undergoing development at time of the study), which has 7 verbal descriptions of ulcers including colour, presence of granulation tissue, evidence of infection, drainage, odour and eschar. Mulder (1994) assessed wound surface area by photoplanimetry. Ulcer volume = ulcer length x width x depth (of deepest ulcer point). The pressure ulcers were assessed using the International Association of Enterostomal Therapists staging system. Only stage 3 and 4 ulcers were included in this study.

(h) The baseline had a larger difference than the difference between the final values therefore the results should be viewed with caution. There was no log transformation of data.

(i) A non-parametric test (Wilcoxon rank-sum) was used but there was no log transformation of data.

Table 45: Clinical evidence profile: low-air-loss bed versus low-air-loss overlay

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Low-air-loss bed	Low-air-loss overlay	Relative (95% CI)	Absolute	Quality	Importance
Median change in ulcer area (cm^2) – people in acute care, mean 24 day follow-up[38]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	3.9 cm2	1.9 cm2	p=0.060	-	Very low	Critical
Mean changes in pressure ulcer surface area– people in acute care, mean 24 day follow-up[38]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	10.2 cm2	3.8 cm2	-	-	Very low	Critical
Proportion of people with pressure ulcers completely healed												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate of change in size of ulcer												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital or NHS care												
-	-	-	-	-	-	-	-	-	-	-	-	-
Patient acceptability												
-	-	-	-	-	-	-	-	-	-	-	-	-
Side effects												
-	-	-	-	-	-	-	-	-	-	-	-	-
Mortality												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) There was very little data provided (median change in area and range). It was unclear (and unlikely) that the outcome assessment was blind to treatment group. No description of co-interventions except skincare protocol applied to both groups; insufficient reporting of incomplete outcome data; high drop-out.
(b) No data were available to analyse in Revman.

Table 46: Clinical evidence profile: air-fluidised therapy (AFT) versus standard or conventional therapies

Quality assessment							No of patients		Effect			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Air-fluidised bed**	**Standard care**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
Proportion with 50% reduction in total surface area – Shea all stages, people in surgery, mean 13 days follow-up[6]												
1	Randomised trial	Serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	9/31 (29%)	8/34 (23.5%)	RR 1.23 (0.54 to 2.8)	54 more per 1000 (from 108 fewer to 424 more)	Very low	Critical
							-	23.5%		54 more per 1000 (from 108 fewer to 423 more)		
Proportion with improvement in pressure ulcers – Shea stage 3 or 4 ulcers, people at home, 36 weeks follow-up[180]												
1	Randomised trial	Very serious[c,i]	No serious inconsistency	No serious indirectness	Serious[d]	None	19/22 (86.4%)o	9/13 (69.2%)o	RR 1.25 (0.84 to 1.86)	173 more per 1000 (from 11 fewer to 595 more)	Very low	Critical
							-	69.2%		173 more per 1000 (from 11 fewer to 595 more)		
Proportion with improvement in pressure ulcers – Shea all stages, people in surgery, mean 13 days follow-up[6]												
1	Randomised trial	Serious[a]	No serious inconsistency	No serious indirectness	Serious[d]	None	22/31 (71%)	16/34 (47.1%)	RR 1.51 (0.99 to	240 more per 1000	Low	Critical

Quality assessment							No of patients		Effect			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Air-fluidised bed**	**Standard care**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
									2.3)	(from 5 fewer to 612 more)		
							-	47.1%		240 more per 1000 (from 5 fewer to 612 more)		
Proportion with improvement in pressure ulcers – Shea all stages (people in surgery and people at home) – meta-analysed[6];[180]												
2	Randomised trials	Serious[a,c]	No serious inconsistency	No serious indirectness	Serious[d]	None	41/53 (77.4%)o	25/47 (53.2%)o	RR 1.4 (1.04 to 1.88)	213 more per 1000 (from 21 more to 468 more)	Low	Critical
							-	58.1%		232 more per 1000 (from 23 more to 511 more)		
Change in mean ulcer area (mm^2) – stage 2 or 3 ulcers (not specified which classification system), people in hospital, 15 days follow-up (final values)[126]												
1	Randomised trial	Very serious[e]	No serious inconsistency	No serious indirectness	Very serious[k]	Serious[l]	1158mm2	2051mm2	-	p=0.05	Very low	Critical
Change in total surface area (median, range) cm^2– Shea all stages, people in surgery, mean 13 days follow-up[6]												
1	Randomised trial	Serious[a]	No serious inconsistency	No serious indirectness	Very serious[f]	Serious[m]	-1.2 (-38.0 to +15.5)	+0.5 (-55.1 to +94.7)	-	Difference (median): -1.7cm2 (95% CI -9.2cm2 to -0.6cm2)	Very low	Critical
Reduction in pain[g]– Shea all stages, people in surgery, mean 13 days follow-up[6]												

Quality assessment							No of patients		Effect			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Air-fluidised bed**	**Standard care**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
1	Randomised trial	Very serious[a,h]	No serious inconsistency	No serious indirectness	Serious[d]	None	8/13 (61.5%)	4/14 (28.6%)	RR 2.15 (0.85 to 5.48)	329 more per 1000 (from 43 fewer to 1000 more)	Very low	Important
Increase in pain[g]– Shea all stages, people in surgery, mean 13 days follow-up[6]												
1	Randomised trial	Very serious[a,h]	No serious inconsistency	No serious indirectness	Very serious[b]	None	0/13 (0%)	3/14 (21.4%)	Peto OR 0.12 (0.01 to 1.31)	183 fewer per 1000 (from 212 fewer to 49 more)	Very low	Important
								21.4%		182 fewer per 1000 (from 212 fewer to 49 more		
Time in hospital (better indicated by lower values) – Shea stage 3 or 4 ulcers, people at home, 36 weeks follow-up[180]												
1	Randomised trial	Very serious[c]	No serious inconsistency	No serious indirectness	Very serious[b]	None	11.5 (s.d 8.8) days n= 47	21.5 (s.d 23.8) days n= 50	-	MD 10 lower (161.64 lower to 141.64 higher)	Very low	Important
Median length of stay in hospital after randomisation– Shea all stages, people in surgery, mean 13 days follow-up[6]												
1	Randomised trial	Serious[a]	No serious inconsistency	No serious indirectness	Very serious[f]	None	16 days	15 days	-	-	Very low	Important
Patient satisfaction (better indicated by higher values) – stage 2 or 3 ulcers (not specified which classification system), people in hospital, 15 days follow-up[126]												
1	Randomised trial	Very serious[e,h]	No serious inconsistency	No serious indirectness	No serious imprecision	None	57.5 (s.d 6.1) n= 8	48.6 (s.d 12.3) n=10	-	MD 8.9 higher (0.18 to 17.62	Low	Critical

Quality assessment							No of patients		Effect			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Air-fluidised bed**	**Standard care**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
										higher)		
Increase in comfort– Shea all stages, people in surgery, mean 13 days follow-up[6]												
1	Randomised trial	Very serious[a,h]	No serious inconsistency	No serious indirectness	Serious[d]	None	8/13 (61.5%)	3/14 (21.4%)	RR 2.87 (0.96 to 8.55)	401 more per 1000 (from 9 fewer to 1000 more)	Very low	Critical
Reduction in comfort– Shea all stages, people in surgery, mean 13 days follow-up[6]												
1	Randomised trial	Very serious[a,h]	No serious inconsistency	No serious indirectness	Very serious[b]	None	1/13 (7.7%)	6/14 (42.9%)	RR 0.18 (0.02 to 1.30)	351 fewer per 1000 (from 420 fewer to 129 more)	Very low	Critical
Mortality – Shea all stages, people in surgery and at home[6];[180]												
2	Randomised trials	Serious[a,c]	No serious inconsistency	No serious indirectness	Very serious[b]	None	22/89 (24.7%)	26/88 (29.5%)	RR 0.83 (0.51 to 1.34)	50 fewer per 1000 (from 145 fewer to 100 more)	Very low	Important
							-	27.9%				
Proportion of patients with pressure ulcers completely healed												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time to complete healing												
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate of change in size of ulcer												
-	-	-	-	-	-	-	-	-	-	-	-	-
Side effects												
-	-	-	-	-	-	-	-	-	-	-	-	-

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Air-fluidised bed	Standard care	Relative (95% CI)	Absolute	Quality	Importance
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) Allman (1987) did not report clear allocation concealment and there were baseline differences. The size of ulcer at baseline was not reported.
(b) The confidence interval crossed both MID points.
(c) Strauss (1991) did not report clear allocation concealment and there was insufficient reporting of incomplete outcome data. The size of ulcer at baselinewas not reported. There was also a high drop-out rate.
(d) The confidence interval crossed 1 MID point.
(e) Munro (1989) did not report clear allocation concealment and no information regarding sample size calculations, randomisation method, blinding, baseline characteristics or extent of follow-up were reported. No raw data was presented in the paper and there was insufficient reporting of incomplete outcome data.
(f) It was not possible to analyse data in Revman.
(g) There was a change in pain intensity from baseline (from asking participants to score 0 to 5 on words to describe pain (none, mild, discomforting, distressing, horrible or excruciating)).
(h) The participant self-reported outcomes.
(i) Improvement was assessed by an independent nurse reviewer's assessment of the participants' pressure ulcere. There was no definition of improvement.
(j) Improvement was defined as those pressure ulcers that had healed, much improved, or a little improved. Non-improvement included those that were unchanged, a little worse, or much worse. This was assessed by an investigator and a plastic surgeon independently from photographs.
(k) The change scores were given by study but it was not possible to analyse data in Revman as no standard deviations were given.
(l) The ulcer size (diameter) at day 1 had a larger difference between the groups than the difference between the ulcer sizes at day 15. There was no log transformation of data.
(m) Non-parametric tests were used but there was no log transformation of data.
(n) Less than half the participants completed the questionnaire.
(o) Strauss used an independent nurse reviewer's assessment of the participants' pressure ulcer, the data was given for both reviewers and then for the purposes of this review, the results were amalgamated for the 35 participants who were assessed.

Table 47: Clinical evidence profile: alternating-pressure mattress versus alternating-pressure mattress

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Alternating-pressure mattress	Alternating-pressure mattress	Relative (95% CI)	Absolute	Quality	Importance
Proportion of people with pressure ulcers completely healed – grade 2 and above (grading system not specified), elderly adults, 4-week follow-up – alternating-pressure mattress (Nimbus 1) versus alternating-pressure mattress (Pegasus Airwave)[55]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	None	10/16 (62.5%)	5/14 (35.7%)	RR 1.75 (0.79 to 3.89)	268 more per 1000 (from 75 fewer to 1000 more)	Very low	Critical
							-	35.7%		268 more per 1000 (from 75 fewer to 1000 more)		
Proportion of pressure ulcers completely healed – grade 2 and above (Torrance classification system), elderly adults, 18 months follow-up – alternating pressure mattress (Nimbus 3) with Aura cushion and 4-hourly turning versus alternating pressure mattress (Pegasus Cairwave Therapy System) with Proactive 2 seating cushion and 8-hourly turning[161]												
1	Randomised trial	Serious[c]	No serious inconsistency	No serious indirectness	No serious imprecision	None	65/71 (91.5%)	65/70 (92.9%)	RR 0.99 (0.9 to 1.09)	9 fewer per 1000 (from 93 fewer to 84 more)	Moderate	Critical
							-	92.9%		9 fewer per 1000 (from 93 fewer to 84 more)		
Proportion of people with decrease in pressure ulcer size– grade 2 and above (grading system not specified), elderly adults, 4-week follow-up– alternating pressure mattress (Nimbus 1) versus alternating pressure mattress (Pegasus Airwave)[55]												
1	Randomised	Very	No serious	No serious	Very	None	4/16	6/14	RR 0.58 (0.21 to	180 fewer per 1000	Very low	Critical

Quality assessment							No of patients		Effect			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Alternating-pressure mattress**	**Alternating-pressure mattress**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
	trial	serious[a]	inconsistency	indirectness	serious[d]		(25%)	(42.9%)	1.65)	(from 339 fewer to 279 more)		
							-	42.9%		180 fewer per 1000 (from 339 fewer to 279 more)		
Proportion of people with increase in pressure ulcer size– grade 2 and above (grading system not specified), elderly adults, 4-week follow-up– alternating pressure mattress (Nimbus 1) versus alternating pressure mattress (Pegasus Airwave)[55]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[d]	None	2/16 (12.5%)	3/14 (21.4%)	RR 0.58 (0.11 to 3.00)	90 fewer per 1000 (from 191 fewer to 429 more)	Very low	Critical
							-	21.4%		90 fewer per 1000 (from 190 fewer to 428 more)		
Median rate of reduction in surface area (cm/day) – grade 2 and above (grading system not specified), elderly adults, 4-week follow-up– alternating pressure mattress (Nimbus 1) versus alternating pressure mattress (Pegasus Airwave)[55]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[e]	Serious[h]	0.089cm2/day	0.107cm2/day	Difference 0.018 cm^2 (95% CI 0.179 to 0.143) p=0.92	-	Very low	Critical
Median absolute reduction in wound surface area per day – grade 2 and above (grading system not specified), elderly adults in hospital and nursing homes, 2 week follow-up – alternating pressure mattress (Nimbus 3) versus alternating pressure mattress (P.Biwave, P.Airwave, P. Cairwave or AlphaXCell) or alternating-pressure mattress overlay (AlphaXCell or Quattro)[56]												

Quality assessment							No of patients		Effect			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Alternating-pressure mattress**	**Alternating-pressure mattress**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
1	Randomised trial	Very serious[f]	No serious inconsistency	No serious indirectness	Very serious[e]	Serious[h]	0.12cm 2 (range 0 to 0.21cm2)	0.08cm2 (range 0.04 to 0.33cm2)	p=0.570	-	Very low	Critical
Median relative reduction in wounds surface area– grade 2 and above (grading system not specified), elderly adults in hospital and nursing homes, 2 week follow-up– alternating pressure mattress (Nimbus 3) versus alternating pressure mattress (P.Biwave, P.Airwave, P. Cairwave or AlphaXCell) or alternating-pressure mattress overlay (AlphaXCell or Quattro)[56]												
1	Randomised trial	Very serious[f]	No serious inconsistency	No serious indirectness	Very serious[e]	Serious[h]	2.44% (range 0-7.14%)	1.34% (range 1.11-2.88%)	p=0.570	-	Very low	Critical
Median absolute reduction in wound surface are per day– grade 2 and above (grading system not specified), elderly adults in hospital and nursing homes, 2 week follow-up– alternating pressure mattress (Nimbus 3) versus alternating pressure mattress (P.Biwave, P.Airwave, P. Cairwave or AlphaXCell) or alternating-pressure mattress overlay (AlphaXCell or Quattro)[56]												
1	Randomised trial	Very serious[f]	No serious inconsistency	No serious indirectness	Very serious[e]	Serious[h]	0.11cm2 (range 0.04 to 0.41cm2)	0.05cm2 (range 0-0.48cm2)	p=0.570	-	Very low	Critical
Median relative reduction in wounds surface area – grade 2 and above (grading system not specified), elderly adults in hospital and nursing homes, 2 week follow-up– alternating pressure mattress (Nimbus 3) versus alternating pressure mattress (P.Biwave, P.Airwave, P. Cairwave or AlphaXCell) or alternating-pressure mattress overlay (AlphaXCell or Quattro)[56]												
1	Randomised trial	Very serious[f]	No serious inconsistency	No serious indirectness	Very serious[e]	Serious[h]	1.57% (range 0.45-5%)	0.99% (range 0-2.54%)	p=0.570	-	Very low	Critical
Mean time in hospital (for those who completed the trial) – grade 2 and above (Torrance classification system), elderly adults in hospital and nursing homes, 18 months follow-up– alternating pressure mattress (Nimbus 3) with Aura cushion and 4-hourly turning versus alternating pressure mattress (Pegasus Cairwave Therapy System) with Proactive 2 seating cushion and 8-hourly turning[161]												
1	Randomised trial	Serious[c]	No serious inconsistency	No serious indirectness	Very serious[e]	None	21.6 days n=57	21.7 days n=55	-	-	Very low	Important
Comfort (people in hospital)– grade 2 and above (grading system not specified), elderly adults in hospital and nursing homes, 2 week follow-up– alternating pressure mattress (Nimbus 3) versus alternating pressure mattress (P.Biwave, P.Airwave, P. Cairwave or AlphaXCell) or alternating-pressure mattress overlay (AlphaXCell or Quattro)[56]												
1	Randomised	Very	No serious	No serious	Very	None	5 (very comfortable	4	p=0.006	-	Very low	Critical

Quality assessment							No of patients		Effect			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Alternating-pressure mattress**	**Alternating-pressure mattress**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
	trial	serious[f,g]	inconsistency	indirectness	serious[e]		)	(comfortable)				
Comfort (people in nursing homes)– grade 2 and above (grading system not specified), elderly adults in hospital and nursing homes, 2 week follow-up– Nimbus 3 versus P.Biwave, P.Airwave, P. Cairwave or AlphaXCell) or alternating-pressure mattress overlay (AlphaXCell or Quattro)[56]												
1	Randomised trial	Very serious[f,g]	No serious inconsistency	No serious indirectness	Very serious[e]	None	5 (very comfortable	4 (comfortable)	p=0.002	-	Very low	Critical
Comfort – grade 2 and above (grading system not specified), elderly adults, 4-week follow-up– alternating pressure mattress (Nimbus 1) versus alternating pressure mattress (Pegasus Airwave)[55]												
1	Randomised trial	Very serious[a,g]	No serious inconsistency	No serious indirectness	Very serious[e]	None	Median 8/10	Median 8/10	-	-	Very low	Critical
Mortality – grade 2 and above (grading system not specified), elderly adults, 4-week follow-up– alternating pressure mattress (Nimbus 1) versus alternating pressure mattress (Pegasus Airwave)[55]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[d]	None	6/22 (27.3%)	5/19 (26.3%)	RR 1.04 (0.38 to 2.86)	11 more per 1000 (from 163 fewer to 489 more)	Very low	Important
							-	26.3%		11 more per 1000 (from 163 fewer to 489 more)		
Mortality – grade 2 and above (Torrance classification system), elderly adults, 18 months follow-up– alternating pressure mattress (Nimbus 3) with Aura cushion and 4-hourly turning versus alternating pressure mattress (Pegasus Cairwave Therapy System) with Proactive 2 seating cushion and 8-hourly turning[161]												
1	Randomised trial	Serious[c]	No serious inconsistency	No serious indirectness	Serious[c]	None	16/71 (22.5%)	10/70 (14.3%)	RR 1.58 (0.77 to 3.23)	83 more per 1000 (from 33 fewer to 319 more)	Low	Important
							-	14.3%		83 more per 1000		

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Alternating-pressure mattress	Alternating-pressure mattress	Relative (95% CI)	Absolute	Quality	Importance
										(from 33 fewer to 319 more)		
Mortality – grade 2 and above (grading system not specified), elderly adults in hospital and nursing homes, 2 week follow-up– alternating pressure mattress (Nimbus 3) versus alternating pressure mattress (P.Biwave, P.Airwave, P. Cairwave or AlphaXCell) or alternating-pressure mattress overlay (AlphaXCell or Quattro) [56]												
1	Randomised trial	Very serious[f]	No serious inconsistency	No serious indirectness	Very serious[d]	None	7/17 (41.2%)	3/15 (20%)	RR 2.06 (0.64 to 6.57)	212 more per 1000 (from 72 fewer to 1000 more)	Very low	Important
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Side effects												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) Devine (1995) did not report whether there was blinding of outcome assessors and there was baseline differences in the groups (more people incontinent of urine in alternating pressure mattress (Nimbus) group, more people catheterised in alternating pressure mattress (Airwave) group). Baseline pressure ulcer size was not reported and there was drop-out higher than event rate. The study used a very small sample size.

(b) The confidence interval crossed 1 MID point.

(c) Russell (2000) did not provide details of the randomisation method and there was unclear allocation concealment.

(d) The confidence interval crossed both MID points.

(e) There was not enough data available to analyse in Revman.

(f) Evans (2000) did not report a method of randomisation and there was unclear allocation concealment. A large proportion of participants did not complete follow-up (11/20 in nursing home group and 75% of hospital group). The study used a very small sample size.

(g) The participants self-reported outcomes.

(h) There was no log transformation of data.

Table 48: Clinical evidence profile: alternating-pressure mattress overlay versus alternating-pressure mattress

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Alternating-pressure mattress overlay	Alternating-pressure mattress	Relative (95% CI)	Absolute	Quality	Importance
Proportion of people with pressure ulcers completely healed– grade 2 and above (classification system not specified), elderly adults, 30 day follow-up[136,138]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	20/59 (33.9%)	19/54 (35.2%)	RR 0.96 (0.58 to 1.6)	14 fewer per 1000 (from 148 fewer to 211 more)	Very low	Critical
							-	35.2%		14 fewer per 1000 (from 148 fewer to 211 more)		
Time to healing (median days)[136,138]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[e]	None	20 days (12 to not estimable)	20 days (10 to not estimable)	-	p=0.86 log-rank test	Very low	Important
Absolute change in surface area (cm^2) - change values (better indicated by higher values) – grade 2 and above (classification system not specified), elderly adults, 30 day follow-up[136,138]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[c]	None	1 (SD 2.3) n=33	2 (SD 6.1) n=36	-	MD 1 lower (3.14 lower to 1.14 higher)	Very low	Critical
% change in surface area (change values) (better indicated by higher values) – grade 2 and above (classification system not specified), elderly adults, 30 day follow-up[136,138]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[c]	None	-35 (SD 605.5) n=33	34.4 (SD 108.6) n=36	-	MD 69.4 lower (279.01 lower to	Very low	Critical

Quality assessment							No of patients		Effect			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Alternating-pressure mattress overlay**	**Alternating-pressure mattress**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
										140.21 higher)		
Pressure ulcer improvement– grade 1 or 2 pressure ulcers (EPUAP classification system), elderly adults, follow-up period not specified[162]												
1	Randomised trial	Very serious[d]	No serious inconsistency	No serious indirectness	No serious	None	56/75 (74.7%)	60/83 (72.3%)	RR 1.03 (0.86 to 1.25)	22 more per 1000 (from 101 fewer to 181 more)	Low	Critical
							-	72.3%		22 more per 1000 (from 101 fewer to 181 more)		
Worsening of pressure ulcers– grade 1 or 2 pressure ulcers (EPUAP classification system), elderly adults, follow-up period not specified[162]												
1	Randomised trial	Very serious[d]	No serious inconsistency	No serious indirectness	Very serious[b]	None	16/75 (21.3%)	22/83 (26.5%)	RR 0.8 (0.46 to 1.41)	53 fewer per 1000 (from 143 fewer to 109 more)	Very low	Critical
							-	26.5%		53 fewer per 1000 (from 143 fewer to 109 more)		
Time in hospital (mean) – grade 1 or 2 pressure ulcers (EPUAP classification system), elderly adults, follow-up period not specified[162]												
1	Randomised trial	Very serious[d]	No serious inconsistency	No serious indirectness	Very serious[e]	None	22.17 days	20.05 days	-	p=0.23	Very low	Important
Patient acceptability (requested changes for comfort or other device-related reasons) – grade 2 and above (classification system not specified), elderly adults, 30 day follow-up[136,138]												
1	Randomised	Serious[a]	No serious	No serious	Serious[c]	None	230/989	186/982	RR 1.23	44 more	Low	Important

Quality assessment							No of patients		Effect			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Alternating-pressure mattress overlay**	**Alternating-pressure mattress**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
	trial		inconsistency	indirectness			(23.3%)	(18.9%)	(1.03 to 1.46)	per 1000 (from 6 more to 87 more)		
							-	18.9%		43 more per 1000 (from 6 more to 87 more)		
Proportion of participants with negative comments on mattress motion– grade 2 and above (classification system not specified), elderly adults, 30 day follow-up[136,138]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[c]	None	328/929 (35.3%)	285/891 (32%)	RR 1.1 (0.97 to 1.26)	32 more per 1000 (from 10 fewer to 83 more)	Very low	Important
							-	32%		32 more per 1000 (from 10 fewer to 83 more)		
Proportion of participants with positive comments for mattress motion– grade 2 and above (classification system not specified), elderly adults, 30 day follow-up[136,138]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious	None	272/929 (29.3%)	263/891 (29.5%)	RR 0.99 (0.86 to 1.14)	3 fewer per 1000 (from 41 fewer to 41 more)	Low	Important
							-	29.5%		3 fewer per 1000 (from 41 fewer to		

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Alternating-pressure mattress overlay	Alternating-pressure mattress	Relative (95% CI)	Absolute	Quality	Importance
										41 more)		
Proportion of participants commenting negatively on getting into or out of bed– grade 2 and above (classification system not specified), elderly adults, 30 day follow-up[136,138]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[c]	None	124/929 (13.3%)	127/891 (14.3%)	RR 0.94 (0.74 to 1.18)	9 fewer per 1000 (from 37 fewer to 26 more)	Low	Important
								14.3%		9 fewer per 1000 (from 37 fewer to 26 more)		
Participants commenting negatively on movement in bed– grade 2 and above (classification system not specified), elderly adults, 30 day follow-up[136,138]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	290/929 (31.2%)	260/891 (29.2%)	RR 1.07 (0.93 to 1.23)	20 more per 1000 (from 20 fewer to 67 more)	Low	Important
							-	29.2%		20 more per 1000 (from 20 fewer to 67 more)		
Proportion of participants commenting positively on movement in bed– grade 2 and above (classification system not specified), elderly adults, 30 day follow-up[136,138]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	25/929 (2.7%)	27/891 (3%)	RR 0.89 (0.52 to 1.52)	3 fewer per 1000 (from 15 fewer to 16 more)	Very low	Important

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Alternating-pressure mattress overlay	Alternating-pressure mattress	Relative (95% CI)	Absolute	Quality	Importance
							-	3%		3 fewer per 1000 (from 14 fewer to 16 more)		
Proportion of participants commenting on temperature as hot or warm– grade 2 and above (classification system not specified), elderly adults, 30 day follow-up[136,138]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[c]	None	67/929 (7.2%)	50/891 (5.6%)	RR 1.29 (0.9 to 1.83)	16 more per 1000 (from 6 fewer to 47 more)	Very low	Important
							-	5.6%		16 more per 1000 (from 6 fewer to 46 more)		
Proportion of participants commenting on sweaty or sticky temperature– grade 2 and above (classification system not specified), elderly adults, 30 day follow-up[136,138]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[c]	None	32/929 (3.4%)	23/891 (2.6%)	RR 1.33 (0.79 to 2.26)	9 more per 1000 (from 5 fewer to 33 more)	Very low	Important
							-	2.6%		9 more per 1000 (from 5 fewer to 33 more)		
Proportion of participants commenting on cold or cool temperature– grade 2 and above (classification system not specified), elderly adults, 30 day follow-up[136,138]												
1	Randomised	Very	No serious	No serious	Very	None	11/929	11/891	RR 0.96	0 fewer	Very	Important

Quality assessment							No of patients		Effect			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Alternating-pressure mattress overlay**	**Alternating-pressure mattress**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
	trial	serious[a]	inconsistency	indirectness	serious[b]		(1.2%)	(1.2%)	(0.42 to 2.2)	per 1000 (from 7 fewer to 15 more)	low	
							-	1.2%		0 fewer per 1000 (from 7 fewer to 14 more)		
Mattress not working or not working properly– grade 2 and above (classification system not specified), elderly adults, 30 day follow-up[136,138]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	16/929 (1.7%)	18/891 (2%)	RR 0.85 (0.44 to 1.66)	3 fewer per 1000 (from 11 fewer to 13 more)	Very low	Important
							-	2%		3 fewer per 1000 (from 11 fewer to 13 more)		
Hard to tuck sheet under or sheets come off or gather ormattress cover slips– grade 2 and above (classification system not specified), elderly adults, 30 day follow-up[136,138]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[c]	None	19/929 (2%)	6/891 (0.7%)	RR 3.04 (1.22 to 7.57)	14 more per 1000 (from 1 more to 44 more)	Very low	Important
							-	0.7%		14 more per 1000 (from 2 more to		

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Alternating-pressure mattress overlay	Alternating-pressure mattress	Relative (95% CI)	Absolute	Quality	Importance
										46 more)		
Mattress or bed too high– grade 2 and above (classification system not specified), elderly adults, 30 day follow-up[136,138]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[c]	None	72/929 (7.8%)	48/891 (5.4%)	RR 1.44 (1.01 to 2.05)	24 more per 1000 (from 1 more to 57 more)	Very low	Important
							-	5.4%		24 more per 1000 (from 1 more to 57 more)		
Mattress slippy– grade 2 and above (classification system not specified), elderly adults, 30 day follow-up[136,138]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	9/929 (1%)	4/891 (0.4%)	RR 2.16 (0.67 to 6.98)	5 more per 1000 (from 1 fewer to 27 more)	Very low	Important
							-	0.5%		6 more per 1000 (from 2 fewer to 30 more)		
Mattress too soft or edges soft or slope– grade 2 and above (classification system not specified), elderly adults, 30 day follow-up[136,138]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[c]	None	19/929 (2%)	29/891 (3.3%)	RR 0.63 (0.35 to 1.11)	12 fewer per 1000 (from 21 fewer to 4 more)	Very low	Important

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Alternating-pressure mattress overlay	Alternating-pressure mattress	Relative (95% CI)	Absolute	Quality	Importance
							-	3.3%		12 fewer per 1000 (from 21 fewer to 4 more)		
Not able to use backrest– grade 2 and above (classification system not specified), elderly adults, 30 day follow-up[136,138]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	4/929 (0.4%)	2/891 (0.2%)	RR 1.92 (0.35 to 10.45)	2 more per 1000 (from 1 fewer to 21 more)	Very low	Important
							-	0.2%		2 more per 1000 (from 1 fewer to 19 more)		
Mattress-related fall[136,138]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[c]	None	0/828 (0%)	4/891 (0.4%)	Peto OR 0.14 (0.02 to 1.03)	4 fewer per 1000 (from 4 fewer to 0 more)	Very low	Important
							-	0.5%		4 fewer per 1000 (from 5 fewer to 0 more)		
Mattress-related suspected contact dermatitis– grade 2 and above (classification system not specified), elderly adults, 30 day follow-up[136,138]												
1	Randomised	Very	No serious	No serious	Very	None	0/929	1/891	Peto OR	1 fewer	Very	Important

Quality assessment							No of patients		Effect			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Alternating-pressure mattress overlay**	**Alternating-pressure mattress**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
	trial	serious[a]	inconsistency	indirectness	serious[b]		(0%)	(0.1%)	0.13 (0 to 6.54)	per 1000 (from 1 fewer to 6 more)	low	
							-	0.1%		1 fewer per 1000 (from 1 fewer to 6 more)		
Mattress-related climbed over or fell through cot sides– grade 2 and above (classification system not specified), elderly adults, 30 day follow-up[136,138]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	2/929 (0.2%)	1/891 (0.1%)	RR 1.92 (0.17 to 21.12)	1 more per 1000 (from 1 fewer to 23 more)	Very low	Important
							-	0.1%		1 more per 1000 (from 1 fewer to 20 more)		
Mattress deflation during transfer– grade 2 and above (classification system not specified), elderly adults, 30 day follow-up[136,138]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	0/929 (0%)	1/891 (0.1%)	Peto OR 0.13 (0 to 6.54)	1 fewer per 1000 (from 1 fewer to 6 more)	Very low	Important
							-	0.1%		1 fewer per 1000 (from 1 fewer to 6		

Adverse events

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Alternating-pressure mattress overlay	Alternating-pressure mattress	Relative (95% CI)	Absolute	Quality	Importance
										more)		
Mortality– grade 2 and above (classification system not specified), elderly adults, 30 day follow-up[136,138]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[c]	None	20/59 (33.9%)	12/54 (22.2%)	RR 1.53 (0.83 to 2.82)	118 more per 1000 (from 38 fewer to 404 more)	Very low	Important
							-	22.2%		118 more per 1000 (from 38 fewer to 404 more)		
Rate of change in size of pressure ulcer												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) Nixon (2006) did not report blinding and the drop-out was higher than the event rate. The outcomes of patient acceptability and side effects were for the study as a whole rather than solely those who had pressure ulcers.
(b) The confidence interval crossed both MID points.
(c) The confidence interval crossed 1 MID point
(d) Russell (2003) did not report blinding and there was unclear allocation concealment.There was insufficient reporting of incomplete outcome data.
(e) There was not enough data to analyse in Revman.
(f) This was a non-validated assessment of outcome.

Table 49: Clinical evidence profile: air-filled devices versus alternating pressure mattress

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Air-filled devices	Alternating-pressure mattress	Relative (95% CI)	Absolute	Quality	Importance
Proportion of people with pressure ulcers completely healed – grade 2 ulcer or above (EPUAP classification system), elderly adults, maximum follow-up 42 days[145]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	7/34 (20.6%)	1/26 (3.8%)	RR 5.35 (0.7 to 40.84)	167 more per 1000 (from 12 fewer to 1000 more)	Very low	Critical
							-	3.9%		170 more per 1000 (from 12 fewer to 1000 more)		
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate of change in size of pressure ulcer												
-	-	-	-	-	-	-	-	-	-	-	-	-
Reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital or NHS care												
-	-	-	-	-	-	-	-	-	-	-	-	-
Patient acceptability												
-	-	-	-	-	-	-	-	-	-	-	-	-
Side effects												

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Air-filled devices	Alternating-pressure mattress	Relative (95% CI)	Absolute	Quality	Importance
-	-	-	-	-	-	-	-	-	-	-	-	-
Mortality												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) Osterbrink (2005) did not report the randomisation method, whether there was allocation concealment or blinding and there was insufficient reporting of incomplete outcome data. The authors did not report baseline ulcer size.

(b) The confidence interval crossed both MID points and there were a limited number of events.

Table 50: Clinical evidence profile: alternating-pressure cushion versus dry flotation cushion

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Alternating-pressure cushion	Dry flotation cushion	Relative (95% CI)	Absolute	Quality	Importance
Proportion of people with pressure ulcers completely healed – grade 2 ulcers or above, elderly adults, mean 51 days follow-up[44]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	3/14 (21.4%)	5/11 (45.5%)	RR 0.47 (0.14 to 1.56)	241 fewer per 1000 (from 391 fewer to 255 more)	Very low	Critical
							-	45.5%		241 fewer per 1000 (from 391 fewer to 255 more)		
Rate of healing (cm^2/day) – grade 2 ulcers or above, elderly adults, mean 51 days follow-up[44]												

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Alternating-pressure cushion**	**Dry flotation cushion**	**Relative (95% CI)**	**Absolute**		
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	Serious[d]	0.13 (SD 0.37)	0.27 (SD 0.56)	-	MD 0.14 lower (0.52 lower to 0.24 higher)	Very low	Critical
Rate of healing (cm^3/day) – grade 2 ulcers or above, elderly adults, mean 51 days follow-up[44]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	Serious[d]	0.56 (SD 0.86)	0.49 (SD 0.86)	-	MD 0.07 higher (0.61 lower to 0.75 higher)	Very low	Critical
% change in area per day– grade 2 ulcers or above, elderly adults, mean 51 days follow-up[44]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[c]	Serious[d]	2.56 (SD 7.86)	5.71 (SD 5.57)	-	MD 3.15 lower (8.42 lower to 2.12 higher)	Very low	Critical
% change in volume per day– grade 2 ulcers or above, elderly adults, mean 51 days follow-up[44]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	Serious[d]	1.00 (SD 1.83)	0.68 (SD 0.86)	-	MD 0.32 higher (0.76 lower to 1.4 higher)	Very low	Critical
Mortality– grade 2 ulcers or above, elderly adults, mean 51 days follow-up[44]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b,e]	None	3/14 (21.4%)	1/11 (9.1%)	RR 2.36 (0.28 to	124 more per 1000	Very low	Important

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Alternating-pressure cushion	Dry flotation cushion	Relative (95% CI)	Absolute	Quality	Importance
									19.66)	(from 65 fewer to 1000 more)		
							-	9.1%		124 more per 1000 (from 66 fewer to 1000 more)		
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Reduction in size or volume of pressure ulcer												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital or NHS care												
-	-	-	-	-	-	-	-	-	-	-	-	-
Patient acceptability												
-	-	-	-	-	-	-	-	-	-	-	-	-
Side effects												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) Clark (1998): unclear details of randomisation; unblinded observer; grading system of ulcers not specified. High drop-out.
(b) Confidence interval crossed both MID points.
(c) Confidence interval crossed 1 MID point.
(d) No log transformation of data.

(e) Limited number of events.

Table 51: Clinical evidence profile: profiling bed versus foam mattress

Quality assessment							No of patients		Effect			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Profiling bed**	**Foam mattress**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
Proportion of people with completely healed pressure ulcers – any grade of pressure ulcers, surgical or medical adults, grade 1 occurred, 5-10 days follow-up[89]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	None	4/4 (100%)	2/10 (20%)	RR 3.96 (1.28 to 12.24)	592 more per 1000 (from 56 more to 1000 more)	Very low	Critical
							-	20%		592 more per 1000 (from 56 more to 1000 more)		
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate of change in size of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital or NHS care												
-	-	-	-	-	-	-	-	-	-	-	-	-
Patient acceptability												
-	-	-	-	-	-	-	-	-	-	-	-	-
Side effects												
-	-	-	-	-	-	-	-	-	-	-	-	-

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Profiling bed	Foam mattress	Relative (95% CI)	Absolute	Quality	Importance
Mortality												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) Keogh (2001) did nto report clear blinding and not all of the study's pre-specified outcomes were reported. Not all participants had pressure ulcers (only 14 had existing pressure ulcers), so there was a small sample size and uneven distribution, with only 4 in the experimental group. Grade 1 pressure ulcers analysed only. The authors did not address incomplete outcome data. There was a high drop out from study and it is not possible to identify how many of those who dropped-out had existing pressure ulcers at start of the trial.

(b) There were a limited number of events.

Table 52: Clinical evidence profile: constant force mattress versus low-air-loss mattress

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Constant force mattress	LAL mattress	Relative (95% CI)	Absolute	Quality	Importance
Mean % rate of closure per week – grade 3 or 4 ulcers (classification system not specified), long-term or subacute people in hospital from wards specialising in ventilator-dependent or extensive wound care needs, at 8 week follow-up[29]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	Serious[c]	9 (s.d 4.8) n= 10	5 (s.d 3.7) n= 8	-	MD 4 higher (0.07 to 7.93 higher)	Very low	Critical
Proportion of people with complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Reduction in size and volume of pressure ulcer												
-	-	-	-	-	-	-	-	-	-	-	-	-

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Constant force mattress	LAL mattress	Relative (95% CI)	Absolute	Quality	Importance
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital or NHS care												
-	-	-	-	-	-	-	-	-	-	-	-	-
Patient acceptability												
-	-	-	-	-	-	-	-	-	-	-	-	-
Side effects												
-	-	-	-	-	-	-	-	-	-	-	-	-
Mortality												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) The randomisation reported was inadequate and there was unclear allocation concealment and blinding. No details of incomplete outcome data, type of analysis, pressure ulcer sizes at baseline or classification of pressure ulcers were given. The study used a very small sample size.

(b) The confidence interval crossed 1 MID point.

(c) The data was not log transformed.

Table 53: Clinical evidence profile: wheelchair cushion with equipped with individualised cyclic pressure-relief protocol versus standard wheelchair cushion[b]

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Wheelchair cushion with cyclic pressure-relief protocol	Standard wheelchair cushion	Relative (95% CI)	Absolute		
Pressure ulcer closure (cm^2)[c] – stage 2 or 3 ulcers (classification system not specified), paraplegic or tetraplegic wheelchair users, 30 days follow-up[108]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	78.5 (s.d 74.4) n=22	12.49 (s.d 52.0) n=22	p<0.001	MD 66.01 higher (28.08 to 103.94 higher)	Low	Critical
Pressure ulcer closure rate (cm^2/day)[c] – stage 2 or 3 ulcers (classification system not specified), paraplegic or tetraplegic wheelchair users, 30 days follow-up[108]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	2.17 (s.d 1.46) n=22	2.3 (s.d 2.04) n=22	p<0.001	MD 1.94 higher (0.89 to 2.99 higher)	Low	Critical
PUSH score improvement[c] – stage 2 or 3 ulcers (classification system not specified), paraplegic or tetraplegic wheelchair users, 30 days follow-up[108]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	2.5 (s.d 2.3) n=22	0.7 (s.d 1.1) n=22	p=0.001	MD 1.8 higher (0.73 to 2.87 higher)	Low	Critical
% surface area reduction[c] – stage 2 or 3 ulcers (classification system not specified), paraplegic or tetraplegic wheelchair users, 30 days follow-up[108]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	45.0 (s.d 22.0) n=22	10.2 (s.d 34.9) n=22	p<0.001	MD 34.8 higher (17.78 to 51.82 higher)	Low	Critical
% PUSH score improvement[c] – stage 2 or 3 ulcers (classification system not specified), paraplegic or tetraplegic wheelchair users, 30 days follow-up[108]												

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Wheelchair cushion with cyclic pressure-relief protocol**	**Standard wheelchair cushion**	**Relative (95% CI)**	**Absolute**		
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	21.9 (s.d 24.6) n=22	5.8 (s.d 9.2) n=22	p=0.003	MD 16.1 higher (5.13 to 27.07 higher)	Low	Critical
Proportion of people with pressure ulcers completely healed												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital or NHS care												
-	-	-	-	-	-	-	-	-	-	-	-	-
Patient acceptability												
-	-	-	-	-	-	-	-	-	-	-	-	-
Side effects												
-	-	-	-	-	-	-	-	-	-	-	-	-
Mortality												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) Makhsous (2010) did not provide details of sequence generation, allocation concealment or blinding. The study used a small sample size.
(b) The study included people who had a spinal cord injury and so would not be able to reposition themselves.
(c) Change scores were presented in the paper.

6.2.1 Economic evidence (adults)

Published literature

One study was included with a relevant comparison.[61] This is summarised in the economic evidence profile below (Table 54). See also the study selection flow chart in Appendix D and study evidence tables in Appendix H.

One study that met the inclusion criteria was selectively excluded[196] – this is summarised in Appendix H, with reasons for exclusion given.

One additional study was found which included devices for the management of pressure ulcers as part of a more complex management strategy.[193] This study was not included as the cost-effectiveness of the strategy as a whole is evaluated, and does not provide information on the cost-effectiveness of the device alone.

Table 54: Economic evidence profile: alternating pressure overlays verses alternating pressure mattress replacements verses high specification foam mattresses

Study	Applicability	Limitations	Other comments	Incremental cost	Incremental effects	Cost effectiveness	Uncertainty
Fleurance 2005[61] (UK)	Partially applicable[a]	Potentially serious limitations[b]	A decision analytic model which compared 3 alternatives: alternating pressure overlays (AO), alternating pressure mattress replacements (AR), and high-specification foam mattresses (SC).	Superficial ulcers - 4 week horizon AR-AO = -£20 SC-AR = £100 Severe ulcers - 4 week horizon AR-AO = -£11 SC-AR = £56	QALYs Superficial ulcers - 4 week horizon AR-AO = 0.00005 SC-AR = -0.00027 Severe ulcers - 4 week horizon AR-AO = 0.00002 SC-AR = -0.00011	Superficial - 4 week horizon AR dominates other options Severe - 4 week horizon AR dominates other options	The probability of AR being the most CE at a threshold of £20,000 was 64% for superficial ulcers at 1 and four weeks, and 61% and 61-62% for severe pressure ulcers at 1 and four weeks respectively.

(a) UK NHS setting; cost year 2003.

(b) Quality of life data is obtained from healthcare professionals rather than from patients, short time horizon may not capture full economic impact of these devices. Estimates of health effect estimated rather than obtained from the literature, baseline health outcomes not based on randomised data.

Unit costs

Unit costs were presented to aid consideration of cost effectiveness (see Table 55).

Table 55: Unit costs

Device	Purchase cost	Rental cost	Source
High specification foam mattresses			
Softform premiere	£199.00	NA	Correspondence with Invacare
Harvest Reflect 2 Replacement Mattress	£140.00	NA	Correspondence with Harvest healtcare
Harvest Prime Comfort Plus	£120.00	NA	Correspondence with Harvest healtcare
Pentaflex (4 way turn, acute)	£204.14	NA	Huntleigh
Constant low pressure			
Breeze	£3,453.70	£12.85 per day[a]	Huntleigh
Alternating pressure			
Nimbus 3	£3,565.18	£13.56 per day[a]	Huntleigh

(a) Minimum of 10 day rental

Note - these prices have been obtained directly from manufacturers, and represent the list price for the NHS. It is acknowledged that prices vary locally; therefore these prices are illustrative only. The devices included in the table are those identified by GDG members as being commonly used, and should not be interpreted as recommended devices.

6.2.2 Clinical evidence (neonates, infants, children and young people)

No RCTs or cohort studies were identified. Recommendations were developed using a modified Delphi consensus technique. Further details can be found in Appendix N.

6.2.3 Economic evidence (neonates, infants, children and young people)

Published literature

No relevant economic evaluations were identified.

Economic considerations

In the absence of economic evidence, the GDG considered relevant UK NHS unit costs of various mattresses and overlays (see Table 56) These were considered alongside clinical evidence obtained from the Delphi consensus panel to inform qualitative judgement about cost-effectiveness.

Table 56: Unit costs

Device	Cost	Source
High specification foam mattresses and overlays		
Softform incubator pad (high specification foam)	£49.48	NHS supply chain catalogue[1]
Softform cot mattress (high specification foam)	£107.63	NHS supply chain catalogue[1]

Device	Cost	Source
Repose babytherm redistributing overlay (with pump)	£91.55	NHS supply chain catalogue[1]
Repose paediatric mattress Overlay (with pump)	£91.55	NHS supply chain catalogue[1]
Repose mattress overlay (with pump)	£106.11	NHS supply chain catalogue[1]
Softform premiere	£199.00	Correspondence with manufacturer
Dynamic support surfaces		
Nimbus paediatric mattress	£13.56 per day rental (purchase price £3,293)	Correspondence with manufacturer
Nimbus 3 mattress	£13.56 per day rental (purchase price £3,565)	Correspondence with manufacturer

Note: the costs above are included for illustrative purposes only and should not be interpreted as recommendations in favour of these particular devices. These are list prices only and local prices may vary.

6.2.4 Evidence statements

6.2.4.1 Clinical (adults)

6.2.4.1.1 Water mattress overlay versus low-tech mattress

- One study (n=120) showed there may be no clinical difference between a water mattress overlay and a low-tech mattress for the proportion of people with pressure ulcers completely healed within trial period, but the direction of the estimate of effect favoured the low-tech mattress (very low quality).
- One study (n=120) showed there may be a clinical benefit for a water mattress overlay compared to a low tech mattress for reducing reduction in pain. No estimate of precision could be derived (very low quality).
- No evidence was found for the following outcomes:
  - Time to complete healing
  - Rate of reduction in size of ulcers
  - Reduction in size and/or volume of pressure ulcer
  - Time in hospital or NHS care
  - Patient acceptability
  - Side effects
  - Mortality (all cause)
  - Health-related quality of life

6.2.4.1.2 3-D macroporous overlay versus gel overlay

- One study (n=72) showed there may be no clinical difference between a 3-D macroporous overlay and a gel overlay for the proportion of people with pressure ulcers completely healed. The direction of the estimate of effect favoured the gel overlay (very low quality).
- One study (n=72) showed a 3-D macroporous overlay may be more clinically effective for reducing mortality (all-cause) when compared to a gel overlay (very low quality).

- One study (n=72) showed a 3-D macroporous overlay is potentially more clinically effective for reducing suspension due to worsening of pressure ulcers when compared to a gel overlay (very low quality).
- One study (n=72) showed a 3-D macroporous overlay may be more clinically effective for reducing suspension due to intolerance when compared to a gel overlay (very low quality).
- One study (n=72) showed a 3-D macroporous overlay is potentially more clinically effective for reducing unchanged/worsened pressure ulcers when compared to a gel overlay (very low quality).
- One study (n=72) showed a 3-D macroporous overlay is potentially more clinically effective for improving pressure ulcers when compared to a gel overlay (very low quality).
- One study (n=72) showed a 3-D macroporous overlay may be more clinically effective for increased comfort when compared to a gel overlay (very low quality).
- One study (n=72) showed a 3-D macroporous overlay is potentially more clinically effective for reducing discomfort when compared to a gel overlay (very low quality).
- No evidence was found for the following outcomes:
  - Time to complete healing (time to event data)
  - Rate of healing (continuous data)
  - Rate of change in size of ulcer (absolute and relative) (continuous data)
  - Reduction in size of ulcer and volume of ulcer
  - Pain (pressure ulcer related)
  - Time in hospital or NHS care (continuous data)
  - Side effects
  - Health-related quality of life (continuous data)

6.2.4.1.3 Low-air loss-bed versus low-tech foam mattress overlay

- One study (n=84) showed a low-air-loss bed is potentially more clinically effective for the proportion of people with pressure ulcers completely healed within the trial period when compared to a low-tech foam mattress overlay (very low quality).
- One study (n=49) showed there may be no clinical harm between a low-air-loss bed and a low tech foam mattress overlay for the proportion of people with pressure ulcers completely healed within the trial period, but the direction of the estimate of effect could favour the low-tech foam mattress overlay (very low quality).
- Two studies (n=133) showed a low-air-loss bed is potentially more clinically effective for the proportion of people with pressure ulcers completely healed within the trial period at when compared to a low-tech foam mattress overlay (very low quality).
- One study (n=49) showed there may be no clinical difference between a low-air-loss bed and a low-tech foam mattress overlay for pressure ulcers reduced by 1 grade or more, including completely healed (very low quality).
- One study (n=84) reported there is potentially a clinical benefit for a low-air-loss bed compared to a low-tech foam mattress overlay for rate of ulcer healing. No estimate of precision could be derived (very low quality).
- One study (n=48) reported a mean difference for change in pressure ulcer size for stage 2 pressure ulcers was 2 higher (0.73 to 3.27) in a low-air-loss bed compared with a low-tech foam mattress overlay. The clinical importance is unknown (very low quality).
- One study (n=29) reported a mean difference for change in pressure ulcer size for stage 3 and stage 4 pressure ulcers was 24.7 higher (20.37 to 29.03)in a low-air-loss bed compared with a low-tech foam mattress overlay. The clinical importance is unknown (very low quality).

- One study (n=39) showed there is no clinical benefit of a low-air-loss bed for patient acceptability (mean comfort score) when compared with a low-tech foam mattress overlay (low quality).
- One study (n=84) showed there may be a clinical harm for a low-air-loss bed compared to a low-tech foam mattress overlay for all-cause mortality (very low quality).
- No evidence was found for the following outcomes:
  - Time to complete healing
  - Pain (prssure ulcer related)
  - Time in hospital or NHS care
  - Side effects
  - Health-related quality of life

6.2.4.1.4 Low-air-loss bed versus low-air-loss overlay

- One study (n=93) showed there may be a clinical benefit for a low-air-loss bed compared to a low-air-loss overlay for reduction in size of pressure ulcer (median change in pressure ulcer area). No estimate of precision could be derived (very low quality).
- One study (n=93) showed there may be a clinical benefit for a low-air-loss bed compared to a low-air-loss overlay for reduction in size of pressure ulcer (mean change in pressure ulcer surface area). No estimate of precision could be derived (very low quality).
- No evidence was found for the following outcomes:
  - Time to complete healing
  - Rate of reduction in size of ulcers
  - Proportion of completely healed within trial period
  - Pain (pressure ulcer-related)
  - Time in hospital or NHS care
  - Patient acceptability
  - Side effects
  - Mortality (all cause)
  - Health-related quality of life

6.2.4.1.5 Air-fluidised therapy (AFT) versus standard/conventional therapies

- One study (n=65) showed there may be no clinical difference between an air-fluidised therapy and a standard/conventional therapy for proportion of people with 50% reduction in total surface area (very low quality).
- One study (n=35) showed air-fluidised therapy is potentially more clinically effective for proportion with improvement in pressure ulcers when compared to standard/conventional therapy (very low quality).
- One study (n=65) showed air-fluidised therapy is potentially more clinically effective for proportion with improvement in pressure ulcers when compared to standard/conventional therapy (low quality).
- Two studies (n=100) showed air-fluidised therapy is potentially more clinically effective for proportion with improvement in pressure ulcers when compared to standard/conventional therapy (low quality).
- One study (n=40) showed there may be a clinical benefit for air-fluidised therapy compared to standard/conventional therapy for change in mean ulcer area (stage 2 or 3 ulcers). No estimate of precision could be derived (very low quality).
- One study (n=65) showed there may be a clinical benefit for air-fluidised therapy compared to standard/conventional therapy for change in total pressure ulcer surface area (very low quality).

- One study (n=18) showed air-fluidised therapy is more clinically effective for patient acceptability (patient satisfaction) when compared to standard/conventional therapy (low quality).
- One study (n=27) showed air-fluidised therapy is potentially more clinically effective for patient acceptability (more people experiencing an increase in comfort) when compared to standard/conventional therapy (very low quality).
- One study (n=27) showed there may be a clinical benefit for air-fluidised therapy compared to standard/conventional therapy for patient acceptability (fewer people experiencing a reduction in comfort) (very low quality).
- One study (n=97) showed there may be a clinical benefit for air-fluidised therapy compared to standard/conventional therapy for time in hospital (very low quality).
- One study (n=27) reported there may be no clinical difference between air-fluidised therapy and standard/conventional therapy length of stay in hospital after randomisation, but the direction of the estimate of effect could favour standard care. No estimate of precision could be derived (very low quality).
- One study (n=27) showed air-fluidised therapy is potentially more clinically effective for pain (more people experiencing a reduction in pain) when compared to standard or conventional therapy (very low quality).
- One study (n=27) showed there may be a clinical benefit for air-fluidised therapy compared to standard/conventional therapy for pain (fewer people experiencing an increase in pain) (very low quality).
- One study (n=112) showed air-fluidised therapy is potentially more clinically effective at reducing all-cause mortality when compared to standard/conventional therapy (very low quality).
- Two studies (n=177) showed there may be no clinical difference between an air-fluidised therapy and standard/conventional therapy at reducing all-cause mortality, the direction of the estimate of effect favoured air-fluidised therapy (very low quality).
- No evidence was found for the following outcomes:
  - Time to complete healing
  - Rate of reduction in size of pressure ulcers
  - Proportion of completely healed within trial period
  - Side effects
  - Health-related quality of life

6.2.4.1.6 Alternating-pressure mattress (Nimbus 1) versus.alternating-pressure mattress (Pegasus Airwave)

- One study (n=30) showed an alternating-pressure mattress (Nimbus 1) is potentially more clinically effective for proportion of people with pressure ulcers completely healed (grade 2 and above) when compared to an alternating-pressure mattress (Pegasus Airwave) (very low quality).
- One study (n=30) showed there may be a clinical harm for a alternating-pressure mattress (Nimbus 1) compared to an alternating-pressure mattress (Pegasus Airwave) for proportion of people with decrease in pressure ulcer size (grade 2 and above) (very low quality).
- One study (n=30) showed an alternating-pressure mattress (Nimbus 1) may be more clinically effective than an alternating-pressure mattress (Pegasus Airwave) for proportion of people with increase in pressure ulcer size (grade 2 and above) (very low quality).
- One study (n=41) reported medians an alternating-pressure mattress (Nimbus 1) and an alternating-pressure mattress (Pegasus Airwave) for patient acceptability (comfort). The median for both interventions was 8/10. No estimate of effect or precision could be derived (very low quality).

- One study (n=41) showed there may be no clinical difference between an alternating-pressure mattress (Nimbus 1)and an alternating-pressure mattress (Pegasus Airwave) for mortality, but the direction of the estimate of effect could favour either intervention (very low quality).
- One study (n=41) reported there may be no clinical difference between an alternating-pressure mattress (Nimbus 1) and an alternating-pressure mattress (Pegasus Airwave) for rate of reduction in pressure ulcer surface area (grade 2 and above), but the direction of the estimate of effect could favour either intervention (very low quality).
- No evidence was found for the following outcomes:
  - Time to complete healing
  - Pain (pressure ulcer related)
  - Time in hospital or NHS care
  - Side effects
  - Health-related quality of life

6.2.4.1.7 Alternating-pressure mattress (Nimbus 3) with cushion (Aura) and 4-hourly turning versus an alternating-pressure mattress (Pegasus Cairwave Therapy System) with seating cushion (Proactive 2) and 8-hourly turning

- One study (n=141) showed no clinical difference between an alternating-pressure mattress (Nimbus 3) with cushion (Aura) and 4-hourly turning for proportion of people with pressure ulcers completely healed (grade 2 and above) when compared with an alternating-pressure mattress (Pegasus Cairwave Therapy System) with seating cushion (Proactive 2) and 8-hourly turning, the direction of the estimate of effect favours the 4-hourly turning (moderate quality).
- One study (n=112) reported the mean difference for time in hospital for an alternating-pressure mattress (Nimbus 3) with cushion (Aura) and 4-hourly turning, and an alternating-pressure mattress (Pegasus Cairwave Therapy System) with seating cushion (Proactive 2) and 8-hourly turning. The mean for the alternating-pressure mattress (Nimbus 3) was 21.6 days and 21.7 days for the alternating-pressure mattress (Pegasus Cairwave Therapy System). No estimate of effect or precision could be derived (very low quality).
- One study (n=141) showed an alternating-pressure mattress (Nimbus 3) with cushion (Aura) and 4-hourly turning is potentially more clinically harmful for mortality when compared to an alternating-pressure mattress (Pegasus Cairwave Therapy System) with seating (Proactive 2)cushion and 8-hourly turning (low quality).
- No evidence was found for the following outcomes:
  - Time to complete healing
  - Rate of reduction in size of ulcers
  - Reduction in size and/or volume of ulcer
  - Pain (pressure ulcer related)
  - Patient acceptability
  - Side effects
  - Health-related quality of life

6.2.4.1.8 Alternating-pressure mattress (Nimbus 3) versus alternating-pressure mattress (Pegasus Biwave, Pegasus Airwave, Pegasus Cairwave or AlphaXCell) or alternating-pressure mattress overlay (AlphaXCell or Quattro)

- One study (n=32) reported medians for patient acceptability (comfort) for people in hospital for an alternating-pressure mattress (Nimbus 3) and a different alternating-pressure mattress (Pegasus Biwave, Pegasus Airwave, Pegasus Cairwave or AlphaXCell) or alternating-pressure mattress overlay (AlphaXCell or Quattro). The median for the alternating-pressure mattress (Nimbus 3) was 5 (very comfortable) and 4 (comfortable) for alternating-pressure mattress

(Pegasus Biwave, Pegasus Airwave, Pegasus Cairwave or AlphaXCell) or alternating-pressure mattress overlay (AlphaXCell or Quattro). No estimate of effect or precision could be derived (very low quality).

- One study (n=32) reported medians for patient acceptability (comfort)for elderly people in a hospital or nursing home for an alternating-pressure mattress (Nimbus 3) and a different alternating-pressure mattress (Pegasus Biwave, Pegasus Airwave, Pegasus Cairwave or AlphaXCell) or alternating-pressure mattress overlay (AlphaXCell or Quattro). The median for the alternating-pressure mattress (Nimbus 3) was 5 (very comfortable) and 4 (comfortable) for alternating-pressure mattress (Pegasus Biwave, Pegasus Airwave, Pegasus Cairwave or AlphaXCell) or alternating-pressure mattress overlay (AlphaXCell or Quattro). No estimate of effect or precision could be derived (very low quality).
- One study (n=32) showed there may be a clinical harm for an alternating-pressure mattress (Nimbus 3) compared to a different alternating-pressure mattress (Pegasus Biwave, Pegasus Airwave, Pegasus Cairwave or AlphaXCell) or alternating-pressure mattress overlay (AlphaXCell or Quattro) for mortality (very low quality).
- One study (n=32) reported medians for absolute reduction in wound surface area per day (grade 2 and above) for people in hospital for an alternating-pressure mattress (Nimbus 3) and a different alternating-pressure mattress (Pegasus Biwave, Pegasus Airwave, Pegasus Cairwave or AlphaXCell) or alternating-pressure mattress overlay (AlphaXCell or Quattro). The median for the Nimbus 3 alternating-pressure mattress was 0.12cm^2 (range 0 to 0.21cm2) and 0.08cm^2(range 0.04 to 0.33cm^2) for alternating-pressure mattress (Pegasus Biwave, Pegasus Airwave, Pegasus Cairwave or AlphaXCell) or alternating-pressure mattress overlay (AlphaXCell or Quattro). No estimate of precision could be derived (very low quality).
- One study (n=32) reported medians for relative reduction in wound surface area (grade 2 and above) for people in hospital for an alternating-pressure mattress (Nimbus 3) and a different alternating-pressure mattress (Pegasus Biwave, Pegasus Airwave, Pegasus Cairwave or AlphaXCell) or alternating-pressure mattress overlay (AlphaXCell or Quattro),. The median for the Nimbus 3 alternating-pressure mattress was 2.44% (range 0 to 7.14%) and 1.34% (range 1.11 to 2.88%) for alternating-pressure mattress (Pegasus Biwave, Pegasus Airwave, Pegasus Cairwave or AlphaXCell) or alternating-pressure mattress overlay (AlphaXCell or Quattro). No estimate of precision could be derived (very low quality).
- One study (n=32) reported medians for absolute reduction in wound surface area per day (grade 2 and above) for elderly people in hospital or a nursing home for an alternating-pressure mattress (Nimbus 3) and a different alternating-pressure mattress (Pegasus Biwave, Pegasus Airwave, Pegasus Cairwave or AlphaXCell) or alternating-pressure mattress overlay (AlphaXCell or Quattro). The median for the Nimbus 3 alternating-pressure mattress was 0.11cm^2 (range 0.04 to 0.41cm^2) and 0.05cm^2(range 0 to 0.48cm^2) for alternating-pressure mattress (Pegasus Biwave, Pegasus Airwave, Pegasus Cairwave or AlphaXCell) or alternating-pressure mattress overlay (AlphaXCell or Quattro). No estimate of precision could be derived (very low quality).
- One study (n=32) reported medians for relative reduction in wound surface area (grade 2 and above)for elderly people in hospital or a nursing home for an alternating-pressure mattress (Nimbus 3) and a different alternating-pressure mattress (Pegasus Biwave, Pegasus Airwave, Pegasus Cairwave or AlphaXCell) or alternating-pressure mattress overlay (AlphaXCell or Quattro). The median for the alternating-pressure mattress (Nimbus 3) was 1.57% (range 0.45 to 5%) and 0.99% (range 0 to 2.54%) for alternating-pressure mattress (Pegasus Biwave, Pegasus Airwave, Pegasus Cairwave or AlphaXCell) or alternating-pressure mattress overlay (AlphaXCell or Quattro). No estimate of precision could be derived (very low quality).
- No evidence was found for the following outcomes:
  - Time to complete healing
  - Proportion of completely healed within trial period

- Pain (pressure ulcer related)
- Time in hospital or NHS care
- Side effects
- Health-related quality of life

6.2.4.1.9 Alternating-pressure mattress overlay versus alternating-pressure mattress

- One study (n=113) showed there may be no clinical difference between an alternating-pressure mattress overlay and an alternating-pressure mattress for proportion of people with pressure ulcers completely healed (grade 2 and above), but the direction of the estimate of effect could favour the alternating-pressure mattress (very low quality).
- One study (n=158) showed there is no clinical benefit of an alternating-pressure mattress overlay for pressure ulcer improvement (grade 1 or 2) when compared with an alternating-pressure mattress (low quality).
- One study (n=158) showed there may be no clinical difference between an alternating-pressure mattress overlay and an alternating-pressure mattress for worsening of pressure ulcers (grade 1 or 2), but the direction of the estimate of effect could favour either intervention (very low quality).
- One study (n=1971) showed there is potentially no clinical difference between an alternating-pressure mattress overlay and an alternating-pressure mattress for patient acceptability (number requesting changes for comfort or other device-related reason) (low quality).
- One study (n=158) reported the mean for time in hospital for an alternating-pressure mattress overlay and an alternating-pressure mattress. The mean for an alternating-pressure mattress was 22.17 days and 20.02 days for an alternating-pressure mattress. No estimate of precision could be derived (very low quality).
- One study (n=113) showed an alternating-pressure mattress overlay is potentially more clinically harmful for mortality when compared to an alternating-pressure mattress (very low quality).
- One study (n=113) reported medians for an alternating-pressure mattress and an alternating-pressure mattress overlay for time to ulcer heading. The median for both interventions was 20 days. No estimate of precision could be derived (very low quality).
- One study (n=69) showed there is potentially no clinical difference between an alternating-pressure mattress and an alternating-pressure mattress overlay for absolute change in pressure ulcer surface area (very low quality).
- One study (n=1820) showed there is potentially no clinical difference between an alternating-pressure mattress overlay and an alternating-pressure mattress for patient acceptability (proportion of people with negative comments on mattress motion). The direction of the estimate of effect favoured the air-filled devices (very low quality).
- One study (n=1820) showed there is no clinical difference between an alternating-pressure mattress overlay for patient acceptability (proportion of people with positive comments on mattress motion) when compared with an alternating-pressure mattress the direction of the estimate of effect favoured the alternating-pressure mattress (low quality).
- One study (n=1820) showed there is potentially no clinical difference between an alternating-pressure mattress overlay and an alternating-pressure mattress for patient acceptability (proportion of people with negative comments on getting into/out of bed). The direction of the estimate of effect favoured the alternating-pressure mattress (low quality).
- One study (n=1820) showed there is no clinical difference between an alternating-pressure mattress overlay for patient acceptability (proportion of people with negative comments on movement in bed) when compared with an alternating-pressure mattress. The direction of the estimate of effect favoured the alternating-pressure mattress (low quality).

- One study (n=1820) showed there may be no clinical difference between an alternating-pressure mattress overlay and an alternating-pressure mattress for patient acceptability (proportion of people with positive comments on movement in bed). The direction of the estimate of effect favoured the alternating-pressure mattress (very low quality).
- One study (n=1820) showed there is potentially no clinical difference between an alternating-pressure mattress overlay and an alternating-pressure mattress for patient acceptability (proportion of people commenting on temperature as hot orwarm). The direction of the estimate of effect favoured the alternating-pressure mattress (very low quality).
- One study (n=1820) showed there is potentially no clinical difference between an alternating-pressure mattress overlay and an alternating-pressure mattress for patient acceptability (proportion of people commenting on temperature as sweaty or sticky). The direction of the estimate of effect favoured the alternating-pressure mattress overlay (very low quality).
- One study (n=1820) showed there may be no clinical difference between an alternating-pressure mattress overlay and an alternating-pressure mattress for patient acceptability (proportion of people commenting on temperature as cold/cool), but the direction of the estimate of effect favoured either intervention (very low quality).
- One study (n=1820) showed there may be no clinical difference between an alternating-pressure mattress overlay and an alternating-pressure mattress for patient acceptability (proportion of people reporting the mattress not working or not working properly). The direction of the estimate of effect favoured the alternating-pressure mattress overlay (very low quality).
- One study (n=1820) showed there is potentially no clinical difference between an alternating-pressure mattress overlay and an alternating-pressure mattress for patient acceptability (proportion of people commenting that it was hard to tuck the sheet under, sheets come off or gather or the mattress cover slips). The direction of the estimate of effect favoured the alternating-pressure mattress overlay (very low quality).
- One study (n=1820) showed there is potentially no clinical difference between an alternating-pressure mattress overlay and an alternating-pressure mattress for patient acceptability (proportion of people commenting the mattress/bed was too high). The direction of the estimate of effect favoured the alternating-pressure mattress overlay (very low quality).
- One study (n=1820) showed there may be no clinical difference between an alternating-pressure mattress overlay and an alternating-pressure mattress for patient acceptability (proportion of people reporting the mattress as slippery). The direction of the estimate of effect favoured the alternating-pressure mattress overlay (very low quality).
- One study (n=1820) showed there is potentially no clinical difference between an alternating-pressure mattress overlay and an alternating-pressure mattress for patient acceptability (proportion of people reporting the mattress as too softor edges soft or sloping). The direction of the estimate of effect favoured the alternating-pressure mattress overlay (very low quality).
- One study (n=1820) showed there may be no clinical difference between an alternating-pressure mattress overlay and an alternating-pressure mattress for patient acceptability (proportion of people reporting they were not able to use backrest). The direction of the estimate of effect favoured the alternating-pressure mattress overlay (very low quality).
- One study (n=1820) showed there is potentially no clinical difference between an alternating-pressure mattress overlay and an alternating-pressure mattress for side effects (mattress related fall). The direction of the estimate of effect favoured the alternating-pressure mattress overlay (very low quality).
- One study (n=1820) showed there may be no clinical difference between an alternating-pressure mattress overlay and an alternating-pressure mattress for side effects (mattress-related suspected contact dermatitis). The direction of the estimate of effect favoured the alternating-pressure mattress overlay (very low quality).

- One study (n=1820) showed there may be no clinical difference between an alternating-pressure mattress overlay and an alternating-pressure mattress for side effects (mattress-related climbed over/fell through cot sides). The direction of the estimate of effect favoured the alternating-pressure mattress overlay (very low quality).
- One study (n=1820) showed there may be no clinical difference between an alternating-pressure mattress overlay and an alternating-pressure mattress for side effects (mattress deflation during transfer). The direction of the estimate of effect favoured the alternating-pressure mattress overlay (very low quality).
- No evidence was found for the following outcomes:
  - Rate of reduction in size of pressure ulcers
  - Pain (pressure ulcer related)
  - Side effects
  - Health-related quality of life

6.2.4.1.10 Air-filled devices versus alternating-pressure mattress

- One study (n=60) showed there may be a clinical benefit for an air filled device compared to an alternating-pressure mattress for the proportion of people with pressure ulcers completely healed (grade 2 and above) (very low quality).
- No evidence was found for the following outcomes:
  - Time to complete healing
  - Rate of reduction in size of pressure ulcers
  - Reduction in size and/or volume of ulcer
  - Pain (pressure ulcer related)
  - Time in hospital or NHS care
  - Patient acceptability
  - Side effects
  - Mortality (all cause)
  - Health-related quality of life

6.2.4.1.11 Alternating-pressure cushion versus dry flotation cushion

- One study (n=25) showed there may be a clinical benefit for a dry flotation cushion for proportion of people with pressure ulcers completely healed (grade 2 and above) compared to an alternating-pressure cushion (very low quality).
- One study (n=25) showed there may be a clinical benefit for a dry flotation cushion for mortality when compared to an alternating-pressure cushion (very low quality).
- One study (n=25) showed there may be a clinical benefit for a dry flotation cushion for rate of ulcer healing (area of ulcer) when compared to an alternating-pressure cushion (very low quality).
- One study (n=25) showed there may be a clinical benefit for an alternating-pressure cushion compared to a dry flotation cushion for rate of ulcer healing (volume of ulcer) (very low quality).
- One study (n=25) showed an alternating-pressure cushion is potentially more clinically effective for percentage change in pressure ulcer area per day when compared to a dry flotation cushion (very low quality).
- One study (n=25) showed there may be a clinical benefit for an alternating-pressure cushion compared to a dry flotation cushion for percentage change in volume of pressure ulcer per day (very low quality).
- No evidence was found for the following outcomes:
  - Time to complete healing

- Reduction in size and/or volume of pressure ulcer
- Pain (pressure ulcer related)
- Time in hospital or NHS care
- Patient acceptability
- Side effects
- Health-related quality of life

6.2.4.1.12 Profiling bed versus foam mattress

- One study (n=14) showed there is potentially a clinical benefit for a profiling bed compared to a foam mattress for the proportion of people with completely healed pressure ulcers (very low quality).
- No evidence was found for the following outcomes:
  - Time to complete healing
  - Rate of reduction in size of pressure ulcers
  - Reduction in size and/or volume of pressure ulcer
  - Pain (pressure ulcer related)
  - Time in hospital or NHS care
  - Patient acceptability
  - Side effects
  - Mortality (all cause)
  - Health-related quality of life

6.2.4.1.13 Constant force mattress versus low-air-loss mattress

- One study (n=18) showed a constant force mattress is potentially more clinically effective for the percentage rate of pressure ulcer closure per week when compared to a low-air-loss mattress (very low quality).
- No evidence was found for the following outcomes:
  - Time to complete healing
  - Reduction in size and/or volume of pressure ulcer
  - Proportion of completely healed within trial period
  - Pain (pressure ulcer related)
  - Time in hospital or NHS care
  - Patient acceptability
  - Side effects
  - Mortality (all cause)
  - Health-related quality of life

6.2.4.1.14 Wheelchair cushion with equipped with individualised cyclic pressure-relief protocol versus standard wheelchair cushion

- One study (n=44) showed a wheelchair cushion equipped with individualised cyclic pressure-relief protocol is more clinically effective for pressure ulcer closure rate (area) when compared to a standard wheelchair cushion (low quality).
- One study (n=44) showed a wheelchair cushion equipped with individualised cyclic pressure-relief protocol is more clinically effective for PUSH score improvement when compared to a standard wheelchair cushion (low quality).

- One study (n=44) showed a wheelchair cushion equipped with individualised cyclic pressure-relief protocol is more clinically effective for percentage surface area reduction improvement when compared to a standard wheelchair cushion (low quality).
- One study (n=44) showed a wheelchair cushion equipped with individualised cyclic pressure-relief protocol is more clinically effective for PUSH score improvement when compared to a standard wheelchair cushion (low quality).
- One study (n=44) showed a wheelchair cushion equipped with individualised cyclic pressure-relief protocol is more clinically effective for percentage PUSH score improvement when compared to a standard wheelchair cushion (low quality).
- No evidence was found for the following outcomes:
  - Time to complete healing
  - Proportion of completely healed within trial period
  - Pain (pressure ulcer related)
  - Time in hospital or NHS care
  - Patient acceptability
  - Side effects
  - Mortality (all cause)
  - Health-related quality of life

6.2.4.2 Economic (adults)

- One cost-utility analysis found that alternating pressure mattress replacements dominate alternating pressure overlays and standard care (high specification foam mattresses) in the treatment of pressure ulcers. This study was assessed to be directly applicable with potentially serious limitations.

6.2.4.3 Clinical (neonates, infants, children and young people)

No evidence was identified.

6.2.4.4 Economic (neonates, infants, children and young people)

No evidence was identified.

6.3 Recommendations and link to evidence

6.3.1 Adults

Recommendations	**18. Use high-specification foam mattresses for adults with a pressure ulcer. If this is not sufficient to redistribute pressure, consider the use of a dynamic support surface.** **19. Do not use standard-specification foam mattresses for adults with a pressure ulcer.** **20. Consider the seating needs of people who have a pressure ulcer who are sitting for prolonged periods.** **21. Consider a high-specification foam or equivalent pressure redistributing cushion for adults who use a wheelchair or who sit for prolonged**

	periods and who have a pressure ulcer.
Relative values of different outcomes	The GDG identified that the proportion of people with pressure ulcers completely healed, time to complete healing, reduction in size and volume and rate of reduction in size and volume of pressure ulcers were the most critical outcomes to inform decision making.
Trade off between clinical benefits and harms	One study showed that a low-air-loss bed was more clinically beneficial than a foam mattress overlay for complete healing. Another study showed no difference between a foam mattress overlay and a low-air-loss bed for grade 3 and 4 pressure ulcers. There was higher mortality in the low-air-loss bed group and there was a clinical benefit of low-air-loss bed for rate of ulcer healing, but no clinical difference for patient acceptability or reduction by 1 grade of pressure ulcer. Air-fluidised therapy beds showed some clinical benefit compared to standard or conventional therapies (these varied and included repositioning and massage, use of a sheepskin, gel pad, heel and elbow protector, alternating pressure mattress, alternating pressure pads, air-filled mattresses, water filled mattresses and pads or high density foam pads) for improvement in pressure ulcers. This study also showed a clinical benefit for the reduction in pain, time in hospital, patient satisfaction, and an increase in comfort. There was no clinical benefit for length of stay in hospital or reduction in mortality. There was no clinical difference between a water mattress overlay and a low-tech mattress for pressure ulcers completely healed but there were less people on the water mattress overlay with pain. There were no clinically beneficial results for alternating-pressure mattress overlays compared to alternating-pressure mattresses except for percentage change in surface area. In this study there were more deaths in the mattress group compared to the mattress overlay group. There was a clinical benefit for air-filled devices compared to alternating pressure mattress for proportion of people with pressure ulcers completely healed. There were varying results for 1 alternating-pressure mattress compared to another alternating-pressure mattress. This however was dependant on the exact device in use. There were no clear outcomes for low-air-loss beds compared to low-air-loss overlays. There was an uncertain clinical benefit for a constant force mattress when compared to a low-air-loss mattress. There was a large clinical benefit for a profiling bed when compared to a foam mattress for complete healing of pressure ulcers. An alternating-pressure cushion was more clinically beneficial than a dry flotation cushion for completely healing grade 2 or above pressure ulcers. There was less mortality in the dry flotation cushion group. A 3-D macroporous overlay compared to a gel overlay showed no clinical difference for pressure ulcers completely healed but a benefit of the 3-D macroporous overlay for reducing mortality, discomfort and suspension due to worsening of pressure ulcers or intolerance, and increasing improvement. A wheelchair cushion equipped with an individualised pressure-relief protocol was more clinically beneficial for the reduction in the size of pressure ulcers. Overall, there is no high quality evidence to suggest a benefit in healing for any particular type of device. However people with pressure ulcers are at risk of developing further pressure ulcers, thus the GDG felt it appropriate to recommend the use of high specification mattresses (which are widely used in current clinical practice) for all people as standard. This recommendation is reflective of preventation strategies for pressure ulcers. The GDG highlighted that standard foam mattresses should not be provided to people who have developed pressure ulcers and developed a recommendation to emphasise this. **Wheelchair cushions** Evidence from one study showed that a wheelchair cushion equipped with

	individualised cyclic pressure-relief protocol had more benefit when compared to a standard wheelchair cushion in spinal cord injured patients, however the GDG felt that the intervention was very complicated and combined a number of other interventions and may not be representative of clinical practice. This was a very small study of low quality and the GDG thought that the study may not have been long enough for patients to reach complete healing of ulcers and the loss to follow up may potentially be large. The GDG therefore chose to develop a recommendation similar to that included in the 'prevention guideline' to highlight that people who use a wheelchair who have pressure ulcers should be provided with a high specification foam cushion as a minimum. The GDG also felt that people who were likely to be seated for a long period, who have a pressure ulcer, should be provided with a high specification foam cushion and should have their seating requirements carefully considered.
Economic considerations	High specification foam mattresses are considered to be cost-effective for the prevention of pressure ulcers, compared to standard mattresses. It can therefore be inferred that it is cost-effective for people to remain on these mattresses once a pressure ulcer develops. The mattress will assist with on-going prevention, and will also aid pressure ulcer treatment. High specification foam mattresses are therefore considered to be cost-effective for the treatment of pressure ulcers, compared to standard mattresses. The GDG considered 1 cost-utility analysis which compared alternating pressure mattresses and alternating pressure overlays to high specification foam mattresses for the treatment of pressure ulcers. The study found that alternating pressure mattresses dominate alternating pressure overlays and high specification mattresses, with reduced costs and increased QALYs. However this study had potentially serious limitations and was considered to be only partially applicable. The GDG also considered the unit costs of various devices, and acknowledged that dynamic support surfaces are more costly than high specification foam mattresses. The GDG discussed that, although there was no clear clinical evidence, the crucial factor when healing pressure ulcers is pressure redistribution, and that the dynamic support surfaces do reduce pressure better than high specification foam. Efficient pressure redistributionwill improve quality of life and up front unit costs will be offset, or at least mitigated, by the reduction in further treatment costs. Based on the existing economic evidence, discussion of unit costs and potential benefits of dynamic surfaces, the GDG agreed that where high specification foam was not sufficient for the healing of a pressure ulcer, the use of dynamic support surfaces was likely to be cost effective.
Quality of evidence	The evidence reviewed was of varying populations, interventions, comparisons, and outcomes which made a conclusion of which type of device was preferential very difficult. The evidence was of low to very low quality due to study limitations and most outcomes had serious to very serious imprecision. The GDG discussed the evidence limitations. They further agreed that that none of the studies followed up people for a sufficient amount of time, which is likely to have limited the apparent effectiveness of the mattresses.
Other considerations	The GDG agreed that high specification foam mattresses are commonly used in the NHS for the prevention of pressure ulcers, thus the group considered that it would be unethical to discontinue the use of this device, if it had been started prior to the development of the pressure ulcer.

6.3.2 Neonates, infants, children and young people

Recommendations	**22. Use a high-specification cot or bed mattress or overlay for all neonates, infants, children and young people with a pressure ulcer.**

Relative values of different outcomes	The GDG identified that the proportion of people with pressure ulcers completely healed, time to complete healing, reduction in size and volume and rate of reduction in size and volume of pressure ulcers were the most critical outcomes to inform decision making.
Trade-off between clinical benefits and harms	The GDG used 2 statements from the Delphi consensus panel to develop the recommendation, 'Healthcare professionals should use a high specification cot or bed mattress for all neonates, infants and children who have developed pressure ulcers' and 'Healthcare professionals should use a high specification cot or bed overlay for all neonates, infants and children who have developed pressure ulcers'. The former was accepted during Round 1 of the Delphi consensus survey, the latter was not accepted. During Round 1, qualitative comments received on the use of high specification bed mattresses highlighted that the provision of a pressure redistributing device should be tailored to the child and that selection should consider the physical, clinical and environmental situation. Other comments emphasised that the use of any pressure redistributing device should only be used in combination will a repositioning regimen. The GDG subsequently discussed the latter statement on the use of overlays as well as the comments received during Round 1, which focused on the benefits of using an overlay where a mattress is unavailable. In particular, comments noted that the use of an overlay would be preferable to delaying pressure redistribution. However, comments also highlighted that there were potential safety issues in the use of certain overlays, particularly where this raises the height of the child above the bed rails. The statement was therefore amended to highlight that an overlay may be considered where a mattress is unavailable but safety should be considered where this is used. The GDG therefore amended the statement to 'Healthcare professionals should consider the use of a high specification cot or bed overlay for neonates, infants and children who have developed pressure ulcers, where a high specification mattress is not available, taking into account safety' for inclusion in Round 2 of the Delphi consensus survey. The amended statement was included in Round 2 of the survey and was agreed by the panel. Qualitative responses gathered in Round 2 emphasised that any overlay used should be high specification and noted that repositioning should still be considered a mainstay of care, regardless of the use of a pressure redistributing device. The GDG discussed both of the agreed statements. The GDG felt that high specification mattresses should be provided as standard to all neonates, infants, children and young people who have developed a pressure ulcer, as the potential benefits in reducing pressure were likely to outweigh any harms. The GDG discussed further the use of high specification overlays. The GDG noted that it was likely that high specification mattresses would be provided to people admitted to secondary care, as these would be given as standard preventative treatment. The GDG therefore felt that the recommendation should provide the option of providing people with pressure ulcers a high specification bed mattress or overlay. The GDG felt, although the Delphi consensus panel had agreed a statement that overlays used only be used in the absence of a mattress, that recommending the provision of either device would help to ensure that pressure was reduced across different settings in which care was provided (for example, in the operating theatre, where care is provided in the home, or in long term residential settings). The GDG felt that the option to provide an overlay to those who had developed a pressure ulcer should remain as pressure reduction was the most urgent

	consideration in this situation and, if the use of an overlay was to facilitate the reduction of pressure, this would be important where there is a delay in providing a high specification foam mattress. Furthermore, the GDG noted that some populations (for example, neonates in neonatal intensive care units) were often provided with high specification cot or bed overlays as standard.
Economic considerations	There are costs associated with high specification foam cots and mattresses and overlays. The estimated purchase costs are £50-£199 (typical products identified by GDG members), and the devices can be used over a number of years, therefore the expected cost per patient is low. The GDG considered these costs likely to be offset by the benefits of the intervention in terms of improvement in the person's quality of life, and reduction in future treatment costs through improved healing.
Quality of evidence	No RCTs or cohort studies were identified for neonates, infants, children or young people. Formal consensus using a modified Delphi was therefore used to develop the recommendation. To inform the recommendation, the GDG used 2 statements which were included in Round 1 of the Delphi consensus survey and reached 83% and 64% consensus agreement. The latter statement was therefore included in Round 2 of the survey, where it reached 86% consensus agreement. Further details can be found in Appendix N.
Other considerations	The GDG highlighted that healthcare professionals should be aware of potential safety considerations in the use of overlays for neonates, infants, children and young people, where the use of an overlay causes the child to be above the height of the bed rails.

Recommendations	**23. If pressure on the affected area cannot be adequately relieved by other means (such as repositioning), consider a dynamic support surface, appropriate to the size and weight of the child or young person with a pressure ulcer, if this can be tolerated.**
Relative values of different outcomes	The GDG identified that the proportion of people with pressure ulcers completely healed, time to complete healing, reduction in size and volume and rate of reduction in size and volume of pressure ulcers were the most critical outcomes to inform decision making.
Trade-off between clinical benefits and harms	The GDG used 1 statement from the Delphi consensus panel to develop the recommendation 'Healthcare professionals should not use dynamic support surface for the treatment of pressure ulcers in neonates, infants and children'. The statement was not accepted during Round 1 of the Delphi consensus survey and was therefore amended for inclusion in Round 2 of the survey. The GDG discussed the use of dynamic support surfaces and the comments received during Round 1, which focused upon considering the appropriateness of a dynamic support surface, taking into account a child's weight, clinical condition and tolerability. The statement was therefore amended to highlight that a dynamic support surface may be considered however, any decision should account for these factors. Additionally, the GDG identified that dynamic support surfaces may be appropriate for both children and young people, depending upon individual factors. Therefore the statement was also amended to include children.

	The GDG therefore developed the statement 'Healthcare professionals should consider the use of a dynamic support surface for children and young people who have developed pressure ulcers, where this can be tolerated, if pressure on the affected area cannot be relieved by other means (such as repositioning). The support surface should be appropriate for the size and weight of the child' which was included in Round 2 of the survey, where it was accepted. The GDG discussed the agreed statement and agreed that a recommendation should be made. Qualitative comments received during round 2 of the survey noted that there were some dynamic support surfaces which would be appropriate for use in infants and children. Comments received from panel members generally felt the use of a dynamic support surface may be appropriate where pressure could not be relieved by any other means, for example repositioning. Comments also highlighted that individual patient factors should be taken into account when assessing the potential benefits that use of a dynamic support surface might bring. The GDG therefore felt that on balance, there were potential benefits of using a dynamic support surface for children and young people who have developed pressure ulcers, where pressure cannot be relieved by other means (for example, where a child cannot be repositioning). Any consideration of using a dynamic support surface should account for the individual patient factors and to minimise any potential harms, the size and weight of the child or young person should be carefully considered and an appropriate dynamic support surface selected.
Economic considerations	Dynamic support surfaces are more costly than high specification devices, for example the Nimbus paediatric mattress which can be rented for £13.56 per day. Pressure redistribution is crucial for the treatment of pressure ulcers, and is greatly facilitated by such dynamic devices. Therefore the GDG agreed that the cost of these devices will likely be offset by improvements in quality of life and reduction in further treatment costs. Note that people with pressure ulcers are considered to be at high risk of developing further pressure ulcers, therefore these devices may also help to prevent further pressure ulcers.
Quality of evidence	No RCTs or cohort studies were identified for neonates, infants, children or young people. Formal consensus using a modified Delphi was therefore used to develop the recommendation. To inform the recommendation, the GDG used 1 statement which was included in Round 1 of the Delphi consensus survey, where it reached 12% consensus. The statement was therefore amended for Round 2, where it was accepted at 95% consensus agreement. Further details can be found in Appendix N.
Other considerations	The GDG emphasised that any dynamic support surface used for a child or young person should be appropriate to the size and weight of the child, to prevent safety issues and ensure optimum effectiveness.

Recommendations	**24. Consider using specialist support surfaces (including dynamic support surfaces where appropriate) for neonates, infants, children and young people with pressure ulcers, taking into account their current pressure ulcer risk and mobility.** **25. Tailor the support surface to the location and cause of the pressure ulcer for neonates, infants, children and young people.**

Relative values of different outcomes	The GDG identified that the proportion of people with pressure ulcers completely healed, time to complete healing, reduction in size and volume and rate of reduction in size and volume of pressure ulcers were the most critical outcomes to inform decision making.
Trade-off between clinical benefits and harms	The GDG used 1 statement from the Delphi consensus panel to develop the recommendation 'Healthcare professionals should not use a standard foam cot/bed mattress for neonates, children, infants or young people who have previously developed pressure ulcers and should use specialist patient support surfaces as clinically indicated.' The statement was not accepted during Round 1 of the Delphi consensus survey and was therefore amended for inclusion in Round 2 of the survey. The GDG discussed comments received during Round 1 which highlighted that this would depend upon the reason for initial pressure ulcer development. The GDG agreed that, given pressure ulcers caused by devices were not included in the current guideline, standard foam mattresses should not be used for those who have developed a pressure ulcer previously, given this would mean that they were at risk of subsequent pressure ulcer development. The GDG therefore amended the statement to reflect that these should not be used routinely, however current risk level should be considered when choosing a specialist support surface for this population. The GDG therefore amended the statement for inclusion in Round 2 of the Delphi consensus to 'Healthcare professionals should not routinely use a standard foam cot/bed mattress for neonates, children, infants or young people who have previously developed pressure ulcers and should consider using specialist support surfaces, taking into account current risk level and mobility.' The statement was accepted. The GDG discussed the agreed statement and agreed that a recommendation should be made. Qualitative comments received during round 2 of the survey generally felt that high specification foam mattresses may be appropriate for this population however, standard foam would not be appropriate for infants, children and young people who had previously had a pressure ulcer. Some panel members noted that some people who had a pressure ulcer were likely to be a lesser risk as their risk was related to an acute situation. The GDG acknowledged this but did not feel that standard foam mattresses should be used for anyone who had previously developed a pressure ulcer, due to the increased risk of developing another pressure ulcer. The GDG also noted that many people in secondary care would be provided with a high specification foam mattress as standard care. The GDG felt that the benefits of providing an alternative foam mattress over a standard foam mattress outweighed any potential harms. A recommendation was therefore developed to reflect this and to highlight that specialist support surfaces, for example, dynamic support surfaces, would be more appropriate for this population. The GDG highlighted that provision of any support surface should take into account current risk level and mobility, as highlighted by comments from the Delphi consensus panel, who noted that a child's level of pressure ulcer risk may vary, depending on the risk factors. Comments from the Delphi consensus panel also highlighted the importance of ensuring that the support surface chosen was appropriate to the location and cause of the pressure ulcer. For example, the GDG noted that some pressure redistributing devices may increase pressure in at a risk site, whilst decreasing the pressure elsewhere. The GDG therefore felt that it was important to highlight that the choice of pressure redistributing surface should be tailored to the location and cause of the pressure ulcer. It was noted that this was particularly important given the specific sites considered to be at risk in neonates, infants, children and young people, for example, the head and scalp. The GDG therefore chose to develop a

	recommendation to reflect this.
Economic considerations	Use of high specification and dynamic support surfaces is considered to be cost-effective for individuals with pressure ulcers and for those at significant risk of developing them; therefore standard foam mattresses are not considered to be an efficient use of resources. Furthermore, high specification foam and dynamic surfaces are current best practice and therefore this is not thought to require a substantial increase in resource. Current risk level, mobility, location, and cause of pressure ulcer should be taken into account when selecting the device in order to ensure that an effective device is implemented and clinical and economic benefits are realised as soon as possible.
Quality of evidence	No RCTs or cohort studies were identified for neonates, infants, children or young people. Formal consensus using a modified Delphi was therefore used to develop the recommendation. To inform the recommendation, the GDG used 1 statement which was included in Round 1 of the Delphi consensus survey, where it reached 72% consensus. The statement was therefore amended for Round 2, where it was accepted at 89% consensus agreement. Further details can be found in Appendix N.
Other considerations	There were no other considerations.

7 Adjunctive therapies

7.1 Negative pressure wound therapy (NPWT) - introduction

The application of controlled levels of negative pressure for prolonged periods of time to heal wounds has been reported as being used to treat a number of indications, including open fractures, burns, diabetic ulcers, venous ulcers, surgical wound infections and pressure ulcers.

The concept is that by applying and maintaining a negative pressure over the wound, healing is encouraged and improved. The technique is considered straightforward and involves plalcing a piece of gauze or foam with an open cell structure into the wound, over which a drain with multiple perforations is placed. This is then sealed into place with a transparent adhesive membrane placed along the edges of the wound. The tube is connected at the other end to a vacuum source and to a reservoir. When the vacuum is activated fluid is drawn from the wound and discharged into the reservoir. The adhesive membrane helps to maintain the vacuum seal while the gauze and foam ensures that the entire surface of the wound is exposed to the negative pressure, avoiding areas of high and low pressures.

The GDG were therefore interested in whether negative pressure wound therapy was clinically or cost effective for the treatment of pressure ulcers.

7.2 Review question: What is the clinical and cost effectiveness of negative pressure wound therapy for the treatment of pressure ulcers?

For full details see review protocol in Appendix C.

7.2.1 Clinical evidence (adults)

One Cochrane review was identified (Ubbink 2008)[197] for negative pressure wound therapy (NPWT) for treating chronic wounds. This was used as a basis for the review, focusing only on the pressure ulcer studies included.

Two studies with pressure ulcers were included in the Cochrane review.[63, 205] One further study was identified since publication of the 2008 Cochrane review (Ashby 2012).[13] These studies are summarised in the clinical GRADE evidence profile below (Table 57). See also the full study evidence tables and forest plots in the Appendix G and I.

Ford 2002[63] included 28 people with grade 3 or 4 ulcers and compared NPWT to modern wound dressings (wound gel products) and followed up for 3 ro 10 weeks. Wanner 2003[205] included 22 paraplegic or tetraplegic people with grade 2 or above pressure ulcers of the pelvic region and compared NPWT to wet-to-dry or wet-to-wet gauze dressings with Ringer's solution. Ashby 2012[13] included 12 participants with grade 3 or 4 pressure ulcers and compared NPWT with spun hydrocolloid dressing, foam dressing or alginate dressing. As the comparators were different, these studies could not be meta-analysed.

Summary of included studies

Study	Study type	Intervention/comparison	Population	Outcomes	Length of study/follow-up
Ashby 2012[13]	Pilot RCT	Vacuum-assisted wound closure (NPWT) versus standard care (spun hydrocolloid dressing, foam dressing or alginate dressing).	People in acute care and or the community with grade 3 or 4 pressure ulcers.	• Time to healing.	2 to 6 months follow-up.
Ford 2002[63]	RCT	Vacuum-assisted wound closure (NPWT) versus modern wound dressings (wound gel products).	People with 1 to 3 full-thickness pressure ulcers (grade 2 or 4) present for a minimum of 4 weeks.	• Proportion of pressure ulcers healed; mean % reduction in pressure ulcer volume.	6 weeks treatment 3 to 10 weeks follow-up.
Wanner 2003[205]	RCT.	Ulcer debridement followed by: Vacuum-assisted wound closure (NPWT) versus wet-to-dry or wet-to wet technique with gauze soaked in Ringer's solution.	Peope with a spinal injury (paraplegic or tetraplegic) with grade 3 or 4 pressure ulcers in the pelvic region.	• Time to reach 50% of the initial volume; mean pressure ulcer volume (%).	56 days.

Table 57: Clinical evidence profile: negative pressure wound therapy versus wet-to-dry or wet-to-wet gauze

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	NPWT	Wet-to-dry/wet-to-wet	Relative (95% CI)	Absolute	Quality	Importance
Time to 50% of initial wound volume (follow-up 42 days; measured with: photograph of wound and plaster wound impression) – paraplegic or tetraplegic adults[205]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	None	27 (SD 10) days n=11	28 (SD 7) days n=11	-	MD 1 lower (8.21 lower to 6.21 higher)	Very low	Critical
Mean reduction in volume (% change) (follow-up 42 days; measured with: photograph of wound and plaster wound impression) – paraplegic or tetraplegic adults[205]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[c]	None	53%	65%	p=0.9[d]	MD 12% larger in control group	Very low	Critical
Mean reduction in volume (actual change) (follow-up 42 days; measured with: photograph of wound and plaster wound impression) – paraplegic or tetraplegic adults[205]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious directness	Very serious[c]	None	26.5ml	27.3ml	p=0.2?	MD 0.8ml larger in control group	Very low	Critical
Proportion of people with pressure ulcers completely healed												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time to healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate of reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital												
-	-	-	-	-	-	-	-	-	-	-	-	-

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	NPWT	Wet-to-dry/wet-to-wet	Relative (95% CI)	Absolute	Quality	Importance
Patient acceptability												
-	-	-	-	-	-	-	-	-	-	-	-	-
Side effects (pain, problems with vacuum sealing, reaction of foam)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Mortality (all-cause)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) No details of sequence generation, allocation concealment or blinding. The mean wound size was larger in the vacuum-assisted than the wet-to-dry/wet-to-wet group.
(b) The confidence interval crossed one MID point.
(c) Data taken from graph, no standard deviations given. Very small sample size.
(d) Wilcoxon rank-sum test result.

Table 58: Clinical evidence profile: negative pressure wound therapy versus modern dressings: wound gel products

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	NPWT	Modern dressings: wound gel products	Relative (95% CI)	Absolute	Quality	Importance
Proportion of pressure ulcers completely healed within 6 weeks (follow-up 3-10 months) [63]												
1	Randomised trial	Serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	2/20 (10%)	2/15 (13.3%)	RR 0.75 (0.12 to 4.73)	33 fewer per 1000 (from 117 fewer to 497 more)	Very low	Critical
							-	13.3%		33 fewer per 1000 (from 117		

Quality assessment							No of patients		Effect			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**NPWT**	**Modern dressings: wound gel products**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
										fewer to 496 more)		
Mean reduction in pressure ulcer volume (% change)[d63]												
1	Randomised trial	Serious[a]	No serious inconsistency	No serious indirectness	Very serious[c]	None	51.8%	42.1%	p=0.46	MD 9.7% larger in intervention group	Very low	Critical
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate of reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital												
-	-	-	-	-	-	-	-	-	-	-	-	-
Patient acceptability												
-	-	-	-	-	-	-	-	-	-	-	-	-
Side effects (pain, problems with vacuum sealing, reaction of foam)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Mortality (all-cause)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) No details of allocation concealment were provided. There was a difference in age at baseline.

(b) The confidence interval crossed both MID points.
(c) No standard deviations were given by the authors. The study used a very small sample size.
(d) There were details of reduction in length, width and depth of pressure ulcer (cm). The Cochrane Review (Ubbink 2008) found the figures to be surprisingly large and contacted the author for verification but received no response. No standard deviations were available for this data.

Table 59: Clinical evidence profile: negative pressure wound therapy versus standard care (spun hydrocolloid, alginate or foam dressings)

Quality assessment							No of patients		Effect			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**NPWT**	**Spun hydrocolloid, foam or alginate dressings - GRADE III and IV**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
Proportion of people with pressure ulcers completely healed[13]												
1	Randomised trial	Serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	1/6 (16.7%)	0/6 (0%)	Peto OR 7.39 (0.15 to 372.38)	170 more per 1000 (from 190 more to 530 more)	Very low	Critical
							-	0%		170 more per 1000 (from 190 more to 530 more)		
Mortality (all-cause)[13]												
1	Randomised trial	Serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	2/6 (33.3%)	0/6 (0%)	Peto OR 9.03 (0.49 to 165.19)	330 more per 1000 (from 70 more to 740 more)	Very low	Important
							-	0%		330 more		

Quality assessment							No of patients		Effect			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**NPWT**	**Spun hydrocolloid, foam or alginate dressings - GRADE III and IV**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
										per 1000 (from 70 more to 740 more)		
Pain (wound-related)[13]												
1	Randomised trial	Serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	1/6 (16.7%)	0/6 (0%)	Peto OR 7.39 (0.15 to 372.38)	170 more per 1000 (from 190 more to 530 more)	Very low	Important
							-	0%		170 more per 1000 (from 190 more to 530 more)		
Time to complete healing												
-	-	-	-	-	-	-	-	-	-	-	-	-
Reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate of reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital												

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	NPWT	Spun hydrocolloid, foam or alginate dressings - GRADE III and IV	Relative (95% CI)	Absolute	Quality	Importance
-	-	-	-	-	-	-	-	-	-	-	-	-
Patient acceptability												
-	-	-	-	-	-	-	-	-	-	-	-	-
Side effects (pain, problems with vacuum sealing, reaction of foam)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) No details of blinding of participants or health care providers were reported by the authors. There were a high number of participants who did not continue treatment (all in the NPWT arm).

(b) The confidence interval crossed both MID points and there were a limited number of events.

7.2.2 Economic evidence (adults)

Published literature

One study was identified that included the relevant comparison.[178] This is summarised in the economic evidence profile below (Table 60). See also the study selection flow chart in Appendix D and study evidence tables in Appendix H.

Table 60: Economic evidence profile: negative pressure wound therapy verses dressings

Study	Applicability	Limitations	Other comments	Costs	Effects	Cost effectiveness	Uncertainty
Soares 2013[178] (UK)	Directly applicable[a]	Potentially serious Limitations[b]	Decision analytic Markov model based on a network meta-analysis. Negative pressure wound therapy (intervention4) is compared to alginate (intervention 1), spun hydrocolloid (intervention 2), and foam (intervention 3).	Intvn1: £15,249 Intvn2: £15,054 Intvn3: £14,178 Intvn4: £17,521	QALYs Intvn1: 1.2662 Intvn2: 1.2676 Intvn3: 1.2681 Intvn4: 1.2701	Foam dressings had the highest net benefit (£20,000 threshold). NPWT had the lowest expected net benefit.	Probability cost-effective (at £20,000 threshold): Foam 32%, NPWT 22%. When data from existing literature was combined with expert elicited information spun hydrocolloid had the highest net benefit. When data from a pilot trial was also included NPWT dominated all other treatments.[c]
NCGC model	Partially applicable[d]	Minor limitations[e]	A cost comparison which compares negative pressure wound therapy to a standard care dressing regimen in adults with pressure ulcers that are exhibiting high exudate levels that require regular dressing changes.	Incremental cost (NPWT – dressings): Small pressure ulcers: £276 Medium pressure ulcers: £230 Large pressure ulcers: £216	N/A	Negative pressure wound therapy is more costly than the standard care dressing regimen.	Deterministic sensitivity analyses included varying the rental cost of the negative pressure wound therapy pump, staff costs, and costs faced in the community. Negative pressure wound therapy remained more costly than standard care dressings in the majority of these analyses.

(a) UK setting; perspective of NHS; QALYs calculated.

(b) The costs of NPWT used in this analysis were not considered to be representative of current costs of this therapy, a limitation which is likely to have a significant impact on the results. In addition, the GDG felt that the comparator should be a dressing regimen rather than individual dressings. Finally, the absolute healing hazard is assumed to be constant over time; this assumption was not considered to be realistic by the GDG. Clinical evidence on the effectiveness of NPWT for the treatment of pressure ulcers is considered to be weak.

(c) The primary purpose of this study was to demonstrate how expert elicited information can be used to supplement existing evidence. The cost-effectiveness of NPWT, and the associated uncertainty are calculated with 3 sets of evidence: 1) existing evidence only, 2) existing evidence + expert elicited evidence, 3) existing evidence + expert elicited evidence + pilot trial data. Base case results are those for scenario 1, as chosen by the GDG.

(d) UK setting and from perspective of UK NHS. Quality of life is not considered.

(e) Health outcomes are not included; no probabilistic analysis of uncertainty.

7.2.2.1 New economic analysis

Negative pressure wound therapy (NPWT) was identified by the GDG as a priority for new economic analysis. A model summary is presented here, with full details in Appendix L. This analysis is also summarised in the economic evidence profile (Table 60).

The analysis compares the cost of negative pressure wound therapy to a standard dressing regimen for the management of pressure ulcers that exhibit high levels of exudate and require regular dressing changes. A cost comparison was chosen as the most appropriate form of analysis because the clinical data on the comparative effectiveness of NPWT is weak, and was considered not sufficiently reliable on which to base a cost-effectiveness or cost-utility analysis. The GDG therefore decided to focus on NPWT for the on-going management of pressure ulcers which exhibit high exudate levels and require regular dressing changes, rather than to look at differential effects on healing. It was felt that cost-savings could potentially be realised through fewer dressing changes required with NPWT than with a standard dressing regimen. The aim of this analysis is to explore this hypothesis further.

Methods

A cost-comparison was undertaken where costs were considered from a UK NHS and personal social services perspective; health outcomes were not considered. The model was developed in Excel.

Two interventions were considered:

- NPWT (foam or gauze)
- A standard care dressing regimen.

The population considered was adults with pressure ulcers that exhibit high exudate levels that require regular dressing changes. The time horizon of the model was 2 weeks.

People in the model were allocated to either NPWT or the standard care dressing regimen. Costs of managing the pressure ulcer using each of these techniques was calculated over the 2 week time horizon. Costs included staff time and materials needed for dressing changes, but did not include adjunct management methods such as pressure relieving devices, as these are assumed constant between the 2 arms of the model.

The model considered 3 separate scenarios, management of small pressure ulcers (requiring dressings approximately 10cmx8cm), medium pressure ulcers (requiring dressings approximately 18cmx12cm) and large pressure ulcers (requiring dressings approximately 25cmx15cm).

Various sensitivity analyses were undertaken to test the robustness of model assumptions and data sources. In these analyses, 1 or more inputs were changed in order to evaluate the impact of these changes on the results of the model. Key parameters for sensitivity analysis were unit costs, frequency of dressing change, and staff time. Probabilistic analysis was not undertaken.

Model Inputs

The standard care dressing regimen was based on advice from the GDG members, and included a combination of alginates, cavity fillers, absorbent dressings and a film membrane in various quantities, depending on size of pressure ulcer. The dressing regimen was chosen to reflect a fairly high cost dressing combination, in order to compare the cost of NPWT against the maximum cost of dressings. Full details are provided in Appendix L.

The GDG identified the key NPWT systems which are most commonly used in the UK for inclusion in the model. For these systems, each dressing change requires 1 primary contact dressing, 1

foam/gauze dressing, and 1 canister. One pump is also required, per person, for the duration of the therapy. The GDG acknowledged that other dressings and NPWT systems are available, however it was decided that the analysis should focus on the NPWT systems most commonly used in the UK.

In the base case it was assumed that the first NPWT dressing change is required after 2 days, and subsequent dressing changes take place every 3 days, while the standard dressing regimen is changed every 2 days throughout the time horizon. It was assumed that half an hour of Band 5 nurse time is required for each dressing change, regardless of the management strategy. 30 minutes of specialist nurse (Band 7) time was also included to account for periodic supervision by a specialist nurse.

The cost of staff time was taken from the PSSRU[47]); each dressing change (NPWT and standard care dressing regimen) costs £42.5 in staff costs.

All material costs (standard care dressings, primary contact dressings, NPWT dressings and NPWT canisters) were obtained from the NHS drug tariff,[134] with the exception of the cost of the NPWT pumps which were obtained directly from the manufacturers (full details in Appendix L). NPWT pumps are typically rented rather than purchased, therefore only rental costs are considered in the analysis. The price of the NPWT pump is subject to regional variation, and was therefore varied extensively within the analysis.

The total cost per dressing change for the dressing regimen and for NPWT can be found in Table 61. The total cost per dressing change for the dressing regimen includes the cost of the dressing materials and the cost of staff time. The total cost per dressing change for NPWT includes the NPWT dressing materials, primary contact dressings, canisters, and staff time changing the dressing. Note that the cost of the pump and the cost of the fortnightly supervision by the specialist nurse are not included. An unweighted mean of the costs of the various NPWT systems is presented per dressing change; the accompanying range shows the highest and lowest costs per dressing change out of the included NPWT systems.

Table 61: Mean cost per dressing change (range)

Ulcer size	Standard care dressing regimen	NPWT[a,b]
Small	£63	£83 (£81 – £85)
Medium	£74	£90 (£88 – £91)
Large	£88	£106 (£105 – £106)

(a) Note these costs do not include the cost of the pump or the fortnightly supervision by the specialist nurse.
(b) The range is included in parenthesis to shows the minimum and maximum totals based on the different NPWT systems included in this analysis

Computations

To compute total costs, the cost per dressing change (including staff costs and material costs (see Table 61) was multiplied by the number of dressing changes required over the 2 week time horizon. For the NPWT arm, the total rental cost of the pump (cost per day multiplied by time horizon), and the cost of fortnightly nurse supervision was also added to this.

Sensitivity analyses

Sensitivity analyses were undertaken to explore the effect of different parameter inputs and assumptions on the results of the model. Sensitivity analyses included extending the time required for a NPWT dressing change to 45 minutes, using a specialist nurse (Band 7) to conduct all dressing changes, removing the requirement for specialist supervision, using community costs, using cost

collected by GDG members to capture the effect of regional variation, and altering the frequency of dressing change and rental costs (full details in Appendix L).

Interpreting results

In the absence of reliable evidence to suggest a clear clinical benefit of NPWT, the GDG agreed that NPWT was only likely to represent an efficient use of resources if it was cost-saving (or cost-neutral) for the management of pressure ulcers.

The GDG did not look at individual products to make recommendations, but rather looked at the more general comparison of standard care dressings compared to NPWT. The focus on specific dressings and NPWT systems used within this analysis should not be interpreted as a recommendation in favour these particular products.

Results

Table 62 shows the base case results of the analysis; these results include all the costs detailed in the previous sections, over the 2 week time horizon. It is clear from the table that, even though fewer dressing changes are required with NPWT, the standard care dressing regimen is still less costly than all of the included negative pressure wound therapy systems, for small, medium and large pressure ulcers.

Table 62: Mean (range) base case results – costs over 2 week time horizon

Ulcer size	Standard care dressing regimen	NPWT[a]	Incremental cost
Small	£440	£716 (£706 – £725)	£276
Medium	£520	£751 (£743 – £757)	£230
Large	£614	£830 (£825 – £833)	£216

(a) The range shows the minimum and maximum totals based on the different NPWT systems included in this analysis

In the majority of sensitivity analyses the cost of the dressing regimen remained less than the NPWT systems, including when local costs were used and when NPWT is used in community settings (full details in Appendix L). Threshold sensitivity analyses revealed NPWT would be cost saving for the management of large and medium pressure ulcers if the rental cost per day of the pump reduced to £4, and cost saving for small pressure ulcers if the rental cost per day decreased to £1 (Appendix L). Overall, the sensitivity analyses demonstrated that the results of this analysis were robust to changes in key assumptions, costs, and frequency of dressing change.

Discussion

This analysis found that a standard care dressing regimen is less costly than NPWT for the management of pressure ulcers exhibiting high fluid secretion. This conclusion was robust to a wide range of sensitivity analyses, demonstrating that although uncertainty surrounds model inputs, variation within reasonable ranges does not change the results. As the existing clinical evidence does not identify any clear benefit of NPWT, the GDG agreed that it is unlikely that NPWT is cost-effective compared to standard care dressings for the treatment of pressure ulcers.

Note that the standard care dressing regimen included in this analysis is just 1 of many possible dressing combinations. The dressing regimen was chosen to reflect a fairly high cost dressing combination, in order to compare the cost of NPWT against the maximum cost of dressings. As NPWT has been found to be more expensive than the costly dressing regimen, it is clear that it would also be more costly than simpler dressing regimens.

The conclusions of this analysis fit with those presented by Soares and colleagues,[178] when their analysis was based only on existing data (note that the GDG wished to avoid placing too much reliance on expert elicited data). In this scenario, Soares and colleagues did not find NPWT to be cost-effective compared to dressings.

7.2.3 Clinical evidence (neonates, infants, children and young people)

No RCTs or cohort studies were identified. Recommendations were developed using a modified Delphi consensus technique. Further details can be found in Appendix N.

7.2.4 Economic evidence (neonates, infants, children and young people)

No economic evidence was identified. The economic model developed above was not intended to apply to this population.

7.2.5 Evidence statements

7.2.5.1 Clinical (adults)

7.2.5.1.1 Negative pressure wound therapy versus wet-to-dry or we-to-wet gauze

- One study (n=22) showed there is potentially no clinical difference between NPWT and wet-to-dry or wet-to-wet gauze for time to reduction of initial wound volume by 50%, but the direction of estimate of effect favoured NPWT (very low quality).
- One study (n=22) reported no clinical difference between NPWT and wet-to-dry or wet-to-wet gauze for mean reduction in volume (% change, actual change), but the direction of estimate of effect favoured the wet-to-dry or wet-to-wet gauze. The imprecision was unknown (very low quality).
- No evidence was found for the following outcomes:
  - Time to complete healing (time to event data)
  - Rate of healing (continuous data)
  - Rate of change in size of ulcer (absolute and relative) (continuous data)
  - Proportion of people completely healed within trial period
  - Pain (wound-related)
  - Time in hospital or NHS care (continuous data)
  - Patient acceptability eg measured by compliance and tolerance
  - Side effects (pain, problems with vacuum sealing, reaction of foam)
  - Mortality (all cause) (dichotomous)
  - Health-related quality of life.

7.2.5.1.2 Negative pressure wound therapy versus modern gel dressings

- One study (n=35) showed there may be no clinical difference between NPWT versus modern wound gel dressings for the number of ulcers healed within 6 weeks, but the direction of estimate of effect favoured modern wound gel dressings (very low quality).
- One study (n=35) reported no clinical difference between NPWT versus modern wound gel dressings for the mean reduction in pressure ulcer volume (% change). The imprecision was unknown (very low quality).
- No evidence was found for the following outcomes:
  - Time to complete healing (time to event data)

- Rate of healing (continuous data)
- Rate of change in size of ulcer (absolute and relative) (continuous data)
- Pain (wound-related)
- Time in hospital or NHS care (continuous data)
- Patient acceptability eg measured by compliance and tolerance
- Side effects (pain, problems with vacuum sealing, reaction to foam)
- Mortality (all cause) (dichotomous)
- Health-related quality of life.

7.2.5.1.3 Negative pressure wound therapy versus standard care

- One study (n=12) showed there may be a clinical benefit of NPWT when compared to standard care (spun hydrocolloid, alginate or foam dressings) for proportion of people with pressure ulcers completely healed (very low quality).
- One study (n=12) showed there may be a clinical harm of NPWT when compared to standard care (spun hydrocolloid, alginate or foam dressings) for increased mortality (very low quality).
- One study (n=12) showed there may be a clinical harm of NPWT when compared to standard care (spun hydrocolloid, alginate or foam dressings) for increased pain (very low quality).
- No evidence was found for the following outcomes:
  - Time to complete healing (time to event data)
  - Rate of healing (continuous data)
  - Rate of change in size of ulcer (absolute and relative) (continuous data)
  - Reduction in size of ulcer and volume of ulcer
  - Time in hospital or NHS care (continuous data)
  - Patient acceptability eg measured by compliance and tolerance
  - Side effects (pain, problems with vacuum sealing, reaction to foam)
  - Health-related quality of life.

7.2.5.2 Economic (adults)

- One cost-utility analysis found NPWT is not cost-effective compared to alginate dressings, spun hydrocolloid dressings, or foam dressings (at £20,000 per QALY gained threshold). This study was assessed as directly applicable with potentially serious limitations.
- One cost-comparison found NPWT to be more costly than standard care dressings for the management of pressure ulcers exhibiting high fluid secretion. This analysis is considered to be partially applicable, with minor limitations.

7.2.5.3 Clinical (neonates, infants, children and young people)

No evidence was identified.

7.2.5.4 Economic (neonates, infants, children and young people)

No evidence was identified.

7.3 Hyperbaric oxygen therapy

Hyperbaric oxygen therapy involves administration of 100% oxygen at a pressure of greater than 1 atmospheric pressure absolute. The therapy has been posited to treat a number of conditions including the treatment of pressure ulcers, as it has been suggested that an increase in the oxygen supply to the wound bed therefore improves the healing process.

Creating the appropriate atmosphere can only be achieved in an environment of elevated atmospheric pressure however, a number of methods of administering hyperbaric oxygen therapy have been developed and it is possible to apply hyperbaric oxygen therapy topically, locally (for example, on an arm) or within a mono or multi-place hyperbaric chamber (for 1 or more people). One of the challenges for treatment is that mono and multi-place chambers are not always available locally, so people often have to travel long distances to achieve necessary treatment.

In clinical practice, hyperbaic oxygen therapy has been used with a variety of objectives, generally to facilitate and augment the healing process. The GDG were therefore interested in whether hyperbaric oxygen therapy was clinically or cost effective for the treatment of pressure ulcers.

7.4 Review question: What is the clinical and cost-effectiveness of hyperbaric oxygen therapy for the treatment of pressure ulcers?

For full details see review protocol in Appendix D.

7.4.1 Clinical evidence (adults)

A search was conducted for randomised trials of hyperbaric oxygen therapy for the treatment of pressure ulcers but none were identified. As per the protocol (see Appendix D) a search was then conducted for cohort studies but none relating to pressure ulcers were found. Therefore no studies were included in this review. One Cochrane Review was found (Kranke 2012) which included 9 trials of diabetic or venous ulcers however, no randomised trials were identified focusing on pressure ulcers.[99]

As outlined in Chapter 3, the GDG chose to exclude evidence relating to other chronic wounds from the review, as the group considered that the mechanism of pressure ulcer development differed significantly from other wounds and therefore, it was likely that treatment regimens would differ in their effectiveness.

7.4.2 Economic evidence (adults)

No relevant economic evaluations assessing the cost-effectiveness of hyperbaric oxygen therapy were identified.

In the absence of recent UK cost-effectiveness analysis, relevant unit costs are provided below to aid consideration of cost effectiveness.

Table 63: Example unit costs – hyperbaric oxygen therapy

Treatment component	Cost	Comment
90 minute HBOT session	£155 – £200 per session	40 sessions required
Consumables (dressings etc)	£383	One-off charge
Total	£6,583 - £8,383	This cost does not include accommodation and transport costs

Source: Treatment components and unit costs are obtained from the HBOT centre in Plymouth and GDG member estimates.

Treatments are usually carried out on consecutive weekdays, thus 40 sessions would be expected to take 8 weeks.

Travel costs are likely to be substantial, depending on the mode of transport required and the distance travelled, and are not included in the total above. When people are required to travel a long way there may also be accommodation costs (although these may be partially offset by freeing up hospital beds elsewhere). Distance travelled may be significant, as there are few hyperbaric oxygen chambers in the UK.

7.4.3 Clinical evidence (neonates, infants, children and young people)

No RCTs or cohort studies were identified. Recommendations were developed using a modified Delphi consensus technique. Further details can be found in Appendix N.

7.4.4 Economic evidence (neonates, infants, children and young people)

No economic evidence was identified. Unit costs are provided in Table 63.

7.5 Electrotherapy

Electrotherapy is a non–invasive treatment that has been used for a variety of health conditions, including pressure ulcers and other chronic wounds such as diabetic foot ulcers, venous and arterial leg ulcers. It has been defined as, 'the use of a capacitive coupled electric current to transfer energy to a wound'. Capacitive coupled electrical stimulation of wound healing involves the transference of electric current through an electrode pad applied to moistened skin or wound bed, which form a wet conductive medium. At least 2 electrodes are needed to complete the circuit. The reported rationale for applying electrical stimulation to chronic non-healing wound is that it minics the natural current of injury and will initiate or accelerate the wound healing process, when other aetiological factors have been both assessed and controlled.

Despite its varied use, it is still generally accepted that mechanism by which electrotherapy may work are little understood, with effectiveness and best practice primarily relying on anecdotal evidence.

The GDG was therefore interested as to whether the use of electrotherapy could be considered clinically or cost effective in the treatment of pressure ulcers.

7.6 Review question: What is the clinical and cost effectiveness of electrotherapy for the treatment of pressure ulcers?

For full details see review protocol in Appendix D.

7.6.1 Clinical evidence (adults)

Fourteen studies were included in the review.[2,3,5,12,14,64,65,67,71,83,84,86,94,208] Evidence from these are summarised in the clinical GRADE evidence profile below (ity

Table 5:Clinical). See also the study selection flow chart in Appendix D, forest plots in Appendix I, study evidence tables in Appendix G and exclusion list in Appendix K.

A search was conducted for randomised trials comparing the effectiveness of electrotherapy versus placebo or usual care for treatment of people with pressure ulcers. Sixteen randomised trials were identified. Various types of electrical stimulation were included as were different populations. One study was included which compared different types of electrical stimulation (as well as to a control group). Another trial looked at different durations of electrotherapy compared to placebo. Studies

that reported pressure ulcers (where each participant could have more than 1 ulcer) were separated from those who reported participants. One study included a mixed population of children and adults (aged 10 to 74) but did not report the results for each population separately. The studies had varying time periods (4 weeks to 5 months) and these were meta-analysed together. No significant heterogeneity was found.

Change from baseline scores were used in preference to final values to calculate the reduction in pressure ulcer size. Outcomes such as size of ulcer were reported separately from other outcomes, as the data were continuous and there was a probability that the data was skewed. This was not corrected with log transformation within the studies. It should therefore be emphasised that these data should be interpreted with caution. In addition, it should also be noted that many of the studies had very small sample sizes.

Summary of included studies

Study	Intervention/comparison	Population	Outcomes	Length of study
Adegoke 2001[2]	Interrupted direct current versus sham interrupted direct current. Both groups received routine nursing care.	People with a spinal cord injury with grade 4 pressure ulcers in the pelvic region	• % reduction in surface area	4 weeks treatment
Adunsky 2005[3]	Direct current versus sham direct current. Both groups received conservative treatment of wounds.	People receiving geriatric rehabilitation with grade 3 pressure ulcers.	• Proportion with complete healing of pressure ulcers; speed of pressure ulcer closure; reduction in absolute pressure ulcer area; reduction in % pressure ulcer size	Treatment lasted 8 weeks (57 days) and followed up at day 147 Results were also given for 45 days.
Ahmad 2008[5]	High-voltage pulsed galvanic stimulation (50µsec, 120 Hz, 100-175 v) (45, 60 and 120 minutes) versus sham treatment and conventional wound therapy, wet dressing and whirlpool therapy. Both groups received debridement before admission to study.	People with an indolent pressure ulcers of grade 2 (Yarkony-Kirk classification) chronic pressure ulcers	• Reduction in pressure ulcer surface area (cm^2)	5 weeks treatment
Asbjornsen 1990[12]	Transcutaneous electrical nerve stimulation (3Hz, 85 ms, 100Hz, 20-30mA) versus placebo transcutaneous electrical nerve stimulation. Both groups received conventional pressure ulcer treatment including measures to improve general condition, adequate local care and avoidance of pressure.	Geriatric participants with pressure ulcers on the heels or the sacral region.	• Proportion with complete healing; proportion of pressure ulcers reduced; proportion of pressure ulcers increased.	6 weeks treatment
Baker 1996[14]	Asymmetric biphasic (100usec, 50 pulses/sec) versus symmetric biphasic	People with a spinal cord injury with 1 or more	• Rate of healing of pressure ulcers .	4 weeks treatment

Study	Intervention/comparison	Population	Outcomes	Length of study
	(300Usec, 50 pulses/sec) versus microcurrent (4mA, 10 usec, 1 pulse/sec versus sham electrical stimulation.	pressure ulcers.		
Franek 2011[65]	High voltage monophasic stimulation (100us, 100Hz, 100v) versus no stimulation. Both groups received pharmacological agents, including wound cleansing with potassium permanganate. The ulcer base was covered with compresses of fibrolan, colistin, and iruxol and wet dressings of 10% sodium chloride.	People undergoing surgery with grade 1 to 3 pressure ulcers.	• Proportion of pressure ulcers completely healed; relative change of total surface area of pressure ulcers; relative change in length, relative change in width, relative change in volume, relative change in Gilman Index.	6 weeks treatment
Franek 2012[64]	Standard care plus high voltage electrical stimulation (voltage exceeded 100V, twin monophasic pulses lasting 100us in total and frequency of 100HZ applied). Five 50-minute procedures per week (1 procedure per day) versus no stimulation. Both groups standard care. Pressure redistribution surfaces and devices and pillows as needed; repositioning; standard topical care including cleansing with potassium permanganate followed by dressings; sharp debridement in small number; cleansing; immobilised people received low-molecular-weight heparin (enoxaparin). Antibiotics for those requiring.	People undergoing surgery with grade 2 and 3 pressure ulcers.	• Change in pressure ulcer surface area (%); change in longest length (%); change in longest width (%); change in cavity volume (%); change in granulation tissue area (%); Gilman parameter.	6 weeks treatment
Gentzkow 1991[67]	Low voltage pulsed direct current (2pps/250 µsec to 128pps/150 µsec) versus placebo low voltage pulsed direct	People with grade 2, 3 or 4 pressure ulcers.	• Proportion of pressure ulcers healed, rate of healing, mean healing , withdrawals due to	4 weeks treatment

Study	Intervention/comparison	Population	Outcomes	Length of study
	current . Both groups received equivalent nursing care - cleansing and application of gel and a dry dressing; wound mechanically debrided. 2 hourly turning.		adverse events, acceptability of treatment	
Griffin 1991[71]	High-voltage pulsed direct current (100pps, 200v) versus placebo high-voltage pulsed direct current. Both groups received equivalent nursing care - cleansing and application of gel and a dry dressing; wound mechanically debrided. 2 hourly turning.	People with a spinal cord injury and grade 2 to 4 pressure ulcers in the pelvic region.	• Change in pressure ulcer surface area; proportion of pressure ulcers completed healed.	20 days treatment
Houghton 2010[83]	Twin peaked high-voltage monophasic pulsed current (50 usec, 50-150v) versus no stimulation. Both groups received a community-based interdisciplinary wound care programme.	People in the community with spinal cord injuries with grade 3 to 4 pressure ulcers.	• % reduction in pressure ulcer surface area; proportion of pressure ulcers reduced by at least 50%; changes in pressure ulcer appearance (PWAT scores); improved PWAT scores; proportion with increased pressure ulcers; proportion with improved PSST scores; proportion of grade 2 pressure ulcers completely healed; proportion of 3, 4 and 5 pressure ulcers healed; proportion of grade 3, 4 and 5 pressure ulcers reduced by at least 50%; EST compliance; adverse reactions.	3 months treatment, 4 months follow-up
Jercinovic 1994[84]	Low frequency pulsed current (biphasic, asymmetric, charge-balanced pusses 40pps, 205µs, 35mA) versus no stimulation. Both groups received standard wound	People with a spinal cord injury with pressure ulcers.	• Rate of healing of pressure ulcers.	4 weeks treatment

Study	Intervention/comparison	Population	Outcomes	Length of study
	care. Debridement; standard dressings; antibiotics in cases of infection; dry-floatation mattresses; repositioning; standard rehabilitation programme.			
Karba 1995[86]	4-second trains of biphasic, charge-balanced asymmetrical current stimuli, which alternated with pauses of the same duration (4 seconds) versu sham treatment. Both groups: cleansing; covered with semi-occlusive foam gel dressings.	Males with a spinal cord injury with pressure ulcers.	• Rate of healing of pressure ulcers.	98 days
Kloth 1988[94]	High voltage pulsed current (105Hz, 50 µsec, 100-175v) versus sham treatments. Both groups received pressure-relieving devices that reduced exogenous cutaneous pressure; high-protein dietary supplement; manual debridement and with enzymes.	People with grade 4 pressure ulcers	• Proportion completely healed; healing rate of pressure ulcers.	16 weeks treatment
Wood 1993[208]	Pulsed low-intensity direct current (600uA, 0.8Hz) versus placebo pulsed low-intensity direct current plus standard treatment. Standard treatment received wound cleansing, simple moist dressing, whirlpool baths.	People with grade 2 and 3 chronic pressure ulcers.	• Proportion of pressure ulcers completely healed; reduction in pressure ulcer area; reduction in pressure ulcer area over 80%, pressure ulcer depth.	8 weeks treatment

Table 64: Clinical evidence profile: electrotherapy versus control (placebo or usual treatment)

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Electrotherapy	Control	Relative (95% CI)	Absolute	Quality	Importance
Proportion of people with pressure ulcers completely healed - end of study (people) people receiving geriatric rehabilitation, grade 3 pressure ulcers (classification system not reported) (Adunsky 2005); geriatric adults, pressure ulcer grade not reported (Asbjornsen 1990); people undergoing surgery, grade 1, 2 and 3 pressure ulcers (classification system not reported, see criteria in evidence table) (Franek 2011); people with a spinal cord injury, grade 2 to 4 pressure ulcers (DeLisa classication system) (Griffin 1991); people with a spinal cord injury in the community, pressure ulcers grade 2 to 4 (NPUAP) (Houghton 2010)[3,12,65,71,83];												
5	Randomised trials	Very serious[a]	Serious inconsistency[b]	No serious indirectness	Serious imprecision[c]	None	26/95 (27.4%)	23/93 (24.7%)	RR 1.09 (0.68 to 1.75)	22 more per 1000 (from 79 fewer to 167 more)	Very low	Critical
							-	22.2%		20 more per 1000 (from 71 fewer to 167 more)		
Proportion of pressure ulcers completely healed - end of study (pressure ulcers) - people with chronic pressure ulcers, grade 2 and 3 (classification system not reported)[208]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious imprecision[e]	None	25/43 (58.1%)	1/31 (3.2%)	RR 18.02 (2.58 to 126.01)	549 more per 1000 (from 51 more to 1000 more)	Very low	Critical
							-	3.2%		545 more per 1000 (from 51 more to 1000 more)		
More than 80% decrease in ulcer area - ulcers- people with chronic pressure ulcers, grade 2 and 3 (classification system not reported) [208]												
1	Randomised trial	Very seriousa	No serious inconsistency	No serious indirectness	No serious imprecision	None	31/43 (72.1%)	4/31 (12.9%)	RR 5.59 (2.2 to	592 more per 1000 (from 155	Low	Important

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Electrotherapy	Control	Relative (95% CI)	Absolute	Quality	Importance
									14.21)	more to 1000 more)		
							-	12.9%		592 more per 1000 (from 155 more to 1000 more)		
Proportion of pressure ulcers that reduced by at least 50% at 3 months (people) – people with a spinal cord injury in the community, pressure ulcers grade 2 to 4 (NPUAP)[83]												
1	Randomised trial	Serious[a]	No serious inconsistency	No serious indirectness	Serious imprecision[c]	None	12/15 (80%)	5/14 (35.7%)	RR 2.24 (1.06 to 4.73)	443 more per 1000 (from 21 more to 1000 more)	Low	Important
							-	35.7%		443 more per 1000 (from 21 more to 1000 more)		
Proportion with improved PWAT scores (people) people with a spinal cord injury in the community, pressure ulcers grade 2 to 4 (NPUAP)[83]												
1	Randomised trial	Serious[a]	No serious inconsistency	No serious indirectness	Serious imprecision[c]	None	12/16 (75%)	8/18 (44.4%)	RR 1.69 (0.94 to 3.04)	307 more per 1000 (from 27 fewer to 907 more)	Low	Important
							-	44.4%		306 more per 1000 (from 27 fewer to		

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Electrotherapy	Control	Relative (95% CI)	Absolute		
										906 more)		
Proportion with improved PSST scores (people) – people with a spinal cord injury in the community, pressure ulcers grade 2 to 4 (NPUAP)[83]												
1	Randomised trial	Serious[a]	No serious inconsistency	No serious indirectness	Very serious imprecision[c]	None	8/16 (50%)	9/18 (50%)	RR 1.00 (0.51 to 1.96)	0 fewer per 1000 (from 245 fewer to 480 more)	Very low	Important
							-	50%		0 fewer per 1000 (from 245 fewer to 480 more)		
Proportion of people with decreased ulcers - geriatric adults, pressure ulcer grade not reported [12]												
1	Randomised trial	Very serious[a]	No serious	No serious indirectness	Very serious[c,e]	None	3/7 (42.9%)	0/9 (0%)	Peto OR 13.98 (1.21 to 162.00)	430 more per 1000 (from 60 fewer to 800 more)	Very low	Important
Proportion of people with increased ulcers - geriatric adults, pressure ulcer grade not reported (Asbjornsen 1990); people with a spinal cord injury in the community, pressure ulcers grade 2 to 4 (NPUAP) (Houghton 2010)[83]; [12]												
2	Randomised trials	Very serious[a]	Very serious[g]	No serious indirectness	Very serious[d,e]	None	3/23 (13%)	4/27 (14.8%)	RR 1.05 (0.02 to 68.36)	7 more per 1000 (from 145 fewer to 1000 more)	Very low	Important
							-	11.1%		6 more per 1000 (from 109 fewer to 1000		

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Electrotherapy	Control	Relative (95% CI)	Absolute	Quality	Importance
										more)		
Proportion of people with increased ulcers – geriatric adults, pressure ulcer grade not reported [12]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[c,e]	None	3/7 (42.9%)	0/9 (0%)	Peto OR 13.98 (1.21 to 162.00)	430 more per 1000 (from 60 fewer to 800 more)	Very low	Important
							-	0%		430 more per 1000 (from 60 fewer to 800 more)		-
Proportion of people with increased ulcers – people with a spinal cord injury in the community, pressure ulcers grade 2 to 4 (NPUAP)[83]												
1	Randomised trial	Serious[a]	No serious inconsistency	No serious indirectness	Serious[c]	None	0/16 (0%)	4/18 (22.2%)	Peto OR 0.13 (0.02 to 0.98)	186 fewer per 1000 (from 3 fewer to 217 fewer)	Low	Important
							-	22.2%		186 fewer per 1000 (from 3 fewer to 216 fewer)	-	-
Proportion of ulcers which increased in size - people with chronic pressure ulcers, grade 2 to 3 (classification system not reported)[208]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious	None	0/43 (0%)	10/31 (32.3%)	Peto OR 0.07 (0.02 to 0.25)	290 fewer per 1000 (from 216 fewer to 313	Very low	Important

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Electrotherapy	Control	Relative (95% CI)	Absolute	Quality	Importance
										fewer)		
							-	32.3%		291 fewer per 1000 (from 1216 fewer to 313 fewer)		
Mortality - geriatric adults, pressure ulcer grade not reported (Asbjornsen 1990); people undergoing surgery, grade 1, 2 and 3 pressure ulcers (classification system not reported, see criteria in evidence table) (Franek 2011); people undergoing surgery with grade 2 and 3 pressure ulcers (Franek 2012); people with a spinal cord injury, grade 2 to 4 pressure ulcers (DeLisa classication system)(Griffin 1991); people with grade 4 pressure ulcers (Kloth 1988); people with chronic pressure ulcers, grade 2 and 3 (classification system not reported) (Wood 1993)[12,64,65,71,94,208]												
6	Randomised trials	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[d]	None	3/120 (2.5%)	5/108 (4.6%)	RR 0.58 (0.18 to 1.88)	19 fewer per 1000 (from 38 fewer to 41 more)	Very low	Important
Time to- complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate of reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital												
-	-	-	-	-	-	-	-	-	-	-	-	-
Acceptability of treatment												
-	-	-	-	-	-	-	-	-	-	-	-	-
Side effects												
-	-	-	-	-	-	-	-	-	-	-	-	-

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Electrotherapy	Control	Relative (95% CI)	Absolute	Quality	Importance
Mortality												
-	-	-	-	-	-	-	-	-	-	-	-	-`
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) Adunsky (2005) did not report details of allocation concealment. There was a hHigh drop-out. Per protocol was used but the authors were unclear about the number analysed in the control group. The authors did not provide details of whether outcome assessors were blinded. Asbjornsen (1990) did not report details of sequence generation or allocation concealment or baseline differences. There was a higher drop-out in the treatment group. No statistical tests were mentioned. Franek (2011) did not use blinding (although the authors say it was not possible for EST), but the outcome assessors were not blinded either. Griffin (1991) did not provide details of sequence generation method or allocation concealment. There was a significant difference in groups for duration of spinal cord injury, which was longer in the treatment group. No blinding of outcome assessors. Houghton (2010) did not blind the caregiver or participant however the outcome assessor was blinded. Kloth (1988) did not report details of allocation concealment, baseline differences, blinding of outcome assessors. No statistical tests mentioned. No details of blinding of outcome assessor were given.There were unclear numberof participants randomised but 49 were entered into study, and 34 completed. No details of withdrawals were given; measured pressure ulcer by using length and width. Wood (1993) did not provide details of sequence generation method.There were more participants in treatment than control group. There was a high drop-out in control group arm.

(b) There were wide variations in follow-up times.

(c) The confidence interval crossed 1 MID point (0.5 x standard deviation for continuous outcomes and 0.75 to 1.25 for dichotomous outcomes).

(d) The confidence interval crossed both MID points (0.5 x standard deviation for continuous outcomes and 0.75 to 1.25 for dichotomous outcomes).

(e) There was a very wide confidence interval.

(f) Peto odds ratio was used as 1 arm had zero events.

(g) I^2 = 77%, p=0.04. Asbjornsen, 1990 was a study which included a majority of heel ulcers.

Table 65: Clinical evidence profile: electrotherapy versus control (placebo or usual treatment)

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Electrotherapy	Control	Relative (95% CI)	Absolute	Quality	Importance
% mean reduction in wound surface area (people) people undergoing surgery with grade 2 and 3 pressure ulcers (Franek 2012); people with a spinal cord injury in the community, pressure ulcers grade 2 to 4 (NPUAP) (Houghton 2010)[64,83]												
2	Randomised trials	Serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	Serious[f]	n=42	n=42	-	MD 40.16 higher	Low	Important

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Electrotherapy	Control	Relative (95% CI)	Absolute	Quality	Importance
										(20.39 to 59.92 higher)		
% mean reduction in wound surface area (pressure ulcers) people with pressure ulcers grade 2, 3 or 4 (classification system not reported but details given – see evidence table)[67]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious imprecision[b]	Serious[f]	49.8 (SD 30.9) n=21	23.4 (SD 47.4) n=19	-	MD 26.4 higher (1.32 to 51.48 higher)	Very low	Important
% median reduction in wound surface area (at 20 days) (people) people with a spinal cord injury, grade 2 to 4 pressure ulcers (DeLisa classification system)[71]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious imprecision[e]	Serious[f]	Median 80% (range 52 to 100%)	Median 52% (range 14% to 100%	p=0.05	MD 28%	Very low	Important
Healing rate (%/week) (people) people with grade 4 pressure ulcers (classification system not reported)[94]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	Serious[f]	44.8 (SD 22.6) n=9	-11.59 (SD 18.6) n=7	-	MD 56.39 higher (36.19 to 76.59 higher)	Very low	Important
Healing rate (%/week) (pressure ulcers) people with a spinal cord injury (classification system not reported (BAKER 1996); patients with pressure ulcers grade 2,3 or 4 (classification system not reported but details given – see evidence table) (Gentzkow 1991)[14,67]												
2	Randomised trials	Very serious[a]	No serious inconsistency[i]	No serious indirectness	Serious imprecision[b]	Serious[f]	n=79	n=44	-	MD 2.99 lower (6.03 lower to 0.05 higher)	Very low	Important
Healing rate (%/day) (people) people with a spinal cord injury (classification system not reported)[86]												
1	Randomised	Very	No serious	No serious	No serious	Serious[f]	7.13 (SD 1.46)	-0.66	-	MD 7.79	Low	Important

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Electrotherapy	Control	Relative (95% CI)	Absolute	Quality	Importance
	trial	serious[a]	inconsistency	indirectness	imprecision		n=6	(SD 1.16) n=6		higher (6.30 to 9.28 higher)		
Healing rate (%/day) - exponential fitting (pressure ulcers) people with a spinal cord injury (classification system not reported)[84]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious imprecision[b]	Serious[f]	5.7 (SD 7.1) n=61	2.7 (SD 3.6) n=48	-	MD 3 higher (0.95 to 5.05 higher)	Very low	Important
Healing rate (%/day) - linear fitting (pressure ulcers) people with a spinal cord injury (classification system not reported)[84]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious imprecision[b]	Serious[f]	2.2 (SD 2.1) n=61	1.5 (SD 1.7) n=48	-	MD 0.7 higher (0.01 lower to 1.41 higher)	Very low	Important
Healing rate (%/day) - exponential fitting - crossover group (pressure ulcers) people with a spinal cord injury (classification system not reported)[84]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious imprecision[b]	Serious[f]	5 (SD 4.2) n=20	1.2 (SD 2.1) n=20	-	MD 3.8 higher (1.74 to 5.86 higher)	Very low	Important
Healing rate (%/day) - linear fitting - crossover group (pressure ulcers) people with a spinal cord injury (classification system not reported)[84]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	Serious[f]	2.4 (SD 1.4) n=20	0.6 (SD 1.5) n=20	-	MD 1.8 higher (0.9 to 2.7 higher)	Very low	Important
Time to complete healing (people) geriatric rehabilitation adults, grade 3 pressure ulcers (classification system not reported)[3]												
1	Randomised trial	Very serious[a]	No serious inconsistency	Serious indirectnesse	No serious imprecision	Serious[f]	63.4 (SD 15.1) n=9	89.7 (9.2)	-	MD 26.3 lower	Very low	Important

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Electrotherapy	Control	Relative (95% CI)	Absolute	Quality	Importance
								n=10		(37.69 to 14.91 lower)		
Speed of healing (% change from baseline – days) (people) geriatric rehabilitation adults, grade 3 pressure ulcers (classification system not reported) [3]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious imprecision[b]	Serious[f]	-0.24 (SD 0.14) n=35	- 0.25 (SD 0.14) n=28	-	MD 0.01 higher (0.06 lower to 0.08 higher)	Very low	Important
Acceptability of treatment – compliance to electrotherapy (hours per day) (people) people with a spinal cord injury in the community, pressure ulcers grade 2 to 4 (NPUAP)[83]												
1	Randomsed trial	Very serious[a]	No serious inconsistency	No serious indirectness	N/A	None	Mean 3.0 (SD 1.5) h/dayg	-	-	-	Very low	Important
Acceptability of treatment – uncomfortable sensation in the ulcer when current was turned on (pressure ulcers) people with pressure ulcers grade 2, 3 or 4 (classification system not reported but details given – see evidence table)[67]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious imprecision[k]	Serious[f]	13.6% n=21	4.2% n= 18	-	MD 9.4%	Very low	Important
Side effects (people) people with a spinal cord injury in the community-, pressure ulcers grade 2 to 4 (NPUAP) [83]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	N/A	Serious[f]	See footnote[h]	-	-	-	-	Important
Mean reduction in length (%) – people undergoing surgery with grade 2 and 3 pressure ulcers [64]												
1	Randomised trial	Serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	Serious[f]	74 (SD 29.6) n=26	36.1 (SD 33.9) n=24	-	MD 37.9 higher (20.2 to 55.6 higher)	Low	Important
Mean reduction in longest width (%) – people undergoing surgery with grade 2 and 3 pressure ulcers[64]												
1	Randomised trial	Serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	Serious[f]	79 (SD 25.1) n=26	36.3 (41.9)	-	MD 42.7 higher	Low	Important

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Electrotherapy	Control	Relative (95% CI)	Absolute	Quality	Importance
								n=24		(23.36 to 62.04 higher)		
Mean reduction in cavity volume (%) –people undergoing surgery with grade 2 and 3 pressure ulcers [64]												
1	Randomised trial	Serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	Serious[f]	100 (SD 0.0001) n=26	54 (SD 39.4) n=24	-	46 higher (30.24 to 61.76 higher)j	Low	Important
Mean reduction in granulation tissue area (%) people undergoing surgery with grade 2 and 3 pressure ulcers[64]												
1	Randomised trial	Serious[a]	No serious inconsistency	No serious indirectness	Very serious imprecision c	Serious[f]	37.66 (SD 76.17) n=26	10.36 (SD 43.46) n=24	-	MD 27.3 higher (6.75 lower to 61.35 higher)	Very low	Important
Gillman parameter – people undergoing surgery, grade 1, 2 and 3 pressure ulcers (classification system not reported, see criteria in evidence table) (Franek 2011); people undergoing surgery with grade 2 and 3 pressure ulcers (Franek 2012)[64,65]												
2	Randomised trials	Serious[a]	No serious inconsistency	No serious indirectness	Serious imprecision[b]	Serious[f]	n=26	n=24	-	MD 0.41 higher (0.28 to 0.54 higher)	Very low	Important
Proportion of people with pressure ulcers completely healed												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time to complete healing of pressure ulcers (time to event data)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital												

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Electrotherapy	Control	Relative (95% CI)	Absolute	Quality	Importance
-	-	-	-	-	-	-	-	-	-	-	-	-
Mortality												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) Adunsky (2005) did not provide details of allocation concealment. There was a high drop-out and per protocol was used bu the authors were unclear about the number analysed in the control group. There were no details provided of whether the outcome assessors were blinded. Non-parametric tests were used so the data was possibly skewed but no log transformations were carried out. Adegoke (2001) did not provide details of sequence generation. There was unclear allocation concealment. No details of blinding of outcome assessors were provided.There was 1 drop-out but no details were provided on which arm this was in.There were differences at baseline. No statistical tests were mentioned. Baker (1996) did not provide details of sequence generation or allocation concealment.There was no blinding except of the outcome assessor.There was unclear missing outcome data. Franek (2011) did not blind (although the authors say it was not possible for EST), but the outcome assessors were not blinded either. Non-parametric test were used the data was possibly skewed but no log-transformations were carried out. Franek (2012) did not provide sham treatment and there was no blinding of participants, caregivers or outcome assessors. Gentzkow (1991) did not provide details of sequence generation method; difference at baseline in ulcer size. Pressure ulcers were measured by using length and width. Griffin (1991) did not provide details of sequence generation method or allocation concealment. There was a significant difference in groups for duration of spinal cord injury, which was longer in the treatment group. There was no blinding of outcome assessors. Non-parametric tests used so possibly skewed data but no log transformations. Houghton (2010) did not provide details ofblinding of caregiver and participant. Outcome assessor was blinded. Jercinovic (1994) did not provide details of sequence generation or allocation concealment. No blinding was carried out. There was an unclear number randomised and missing outcome data. Kloth (1988) did not provide details of allocation concealment, baseline differences, blinding of outcome assessors. No statistical tests mentioned.

(b) The confidence interval crossed 1 MID point (0.5 x standard deviation for continuous outcomes and 0.75 to 1.25 for dichotomous outcomes).

(c) The confidence interval crossed both MID points (0.5 x standard deviation for continuous outcomes and 0.75 to 1.25 for dichotomous outcomes).

(d) The confidence interval crossed 1 MID point (0.5 x standard deviation for continuous outcomes and 0.75 to 1.25 for dichotomous outcomes) and limited number of events.

(e) Medians given, no standard deviations given.

(f) The data was skewed data and no log transformations were done.

(g) Recommended treatment time 8 hours per day. Proportion using the recommended time: 4/16. Those who healed used the electrotherapy the longest (539 total hours; 2.54h/day); those who did not heal 331 total hours; 2.24h/day; Average for those who healed: 136.4 days (4.5 months).

(h) Red area or burn under the active electrode after EST treatment, area resolved within 48 hours and remedied by turning down the intensity of subsequent electrotherapy treatments. One participant complained of dizziness and delusions while receiving electrotherapy but was evaluated as withdrawal from narcotics after a lapse in prescription.

(i) Baker (1996) included 3 treatments and treatment B (symmetric biphasic 200usec, 50 pulses/sec) was the most similar to Gentzkow (1991) which was pulsed electrical current (2pulses/sec/350usec to 128pulses/sec/150usec).

(j) A standard deviation of 0.001 was used in Revman as the standard deviation of zero showed no result.

(k) No numerator or denominator given so unable to analyse in Revman.

Table 66: Clinical evidence profile: asymmetric biphasic electrostimulation at 100µs versus control

Quality assessment							No of patients		Effect			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Asymmetric biphasic electrostimulation at 100us**	**Control**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
Mean reduction in wound surface area (% per week)–- people with a spinal cord injury (classification system not reported)[14]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious imprecision[b]	Serious[c]	36.40 (SD 6.2) n=67	32.7 (SD 7) n=25	-	MD 3.7 higher (0.58 to 6.82 higher)	Very low	Important
Proportion of people with pressure ulcers completely healed												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate of reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital												
-	-	-	-	-	-	-	-	-	-	-	-	-
Acceptability of treatment												
-	-	-	-	-	-	-	-	-	-	-	-	-
Side effects												
-	-	-	-	-	-	-	-	-	-	-	-	-
Mortality												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) Baker (1996) did not provide details of sequence generation or allocation concealment. No blinding was carried out except for the outcome assessor.There was unclear missing outcome data.
(b) The confidence interval crossed 1 MID point (0.5 x standard deviation for continuous variables).
(c) The data were possibly skewed but no log transformation was carried out.

Table 67: Clinical evidence profile: symmetric biphasic electrostimulation 300 µsec versus control

Quality assessment							No of patients		Effect			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Symmetric biphasic electrostimulation 300 usec**	**Control**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
Mean reduction in wound surface area (% per week) – people with a spinal cord injury (classification system not reported)[14]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious imprecision[b]	Serious[c]	n=58	n=25	-	MD 3 lower (6.04 lower to 0.04 higher)	Very low	Important
Proportion of people with pressure ulcers completely healed												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital												
-	-	-	-	-	-	-	-	-	-	-	-	-
Acceptability of treatment												
-	-	-	-	-	-	-	-	-	-	-	-	-
Side effects												
-	-	-	-	-	-	-	-	-	-	-	-	-
Mortality												
-	-	-	-	-	-	-	-	-	-	-	-	-

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Symmetric biphasic electrostimulation 300 usec	Control	Relative (95% CI)	Absolute	Quality	Importance
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) Baker (1996) did not report details of sequence generation or allocation concealment. There was no blinding except of the outcome assessor. There was unclear missing outcome data.
(b) The confidence interval crossed 1 MID point (0.5 x standard deviation for continuous variables).
(c) The data were possibly skewed but no log transformation was carried out.

Table 68: Clinical evidence profile: microcurrent versus control

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Microcurrent	Control	Relative (95% CI)	Absolute	Quality	Importance
Mean reduction in wound surface area (% per week) – people with a spinal cord injury (classification system not reported)[14]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious imprecision[b]	Serious[c]	n=42	n=25	-	MD 9.4 lower (12.5 to 6.3 lower)	Very low	Important
Proportion of people with pressure ulcers completely healed												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital												
-	-	-	-	-	-	-	-	-	-	-	-	-

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Microcurrent	Control	Relative (95% CI)	Absolute	Quality	Importance
Acceptability of treatment												
-	-	-	-	-	-	-	-	-	-	-	-	-
Side effects												
-	-	-	-	-	-	-	-	-	-	-	-	-
Mortality												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) Baker (1996) did not report details of sequence generation or allocation concealment. No blinding except of outcome assessor. There was unclear missing outcome data.
(b) Confidence interval crossed 1 MID point (0.5 x standard deviation for continuous variables).
(c) The data were possibly skewed but no log transformation was carried out.

Table 69: Clinical evidence profile: asymmetric biphasic electrostimulation 100µsec versus 300µsec

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Asymmetric biphasic electrostimulation 100µsec	300 µsec	Relative (95% CI)	Absolute		
Mean reduction in wound surface area (% per week) – people with a spinal cord injury (classification system not reported)[14]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	Serious[b]	36.4 (SD 6.2) n=67	29.7 (SD 5.1) n=58	-	MD 6.7 higher (4.72 to 8.68 higher)	Very low	Important
Proportion of people with pressure ulcers completely healed												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time to complete healing of pressure ulcers												

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Asymmetric biphasic electrostimulation 100µsec	300 µsec	Relative (95% CI)	Absolute		
-	-	-	-	-	-	-	-	-	-	-	-	-
Reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital												
-	-	-	-	-	-	-	-	-	-	-	-	-
Acceptability of treatment												
-	-	-	-	-	-	-	-	-	-	-	-	-
Side effects												
-	-	-	-	-	-	-	-	-	-	-	-	-
Mortality												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) Baker (1996) did not provide details of sequence generation or allocation concealment. There was no blinding except of outcome assessor. There was unclear missing outcome data.
(b) The data were possibly skewed but no log transformation was carried out.

Table 70: Clinical evidence profile: asymmetric biphasic electrostimulation 100µsec versus microcurrent

Quality assessment	No of patients	Effect	Quality	Importance

No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Asymmetric biphasic electrostimulation 100usec	Microcurrent	Relative (95% CI)	Absolute		
Mean reduction in wound surface area (% per week) – people with a spinal cord injury (classification system not reported)[14]												
1	Randomised trial	Very serious [a]	No serious inconsistency	No serious indirectness	No serious imprecision	Serious[b]	36.4 (SD 6.2) n=67	23.3 (SD 4.8) n=42	-	MD 13.1 higher (11.02 to 15.18 higher)	Very low	Important
Proportion of people with pressure ulcers completely healed												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital												
-	-	-	-	-	-	-	-	-	-	-	-	-
Acceptability of treatment												
-	-	-	-	-	-	-	-	-	-	-	-	-
Side effects												
-	-	-	-	-	-	-	-	-	-	-	-	-
Mortality												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) Baker (1996) did not provide details of sequence generation or allocation concealment.There was no blinding except of the outcome assessor. There was unclear missing outcome data.
(b) The data were possibly skewed but no log transformation as carried out.

Table 71: Clinical evidence profile: asymmetric biphasic electrostimulation 300µsec versus microcurrent

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Asymmetric biphasic electrostimulation 300usec	Microcurrent	Relative (95% CI)	Absolute	Quality	Importance
Mean reduction in wound surface area (% per week) – people with a spinal cord injury (classification system not reported)[14]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	Serious[b]	29.7 (SD 5.1) n=58	23.3 (SD 4.8) n=42	-	MD 6.4 higher (4.44 to 8.36 higher)	Very low	Important
Proportion of people with complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital												
-	-	-	-	-	-	-	-	-	-	-	-	-
Acceptability of treatment												
-	-	-	-	-	-	-	-	-	-	-	-	-
Side effects												
-	-	-	-	-	-	-	-	-	-	-	-	-
Mortality												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) Baker (1996) did not provide details of sequence generation or allocation concealment. There was no blinding except of the outcome assessor. There was unclear missing outcome data.
(b) The data were possibly skewed but no log transformation was carried out.

Table 72: Clinical evidence profile: electrotherapy versus control group (grade 3 and 4 pressure ulcers)

Quality assessment							No of patients		Effect			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Electrotherapy**	**Control**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
Proportion of participants completely healed - at end of study (people) geriatric rehabilitation adults, grade 3 pressure ulcers (classification system not reported) (Adunsky 2005); people with a spinal cord injury, grade 2 to 4 pressure ulcers (DeLisa classification system)(Griffin 1991); people in the community with a spinal cord injury, pressure ulcers grade 2 to 4 (NPUAP) (Houghton 2010) [3]												
3	Randomised trials	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	15/56 (26.8%)	11/49 (22.4%)	RR 1.14 (0.6 to 2.2)	31 more per 1000 (from 90 fewer to 269 more)	Very low	Critical
							-	7.1%		10 more per 1000 (from 28 fewer to 85 more)		
Mortality - people with grade 4 pressure ulcers (classification system not reported) (Kloth 1988)[94]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	0/9 (0%)	0/7 (0%)	Not pooled	Not pooled	Low	Important
							-	0%		Not pooled		
Absolute reduction in size of pressure ulcer (cm) at end of treatment (better indicated by higher values) - geriatric rehabilitation adults, grade 3 pressure ulcers (classification system not reported) (Adunsky 2005)[3]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision[b]	None	11.15 (SD 1.1) n=21	16.7 (SD 1) n=25	-	MD 5.55 lower (6.16 to 4.94 lower)	Low	Critical
Absolute reduction in size of pressure ulcer (cm) at end of follow-up (better indicated by higher values) - Geriatric rehabilitation adults, grade 3 pressure ulcers (classification system not reported) (Adunsky 2005)[3]												

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Electrotherapy	Control	Relative (95% CI)	Absolute	Quality	Importance
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[c]	None	2.53 (SD 2.11) n=21	2.88 (SD 1.92) n=25	-	MD 0.35 lower (1.53 lower to 0.83 higher)	Very low	Critical
Healing rate (%/week) (people) (better indicated by higher values) – people with grade 4 pressure ulcers (Kloth 1988)[94]												
1	Randomised trial	Very serious[d]	No serious inconsistency	No serious indirectness	No serious imprecision	None	44.8 (SD 22.6) n=9	-11.59 (SD 18.6) n=7	-	MD 56.39 higher (36.19 to 76.59 higher)	Low	Critical
Time to complete healing (days) (better indicated by lower values) geriatric rehabilitation adults, grade 3 pressure ulcers (classification system not reported) (Adunsky 2005)												
1	Randomised trial	Very serious[a]	No serious inconsistency	Serious indirectness[e]	No serious imprecision	None	63.4 (SD 15.1) n=9	89.7 (SD 9.2) n=10	-	MD 26.3 lower (37.69 to 14.91 lower)	Very low	Critical
Speed of healing (% change from baseline - days) (better indicated by lower values) geriatric rehabilitation adults, grade 3 pressure ulcers (classification system not reported) (Adunsky 2005)												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[c]	None	-0.24 (SD 0.14) n=35	-0.25 (SD 0.14) n=28	-	MD 0.01 higher (0.06 lower to 0.08 higher)	Very low	Critical
Time to complete healing of pressure ulcers (time to event data)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Electrotherapy	Control	Relative (95% CI)	Absolute	Quality	Importance
Time in hospital												
-	-	-	-	-	-	-	-	-	-	-	-	-
Acceptability of treatment												
-	-	-	-	-	-	-	-	-	-	-	-	-
Side effects												
-	-	-	-	-	-	-	-	-	-	-	-	-
Mortality												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) Adunsky (2005): no details of allocation concealment were reported by the authors. There was a high drop-out and per protocol was used but was unclear about number analysed in the control group. No details of whether outcome assessors were blinded was reported by the authors. Non-parametric tests were used so the data were possibly skewed but no log transformations were carried out. Adegoke (2001) No details of sequence generation were reported by the authors. There was unclear allocation concealment. No details of blinding of outcome assessors was reported by the authors. There was 1 drop-out but no details of which arm were provided. The groups were different at baseline. No statistical tests were mentioned. Baker (1996): no details of sequence generation or allocation concealment were reported by the authors. No blinding except of outcome assessor was reported. There was unclear missing outcome data. Franek (2011): no blinding (although the authors say it was not possible for EST), but the outcome assessors were not blinded either. Non-parametric test used so possibly skewed data but no log-transformations. Franek (2012) No sham treatment, no blinding of participants, caregivers or outcome assessors. Gentzkow (1991): Mo details of sequence generation method; difference at baseline in ulcer size; measured pressure ulcer by using length and width. Griffin (1991): no details of sequence generation method or allocation concealment. There was a significant difference in groups for duration of spinal cord injury, which was longer in the treatment group. No blinding of outcome assessors. Non-parametric tests used so possibly skewed data but no log transformations. Houghton (2010): no blinding of caregiver and participant. Outcome assessor was blinded. Jercinovic (1994) No details of sequence generation or allocation concealment. No blinding. Unclear number randomised and missing outcome data. Kloth (1988) No details of allocation concealment, baseline differences, blinding of outcome assessors. No statistical tests mentioned. Ullah (2007): no details of sequence generation or allocation concealment. No details of missing data, how they measured ulcer size, baseline differences or whether outcome assessors were blinded.

(b) Confidence interval crossed both MID points.

(c) Confidence interval crossed 1 MID point.

(d) Kloth (1988) No details of allocation concealment, baseline differences, blinding of outcome assessors. No statistical tests mentioned. No details of blinding of outcome assessor. Unclear number randomised but 49 were entered into study, and 34 completed, no detail of withdrawals; measured pressure ulcer by using length and width.

(e) Time to event data not given as hazard ratio, high risk of bias from mean values.

7.6.1 Economic evidence (adults)

One study was included with the relevant comparison.[118] This is summarised in the economic evidence profile below (Table 73). See also the study selection flow chart in Appendix D and study evidence table in Appendix H.

Table 73: Economic evidence profile: Electrotherapy versus standard wound care

Study	Applicability	Limitations	Other comments	Incremental cost	Incremental effects	Cost effectiveness	Uncertainty
Mittmann 2011[118] (Canada)	Partially applicable[a]	Potentially serious limitations[b]	A decision analytic model to calculate the incremental cost per pressure ulcer healed when electrical simulation therapy (ES) plus standard wound care (SWC) is compared to SWC in patients with grade 3-4 pressure ulcers and spinal cord injury.	-£123	0.164 pressure ulcers healed per year	ES+SWC dominates SWC	One-way sensitivity analyses were carried out to identify model drivers; the percentage of pressure ulcers healed was the largest driver of the model. Probabilistic sensitivity analyses revealed a probability that ES+WSC dominates SWC of 61.5%.

(a) This study is based on the Canadian health care system and does not consider quality of life. The intervention is assessed within a spinal cord injury population thus generalisation to all those with pressure ulcers may not be appropriate.

(b) The authors have made several assumptions around transition probabilities, for example using a 3 month healing rate taken from Houghton (2010) for 12 month probability of ulcers healing, whereas the rate for relapse was a 9 month rate also assumed to be annual. Estimates of costs and resource use are calculated from the Houghton trial rather than a systematic procedure. The time horizon is only 1 year, thus relevant costs and benefits may not have been accounted for. It is unclear how costs have been calculated.

7.6.2 Clinical evidence (neonates, infants, children and young people)

No RCTs or cohort studies were identified. Recommendations were developed using a modified Delphi consensus technique. Further details can be found in Appendix N.

7.6.3 Economic evidence (neonates, infants, children and young people)

No economic evidence was identified.

7.6.4 Evidence statements

7.6.4.1 Clinical evidence (adults)

- Five studies (n=188) showed there is potentially no clinical difference between electrotherapy and a placebo or usual treatment for the proportion of people with pressure ulcers completely healed, the direction of the estimate of effect favoured the electrotherapy group (very low quality).
- One study (n=74) showed electrotherapy is potentially more clinically effective than placebo or usual treatment for the proportion of pressure ulcers completely healed (very low quality).
- One study (n=74) showed electrotherapy is more clinically effective than placebo or usual treatment for the proportion of people with over 80% decrease in pressure ulcer area (low quality).
- One study (n=29) showed electrotherapy is potentially more clinically effective than placebo or usual treatment for the proportion of pressure ulcers that reduced by at least 50% (low quality).
- One study (n=34) showed electrotherapy is potentially more clinically effective than placebo or usual treatment for the improvement of PWAT scores (low quality).
- One study (n=34) showed there may be no clinical difference between electrotherapy and a placebo or usual treatment for improvement of PSST scores (very low quality).
- One study (n=16) showed electrotherapy may be more clinically effective than placebo or usual treatment for the proportion of people with decreased pressure ulcers (very low quality)
- Two studies (n=50) showed there may be no clinical difference between electrotherapy and a placebo or usual treatment in a geriatric and spinal cord injured population for the proportion of people with increased pressure ulcers, the direction of the estimate of effect favoured the placebo or usual treatment (very low quality).
- One study (n=16) showed placebo or usual treatment may be more clinically effective than electrotherapy in a geriatric population for reducing the proportion of people with increased pressure ulcers (very low quality).
- One study (n=34) showed electrotherapy is possibly more clinically effective than placebo or usual treatment in a spinal cord injured population for reducing the proportion of people with increased pressure ulcers (low quality).
- One study (n=74) showed electrotherapy is more clinically effective than placebo or usual treatment for the proportion of pressure ulcers which increased in size (very low quality).
- Six studies (n=228) showed there may be no clinical difference between electrotherapy and placebo or usual treatment for all-cause mortality, the direction of the estimate of effect favoured electrotherapy (very low quality).
- Two studies (n=84) showed electrotherapy is potentially more clinically effective than placebo or usual treatment for achieving a higher % mean reduction in wound surface area for surgical inpatients and people in the community with spinal cord injuries (very low quality)
- One study (n=40) showed that electrotherapy may be more clinically effective at achieving higher % mean reduction in wound surface area than placebo or usual treatment (very low quality)

- One study reported that electrotherapy may be more clinically effective at achieving higher % median reduction in wound surface area than placebo or usual treatment (very low quality).
- One study (n=16) showed electrotherapy is more clinically effective than placebo or usual treatment for achieving a higher rate of healing (%/week) (very low quality).
- Two studies (n=123) showed electrotherapy is potentially more clinically effective than placebo or usual treatment for having a higher healing rate (%/week) in people with a spinal cord injury and general participants (very low quality).
- One study (n=12) showed electrotherapy is more clinically effective than placebo or usual treatment for having a higher healing rate (%/day) for people with a spinal cord injury (low quality).
- One study (n=109) showed there is potentially no clinical difference between electrotherapy and placebo or usual treatment for % healing rate per day when data were fitted linearly and exponentially for people with a spinal cord injury, but the direction of the estimate of effect favoured electrotherapy (very low quality).
- One study (n=19) showed electrotherapy is more clinically effective than placebo/usual treatment for delaying time to complete healing (very low quality).
- One study (n=63) showed there is potentially no clinical difference between electrotherapy and placebo/usual treatment for speed of healing (days, percentage change from baseline), the direction of the estimate of effect favoured either intervention (very low quality).
- One study (n= 34) reported red area or burn under the active electrode after EST treatment, area resolved within 48 hours and remedied by turning down the intensity of subsequent electrotherapy treatments (very low quality).
- One study (n=16) reported mean 3.0 (s.d 1.5) hours per day for compliance to electrotherapy treatment but there was no results for the placebo/usual treatment group (very low quality).
- One study (n=39) reported there may be a clinical harm of electrotherapy when compared to placebo or usual treatment for an uncomfortable sensation in the ulcer when current was turned on (very low quality).
- One study (n=50) showed electrotherapy may be more clinically effective than placebo or usual treatment for achieving a higher % mean reduction in length (low quality).
- One study (n=50) showed electrotherapy may be more clinically effective than placebo or usual treatment for achieving a higher % mean reduction in longest width (low quality).
- One study (n=50) showed electrotherapy may be more clinically effective than placebo or usual treatment for achieving a higher % mean reduction in cavity volume (low quality).
- One study (n=50) showed electrotherapy is potentially more clinically effective than placebo or usual treatment for achieving a higher % mean reduction in granulation tissue area (low quality).
- One study (n=50) showed there is potentially no clinical difference between electrotherapy and placebo or usual treatment for reducing the Gilman parameter, the direction of the estimate of effect favoured either intervention (very low quality).
- One study (n=92) showed there is potentially no clinical difference between asymmetric biphasic electrostimulation at 100µs compared to control for mean reduction in % per week mean wound surface area reduction, the direction of the estimate of effect favoured the asymmetric biphasic electrostimulation at 100µs (very low quality).
- One study (n=83) showed there is potentially no clinical difference between symmetric biphaseic electrostimulation 300µs compared to control for mean reduction in % per week mean wound surface area reduction, the direction of the estimate of effect favoured control (very low quality).
- One study (n=67) showed there is potentially no clinical difference between microcurrent compared to control for mean reduction in % per week mean wound surface area reduction, the direction of the estimate of effect favoured the control (very low quality).

- One study (n=125) showed there is potentially no clinical difference between asymmetric biphasic electrostimulation at 100µs compared to 300µs for mean reduction in % per week mean wound surface area reduction, the direction of the estimate of effect favoured the asymmetric biphasic electrostimulation at 100µs (very low quality).
- One study (n=109) showed there is potentially no clinical difference between asymmetric biphasic electrostimulation at 100µs compared to microcurrent for mean reduction in % per week mean wound surface area reduction, the direction of the estimate of effect favoured the asymmetric biphasic electrostimulation at 100µs (very low quality).
- One study (n=100) showed there is potentially no clinical difference between asymmetric biphasic electrostimulation at 300µs compared to microcurrent for mean reduction in % per week mean wound surface area reduction, the direction of the estimate of effect favoured the asymmetric biphasic electrostimulation at 300µs (very low quality).
- Three studies (n=105) showed there may be no clinical difference between electrotherapy and control group for complete healing for grade 3 and above pressure ulcers, the direction of the estimate of effect favours electrotherapy (very low quality).
- One study (n=16) showed there is no clinical difference between electrotherapy and control group for mortality for those with grade 4 pressure ulcers, the direction of the estimate of effect favours either intervention (low quality).
- One study (n=46) showed there is no clinical difference between electrotherapy and control group for absolute reduction in size of pressure ulcer (cm) at end of treatment for those with grade 3 pressure ulcers, the direction of the estimate of effect favours the control (very low quality).
- One study (n=46) showed there is no clinical difference between electrotherapy and control group for absolute reduction in size of pressure ulcer (cm) at end of follow-up for those with grade 4 pressure ulcers, the direction of estimate of effect favoured either intervention (low quality).
- One study (n=16) showed there is no clinical difference between electrotherapy and control group for % healing rate per week for those with grade 3 pressure ulcers, the direction of estimate of effect favours the control group (very low quality).
- One study (n=19) showed electrotherapy was more clinically effective than the control group for time to complete healing (days) for those with grade 3 pressure ulcers, the direction of estimate of effect favours the control (very low quality).
- One study (n=63) showed there is potentially no clinical difference between electrotherapy and control group for speed of healing (% change from baseline, days) for those with grade 3 pressure ulcers, the direction of estimate of effect favours either intervention (very low quality).
- No evidence was found for the following outcomes:
  - Pain (wound-related)
  - Time in hospital or NHS care
  - Health-related quality of life

7.6.4.2 Economic evidence (adults)

- One cost-effectiveness analysis found electrical stimulation in combination with standard wound care to dominate standard wound care, in people with a spinal cord injury with grade 3-4 pressure ulcers. This study was assessed as partially applicable, with potentially serious limitations.

7.6.4.3 Clinical evidence (neonates, infants, children and young people)

No RCTs or cohort studies were identified. Recommendations were developed using a modified Delphi consensus technique. Further details can be found in Appendix N.

7.6.4.4 Economic evidence (neonates, infants, children and young people)

No economic evidence was identified.

7.7 Recommendations and link to evidence

7.7.1.1 Adults

Recommendations	**26. Do not routinely offer adults negative pressure wound therapy to treat a pressure ulcer, unless it is necessary to reduce the number of dressing changes (for example, in a wound with a large amount of exudate).** **27. Do not offer the following to adults to treat a pressure ulcer:** • **electrotherapy** • **hyperbaric oxygen therapy.**
Relative values of different outcomes	The GDG identified that the proportion of people with pressure ulcers completely healed, time to complete healing, reduction in size and volume and rate of reduction in size and volume of pressure ulcers were the most critical outcomes to inform decision making.
Trade off between clinical benefits and harms	**Electrotherapy** Electrotherapy was found to be more clinically beneficial than placebo (or usual treatment) for the proportion of pressure ulcers completely healed in 1 small trial, however it was not found to be clinically beneficial for the proportion of people with pressure ulcers completely healed when 5 trials were meta-analysed. Electrotherapy was clinically beneficial for reducing the size of pressure ulcer area and had a faster healing rate. There were however differing results as to whether electrotherapy also increased the size of ulcers. The GDG considered that electrotherapy was likely to be most beneficial for pressure ulcers of grade 3 and 4, however no clinical benefit was found for the proportion of people completely healed, yet there was a clinical benefit for placebo/usual treatment for the reduction in size of pressure ulcer. There was a clinical benefit for healing rate and time to complete healing. There were no results for electrotherapy compared to other interventions. The GDG felt that any benefit of electrotherapy in clinical practice was likely to be in pressure ulcers of grade 3 and 4. However, the limited and conflicting evidence for these grade mostly demonstrated no clinical benefit of electrotherapy. **Hyperbaric oxygen therapy** No studies were found for hyperbaric oxygen therapy. The GDG considered that hyperbaric oxygen therapy can cause discomfort and may not be tolerable, therefore in the absence of any evidence of benefit the GDG felt that it should not be used for the treatment of pressure ulcers. **Negative pressure wound therapy** There was limited evidence for negative pressure wound therapy in pressure ulcers, with only 3 randomised controlled studies found. Two of the studies looked at negative pressure wound therapy compared to gel dressings or gauze dressing, and no clinical benefit was shown either way. One very small study showed clinical benefit of negative pressure wound therapy compared to standard care (spun hydrocolloid, alginate or foam dressings) for pressure ulcers completely healed, however there was more clinical harm from increased pain and mortality in the negative pressure wound therapy group.

	The evidence for the benefit of negative pressure wound therapy was limited and thus could not be recommended for use in routine clinical practice. However, the GDG acknowledged that there were some individuals in which the use of negative pressure wound therapy may have some benefits, most notably in people who require a large number of dressing changes because of a significant amount of exudate. The GDG therefore felt that there may be specific clinical situations in which the negative pressure wound therapy may be used. Finally, the GDG also wished to highlight the need for further high quality research in the area and highlighted in the recommendations that the use of negative pressure wound therapy may be conducted in the context of a clinical trial.
Economic considerations	**Electrotherapy** One economic study found electrical stimulation in combination with standard pressure ulcer care to dominate standard pressure ulcer care. However, this study was based on clinical effectiveness evidence which showed greater effect than found in the review of the clinical literature, and it also had several other limitations. Given the limitations and the partial applicability of this study, the GDG did not feel that the conclusions of this economic evaluation would apply within a UK NHS setting. The GDG felt that given the absence of any clear evidence to suggest a clinical benefit of electrotherapy for the treatment of pressure ulcers, the substantial additional resource use associated with this therapy could not be justified. Electrotherapy is not considered to be cost-effective. **Hyperbaric oxygen therapy** In the absence of relevant economic evidence the GDG considered the unit costs of hyperbaric oxygen therapy. The GDG noted that this is an expensive therapy, costing up to £8,383 before accounting for travel and accommodation costs. Given that no evidence of clinical effect was identified, the GDG felt that the high costs of this therapy could not be justified for the management of pressure ulcers. Hyperbaric oxygen therapy is not considered to be cost-effective. **Negative pressure wound therapy** The GDG considered 1 existing cost-utility analysis; the study found that NPWT dominates dressings (in the base case). However, as no evidence of clinical benefit was found in the clinical review, the GDG were concerned that the economic evidence was based on weak evidence of clinical effectiveness, and for this reason was insufficient on which to base a recommendation. The GDG felt that, in the absence of clinical effectiveness evidence for the healing of pressure ulcers, NPWT may be cost saving for exudate management, as NPWT dressings are changed less frequently. A cost comparison was therefore carried out, looking at NPWT compared to a standard care dressing regime for pressure ulcers with high fluid secretion that require regular dressing changes. This analysis revealed that NPWT was more expensive than standard care dressings in all scenarios (increases of £276, £230, and £216 for small, medium, and large pressure ulcers respectively); therefore NPWT was not cost saving compared to standard care for the management of pressure ulcers. In light of the additional cost of using NPWT, and lack of clear evidence of clinical benefit, the GDG did not feel there was sufficient evidence to suggest that NPWT is cost-effective compared to standard care.
Quality of evidence	For the electrotherapy review the majority of evidence available for the included outcomes was very low or low quality, due to having serious or very serious imprecision and study limitations. There was no evidence for hyperbaric oxygen therapy and limited evidence for negative pressure wound therapy. For the 3studies available for negative pressure wound therapy there was little clinical benefit found.

	Where there was benefit or harm shown the outcomes had very serious imprecision and were graded very low quality.
Other considerations	The GDG acknowledged that there may be evidence available on the use of adjunctive therapies for chronic wounds, however as per Chapter 3, the GDG decided not to consider indirect evidence. **Negative pressure wound therapy** There is some suggestion of benefit in reducing the number of dressing changes and therefore reducing consequent pain and discomfort from a patient perspective, therefore NPWT might have some benefit in a subset of people with high pain levels or those with high exudate levels who require very frequent dressing changes. The tolerability of NPWT was discussed. It can be very uncomfortable and noisy and thus not suitable for many people.

7.7.1.2 Neonates, infants, children and young people

Recommendations	**28. Do not routinely use negative pressure wound therapy to treat a pressure ulcer in neonates, infants, children and young people.** **29. Do not use the following to treat a pressure ulcer in neonates, infants, children and young people:** • **electrotherapy** • **hyperbaric oxygen therapy.**
Relative values of different outcomes	The GDG identified that the proportion of people with pressure ulcers completely healed, time to complete healing, reduction in size and volume and rate of reduction in size and volume of pressure ulcers were the most critical outcomes to inform decision making.
Trade-off between clinical benefits and harms	The GDG used 3 statements from the Delphi consensus to inform the recommendation on the use of adjunctive therapies in neonates, infants, children and young people. These statements were 'Healthcare professionals should not use negative pressure wound therapy for the treatment of pressure ulcers in neonates, infants, children and young people', 'Healthcare professionals should not use hyperbaric oxygen therapy for the treatment of pressure ulcers in neonates, infants, children and young people' and 'Healthcare professionals should not routinely use electrotherapy for the treatment of neonates, infants, children and young people with pressure ulcers'. Two statements were then amended for inclusion in Round 2 of the survey. Further detail on the Delphi consensus survey can be found in Appendix N. **Negative pressure wound therapy** For negative pressure wound therapy, the statement was not accepted by the Delphi consensus panel in Round 1 and the statement was amended for inclusion in Round 2. Comments received during Round 1 of the survey suggested that some healthcare professionals felt that negative pressure wound therapy was helpful to promote healing in some children and young people, with some individuals highlighting that this was particularly helpful for the management of grade 3 and 4 pressure ulcers, or those in hard to reach sites. However, the GDG did not feel that, given the limited evidence to suggest significant benefits of negative pressure wound therapy in adults and the possible harms identified, it was appropriate to amend the statement to promote the use of negative pressure wound therapy. The statement was therefore amended for Round 2 of the survey to reflect that there may be specific situations in which negative pressure wound therapy may be considered however, this should not

	be routinely used ('Healthcare professionals should not routinely use negative pressure wound therapy for the treatment of pressure ulcers in neonates, infants, children and young people.'). During Round 2 of the Delphi consensus, this statement was not accepted by the Delphi consensus panel at the 75% level. Comments received during Round 2 of the Delphi consensus panel did however, highlight that negative pressure wound therapy should only be used in these populations with specialist advice and noted again that its role was reserved for hard to heal wounds and those in difficult sites. The GDG therefore accepted that, in the absence of evidence, there may be some situations in which negative pressure wound therapy may have some benefits, particularly for grade 3-4 pressure ulcers and those in difficult sites, with specialist advice. However, given the lack of evidence available to suggest a benefit of negative pressure wound therapy on the management of pressure ulcers in adults, the GDG did not feel that it was appropriate to recommend its use in neonates, infants, children and young people. As such, the GDG extrapolated from the recommendation developed for adults and agreed that the use of negative pressure wound therapy was not routinely recommended in these populations. **Hyperbaric oxygen therapy** For hyperbaric oxygen therapy, 1 statement was not accepted by the Delphi consensus panel in Round 1 and the statement was amended for inclusion in Round 2, following concerns from the GDG that some members of the Delphi consensus panel may be unclear as to the treatment being considered. The statement was therefore amended for inclusion in Round 2 ('Healthcare professionals should not use hyperbaric oxygen therapy (the use of 'above atmospheric pressure' to increase the oxygen supply to the wound bed) for the treatment of pressure ulcers in neonates, infants, children and young people.'), however, the statement did not reach consensus. However, given the potential risk of adverse events and safety concerns highlighted by the Delphi consensus panel (including the development of retinopathy of prematurity in neonates) and the GDG, the GDG did not feel that it was appropriate to recommend the use of hyperbaric oxygen therapy in these populations. The GDG therefore extrapolated from the recommendation developed for adults and agreed that the use of hyperbaric oxygen therapy was not routinely recommended in neonates, infants, children and young people. **Electrotherapy** For electrotherapy, the statement was accepted by the Delphi consensus panel in Round 1 of the survey. The GDG therefore agreed that a recommendation should be developed to not routinely use electrotherapy for the treatment of pressure ulcers in neonates, infants, children and young people. Comments received from panel members highlighted that they were unaware of evidence to support the use of electrotherapy. However, some comments suggested that there may be circumstances in which the use of electrotherapy would be beneficial, for example for those with chronic wounds, following holistic assessment and under medical supervision. Therefore, the GDG felt that a recommendation to not routinely use electrotherapy would be appropriate.
Economic considerations	No economic studies on the use of electrotherapy, negative pressure wound therapy or hyperbaric oxygen therapy were identified. The GDG identified that there were significant cost implications in the use of these therapies for the management or treatment of pressure ulcers, and that there were

	safety concerns in these populations. The GDG agreed that use of these therapies in these populations would not be cost-effective.
Quality of evidence	No RCTs or cohort studies were identified for neonates, infants, children or young people. Formal consensus using a modified Delphi was therefore used to develop the recommendation. **Negative pressure wound therapy** To inform the recommendation, the GDG used 1 statement which was included in Round 1 of the Delphi consensus survey and reached 11% consensus agreement. The statement was therefore amended and included in Round 2 of the Delphi consensus survey, where it reached 67% consensus. The GDG therefore extrapolated from the recommendation developed for adults. **Hyperbaric oxygen therapy** To inform the recommendation, the GDG used 1 statement which was included in Round 1 of the Delphi consensus survey and reached 43% consensus agreement. The statement was therefore amended and included in Round 2 of the Delphi consensus survey, where it reached 65% consensus. **Electrotherapy** To inform the recommendation, the GDG used 1 statement which was included in Round 1 of the Delphi consensus survey and reached 77% consensus agreement. Further details can be found in Appendix N.
Other considerations	There were no other considerations.

8 Debridement

Debridement is the removal of necrotic tissue from a wound. Generally, the presence of necrotic or dead tissue is seen as a delaying factor in pressure ulcer healing, preventing the formation of healthy granulation tissue and a good environment to harbour more bacteria, thereby increasing the risk of further sepsis.

Necrotic tissue is removed during natural wound healing due to autolytic debridement and this process may be helped by the application of a moist wound dressing. Other forms of debridement include enzymatic (via an agent impregnated in a dressing or applied directly to the pressure ulcer), mechanical (via the physical removal of dead tissue by water either under low or high pressure or by allowing a dressing to stick to the pressure ulcer before removal (wet to dry dressing)) and sharp debridement. Sharp debridement includes debridement of totally dead or necrotic tissue using a scalpel or scissors and the more extensive removal of tissue under anaesthesia (when a surgeon removes enough tissue until tissue with a good bleeding capillary base is found.

The choice of debridement method depends upon the nature of the wound, the skill set of the practitioner, access to equipment and dressings, and the condition of the individual. Given the range of debridement options available, the GDG was interested in identifying the most effective method of debridement of non-viable tissue to treat pressure ulcers.

8.1 Review question: What are the most clinically and cost effective methods of debridement of non-viable tissue for the treatment of pressure ulcers?

For full details see review protocol in Appendix D.

8.1.1 Clinical evidence (adults)

Nine randomised trials were identified as meeting the inclusion criteria and were included in this review. All study evidence tables and forest plots are presented in Appendix G and I.

Summry of included studies

Study	Intervention/comparator	Population	Outcome	Length of study
Agren,1985[4]	Zinc oxide Streptokinase-streptodornase ointment.	Geriatric adults with necrotic pressure ulcer.	• Reduction in ulcer area • Side effects	8 weeks of treatment
Alvarez, 2000[8]	Collagenase ointment (Santyl) versus papain/urea ointment (Accuzyme).	People with pressure ulcers requiring debridement, who were stable or improving after a 2 week screening period.	• Percent reduction of ulcer size from baseline • Side effects	2 weeks screening and 4 weeks period of the study
Burgos, 2000 (a)[36]	Collagenase ointment (Iruxol) versus hydrocolloid dressing (Varihesive).	People of at least 55 years presenting with grade 3 pressure ulcers (skin disruption, tissue damage and exudate and subcutaneous tissue involvement).	• Proportion of people with reduction in pressure ulcer area after 12 weeks of treatment • Proportion of people with complete healing of pressure ulcer after 12 weeks of treatment • Mean reduction in ulcer area after 12 weeks of treatment (cm^2) • Decrease in pain intensity • Adverse reactions	12 weeks of treatment or until healing of the pressure ulcer, whichever occurred first.
Burgos, 2000 (b)[35]	Collagenase ointment application every 24 hours versus collagenase ointment application every 48 hours.	Hospitalised or institutionalised people aged 55 years or older presenting with grade 3 pressure ulcer for less than 1 year.	• Proportion of pressure ulcers that showed complete healing after 8 weeks (intention-to-treat). • Relative risk of non-healing among group 2 (collagenase ointment every 48 hours) as compared with group 1	Treatment during maximum 8 weeks or until complete healing of the pressure ulcer whatever occurred first.

Study	Intervention/comparator	Population	Outcome	Length of study
			(collagenase ointment every 24 hours)after 8 weeks (intention-to-treat) when granulation tissue covered 11 to 30% of the ulcer surface. • Mean reduction of pressure ulcer area (cm^2) during 8 weeks (per-protocol). • Decrease in pain intensity after 8 weeks (intention-to-treat). • Decrease in pain intensity after 8 weeks (per-protocol). • Proportion with adverse reactions after 8 weeks.	
Lee, 1975[103]	Collagenase ointment (Santyl) versus preparation of inactivated collagenase.	11 adults with chronic diseases. Four had neoplastic disease; 4 atherosclerotic heart diseases or cerebrovascular accident or both; 2 had Parkinson's disease and 1 had a femoral neck fracture.	• Proportion of pressure ulcers that reduced in volume assessed with the aid of a volume mould • Proportion of pressure ulcers that increased in volume assessed with the aid of a volume mould • Proportion of pressure ulcers with odour at the end of treatment • Side effects	4 weeks of treatment and follow-up unless complications developed or participant died.
Milne, 2012, 2010[117]	Colleganase ointment (Santyl) versus hydrogel dressing (SoloSite Gel).	People in a long-term care facility.	• Proportion of people completely healed; mean reduction in PUSH tool	84 days

Study	Intervention/comparator	Population	Outcome	Length of study
			score; mortality (all-cause).	
Müller 2001[125]	Hydrocolloid dressing (Duoderm) versus collagenase dressing (Novuxol).	Females with a grade 4 heel pressure ulcers	• Proportion of peoplecompletely healed • Time to healing.	Maximum 16 weeks
Parish, 1979[146]	Dextranomer powder (Debrisan) versus collagenase ointment (Santyl) versus sugar and egg white.	People with pressure ulcers in a long-term care institution for the chronically ill and physically disabled.	• Proportion of pressure ulcers improved for people treated with dextranomer versus people treated with collagenase (%). • Proportion of pressure ulcers improved for people treated with collagenase versus people treated with sugar and egg white. • Proportion of people with ulcer closure for people treated with dextranomer versus people treated with collagenase. • Proportion of people with ulcers closure for people treated with collagenase versus people treated with sugar and egg white. • Proportion of pressure ulcers closed for people treated with dextranomer versus	The initial study was to have lasted 4 weeks, but many subjects were treated and observed for up to 4 months or longer.

Study	Intervention/comparator	Population	Outcome	Length of study
			people treated with collagenase. • Proportion of pressure ulcers closed for people treated with collagenase versus people treated with sugar and egg white. • Proportion of people improved treated with dextranomer versus people treated with collagenase. • Proportion of pressure ulcer closed treated with dextranomer versus collagenase after 1 week. • Proportion of pressure ulcers closed treated with dextranomer versus collagenase after 1 month. • Proportion of pressure ulcers closed treated with dextranomer versus collagenase after 2 months. • Proportion of pressure ulcers closed treated with dextranomer versus collagenase after more than 2 months. • Proportion of people improved treated with	

Study	Intervention/comparator	Population	Outcome	Length of study
			collagenase versus people treated with sugar and egg white. • Proportion of pressure ulcers closed treated with collagenase versus sugar and egg white after 1 week. • Proportion of pressure ulcers closed treated with collagenase versus sugar and egg white after 1 month. • Proportion of pressure ulcers closed treated with collagenase versus sugar and egg white after 2 months • Proportion of pressure ulcers closed treated with collagenase versus sugar and egg white after more than 2 months • Side effects	
Püllen, 2002[152]	Twice-daily treatment with collagenase ointment (1.2 U/g) (Novuxal) versus twice-daily treatment fibrinolysin/DNAse ointment (1 U Loomis and 666 Christensen/g) (Fibrolan)	Adults with pressure ulcers, Seiler grade 2,3 or 4, in the pelvic region with fibrinous or necrotic slough from 17 hospitals.	• Proportion of peoples reporting adverse events • Proportion of serious adverse events reported	Four weeks of treatment or until complete wound debridement whichever occurred first.

Table 74: Clinical evidence profile: collagenase ointment versus preparation of inactivated collagenase

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Collagenase	Preparation of inactivated collagenase	Relative (95% CI)	Absolute	Quality	Importance
Proportion of pressure ulcers that decreased in volume – people with chronic diseases- grade not reported- classification system not reported- follow-up 4 weeks[103]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[d]	None	8/17 (47.1%)	0/11 (0%)	Peto OR 9.24 (1.78 to 48.04)	470 more per 1000 (from 210 more to 730 more)	Very low	Critical
							-	0%		470 more per 1000 (from 210 more to 730 more)		
Proportion of pressure ulcers that increased in volume – people with chronic diseases- grade not reported- classification system not reported- follow-up 4 weeks[103]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	None	4/17 (23.5%)	6/11 (54.5%)	RR 0.43 (0.16 to 1.19)	311 fewer per 1000 (from 458 fewer to 104 more)	Very low	Critical
							-	54.6%		311 fewer per 1000 (from 459 fewer to 104 more)		
Proportion of pressure ulcers with odour at the end of treatment– people with chronic diseases- grade not reported- claasification system not reported- follow-up 4 weeks[103]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[c]	None	7/17 (41.2%)	5/11 (45.5%)	RR 0.91 (0.38 to 2.14)	41 fewer per 1000 (from 282 fewer to 518 more)	Very low	Important
							-	45.5%		41 fewer per 1000 (from 282 fewer to 519 more)		
Number of side effects observed– people with chronic diseases- grade not reported- classification system not reported- follow-up 4 weeks[103]												

Quality assessment							No of patients		Effect			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Collagenase**	**Preparation of inactivated collagenase**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[c,d]	None	1/17 (5.9%)	0/11 (0%)	Peto OR 5.19 (0.09 to 287.21)	60 more per 1000 (from 11 less to 23 more)	Very low	Important
							-	0%		60 more per 1000 (from 11 less to 23 more)		
Mortality (all-cause) [103]												
1	Randomised trial	Very seriousa	No serious inconsistency	No serious indirectness	No serious	None	0/17 (0%)	0/11 (0%)	Not pooled	Not pooled	Low	Important
Proportion of people with pressure ulcers completely healed												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate of change in size of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital or NHS care												
-	-	-	-	-	-	-	-	-	-	-	-	-
Patient acceptability												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Collagenase	Preparation of inactivated collagenase	Relative (95% CI)	Absolute	Quality	Importance
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) The process for randomisation was unclear. The method of allocation concealment and blinding were unclear.
(b) The confidence interval crossed 1 MID point.
(c) The confidence interval crossed both MID points.
(d) There were a limited number of events.

Table 75: Clinical evidence profile: collagenase ointment versus dextranomer

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Collagenase	Dextranomer	Relative (95% CI)	Absolute	Quality	Importance
Proportion of pressure ulcers that improved –chronically ill and disabled people- grade not reported – classification system not reported[146]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	None	5/11 (45.5%)	12/14 (85.7%)	RR 0.53 (0.27 to 1.05)	403 fewer per 1000 (from 626 fewer to 43 more)	Very low	Critical
							-	85.7%		403 fewer per 1000 (from 626 fewer to 43 more)		
Proportion of pressure ulcers completely healed–chronically ill and disabled people- grade not reported – classification system not reported[146]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[c]	None	1/11 (9.1%)	6/14 (42.9%)	RR 0.21 (0.03 to 1.51)	339 fewer per 1000 (from 416 fewer to 219 more)	Very low	Critical

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Collagenase	Dextranomer	Relative (95% CI)	Absolute	Quality	Importance
							-	42.9%		339 fewer per 1000 (from 416 fewer to 219 more)		
Proportion of people with pressure ulcers completely healed –chronically ill and disabled people - grade not reported – classification system not reported[146]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[c]	None	1/5 (20%)	4/7 (57.1%)	RR 0.35 (0.05 to 2.26)	371 fewer per 1000 (from 543 fewer to 720 more)	Very low	Critical
							-	57.1%		371 fewer per 1000 (from 542 fewer to 719 more)		
Proportion of people that improved–chronically ill and disabled people - grade not reported – classification system not reported[146]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	None	2/5 (40%)	7/7 (100%)	RR 0.44 (0.17 to 1.16)	560 fewer per 1000 (from 830 fewer to 160 more)	Very low	Critical
							-	100%		560 fewer per 1000 (from 830 fewer to 160 more)		
Proportion of pressure ulcers improved after 1 week–chronically ill and disabled people - grade not reported – classification system not reported[146]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[d]	None	0/11 (0%)	6/14 (42.9%)	Peto OR 0.1 (0.02 to	430 fewer per 1000 (from 700	Very low	Critical

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Collagenase	Dextranomer	Relative (95% CI)	Absolute		
									0.64)	fewer to 150 fewer)		
							-	42.9%		430 fewer per 1000 (from 700 fewer to 150 fewer)		
Proportion of pressure ulcers improved after 1 month–chronically ill and disabled people - grade not reported – classification system not reported[146]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[c]	None	3/11 (27.3%)	8/14 (57.1%)	RR 0.48 (0.16 to 1.39)	297 fewer per 1000 (from 480 fewer to 223 more)	Very low	Critical
							-	57.1%		297 fewer per 1000 (from 480 fewer to 223 more)		
Proportion of pressure ulcers improved after 2 months–chronically ill and disabled people - grade not reported – classification system not reported[146]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[c]	None	5/11 (45.5%)	8/14 (57.1%)	RR 0.8 (0.36 to 1.75)	114 fewer per 1000 (from 366 fewer to 429 more)	Very low	Critical
							-	57.1%		114 fewer per 1000 (from 365 fewer to 428 more)		
Proportion improved after 2 months–chronically ill and disabled people- grade not reported – classification system not reported[146]												
1	Randomised	Very	No serious	No serious	Serious[b]	None	5/11	12/14	RR 0.53	403 fewer	Very low	Critical

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Collagenase	Dextranomer	Relative (95% CI)	Absolute	Quality	Importance
	trial	serious[a]	inconsistency	indirectness			(45.5%)	(85.7%)	(0.27 to 1.05)	per 1000 (from 626 fewer to 43 more)		
							-	85.7%		403 fewer per 1000 (from 626 fewer to 43 more)		
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate of change in size of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital or NHS care												
-	-	-	-	-	-	-	-	-	-	-	-	-
Patient acceptability												
-	-	-	-	-	-	-	-	-	-	-	-	-
Side effects												
-	-	-	-	-	-	-	-	-	-	-	-	-
Mortality (all-cause)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) The randomisation and concealment methods were not reported by the authors. Blinding failed.
(b) The confidence interval crossed 1 MID point.
(c) The confidence interval crossed both MID points.
(d) There were a limited number of events.

Table 76: Clinical evidence profile: collagenase ointment versus sugar and egg white

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Collagenase	Sugar and egg white	Relative (95% CI)	Absolute	Quality	Importance
Proportion of pressure ulcers completely healed– chronically ill and disabled people- no grade reported- no classification system reported[146]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b,c]	None	1/11 (9.1%)	0/9 (0%)	Peto OR 6.16 (0.12 to 316.67)	90 more per 1000 (from 140 more to 320 more)	Very low	Critical
							-	0%		90 more per 1000 (from 140 more to 320 more)		
Proportion of people with pressure ulcer completely healed– chronically ill and disabled people - no grade reported- no classification system reported[146]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b,c]	None	1/5 (20%)	0/5 (0%)	Peto OR 7.39 (0.15 to 372.38)	200 more per 1000 (from 210 less to 610 more)	Very low	Critical
							-	0%		200 more per 1000 (from 210 less to 610 more)		
Proportion of people that improved– chronically ill and disabled people - no grade reported- no classification system reported[146]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b,c]	None	2/5 (40%)	0/5 (0%)	Peto OR 9.49 (0.5 to 179.46)	400 more per 1000 (from 50 more to 850 more)	Very low	Critical
							-	0%		400 more per 1000 (from 50 more to 850 more)		
Proportion of pressure ulcers that improved – chronically ill and disabled people - no grade reported- no classification system reported[146]												
1	Randomised	Very	No serious	No serious	Serious[c]	None	5/11	0/9	Peto OR	450 more per	Very low	Critical

Quality assessment							No of patients		Effect			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Collagenase**	**Sugar and egg white**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
	trial	serious[a]	inconsistency	indirectness			(45.5%)	(0%)	10.00 (1.38 to 146.4)	1000 (from 140 more to 770 more)		
							-	0%		450 more per 1000 (from 140 more to 770 more)		
Proportion of pressure ulcers improved after 1 week– chronically ill and disabled people - no grade reported- no classification system reported[146]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious	None	0/11 (0%)	0/9 (0%)	Not pooled	Not pooled	Very low	Critical
							-	0%		Not pooled		
Proportion of pressure ulcers improved after 1 month– chronically ill and disabled people - no grade reported- no classification system reported[146]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b,c]	None	3/11 (27.3%)	0/9 (0%)	Peto OR 7.63 (0.69 to 84.5)	270 more per 1000 (from 20 fewer to 560 more)	Very low	Critical
							-	0%		270 more per 1000 (from 20 fewer to 560 more)		
Proportion of pressure ulcers improved after 2 months– chronically ill and disabled people - no grade reported- no classification system reported[146]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious[c]	None	5/11 (45.5%)	0/9 (0%)	Peto OR 10.00 (1.38 to 72.67)	450 more per 1000 (from 140 more to 770 more)	Low	Critical
							-	0%		450 more per 1000 (from 140 more to 770 more)		

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Collagenase	Sugar and egg white	Relative (95% CI)	Absolute	Quality	Importance
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate of change in size of pressure ulcer												
-	-	-	-	-	-	-	-	-	-	-	-	-
Reduction in size and volume of pressure ulcer												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital or NHS care												
-	-	-	-	-	-	-	-	-	-	-	-	-
Patient acceptability												
-	-	-	-	-	-	-	-	-	-	-	-	-
Side effects												
-	-	-	-	-	-	-	-	-	-	-	-	-
Mortality (all-cause)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) *The randomisation and concealment methods were not reported. Blinding failed.*

(b) *The confidence interval crossed both MID points.*

(c) *There were a limited number of events.*

Table 77: Clinical evidence profile: collagenase ointment versus papainm and urea ointment

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Collagenase	papain/ urea	Relative (95% CI)	Absolute	Quality	Importance
Percentage reduction in pressure ulcer size after 1 week – people with pressure ulcers- grade 2-4- classification system not reported[8]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	5.8 (n=10)	1.9 (n=11)	-	MD 3.9 higher (7.78 lower to 15.58 higher)	Very low	Critical
Percentage reduction in pressure ulcer size after 2 weeks (follow-up 4 weeks; better indicated by lower values) [8]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	19.9 (n=10)	23.7 (n=11)	-	MD 3.8 lower (27.46 lower to 19.86 higher)	Very low	Critical
Percentage reduction in pressure ulcer size after 3 weeks – people with pressure ulcers- grade 2-4- classification system not reported[8]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	27.3 (n=10)	34.8 (n=11)	-	MD 7.5 lower (30.6 lower to 15.6 higher)	Very low	Critical
Percentage reduction in pressure ulcer size after 4 weeks – people with pressure ulcers- grade 2-4- classification system not reported[8]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	33.9 (n=10)	55.4 (n=11)	-	MD 21.5 lower (47.09 lower to 4.09 higher)	Very low	Critical
Number of side effects observed (follow-up 4 weeks) – people with pressure ulcers- grade 2-4- classification system not reported[8]												
1	Randomised	Very	No serious	No serious	Very serious[c]	None	1/10	0/11	Peto OR	100 more	Very low	Critical

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Collagenase	papain/ urea	Relative (95% CI)	Absolute	Quality	Importance
	trial	serious[a]	inconsistency	indirectness			(10%)	(0%)	8.17 (0.16 to 413.39)	per 1000 (from 130 more to 330 more)		
Proportion of people with pressure ulcers completely healed												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate of reduction in size of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital or NHS care												
-	-	-	-	-	-	-	-	-	-	-	-	-
Patient acceptability												
-	-	-	-	-	-	-	-	-	-	-	-	-
Mortality (all-cause)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life.												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) The methods of concealment and blinding were not reported
(b) There was a small sample. The mean difference is greater or smaller than the standard deviation in control group
(c) The confidence interval crossed both MID points. There were a limited number of events,

Table 78: Clinical evidence profile: collagenase ointment versus fibrinolysis/DNAse ointment

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Collagenase	Fibrinolysis /DNAse	Relative (95% CI)	Absolute	Quality	Importance
Proportion of people reporting adverse events -elderly people with pressure ulcer in pelvic region- grade 2-4- Seiler classification[152]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	None	45/66 (68.2%)	34/69 (49.3%)	RR 1.38 (1.03 to 1.85)	187 more per 1000 (from 15 more to 419 more)	Very low	Important
							-	49.3%		187 more per 1000 (from 15 more to 419 more)		
Proportion of people reporting serious adverse events -elderly people with pressure ulcer in pelvic region- grade 2-4- Seiler classification[152]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	54/118 (45.8%)	24/103 (23.3%)	RR 1.96 (1.31 to 2.93)	224 more per 1000 (from 72 more to 450 more)	Low	Important
							-	23.3%		224 more per 1000 (from 72 more to 450 more)		
Proportion of people with pressure ulcers completely healed												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate of reduction in size of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Reduction in size or volume of pressure ulcers												

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Collagenase	Fibrinolysis /DNAse	Relative (95% CI)	Absolute	Quality	Importance
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital or NHS care												
-	-	-	-	-	-	-	-	-	-	-	-	-
Patient acceptability												
-	-	-	-	-	-	-	-	-	-	-	-	-
Mortality (all-cause)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) Unclear sequence generation was reported by the authors. There was unclear allocation concealment and a relatively high drop out rate.
(b) Confidece interval crossed 1 MID point.

Table 79: Clinical evidence profile: collagenase ointment versus hydrocolloid dressing

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Collagenase	Hydrocolloid dressing	Relative (95% CI)	Absolute	Quality	Importance
Proportion of people with reduction in pressure ulcer area – people with pressure ulcer grade 2- classification system not reported[36]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	None	15/18 (83.3%)	14/19 (73.7%)	RR 1.13 (0.81 to 1.59)	96 more per 1000 (from 140 fewer to 435 more)	Very low	Critical
							-	73.7%		96 more per 1000 (from 140 fewer to 435 more)		
Proportion of people with complete healing of pressure ulcers– people with pressure ulcer grade 2 and 4- classification system not reported[36,125]												
2	Randomised trials	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	None	14/30 (46.7%)	10/30 (33.3%)	RR 1.33 (0.8 to 2.23)	110 more per 1000 (from 67 fewer to 410 more)	Very low	Critical
							-	39.7%		131 more per 1000 (from 79 fewer to 488 more)		
Mean reduction in pressure ulcer area after 12 weeks of treatment – people with pressure ulcer grade 2- classification system not reported[36]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[c]	None	9.1 (n=18)	6.2 (n=19)	-	MD 2.9 higher (4.44 lower to 10.24 higher)	Very low	Critical
Proportion of people reporting adverse events-– people with pressure ulcer grade 2- classification system not reported[36]												

Quality assessment							No of patients		Effect			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Collagenase**	**Hydrocolloid dressing**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[c]	None	1/18 (5.6%)	2/19 (10.5%)	RR 0.53 (0.05 to 5.33)	49 fewer per 1000 (from 100 fewer to 456 more)	Very low	Important
							-	10.5%		49 fewer per 1000 (from 100 fewer to 455 more)		
Mean time to healing (weeks) of pressure ulcer- female hospitalised people- grade 4 heel ulcers-classification system not reported[125]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[c]	None	12 (n=12)	11 (n=11)	-	MD 4 lower (5.11 to 2.89 lower)	Very low	Critical
Mortality (all-cause) [36,125]												
2	Randomised trials	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[c,d]	None	3/30 (10%)	1/31 (3.2%)	RR 3.17 (0.36 to 27.72)	70 more per 1000 (from 21 fewer to 862 more)	Very low	Important
							-	2.6%		56 more per 1000 (from 17 fewer to 695 more)		
Rate of reduction in size of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-		-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-		-

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Collagenase	Hydrocolloid dressing	Relative (95% CI)	Absolute	Quality	Importance
Time in hospital or NHS care												
-	-	-	-	-	-	-	-	-	-	-		-
Patient acceptability												
-	-	-	-	-	-	-	-	-	-	-		-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-		-

(a) The method of allocation concealment was unclear and not all assessors were blinded. There was a relatively high drop-out but no baseline differences were reported.
(b) The confidence interval crossed 1 MID point.
(c) The confidence interval crossed both MID points.
(d) There were a limited number of events.

Table 80: Clinical evidence profile: collagenase ointment application every 24 hours versus every 48 hours

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Collagenase ointment application every 24 hours	Collagenase ointment application every 48 hours	Relative (95% CI)	Absolute	Quality	Importance
Proportion of pressure ulcers with complete healing after 8 weeks –hospitalised people -grade 3- NPUAP classification[35]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	12/43 (27.9%)	9/43 (20.9%)	RR 1.33 (0.63 to 2.83)	69 more per 1000 (from 77 fewer to 383 more)	Very low	Critical
							-	20.9%		69 more per 1000 (from 77 fewer to		

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Collagenase ointment application every 24 hours	Collagenase ointment application every 48 hours	Relative (95% CI)	Absolute	Quality	Importance
										382 more)		
Proportion of people reporting adverse events (rash, necrosis in ulcer bed, ulcer worsening, infection) –hospitalised people -grade 3- NPUAP classification[35]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	3/46 (6.5%)	3/46 (6.5%)	RR 1 (0.21 to 4.7)	0 fewer per 1000 (from 52 fewer to 241 more)	Very low	Critical
							-	6.5%		0 fewer per 1000 (from 51 fewer to 240 more)		
Mortality (all-cause) [35]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	4/46 (8.7%)	7/46 (15.2%)	RR 0.57 (0.18 to 1.82)	65 fewer per 1000 (from 125 fewer to 125 more)	Very low	Important
							-	15.2%		65 fewer per 1000 (from 125 fewer to 125 more)		
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate of reduction in size of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Collagenase ointment application every 24 hours	Collagenase ointment application every 48 hours	Relative (95% CI)	Absolute	Quality	Importance
Reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital or NHS care												
-	-	-	-	-	-	-	-	-	-	-	-	-
Patient acceptability												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) There were unclear methods of allocation concealment and not all assessors were blinded. There was a relatively high drop out and no baseline differences reported.
(b) The confidence interval crossed both MID points.

Table 81: Clinical evidence profile: collagenase ointment versus hydrogel dressing

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Collagenase versus hydrogel	Control	Relative (95% CI)	Absolute	Quality	Importance
Proportion of people with pressure ulcers completely healed[117]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	None	9/13 (69.2%)	3/14 (21.4%)	RR 3.23 (1.11 to 9.39)	478 more per 1000 (from 24 more to 1000	Very low	Critical

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Collagenase versus hydrogel	Control	Relative (95% CI)	Absolute	Quality	Importance
										more)		
							-	21.4%		477 more per 1000 (from 24 more to 1000 more)		
Mean reduction in PUSH tool score (at day 42) [117]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[c]	None	5.03 (no s.d) n=13	3.99 (no s.d) n=14	MD 1.04 higher	-	Very low	Critical
Mortality[117]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	0/13 (0%)	0/14 (0%)	Not pooled	Not pooled	Low	Important
							-	0%		Not pooled		
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate of reduction in size of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Reduction in size and volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital or NHS care												
-	-	-	-	-	-	-	-	-	-	-	-	-
Patient acceptability												

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Collagenase versus hydrogel	Control	Relative (95% CI)	Absolute	Quality	Importance
-	-	-	-	-	-	-	-	-	-	-	-	-
Side effects												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) No details of sequence generation or allocation concealment were reported.There were baseline differences in pressure ulcer size.
(b) The confidence interval crossed 1 MID point.
(c) No standard deviations were reported so they were calculated from mean initial PUSH tool score and mean at day 42. There was a small sample size.

Table 82: Clinical evidence profile: zinc oxide versus streptokinase-streptodornase ointment[4]

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Zinc oxide	Streptokinase-streptodornase	Relative (95% CI)	Absolute	Quality	Importance
Median percentage reduction in ulcer area – elderly people – necrotic pressure ulcers - classification method not reported[4]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	24 (n=14)	-18.7 (n=14)	-	Not pooled	Very low	Critical
Proportion of people with an infection – elderly people – necrotic pressure ulcers - classification method not reported[4]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[c]	None	0/14 (0%)	1/14 (7.1%)	OR 0.14 (0 to 6.82)	61 fewer per 1000 (from 71 fewer to 273 more)	Very low	Critical
							-	7.1%		60 fewer per 1000 (from 71		

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Zinc oxide	Streptokinase-streptodornase	Relative (95% CI)	Absolute	Quality	Importance
										fewer to 272 more)		
Proportion of people with skin reaction – elderly people – necrotic pressure ulcers - classification method not reported[4]												
1	Randomised trial	Very serious[b]	No serious inconsistency	No serious indirectness	Very serious[c]	None	0/14 (0%)	1/14 (7.1%)	OR 0.14 (0 to 6.82)	61 fewer per 1000 (from 71 fewer to 273 more)	Very low	Important
							-	7.1%		60 fewer per 1000 (from 71 fewer to 272 more)		
Mortality (all-cause) [4]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious	None	0/14 (0%)	0/14 (0%)	Not pooled	Not pooled	Low	Important
							-	0%	-	Not pooled		
Proportion of people with pressure ulcers completely healed												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate of reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Zinc oxide	Streptokinase-streptodornase	Relative (95% CI)	Absolute	Quality	Importance
Time in hospital												
-	-	-	-	-	-	-	-	-	-	-	-	-
Acceptability of treatment												
-	-	-	-	-	-	-	-	-	-	-	-	-
Side effects												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) Sequence generation was by matched pairs. The authors did not report the method of allocation concealment and there was no blinding of participants or nurses. No log-transformation of data was carried out.

(b) No standard deviation was reported. There was a small sample size.

(c) The confidence interval crossed both MID points.

(d) This comparison was also included in topical agents review (see Chapter X).

8.1.1 Economic evidence (adults)

Five studies were included with relevant comparisons.[27,36,121,125] These are summarised in the economic evidence profiles below (Table 83- Table 87). See also the study selection flow chart in Appendix C and study evidence tables in Appendix F.

Two of the included studies[36,125] compare collagenase ointment to a hydrocolloid dressing (Table 190). However, the conclusions of these 2 studies differ; Burgos and colleagues (2000) found collagenase ointment to be more effective and more costly than hydrocolloid dressing, whereas Müller and colleagues (2001) found collagenase to be more effective and less costly than hydrocolloid. This is because a higher proportion of people were heeled in the Müller study compared to the Burgos study (Appendix H), and a greater incremental difference in people healed between the trail arms can be seen. This could be partly due to the differences in the populations studied in the trials. The Burgos study was based in Spain (costs are calculated in Spanish pesetas) amongst a group which was 46% male and all of whom had stage 3 pressure ulcers. The Müller study, on the other hand, was conducted in Holland (costs are calculated in Dutch guilders), amongst a population who were all female, and all had stage 4 heel pressure ulcers. Note also that the time horizon of the Müller study was 16 weeks, compared to 12 weeks in the Burgos study.

Both studies report that collagenase was applied once daily and hydrocolloid every 3 days (or twice a week). Consequently, Burgos and colleagues report higher staff and auxiliary supply costs (per patient) in the collagenase group than in the hydrocolloid group. The higher staff cost and ancillary supplies required for the more frequent dressing changes in the collagenase arm result in this arm being more costly per person than the hydrocolloid arm, despite a lower pharmaceutical cost of collagenase. However, Müller and colleagues report lower personnel costs for collagenase than for hydrocolloid. They attribute this to fewer doctors' appointments required in the collagenase group due to a shorter healing time. Müller and colleagues find personnel costs and material costs to be lower in the collagenase arm, and thus conclude collagenase is cheaper than hydrocolloid.

One study that met the inclusion criteria was selectively excluded[191] – this is summarised in Appendix K, with reasons for exclusion given.

Table 83: Economic evidence profile: hydrocolloid dressing versus collagenase dressing

Study	Applicability	Limitations	Other comments	Incremental cost	Incremental effects	Co ef
Burgos 2000[36] (Spain)	Partially applicable[a]	Potentially serious limitations[b]	Within trial analysis of a collagenase dressing compared to a hydrocolloid dressing, based on analysis of individual level resource use with unit costs applied.	-£46 (p <0.0001)	Pressure ulcers healed: -0.01 (p=0.451)	Co bo ex m th hy
Müller 2001[125] (Netherlands)	Partially applicable[c]	Potentially serious limitations[d]	Within trial analysis of a collagenase dressing compared to a hydrocolloid dressing for heel ulcers, based on analysis of individual level resource use with unit costs applied.	£25	Pressure ulcers healed: -0.29 (p <0.005)	Co do hy

(a) Study based in Spain, quality of life not considered, costs based on 1998 values
(b) no consideration of quality of life, no analysis of uncertainty reported, unit costs are based on prices faced by patients and could be substantially different to those faced by hospitals
(c) Study based in the Netherlands, quality of life not considered, costs based on 1998 values
(d) Small study, no unit cost source reported, no consideration of quality of life, no useful analysis of uncertainty reported

Table 84: Economic evidence profile: hydrogel dressing versus collagenase dressing

Study	Applicability	Limitations	Other comments	Incremental cost	Incremental effects	Co ef
Waycaster 2013[206] (US)	Partially applicable[a]	Potentially serious limitations[b]	Markov model based on a single RCT. Three states: inflamed wound, healing wound, healed wound. Hydrogel dressings are compared to collagenase dressings.	£2,297	Days spent with non-healed pressure ulcer: 99	Co dr do hy dr co da no pr

(c) US healthcare system, quality of life not considered
(d) Based on single RCT. The study does not fully describe cost sources or resource usage. No consideration is given to quality of life. Analysis of uncertainty is incomplete.

Table 85: Economic evidence profile: gauze versus impregnated gauze versus calcium alginate versus hydroactive wound dressing (with collagenase)

Study	Applicability	Limitations	Other comments	Costs	Effects	Co ef
Bergermann 1999[27](Germany)	Partially applicable[a]	Potentially serious limitations[b]	A model comparing gauze, ointment impregnated gauze, calcium alginate, and a hydroactive wound dressing (in combination with collagenase) in the treatment of four sizes of PU: 5cm x 8 cm, 8cm x 12 cm, 10cm x 15cm, 12cm x 20cm. Cost-comparison only.	Total costs (per patient, median) for 12x20cm ulcer: Intvn 1: £3,813 Intvn 2: £1,501 Intvn 3: £1,677 Intvn 4: £592	None	Ef as th th 4 i ef ha co

(a) Based in Germany, quality of life not considered, health outcomes not considered (assumed equivalent)

(b) Unclear whether unit costs are nationally representative, efficacy is assumed the same, it is assumed (not based on evidence) that treatment with hydroactive wound dressing reduces inpatient stay by 10%

Table 86: Economic evidence profile: autolysis versus wet-to-dry dressings versus collagenase versus fibrinolysin

Study	Applicability	Limitations	Other comments	Cost	Incremental effects	Co ef
Mosher 1999 (US)[121]	Partially applicable[a]	Potentially serious limitations[b]	Decision analytic model to calculate the costs of autolytic debridement, wet-to-dry saline dressings, collagenase and fibrinolysin. The key clinical outcomes were the probability of achieving a clean wound bed and the probability of infection.	Autolysis: £591 Wet-to-dry saline dressings: £648 Collagenase: £392 Fibrinolysin: £633	None	Co th of m de

(a) Study based in the US, quality of life not considered, costs based on 1995 values
(b) Unclear whether unity costs are nationally representative, efficacy is based on expert opinion (small sample of only 9 experts), the time hoizon is short and therefore the model may not capture the full cost impact between the different strategies.

8.1.2 Clinical evidence (neonates, infants, children and young people)

No RCTs or cohort studies were identified. Recommendations were developed using a modified Delphi consensus technique. Further details can be found in Appendix N.

8.1.3 Economic (neonates, infants, children and young people)

No economic evidence was identified.

8.1.4 Evidence statements

8.1.4.1 Clinical (adults)

8.1.4.1.1 Collagenase ointment versus preparation of inactivated collagenase

- One study (n=28) showed collagenase ointment is potentially more clinically effective for decreasing volume of pressure ulcers compared to a preparation of inactivated collagenase (very low quality).
- One study (n=28) showed inactivated collagenase is potentially more clinically harmful for increasing the size of volume of pressure ulcers compared to collagenase ointment (very low quality).
- One study (n=28) showed there may be no clinical difference between collagenase ointment and a preparation of inactivated collagenase for proportion of pressure ulcers with odour at the end of treatment, the direction of the estimate of effect favoured collagenase (very low quality).
- One study (n=28) showed there may be no clinical difference between collagenase ointment and a preparation of inactivated collagenase for side effects, the direction of the estimate of effect favoured the preparation of inactivated collagenase (very low quality).
- One study (n=28) showed there is no clinical difference between collagenase ointment and a preparation of inactivated collagenase for mortality (all-cause) (low quality).
- No evidence was found for the following outcomes:
  - Proportion of people with pressure ulcers completely healed
  - Time to complete healing of pressure ulcers

- Rate of change in size or volume of pressure ulcers
- Pain (wound-related)
- Time in hospital or NHS care
- Patient acceptability
- Health-related quality of life

8.1.4.1.2 Collagenase ointment versus dextranomer powder

- One study (n=28) showed dextranomer may be more clinically effective for complete healing of pressure ulcers when compared to collagenase ointment (very low quality).
- One study (n=25) (chronically ill and disabled people) showed dextranomer may be more clinically effective for proportion of people with complete healing of pressure ulcers when compared to collagenase ointment (very low quality).
- One study (n=25) showed dextranomer is potentially more clinically effective for proportion of pressure ulcers improved when compared to collagenase ointment (very low quality).
- One study (n=28) showed dextranomer is potentially more clinically effective for proportion of people with pressure ulcers improved when compared to collagenase ointment (very low quality).
- One study (n=28) showed dextranomer is potentially more clinically effective for proportion of people with pressure ulcers improved after 1 week when compared to collagenase ointment (very low quality).
- One study (n=28) showed dextranomer is potentially more clinically effective for proportion of people with pressure ulcers improved after 1 month when compared to collagenase ointment (very low quality).
- One study (n=28) showed dextranomer may be more clinically effective for proportion of people with pressure ulcers improved after 2 months when compared to collagenase ointment (very low quality).
- One study (n=28) showed dextranomer is potentially more clinically effective for proportion of people with pressure ulcers improved after over 2 months when compared to collagenase ointment (very low quality).
- No evidence was found for the following outcomes:
  - Time to complete healing of pressure ulcers
  - Rate of change in size or volume of pressure ulcers
  - Pain (wound-related)
  - Time in hospital or NHS care
  - Patient acceptability
  - Side effects
  - Mortality (all-cause)
  - Health-related quality of life

8.1.4.1.3 Collagenase ointment versus sugar and egg white

- One study (n=20) showed collagenase ointment may be more clinically effective for proportion of people with pressure ulcers completely healed when compared to sugar and egg white (very low quality).
- One study (n=20) showed collagenase ointment may be more clinically effective for complete healing of pressure ulcers when compared to sugar and egg white (very low quality).

- One study (n=20) showed collagenase ointment may be more clinically effective for improving pressure ulcers when compared to sugar and egg white (very low quality).
- One study (n=20) showed collagenase ointment no clinical difference between sugar and egg white for improving pressure ulcers at 1 week, the direction of estimate of effect could favour either intervention (low quality).
- One study (n=20) showed collagenase ointment may be more clinically effective for improving pressure ulcers when compared to sugar and egg white at 1 month (very low quality).
- One study (n=20) showed collagenase ointment is more clinically effective for improving pressure ulcers when compared to sugar and egg white at 2 months (low quality).
- One study (n=20) showed collagenase ointment is more clinically effective for reducing proportion of people with pressure ulcers when compared to sugar and egg white (very low quality).
- No evidence was found for the following outcomes:
  - Time to complete healing of pressure ulcers
  - Rate of change in size or volume of pressure ulcers
  - Pain (wound-related)
  - Time in hospital or NHS care
  - Patient acceptability
  - Side effects
  - Mortality (all-cause)
  - Health-related quality of life

8.1.4.1.4 Collagenase ointment versus papain/urea ointment

- One study (n=21) showed there may be no clinical difference between collagenase ointment and papain/urea for reducing pressure ulcers size (%) at 1 week, the direction of estimate of effect favoured papain/urea (very low quality).
- One study (n=21) showed there may be no clinical difference between collagenase ointment and papain/urea for reducing pressure ulcers size (%) at 2 week2, the direction of estimate of effect favoured papain/urea (very low quality).
- One study (n=21) showed there may be no clinical difference between collagenase ointment and papain/urea for reducing pressure ulcers size (%) at 3 week2, the direction of estimate of effect favoured papain/urea (very low quality).
- One study (n=21) showed there may be no clinical difference between collagenase ointment and papain/urea for reducing pressure ulcers size (%) at 4 weeks, the direction of estimate of effect favoured papain/urea (very low quality).
- One study (n=21) showed collagenase ointment may be more clinically harmful than papain/urea for adverse events observed (very low quality).
- No evidence was found for the following outcomes:
  - Proportion of people with pressure ulcers completely healed
  - Time to complete healing of pressure ulcers
  - Rate of change in size or volume of pressure ulcers
  - Pain (wound-related)
  - Time in hospital or NHS care
  - Patient acceptability
  - Mortality (all-cause)
  - Health-related quality of life

8.1.4.1.5 Collagenase ointment versus fibrinolysis/DNAse ointment

- One study (n=135) showed collagenase ointment is potentially more clinically harmful than fibrinolysis/DNAse for adverse events observed (very low quality).
- One study (n=135) showed collagenase ointment is more clinically harmful than fibrinolysis/DNAse for serious adverse events observed (low quality).
- No evidence was found for the following outcomes:
  - Proportion of people with pressure ulcers completely healed
  - Time to complete healing of pressure ulcers
  - Rate of change in size or volume of pressure ulcers
  - Reduction in size or volume of pressure ulcers
  - Pain (wound-related)
  - Time in hospital or NHS care
  - Patient acceptability
  - Mortality (all-cause)
  - Health-related quality of life

8.1.4.1.6 Collagenase dressing versus hydrocolloid dressing

- One study (n=37) showed no clinical difference between collagenase dressing and hydrocolloid dressing for reducing pressure ulcer area (very low quality).
- One study (n=37) showed collagenase dressing may be more clinically effective than hydrocolloid dressing for complete healing of pressure ulcers (very low quality).
- One study (n=37) showed there may be no clinical difference between collagenase dressing and hydrocolloid dressing for mean reduction in pressure ulcer area, the direction of the estimate of effect favoured the collagenase dressing (very low quality).
- One study (n=37) showed there may be no clinical difference between hydrocolloid dressing and collagenase dressing for adverse events observed, the direction of estimate of effect favoured collagenase (very low quality).
- One study (n=22) showed collagenase dressing may be more clinically effective than hydrocolloid dressing for delaying time to complete healing of pressure ulcers (very low quality).
- Two studies (n=61) showed there may be no clinical difference between collagenase dressing and hydrocolloid dressing for mortality, the direction of effect favours the hydrocolloid dressing (very low quality).
- No evidence was found for the following outcomes:
  - Rate of change in size or volume of pressure ulcers
  - Pain (wound-related)
  - Time in hospital or NHS care
  - Patient acceptability
  - Health-related quality of life

8.1.4.1.7 Collagenase ointment 24 hours versus 48 hour application

- One study (n=86) showed there may be no clinical difference between collagenase ointment applied 24 hours compared to 48 hours for the proportion of pressure ulcers completely healed, the direction of effect favours 24 hours (very low quality).

- One study (n=92) showed there may be no clinical difference between collagenase ointment applied 24 hours compared to 48 hours for adverse events observed, the direction of effect could favour either application (very low quality).
- One study (n=86) showed there may be no clinical difference between collagenase ointment applied 24 hours compared to 48 hours for mortality, the direction of effect favours 24 hours (very low quality).
- No evidence was found for the following outcomes:
  - Time to complete healing of pressure ulcers
  - Rate of change in size or volume of pressure ulcers
  - Reduction in size or volume of pressure ulcers
  - Pain (wound-related)
  - Time in hospital or NHS care
  - Patient acceptability
  - Health-related quality of life

8.1.4.1.8 Collagenase ointment versus hydrogel dressing

- One study (n=27) showed collagenase ointment is potentially more clinically effective than hydrogel for proportion of people with pressure ulcers completely healed (very low quality).
- One study (n=27) showed there may be no clinical difference between collagenase ointment and hydrogel for reducing mean PUSH tool score, direction of estimate of effect favours collagenase (very low quality).
- One study (n=27) showed no clinical difference between collagenase ointment and hydrogel for mortality (low quality).
- No evidence was found for the following outcomes:
  - Time to complete healing of pressure ulcers
  - Rate of change in size or volume of pressure ulcers
  - Reduction in size or volume of pressure ulcers
  - Pain (wound-related)
  - Time in hospital or NHS care
  - Patient acceptability
  - Side effects
  - Mortality (all-cause)
  - Health-related quality of life

8.1.4.1.9 Zinc oxide versus streptokinase-streptodornase ointment

- One study (n=28) reported zinc oxide ointment may be more effective at reducing percentage of ulcer area compared to streptokinase-streptodornase. The clinical importance is unknown (very low quality).
- One study (n=28) showed that there may be no clinical difference between zinc oxide and streptokinase-streptodornase ointment for proportion of people with an infection, the direction of the estimate of effect favours zinc oxide (very low quality).
- One study (n=28) showed that there may be no clinical difference between zinc oxide and streptokinase-streptodornase ointment for proportion of people with a skin reaction, the direction of the estimate of effect favours zinc oxide (very low quality).

- One study (n=28) showed there is no clinical difference between zinc oxide and streptokinase-streptodornase ointment for mortality (all-cause), the direction of the estimate of effect could favour either intervention (low quality).
- No evidence was found for the following outcomes:
  - Proportion of people with pressure ulcers completely healed
  - Time to complete healing of pressure ulcers
  - Rate of change in size or volume of pressure ulcers
  - Pain (wound-related)
  - Time in hospital or NHS care
  - Patient acceptability
  - Side effects
  - Mortality (all-cause)
  - Health-related quality of life

8.1.4.2 Economic (adults)

- One cost-effectiveness analyses found collagenase is likely to be more expensive and more effective than hydrocolloid for healing people with pressure ulcers; 1 additional cost-effectiveness analysis found that collagen is likely to dominate hydrocolloid (collagen is less costly and more effective) in the treatment of heel pressure ulcers. Both studies were partially applicable with potentially serious limitations.
- One cost-consequence analysis found collagenase dressings dominate hydrogel dressings, with lower costs and fewer days spent with a pressure ulcer. This study was assessed to be partially applicable with potentially serious limitations.
- One cost comparison found the combination of a hydroactive wound dressing and collagenase to be less costly than gauze, impregnated gauze and calcium alginate. This study was partially applicable with potentially serious limitations.
- One cost comparison found collagenase to be less costly than autolysis, wet-to-dry saline dressings and fibrinolysin and desoxyribonuclease combined. This study was partially applicable with potentially serious limitations.

8.1.4.3 Clinical (neonates, infants, children and young people)

No evidence was identified.

8.1.4.4 Economic (neonates, infants, children and young people)

No relevant economic evaluations were identified.

8.2 Maggot (larval) therapy

Maggot therapy, also known as larval therapy, is an alternative method of debridement. The maggots used for debridement are from sterile fly larvae of the sheep blowfly Luciliasericata (Diptera: Calliphoridae). These maggots are ideal for debridement because the enzymes produced by this species dissolve only dead tissue in human wounds, thus the maggots are unable to damage healthy tissue. Maggot secretions also contain chemicals with inherent antimicrobial properties, which may help to combat infection by having an inhibitory effect on the growth of bacteria. In addition it has been postulated that maggot therapy may result in more rapid debridement and less pain than some other therapies.

The GDG was interested in identifying the the most clinical and cost effective method of maggot debridement.

8.3 Review question: What are the most clinically and cost effective methods of maggot debridement of non-viable tissue for treatment of pressure ulcers?

For full details see review protocol in Appendix D.

8.3.1 Clinical evidence (adults)

No randomised trials were identified for inclusion of the review, therefore a search for cohort studies was conducted (as per the protocol in Appendix C). Three records were subsequently included in this review. Evidence from these studies is summarised below and the clinical GRADE evidence profiles in Table 74 onwards. All study evidence tables and forest plots are presented in respectively Appendix G and Appendix I.

Summary of studies included in the review

Study	Intervention/comparator	Population	Outcome	Length of study
Sherman, 1995[175]	Maggot therapy administered by disinfected fly larvae of the species Phaeniciasericata versus conventional treatment.	Participants with pressure ulcers stage 3 or 4 for at least 1 month.	• Average change in surface area per week	Participantswere followed up for 3 to 4 weeks prior to maggot therapy
Sherman, 2002[174]	Maggot therapy administered by applying disinfectedfly larvae (Phaeniciasericata) to the wound at a density offive to eight per cm2 versus conventional treatment prescribed by their primary care provider or the hospital's wound care team.	People with pressure ulcers.	• Change in surface area during treatment (cm²) • Change in surface area per week • Percentage of wounds which decreased in surface area within 4 weeks • Healing rate at 4 weeks • Healing rate at 8 weeks • Percentage of wounds that completely healed • Average time until wounds completely healed (weeks) • Proportion of wounds decreased during treatment	Wounds were first followed for 2 to 8 weeks (average 4.8 weeks) while still receiving conventional therapy. Then the wounds were treated for 2 weeks or more (average 5.2 weeks) with maggot therapy.
Wang, 2010[204]	Maggot therapy administered by applying disinfected larvae of Luciliasericata to the wound at a density of 5 to 10 per cm² versus a dressing applied daily with normal saline only and if necessary surgical debridement.	People with pressure ulcers after spinal cord injury treated in the hospital.	• Time to wound healing (days)	All participants were followed up for 2 to 6 months (mean 3.5 months).

Table 87: Clinical evidence profile: maggot therapy versus conservative treatment

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Maggot therapy	Conservative treatment	Relative (95% CI)	Absolute	Quality	Importance
Change in surface area during treatment (cm^2) in people with pressure ulcers (grade 3 to 4) -classification system not reported - follow-up mean 5.2 weeks[174]												
1	Cohort study	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	-7.3 (n=43)	6.3 (n=49)	-	MD 13.6 lower (15.01 to 12.19 lower)	Very low	Critical
Change in surface area per week in people with pressure ulcers (grade 3 to 4) (classification system not reported)- follow-up mean 5.2 weeks[174]												
1	Cohort study	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	-1.5 (n=43)	1.4 (n= 49)	-	MD 2.9 lower (3.25 to 2.55 lower)	Very low	Critical
Proportion wounds decreased in surface area within 4 weeks in people with pressure ulcers (grade 3 to 4) (classification system not reported) - follow-up mean 5.2 weeks[174]												
1	Cohort study	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	34/43 (79.1%)	22/49 (44.9%)	RR 1.76 (1.25 to 2.49)	341 more per 1000 (from 112 more to 669 more)	Very low	Critical
							-	44.9%		341 more per 1000 (from 112 more to 669 more)		
Proportion of wounds decreased during treatment in people with pressure ulcers (grade 3 to 4) (classification system not reported) - follow-up mean 5.2 weeks[174]												
1	Cohort study	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	36/43 (83.7%)	18/49 (36.7%)	RR 2.28 (1.54 to 3.37)	470 more per 1000 (from 198 more to 871 more)	Very low	Critical
							-	36.7%		470 more per 1000 (from 198 more to 870 more)		
Healing rate at 8 weeks in people with pressure ulcers (grade 3 to 4) (classification system not reported)- follow-up mean 5.2 weeks[174]												
1	Cohort study	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	0.096 (n=43)	0.027 (n=49)	-	MD 0.12 higher (0.11 to 0.14	Very low	Critical

Quality assessment							No of patients		Effect			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Maggot therapy**	**Conservative treatment**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
										higher)		
Proportion of wounds that completely healed in people with pressure ulcers (grade 3 to 4) (classification system not reported)- follow-up mean 5.2 weeks[174]												
1	Cohort study	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[c]	None	17/43 (39.5%)	10/49 (20.4%)	RR 1.94 (1 to 3.77)	192 more per 1000 (from 0 more to 565 more)	Very low	Critical
								20.4%		192 more per 1000 (from 0 more to 565 more)		
Time to wound healing (days) Sherman 2002: in people with pressure ulcers (grade 3 to 4) (classification system not reported - follow-up mean 5.2 weeks; Wang 2010: people with a spinal cord injury with pressure ulcers –follow-up mean 3.5 months[174,204]												
2	Cohort study	Very serious[a]	Serious[d]	No serious indirectness 4	Serious[c]	None	71.7 (n=53)	85.1 n=57	-	MD 11.27 lower (19.97 to 2.57 lower)	Very low	Critical
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital or NHS care												
-	-	-	-	-	-	-	-	-	-	-	-	-
Patient acceptability												
-	-	-	-	-	-	-	-	-	-	-	-	-
Side effects												
-	-	-	-	-	-	-	-	-	-	-	-	-
Mortality (all-cause)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) There was a high risk of selection bias (the method of allocation was potentially related to confounding factors, there were no attempts to balance comparison groups and comparison groups were not comparable at baseline), there was a high risk of performance bias (as both participants and administrators of care were blinded to treatment allocation), there was a high risk of detection bias (investigators were not kept blind for exposure to intervention and other confounding/prognostic factors).

(b) The confidence interval crossed both MID points (0.5 x standard deviation for continuous outcomes and 0.75 to 1.25 for dichotomous outcomes).

(c) The confidence interval crossed 1e MID point (0.5 x standard deviation for continuous outcomes and 0.75 to 1.25 for dichotomous outcomes).

(d) Heterogeneity shows a low p-value.

8.3.2 Economic evidence (adults)

Published literature

No relevant economic evaluations were identified. One study that met the inclusion criteria was selectively excluded[191] – reasons for exclusion are given in Appendix K.

Unit costs

To aid consideration of cost effectiveness, relevant unit costs were obtained from the UK supplier of maggots (BioMond UK). List prices indicate that a 5x6cm BioBag (without sudocrem) costs £245. Assuming (based on GDG estimate) that each patient has a maximum of 3-4 applications, the cost of debridement with maggots could cost up to £980.

8.3.3 Clinical evidence (neonates, infants, children and young people)

No RCTs or cohort studies were identified. Recommendations were developed using a modified Delphi consensus technique. Further details can be found in Appendix N.

8.3.4 Economic evidence (neonates, infants, children and young people)

No relevant economic evaluations were identified.

8.3.5 Evidence statements

8.3.5.1 Clinical (adults)

- One study (n=92) reported maggot therapy was more clinically effective than conservative treatment for reducing the surface area of pressure ulcers during treatment (very low quality).
- One study (n=92) showed that there may be no clinical difference between maggot therapy and conservative treatment for the change in surface area per week. The direction of the effect favoured maggot therapy (very low quality).
- One study (n=92) showed that maggot therapy was more clinically effective than conservative treatment for decreasing the surface area of pressure ulcers within 4 weeks (very low quality).
- One study (n=92) showed that there is no clinical difference between maggot therapy and conservative treatment for healing rate at 8 weeks. The direction of the effect favoured maggot therapy (very low quality).
- One study (n=92) showed that there is potentially no clinical difference between maggot therapy and conservative treatment for the proportion of wounds completely healed. The direction of the effect favoured the maggot therapy (very low quality).
- Two studies (n=110) showed that maggot therapy is potentially more clinically effective than conservative treatment for time to wound healing (very low quality).
- No evidence was found for the following outcomes:
  - Pain (wound-related)
  - Time in hospital or NHS care
  - Patient acceptability
  - Side effects
  - Mortality (all-cause)
  - Health-related quality of life

8.3.5.2 Economic (adults)

No economic evidence was identified.

8.3.5.3 Clinical (neonates, infants, children and young people)

No evidence was identified.

8.3.5.4 Economic (neonates, infants, children and young people)

No economic evidence was identified.

8.4 Recommendations and link to evidence

8.4.1 Adults

Recommendations	**30. Assess the need to debride a pressure ulcer in adults, taking into consideration:** • **the amount of necrotic tissue** • **the grade, size and extent of the pressure ulcer** • **patient tolerance** • **any comorbidities** **31. Offer debridement to adults if identified as needed in the assessment:** • **use autolytic debridement, using an appropriate dressing to support it** • **consider using sharp debridement if autolytic debridement is likely to take longer and prolong healing time.**
Relative values of different outcomes	The GDG identified that the proportion of people with pressure ulcers completely healed, time to complete healing, reduction in size and volume and rate of reduction in size and volume of pressure ulcers were the most critical outcomes to inform decision making. This recommendation was developed from GDG consensus after reviewing the evidence for debridement, to establish whether debridement is required and what type of debridement would be preferable.
Trade-off between clinical benefits and harms	In order to determine whether debridement should be carried out for the treatment of pressure ulcers, the GDG considered evidence looking at different debridement techniques. There was no evidence comparing different techniques of debridement except for the comparison of enzymatic debridement to autolytic debridement (with the use of hydrogel or hydrocolloid dressings). Enzymatic debridement (collagenase) showed some benefit over autolytic debridement (hydrogel dressing). However the GDG noted that there were certain benefits in allowing debridement to occur naturally, as enzymatic debridement can result in the removal of tissue which might otherwise survive. The GDG felt that the use of collagenase was slower than the use of surgical debridement, and therefore surgical debridement would be preferential over enzymatic debridement. Despite the lack of evidence, the GDG considered that debridement is required

	physiologically for the healing process in some pressure ulcers. Therefore, in order to identify where this would be required, the GDG felt that it was necessary to assess the pressure ulcer. The group therefore used informal consensus to develop a list of considerations to aid an assessment of need for and technique of debridement. The GDG felt that an experienced individual should carry out the debridement. Careful consideration would be needed as to who this should be and in what environment this should be done. The GDG noted that debridement can also be carried out in the community. There is also a need to consider if specialist referral is appropriate. Debridement should be prompt and timely to ensure that there is no delay in initiating treatment. The timing of debridement methods should be dependent upon the individuals clinical need.
Economic considerations	The GDG considered the economic implications of debridement. It was agreed that debridement was necessary to promote healing in some cases, and has long term benefits in the form of improved quality of life and reduced treatment costs. The GDG considered 5 economic evaluations which assessed different methods of debridement, all of which were only partially applicable, and had potentially serious limitations. All 5 analyses indicated that collagenase (enzymatic debridement) is cost-effective (compared to hydrocolloid dressings, hydrogel dressings, gauze, calcium alginate, autolysis, wet-to-dry dressings and fibrinolysin). However, none of these studies were from the UK, and pressure ulcers are not a licensed indication for the use of collagenase in the UK. Due to the limitations of these studies and the limited applicability in a UK NHS setting, the GDG felt that these studies were of little benefit in determining cost-effectiveness, and noted that a more relevant comparison would be sharp debridement compared to enzymatic debridement. The GDG agreed that where debridement was required, it is likely that sharp debridement would be cost effective compared to other methods, as it is a quicker process, thus healing can begin sooner and quality of life improvements realised from an earlier stage. In most cases, sharp debridement does not require anaesthetic as only dead tissue is removed, and can be done at the bedside, meaning it can be achieved quickly and efficiently. The GDG did note however, that in a small number of cases sharp debridement would need to be conducted in an operating theatre which would increase the cost on these occasions. The GDG agreed that the upfront cost of sharp debridement would be offset by future savings from a reduced time to healing and improvements in quality of life. The GDG noted that where autolytic debridement was likely to be sufficient, this method of debridement would be likely to offer a cost-effective solution, as it requires no additional resources over the use of an appropriate dressing (as recommended in Chapter 10. The GDG therefore agreed that where active steps for debridement are required sharp debridement is likely to be the cost-effective strategy, and where autolytic debridement is likely to be sufficient, autolytic debridement is likely to be the cost-effective option. No economic evaluations were included which assessed the cost-effectiveness of larval therapy for debridement; therefore the GDG considered relevant unit costs. The GDG noted that debridement with maggots is substantially more expensive than debridement by other means. As there was limited clinical evidence to suggest a benefit of using larval therapy, the GDG did not think that the additional cost was justified. Larval therapy is not considered to be cost-effective compared to other methods of debridement.

Quality of evidence	This recommendation was based on the GDG's experience and was developed after reviewing the limited evidence for debridement. **Maggot therapy** No randomised trials were found, therefore cohort studies were included in the review. The majority of outcomes came from 1 cohort study. The evidence was limited to 3 cohort studies which had very serious limitations and small sample sizes. There was no serious imprecision for the proportion of pressure ulcers decreased in surface area and healing rate. There was serious imprecision for the proportion of pressure ulcers completely healed and time to healing. The conventional treatment involved a variety of treatments including dressings, surgical and enzymatic debridement. **Enzymatic debridement** The evidence was weak as the studies had small sample sizes and the evidence was downgraded for serious and very serious imprecision for almost all outcomes. All the studies had very serious risk of bias. Therefore there is a lot of uncertainty in the results. The GDG noted that outcomes such as reduction in the area of pressure ulcer were sometimes difficult to interpret as debridement may increase the size of the wound whilst being beneficial to healing.
Other considerations	The GDG noted that debridement methods need to be considered on an individual basis. Such consideration includes patient preference and tolerability. The GDG also identified a concern that people who are involved in the treatment of pressure ulcers do not often have the relevant experience needed to debride. Thus, any such undertaking must be done by a person who is trained and competent to ensure debridement is successful.

Recommendations	**32.Do not routinely offer adults:** • **larval (maggot) therapy** • **enzymatic debridement.** **Consider larval therapy if debridement is needed but sharp debridement is contraindicated or if there is associated vascular insufficiency.**
Relative values of different outcomes	The GDG identified that the proportion of people with pressure ulcers completely healed, time to complete healing, reduction in size and volume and rate of reduction in size and volume of pressure ulcers were the most critical outcomes to inform decision making.
Trade off between clinical benefits and harms	**Maggot therapy** There was limited evidence for maggot debridement, with only 3 small cohort studies comparing maggot treatment to conservative treatment. These studies showed a clinical benefit of maggot debridement for the proportion of pressure ulcers completely healed, shorter time to healing and proportion of pressure ulcers which decreased in surface area. There was no clinical benefit for healing rate and it was unclear for change in surface area. There was no evidence for which method of maggot debridement is more effective (that is maggots in a bag compared to free-roaming maggots). The evidence used maggots that were free-roaming, with dressings to hold them in place. The GDG discussed the high cost associated with maggot debridement and that

	larval therapy was not considered to be cost effective (see Economic considerations). However, it was agreed that some people may benefit from the use of maggot debridement where there are contraindications to other methods of debridement (for example, those with comorbidities, where anaesthetic could be required for sharp debridement but cannot be given or where ulcers are in difficult sites) and that it may be necessary to consider the use of laval therapy in these individuals. **Enzymatic debridement** The evidence was very limited with a lot of uncertainty in the results. There was only 1 study found per comparison. Collagenase was found to be more clinically beneficial when compared to hydrocolloid or hydrogel dressing for complete healing compared to hydrocolloid dressing. There was no clinical benefit of collagenase for reduction in pressure ulcer size, reduction in adverse events and for time to healing when compared to hydrocolloid dressing and no clinical harm for mortality (all-cause) when compared to hydrogel or hydrocolloid dressing. Collagenase was more clinically beneficial than inactivated collagenase for proportion of ulcers that increased/decreased in size. Collagenase was more effective at improving pressure ulcers and complete healing of pressure ulcers when compared to sugar and egg white. There was no clinical benefit for collagenase compared to inactivated collagenase to reduce the odour at the end of treatment, the number of side effects or mortality. Collagenase was also more clinically beneficial than papain/urea for reduction pressure ulcers size at 4 weeks, although collagenase had higher side effects, as it did when compared to fibrinolysis/DNAse. Frequency of collagenase ointment application did not show a clinical benefit for 24 hours when compared to 48 hours for complete healing, adverse events or reducing all-cause mortality. Dextranomer was clinically more beneficial than collagenase for completely healing and improving pressure ulcers. Zinc oxide showed no clinical difference for infection, skin reaction and mortality when compared to streptokinase-streptodornase. There was no evidence comparing different techniques of debridement except for the comparison of enzymatic debridement to autolytic debridement (with the use of hydrogel or hydrocolloid dressings). Enzymatic debridement (collagenase) showed some benefit over autolytic debridement (hydrogel dressing). However the GDG noted that there were certain benefits in allowing debridement to occur naturally, as enzymatic debridement can result in the removal of tissue which might otherwise survive. The GDG felt that the use of collagenase was slower than the use of surgical debridement, and therefore surgical debridement would be preferential over enzymatic debridement.
Economic considerations	**Maggot therapy** No economic evaluations were included which assessed the cost-effectiveness of larval therapy for debridement; therefore the GDG considered relevant unit costs. The GDG noted that debridement with maggots is substantially more expensive than debridement by other means. As there was limited clinical evidence to suggest a benefit of using larval therapy, the GDG did not think that the additional cost was justified. Larval therapy is not considered to be cost-effective compared to other methods of debridement. **Enzymatic debridement** See recommendation 27.
Quality of evidence	**Maggot therapy** No randomised trials were found, therefore cohort studies were included in the review. The majority of outcomes came from 1 cohort study. The evidence was limited to 3 cohort studies which had very serious limitations and

	small sample sizes. There was no serious imprecision for the proportion of pressure ulcers decreased in surface area and healing rate. There was serious imprecision for the proportion of pressure ulcers completely healed and time to healing. The conventional treatment involved a variety of treatments including dressings, surgical and enzymatic debridement. **Enzymatic debridement** The evidence was weak as the studies had small sample sizes and the evidence was downgraded for serious and very serious imprecision for almost all outcomes. All the studies had very serious risk of bias. Therefore there is a lot of uncertainty in the results. The GDG noted that outcomes such as reduction in the area of pressure ulcer were sometimes difficult to interpret as debridement may increase the size of the wound whilst being beneficial to healing.
Other considerations	**Maggot therapy** The GDG noted that there can be some discomfort experienced by the individual when using maggots thus affecting tolerability of the treatment. The GDG stated that maggots were available either in a bagged form so that the maggots are contained or as free roaming maggots. Free roaming maggots are contained in the wound by a dressing put over the top. In addition, it was stated that there is at least a 1 day delay in obtaining the maggots as they cannot be stored as they need to be freshly ordered. This can be particularly problematic when wishing to obtain them over weekends and bank holidays. The GDG felt that the effectiveness of the maggots was also dependent upon the skill of the healthcare professional that uses them. It was acknowledged that the actual time taken to conduct the debridement is faster for maggot debridement than sharp debridement because maggots are quicker to apply and would require less staff time. However, both forms of debridement would require a specialist nurse. **Enzymatic debridement** The GDG discussed the current use of debriding agents. They informed that collagenase debridement was previously used in the UK and is used throughout the rest of the world, however it is not currently used routinely in most units. The GDG noted that in the NHS, healthcare professionals undertaking surgical debridement need to have suitable qualifications, and thus there are often limited availability for nurses to undertake this. It was therefore felt that this can increase the popularity of using enzymatic debridement methods.

8.4.2 Neonates, infants, children and young people

Recommendations	**33. Consider autolytic debridement with appropriate dressings for dead tissue in neonates, infants, children and young people. Consider sharp and surgical debridement by trained staff if autolytic debridement is unsuccessful.**
Relative values of different outcomes	The GDG identified that the proportion of people with pressure ulcers completely healed, time to complete healing, reduction in size and volume and rate of reduction in size and volume of pressure ulcers were the most critical outcomes to inform decision making.
Trade-off between clinical benefits and	The GDG used 2 statements from the Delphi consensus survey to help develop the recommendation on debridement in neonates, infants, children and young people.

harms	The statements were: 'Healthcare professionals should use autolytic debridement, by the use of appropriate dressings, for the debridement of devitalized tissue in neonates, infants, children and young people' and' Healthcare professionals should consider the use of sharp and surgical debridement in neonates, infants, children and young people, where autolytic debridement is insufficient.' The statement on autolytic debridement was accepted by the Delphi consensus panel during Round 1 of the survey. The statement on surgical debridement was amended for Round 2 of the survey on the basis of comments received from the panel. The GDG discussed the comments received during Round 1, which focused on ensuring that a suitably qualified individual carried out any surgical or sharp debridement (for example a member of the surgical team or a trained tissue viability nurse). The GDG amended the statement to highlight this. The GDG felt that the statement should also be amended to highlight that autolytic debridement with appropriate dressings would be used before any sharp or surgical debridement was considered. The statement included in Round 2 of the survey was 'Healthcare professionals should consider the use of sharp and surgical debridement by appropriately qualified staff, where autolytic debridement via the use of appropriate dressings is insufficient, in neonates, infants, children and young people.' The statement was accepted during Round 2 of the survey. The GDG discussed the results of the survey and developed a recommendation. The GDG agreed that for some pressure ulcers (for example, those with non-viable tissue), debridement was necessary to ensure that the healing process could be completed. The GDG felt that in the majority of situations, autolytic debridement should be considered the most appropriate method of debridement as this would be achieved naturally, facilitated by the use of a dressing . Comments from the Delphi consensus panel supported this recommendation. However, the GDG acknowledged that there were some situations in which autolytic debridement was likely to be inappropriate or insufficient to remove the non-viable tissue and allow for healing of the pressure ulcer. Comments from the Delphi consensus panel supported this and highlighted that there were situations in which sharp debridement should be considered as an alternative to autolytic debridement, where this is insufficient. The GDG therefore added to the recommendation, to highlight that sharp debridement should be considered where autolytic debridement was insufficient. The GDG and Delphi consensus panel both highlighted that sharp debridement should only be carried out by an appropriate qualified healthcare professional but noted that this may vary by location.
Economic considerations	The GDG noted that autolytic debridement requires no additional resources over the use of an appropriate dressing, as recommended in Chapter 10. Where autolytic debridement is unsuccessful, there may be economic and clinical benefits to sharp debridement. Sharp debridement can speed up the healing process, thus reducing future treatment costs and improving quality of life. The GDG noted that there would be a small upfront cost of sharp debridement, but that this would be offset by future savings from a reduced time to healing and improvements in quality of life.
Quality of evidence	No RCTs or cohort studies were identified for neonates, infants, children or young people. Formal consensus using a modified Delphi was therefore used to develop the recommendation. To inform the recommendation, the GDG used 1 statement which was included in Round 1 of the Delphi consensus survey and reached 84% consensus agreement. A second statement was included in Round 1 of the Delphi consensus, which reached

	63% consensus. This statement was amended for inclusion in Round 2 of the Delphi consensus survey, where it reached 84% consensus agreement. Further details can be found in Appendix N.
Other considerations	The GDG noted that recommendations on assessment to identify need for and techniques of debridement were also likely to be applicable to neonatal, infant, child and young person populations.

9 Systemic antibiotics

The role of microorganisms in the aetiology and persistence of chronic wounds, including pressure ulcers, remains poorly understood. All chronic wounds are presumed to be bacterially contaminated, but the point at which this contamination becomes problematic still needs to be determined.

Current practice in terms of identifying indications for systemic antimicrobials (largely, antibiotic therapy) is diverse and based on expert opinion. Whilst many healthcare professionals do not feel that it is appropriate to provide systemic antibiotics for pressure ulcers which present only with clinical signs of local infection, others feel that some local infection may also require treatment with systemic antibiotics, especially when the virulence of the organism and the host defences have been taken into account.

The GDG was therefore interested in identifying what the most clinically and cost effective antimicrobial agents are in the treatment of pressure ulcers. For the purposes of the review, systemic antibiotics and antifungals were considered.

9.1 Review question: What are the most clinically and cost effective systemic agents for the treatment of pressure ulcers?

For full details see review protocol in Appendix D.

9.1.1 Clinical evidence (adults)

A systematic search for randomised trials identified 6 studies of potential relevance to the review question of which all were subsequently excluded. Reasons for exclusion can be found in Appendix K.

A systematic search for cohort studies was subsequently carried out. Eleven studies met the inclusion criteria and were reviewed in detail. All 11 records were excluded. The flow chart and reason for exclusion are presented in Appendix D and J.

9.1.2 Economic evidence (adults)

No relevant economic evaluations were identified.

9.1.3 Clinical evidence (neonates, infants, children and young people)

No RCTs or cohort studies were identified. Recommendations were developed using a modified Delphi consensus technique. Further details can be found in Appendix N.

9.1.4 Economic evidence (neonates, infants, children and young people)

No relevant economic evaluations were identified.

9.1.5 Evidence statements

9.1.5.1 Clinical (adults)

No evidence was identified.

9.1.5.2 Economic (adults)

No evidence was identified.

9.1.5.3 Clinical (neonates, infants, children and young people)

No evidence was identified.

9.1.5.4 Economic (neonates, infants, children and young people)

No evidence was identified.

9.1.6 Recommendations and link to evidence

9.1.6.1 Adults

Recommendations	**34. Do not offer systemic antibiotics specifically to heal pressure ulcers in adults.**
Relative values of different outcomes	The GDG identified that the proportion of people with pressure ulcers completely healed, time to complete healing, reduction in size and volume and rate of reduction in size and volume of pressure ulcers were the most critical outcomes to inform decision making.
Trade off between clinical benefits and harms	There was no evidence identified on the use of systemic agents for the healing of pressure ulcers, therefore this recommendation was based on GDG informal consensus. The GDG stated that it is not possible to recommend the use of systemic agents for the treatment of pressure ulcers, however these agents may be used for related conditions. The GDG highlighted that there are some systemic agents such as steroids which are detrimental to the healing of pressure ulcers.
Economic considerations	No evidence was identified to suggest that systemic agents were clinically effective in the treatment of pressure ulcers, and the GDG agreed that they are unlikely to promote pressure ulcer healing. Use of systemic agents has a resource implication, thus in the absence of clinical benefit the GDG agreed that the use of systemic agents would not be cost-effective.
Quality of evidence	There were no RCTs or cohort studies identified on the use of systemic agents for the healing of pressure ulcers, therefore the recommendation was developed by GDG informal consensus.
Other considerations	The GDG felt that systemic agents should be reserved for signs and symptoms of systemic sepsis, spreading cellulitis and underlying osteomyelitis. It should be noted that the use of systemic agents should only be prescribed following full assessment of the individual.

Recommendations	**35. After a skin assessment, offer systemic antibiotics to adults with a pressure ulcer if there are any of the following:** • **clinical evidence of systemic sepsis** • **spreading cellulitis** • **underlying osteomyelitis.** **36. Discuss with the local hospital microbiology department which antibiotic to offer adults to ensure that the systemic antibiotic is effective against local strains of infection.**
Relative values of different outcomes	The GDG identified that the proportion of people with pressure ulcers completely healed, time to complete healing, reduction in size and volume and rate of reduction

	in size and volume of pressure ulcers were the most critical outcomes to inform decision making.
Trade off between clinical benefits and harms	There was no evidence identified on the use of systemic antibiotics for the healing of pressure ulcers, therefore this recommendation was based on GDG informal consensus. The GDG noted that the use of systemic antibiotics should be reserved for when there are signs and symptoms of systemic sepsis, spreading cellulitis and underlying osteomyelitis. The GDG felt that it would be necessary to have a full assessment of the individual to identify if systemic agents would be required. The GDG therefore used informal consensus to develop a recommendation identifying possible signs of infection which would benefit from treatment using systemic antibiotics. The GDG felt that it was important to highlight that where systemic antibiotics are offered, these should only be offered following discussion with the local microbiology department. The group felt that this was important to ensure that local guidelines on the use of antibiotics were followed and to ensure that the antibiotis being used is effective against local strains of infection. A recommendation was therefore developed using informal consensus to emphasise the importance of this.
Economic considerations	The GDG noted that whilst systemic agents such as antibiotics are unlikely to be cost-effective solely for the treatment of pressure ulcers, there are additional factors to consider when there are signs of systemic sepsis, spreading cellulitis or underlying osteomyelitis. Systemic agents are required to treat these conditions, and are generally inexpensive. The GDG agreed that the small cost of treating these conditions would be outweighed by substantial increases in quality of life, and cost savings would most likely be realised through reductions in further treatment costs.
Quality of evidence	There was no evidence identified on the use of systemic antibiotics for the healing of pressure ulcers, therefore the recommendation was developed by GDG informal consensus.
Other considerations	The GDG stated that it was important to be aware of the unnecessary use of antibiotics as this may lead to the development of antibiotic resistant strains and the group highlighted that there was evidence of the development of drug resistance from other uses of antibiotics. It was also acknowledged that local resistance should be taken into consideration when deciding which antibiotics should be used.

Recommendations	**37. Do not offer systemic antibiotics to adults based only on positive wound cultures without clinical evidence of infection.**
Relative values of different outcomes	The GDG identified that the proportion of people with pressure ulcers completely healed, time to complete healing, reduction in size and volume and rate of reduction in size and volume of pressure ulcers were the most critical outcomes to inform decision making.
Trade off between clinical benefits and harms	There was no evidence identified on the use of systemic antibiotics for the healing of pressure ulcer, therefore this recommendation was based on GDG informal consensus. The GDG felt that a positive wound culture does not necessarily mean that the wound is infected as it may be due to normal bacteria. Therefore further clinical evidence is required to confirm that the pressure ulcer is infected, via a full assessment.
Economic	The GDG noted that identification of positive wound cultures did not mean systemic

considerations	antibiotics were required. No evidence was identified to suggest that systemic antibiotics were clinically effective in the treatment of pressure ulcers, and the GDG agreed that they are unlikely to promote pressure ulcer healing. Use of systemic antibiotics has a resource implication, thus in the absence of clinical benefit the GDG agreed that the use of systemic agents would not be cost-effective if there was no clinical evidence of infection.
Quality of evidence	There was no evidence identified on the use of systemic agents for the healing of pressure ulcers, therefore the recommendation was developed by GDG informal consensus.
Other considerations	The GDG stated that it was important to be aware of the unnecessary use of antibiotics as this may lead to the development of antibiotic resistant strains and the group highlighted that there was evidence of the development of drug resistance from other uses of antibiotics. It was also acknowledged that local resistance should be taken into consideration when deciding which antibiotics should be used.

9.1.6.2 Neonates, infants, children and young people

Recommendations	**38. Consider systemic antibiotics for neonates, infants, children and young people with pressure ulcers with clinical evidence of local or systemic infection.**
Relative values of different outcomes	The GDG identified that the proportion of people with pressure ulcers completely healed, time to complete healing, reduction in size and volume and rate of reduction in size and volume of pressure ulcers were the most critical outcomes to inform decision making.
Trade off between clinical benefits and harms	The GDG used 2 statements from the Delphi consensus panel to develop the recommendation, 'Healthcare professionals should use appropriate systemic antibiotics for the treatment of infected pressure ulcers (ie. advancing cellulitis, osteomyelitis or systemic infection) in neonates, infants, children and young people, as specified in the British National Formulary for Children (BNFc)' and 'Healthcare professionals should only use systemic antibiotic therapy for neonates, infants, children and young people, where clinically indicated (for example a positive wound swab or when 2 or more clinical signs of infection are present at the same time).' Both statements were accepted in Round 1 of the Delphi consensus survey. The GDG agreed that a recommendation should be developed to highlight that systemic antibiotics should be considered for pressure ulcers with signs of local or systemic infection. This was supported by qualitative comments received during Round 1 of the Delphi consensus, which noted that treatment with antibiotics should be carefully considered on an individual basis, accounting for the clinical state and history of the child. The GDG wished to highlight that antibiotics should only be considered where there signs of local or systemic infection, that is where there are signs and symptoms of systemic sepsis, spreading cellulitis or underlying osteomyelitis.
Economic considerations	The GDG noted that systemic antibiotics are often required to treat infection, and are generally inexpensive. The GDG agreed that the small cost of treating infection would be outweighed by substantial increases in quality of life, and cost savings would most likely be realised through reductions in further treatment costs. Systematic antibiotics are only thought to be cost-effective when there are signs of systemic or local infection.
Quality of evidence	No RCTs or cohort studies were identified for neonates, infants, children or young people. Formal consensus using a modified Delphi was therefore used to develop the

	recommendation. To inform the recommendation, the GDG used 2 statements which were included in Round 1 of the Delphi consensus survey and reached 96% and 80% consensus agreement. Further details can be found in Appendix N.
Other considerations	The GDG stated that it was important to be aware of the unnecessary use of antibiotics as this may lead to the development of antibiotic resistant strains. It was also acknowledged that local resistance should be taken into consideration when deciding which antibiotics should be used.

Recommendations	**39. Discuss with a local hospital microbiology department which antibiotic to offer neonates, infants, children and young people to ensure that the chosen systemic antibiotic is effective against local strains of bacteria.**
Relative values of different outcomes	The GDG identified that the proportion of people with pressure ulcers completely healed, time to complete healing, reduction in size and volume and rate of reduction in size and volume of pressure ulcers were the most critical outcomes to inform decision making.
Trade off between clinical benefits and harms	The GDG used 1 statement from the Delphi consensus panel to develop the recommendation 'Healthcare professionals should account for local sensitivities in antibiotic resistance, in conjunction with the microbiology department of their local hospital'. The statement was agreed in Round 1of the Delphi consensus survey and a recommendation was therefore developed. The GDG felt that it was important to highlight that the offering of an antibiotic should only be given in conjunction and after discussion with, the local microbiology department. The GDG emphasised the importance of doing so to ensure that the most effective antibiotics are provided to combat local strains. Qualitative comments receiving during Round 1 agreed and noted that there are often local guidelines in place to help guide and advise healthcare professionals on the use of systemic antibiotics and treating infection.
Economic considerations	Discussion with the microbiology department will help promote efficient use of resources, as this will ensure that effective drugs are used, thereby minimising wastage and promoting healing of pressure ulcers.
Quality of evidence	No RCTs or cohort studies were identified for neonates, infants, children or young people. Formal consensus using a modified Delphi was therefore used to develop the recommendation. To inform the recommendation, the GDG used 1 statement which were included in Round 1 of the Delphi consensus survey and reached 95% consensus agreement. Further details can be found in Appendix N.
Other considerations	The GDG stated that it was important to be aware of the unnecessary use of antibiotics as this may lead to the development of antibiotic resistant strains. It was also acknowledged that local resistance should be taken into consideration when deciding which antibiotics should be used.

10 Topical antimicrobials and antiseptics

A number of topical agents have been used over the years for the treatment of pressure ulcers. These range from antiseptics to antibiotics and newer biological agents such as platelet derived growth factors and nerve growth factors. While many claims have been made for the superiority of individual topical agents, it has been difficult to find and develop the evidence for these. Local cytotoxicity has been an area of concern with a number of agents and the situation is further complicated by the addition of new formulations every year.

While topical agents are often grouped together, they are thought to have widely differing mechanisms of action. Reduction in bio burden, antisepsis, disruption of biofilms, prevention of infection and creation of an occlusive barrier have all been proposed as mechanisms by which topical agents can exert a beneficial effect. In addition to aiding pressure ulcer healing, it has been suggested that they reduce the likelihood of systemic antibiotic use, reduce the likelihood of resistant bacterial strains emerging and reduce the local complications associated with pressure ulcers.

The GDG were interested in identifying studies that support or negate a role for any of the individual topical agents or a group of agents in the treatment of pressure ulcers.

10.1 Review question: What are the most clinically and cost effective topical agents for the treatment of pressure ulcers?

For full details see review protocol in Appendix D.

10.1.1 Clinical evidence (adults)

A Cochrane review on wound cleansing for pressure ulcer by Moore and Cowman (2011) was identified. A systematic search was undertaken to update the Cochrane review and identify any evidence on other categories of topical agents. Fifty four records were identified as potentially relevant for inclusion and 19 records were excluded. The remaining 35 studies were included in this review.

The Cochrane review by Moore and Cowman (2011)[120] included 3 RCTs,[23,37,72] of which 2 were excluded because they did not meet the inclusion criteria of this review. One was excluded as it was a study on hydrotherapy[37] and was identified as more appropriate for the debridement review. The other study did not report separate outcomes for people with pressure ulcers[72]. The flow chart and reasons for exclusion are presented in Appendix D and K.

Thirty-six randomized controlled trials were included in this review[4,7,23,41,43,68,74,79,81,87,93,95,98,100,101,106,110,119,128,129,133,144,147,148,153,155-159,176,181,190,200,209,211]. Evidence from the included studies is summarised in the clinical GRADE evidence profiles (Table 90). All forest plots and study evidence tables are presented in respectively Appendix D and J.

Various types of topical agents are used to treat pressure ulcers. A definition of the different topical agents is provided in Table 89. In this review different types of topical agents are compared to each other or to placebo. The following categories were included in the review:

- Cleansers: soap, water, detergent, and solvent
- Moisturisers (emollients): glycerine, oil, cream and ointment
- Protective agents: for example talc, zinc oxide
- Antiseptic agents: alcohol, iodine solution, chlorhexidine, chlor oxydantia, peroxide, quaternary ammonium compounds, Oxyquinoline, mercury, gentian violet, silver preparation

- Antibiotics
- Anti-inflammatory agents
- Anti-fungal agents
- Insulin
- Growth factors

Summary of included studies

Study	Intervention/comparator	Population	Outcome	Study length
Agren 1985[4]	Zinc oxide Streptokinase-streptodornase ointment	Geriatric adults with necrotic pressure ulcers	• Reduction in ulcer area • Side effects	Eight weeks of treatment
Alm 1989[7]	Saline-soaked gauze Hydrocolloid	People in long term care with pressure ulcers	• Reduction in ulcer area • Side effects	Six weeks of treatment and additional 3 and 6 weeks of follow-up
Bellingeri 2004[23]	Aloe vera, silver chloride and decyl glucoside Isotonic saline	Elderly adults in a home care with a grade 2 to 4 pressure ulcers (NPUAP classification)	• Reduction in PSST score	14 days of treatment
Chang 1998[41]	Saline-soaked gauze Hydrocolloid	People with a grade 2 or 3 pressure ulcers	• Reduction in ulcer area • Side effects	Eight weeks of treatment or until complete healing
Chuansuwanich 2011[43]	Silver sulfadiazine cream Silver dressing	People in hospital with a grade 3 or 4 pressure ulcer (NPUAP classification)	• Rate of healing • Reduction in PUSH score • Side effects	Eight weeks of treatment
Gerding 1992[68]	Oxyquinoline A&D ointment	People in palliative care with a grade 2 or 3 pressure ulcer (NPUAP classification)	• Proportion of ulcers completely healed • Proportion of ulcers improved • Proportion of ulcers not changed • Proportion of ulcers worsened • Healing rate	28 days of treatment or until complete healing
Günes 2007[74]	Ethoxydiaminoacridine plus nitrofurazone Honey	Hospitalised adults older than 18 years with a grade 2 or 3 pressure ulcer (AHCPR classification)	• Proportion of ulcers completely healed • Reduction in PUSH score • Reduction in ulcer size • Side effects	Five weeks of treatment or until complete healing

Study	Intervention/comparator	Population	Outcome	Study length
Hirshberg 2003[79]	Growth factors Placebo	People in hospital with a grade 3 or 4 pressure ulcer(NPUAP classification)	• Proportion of ulcers completely healed • Reduction in ulcer area • Reduction in ulcer volume	16 weeks or until complete healing
Hollisaz 2004[81]	Phenytoin cream Saline-soaked gauze Hydrocolloid	People with a spinal cord injury and a grade 1 or 2 pressure ulcer (NPUAP or Shea classification)	• Proportion of ulcers completely healed • Proportion of ulcers improved • Proportion of ulcers worsened • Proportion of people completely healed	Eight weeks of treatment
Kaya 2005[87]	Povidone-iodine Hydrogel	Hospitalised adults with a spinal cord injury and a grade 1 to 3 pressure ulcer (NPUAP classification)	• Healing rate	Not reported
Kim 1996[93]	Povidone Hydrocolloid	People with a grade 1 to 2 pressure ulcer (NPUAP classification)	• Proportion of people completely healed • Healing rate • Healing speed • Side effects	Mean duration of 18.9 days and 24.3 in group 1 and 2 respectively
Knudsen 1982[95]	Dialysate Placebo	People with a spinal cord injury and a pressure ulcer.	• Decrease in ulcer size • Healing half-time • Side effects	Three weeks of treatment
Kraft 1993[98]	Saline-soaked gauze Foam dressing	Males with a grade 2 or 3 pressur eulcers (Enterstomal Therapy definition)	• Proportion of people completely healed	24 days of treatment
Kuflik 2001[100]	Ointment (Resurflix®) Petrolatum	Elderly adults with a grade I or 2 pressure ulcer (AHCPR	• Proportion of ulcers completely healed	Six weeks of treatment

Study	Intervention/comparator	Population	Outcome	Study length
		classification)	• Proportion of ulcers improved • Proportion of ulcers not changed • Proportion of ulcers worsened	
Landi 2003[101]	Nerve growth factor Placebo	Adults in a nursing home with a grade 2 to 5 foot pressure ulcer (Yarkony classification)	• Proportion of people completely healed • Proportion of people improved in pressure ulcer grade • Reduction in ulcer area • Side effects	Six weeks of treatment or until complete healing
Ljungberg 2009[106]	Saline-soaked gauze Dextranomer	Males with a spinal cord injury and exudative pressure ulcers (Eltorai classification)	• Proportion of ulcers improved • Side effects	14 days of treatment
Matzen 1999[110]	Saline-soaked gauze Hydrocolloid dressing	Adults with a grade 3 or 4 pressure ulcer (Lowthian classification)	• Proportion of people completely healed • Reduction in ulcer volume • Side effects	12 weeks of treatment or until complete healing
Moberg 1983[119]	Iodine Standard treatment	Hospitalised adults with an deep or superficial pressure ulcer	• Proportion of ulcers reduced with 50% • Reduction in ulcer area	Three weeks of treatment
Mustoe 1994[128]	Growth factors Placebo	Adults with a grade 3 or 4 pressure ulcer	• Proportion of people completely healed • Ulcer volume	29 days of treatment and up to five months of follow-up
Nasar 1982[129]	Chlorinated lime solution (Eusol) and paraffin Dextranomer	Adults with a deep pressure ulcer	• Time to healing (defined as granulation and less than 25% of original	Until healing

Study	Intervention/comparator	Population	Outcome	Study length
			ulcer area) • Pain	
Neill 1989[133]	Saline-soaked gauze Hydrocolloid dressing	Adults with a grade 2 or 3 pressure ulcer (Shea classification)	• Proportion of ulcers completely healed • Proportion of people worsened • Reduction in ulcer area • Side effects	Eight weeks of treatment
Oleske 1986[144]	Saline-soaked gauze Polyurethane dressing	People in hospital with a grade 1 or 2 pressure ulcer (Enis and Sarmiento classification)	• Proportion of ulcers completely healed • Proportion of ulcers worsened • Reduction in ulcer area	10 days of treatment
Payne 2001[147]	Growth factors Placebo	People in hospital with a grade 3 or 4 pressure ulcer	• Proportion of people completely healed • Proportion of people worsened	35 days of treatment and 1 year of follow-up
Payne 2009[148]	Saline Foam dressing	People in hospital with a grade 2 pressure ulcer (NPUAP classification)	• Proportion of people completely healed • Time to healing	Four weeks of treatment or until complete healing
Rees 1999[153]	Growth factor Placebo	People with a grade 3 or 4 pressure ulcer (NPUAP classification)	• Proportion of people completely healed • Proportion of people healed ≥ 90% • Reduction in ulcer volume • Side effects	16 weeks of treatment or until complete healing
Rhodes 2001[155]	Phenytoin Triple antibiotics Hydrocolloid	People in a nursing home with a grade 2 pressure ulcer (AHCPR classification)	• Healing time • Side effects • Pain	Not reported

Study	Intervention/comparator	Population	Outcome	Study length
Robson 1992a[158]	Growth factors Placebo	People with denervated ulcers and a grade 3 or 4 pressure ulcer	• Proportion of people healed > 70% • Reduction in ulcer volume	30 days of treatment and 5 months of follow-up
Robson 1992[159]	Growth factors Placebo	People with denervated ulcers and a grade 3 or 4 pressure ulcer	• Proportion of people completely healed • Reduction in ulcer depth • Side effects	Four weeks of treatment and five months of follow-up
Robson 1994[156]	Growth factors Placebo	People with denervated ulcers and a grade 3 or 4 pressure ulcer	• Proportion of people completely healed • Reduction in ulcer area	28 days of treatment and 3 months of follow-up
Robson 2000[157]	Growth factors Placebo	People with a grade 3 or 4 pressure ulcer	• Reduction in ulcer area	35 days of treatment
Sipponen 2008[176]	Resin salve Hydrofibre	Hospitalised people with a grade 2 to 4 pressure ulcer (NPUAP classification)	• Proportion of people completely healed • Proportion of ulcers completely healed • Proportion of ulcers improved • Proportion of ulcers worsened • Reduction in ulcer width and depth • Healing speed • Side effects	Six months of treatment
Subbanna 2007[181]	Phenytoin Saline-soaked gauze	People with a spinal cord injury and a grade 2 pressure ulcer (NPUAP classification).	• Reduction in ulcer size • Reduction in ulcer volume • Reduction in PUSH score • Side effects	15 days of treatment

Study	Intervention/comparator	Population	Outcome	Study length
Thomas 1998[190]	Saline-soaked gauze Hydrogel	People with a grade 2, 3 or 4 pressure ulcer.	• Proportion of people completely healed • Proportion of people worsened • Reduction in ulcer area • Time to healing	Ten weeks of treatment or until complete healing
Van Ort 1976[200]	Insulin Standard treatment	People in a nursing home with a pressure ulcer	• Healing rate	Fifteen days of treatment
Xakellis 1992[209]	Saline-soaked gauze Hydrocolloid dressing	People in long term care with a grade 2 or 3 pressur eulcer (Shea classification)	• Proportion of people completely healed • Time to healing	Six months of treatment
Yastrub 2004[211]	Antibiotic ointment Foam dressing	People in long term care with a grade 2 pressure ulcer (AHCPR classification)	• Proportion of people improved • PUSH score	Four weeks of treatment

Table 88: Categories of topical agents

	Saline	Phenytoin	Solcoseryl	Aloe vera	Petrolatum	Zinc oxide	A&D ointment	Silver sulfazidine	Ethoxy-diaminoacridine	Oxy-quinoline	Chlorinated lime	Iodophor such as (Povidone)-iodine	Resin salve	Nitrofurazone	Silvadene
Cleanser	X														
Moisturiser		X	X	X	X										
Protecting agent						X	X								
Antiseptic agent (a)								X	X	X	X	X	X	X	
Antibiotic agent (a)													X	X	X
Anti-inflammatory agent (a)												X	X	X	
Antifungal agent (a)												X	X	X	

(a) Antimicrobial agents.

Table 89: Definition topical agents

Topical Agent	Definition
Saline	An isotonic solution of sodium chloride in distilled water.
Phenytoin	Possible mechanisms of action of phenytoin on wound healing are by decreasing serum corticosteroid and by acceleration of assembly and presence of collagen and fibrin in the ulcer area, and stimulation of alkaline phosphatase secretion.
Dialysate (Solcoseryl)	Contains a free protein extract of calf blood that possesses metabolic function in the tissue. Solcoseryl contains a mixture of biologically active substances like aminoacids, irreplaceable microelements, glycolipids, nucleotides, nucleosides.
Petrolatum	Vaseline.
Zinc oxide	A topical astringent and protectant.
Streptokinase-streptodornase	A mixture of enzymes elaborated by hemolytic streptococci; used as a proteolytic and fibrinolytic agent.
Povidone-iodine	An antiseptic that is used for disinfecting skin.
Cadexomer	A dry powder consisting of spherical microbeads that range in diameter from 100 to 315 3 dimensional network of a modified starch polymer containing iodine, which is physically immobilized within the matrix at a concentration of 0.9%. One gram of powder can absorb as much as 7ml of fluid.
Silver sulfazidine	The cream vehicle consists of white petrolatum, stearyl alcohol, isopropyl myristate, sorbitan monooleate, polyoxyl 40 stearate, propylene glycol, and water, with methylparaben 0.3% as a preservative and sulfa antibiotics.
Resin salve	A pure spruce resin.
Growth factors	Including: • Topical growth factor – Beta 3 • Mouse nevre groth factor • Recombinant platelet-derived growth factor-BB • Granulo-macrophage/colony-stimulating factor • Basic fibroblast growth factor • Interleukin 1-beta

Table 90: Clinical evidence profile: saline-soaked gauze versus hydrocolloid dressing

Quality assessment							No of patients/ulcers		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Saline	Hydro-colloid	Relative (95% CI)	Absolute	Quality	Importance
Proportion of people completely healed – general population and people with a spinal cord injury (meta-analysed) – all grade (grade 1 and above) – Lowthian and Shea classification[m,81,110,209]												
3	Randomised trials	Very serious[a,b,c]	Very serious[h]	No serious indirectness	Serious[d]	None	26/63 (41.3 %)	41/63 (65.1%)	RR 0.50 (0.14 to 1.74)	325 fewer per 1000 (from 560 fewer to 482 fewer)	Very low	Critical
							-	71.4%		357 fewer per 1000 (from 614 fewer to 528 fewer)		
Proportion of people completely healed – general population (analysed separately due to population) – all grade (grade 1 and above) – Lowthian and Shea classification[110,209]												
2	Randomised trials	Very serious[a,c]	Very serious[h]	No serious indirectness	Serious[d]	None	18/36 (50%)	21/35 (60%)	RR 0.38 (0.01 to 10.16)	372 fewer per 1000 (from 594 fewer to 1000 more)	Very low	Critical
							-	59.2%		367 fewer per 1000 (from 586 fewer to 1000 more)		
Proportion of people completely healed - people with a spinal cord injury (analysed separately due to population) – all grade (grade 1 and above) – Shea classification[81]												
1	Randomised trial	Serious[b]	No serious inconsistency	No serious indirectness	Serious[d]	None	8/27 (29.6 %)	20/28 (71.4%)	RR 0.41 (0.22 to 0.78)	421 fewer per 1000 (from 157 fewer to 557 fewer)	Low	Critical
							-	71.4%		421 fewer per 1000 (from 157 fewer to 557 fewer)		
Proportion of ulcers completely healed (all sites) - general population and people with a spinal cord injury (meta-analysed) – all grade (grade 1 to 3) – Shea classification[81,133]												
2	Randomised	Very	Serious[f]	No serious	Serious[d]	None	18/75	36/73	RR 0.49	280 fewer	Very low	Critical

Quality assessment							No of patients/ulcers		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Saline**	**Hydro-colloid**	**Relative (95% CI)**	**Absolute**		
	trials	serious[b,e]		indirectness			(24%)	(49.3%)	(0.31 to 0.78)	(from 660 fewer to 100 more		
							-	52.6%		280 fewer (from 660 fewer to 100 more		
Proportion of ulcers completely healed (all sites) - general population (analysed separately due to population and grade 2 and above only)(grade 2 to 3)– Shea classification[133]												
1	Randomised trial	Very serious[e]	No serious inconsistency	No serious indirectness	Very serious[g]	None	10/45 (22.2 %)	13/42 (31%)	RR 0.72 (0.35 to 1.46)	87 fewer per 1000 (from 201 fewer to 142 more)	Very low	Critical
							-	31%		87 fewer per 1000 (from 201 fewer to 143 more)		
Proportion of ulcers completely healed (all sites) - people with a spinal cord injury (analysed separately due to population) – grade 1 and above (grade 1 and 2) – Shea classification[81]												
1	Randomised trial	Serious[b]	No serious inconsistency	No serious indirectness	No serious imprecision	None	8/30 (26.7 %)	23/31 (74.2%)	RR 0.36 (0.19 to 0.67)	475 fewer per 1000 (from 245 fewer to 601 fewer)	Moderate	Critical
							-	74.2%		475 fewer per 1000 (from 245 fewer to 601 fewer)		
Proportion of ulcers completely healed (all sites) - people with a spinal cord injury (analysed separately due to grade of pressure ulcer) – grade 1 - Shea classification[81]												
1	Randomised trial	Serious[b]	No serious inconsistency	No serious indirectness	Serious[d]	None	5/11 (45.5 %)	11/13 (84.6%)	RR 0.54 (0.27 to 1.07)	389 fewer per 1000 (from 618 fewer to 59 more)	Low	Critical
							-	84.6%		389 fewer per		

Quality assessment							No of patients/ulcers		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Saline**	**Hydro-colloid**	**Relative (95% CI)**	**Absolute**		
										1000 (from 618 fewer to 59 more)		
Proportion of ulcers completely healed (all sites) - general population and people with a spinal cord injury (meta-analysed population, analysed grade of pressure ulcer separately) grade 2 - Shea classification[81,133]												
2	Randomised trials	Very serious[b,e]	No serious inconsistency	No serious indirectness	No serious imprecision	None	6/53 (11.3 %)	23/43 (53.5%)	RR 0.22 (0.1 to 0.48)	417 fewer per 1000 (from 278 fewer to 481 fewer)	Low	Critical
							-	55.3%		431 fewer per 1000 (from 288 fewer to 498 fewer)		
Proportion of ulcers completely healed (all sites) - general population (analysed population and grade of ulcer separately) – grade 2 - Shea classification[133]												
1	Randomised trial	Very serious[e]	No serious inconsistency	No serious indirectness	No serious imprecision	None	3/34 (8.8%)	11/25 (44%)	RR 0.2 (0.06 to 0.64)	352 fewer per 1000 (from 158 fewer to 414 fewer)	Low	Critical
							-	44%		352 fewer per 1000 (from 158 fewer to 414 fewer)		
Proportion of ulcers completely healed (all sites) - people with a spinal cord injury (analysed population separately and grade of pressure ulcer separately) – grade 2 - Shea classification[81]												
1	Randomised trial	Serious[b]	No serious inconsistency	No serious indirectness	No serious imprecision	None	3/19 (15.8 %)	12/18 (66.7%)	RR 0.24 (0.08 to 0.7)	507 fewer per 1000 (from 200 fewer to 613 fewer)	Moderate	Critical
							-	66.7%		507 fewer per 1000 (from 200 fewer to 614		

Quality assessment							No of patients/ulcers		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Saline	Hydro-colloid	Relative (95% CI)	Absolute		
										fewer)		
Proportion of ulcers completely healed (all sites) - general population (analysed population separately and grade of pressure ulcer separately) – grade 3 - Shea classification[133]												
1	Randomised trial	Very serious[e]	No serious inconsistency	No serious indirectness	Very serious[d,n]	None	1/11 (9.1%)	2/17 (11.8%)	RR 0.77 (0.08 to 7.54)	27 fewer per 1000 (from 108 fewer to 769 more)	Very low	Critical
							-	11.8%		27 fewer per 1000 (from 109 fewer to 772 more)		
Proportion of ulcers completely healed (sacral area) - people with a spinal cord injury (analysed population and area separately) – grade 1 and above (grade 1 and 2) – Shea classification[81]												
1	Randomised trials	Serious[b]	No serious inconsistency	No serious indirectness	Very serious[d,n]	None	4/8 (50%)	0/7 (0%)	OR 10.87 (1.19 to 99.73)	100 fewer (from 650 fewer to 450 more)	Very low	Critical
							-	0%		100 fewer (from 650 fewer to 450 more)		
Proportion of ulcers improved - people with a spinal cord injury (analysed population separately) – grade 1 and above (grade 1 and 2) – Shea classification[81]												
1	Randomised trials	Serious[b]	No serious inconsistency	No serious indirectness	No serious imprecision	None	29/60 (48.3 %)	27/31 (87.1%)	RR 0.55 (0.41 to 0.75)	392 fewer per 1000 (from 218 fewer to 514 fewer)	Moderate	Critical
							-	87.1%		392 fewer per 1000 (from 218 fewer to 514 fewer)		
Proportion of ulcers worsened - general population and people with a spinal cord injury (meta-analysed population) – grade 1 and above (grade 1 to 3) – Shea classification[81,133]												
2	Randomised	Very	Very serious[h]	No serious	Very	None	24/75	16/73	RR 1.88	193 more per	Very low	Critical

Quality assessment							No of patients/ulcers		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Saline**	**Hydro-colloid**	**Relative (95% CI)**	**Absolute**		
	trials	serious[b,e]		indirectness	serious[g]		(32%)	(21.9%)	(0.41 to 8.68)	1000 (from 129 fewer to 1000 more)		
							-	19.9%		175 more per 1000 (from 117 fewer to 1000 more)		
Proportion of ulcers worsened - general population (analysed population and grade 2 and above separately) – grade 2 and above (grade 2 and 3) – Shea classification[133]												
1	Randomised trial	Very serious[e]	No serious inconsistency	No serious indirectness	Very serious[g]	None	15/45 (33.3 %)	14/42 (33.3%)	RR 1 (0.55 to 1.81)	0 fewer per 1000 (from 150 fewer to 270 more)	Very low	Critical
							-	33.3%		0 fewer per 1000 (from 150 fewer to 270 more)		
Proportion of ulcers worsened - people with a spinal cord injury (population analysed separately) – grade 1 and above (grade 1 and 2) – Shea classification[81]												
1	Randomised trial	Serious[b]	No serious inconsistency	No serious indirectness	Very serious[d,n]	None	9/30 (30%)	2/31 (6.5%)	RR 4.65 (1.09 to 19.78)	235 more per 1000 (from 6 more to 1000 more)	Very low	Critical
							-	6.5%		237 more per 1000 (from 6 more to 1000 more)		
Proportion of ulcers worsened - general population (population analysed separately and grade of pressure ulcer separately) – grade 2 – Shea classification[133]												
1	Randomised trial	Very serious[e]	No serious inconsistency	No serious indirectness	Very serious[g]	None	11/34 (32.4 %)	7/25 (28%)	RR 1.16 (0.52 to 2.56)	45 more per 1000 (from 134 fewer to 437 more)	Very low	Critical
							-	28%		45 more per		

Quality assessment							No of patients/ulcers		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Saline	Hydro-colloid	Relative (95% CI)	Absolute		
										1000 (from 134 fewer to 437 more)		
Proportion of ulcers worsened - general population (population analysed separately and grade of pressure ulcer separately) – grade 3 – Shea classification[133]												
1	Randomised trial	Very serious[e]	No serious inconsistency	No serious indirectness	Very serious[g]	None	4/11 (36.4 %)	7/17 (41.2%)	RR 0.88 (0.34 to 2.32)	49 fewer per 1000 (from 272 fewer to 544 more)	Very low	Critical
								41.2%		49 fewer per 1000 (from 272 fewer to 544 more)		
Mean percentage reduction in ulcer area – general population – grade 2 and above (grade 2 and 3) – classification method not reported[41]												
1	Randomised trial	Very serious[i]	No serious inconsistency	No serious indirectness	Serious[d]	None	-9 (SD 102.45)	34 (SD 102.45)	-	MD 43 lower (111.87 lower to 25.87 higher)	Very low	Critical
Mean percentage reduction in ulcer volume – general population – grade 2 and above (grade 3 and 4) – Lowthian classification[110]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	64 (SD 16)	26 (SD 20)	-	MD 38 higher (28.61 to 47.39 higher)	Low	Critical
Median percentage reduction in ulcer area – people in long-term care – pressure ulcer grade not reported – classification method not reported[7]												
1	Randomised trial	Very serious[j]	No serious inconsistency	No serious indirectness	Very serious[k]	None	85.7 (n=21)	100 (n=29)	-	Not pooled	Very low	Critical
Median percentage reduction in ulcer size - general population – grade 2– Shea classification[133]												
1	Randomised trial	Very serious[e]	No serious inconsistency	No serious indirectness	Very serious[k]	None	48 (n=34)	91 (n=25)	p>0.05	Not pooled	Very low	Critical
Median percentage reduction in ulcer size - general population – grade 3 – Shea classification[133]												
1	Randomised	Very	No serious	No serious	Very	None	30	(0.3)	p>0.05	Not pooled	Very low	Critical

Quality assessment							No of patients/ulcers		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Saline**	**Hydro-colloid**	**Relative (95% CI)**	**Absolute**		
	trial	serious[e]	inconsistency	indirectness	serious[k]		(n=11)	(n=17)				
Median days to healing – people in long-term care – grade 2 and 3 – Shea classification[209]												
1	Randomised trial	Very serious[c]	No serious inconsistency	No serious indirectness	Very serious[k]	None	11 (n=21)	9 (n=18)	p=0.12	Not pooled	Very low	Critical
Healing distribution function – people in long-term care – pressure ulcer grade not reported – classification method not reported[7]												
1	Randomised trial	Very serious[j]	No serious inconsistency	No serious indirectness	Very serious[l]	None	n=21	n=29	p=0.15 (favours hydrocolloid)	Not pooled	Very low	Critical
Proportion of people with pain at dressing removal – general population –grade 2 and 3– classification method not reported[41]												
1	Randomised trial	Very serious[i]	No serious inconsistency	No serious indirectness	No serious imprecision	None	0/17 (0%)	7/17 (41.2%)	OR 0.09 (0.02 to 0.45)	352 fewer per 1000 (from 172 fewer to 398 fewer)	Low	Important
							-	41.2%		353 fewer per 1000 (from 172 fewer to 398 fewer)		
Median pain score during treatment (scoring system not reported) – general population – grade 3 and 4 – Lowthian classification[110]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[k]	None	2.0 (range: 1-3) (n=15)	2.0 (range: 1-4) (n=17)	-	Not pooled	Very low	Important
Proportion of people with discomfort at dressing removal – general population – grade 2 and 3 – classification method not reported[41]												
1	Randomised trial	Very serious[i]	No serious inconsistency	No serious indirectness	No serious imprecision	None	0/17 (0%)	9/17 (52.9%)	OR 0.07 (0.02 to 0.32)	456 fewer per 1000 (from 265 fewer to 507 fewer)	Low	Important
							-	52.9%		456 fewer per 1000 (from 265		

Quality assessment							No of patients/ulcers		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Saline**	**Hydro-colloid**	**Relative (95% CI)**	**Absolute**		
										fewer to 507 fewer)		
Median comfort score during treatment (scoring system not reported) – general population – grade 3 and 4 – Lowthian classification[110]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[k]	None	3.0 (range : 2-4) (n=15)	4.0 (range: 3-4) (n=17)	-	Not pooled	Very low	Important
Proportion of people with an infection – general population – grade 2 and 3 – classification method not reported[41]												
1	Randomised trial	Very serious[i]	No serious inconsistency	No serious indirectness	No serious imprecision	None	0/17 (0%)	0/17 (0%)	Not pooled	Not pooled	Low	Important
							-	0%		Not pooled		
Median smell score during treatment (scoring system not reported) – general population – grade 3 and 4 – Lowthian classification[110]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[k]	None	2.0 (range : 1-4) (n=15)	2.0 (range: 1-3) (n=17)	-	Not pooled	Very low	Important
Proportion of people with skin irritation - general population – grade 2 and 3 – Shea classification[133]												
1	Randomised trial	Very serious[e]	No serious inconsistency	No serious indirectness	No serious imprecision	None	0/50 (0%)	9/50 (18%)	OR 0.11 (0.03 to 0.44)	156 fewer per 1000 (from 92 fewer to 173 fewer)	Very low	Important
							-	18%		156 fewer per 1000 (from 92 fewer to 173 fewer)		
Mortality (all-cause) – general population and people with a spinal cord injury – all grade (1 and above) [41,81,110,209]												
4	Randomised trials	Very serious[a,b,c,i]	No serious inconsistency	No serious indirectness	Very serious imprecision[g]	None	4/80 (5%)	2/80 (2.5%)	RR 1.79 (0.38 to 8.46)	20 more per 1000 (from 16 fewer to 186 more)	Very low	Important

Quality assessment							No of patients/ulcers		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Saline	Hydro-colloid	Relative (95% CI)	Absolute	Quality	Importance
							-	0%	-	20 more per 1000 (from 16 fewer to 186 more)		
Time to complete healing												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) Matzen (1999) did not report or reported insufficient information on sequence generation, allocation concealment and blinding. No log-transformation of data was carried out.
(b) Hollisaz (2004) only reported blinding of the outcome assessor.
(c) Xakellis (1992) did not report on sequence generation and blinding.
(d) The confidence interval crossed 1 MID point.
(e) Neill (1989) did not report on sequence generation, allocation concealment and blinding. No ITT analysis or log-transformation of data was carried out.
(f) The study used different populations and there was high heterogeneity (less than 50%) but p-value > 0.1.
(g) The confidence interval crossed both MID points.
(h) The study used different populations and there was high heterogeneity (less than 50%) but p-value > 0.1.
(i) Chang (1998) did not report on sequence generation, allocation concealment or blinding. No log-transformation of data was carried out.
(j) Alm (1989) did not report on sequence generation; allocation concealment by stratification according to Norton score; only blinding of outcome assessor; no log-transformation of data
(k) No standard deviation; unknown if sample size was sufficient
(l) Only p-value reported
(m) Matzen (1999): Lowthian classification; Xakellis (1992) and Hollisaz (2004): Shea classification
(n) Limited number of events.

Table 91: Clinical evidence profile: saline-soaked gauze versus hydrogel dressing

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Saline	Hydrogel	Relative (95% CI)	Absolute		
Proportion of people completely healed – general population – grade 2 to 4 – classification method not reported[190]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	9/14 (64.3%)	10/16 (62.5%)	RR 1.03 (0.6 to 1.77)	19 more per 1000 (from 250 fewer to 481 more)	Very low	Critical
							-	62.5%		19 more per 1000 (from 250 fewer to 481 more)		
Proportion of people worsened – general population – grade 2 to 4 – classification method not reported[190]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	1/19 (5.3%)	1/22 (4.5%)	RR 1.16 (0.08 to 17.28)	7 more per 1000 (from 42 fewer to 740 more)	Very low	Critical
							-	4.6%		7 more per 1000 (from 42 fewer to 749 more)		
Percentage healing rate – general population – grade 2 to 4 – classification method not reported[190]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[c]	None	64 (n=14)	63 (n=16)	-	Not pooled	Very low	Critical
Mean weeks to healing – general population – grade 2 to 4 – classification method not reported[190]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	5.2 (SD 2.4)	5.3 (SD 2.3)	-	MD 0.1 lower (1.79 lower to	Very low	Critical

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Saline	Hydrogel	Relative (95% CI)	Absolute	Quality	Importance
										1.59 higher)		
Mortality (all-cause) [190]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[c]	None	2/19 (10.5%)	4/22 (18.2%)	RR 0.58 (0.12 to 2.82)	76 fewer per 1000 (from 160 fewer to 331 more)	Very low	Important
								25%		76 fewer per 1000 (from 160 fewer to 331 more)		
Time to complete healing (time to event data)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Reduction in size and volume of pressure ulcer												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital												
-	-	-	-	-	-	-	-	-	-	-	-	-
Acceptability of treatment												
-	-	-	-	-	-	-	-	-	-	-	-	-
Side effects												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(c) The authors did not report on sequence generation, allocation concealment or blinding. Nno log-transformation of data was carried out.

(d) The confidence interval crossed both MID points.
(e) No standard deviation; unknown if sample size was sufficient

Table 92: Clinical evidence profile: saline-soaked gauze versus foam dressing

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Saline	Foam	Relative (95% CI)	Absolute	Quality	Importance
Proportion of people completely healed – general population – grade 2 or 3 – Enterostomal Therapy and NPUAP classification[d98,148]												
2	Randomised trials	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	None	9/30 (30%)	20/44 (45.5%)	RR 0.64 (0.34 to 1.22)	164 fewer per 1000 (from 300 fewer to 100 more)	Very low	Critical
							-	45.8%		165 fewer per 1000 (from 302 fewer to 101 more)		
Median days to 50% healing – general population – grade 2 – NPUAP classification[148]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[c]	None	28 (n=16)	28 (n=20)	-	Not pooled	Very low	Critical
Mortality (all-cause)[98,148]												
2	Randomised trials	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	None	4/30 (13.3%)	3/44 (6.8%)	RR 1.76 (0.49 to 6.34)	52 more per 1000 (from 35 fewer to 364 more)	Very low	Important
								7.5%		57 more per 1000 (from 38 fewer to 401 more)		
Time to complete healing (time to event data)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate of reduction in size and volume of pressure ulcers												

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Saline	Foam	Relative (95% CI)	Absolute	Quality	Importance
-	-	-	-	-	-	-	-	-	-	-	-	-
Reduction in size and volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital												
-	-	-	-	-	-	-	-	-	-	-	-	-
Acceptability of treatment												
-	-	-	-	-	-	-	-	-	-	-	-	-
Side effects												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) The authors did not report on sequence generation, allocation concealment or blinding.
(b) The confidence interval crossed 1 MID point.
(c) No standard deviation; unknown if sample size was sufficient.
(d) Kraft (1993): Enterostomal Therapy classification; Payne (2009): NPUAP classification.

Table 93: Clinical evidence profile: saline-soaked gauze versus polyurethane dressing

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Saline	Poly-urethane	Relative (95% CI)	Absolute	Quality	Importance
Proportion of ulcers completely healed – general population – grade 1 and 2 – Ernis and Sarmiento classification[144]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	0/10 (0%)	1/9 (11.1%)	OR 0.12 (0 to 6.14)	96 fewer per 1000 (from 111	Very low	Critical

Quality assessment							No of patients		Effect			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Saline**	**Poly-urethane**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
										fewer to 323 more)		
							-	11.1%		96 fewer per 1000 (from 111 fewer to 323 more)		
Proportion of ulcers worsened – general population – grade 1 and 2 – Ernis and Sarmiento classification[144]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	2/10 (20%)	1/9 (11.1%)	RR 1.8 (0.19 to 16.66)	89 more per 1000 (from 90 fewer to 1000 more)	Very low	Critical
							-	11.1%		89 more per 1000 (from 90 fewer to 1000 more)		
Mean percentage reduction in ulcer area – general population – grade 1 and 2 – Ernis and Sarmiento classification[144]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[c]	None	2.5 (n=10)	42.9 (n=9)	-	Not pooled	Very low	Critical
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate of reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital												

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Saline	Poly-urethane	Relative (95% CI)	Absolute	Quality	Importance
-	-	-	-	-	-	-	-	-	-	-	-	-
Acceptability of treatment												
-	-	-	-	-	-	-	-	-	-	-	-	-
Side effects												
-	-	-	-	-	-	-	-	-	-	-	-	-
Mortality (all-cause)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) The authors did not report on sequence generation, allocation concealment and blinding; no log-transformation
(b) The confidence interval crossed both MID points
(c) The authors did not report standard deviation. It was unknown if sample size was sufficient

Table 94: Clinical evidence profile: saline-soaked gauze versus dextranomer

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Saline	Dextranomer	Relative (95% CI)	Absolute	Quality	Importance
Proportion of ulcers improved – people with a spinal cord injury - grade 2 to 4 – Eltotai classification[106]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	2/15 (13.3%)	11/15 (73.3%)	RR 0.18 (0.05 to 0.68)	601 fewer per 1000 (from 235 fewer to 697 fewer)	Low	Critical
							-	73.3%		601 fewer per 1000 (from 235 fewer to 696 fewer)		
Proportion of people with adverse events – people with a spinal cord injury - grade 2 to 4 – Eltotai classification[106]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	0/15 (0%)	0/15 (0%)	Not pooled	Not pooled	Low	Important
								0%		Not pooled		
Proportion of people with pressure ulcers completely healed												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate of reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Saline	Dextranomer	Relative (95% CI)	Absolute	Quality	Importance
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital												
-	-	-	-	-	-	-	-	-	-	-	-	-
Acceptability of treatment												
-	-	-	-	-	-	-	-	-	-	-	-	-
Side effects												
-	-	-	-	-	-	-	-	-	-	-	-	-
Mortality (all-cause)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) The authors did not report on sequence generation, allocation concealment or blinding.

Table 95: Clinical evidence profile: phenytoin versus hydrocolloid dressing

Quality assessment							No of patients/ulcers		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Phenytoin	Hydrocolloid	Relative (95% CI)	Absolute	Quality	Importance
Proportion of people completely healed – people with a spinal cord injury – grade 1 and 2 pressure ulcers – NPUAP classification[81]												
1	Randomised trial	Serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	None	11/28 (39.3%)	20/28 (71.4%)	RR 0.55 (0.33 to 0.92)	321 fewer per 1000 (from 57 fewer to 479 fewer)	Low	Critical
							-	71.4%		321 fewer per 1000		

Quality assessment							No of patients/ulcers		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Phenytoin**	**Hydrocolloid**	**Relative (95% CI)**	**Absolute**		
										(from 57 fewer to 478 fewer)		
Proportion of ulcers completely healed (all sites) – people with a spinal cord injury – grade 1 and 2 pressure ulcers – NPUAP classification[81]												
1	Randomised trial	Serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	None	12/30 (40%)	23/31 (74.2%)	RR 0.54 (0.33 to 0.88)	341 fewer per 1000 (from 89 fewer to 497 fewer)	Low	Critical
							-	74.2%		341 fewer per 1000 (from 89 fewer to 497 fewer)		
Proportion of ulcers completely healed (all sites) – people with a spinal cord injury - grade 1 – NPUAP classification[81]												
1	Randomised trial	Serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	None	2/9 (22.2%)	11/13 (84.6%)	RR 0.26 (0.08 to 0.91)	626 fewer per 1000 (from 76 fewer to 778 fewer)	Low	Critical
								84.6%		626 fewer per 1000 (from 76 fewer to 778 fewer)		
Proportion of ulcers completely healed (all sites) – people with a spinal cord injury – grade 2 – NPUAP classification[81]												
1	Randomised trial	Serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	None	10/21 (47.6%)	12/18 (66.7%)	RR 0.71 (0.41 to 1.24)	193 fewer per 1000 (from 393 fewer to 160 more)	Low	Critical

Quality assessment							No of patients/ulcers		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Phenytoin**	**Hydrocolloid**	**Relative (95% CI)**	**Absolute**		
							-	66.7%		193 fewer per 1000 (from 394 fewer to 160 more)		
Proportion of ulcers completely healed (sacral) – people with a spinal cord injury – grade 1 and 2 pressure ulcers – NPUAP classification[81]												
1	Randomised trial	Serious[a]	No serious inconsistency	No serious indirectness	Very serious[c]	None	4/8 (50%)	4/7 (57.1%)	RR 0.88 (0.34 to 2.25)	69 fewer per 1000 (from 377 fewer to 714 more)	Very low	Critical
							-	57.1%		69 fewer per 1000 (from 377 fewer to 714 more)		
Proportion of ulcers improved – people with a spinal cord injury – grade 1 and 2 pressure ulcers – NPUAP classification[81]												
1	Randomised trial	Serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	None	16/30 (53.3%)	27/31 (87.1%)	RR 0.61 (0.43 to 0.88)	340 fewer per 1000 (from 105 fewer to 496 fewer)	Low	Critical
							-	87.1%		340 fewer per 1000 (from 105 fewer to 496 fewer)		
Proportion of ulcers worsened– people with a spinal cord injury – grade 1 and 2 pressure ulcers– NPUAP classification[81]												
1	Randomised trial	Serious[a]	No serious inconsistency	No serious indirectness	Very serious[c]	None	2/30 (6.7%)	2/31 (6.5%)	RR 1.03 (0.16 to 6.87)	2 more per 1000 (from 54 fewer to 379 more)	Very low	Critical

Quality assessment							No of patients/ulcers		Effect			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Phenytoin**	**Hydrocolloid**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
							-	6.5%		2 more per 1000 (from 55 fewer to 382 more)		
Mean days to healing – – people in a nursing home – grade 2 pressure ulcers - (AHCPR classification)[155]												
1	Randomised trial	Very serious[d]	No serious inconsistency	No serious indirectness	Serious[b]	None	35.3 (SD 14.3)	51.8 (SD 19.6)	-	MD 16.5 lower (29.38 to 3.62 lower)	Very low	Critical
Proportion of people with pain – people in a nursing home – grade 2 pressure ulcers - AHCPR classification[155]												
1	Randomised trial	Very serious[d]	No serious inconsistency	No serious indirectness	Very serious[e]	None	-	-	Minimal pain was reported in both groups	Not pooled	Very low	Important
							-	0%		Not pooled		
Proportion of people with treatment related adverse events – people in a nursing home - grade 2 pressure ulcers -AHCPR classification[155]												
1	Randomised trial	Very serious[d]	No serious inconsistency	No serious indirectness	No serious imprecision	None	0/15 (0%)	0/13 (0%)	Not pooled	Not pooled	Low	Important
							-	0%		Not pooled		
Mortality (all-cause)[81,155]												
2	Randomised trials	Serious[a]	No serious inconsistency	No serious indirectness	Very serious[c]	None	2/46 (4.3%)	2/44 (4.5%)	RR 0.89 (0.14 to 5.6)	5 fewer per 1000 (from 39 fewer to 209 more)	Very low	Important
							-	6.3%		7 fewer per 1000 (from 54 fewer to 290 more)		
Time to complete healing of pressure ulcers (time to event data)												
-	-	-	-	-	-	-	-	-	-	-	-	-

Quality assessment							No of patients/ulcers		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Phenytoin	Hydrocolloid	Relative (95% CI)	Absolute	Quality	Importance
Rate of reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital												
-	-	-	-	-	-	-	-	-	-	-	-	-
Acceptability of treatment												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) No blinding of participants or nurses was reported.
(b) The confidence interval crossed 1 MID point.
(c) The confidence interval crossed both MID points.
(d) The authors did not report on allocation concealment, sequence generation or blinding. There was no ITT analysis.
(e) No figures reported, no p-value.

Table 96: Clinical evidence profile: phenytoin versus triple antibiotics

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Phenytoin	Triple antibiotics	Relative (95% CI)	Absolute	Quality	Importance
Mean days to healing – people in a nursing home – grade 2 pressure ulcers - AHCPR classification[155]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	35.3 (SD 14.3)	53.8 (SD 8.5)	-	MD 18.5 lower (27.31 to 9.69 lower)	Low	Critical
Proportion of people with pain – people in a nursing home – grade 2 pressure ulcers - AHCPR classification[155]												
1	Randomised	Very	No serious	No serious	Very serious[b]	None	-	-	Minimal	Not pooled	Very	Important

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Phenytoin	Triple antibiotics	Relative (95% CI)	Absolute		
	trial	serious[a]	inconsistency	indirectness			-	0%	pain was reported in both groups	Not pooled	low	
Proportion of people with treatment related adverse events – people in a nursing home – grade 2 pressure ulcers - AHCPR classification[155]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	0/15 (0%)	0/11 (0%)	Not pooled	Not pooled	Low	Important
								0%		Not pooled		
Mortality (all-cause)[155]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	2/16 (12.5%)	1/13 (7.7%)	RR 1.63 (0.17 to 15.99)	48 more per 1000 (from 64 fewer to 1000 more)	Very low	Important
							-	7.7%	-	48 more per 1000 (from 64 fewer to 1000 more)		
Proportion of people with pressure ulcers completely healed												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time to complete healing (time to event data)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate of reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital												
-	-	-	-	-	-	-	-	-	-	-	-	-
Acceptability of treatment												

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Phenytoin	Triple antibiotics	Relative (95% CI)	Absolute	Quality	Importance
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) The authors did not report on allocation concealment, sequence generation or blinding. There was no ITT analysis
(b) No figures reported; no p-value

Table 97: Clinical evidence profile: aloe vera, silver chloride and decyl glucoside versus isotonic saline

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Aloe vera	Saline	Relative (95% CI)	Absolute	Quality	Importance
Mean percentage reduction in PSST – elderly adults – grade 2 to 4 – NPUAP classification [23]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	22.7 (SD 31.3) (n=?)	20.5 (SD 24.1) (n=?)	-	Not pooled	Very low	Critical
Proportion of people with pressure ulcers completely healed												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate of reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Aloe vera	Saline	Relative (95% CI)	Absolute	Quality	Importance
Time in hospital												
-	-	-	-	-	-	-	-	-	-	-	-	-
Acceptability of treatment												
-	-	-	-	-	-	-	-	-	-	-	-	-
Side effects												
-	-	-	-	-	-	-	-	-	-	-	-	-
Mortality (all-cause)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) The authors did not report on allocation concealment, sequence generation or blinding. There was no ITT analysis
(b) No figures reported; no p-value

Table 98: Clinical evidence profile: dialysate versus placebo

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Dialysate	Placebo	Relative (95% CI)	Absolute	Quality	Importance
Mean ml reduction in ulcer area - people with a spinal cord injury – pressure ulcer grade not reported – classification method not reported[95]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	None	13.4 (SD 10.02)	6.57 (SD 4.88)	-	MD 6.83 higher (3.54 lower to 17.2 higher)	Very low	Critical
Mean percentage reduction in ulcer area at day 10 - people with a spinal cord injury – pressure ulcer grade not reported – classification method not reported[95]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	None	39 (n=5)	28 (n=3)	-	Not pooled	Very low	Critical
Mean percentage reduction in ulcer area at day 20 - - people with a spinal cord injury – pressure ulcer grade not reported – classification method not reported[95]												

Quality assessment							No of patients		Effect			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Dialysate**	**Placebo**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	None	80 (n=5)	59 (n=3)	-	Not pooled	Very low	Critical
Mean healing half-time (days) people with a spinal cord injury – pressure ulcer grade not reported – classification method not reported[95]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	None	8.52 (2.36)	24 (SD 18.43)	-	MD 15.48 lower (36.44 lower to 5.48 higher)	Very low	Critical
Proportion of people **with treatment related adverse events people with a spinal cord injury – pressure ulcer grade not reported – classification method not reported[95]**												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	0/5 (0%)	0/3 (0%)	Not pooled	Not pooled	Low	Important
								0%		Not pooled		
Proportion of people with pressure ulcers completely healed												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time to complete healing of pressure ulcers												
Rate of reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital												
-	-	-	-	-	-	-	-	-	-	-	-	-
Acceptability of treatment												
-	-	-	-	-	-	-	-	-	-	-	-	-
Mortality (all-cause)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Dialysate	Placebo	Relative (95% CI)	Absolute	Quality	Importance
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) The authors did not report on allocation concealment and sequence generation; double-blinded, but no further information. There was no ITT analysis or log-transformation of data.
(b) Confidence interval crossed 1 MID point

Table 99: Clinical evidence profile: petrolatum ointment versus petrolatum (base component)

Quality assessment							No of ulcers		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Topical ointment with petrolatum	Petrolatum (base component)	Relative (95% CI)	Absolute	Quality	Importance
Proportion of ulcers completely healed – elderly adult – grade I and 2 – AHCPR classification[100]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	5/10 (50%)	2/9 (22.2%)	RR 2.25 (0.57 to 8.86)	358 more per 1000 (from 29 fewer to 751 more)	Very low	Critical
							-	16.7%		269 more per 1000 (from 22 fewer to 564 more)		
Proportion of ulcers completely healed - grade 2– elderly adults – AHCPR classification[100]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	1/5 (20%)	0/3 (0%)	OR 4.95 (0.09 to 283.86)	200 more (from 270 fewer to 670	Very low	Critical

Quality assessment							No of ulcers		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Topical ointment with petrolatum	Petrolatum (base component)	Relative (95% CI)	Absolute	Quality	Importance
										more)		
							-	0%		200 more (from 270 fewer to 670 more)		
Proportion of ulcers improved – elderly adults – grade I and 2 – AHCPR classification[100]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[c]	None	4/10 (40%)	0/9 (0%)	OR 9.78 (1.14 to 83.93)	400 more (from 80 more to 720 more)	Very low	Critical
							-	0%		400 more (from 80 more to 720 more)		
Proportion of ulcers improved - Grade 2– elderly adults – AHCPR classification[100]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	3/5 (60%)	0/3 (0%)	OR 9.39 (0.59 to 149.25)	600 more (from 90 fewer to 1110 more)	Very low	Critical
							-	0%		600 more (from 90 fewer to 1110 more)		

Quality assessment							No of ulcers		Effect			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Topical ointment with petrolatum**	**Petrolatum (base component)**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
Proportion of ulcers worsened - grade I and 2 – elderly adults – AHCPR classification[100]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Vno serious	None	0/5 (0%)	3/6 (50%)	OR 0.05 (0.01 to 0.35)	670 fewer (from 990 fewer to 350 fewer)	Low	Critical
							-	50%		670 fewer (from 990 fewer to 350 fewer)		
Proportion of ulcers worsened - grade 2 – elderly adults– AHCPR classification[100]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	0/5 (0%)	3/3 (100%)	OR 0.02 (0 to 0.38)	1000 fewer per 1000 (from 1390 fewer to 610 fewer)	Low	Critical
							-	100%		1000 fewer per 1000 (from 1390 fewer to		

Quality assessment							No of ulcers		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Topical ointment with petrolatum	Petrolatum (base component)	Relative (95% CI)	Absolute	Quality	Importance
										610 fewer)		
Mortality (all-cause) [100]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	0/10 (0%)	0/9 (0%) 0%	Not pooled -	Not pooled Not pooled	Low	Important
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate of reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital												
-	-	-	-	-	-	-	-	-	-	-	-	-
Acceptability of treatment												
-	-	-	-	-	-	-	-	-	-	-	-	-
Side effects												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) There was insufficient information on sequence generation and there was no report on allocation concealment or blinding of outcome assessors.
(b) The confidence interval crossed both MID points.
(c) The confidence interval crossed 1 MID point. Very wide confidence interval.

Table 100: Clinical evidence profile: zinc oxide versus streptokinase-streptodornase[d]

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Zinc oxide	Streptokinase-streptodornase	Relative (95% CI)	Absolute		
Median percentage reduction in ulcer area – elderly adults – necrotic pressure ulcer - classification method not reported[4]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	24 (n=14)	-18.7 (n=14)	-	Not pooled	Very low	Critical
Proportion of people with an infection – elderly adults – necrotic pressure ulcer - classification method not reported[4]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[c]	None	0/14 (0%)	1/14 (7.1%)	OR 0.14 (0 to 6.82)	61 fewer per 1000 (from 71 fewer to 273 more)	Very low	Critical
							-	7.1%		60 fewer per 1000 (from 71 fewer to 272 more)		
Proportion of people with skin reaction – elderly adults – necrotic pressure ulcer - classification method not reported[4]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[c]	None	0/14 (0%)	1/14 (7.1%)	OR 0.14 (0 to 6.82)	61 fewer per 1000 (from 71 fewer to 273 more)	Very low	Important
							-	7.1%		60 fewer per 1000 (from 71 fewer to 272 more)		
Mortality (all-cause) [4]												

Quality assessment							No of patients		Effect			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Zinc oxide**	**Streptokinase-streptodornase**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious	None	0/14 (0%)	0/14 (0%)	Not pooled	Not pooled	Low	Important
							-	0%	-	Not pooled		
Proportion of people with pressure ulcers completely healed												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate of reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital												
-	-	-	-	-	-	-	-	-	-	-	-	-
Acceptability of treatment												
-	-	-	-	-	-	-	-	-	-	-	-	-
Side effects												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) Sequence generation was carried out by matched pairs. The authors did not report on allocation concealment and no blinding of participant or nurses. There was no log-transformation of data.

(b) No standard deviation reported. There was a small sample size.

(c) The confidence interval crossed both MID points.

(d) This comparison was also included in debridement review, see Chapter X.

Table 101: Clinical evidence profile: oxyquinoline versus vitamin A&D treatment (cream)

Quality assessment							No of ulcers		Effect			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Oxyquinoline**	**A&D treatment**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
Proportion of ulcers completely healed (all grades) – people in palliative care – grade 1 and 2 pressure ulcers – NPUAP classification[68]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	None	43/86 (50%)	21/51 (41.2%)	RR 1.21 (0.82 to 1.79)	86 more per 1000 (from 74 fewer to 325 more)	Very low	Critical
							-	41.2%		87 more per 1000 (from 74 fewer to 325 more)		
Proportion of ulcers completely healed– people in palliative care – grade 2 pressure ulcers – NPUAP classification[68]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	None	20/45 (44.4%)	5/23 (21.7%)	RR 2.04 (0.88 to 4.74)	226 more per 1000 (from 26 fewer to 813 more)	Very low	Critical
							-	21.7%		226 more per 1000 (from 26 fewer to 812 more)		
Proportion of ulcers improved after 15 days– people in palliative care – grade 1 pressure ulcers – NPUAP classification[68]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	None	15/41 (36.6%)	6/28 (21.4%)	RR 1.71 (0.76 to	152 more per 1000	Very low	Critical

Quality assessment							No of ulcers		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Oxyquinoline	A&D treatment	Relative (95% CI)	Absolute	Quality	Importance
									3.86)	(from 51 fewer to 613 more)		
							-	21.4%		152 more per 1000 (from 51 fewer to 612 more)		
Proportion of ulcers improved after 22 days– people in palliative care – grade 2 pressure ulcers – NPUAP classification[68]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[c]	None	19/45 (42.2%)	8/23 (34.8%)	RR 1.21 (0.63 to 2.34)	73 more per 1000 (from 129 fewer to 466 more)	Very low	Critical
							-	34.8%		73 more per 1000 (from 129 fewer to 466 more)		
Proportion of ulcers not changed on day 15– people in palliative care – grade 1 pressure ulcers – NPUAP classification[68]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[c]	None	4/41 (9.8%)	4/28 (14.3%)	RR 0.68 (0.19 to 2.51)	46 fewer per 1000 (from 116 fewer to 216 more)	Very low	Critical
							-	14.3%		46 fewer		

Quality assessment							No of ulcers		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Oxyquinoline	A&D treatment	Relative (95% CI)	Absolute		
										per 1000 (from 116 fewer to 216 more)		
Proportion of ulcers not changed on day 22– people in palliative care – grade 2 pressure ulcers – NPUAP classification[68]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	None	5/45 (11.1%)	7/23 (30.4%)	RR 0.37 (0.13 to 1.02)	192 fewer per 1000 (from 265 fewer to 6 more)	Very low	Critical
								30.4%		192 fewer per 1000 (from 264 fewer to 6 more)		
Proportion of ulcers worsened on day 15– people in palliative care – grade 1 pressure ulcers – NPUAP classification[68]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[c]	None	0/41 (0%)	2/28 (7.1%)	OR 0.08 (0 to 1.41)	65 fewer per 1000 (from 71 fewer to 26 more)	Very low	Critical
							-	7.1%		65 fewer per 1000 (from 71 fewer to 26 more)		
Proportion of ulcers worsened on day 22– people in palliative care – grade 2 pressure ulcers – NPUAP classification[68]												

Quality assessment							No of ulcers		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Oxyquinoline**	**A&D treatment**	**Relative (95% CI)**	**Absolute**		
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[c]	None	1/45 (2.2%)	3/23 (13%)	RR 0.17 (0.02 to 1.55)	108 fewer per 1000 (from 128 fewer to 72 more)	Very low	Critical
							-	13%		108 fewer per 1000 (from 127 fewer to 71 more)		
Mean days to complete healing– people in palliative care – grade 1 and 2 pressure ulcers – NPUAP classification[68]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	None	7.23 (SD 4.15)	8.62 (SD 5.16)	-	MD 1.39 lower (3.06 lower to 0.28 higher)	Very low	Critical
Mean days to complete healing– people in palliative care – grade 1 pressure ulcers – NPUAP classification[68]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	None	6.75 (SD 3.9)	7.25 (SD 4.8)	-	MD 0.5 lower (2.64 lower to 1.64 higher)	Very low	Critical
Mean days to complete healing– people in palliative care – grade 2 pressure ulcers – NPUAP classification[68]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	7.8 (SD 4.47)	13 (SD 3.94)	-	MD 5.2 lower (7.27 lower to 3.13	Low	Critical

Quality assessment							No of ulcers		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Oxyquinoline	A&D treatment	Relative (95% CI)	Absolute	Quality	Importance
										lower)		
Time to complete healing (time to event data)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate of reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital												
-	-	-	-	-	-	-	-	-	-	-	-	-
Acceptability of treatment												
-	-	-	-	-	-	-	-	-	-	-	-	-
Side effects												
-	-	-	-	-	-	-	-	-	-	-	-	-
Mortality (all-cause)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) The authors did not report on allocation concealment. Only blinding of outcome assessor was conducted.
(b) The confidence interval crossed 1 MID point.
(c) The confidence interval crossed both MID points.

Table 102: Clinical evidence profile: ethoxy-diaminoacridine plus nitrofuazone versus honey

Quality assessment							No of patients/ulcers		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Ethoxy-diaminoacridine plus nitrofuazone	Honey	Relative (95% CI)	Absolute	Quality	Importance
Proportion of ulcers completely healed – general population – grade 2 and 3 pressure ulcers – AHCPR classification[74]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	0/25 (0%)	5/25 (33.3%)	OR 0.11 (0.02 to 0.71)	173 fewer per 1000 (from 49 fewer to 195 fewer)	Low	Critical
							-	33.3%		272 fewer per 1000 (from 28 fewer to 323 fewer)		
Mean percentage reduction in PUSH score – general population – grade 2 and 3 pressure ulcers – AHCPR classification[74]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	12.9 (SD 28.92)	56.3 (SD 28.92)	-	MD 43.4 lower (59.43 to 27.37 lower)	Low	Critical
Mean percentage reduction in ulcer size – general population – grade 2 and 3 pressure ulcers – AHCPR classification[74]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	13 (SD 29.39)	56 (SD 29.39)	-	MD 43 lower (59.29 to 26.71 lower)	Low	Critical
Proportion of people **with treatment related adverse events – general population grade 2 and 3 pressure ulcers – AHCPR classification[74]**												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	0/11 (0%)	0/15 (0%)	Not pooled	Not pooled	Low	Important
							-	0%		Not pooled		
Mortality (all-cause) [74]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	1/12 (8.3%)	0/15 (0%)	OR 9.49 (0.18 to	80 more per 1000 (from	Low	Important

Quality assessment							No of patients/ulcers		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Ethoxy-diaminoacridine plus nitrofuazone	Honey	Relative (95% CI)	Absolute	Quality	Importance
									489.97)	110 fewer to 280 more)		
							-	0%		80 more per 1000 (from 110 fewer to 280 more)		
Time to complete healing												
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate of reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital												
-	-	-	-	-	-	-	-	-	-	-	-	-
Acceptability of treatment												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) The authors did not report on allocation concealment, sequence generation or blinding. There was no ITT analysis or log-transformation of data.

Table 103: Clinical evidence profile: povidone-iodine versus hydrocolloid

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Povidone-iodine	Hydrocolloid	Relative (95% CI)	Absolute		
Proportion of people completely healed – general population – grade 1 and 2 pressure ulcers – NPUAP classification[93]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	14/18 (77.8%)	21/26 (80.8%)	RR 0.96 (0.71 to 1.31)	32 fewer per 1000 (from 234 fewer to 250 more)	Very low	Critical
							-	80.8%		32 fewer per 1000 (from 234 fewer to 250 more)		
Percentage rate of healing – general population – grade 1 and 2 pressure ulcers – NPUAP classification[93]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[c]	None	77.8 (n=18)	80.8 (n=26)	-	Not pooled	Very low	Critical
Mean speed of healing (mm²/day) – general population – grade 1 and 2 pressure ulcers – NPUAP classification[93]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[d]	None	7.9 (SD 4.7)	9.1 (SD 5.4)	-	MD 1.2 lower (4.2 lower to 1.8 higher)	Very low	Critical
Proportion of people with hypergranulation – general population – grade 1 and 2 pressure ulcers – NPUAP classification[93]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	0/18 (0%)	3/26 (11.5%)	OR 0.17 (0.02 to 1.79)	94 fewer per 1000 (from 113 fewer to 74 more)	Very low	Important
								11.5%		93 fewer per 1000 (from 112 fewer to 74 more)		
Mortality (all-cause) [93]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious	None	0/18 (0%)	0/26 (0%)	Not pooled	Not pooled	Low	Important

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Povidone-iodine	Hydrocolloid	Relative (95% CI)	Absolute	Quality	Importance
								0%		Not pooled		
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital												
-	-	-	-	-	-	-	-	-	-	-	-	-
Acceptability of treatment												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) The authors did not report on allocation concealment, sequence generation or blinding. There was no log-transformation of data.
(b) The confidence interval crossed both MID points.
(c) No standard deviation reported; unclear if sample size was sufficient
(d) The confidence interval crossed 1 MID point.

Table 104: Clinical evidence profile: povidone-iodine versus hydrogel dressing

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Povidone-iodine	Hydrogel	Relative (95% CI)	Absolute	Quality	Importance
Mean cm²/day to healing – people with a spinal cord injury – grade 1 to 3 – NPUAP classification[87]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	None	0.09 (SD 0.05)	0.12 (SD 0.16)	-	MD 0.03 lower (0.1 lower to	Very low	Critical

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Povidone-iodine	Hydrogel	Relative (95% CI)	Absolute	Quality	Importance
										0.04 higher)		
Proportion of people with pressure ulcers completely healed												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital												
-	-	-	-	-	-	-	-	-	-	-	-	-
Acceptability of treatment												
-	-	-	-	-	-	-	-	-	-	-	-	-
Side effects												
-	-	-	-	-	-	-	-	-	-	-	-	-
Mortality (all-cause)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) The authors did not report on allocation concealment, sequence generation or blinding. There was no ITT analysis or log-transformation of data.
(b) Confidence interval crossed 1 MID point

Table 105: Clinical evidence profile: cadexomer iodine versus standard treatment

Quality assessment							No of ulcers		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Cadexomer iodine	Standard treatment	Relative (95% CI)	Absolute	Quality	Importance
Proportion of ulcers reduced with 50% - general population – superficial or deep pressure ulcer – classification method not reported[119]												
1	Randomised trials	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	8/16 (50%)	1/18 (5.6%)	RR 9 (1.26 to 64.33)	444 more per 1000 (from 14 more to 1000 more)	Low	Critical
							-	5.6%		448 more per 1000 (from 15 more to 1000 more)		
Mean cm² reduction in ulcer area - general population – superficial or deep pressure ulcer – classification method not reported[119]												
1	Randomised trials	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	2.9 (SD 5.2)	2.5 (SD 4.67)	-	MD 0.4 higher (2.94 lower to 3.74 higher)	Low	Critical
Mean percentage reduction in ulcer area - general population – superficial or deep pressure ulcer – classification method not reported[119]												
1	Randomised trials	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	30.9 (SD 46)	19.6 (SD 83.16)	-	MD 11.3 higher (33.24 lower to 55.84 higher)	Low	Critical
Mortality (all-cause) [119]												
1	Randomised	Very	No serious	No serious	No serious	None	0/19	0/19	Not	Not	Low	Important

Quality assessment							No of ulcers		Effect			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Cadexomer iodine**	**Standard treatment**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
	trials	serious[a]	inconsistency	indirectness	imprecision		(0%)	(0%)	pooled	pooled		
							-	0%		Not pooled		
Proportion of people with pressure ulcers completely healed												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate of reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital												
-	-	-	-	-	-	-	-	-	-	-	-	-
Acceptability of treatment												
-	-	-	-	-	-	-	-	-	-	-	-	-
Side effects												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) The authors did not report on allocation concealment ord blinding. No ITT analysis or log-transformation of data was carried out.

Table 106: Clinical evidence profile: silver sulfazidine cream versus silver dressing

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Silver sulfazidine	Silver dressing	Relative (95% CI)	Absolute	Quality	Importance
Mean percentage reduction in ulcer area – in- and outpatients – grade 4 – NPUAP classification[43]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	25.06 (SD 56.13)	36.95 (SD 56.13)	-	MD 11.89 lower (46.68 lower to 22.9 higher)	Very low	Critical
Percentage reduction in PUSH score – in- and outpatients – grade 4 – NPUAP classification[43]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[c]	None	34.51 (n=20)	28.15 (SD 20)	p=0.473	Not pooled	Very low	Critical
Proportion of people with adverse events – in- and outpatients – grade 4 – NPUAP classification[43]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	0/20 (0%)	0/20 (0%)	Not pooled	Not pooled	Low	Important
							-	0%		Not pooled		
Mortality (all-cause) [43]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	0/17 (0%)	0/17 (0%)	Not pooled	Not pooled	Low	Important
							-	0%		Not pooled		
Proportion of people with pressure ulcers completely healed												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate of reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Silver sulfazidine	Silver dressing	Relative (95% CI)	Absolute	Quality	Importance
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital												
-	-	-	-	-	-	-	-	-	-	-	-	-
Acceptability of treatment												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) The authors did not report on sequence generation, allocation concealment or blinding. There was no log-transformation of data.
(b) The confidence interval crossed both MID points.
(c) No standard deviation; unknown if sample size was sufficient

Table 107: Clinical evidence profile: resin salve versus hydrofibre

Quality assessment							No of patients/ulcers		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Resin salve	Hydrofibre	Relative (95% CI)	Absolute	Quality	Importance
Proportion of people completely healed – general population – grade 2 to 4 pressure ulcers – NPUAP classification[176]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	None	12/13 (92.3%)	4/9 (44.4%)	RR 2.08 (0.98 to 4.38)	480 more per 1000 (from 9 fewer to 1000 more)	Very low	Critical
								44.4%		480 more per 1000 (from 9 fewer to 1000 more)		

Quality assessment							No of patients/ulcers		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Resin salve	Hydrofibre	Relative (95% CI)	Absolute		
Proportion of ulcers completely healed – general population – grade 2 to 4 pressure ulcers – NPUAP classification[176]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	None	17/18 (94.4%)	4/11 (36.4%)	RR 2.6 (1.18 to 5.72)	582 more per 1000 (from 65 more to 1000 more)	Very low	Critical
								36.4%		582 more per 1000 (from 66 more to 1000 more)		
Proportion of ulcers improved – general population – grade 2 to 4 pressure ulcers – NPUAP classification[176]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	None	18/18 (100%)	10/11 (90.9%)	RR 1.11 (0.89 to 1.4)	100 more per 1000 (from 100 fewer to 364 more)	Very low	Critical
								90.9%		100 more per 1000 (from 100 fewer to 364 more)		
Proportion of ulcers worsened – general population – grade 2 to 4 pressure ulcers – NPUAP classification[176]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[c]	None	0/18 (0%)	1/11 (9.1%)	OR 0.07 (0.00 to	84 fewer per 1000 (from 91	Very low	Critical

Quality assessment							No of patients/ulcers		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Resin salve	Hydrofibre	Relative (95% CI)	Absolute		
									4.07)	fewer to 198 more)		
								9.1%		84 fewer per 1000 (from 91 fewer to 198 more)		
Mean percentage reduction in ulcer width – general population – grade 2 to 4 pressure ulcers – NPUAP classification[176]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[d]	None	93.75 (n=18)	57.14 (n=11)	-	Not pooled	Very low	Critical
Mean percentage reduction in ulcer depth – general population – grade 2 to 4 pressure ulcers – NPUAP classification[176]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[d]	None	88.46 (n=18)	-1.89 (n=11)	-	Not pooled	Very low	Critical
Speed of healing (days) – general population – grade 2 to 4 pressure ulcers – NPUAP classification[176]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[e]	None	(n=18)	(n=11)	p=0.013 (log-rank-test) (favour resin salve)	Not pooled	Very low	Critical
Proportion of people with allergic skin reactions – general population – grade 2 to 4 pressure ulcers – NPUAP classification[176]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[c]	None	1/21 (4.8%)	0/16 (0%)	OR 5.82 (0.11 to 304.33)	50 more (from 80 fewer to 180 more)	Very low	Important
								0%		50 more		

Quality assessment							No of patients/ulcers		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Resin salve	Hydrofibre	Relative (95% CI)	Absolute		
										(from 80 fewer to 180 more)		
Mortality (all-cause) [176]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[c]	None	3/21 (14.3%)	4/16 (25%)	RR 0.57 (0.15 to 2.2)	108 fewer per 1000 (from 213 fewer to 300 more)	Very low	Important
								25%		108 fewer per 1000 (from 213 fewer to 300 more)		
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital												
-	-	-	-	-	-	-	-	-	-	-	-	-
Acceptability of treatment												
-	-	-	-	-	-	-	-	-	-	-	-	-
Side effects												

Quality assessment							No of patients/ulcers		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Resin salve	Hydrofibre	Relative (95% CI)	Absolute	Quality	Importance
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) The authors did not report blinding. There was no ITT analysis or log-transformation of data.
(b) Confidence interval crossed 1 MID point.
(c) Confidence interval crossed both MID points.
(d) No standard deviation reported; small sample size.
(e) Only p-value reported.

Table 108: Clinical evidence profile: antibiotic ointment versus foam dressing

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Antibiotic	Foam dressing	Relative (95% CI)	Absolute	Quality	Importance
Proportion of people completely healed – institutionalised elderly adults – grade 2 pressure ulcers – NPUAP classification[211]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	15/23 (65.2%)	18/21 (85.7%)	RR 0.76 (0.54 to 1.08)	206 fewer per 1000 (from 394 fewer to 69 more)	Very low	Critical
							-	85.7%		206 fewer per 1000 (from 394 fewer to 69 more)		
Mean PUSH score at end of treatment – institutionalised elderly adults – grade 2 pressure ulcers – NPUAP classification[211]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[c]	None	1.61 (n=19)	3.24 (n=23)	p>0.05	Not pooled	Very low	Critical
Time to complete healing of pressure ulcers												

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Antibiotic	Foam dressing	Relative (95% CI)	Absolute	Quality	Importance
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate of reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital												
-	-	-	-	-	-	-	-	-	-	-	-	-
Acceptability of treatment												
-	-	-	-	-	-	-	-	-	-	-	-	-
Side effects												
-	-	-	-	-	-	-	-	-	-	-	-	-
Mortality (all-cause)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) The authors did not report on sequence generation, allocation concealment or blinding.
(b) Confidence interval crossed 1 MID point.
(c) No standard deviation; unknown if sample size was sufficient.

Table 109: Clinical evidence profile: insulin versus standard treatment

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Insulin	Placebo	Relative (95% CI)	Absolute	Quality	Importance
Mean rate of healing – people in a nursing home – grade not reported – pressure ulcer definition was reported[c200]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	n=6	n=8	p=0.05 (favour insulin group)	Not pooled	Very low	Critical
Mortality (all-cause) [200]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious	None	0/6 (0%)	0/6 (0%)	Not pooled	Not pooled	Low	Important
								0%		Not pooled		
Proportion of people with pressure ulcers completely healed												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time to complete healing												
-	-	-	-	-	-	-	-	-	-	-	-	-
Reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital												
-	-	-	-	-	-	-	-	-	-	-	-	-
Acceptability of treatment												
-	-	-	-	-	-	-	-	-	-	-	-	-
Side effects												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) The authors did not report on allocation concealment and blinding.
(b) Only p-value reported.
(c) Pressure ulcers were defined as a break in skin continuity as evidenced by epidermal or dermal injury involving erythema, pallor, cyanosis, and superficial erosion.

Table 110: Clinical evidence profile: different growth factors versus placebo

Quality assessment							No of patients		Effect			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Growth factors**	**Placebo**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
Proportion of people completely healed – general population and denervated adults – grade 2 and above – NPUAP and Yarkony classification[i79,101,128,147,153,156,159]												
6	Randomised trials	Very serious[a]	Very serious[b]	No serious indirectness	Very serious[d]	None	54/222 (24.3%)	12/94 (12.8%)	RR 2.33 (0.54 to 10.02)	170 more per 1000 (from 59 more to 1000 more)	Very low	Critical
							-	0%		170 more per 1000 (from 59 more to 1000 more)		
Proportion of people completely healed - TGF-β3j versus placebo – inpatients – grade 3 and 4 – NPUAP classification[79]												
1	Randomised trial	Very serious[c]	No serious inconsistency	No serious indirectness	Very serious[d]	None	1/9 (11.1%)	0/5 (0%)	OR 4.74 (0.08 to 283.15)	200 fewer per 1000 (from 200 fewer to 420 more)	Very low	Critical
							-	0%		200 fewer per 1000 (from 200		

Quality assessment							No of patients		Effect			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Growth factors**	**Placebo**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
										fewer to 420 more)		
Proportion of people completely healed (foot ulcers) - mNGF j versus placebo – people in a nursing home– grade 2 and above - Yarkony classification[101]												
1	Randomised trial	Serious[e]	No serious inconsistency	No serious indirectness	No serious imprecision	None	8/18 (44.4%)	1/18 (5.6%)	RR 8.00 (1.11 to 57.57)	389 more per 1000 (from 6 more to 1000 more)	Moderate	Critical
							-	5.6%		392 more per 1000 (from 6 more to 1000 more)		
Proportion of people completely healed - rPDGF-BB j versus placebo – general population and denervated people – grade 3 and 4 – NPUAP classification[i128,153,159]												
3	Randomised trials	Very serious[f]	No serious inconsistency	No serious indirectness	Very serious[d]	None	18/136 (13.2%)	1/52 (1.9%)	RR 2.55 (0.56 to 11.65)	30 more per 1000 (from 8 more to 205 more)	Very low	Critical
								0%		30 more per 1000 (from 8 more to 205 more)		
Proportion of people completely healed - bFGF or GM-CSF j versus placebo – inpatients – grade 3 and 4 – classification system not reported[147]												
1	Randomised	Very	No serious	No serious	Very	None	27/41	10/13	RR 0.86 (0.59 to	108 fewer	Very low	Critical

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Growth factors	Placebo	Relative (95% CI)	Absolute		
	trial	serious[g]	inconsistency	indirectness	serious[d]		(65.9%)	(76.9%)	1.24)	per 1000 (from 315 fewer to 185 more)		
							-	76.9%		108 fewer per 1000 (from 315 fewer to 185 more)		
Proportion of people completely healed - rIL-1β j versus placebo – denervated people – grade 3 and 4 – classification system not reported[156]												
1	Randomised trial	Very serious[h]	No serious inconsistency	No serious indirectness	No serious imprecision	None	0/18 (0%)	0/6 (0%)	not pooled	not pooled	Low	Critical
							-	0%		not pooled		
Mortality (all-cause)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate of reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Growth factors	Placebo	Relative (95% CI)	Absolute	Quality	Importance
Time in hospital												
-	-	-	-	-	-	-	-	-	-	-	-	-
Acceptability of treatment												
-	-	-	-	-	-	-	-	-	-	-	-	-
Side effects												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) Hirshberg (2003): no report on sequence generation and allocation concealment and report of blinding, but no further information; Landi (2003): allocation according to age, group, sex and ulcer area and blinding of nurses and outcome assessor, but no blinding of participants; Mustoe (1994), Payne (2001) and Robson (1994): no report on sequence generation, allocation concealment and report of double blinding, but no further information; Rees (1999): no report on sequence generation, allocation concealment and blinding; Robson (1992b): no report on sequence generation, unequal allocation and only blinding of outcome assessor

(b) Heterogeneity: p-value < 0.1 and I^2 > 50%

(c) Hirshberg (2003): no report on sequence generation and allocation concealment and report of blinding, but no further information

(d) Confidence interval crossed both MID points

(e) Landi (2003): allocation according to age, group, sex and ulcer area and blinding of nurses and outcome assessor, but no blinding of participant

(f) No explanation was provided

(g) Payne (2001): no report on sequence generation, allocation concealment and report of double blinding, but no further information

(h) Robson (1994): no report on sequence generation, allocation concealment and report of double blinding, but no further information

(i) Hirshberg (2003) and Rees (1999): NPUAP classification; Landi (2003): Yarkony classification; Mustoe (1994), Robson (1992b and 1994), and Payne (2001): classification system not reported

(j) TGF-µ3: topical growth factor; mNGF: S murine nerve growth factor; rPDGF-BB: recombinant platelet-derived growth factor –BB; bFGF: basic fibroblast growth factor; GM-CSF: granulocyte-macrophage/colony-stimulating factor; rIL-1 interleukin

Table 111: Clinical evidence profile: topical growth factor – beta 3 (1.0µg/cm²) versus placebo

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	TGF-β3 (1.0µg/cm²)	Placebo	Relative (95% CI)	Absolute	Quality	Importance
Proportion of people completely healed – inpatients – grade 3 and 4 – NPUAP classification[79]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	0/4 (0%)	0/5 (0%)	Not pooled	Not pooled	Low	Critical
							-	0%		Not pooled		
Mean percentage reduction in ulcer area – inpatients – grade 3 and 4 – NPUAP classification[79]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	70 (n=4)	30 (n=5)	-	Not pooled	Very low	Critical
Mean percentage reduction in ulcer volume – inpatients – grade 3 and 4 – NPUAP classification[79]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	75 (n=4)	20 (n=5)	-	Not pooled	Very low	Critical
Mortality (all-cause) [79]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[c,d]	None	1/4 (25%)	0/5 (0%)	OR 9.49 (0.18 to 489.97)	250 more per 1000 (from 210 fewer to 710 more)	Very low	Important
							-	0%		250 more per 1000 (from 210 fewer to 710 more)		
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate of reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	TGF-β3 (1.0µg/cm²)	Placebo	Relative (95% CI)	Absolute		
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital												
-	-	-	-	-	-	-	-	-	-	-	-	-
Acceptability of treatment												
-	-	-	-	-	-	-	-	-	-	-	-	-
Side effects												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) Hirshberg (2003): no report on sequence generation and allocation concealment and report of blinding, but no further information; no log-transformation of data
(b) No standard deviation; small sample size
(c) Confidence interval crossed both MID points
(d) Limited number of events.

Table 112: Clinical evidence profile: topical growth factor – beta 3 (1.0µg/cm²) versus topical growth factor – beta 3 (2.5µg/cm²)

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	TGF-β3 (1.0µg/cm²)	TGF-β3 (2.5µg/cm²)	Relative (95% CI)	Absolute		
Proportion of people completely healed – inpatients – grade 3 and 4 – NPUAP classification[79]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	0/4 (0%)	1/5 (20%)	OR 0.17 (0 to 8.54)	159 fewer per 1000 (from 200 fewer to	Very low	Critical

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	TGF-β3 (1.0µg/cm²)	TGF-β3 (2.5µg/cm²)	Relative (95% CI)	Absolute		
										481 more)		
							-	20%		159 fewer per 1000 (from 200 fewer to 481 more)		
Mean percentage reduction in ulcer area – inpatients – grade 3 and 4 – NPUAP classification[79]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[c]	None	70 (n=4)	60 (n=5)	-	Not pooled	Very low	Critical
Mean percentage reduction in ulcer volume – inpatients – grade 3 and 4 – NPUAP classification[79]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[c]	None	75 (n=4)	60 (n=5)	-	Not pooled	Very low	Critical
Mortality (all-cause) [79]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b,d]	None	1/4 (25%)	0/5 (0%)	OR 9.49 (0.18 to 489.97)	250 more per 1000 (from 210 fewer to 710 more)	Very low	Critical
							-	0%		250 more per 1000 (from 210 fewer to 710 more)		

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	TGF-β3 (1.0µg/cm²)	TGF-β3 (2.5µg/cm²)	Relative (95% CI)	Absolute	Quality	Importance
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate of reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital												
-	-	-	-	-	-	-	-	-	-	-	-	-
Acceptability of treatment												
-	-	-	-	-	-	-	-	-	-	-	-	-
Side effects												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) Hirshberg (2003): no report on sequence generation and allocation concealment and report of blinding, but no further information; no log-transformation of data
(b) Confidence interval crossed both MID points
(c) No standard deviation; small sample size
(d) Limited number of events.

Table 113: Clinical evidence profile: topical growth factor – beta 3 (2.5µg/cm²) versus placebo

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	TGF-β3 (2.5µg/cm²)	Placebo	Relative (95% CI)	Absolute	Quality	Importance
Proportion of people completely healed – inpatients – grade 3 and 4 – NPUAP classification[79]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	1/5 (20%)	0/5 (0%)	OR 7.39 (0.15 to 372.38)	200 more per 1000 (from 210 fewer to 610 more)	Very low	Critical
							-	0%		200 more per 1000 (from 210 fewer to 610 more)		
Mean percentage reduction in ulcer area – inpatients – grade 3 and 4 – NPUAP classification[79]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[c]	None	60 (n=5)	30 (n=5)	-	Not pooled	Very low	Critical
Mean percentage reduction in ulcer volume – inpatients – grade 3 and 4 – NPUAP classification[79]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[c]	None	60 (n=5)	20 (n=5)	-	Not pooled	Very low	Critical
Mortality (all-cause) [79]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[c]	None	0/5 (0%)	1/4 (25%)	OR 0.11 (0 to 5.44)	215 fewer per 1000 (from 250 fewer to 395 more)	Very low	Important
							-	25%	-	215 fewer per 1000 (from 250		

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	TGF-β3 (2.5µg/cm²)	Placebo	Relative (95% CI)	Absolute	Quality	Importance
										fewer to 395 more)		
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate of reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital												
-	-	-	-	-	-	-	-	-	-	-	-	-
Acceptability of treatment												
-	-	-	-	-	-	-	-	-	-	-	-	-
Side effects												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) Hirshberg (2003): no report on sequence generation and allocation concealment and report of blinding, but no further information; no log-transformation of data
(b) Confidence interval crossed both MID points
(c) No standard deviation; small sample size

Table 114: Clinical evidence profile: nerve growth factor (2.5 S murine) versus placebo

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	NGF	Placebo	Relative (95% CI)	Absolute	Quality	Importance
Proportion of people completely healed (foot ulcers) – people in a nursing home – grade 2 and above - Yarkony classification[101]												
1	Randomised trial	Serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	None	8/18 (44.4%)	1/18 (5.6%)	RR 8 (1.11 to 57.57)	389 more per 1000 (from 6 more to 1000 more)	Low	Critical
								5.6%		392 more per 1000 (from 6 more to 1000 more)		
Proportion of people improved by 3 or more grade (foot ulcers) – people in a nursing home – grade 2 and above - Yarkony classification[101]												
1	Randomised trial	Serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	5/18 (27.8%)	0/18 (0%)	OR 9.56 (1.48 to 61.61)	280 more (from 60 more to 490 more)	Moderate	Critical
								0%		280 more (from 60 more to 490 more)		
Proportion of peoples improved by 2 grade (foot ulcers) – people in a nursing home – grade 2 and above - Yarkony classification[101]												
1	Randomised trial	Serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	14/18 (77.8%)	2/18 (11.1%)	RR 7 (1.85 to 26.46)	667 more per 1000 (from 94 more to 1000 more)	Moderate	Critical
								11.1%		666 more		

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	NGF	Placebo	Relative (95% CI)	Absolute		
										per 1000 (from 94 more to 1000 more)		
Proportion of people improved by 1 grade (foot ulcers) – nursing home patients – grade II and above - Yarkony classification[101]												
1	Randomised trial	Serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	18/18 (100%)	8/18 (44.4%)	RR 2.18 (1.31 to 3.61)	524 more per 1000 (from 138 more to 1000 more)	Moderate	Critical
								44.4%		524 more per 1000 (from 138 more to 1000 more)		
Mean mm² reduction in ulcer area (foot ulcers) – people in a nursing home – grade 2 and above - Yarkony classification[101]												
1	Randomised trial	Serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	None	738 (SD 393)	485 (SD 384)	-	MD 253 higher (0.83 lower to 506.83 higher)	Low	Critical
Mean mm² reduction in ulcer (foot ulcers) – people in a nursing home – grade 2 and above - Yarkony classification[101]												
1	Randomised trial	Serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	6.5 (SD 0.3)	5.9 (SD 0.3)	-	MD 0.6 higher (0.4 to 0.8 higher) (adjusted for	Moderate	Critical

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	NGF	Placebo	Relative (95% CI)	Absolute		
										baseline ulcer area, location and duration)		
Proportion of people with adverse events (foot ulcers) – people in a nursing home – grade 2 and above - Yarkony classification[101]												
1	Randomised trial	Serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	0/18 (0%)	0/18 (0%)	Not pooled	Not pooled	Moderate	Critical
								0%		Not pooled		
Mortality (all-cause) [101]												
1	Randomised trial	Serious[a]	No serious inconsistency	No serious indirectness	Very serious[c]	None	1/19 (5.3%)	0/19 (0%)	OR 7.39 (0.15 to 372.38)	50 more per 1000 (from 80 fewer to 190 more)	Very low	Important
								0%		50 more per 1000 (from 80 fewer to 190 more)		
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate of reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital												

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	NGF	Placebo	Relative (95% CI)	Absolute		
-	-	-	-	-	-	-	-	-	-	-	-	-
Acceptability of treatment												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) Landi (2003): allocation according to age, group, sex and ulcer area and blinding of nurses and outcome assessor, but no blinding of participant
(b) The confidence interval crossed 1 MID point
(c) The confidence interval crossed both MID points. There were a limited number of events.

Table 115: Clinical evidence profile: recombinant platelet-derived growth factor-BB (100µg/ml) versus placebo

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	rPDGF-BB (100µg/ml)	Placebo	Relative (95% CI)	Absolute		
Proportion of people completely healed – general population and denervated people – grade 3 and 4 – NPUAP classification[e128,153,159]												
2	Randomised trials	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	8/29 (27.6%)	2/21 (9.5%)	RR 2.68 (0.74 to 9.74)	160 more per 1000 (from 25 fewer to 832 more)	Very low	Critical
							-	7.1%		119 more per 1000 (from 18 fewer to 621 more)		
Ulcer volume[g] at end of treatment – general population – grade 3 and 4 – classification system not reported[128]												
1	Randomised	Very	No serious	No serious	Very	None	1.75	3.5	-	Not	Very	Critical

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	rPDGF-BB (100µg/ml)	Placebo	Relative (95% CI)	Absolute	Quality	Importance
	trial	serious[c]	inconsistency	indirectness	serious[d]		(n=16)	(n=14)		pooled (adjusted for initial volume)	low	
Mortality (all-cause)[159]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious	None	0/35 (0%)	0/15 (0%)	Not pooled	Not pooled	Very low	Important
							-	0%		Not pooled		
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate of reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital												
-	-	-	-	-	-	-	-	-	-	-	-	-
Acceptability of treatment												
-	-	-	-	-	-	-	-	-	-	-	-	-
Side effects												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) Mustoe (1994) did not report on sequence generation, allocation concealment and report of double blinding, but no further information; Robson (1992b) did not report on sequence generation, unequal allocation and only the outcome assessor was blinded.

(b) The confidence interval crossed 1 MID point
(c) Mustoe (1994) did not report on sequence generation, allocation concealment and report of double blinding, but no further information
(d) No standard deviation was reported and there was a small sample size.
(e) Mustoe (1994) did not report the classification system used; Robson (1992b): NPUAP classification.

Table 116: Clinical evidence profile: recombinant platelet-derived growth factor-BB (100µg/ml) versus recombinant platelet-derived growth factor-BB (300mg/ml)

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	rPDGF-BB (100µg/ml)	rPDGF-BB (300ug/ml)	Relative (95% CI)	Absolute	Quality	Importance
Proportion of people completely healed – general population – grade 3 and 4 – classification system not reported[128]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	6/16 (37.5%)	3/12 (25%)	RR 1.5 (0.47 to 4.82)	125 more per 1000 (from 132 fewer to 955 more)	Very low	Critical
							-	25%		125 more per 1000 (from 132 fewer to 955 more)		
Ulcer volume[g] at end of treatment – general population – grade 3 and 4 – classification system not reported[128]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[c]	None	1.75 (n=16)	2.0 (n=12)	-	Not pooled (adjusted for initial volume)	Very low	Critical
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate of reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	rPDGF-BB (100µg/ml)	rPDGF-BB (300ug/ml)	Relative (95% CI)	Absolute	Quality	Importance
Reduction in size or volume of pressure ulcers												
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital												
-	-	-	-	-	-	-	-	-	-	-	-	-
Acceptability of treatment												
-	-	-	-	-	-	-	-	-	-	-	-	-
Side effects												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) Mustoe (1994) did not report on sequence generation, allocation concealment and report of double blinding, but no further information was provided.
(b) The confidence interval crossed both MID points.
(c) There was no standard deviation reported and the study used a small sample size.

Table 117: Clinical evidence profile: recombinant platelet-derived growth factor-BB (300µg/ml) versus placebo

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	rPDGF-BB (300µg/ml)	Placebo	Relative (95% CI)	Absolute	Quality	Importance
Proportion of people completely healed – general population – grade 3 and 4 – classification system not reported[128]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	3/12 (25%)	2/14 (14.3%)	RR 1.75 (0.35 to 8.79)	107 more per 1000 (from 93 fewer to 1000 more)	Very low	Critical
							-	14.3%		107 more per		

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	rPDGF-BB (300µg/ml)	Placebo	Relative (95% CI)	Absolute	Quality	Importance
										1000 (from 93 fewer to 1000 more)		
Ulcer volume[g] at end of treatment – general population – grade 3 and 4 – classification system not reported[128]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[c]	None	2.0 (n=12)	3.5 (n=14)	-	Not pooled (adjusted for initial volume)	Very low	Critical
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate of reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital												
-	-	-	-	-	-	-	-	-	-	-	-	-
Acceptability of treatment												
-	-	-	-	-	-	-	-	-	-	-	-	-
Side effects												
-	-	-	-	-	-	-	-	-	-	-	-	-
Mortality (all-cause)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) Mustoe (1994) did not report on sequence generation, allocation concealment and report of double blinding, but no further information was provided.
(b) The confidence interval crossed both MID points.

(c) There was no standard deviation reported and the study used a small sample size.

Table 118: Clinical evidence profile: granulo-macrophage/colony-stimulating factor (2.0µg/cm²) versus placebo

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	rGM-CSF (2.0µg/cm²)	Placebo	Relative (95% CI)	Absolute	Quality	Importance
Proportion of people completely healed (after 1 year) – inpatients – grade 3 and 4 – classification not reported[147]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	8/14 (57.1%)	10/13 (76.9%)	RR 0.74 (0.43 to 1.28)	200 fewer per 1000 (from 438 fewer to 215 more)	Very low	Critical
							-	76.9%		200 fewer per 1000 (from 438 fewer to 215 more)		
Proportion of people worsened (after 1 year) – inpatients – grade 3 and 4 – classification not reported[147]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	2/14 (14.3%)	0/13 (0%)	OR 7.43 (0.44 to 125.76)	140 more (from 70 fewer to 360 more)	Very low	Critical
							-	0%		140 more (from 70 fewer to 360 more)		
Mean percentage reduction in ulcer area – inpatients – grade 3 and 4 – classification not reported[157]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	67 (SD 24)	71 (SD 11)	-	MD 4 lower (17.36 lower to 9.36 higher)	Very low	Critical
Median percentage reduction in ulcer area – inpatients – grade 3 and 4 – classification not reported[157]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[c]	None	70 (range: 3-93) (n=15)	72 (range: 39-84) (n=15)	-	Not pooled	Very low	Critical

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	rGM-CSF (2.0µg/cm²)	Placebo	Relative (95% CI)	Absolute	Quality	Importance
Mortality (all-cause) [157]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious	None	0/15 (0%)	0/15 (0%)	Not pooled	Not pooled	Low	Important
							-	0%		Not pooled		
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate of reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital												
-	-	-	-	-	-	-	-	-	-	-	-	-
Acceptability of treatment												
-	-	-	-	-	-	-	-	-	-	-	-	-
Side effects												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) There was no report on sequence generation, allocation concealment and report of double blinding, but no further information was provided.
(b) The confidence interval crossed both MID points.
(c) There was no standard deviation reported and the study used a small sample size.
(d) No log-transformation of data was carried out.

Table 119: Clinical evidence profile: granulo-macrophage/colony-stimulating factor (2.0µg/cm²) versus basic fibroblast growth factor (5.0µ/cm²)

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	rGM-CSF (2.0ug/cm²)	rBFGF (5.0ug/cm²)	Relative (95% CI)	Absolute	Quality	Importance
Proportion of people completely healed (after 1 year) – inpatients – grade 3 and 4 – classification not reported[147]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	8/14 (57.1%)	10/14 (71.4%)	RR 0.8 (0.46 to 1.4)	143 fewer per 1000 (from 386 fewer to 286 more)	Very low	Critical
								71.4%		143 fewer per 1000 (from 386 fewer to 286 more)		
Proportion of people worsened (after 1 year) – inpatients – grade 3 and 4 – classification not reported[147]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	2/14 (14.3%)	4/14 (28.6%)	RR 0.5 (0.11 to 2.3)	143 fewer per 1000 (from 254 fewer to 371 more)	Very low	Critical
							-	28.6%		143 fewer per 1000 (from 255		

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	rGM-CSF (2.0ug/cm²)	rBFGF (5.0ug/cm²)	Relative (95% CI)	Absolute		
										fewer to 372 more)		
Mean percentage reduction in ulcer area – inpatients – grade 3 and 4 – classification not reported[157]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[c]	None	67 (SD 24)	75 (SD 19)	-	MD 8 lower (23.49 lower to 7.49 higher)	Very low	Critical
Median percentage reduction in ulcer area – inpatients – grade 3 and 4 – classification not reported[157]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[d]	None	70 (range:3-93) (n=15)	79 (range:42-99) (n=15)	-	Not pooled	Very low	Critical
Mortality (all-cause)[157]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious	None	0/15 (0%)	0/15 (0%)	Not pooled	Not pooled	Low	Important
							-	0%	-	Not pooled		
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate of reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital												
-	-	-	-	-	-	-	-	-	-	-	-	-

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	rGM-CSF (2.0ug/cm²)	rBFGF (5.0ug/cm²)	Relative (95% CI)	Absolute	Quality	Importance
Acceptability of treatment												
-	-	-	-	-	-	-	-	-	-	-	-	-
Side effects												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) There was no report on sequence generation, allocation concealment and report of double blinding, but no further information was provided.
(b) The confidence interval crossed both MID points.
(c) Theconfidence interval crossed 1 MID point.
(d) There was no standard deviation reported and the study used a small sample size.
(e) No log-transformation of data was conducted.

Table 120: Clinical evidence profile: granulo-macrophage/colony-stimulating factor (2.0µg/cm²) versus granulo-macrophage/colony-stimulating factor (2.0mg/cm²) and basic fibroblast growth factor (5.0µg/cm²)

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	rGM-CSF	rGM-CSF/rBFGF	Relative (95% CI)	Absolute	Quality	Importance
Proportion of people completely healed (after 1 year) – inpatients – grade 3 and 4 – classification not reported[147]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	8/14 (57.1%)	9/13 (69.2%)	RR 0.83 (0.46 to 1.48)	118 fewer per 1000 (from 374 fewer to 332 more)	Very low	Critical
							-	69.2%		118 fewer per 1000 (from 374 fewer to 332 more)		

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	rGM-CSF	rGM-CSF/rBFGF	Relative (95% CI)	Absolute	Quality	Importance
Proportion of people worsened (after 1 year) – inpatients – grade 3 and 4 – classification not reported[147]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	2/14 (14.3%)	1/13 (7.7%)	RR 1.86 (0.19 to 18.13)	66 more per 1000 (from 62 fewer to 1000 more)	Very low	Critical
							-	7.7%		66 more per 1000 (from 62 fewer to 1000 more)		
Mean percentage reduction in ulcer area – inpatients – grade 3 and 4 – classification not reported[157]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	67 (SD 24)	68 (SD 21)	-	MD 1 lower (16.92 lower to 14.92 higher)	Very low	Critical
Median percentage reduction in ulcer area – inpatients – grade 3 and 4 – classification not reported[157]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[c]	None	70 (range: 3-93) (n=15)	73 (range:29-98) (n=16)	-	Not pooled	Very low	Critical
Mortality (all-cause) [157]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious	None	0/15 (0%)	0/16 (0%)	Not pooled	Not pooled	Low	Important
							-	-	-	Not pooled		
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate of reduction in size or volume of pressure ulcers												

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	rGM-CSF	rGM-CSF/rBFGF	Relative (95% CI)	Absolute	Quality	Importance
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital												
-	-	-	-	-	-	-	-	-	-	-	-	-
Acceptability of treatment												
-	-	-	-	-	-	-	-	-	-	-	-	-
Side effects												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) There was no report on sequence generation, allocation concealment and report of double blinding, but no further information was provided.
(b) The confidence interval crossed both MID points.
(c) There was no standard deviation reported and the study used a small sample size.

Table 121: Clinical evidence profile: basic fibroblast growth factor (5.0µg/cm²) versus placebo

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	rBFGF	Placebo	Relative (95% CI)	Absolute	Quality	Importance
Proportion of peoplecompletely healed (after 1 year) – inpatients – grade 3 and 4 – classification not reported[147]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	10/14 (71.4%)	10/13 (76.9%)	RR 0.93 (0.59 to 1.45)	54 fewer per 1000 (from 315 fewer to 346 more)	Very low	Critical
							-	76.9%		54 fewer per 1000 (from 315 fewer to 346 more)		

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	rBFGF	Placebo	Relative (95% CI)	Absolute	Quality	Importance
Proportion of people worsened (after 1 year) – inpatients – grade 3 and 4 – classification not reported[147]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[c]	None	4/14 (28.6%)	0/13 (0%)	OR 8.85 (1.1 to 71.2)	290 more (from 30 fewer to 540 more)	Very low	Critical
								0%		290 more (from 30 fewer to 540 more)		
Mean percentage reduction in ulcer area – inpatients – grade 3 and 4 – classification not reported[157]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[c]	None	79 (SD 19)	71 (SD 11)	-	MD 4 higher (7.11 lower to 15.11 higher)	Very low	Critical
Median percentage reduction in ulcer area – inpatients – grade 3 and 4 – classification not reported[157]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[d]	None	79 (range:42-99) (n=15)	72 (range:39-84) (n=15)	-	Not pooled	Very low	Critical
Mortality (all-cause)[157]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious	None	0/15 (0%)	0/15 (0%)	Not pooled	Not pooled	Low	Important
							-	0%	-	Not pooled		
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate of reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital												
-	-	-	-	-	-	-	-	-	-	-	-	-
Acceptability of treatment												

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	rBFGF	Placebo	Relative (95% CI)	Absolute	Quality	Importance
-	-	-	-	-	-	-	-	-	-	-	-	-
Side effects												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) There was no report on sequence generation, allocation concealment and report of double blinding, but no further information was provided.
(b) The confidence interval crossed both MID points.
(c) The confidence interval crossed 1 MID point.
(d) There was no standard deviation reported and the study used a small sample size.
(e) No log-transformation of data was conducted.

Table 122: Clinical evidence profile: basic fibroblast growth factor (5.0µg/cm²) versus granulo-macrophage/colony-stimulating factor (2.0µg/cm²) and basic fibroblast growth factor (5.0mg/cm²)

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	rBFGF	rGM-CSF/rBFGF	Relative (95% CI)	Absolute	Quality	Importance
Proportion of people completely healed (after 1 year) – inpatients – grade 3 and 4 – classification not reported[147]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	10/14 (71.4%)	9/13 (69.2%)	RR 1.03 (0.63 to 1.69)	21 more per 1000 (from 256 fewer to 478 more)	Very low	Critical
							-	69.2%		21 more per 1000 (from 256 fewer to 477 more)		
Proportion of people worsened (after 1 year) – inpatients – grade 3 and 4 – classification not reported[147]												

Quality assessment							No of patients		Effect			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**rBFGF**	**rGM-CSF/rBFGF**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	4/14 (28.6%)	1/13 (7.7%)	RR 3.71 (0.47 to 29.06)	208 more per 1000 (from 41 fewer to 1000 more)	Very low	Critical
							-	7.7%		209 more per 1000 (from 41 fewer to 1000 more)		
Mean percentage reduction in ulcer area – inpatients – grade 3 and 4 – classification not reported[157]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[c]	None	75 (SD 19)	68 (SD 21)	-	MD 7 higher (7.08 lower to 21.08 higher)	Very low	Critical
Median percentage reduction in ulcer area – inpatients – grade 3 and 4 – classification not reported[157]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[d]	None	79 (range: 42-99) (n=15)	73 (range: 29-98) (n=16)	-	Not pooled	Very low	Critical
Mortality (all-cause) [157]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious	None	0/15 (0%)	0/16 (0%)	Not pooled	Not pooled	Low	Important
							-	-	-	Not pooled		
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate of reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	rBFGF	rGM-CSF/rBFGF	Relative (95% CI)	Absolute	Quality	Importance
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital												
-	-	-	-	-	-	-	-	-	-	-	-	-
Acceptability of treatment												
-	-	-	-	-	-	-	-	-	-	-	-	-
Side effects												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) There was no report on sequence generation, allocation concealment and report of double blinding, but no further information was provided.
(b) The confidence interval crossed both MID points.
(c) The confidence interval crossed 1 MID point.
(d) There was no standard deviation and the study used asmall sample size.
(e) No log-transformation of data was conducted.

Table 123: Clinical evidence profile: granulo-macrophage/colony-stimulating factor (2.0µg/cm²) and basic fibroblast growth factor (5.0µg/cm²) versus placebo

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	rGM-CSF/rBFGF	Placebo	Relative (95% CI)	Absolute	Quality	Importance
Proportion of people completely healed (after 1 year) – inpatients – grade 3 and 4 – classification not reported[147]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	9/13 (69.2%)	10/13 (76.9%)	RR 0.9 (0.56 to 1.44)	77 fewer per 1000 (from 338 fewer to 338 more)	Very low	Critical
							-	76.9%		77 fewer per 1000 (from		

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	rGM-CSF/rBFGF	Placebo	Relative (95% CI)	Absolute	Quality	Importance
										338 fewer to 338 more)		
Proportion of people worsened (after 1 year) – inpatients – grade 3 and 4 – classification not reported[147]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	1/13 (7.7%)	0/13 (0%)	OR 7.39 (0.15 to 372.38)	80 more (from 110 fewer to 270 more)	Very low	Critical
							-	0%		80 more (from 110 fewer to 270 more)		
Mean percentage reduction in ulcer area – inpatients – grade 3 and 4 – classification not reported[157]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	168 (SD 21)	71 (SD 11)	-	MD 3 lower (14.7 lower to 8.7 higher)	Very low	Critical
Median percentage reduction in ulcer area – inpatients – grade 3 and 4 – classification not reported[157]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[c]	None	73 (range:29-98) (n=16)	72 (range:39-84) (n=15)	-	Not pooled	Very low	Critical
Mortality (all-cause)[157]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	no serious	None	0/16 (0%)	0/15 (0%)	Not pooled	Not pooled	Low	Important
							-	0%	-	Not pooled		
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate of reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	rGM-CSF/rBFGF	Placebo	Relative (95% CI)	Absolute	Quality	Importance
Time in hospital												
-	-	-	-	-	-	-	-	-	-	-	-	-
Acceptability of treatment												
-	-	-	-	-	-	-	-	-	-	-	-	-
Side effects												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) There was no report on sequence generation, allocation concealment and report of double blinding, but no further information was provided.
(b) The confidence interval crossed both MID points.
(c) No standard deviation was reported and the study used a small sample size.
(d) No log-transformation of data was conducted.

Table 124: Clinical evidence profile: recombinant platelet-derived growth factor-BB (100.0µg/g) versus placebo

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	rPDGF-BB	Placebo	Relative (95% CI)	Absolute	Quality	Importance
Proportion of people completely healed – general population – grade 3 and 4 – NPUAP classification[153]												
1	Randomised trials	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	7/31 (22.6%)	0/31 (0%)	OR 9.19 (1.93 to 43.75)	230 more (from 70 more to 380 more)	Low	Critical
							-	0%		230 more (from 70 more to 380		

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	rPDGF-BB	Placebo	Relative (95% CI)	Absolute		
										more)		
Proportion of people healed 90% or higher – general population – grade 3 and 4 – NPUAP classification[153]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	None	18/31 (58.1%)	9/31 (29%)	RR 2 (1.07 to 3.74)	290 more per 1000 (from 20 more to 795 more)	Very low	Critical
							-	29%		290 more per 1000 (from 20 more to 795 more)		
Median percentage reduction in ulcer volume – general population – grade 3 and 4 – NPUAP classification[153]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[c]	None	99.6 (n=31)	99.1 (n=31)	p=0.013	Not pooled	Very low	Critical
Proportion of people with osteomyelitis – general population – grade 3 and 4 – NPUAP classification[153]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[d]	None	2/31 (6.5%)	1/31 (3.2%)	RR 2 (0.19 to 20.93)	32 more per 1000 (from 26 fewer to 643 more)	Very low	Important
							-	3.2%		32 more per 1000 (from 26 fewer to 638 more)		
Proportion of peoples with infection – general population – grade 3 and 4 – NPUAP classification[153]												

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	rPDGF-BB	Placebo	Relative (95% CI)	Absolute		
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[d]	None	0/31 (0%)	1/31 (3.2%)	OR 0.14 (0 to 6.82)	28 fewer per 1000 (from 32 fewer to 153 more)	Very low	Important
							-	3.2%		27 fewer per 1000 (from 32 fewer to 152 more)		
Proportion of people with sepsis – general population – grade 3 and 4 – NPUAP classification[153]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	0/31 (0%)	0/31 (0%)	Not pooled	Not pooled	Low	Important
							-	0%		Not pooled		
Proportion of people with adverse events other than osteomyelitis, infection and sepsis – general population – grade 3 and 4 – NPUAP classification[153]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[d]	None	2/31 (6.5%)	2/31 (6.5%)	RR 1 (0.15 to 6.66)	0 fewer per 1000 (from 55 fewer to 365 more)	Very low	Important
								6.5%		0 fewer per 1000 (from 55 fewer to 368 more)		
Mortality (all-cause) [153]												

Quality assessment							No of patients		Effect			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**rPDGF-BB**	**Placebo**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	0/31 (0%)	0/31 (0%)	Not pooled	Not pooled	Low	Important
							-	0%	-	Not pooled		
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate or reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital												
-	-	-	-	-	-	-	-	-	-	-	-	-
Acceptability of treatment												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) Rees (1999) did not report on sequence generation, allocation concealment and blinding;no log-transformation of data was conducted.
(b) The confidence interval crossed 1 MID point.
(c) No standard deviation was reported. It was unknown if sample size was sufficient.
(d) The confidence interval crossed both MID points.

Table 125: Clinical evidence profile: recombinant platelet-derived growth factor-BB (100.0mg/g) versus recombinant platelet-derived growth factor-BB (300.0mg/g) alternated with placebo

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	rPDGF-BB (100µg/g)	rPDGF-BB (300µg/g) alternated with placebo	Relative (95% CI)	Absolute		
Proportion of people completely healed – general population – grade 3 and 4 – NPUAP classification[153]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	7/31 (22.6%)	6/32 (18.8%)	RR 1.2 (0.46 to 3.18)	38 more per 1000 (from 101 fewer to 409 more)	Very low	Critical
							-	18.8%		38 more per 1000 (from 102 fewer to 410 more)		
Proportion of people healed 90% or higher – general population – grade 3 and 4 – NPUAP classification[153]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	18/31 (58.1%)	19/32 (59.4%)	RR 0.98 (0.65 to 1.48)	12 fewer per 1000 (from 208 fewer to 285 more)	Very low	Critical
							-	59.4%		12 fewer per 1000 (from 208 fewer to 285 more)		

Quality assessment							No of patients		Effect			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**rPDGF-BB (100µg/g)**	**rPDGF-BB (300µg/g) alternated with placebo**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
Median percentage reduction in ulcer volume – general population – grade 3 and 4 – NPUAP classification[153]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[c]	None	99.6 (n=31)	99.7 (n=32)	-	Not pooled	Very low	Critical
Proportion of people with osteomyelitis – general population – grade 3 and 4 – NPUAP classification[153]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	2/31 (6.5%)	1/32 (3.1%)	RR 2.06 (0.2 to 21.63)	33 more per 1000 (from 25 fewer to 645 more)	Very low	Important
							-	3.1%		33 more per 1000 (from 25 fewer to 640 more)		
Proportion of people with infection – general population – grade 3 and 4 – NPUAP classification[153]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	0/31 (0%)	0/32 (0%)	Not pooled	Not pooled	Low	Important
							-	0%		Not pooled		
Proportion of people with sepsis – general population – grade 3 and 4 – NPUAP classification[153]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	0/31 (0%)	1/32 (3.1%)	OR 0.14 (0 to 7.04)	27 fewer per 1000 (from 31 fewer to 154 more)	Very low	Important

Quality assessment							No of patients		Effect			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**rPDGF-BB (100µg/g)**	**rPDGF-BB (300µg/g) alternated with placebo**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
							-	3.1%		27 fewer per 1000 (from 31 fewer to 153 more)		
Proportion of people with adverse events other than osteomyelitis, infection and sepsis – general population – grade 3 and 4 – NPUAP classification[153]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	2/31 (6.5%)	3/32 (9.4%)	RR 0.69 (0.12 to 3.84)	29 fewer per 1000 (from 83 fewer to 266 more)	Very low	Important
							-	9.4%		29 fewer per 1000 (from 83 fewer to 267 more)		
Mortality (all-cause) [153]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	0/31 (0%)	0/32 (0%)	Not pooled	Not pooled	Low	Important
							-	0%	-	Not pooled		
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate of reduction in size or volume of pressure ulcers												

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	rPDGF-BB (100µg/g)	rPDGF-BB (300µg/g) alternated with placebo	Relative (95% CI)	Absolute	Quality	Importance
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital												
-	-	-	-	-	-	-	-	-	-	-	-	-
Acceptability of treatment												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) Rees (1999): no report on sequence generation, allocation concealment and blinding; ; no log-transformation of data;
(b) Confidence interval crossed both MID points
(c) No standard deviation; unknown if sample size was sufficient

Table 126: Clinical evidence profile: recombinant platelet-derived growth factor-BB (100.0µg/g) versus recombinant platelet-derived growth factor-BB (300.0µg/g)

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	rPDGF-BB (100ug/g)	rPDGF-BB (300ug/g)	Relative (95% CI)	Absolute	Quality	Importance
Proportion of people completely healed – general population – grade 3 and 4 – NPUAP classification[153]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	None	7/31 (22.6%)	1/30 (3.3%)	RR 6.77 (0.89 to 51.8)	192 more per 1000 (from 4 fewer to 1000	Very low	Critical

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	rPDGF-BB (100ug/g)	rPDGF-BB (300ug/g)	Relative (95% CI)	Absolute		
										more)		
							-	3.3%		190 more per 1000 (from 4 fewer to 1000 more)		
Proportion of peoples healed 90% or higher – general population – grade 3 and 4 – NPUAP classification[153]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	None	18/31 (58.1%)	12/30 (40%)	RR 1.45 (0.85 to 2.47)	180 more per 1000 (from 60 fewer to 588 more)	Very low	Critical
							-	40%		180 more per 1000 (from 60 fewer to 588 more)		
Median percentage reduction in ulcer volume – general population – grade 3 and 4 – NPUAP classification[153]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[c]	None	99.6 (n=31)	98.6 (n=30)	-	Not pooled	Very low	Critical
Proportion of people with osteomyelitis – general population – grade 3 and 4 – NPUAP classification[153]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[d]	None	2/31 (6.5%)	0/30 (0%)	OR 7.4 (0.45 to 121.11)	60 more (from 40 fewer to 170 more)	Very low	Important
							-	0%		60 more (from 40		

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	rPDGF-BB (100ug/g)	rPDGF-BB (300ug/g)	Relative (95% CI)	Absolute	Quality	Importance
										fewer to 170 more)		
Proportion of people with infection – general population – grade 3 and 4 – NPUAP classification[153]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[d]	None	0/31 (0%)	1/30 (3.3%)	OR 0.13 (0 to 6.6)	29 fewer per 1000 (from 33 fewer to 152 more)	Very low	Important
							-	3.3%		29 fewer per 1000 (from 33 fewer to 151 more)		
Proportion of people with sepsis – general population – grade 3 and 4 – NPUAP classification[153]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious	None	0/31 (0%)	0/30 (0%)	Not pooled	Not pooled	Very low	Important
							-	0%		Not pooled		
Proportion of people with adverse events other than osteomyelitis, infection and sepsis – general population – grade 3 and 4 – NPUAP classification[153]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[d]	None	2/31 (6.5%)	2/30 (6.7%)	RR 0.97 (0.15 to 6.44)	2 fewer per 1000 (from 57 fewer to 363 more)	Very low	Important
							-	6.7%		2 fewer per 1000 (from 57		

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	rPDGF-BB (100ug/g)	rPDGF-BB (300ug/g)	Relative (95% CI)	Absolute		
										fewer to 364 more)		
Mortality (all-cause) [153]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	0/31 (0%)	0/30 (0%)	Not pooled	Not pooled	Low	Important
							-	-	-	Not pooled		
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate of reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital												
-	-	-	-	-	-	-	-	-	-	-	-	-
Acceptability of treatment												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) Rees (1999) did not report on sequence generation, allocation concealment and blinding; no log-transformation of data was conducted.
(b) The confidence interval crossed 1 MID point.
(c) No standard deviation was reported and it was unknown if sample size was sufficient.
(d) The confidence interval crossed both MID points.

Table 127: Clinical evidence profile: recombinant platelet-derived growth factor-BB (300.0µg/g) alternated with placebo versus placebo

Quality assessment	No of patients	Effect	Quality	Importance

No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**rPDGF-BB (300µg/g) alternated with placebo**	**Placebo**	**Relative (95% CI)**	**Absolute**		
Proportion of people completely healed – general population – grade 3 and 4 – NPUAP classification[153]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	6/32 (18.8%)	0/31 (0%)	OR 8.51 (1.6 to 45.18)	190 more (from 50 more to 330 more)	Low	Critical
							-	0%		190 more (from 50 more to 330 more)		
Proportion of people healed 90% or higher – general population – grade 3 and 4 – NPUAP classification[153]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	None	19/32 (59.4%)	9/31 (29%)	RR 2.05 (1.1 to 3.8)	305 more per 1000 (from 29 more to 813 more)	Very low	Critical
							-	29%		304 more per 1000 (from 29 more to 812 more)		
Median percentage reduction in ulcer volume – general population – grade 3 and 4 – NPUAP classification[153]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[c]	None	99.7 (n=32)	99.1 (n=31)	p=0.011	Not pooled	Very low	Critical
Proportion of people with osteomyelitis – general population – grade 3 and 4 – NPUAP classification[153]												
1	Randomised	Very	No serious	No serious	Very serious[d]	None	2/31	1/31	RR 2	32 more	Very	Important

Quality assessment							No of patients		Effect			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**rPDGF-BB (300µg/g) alternated with placebo**	**Placebo**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
	trial	serious[a]	inconsistency	indirectness			(6.5%)	(3.2%)	(0.19 to 20.93)	per 1000 (from 26 fewer to 643 more)	low	
							-	3.2%		32 more per 1000 (from 26 fewer to 638 more)		
Proportion of people with infection – general population – grade 3 and 4 – NPUAP classification[153]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[d]	None	0/32 (0%)	1/31 (3.2%)	OR 0.13 (0 to 6.61)	28 fewer per 1000 (from 32 fewer to 148 more)	Very low	Important
							-	3.2%		28 fewer per 1000 (from 32 fewer to 147 more)		
Proportion of people with sepsis – general population – grade 3 and 4 – NPUAP classification[153]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[d]	None	1/32 (3.1%)	0/31 (0%)	OR 7.16 (0.14 to	30 more (from 50 fewer to	Very low	Important

Quality assessment							No of patients		Effect			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**rPDGF-BB (300µg/g) alternated with placebo**	**Placebo**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
									361.11)	110 more)-		
							-	0%		-		
Proportion of people with adverse events other than osteomyelitis, infection and sepsis – general population – grade 3 and 4 – NPUAP classification[153]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[d]	None	3/32 (9.4%)	2/31 (6.5%)	RR 1.45 (0.26 to 8.11)	29 more per 1000 (from 48 fewer to 459 more)	Very low	Important
							-	6.5%		29 more per 1000 (from 48 fewer to 462 more)		
Mortality (all-cause) [153]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	0/32 (0%)	0/31 (0%)	Not pooled	Not pooled	Low	Important
							-	0%	-	Not pooled		
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate or reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	rPDGF-BB (300µg/g) alternated with placebo	Placebo	Relative (95% CI)	Absolute	Quality	Importance
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital												
-	-	-	-	-	-	-	-	-	-	-	-	-
Acceptability of treatment												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) Rees (1999) did not report on sequence generation, allocation concealment and blinding. There was no log-transformation of data.
(b) The confidence interval crossed 1 MID point.
(c) No standard deviation was reported and it was unknown if sample size was sufficient.
(d) The confidence interval crossed both MID points.

Table 128: Clinical evidence profile: recombinant platelet-derived growth factor-BB (300.0µg/g) alternated with placebo versus recombinant platelet-derived growth factor-BB (300.0µg/g)

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	rPDGF-BB (300µg/g) alternated with placebo	rPDGF-BB (300µg/g)	Relative (95% CI)	Absolute	Quality	Importance
Proportion of people completely healed – general population – grade 3 and 4 – NPUAP classification[153]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	6/32 (18.8%)	1/30 (3.3%)	RR 5.63 (0.72 to 44.03)	154 more per 1000 (from 9 fewer to	Very low	Critical

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**rPDGF-BB (300µg/g) alternated with placebo**	**rPDGF-BB (300µg/g)**	**Relative (95% CI)**	**Absolute**		
										1000 more)		
							-	3.3%		152 more per 1000 (from 9 fewer to 1000 more)		
Proportion of people healed 90% or higher – general population – grade 3 and 4 – NPUAP classification[153]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[c]	None	19/32 (59.4%)	12/30 (40%)	RR 1.48 (0.88 to 2.51)	192 more per 1000 (from 48 fewer to 604 more)	Very low	Critical
							-	40%		192 more per 1000 (from 48 fewer to 604 more)		
Median percentage reduction in ulcer volume – general population – grade 3 and 4 – NPUAP classification[153]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[d]	None	99.7 (n=32)	98.6 (n=30)	-	Not pooled	Very low	Critical
Proportion of people with osteomyelitis – general population – grade 3 and 4 – NPUAP classification[153]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	1/32 (3.1%)	0/30 (0%)	OR 6.94 (0.14 to	30 more (from 50	Very low	Important

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	rPDGF-BB (300µg/g) alternated with placebo	rPDGF-BB (300µg/g)	Relative (95% CI)	Absolute		
									350.54)	fewer to 120 more)		
							-	0%		-		
Proportion of people with infection – general population – grade 3 and 4 – NPUAP classification[153]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	0/32 (0%)	1/30 (3.3%)	OR 0.13 (0 to 6.39)	29 fewer per 1000 (from 33 fewer to 147 more)	Very low	Important
							-	3.3%		29 fewer per 1000 (from 33 fewer to 146 more)		
Proportion of people with sepsis – general population – grade 3 and 4 – NPUAP classification[153]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	1/32 (3.1%)	0/30 (0%)	OR 6.94 (0.14 to 350.54)	30 more (from 50 fewer to 120 more)	Very low	Important
							-	0%		30 more (from 50 fewer to 120 more)		

Quality assessment							No of patients		Effect			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**rPDGF-BB (300µg/g) alternated with placebo**	**rPDGF-BB (300µg/g)**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
Proportion of people with adverse events other than osteomyelitis, infection and sepsis – general population – grade 3 and 4 – NPUAP classification[153]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	3/32 (9.4%)	2/30 (6.7%)	RR 1.41 (0.25 to 7.84)	27 more per 1000 (from 50 fewer to 456 more)	Very low	Important
							-	6.7%		27 more per 1000 (from 50 fewer to 458 more)		
Mortality (all-cause) [153]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	0/32 (0%)	0/30 (0%)	Not pooled	Not pooled	Low	Important
							-	0%		Not pooled		
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate of reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital												
-	-	-	-	-	-	-	-	-	-	-	-	-

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	rPDGF-BB (300µg/g) alternated with placebo	rPDGF-BB (300µg/g)	Relative (95% CI)	Absolute	Quality	Importance
Acceptability of treatment												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) Rees (1999) did not report on sequence generation, allocation concealment and blinding; no log-transformation of data was conducted.
(b) The confidence interval crossed both MID points.
(c) The confidence interval crossed 1 MID point.
(d) No standard deviation was reported; unknown if sample size was sufficient.

Table 129: Clinical evidence profile: recombinant platelet-derived growth factor-BB (300.0µg/g) versus placebo

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	rPDGF-BB (300µg/g)	Placebo	Relative (95% CI)	Absolute	Quality	Importance
Proportion of people completely healed – general population – grade 3 and 4 – NPUAP classification[153]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	1/30 (3.3%)	0/31 (0%)	OR 7.64 (0.15 to 385.21)	30 more (from 50 fewer to 120 more)	Very low	Critical
							-	0%		30 more (from 50 fewer to 120 more)		
Proportion of people healed 90% or higher – general population – grade 3 and 4 – NPUAP classification[153]												

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	rPDGF-BB (300µg/g)	Placebo	Relative (95% CI)	Absolute		
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	12/30 (40%)	9/31 (29%)	RR 1.38 (0.68 to 2.78)	110 more per 1000 (from 93 fewer to 517 more)	Very low	Critical
							-	29%		110 more per 1000 (from 93 fewer to 516 more)		
Median percentage reduction in ulcer volume – general population – grade 3 and 4 – NPUAP classification[153]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[c]	None	98.6 (n=30)	99.1 (n=31)	-	Not pooled	Very low	Critical
Proportion of people with osteomyelitis – general population – grade 3 and 4 – NPUAP classification[153]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	0/30 (0%)	1/31 (3.2%)	OR 0.14 (0 to 7.05)	28 fewer per 1000 (from 32 fewer to 158 more)	Very low	Important
							-	3.2%		27 fewer per 1000 (from 32 fewer to 157 more)		
Proportion of people with infection – general population – grade 3 and 4 – NPUAP classification[153]												
1	Randomised	Very	No serious	No serious	Very serious[b]	None	1/30	1/31	RR 1.03	1 more	Very	Important

Quality assessment							No of patients		Effect			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**rPDGF-BB (300µg/g)**	**Placebo**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
	trial	serious[a]	inconsistency	indirectness			(3.3%)	(3.2%)	(0.07 to 15.78)	per 1000 (from 30 fewer to 477 more)	low	
							-	3.2%		1 more per 1000 (from 30 fewer to 473 more)		
Proportion of peoples with sepsis – general population – grade 3 and 4 – NPUAP classification[153]												
1	Randomised trial	Very seriousa	No serious inconsistency	No serious indirectness	No serious imprecision	None	0/30 (0%)	0/31 (0%)	Not pooled	Not pooled	Low	Important
								0%		Not pooled		
Proportion of people with adverse events other than osteomyelitis, infection and sepsis – general population – grade 3 and 4 – NPUAP classification[153]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	2/30 (6.7%)	2/31 (6.5%)	RR 1.03 (0.16 to 6.87)	2 more per 1000 (from 54 fewer to 379 more)	Very low	Important
							-	6.5%		2 more per 1000 (from 55 fewer to 382 more)		
Mortality (all-cause)[153]												
1	Randomisd	Very	No serious	No serious	No serious	None	0/30	0/31	Not	Not	Low	Important

Quality assessment							No of patients		Effect			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**rPDGF-BB (300µg/g)**	**Placebo**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
	trials	serious[a]	inconsistency	indirectness	imprecision		(0%)	(0%)	pooled	pooled		
							-	0%		Not pooled		
Time to complete healing of pressure ulcers[153]												
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate of reduction in size or volume of pressure ulcers[153]												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related) [153]												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital[153]												
-	-	-	-	-	-	-	-	-	-	-	-	-
Acceptability of treatment[153]												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life[153]												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) Rees (1999) did not report on sequence generation, allocation concealment and blinding; no log-transformation of data was conducted.
(b) The confidence interval crossed both MID points.
(c) No standard deviation was reported. It was unknown if sample size was sufficient.

Table 130: Clinical evidence profile: recombinant platelet-derived growth factor-BB (1.0µg/g) versus placebo

Quality assessment							No of patients		Effect			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**RPDGF-BB (1.0µg/ml)**	**Placebo**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
Proportion of peoples completely healed – denervated people – grade 3 and 4 – classification not reported[159]												
1	Randomised	Very	No serious	No serious	No serious	None	0/4	0/7	Not pooled	Not pooled	Low	Critical

Quality assessment							No of patients		Effect			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**RPDGF-BB (1.0μg/ml)**	**Placebo**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
	trial	serious[a]	inconsistency	indirectness	imprecision		(0%)	(0%)				
							-	0%		Not pooled		
Proportion of people with infection – denervated people – grade 3 and 4 – classification not reported[159]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	0/4 (0%)	0/7 (0%)	Not pooled	Not pooled	Low	Important
							--	0%		Not pooled		
Mortality (all-cause) [159]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	0/4 (0%)	0/7 (0%)	Not pooled	Not pooled	Low	Important
							-	0%		Not pooled		
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate or reduction in size or volume of pressure ulcers												
Reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital												
-	-	-	-	-	-	-	-	-	-	-	-	-
Acceptability of treatment												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) Robson (1992b) did not report on sequence generation, unequal allocation and only blinding of outcome assessor was carried out.

Table 131: Clinical evidence profile: recombinant platelet-derived growth factor-BB (1.0µg/g) versus. recombinant platelet-derived growth factor-BB (10.0µg/g)

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	rPDGF-BB (1.0µg/ml)	rPDGF-BB (10.0µg/ml)	Relative (95% CI)	Absolute	Quality	Importance
Proportion of people completely healed – denervated people – grade 3 and 4 – classification not reported[159]												
1	Randomised trials	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	0/4 (0%)	0/4 (0%)	Not pooled	Not pooled	Low	Critical
							-	0%		Not pooled		
Proportion of people with infection – denervated people – grade 3 and 4 – classification not reported[159]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	0/4 (0%)	0/4 (0%)	Not pooled	Not pooled	Low	Important
							-	0%		Not pooled		
Mortality (all-cause) [159]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	0/4 (0%)	0/4 (0%)	Not pooled	Not pooled	Low	Important
							-	0%	-	Not pooled		
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate or reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital												
-	-	-	-	-	-	-	-	-	-	-	-	-

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	rPDGF-BB (1.0µg/ml)	rPDGF-BB (10.0µg/ml)	Relative (95% CI)	Absolute	Quality	Importance
Acceptability of treatment												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) Robson (1992b) did not report on sequence generation, unequal allocation and only blinding of outcome assessor was carried out.

Table 132: Recombinant platelet-derived growth factor-BB (1.0µg/g) versus recombinant platelet-derived growth factor-BB (100.0µg/g)

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	RPDGF-BB (1.0µg/ml)	rPDGF-BB (100µg/ml)	Relative (95% CI)	Absolute	Quality	Importance
Proportion of people completely healed – denervated people – grade 3 and 4 – classification not reported												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	0/4 (0%)	2/5 (40%)	OR 0.13 (0.01 to 2.52)	320 fewer per 1000 (from 393 fewer to 227 more)	Very low	Critical
							-	40%		320 fewer per 1000 (from 393 fewer to 227 more)		
Proportion of people with infection – denervated people – grade 3 and 4 – classification not reported												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	0/4 (0%)	0/5 (0%)	Not pooled	Not pooled	Low	Important
							-	0%		Not		

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	RPDGF-BB (1.0µg/ml)	rPDGF-BB (100µg/ml)	Relative (95% CI)	Absolute	Quality	Importance
										pooled		
Mortality (all-cause)												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	0/4 (0%)	0/5 (0%)	Not pooled	Not pooled	Low	Important
							-	0%		Not pooled		
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate or reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital												
-	-	-	-	-	-	-	-	-	-	-	-	-
Acceptability of treatment												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) Robson (1992b) did not report on sequence generation, unequal allocation and only blinding of outcome assessor was carried out.
(b) The confidence interval crossed both MID points.

Table 133: Clinical evidence profile: recombinant platelet-derived growth factor-BB (10.0µg/g) versus placebo

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	rPDGF-BB (10.0µg/ml)	Placebo	Relative (95% CI)	Absolute	Quality	Importance
Proportion of people completely healed – denervated people – grade 3 and 4 – classification not reported[159]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	0/4 (0%) -	0/7 (0%) 0%	Not pooled	Not pooled Not pooled	Low	Critical
Proportion of people with infection – denervated people – grade 3 and 4 – classification not reported[159]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	0/4 (0%) -	0/7 (0%) 0%	Not pooled	Not pooled Not pooled	Low	Important
Mortality (all-cause) [159]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	0/4 (0%) -	0/7 (0%) 0%	Not pooled	Not pooled Not pooled	Low	Important
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate of reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital												
-	-	-	-	-	-	-	-	-	-	-	-	-

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	rPDGF-BB (10.0µg/ml)	Placebo	Relative (95% CI)	Absolute	Quality	Importance
Acceptability of treatment												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) Robson (1992b) did no report on sequence generation, unequal allocation and only blinding of outcome assessor was carried out.

Table 134: Clinical evidence profile: recombinant platelet-derived growth factor-BB (10.0µg/g) versus recombinant platelet-derived growth factor-BB (100.0µg/g)

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	rPDGF-BB (10.0µg/ml)	rPDGF-BB (100µg/ml)	Relative (95% CI)	Absolute	Quality	Importance
Proportion of people completely healed – denervated people – grade 3 and 4 – classification not reported [159]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	0/4 (0%)	2/5 (40%)	OR 0.13 (0.01 to 2.52)	320 fewer per 1000 (from 393 fewer to 227 more)	Very low	Critical
								40%		320 fewer per 1000 (from 393 fewer to 227 more)		
Proportion of people with infection – denervated people – grade 3 and 4 – classification not reported												

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	rPDGF-BB (10.0μg/ml)	rPDGF-BB (100μg/ml)	Relative (95% CI)	Absolute		
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	0/4 (0%)	0/5 (0%)	Not pooled	Not pooled	Low	Important
								0%		Not pooled		
Mortality (all-cause)												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	0/4 (0%)	0/5 (0%)	Not pooled	Not pooled	Low	Important
								0%		Not pooled		
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate of reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital												
-	-	-	-	-	-	-	-	-	-	-	-	-
Acceptability of treatment												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) Robson (1992b) did not report on sequence generation, unequal allocation and only blinding of outcome assessor was carried out.
(b) The confidence interval crossed both MID points.

Table 135: Clinical evidence profile: recombinant platelet-derived growth factor-BB (100.0µg/g) versus placebo

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	rPDGF-BB (100uµg/ml)	Placebo	Relative (95% CI)	Absolute		
Proportion of people completely healed – denervated people – grade 3 and 4 – classification not reported[159]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	2/5 (40%)	0/7 (0%) 0%	OR 14.01 (0.73 to 267.29)	400 more (from 30 fewer to 830 more) 400 more (from 30 fewer to 830 more)	Very low	Critical
Mean percentage reduction in ulcer depth – denervated people – grade 3 and 4 – classification not reported[159]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	85.9 (SD 14.8)	65.1 (SD 13.4)	-	MD 20.8 higher (4.47 to 37.13 higher)	Low	Critical
Mean percentage reduction in ulcer volume – denervated people – grade 3 and 4 – classification not reported[159]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	93.6 (SD 4)	78.2 (SD 5.6)	-	MD 15.4 higher (4.54 to 26.26 higher)	Low	Critical
Proportion of people with infection – denervated people – grade 3 and 4 – classification not reported[159]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	0/5 (0%)	0/7 (0%) 0%	Not pooled	Not pooled not pooled	Low	Important

Mortality (all-cause) [159]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	0/5 (0%) 0%	0/7 (0%) 0%	Not pooled Not pooled	Not pooled Not pooled	Low	Important
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate of reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital												
-	-	-	-	-	-	-	-	-	-	-	-	-
Acceptability of treatment												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) Robson (1992b) did not report on sequence generation, unequal allocation and only blinding of outcome assessor; no log-transformation of data was conducted.
(b) The confidence interval crossed both MID points.

Table 136: Clinical evidence profile: basic fibroblast growth factor (different schedules and doses) versus placebo

Quality assessment							No of patients		Effect			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**bFGF**	**Placebo**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
Proportion of people healed 70% or more – denervated people – grade 3 and 4 – classification not reported[158]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	None	21/35 (60%)	4/14 (28.6%)	RR 2.1 (0.88 to 5.02)	314 more per 1000 (from 34 fewer to 1000 more)	Very low	Critical

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	bFGF	Placebo	Relative (95% CI)	Absolute	Quality	Importance
								28.6%		315 more per 1000 (from 34 fewer to 1000 more)		
Mean percentage reduction in volume – denervated people – grade 3 and 4 – classification not reported[158]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[c]	None	69 (n=35)	59 (n=14)	-	Not pooled	Very low	Critical
Mortality (all-cause)[158]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious	None	0/35 (0%)	0/15 (0%)	Not pooled	Not pooled	Low	Important
								0%		Not pooled		
Proportion of people with pressure ulcers completely healed												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate of reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-relate)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital												
-	-	-	-	-	-	-	-	-	-	-	-	-
Acceptability of treatment												
-	-	-	-	-	-	-	-	-	-	-	-	-
Side effects												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	bFGF	Placebo	Relative (95% CI)	Absolute	Quality	Importance
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) Robson (1992a) did not report on sequence generation, unequal allocation and only blinding of outcome assessor; no log-transformation of data was conducted.
(b) The confidence interval crossed 1 MID point.
(c) No standard deviation was reported and the study used a small sample size.

Table 137: Clinical evidence profile: interleukin 1-beta (0.01µg/cm²) versus placebo

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	rIL-1beta (0.01µg/cm²)	Placebo	Relative (95% CI)	Absolute		
Proportion of people completely healed – denervated people – grade 3 and 4– classification not reported[156]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	0/6 (0%)	0/6 (0%)	Not pooled	Not pooled	Low	Critical
								0%		Not pooled		
Mortality (all-cause)[156]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	0/6 (0%)	0/6 (0%)	Not pooled	Not pooled	Low	Important
								0%		Not pooled		
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate of reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	rIL-1beta (0.01µg/cm²)	Placebo	Relative (95% CI)	Absolute		
Time in hospital												
-	-	-	-	-	-	-	-	-	-	-	-	-
Acceptability of treatment												
-	-	-	-	-	-	-	-	-	-	-	-	-
Side effects												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												

(a) Robson (1994) did not report on sequence generation, allocation concealment and report of double blinding, but no further information was provided.

Table 138: Clinical evidence profile: interleukin 1-beta (0.01µg/cm²) versus interleukin 1-beta (0.1µg/cm²)

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	rIL-1beta (0.01µg/cm²)	rIL-1beta (0.1µg/cm²)	Relative (95% CI)	Absolute		
Proportion of people completely healed – denervated people – grade 3 and 4 – classification not reported												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	0/6 (0%)	0/6 (0%)	Not pooled	Not pooled	Low	Critical
							-	0%		Not pooled		
Mortality (all-cause)												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	0/6 (0%)	0/6 (0%)	Not pooled	Not pooled	Low	Important
							-	0%		Not pooled		
Time to complete healing of pressure ulcers												

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	rIL-1beta (0.01µg/cm²)	rIL-1beta (0.1µg/cm²)	Relative (95% CI)	Absolute	Quality	Importance
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate of reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital												
-	-	-	-	-	-	-	-	-	-	-	-	-
Acceptability of treatment												
-	-	-	-	-	-	-	-	-	-	-	-	-
Side effects												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) Robson (1994) did not report on sequence generation, allocation concealment and report of double blinding, but no further information was provided.

Table 139: Clinical evidence profile: interleukin 1-beta (0.01µg/cm²) versus interleukin 1-beta (1.0µg/cm²)

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	rIL-1beta (0.01µg/cm²)	rIL-1beta (1.0µg/cm²)	Relative (95% CI)	Absolute	Quality	Importance
Proportion of people completely healed – denervated people – grade 3 and 4 – classification not reported[156]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	0/6 (0%)	0/6 (0%)	Not pooled	Not pooled	Low	Critical
							-	0%		Not		

Quality assessment							No of patients		Effect			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**rIL-1beta (0.01µg/cm²)**	**rIL-1beta (1.0µg/cm²)**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
										pooled		
Mortality (all-cause)[156]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	0/6 (0%)	0/6 (0%)	Not pooled	Not pooled	Low	Important
							-	0%		Not pooled		
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate of reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital												
-	-	-	-	-	-	-	-	-	-	-	-	-
Acceptability of treatment												
-	-	-	-	-	-	-	-	-	-	-	-	-
Side effects												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) Robson (1994) did not report on sequence generation, allocation concealment and report of double blinding, but no further information was provided.

Table 140: Clinical evidence profile: interleukin 1-beta (0.1µg/cm²) versus placebo

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	rIL-1beta (0.1µg/cm²)	Placebo	Relative (95% CI)	Absolute	Quality	Importance
Proportion of people completely healed – denervated people – grade 3 and 4 – classification not reported[156]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	0/6 (0%)	0/6 (0%)	Not pooled	Not pooled	Low	Critical
							-	0%		Not pooled		
Mortality (all-cause) [156]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	0/6 (0%)	0/6 (0%)	Not pooled	Not pooled	Low	Important
							-	0%	-	Not pooled		
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate of reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital												
-	-	-	-	-	-	-	-	-	-	-	-	-
Acceptability of treatment												
-	-	-	-	-	-	-	-	-	-	-	-	-
Side effects												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	rIL-1beta (0.1µg/cm²)	Placebo	Relative (95% CI)	Absolute	Quality	Importance
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) Robson (1994) did not report on sequence generation, allocation concealment and report of double blinding, but no further information was provided.

Table 141: Clinical evidence profile: interleukin 1-beta (0.1µg/cm²) versus interleukin 1-beta (1.0µg/cm²)

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	rIL-1beta (0.1µg/cm²)	rIL-1beta (1.0µg/cm²)	Relative (95% CI)	Absolute	Quality	Importance
Proportion of people completely healed – denervated people – grade 3 and 4 – classification not reported[156]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	0/6 (0%)	0/6 (0%)	Not pooled	Not pooled	Low	Critical
							-	0%		Not pooled		
Mortality (all-cause)[156]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	0/6 (0%)	0/6 (0%)	Not pooled	Not pooled	Low	Important
							-	0%	-	Not pooled		
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate of reduction in size or volume of pressure ulcers												
Reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	rIL-1beta (0.1µg/cm²)	rIL-1beta (1.0µg/cm²)	Relative (95% CI)	Absolute	Quality	Importance
Time in hospital												
-	-	-	-	-	-	-	-	-	-	-	-	-
Acceptability of treatment												
-	-	-	-	-	-	-	-	-	-	-	-	-
Side effects												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) Robson (1994) did not report on sequence generation, allocation concealment and report of double blinding, but no further information was provided.

Table 142: Clinical evidence profile: interleukin 1-beta (1.0µg/cm²) versus placebo

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	rIL-1beta (1.0µg/cm²)	Placebo	Relative (95% CI)	Absolute	Quality	Importance
Proportion of people completely healed – denervated people – grade 3 and 4 – classification not reported[156]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	0/6 (0%)	0/6 (0%)	Not pooled	Not pooled	Low	Critical
							-	0%		Not pooled		
Mortality (all-cause) [156]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	0/6 (0%)	0/6 (0%)	Not pooled	Not pooled	Low	Important
							-	0%	-	Not pooled		
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate of reduction in size or volume of pressure ulcers												

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	rIL-1beta (1.0µg/cm²)	Placebo	Relative (95% CI)	Absolute	Quality	Importance
-	-	-	-	-	-	-	-	-	-	-	-	-
Reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital												
-	-	-	-	-	-	-	-	-	-	-	-	-
Acceptability of treatment												
-	-	-	-	-	-	-	-	-	-	-	-	-
Side effects												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) Robson (1994) did not report on sequence generation, allocation concealment and report of double blinding, but no further information was provided.

Table 143: Clinical evidence profile: chlorinated lime solution versus dextranomer

Quality assessment							No of patients/ulcers		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Chlorinated lime solution	Dextranomer	Relative (95% CI)	Absolute	Quality	Importance
Time to healing (defined as granulation and less than 25% of original ulcer area) (days) – elderly adults – grade not reported – classification system not reported[129]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	None	61.8 (SD 13.86)	39.3 (SD 17.67)	-	MD 22.5 higher (3.86 to 41.14 higher)	Very low	Critical

Quality assessment							No of patients/ulcers		Effect			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Chlorinated lime solution**	**Dextranomer**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
Proportion of people with pain – elderly adults– grade not reported – classification system not reported[129]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[c]	None	3/?	1/?	Not pooled	Not pooled	Very low	Important
							-	-		Not pooled		
Mortality[129]												
1	Randomised trial	Very seriousa	No serious inconsistency	No serious indirectness	Very serious[c]	None	0/8 (0%)	1/8 (12.5%)	OR 0.14 (0 to 6.82)	105 fewer per 1000 (from 125 fewer to 368 more)	Very low	Important
							-	12.5%	-	105 fewer per 1000 (from 125 fewer to 368 more)		
Proportion of people with pressure ulcers completely healed												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time to complete healing (time to event data)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate of reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Reduction in size or volume of pressure ulcers												

Quality assessment							No of patients/ulcers		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Chlorinated lime solution	Dextranomer	Relative (95% CI)	Absolute	Quality	Importance
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital												
-	-	-	-	-	-	-	-	-	-	-	-	-
Acceptability of treatment												
-	-	-	-	-	-	-	-	-	-	-	-	-
Side effects												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) No report on allocation concealment, sequence generation, blinding; no ITT analysis.
(b) The confidence interval crossed 1 MID point.
(c) It was unclear how many people were included in each group

10.1.2 Economic evidence (adults)

Published literature

One study was included which compared saline soaked gauze to a polyurethane self-adhesive foam dressing.[148] This is summarised in the economic evidence profile below (Table 144). See also the study selection flow chart in Appendix D and study evidence tables in Appendix H.

One study that met the inclusion criteria was selectively excluded due to methodological limitations[157] – this is summarised in Appendix K, with reasons for exclusion given.

Table 144: Economic evidence profile: saline soaked gauze verses polyurethane self-adhesive foam dressing

Study	Applicability	Limitations	Other comments	Incremental cost	Incremental effects	Cost effectiveness	Uncertainty
Payne 2009[148] (US)	Partially applicable[a]	Minor limitations[b]	Within trial analysis with analysis of individual level resource use. Patients randomised to receive saline soaked gauze or polyurethane self-adhesive foam dressing.	-£301	Pressure ulcer free days: 2.4 Ulcers healed by day 28: 12%	Polyurethane self-adhesive foam dressing dominates saline soaked gauze	Costs for patients who dropped out were included only up until the point of withdrawal in a deterministic sensitivity analysis.[c] The foam dressing remained dominant compared to saline soaked gauze.

(a) The analysis is based in the US; quality of life is not considered

(b) All resource use and health outcomes are obtained from within the trial rather than via a systematic procedure. The cost of the saline soaked gauze is calculated to be the same cost as the foam dressing. Exploration of uncertainty is inadequate. There is also a potential conflict of interest as the study is carried out by manufacturer of the foam dressing.

(c) In the base case analysis, per day treatment costs were continued until the 28 day time horizon even if the patient withdrew from the trial

10.1.3 Clinical evidence (neonates, infants, children and young people)

No RCTs or cohort studies were identified. Recommendations were developed using a modified Delphi consensus technique. Further details can be found in Appendix N.

10.1.4 Economic evidence (neonates, infants, children and young people)

No relevant economic evidence was identified.

10.1.5 Evidence statements

10.1.5.1 Clinical (adults)

10.1.5.1.1 Saline-soaked gauze versus hydrocolloid dressing

- Three studies (n=126) (general population and people with a spinal cord injury) showed that hydrocolloid dressing is potentially more clinically effective than saline-soaked gauze for complete healing of (grade 1 and above pressure ulcers) (very low quality).
- Two studies (n=71) (general population) showed that hydrocolloid is potentially more clinically effective compared to saline for complete healing of (grade 1 and above pressure ulcers) (very low quality).
- One study (n=55) (people with a spinal cord injury) showed that hydrocolloid is potentially clinically more effective than saline for complete healing of pressure ulcers (grade 1 and 2) (low quality).
- Two studies (n=148) (general population and people with a spinal cord injury) showed that a hydrocolloid is potentially more effective compared to saline for complete healing of pressure ulcers (grade 1 to 3) (very low quality).
- One study (n=87) (general population) showed that a hydrocolloid may be more clinically effective compared to saline for complete healing of pressure ulcers (grade 2 to 3) (very low quality).
- One study (n=61) (people with a spinal cord injury) showed that a hydrocolloid is clinically more effective compared to saline for complete healing of pressure ulcers (grade 1 to 2) (moderate quality).
- One study (n=24) (people with a spinal cord injury) showed that a hydrocolloid is potentially more clinically effective compared to saline for complete healing of pressure ulcers (grade 1) (low quality).
- Two studies (n=96) (general population and people with a spinal cord injury) showed that a hydrocolloid is more clinically effective compared to saline for complete healing of pressure ulcers (grade 2) (low quality).
- One study (n=59) (general population) showed that that a hydrocolloid is more clinically effective compared to saline for complete healing of pressure ulcers (grade 2) (low quality).
- One study (n=37) (people with a spinal cord injury) showed that that a hydrocolloid is more clinically effective compared to saline for complete healing of pressure ulcers (grade 2) (moderate quality).
- One study (n=28) (general population) showed that there may be no clinical difference between saline and a hydrocolloid for complete healing of pressure ulcers (grade 3), the direction of the estimate of the effect favoured the hydrocolloid dressing (very low quality).
- One study (n=15) (people with a spinal cord injury) showed that a hydrocolloid is potentially more clinically effective compared to saline for complete healing of pressure ulcers (grade 1 and 2) (sacral area) (very low quality).

- One study (n=91) (people with a spinal cord injury) showed that a hydrocolloid is more clinically effective compared to saline to improve healing of pressure ulcers (grade 1 and 2) (moderate quality).
- Two studies (n=148) (general population and people with a spinal cord injury) showed saline may be more clinically harmful than a hydrocolloid dressing for worsening of pressure ulcers (grade 1 to 3) (all sites) (very low quality).
- One study (n=87) (general population) showed that there may be no difference between saline and a hydrocolloid for worsening of pressure ulcers (grade 2 and 3), the direction of the estimate of the effect could favour either intervention (very low quality).
- One study (n=61) (people with a spinal cord injury) showed that a hydrocolloid is potentially more clinically effective compared to saline to reduce pressure ulcers worsening (grade 1 and 2) (all sites) (very low quality).
- One study (n=59) (general population) showed that there may be no clinical difference between saline and a hydrocolloid for worsening of pressure ulcers (grade 2), the direction of the estimate of the effect favoured the hydrocolloid dressing (very low quality).
- One study (n=28) (general population) showed that there may be no clinical difference between saline and a hydrocolloid for worsening of pressure ulcers (grade 3) , the direction of the estimate of the effect favoured the hydrocolloid dressing (very low quality).
- One study (n=34) (general population) showed that there is potentially no clinical difference between saline and a hydrocolloid for mean percentage reduction in pressure ulcer area (grade 2 and 3), the direction of the estimate of the effect favoured the hydrocolloid dressing (very low quality).
- One study (n=32) (general population) showed that saline is more clinically effective for mean percentage reduction in pressure ulcer volume (grade 3 and 4) (low quality).
- One study (n=50) (people in long-term care) reported a median percentage reduction in pressure ulcer area (grade not reported) for saline and a hydrocolloid. The median for saline was 85.7% and 100% for hydrocolloid. No estimate of effect or precision could be derived (very low quality).
- One study (n=59) (general population) reported a median percentage reduction in ulcer size (grade 2) for saline and a hydrocolloid. The median for saline was 48% and 91% for hydrocolloid. A p-value > 0.05 was reported (very low quality).
- One study (n=28) (general population) reported a median percentage reduction in pressure ulcer size (grade 3) for saline and a hydrocolloid. The median for saline was 30% and 0.3% for hydrocolloid. A p-value > 0.05 was reported (very low quality).
- One study (n=39) (people in long-term care) reported median days to healing of pressure ulcers (grade 2 and 3) for saline and a hydrocolloid. The median for saline was 11 days and 9 days for hydrocolloid. A p-value of 0.12 was reported (very low quality).
- One study (n=50) (people in long-term care) reported a healing distribution function (grade not reported) for saline and a hydrocolloid. A p-value of 0.15 was reported (very low quality).
- One study (n=34) (general population) showed that saline is more clinically effective compared to a hydrocolloid in terms of pain at dressing removal (low quality).
- One study (n=32) (general population) reported a median pain score during treatment (grade 3 and 4) for saline and a hydrocolloid. The median for saline was 2.0 (range 1-3) and 2.0 (range1-4) for hydrocolloid. No estimate of effect or precision could be derived (very low quality).
- One study (n=34) (general population) showed that saline is more clinically effective compared to a hydrocolloid in terms of discomfort at dressing removal (low quality).
- One study (n=32) (general population) reported a median comfort score during treatment (grade 3 and 4) for saline and a hydrocolloid. The median for saline was 3.0 (range 2-4) and 4.0 (range 3-4) for hydrocolloid. No estimate of effect or precision could be derived (very low quality).

- One study (n=34) (general population) showed no clinical difference between saline and a hydrocolloid to reduce the incidence of infections (grade 2 and 3) (low quality).
- One study (n=32) (general population) reported a median comfort score during treatment (grade 3 and 4) for saline and a hydrocolloid. The median for saline was 2.0 (range 1-4) and 2.0 (range 1-3) for hydrocolloid. No estimate of effect or precision could be derived (very low quality).
- One study (n=100) (general population) showed that saline is more clinically effective compared to hydrocolloid to reduce the incidence of skin irritation (very low quality).
- One study (n=160) (general and spinal cord injured population) showed that there may be no clinical difference between saline and hydrocolloid for mortality (all-cause)(grade 1 and above pressure ulcers) (very low quality).
- No evidence was found for the outcomes:
  - Time to complete healing
  - Time in hospital

10.1.5.1.2 Saline-soaked gauze versus hydrogel dressing

- One study (n=30) (general population) showed that there may be no clinical difference between saline and hydrogel for complete healing of pressure ulcers (grade 2 to 4), the direction of the estimate of the effect favoured the saline (very low quality).
- One study (n=41) (general population) showed that there may be no clinical difference between saline and hydrogel for worsening of pressure ulcers (grade 2 to 4 pressure ulcers), the direction of the estimate of the effect favoured the hydrogel (very low quality).
- One study (n=30) (general population) reported a percentage healing rate of pressure ulcers (grade 2 to 4) for saline and hydrogel. The rate for saline was 64% and 63% for hydrogel. No estimate of effect or precision could be derived (very low quality).
- One study (n=30) (general population) showed that there may be no clinical difference between saline and hydrogel for mean weeks to healing of pressure ulcers (grade 2 to 4), the direction of the estimate of the effect favoured the hydrogel (very low quality).
- One study (n=41) (general population) showed there may be no clinical difference between saline and hydrogel for mortality (all-cause) (grade 2 to 4 pressure ulcers) (very low quality).
- No evidence was found for the following outcomes:
  - Time to complete healing (time to event data)
  - Pain (wound-related)
  - Time in hospital
  - Acceptability of treatment
  - Side effects
  - Health-related quality of life

10.1.5.1.3 Saline-soaked gauze versus foam dressing

- Two studies (n=74) (general population) showed that a foam dressing is potentially more clinically effective compared to saline for complete healing of pressure ulcers (grade 2 and 3) (very low quality).
- One study (n=36) (general population) reported a median days to healing of 50% of the patients (grade II) for saline and a foam. The median for both saline and hydrogel of 28 days. No estimate of effect or precision could be derived (very low quality).
- Two studies (n=74) (general population) showed there is potentially no clinical difference between a foam dressing and saline for mortality (grade 2 and 3 pressure ulcers) (very low quality).

- No evidence was found for the following outcomes:
  - Time to complete healing (time to event data)
  - Rate of reduction in size and volume of pressure ulcers
  - Reduction in size and volume of pressure ulcers
  - Pain (wound-related)
  - Time in hospital
  - Acceptability of treatment
  - Side effects
  - Health-related quality of life

10.1.5.1.4 Saline-soaked gauze versus polyurethane dressing

- One study (n=19) (general population) showed that a polyurethane dressing may be more clinically effective compared to saline at complete healing of pressure ulcers (grade 1 and 2)(very low quality).
- One study (n=19) (general population) showed that a polyurethane dressing may be more clinically effective compared to saline to reduce pressure ulcers worsening (grade 1 and 2 pressure ulcers) (very low quality).
- One study (n=19) (general population) reported a mean percentage reduction in pressure ulcer area (grade 1 and 2) for saline and polyurethane. The mean for saline was 2.5% and 42.9% for polyurethane. No estimate of effect or precision could be derived (very low quality).
- No evidence was found for the following outcomes:
  - Time to complete healing of pressure ulcers
  - Rate of reduction in size or volume of pressure ulcers
  - Pain (wound-related)
  - Time in hospital
  - Acceptability of treatment
  - Side effects
  - Mortality (all-cause)
  - Health-related quality of life

10.1.5.1.5 Saline-soaked gauze versus dextranomer

- One study (n=30) (people with a spinal cord injury) showed that dextranomer is more clinically effective to improve healing of pressure ulcers (grade 2 to 4) (low quality).
- One study (n=30) (people with a spinal cord injury) showed no clinical difference for incidence of adverse events between saline and dextranomer (low quality).
- No evidence was found for the following outcomes:
  - Proportion of people with pressure ulcers completely healed
  - Time to complete healing of pressure ulcers
  - Rate of reduction in size or volume of pressure ulcers
  - Reduction in size or volume of pressure ulcers
  - Pain (wound-related)
  - Time in hospital
  - Acceptability of treatment

- Side effects
- Mortality (all-cause)

10.1.5.1.6 Phenytoin versus saline-soaked gauze

- One study (n=55) (people with a spinal cord injury) showed that phenytoin may be more clinically effective compared to saline for proportion of people with complete healing of pressure ulcers (grade 1 and 2) (very low quality).
- One study (n=60) (people with a spinal cord injury) showed that phenytoin may be more clinically effective compared to saline for complete healing of pressure ulcers (grade 1 and 2) (very low quality).
- One study (n=40) (people with a spinal cord injury) showed that phenytoin is potentially more clinically effective compared to saline for complete healing of pressure ulcers (grade 2) (very low quality).
- One study (n=60) (people with a spinal cord injury) showed that phenytoin may be more clinically effective than saline for improved healing of pressure ulcers (grade 1 and 2) (very low quality).
- One study (n=60) (people with a spinal cord injury) showed that phenytoin is potentially more clinically effective compared to saline to reduce pressure ulcer worsening (grade 1 and 2) (very low quality).
- One study (n=26) (people with a spinal cord injury) showed that phenytoin is potentially more clinically effective compared to saline for mean percentage reduction in pressure ulcer size (grade 2) (very low quality).
- One study (n=26) (people with a spinal cord injury) showed that there may be no clinical difference between phenytoin and saline for mean percentage reduction in pressure ulcer volume (grade 2) (very low quality).
- One study (n=26) (people with a spinal cord injury) showed that phenytoin may be more clinically effective compared to saline for mean percentage reduction in PUSH score (grade 2) (very low quality).
- One study (n=30) (people with a spinal cord injury) showed no clinical difference for incidence of adverse events between saline and phenytoin, the direction of the estimate of effect favoured (low quality).
- Two studies (n=84) showed no clinical difference between phenytoin and saline for mortality (all-cause), the direction of the estimate of effect favoured either intervention (moderate quality).
- No evidence was found for the following outcomes:
  - Time to complete healing of pressure ulcers
  - Rate of reduction in size or volume of pressure ulcers
  - Pain (wound-related)
  - Time in hospital
  - Acceptability of treatment
  - Side effects
  - Health-related quality of life

10.1.5.1.7 Phenytoin versus hydrocolloid dressing

- One study (n=56) (people with a spinal cord injury) showed that a hydrocolloid is potentially more clinically effective compared to phenytoin for proportion of people with complete healing of pressure ulcers (grade 1 and 2) (low quality).

- One study (n=61) (people with a spinal cord injury) showed that a hydrocolloid is potentially more clinically effective compared to phenytoin for pressure ulcers completely healed (grade 1 and 2 pressure ulcers) (low quality).
- One study (n=22) (people with a spinal cord injury) showed that a hydrocolloid is potentially more clinically effective compared to phenytoin for pressure ulcers completely healed (grade 1) (low quality).
- One study (n=39) (people with a spinal cord injury) showed that a hydrocolloid is potentially more clinically effective compared to phenytoin for pressure ulcers completely healed (grade 2) (low quality).
- One study (n=15) (people with a spinal cord injury) showed that there may be no clinical difference between phenytoin and a hydrocolloid for complete healing of pressure ulcers (grade 1 and 2) in the sacral area (very low quality).
- One study (n=61) (people with a spinal cord injury) showed that a hydrocolloid is potentially more clinically effective compared to phenytoin to improve healing pressure ulcers (grade 1 and 2) (low quality).
- One study (n=61) (people with a spinal cord injury) showed that there may be no clinical difference between phenytoin and a hydrocolloid for pressure ulcer worsening (grade 1 and 2 pressure ulcers) (very low quality).
- One study (n=28) (people in a nursing home) showed that phenytoin is potentially more clinically effective compared to a hydrocolloid for mean days to healing (grade 2 pressure ulcers) (low quality).
- One study (n=28) (people in a nursing home) reported minimal pain in people receiving phenytoin and a hydrocolloid dressing (grade 2 pressure ulcers). No estimate of effect or precision could be derived (very low quality).
- One study (n=28) (people in a nursing home) showed no clinical difference between phenytoin and a hydrocolloid to reduce the incidence of adverse events (grade 2 pressure ulcers) (low quality).
- Two studies (n=90) (people in a nursing home) showed there may be no clinical difference between phenytoin and a hydrocolloid for mortality (all-cause) (grade 2 pressure ulcers), the direction of the estimate of effect could favoured phenytoin (low quality).
- No evidence was found for the following outcomes:
  - Time to complete healing of pressure ulcers (time to event data)
  - Rate of reduction in size or volume of pressure ulcedrs
  - Reduction in size or volume of pressure ulcers
  - Time in hospital
  - Acceptability of treatment
  - Health-related quality of life

10.1.5.1.8 Phenytoin versus triple antibiotics

- One study (n=26) (people in a nursing home) showed that phenytoin is clinically more effective compared to triple antibiotics for mean days to healing (grade 2) (low quality).
- One study (n=26) (people in a nursing home) reported minimal pain in people receiving phenytoin and triple antibiotics. No estimate of effect or precision could be derived (very low quality).
- One study (n=26) (people in a nursing home) showed no clinical difference between phenytoin and triple antibiotics to reduce the incidence of adverse events (low quality).
- One study (n=26) (people in a nursing home) showed there may be no clinical difference between phenytoin and triple antibiotics for mortality (all-cause) (very low quality).

- No evidence was found for the following outcomes:
  - Proportion of people with pressure ulcers completely healed
  - Time to complete healing of pressure ulcers
  - Time to complete healing (time to event data)
  - Rate of reduction in size or volume of pressure ulcers
  - Reduction in size or volume of pressure ulcers
  - Time in hospital
  - Acceptability of treatment
  - Health-related quality of life

10.1.5.1.9 Aloe vera, silver chloride and decyl glucoside versus saline

- One study (number of participants) (elderly adults) reported a mean percentage reduction in PSST score (grade 2 to 4 pressure ulcers) for aloe vera, solver chloride and decyl glucoside versus saline. The mean for aloe vera was 22.7% and 20.5% for saline. No estimate of effect or precision could be derived (very low quality).
- No evidence was found for the following outcomes:
  - Proportion of people with pressure ulcers completely healed
  - Time to complete healing of pressure ulcers
  - Rate of reduction in size or volume of pressure ulcers
  - Reduction in size or volume of pressure ulcers
  - Pain (wound-related)
  - Time in hospital
  - Acceptability of treatment
  - Side effects
  - Mortality (all-cause)
  - Health-related quality of life

10.1.5.1.10 Dialysate versus placebo

- One study (n=8) (people with a spinal cord injury) showed that dialysate is potentially more clinically effective compared to placebo for reducing mean ml in pressure ulcer area (very low quality).
- One study (n=8) (people with a spinal cord injury) reported mean percentage reduction in pressure ulcer area at day 10 for dialysate and placebo. The mean for dialysate was 39% and 28% for placebo. No estimate of effect or precision could be derived (very low quality).
- One study (n=8) (people with a spinal cord injury) reported mean percentage reduction in pressure ulcer area at day 20 for dialysate and placebo. The mean for dialysate was 80% and 59% for placebo. No estimate of effect or precision could be derived (very low quality).
- One study (n=8) (people with a spinal cord injury) showed that dialysate is potentially more clinically effective compared to placebo for mean healing half-time (very low quality).
- One study (n=8) (people with a spinal cord injury) showed no clinical difference between dialysate and placebo for treatment-related adverse events (low quality).
- No evidence was found for the following outcomes:
  - Proportion of people with pressure ulcers completely healed
  - Time to complete healing of pressure ulcers

- Rate of reduction in size or volume of pressure ulcers
- Pain (wound-related)
- Time in hospital
- Acceptability of treatment
- Mortality (all-cause)
- Health-related quality of life

10.1.5.1.11 Petrolatum ointment versus petrolatum (base component)

- One study (n=19) (elderly people) showed that petrolatum ointment may be more clinically effective compared to petrolatum (base component) for pressure ulcers completely healed (grade 1 and 2 pressure ulcers) (very low quality).
- One study (n=8) (elderly people) showed that petrolatum ointment may be more clinically effective compared to petrolatum (base component) for pressure ulcers completely healed (grade 2 pressure ulcers) (very low quality).
- One study (n=19) (elderly people) showed that petrolatum ointment may be more clinically effective compared to petrolatum (base component) to improve healing of pressure ulcers (grade 1 and 2) (very low quality).
- One study (n=8) (elderly people) showed that petrolatum ointment may be more clinically effective compared to petrolatum (base component) to improve healing of pressure ulcers (grade 2) (very low quality).
- One study (n=19) (elderly people) showed that petrolatum ointment is clinically more clinically effective compared to petrolatum (base component) to reduce pressure ulcers (grade 1 and 2) worsening (low quality).
- One study (n=8) (elderly people) showed that petrolatum ointment is clinically more effective compared to petrolatum (base component) to reduce pressure ulcers (grade 2) worsening (low quality).
- One study (n=19) (elderly people) showed no clinical difference between petrolatum ointment and petrolatum (base component) for mortality (grade 2 pressure ulcers) (low quality).
- No evidence was found for the following outcomes:
  - Time to complete healing of pressure ulcers
  - Rate of reduction in size or volume of pressure ulcers
  - Reduction in size or volume of pressure ulcers
  - Pain (wound-related)
  - Time in hospital
  - Acceptability of treatment
  - Side effects
  - Health-related quality of life

10.1.5.1.12 Zinc oxide versus streptokinase-streptodornase

- One study (n=28) (elderly people) reported a median percentage reduction in pressure ulcer area (necrotic PUs) for zinc oxide and streptokinase-streptodornase. The median for zinc oxide was 24% and -18.7% for streptokinase-streptodornase. No estimate of effect or precision could be derived (very low quality).

- One study (n=28) (elderly people) showed that there may be no clinical difference between zinc oxide and streptokinase-streptodornase for reducing the incidence of infections, the direction of effect favoured zinc oxide (very low quality).
- One study (n=28) (elderly people) showed that there may be no clinical difference between zinc oxide and streptokinase-streptodornase for reducing the incidence of skin reactions, the direction of effect favoured zinc oxide (very low quality).
- One study (n=28) (elderly people) showed no clinical difference between zinc oxide and streptokinase-streptodornase for mortality (all-cause), the direction of the estimate of effect favoured either direction (low quality).
- No evidence was found for the following outcomes:
  - Proportion of people with pressure ulcers completely healed
  - Time to complete healing of pressure ulcers
  - Rate of reduction in size or volume of pressure ulcers
  - Pain (wound-related)
  - Time in hospital
  - Acceptability of treatment
  - Side effects
  - Health-related quality of life

10.1.5.1.13 Oxyquinoline versus vitamin A&D treatment (cream)

- One study (n=137) (people receiving palliative care) showed that oxyquinoline is potentially more clinically effective compared to Vitamin A&D treatment (cream) for pressure ulcers completely healed (grade 1 and 2) (very low quality).
- One study (n=68) (people receiving palliative care) showed that oxyquinoline is potentially more clinically effective compared to Vitamin A&D treatment (cream) for pressure ulcers completely healed (grade 2) (very low quality).
- One study (n=69) (people receiving palliative care) showed that oxyquinoline is potentially more clinically effective compared to Vitamin A&D treatment (cream) to improve healing of pressure ulcers (grade 1) (very low quality).
- One study (n=68) (people receiving palliative care) showed that there may be no clinical difference between oxyquinoline and Vitamin A&D treatment (cream) to improve healing of pressure ulcers (grade 2), the direction of the estimate of the effect favoured the oxyquinoline (very low quality).
- One study (n=68) (people receiving palliative care) showed that oxyquinoline may be more clinically effective compared to Vitamin A&D treatment (cream) to reduce the incidence of pressure ulcers (grade 2) not changed (very low quality).
- One study (n=69) (people receiving palliative care) showed no clinical difference between oxyquinoline and Vitamin A&D treatment (cream) to reduce the incidence of pressure ulcers (grade 1) worsened (very low quality).
- One study (n=68) (people receiving palliative care) showed that oxyquinoline may be more clinically effective compared to Vitamin A&D treatment (cream) to reduce the incidence of pressure ulcers (grade 2) worsening (very low quality).
- One study (n=137) (people receiving palliative care) showed that there is potentially no clinical difference between oxyquinoline and Vitamin A&D treatment (cream) for mean days to complete healing of pressure ulcers (grade 1 and 2), the direction of the estimate of the effect favoured the oxyquinoline (very low quality).

- One study (n=69) (people receiving palliative care) showed that there is potentially no clinical difference between oxyquinoline and Vitamin A&D treatment (cream) for mean days to complete healing of pressure ulcers (grade 1), the direction of the estimate of the effect favoured the oxyquinoline (very low quality).
- One study (n=68) (people receiving palliative care) showed that oxyquinoline is more clinically effective compared to Vitamin A&D treatment (cream) for mean days to complete healing of pressure ulcers (grade 2) (low quality).
- No evidence was found for the following outcomes:
  - Time to complete healing (time to event data)
  - Rate of reduction in size or volume of pressure ulcers
  - Reduction in size or volume of pressure ulcers
  - Pain (wound-related)
  - Time in hospital
  - Acceptability of treatment
  - Side effects
  - Mortality (all-cause)
  - Health-related quality of life

10.1.5.1.14 Ethoxy-diaminoacridine plus nitrofuazone versus honey

- One study (n=50) (general populations) showed that honey is clinically more clinically effective compared to ethoxy-diaminoacridine plus nitrofuazone for pressure ulcers completely healed (grade 2 and 3) (low quality).
- One study (n=50) (general populations) showed that honey is clinically more clinically effective compared to ethoxy-diaminoacridine plus nitrofuazone for mean percentage reduction in PUSH score (grade 2 and 3 pressure ulcers) (low quality).
- One study (n=50) (general populations) showed that honey is clinically more clinically effective compared to ethoxy-diaminoacridine plus nitrofuazone for mean percentage reduction in ulcer size (grade 2 and 3 pressure ulcers) (low quality).
- One study (n=50) (general populations) showed that there is no clinical difference between honey and ethoxy-diaminoacridine plus nitrofuazone to reduce the incidence of treatment-related adverse events, the direction of the estimate of effect could favour either intervention (low quality).
- One study (n=50) (general populations) showed that there is no clinical difference between honey and ethoxy-diaminoacridine plus nitrofuazone for mortality (all-cause), the direction of the estimate of effect favours honey (low quality).
- No evidence was found for the following outcomes:
  - Time to complete healing
  - Rate or reduction n in size or volume of pressure ulcers
  - Pain (wound-related)
  - Time in hospital
  - Acceptability of treatment
  - Health-related quality of life

10.1.5.1.15 Povidone-iodine versus hydrocolloid dressing

- One study (n=44) (general populations) showed that there may be no clinical difference between povidone-iodine and hydrocolloid for proportion of people with pressure ulcers completely healed (grade 1 and 2), the direction of the estimate of the effect favoured the hydrocolloid (very low quality).
- One study (n=44) (general populations) reported percentage healing rate for povidone-iodine and hydrocolloid. The healing rate for povidone-iodine was 77.8% and 80.8% for hydrocolloid dressing. No estimate of effect or precision could be derived (very low quality).
- One study (n=44) (general populations) showed that a hydrocolloid is potentially more clinically effective compared to povidone-iodine for mean speed of healing of pressure ulcers (grade 1 and 2) (very low quality).
- One study (n=44) (general populations) showed that a hydrocolloid dressing may be more clinically effective for increasing hypergranulation than povidone-iodine (grade 1 and 2 pressure ulcers) (very low quality).
- One study (n=44) (general populations) showed that there may be no clinical difference between povidone-iodine and hydrocolloid for mortality (all-cause) (grade 1 and 2 pressure ulcers), the direction of the estimate of effect could favour either direction (very low quality).
- No evidence was found for the following outcomes:
  - Time to complete healing of pressure ulcers
  - Reduction in size or volume of pressure ulcers
  - Pain (wound-related)
  - Time in hospital
  - Acceptability of treatment
  - Health-related quality of life

10.1.5.1.16 Povidone-iodine versus hydrogel dressing

One study (n=49) (general populations) showed that there is potentially no clinical difference between hydrogel and povidone-iodine for mean speed of healing of pressure ulcers, the direction of the estimate of effect favours hydrogel (grade 1 to 3 pressure ulcers) (very low quality).

- No evidence was found for the following outcomes:
  - Proportion of people with pressure ulcers completely healed
  - Time to complete healing of pressure ulcers
  - Reduction in size or volume of pressure ulcers
  - Pain (wound-related)
  - Time in hospital
  - Acceptability of treatment
  - Side effects
  - Mortality (all-cause)
  - Health-related quality of life

10.1.5.1.17 Cadexomer iodine versus standard treatment

- One study (n=34) (general populations) showed that cadexomer iodine is more clinically effective compared to standard treatment to reduce the proportion of deep and superficial pressure ulcers healed by 50% (low quality).

- One study (n=34) (general populations) showed there is no clinical difference between cadexomer iodine and standard treatment for mean cm^2 reduction in pressure ulcer area, the direction of the estimate of effect favours cadexomer iodine (low quality).
- One study (n=34) (general populations) showed that there is no clinical difference between cadexomer iodine and standard treatment for mean percentage reduction in pressure ulcer area, the direction of the estimate of effect favoured cadexomer iodine (low quality).
- One study (n=34) (general populations) showed there is no clinical difference between cadexomer iodine and standard treatment for mortality (all-cause) (low quality).
- No evidence was found for the following outcomes:
  - Proportion of people with pressure ulcers completely healed
  - Time to complete healing of pressure ulcers
  - Rate of reduction in size or volume of pressure ulcers
  - Pain (wound-related)
  - Time in hospital
  - Acceptability of treatment
  - Side effects
  - Health-related quality of life

10.1.5.1.18 Silver sulfazidine cream versus silver dressing

- One study (n=40) (general populations) showed that there may be no clinical difference between silver sulfazidine cream and a silver dressing for mean percentage reduction in pressure ulcer area (grade 4 pressure ulcers) (very low quality).
- One study (n=40) (general populations) reported percentage reduction in PUSH score (grade IV PUs) for silver sulfazidine cream and a silver dressing. The mean for silver sulfazidine cream was 34.51% and 28.15% for silver dressing. A p-value of p=0.473 was reported (very low quality).
- One study (n=40) (general populations) showed no difference between silver sulfazidine cream and a silver dressing to reduce the incidence of adverse events, the direction of the estimate of effect favours either intervention (low quality).
- One study (n=40) (general populations) showed no difference between silver sulfazidine cream and a silver dressing for mortality (all-cause) (low quality).
- No evidence was found for the following outcomes:
  - Proportion of people with pressure ulcers completely healed
  - Time to complete healing of pressure ulcers
  - Rate of reduction in size or volume of pressure ulcers
  - Pain (wound-related)
  - Time in hospital
  - Acceptability of treatment
  - Health-related quality of life

10.1.5.1.19 Resin salve versus hydrofibre

- One study (n=22) (general populations) showed that resin salve is potentially more clinically effective compared to a hydrofibre for proportion of people with pressure ulcers completely healed (grade 2 to 4) (very low quality).

- One study (n=29) (general populations) showed that resin salve is potentially more clinically effective compared to a hydrofibre for pressure ulcers completely healed (grade 2 to 4) (very low quality).
- One study (n=29) (general populations) showed that there is potentially no clinical difference between resin salve and a hydrofibre to improve healing of pressure ulcers (grade 2 to 4), the direction of the estimate of the effect favoured the resin salve (very low quality).
- One study (n=29) (general populations) showed there may be no clinical difference between resin salve and hydrofibre to reduce pressure ulcers (grade 2 to 4) worsening (very low quality).
- One study (n=29) (general populations) reported mean percentage reduction in ulcer width for resin salve and hydrofibre. The mean for resin salve was 93.75% and 57.14% for hydrofibre. No estimate of effect or precision could be derived (very low quality).
- One study (n=29) (general populations) reported mean percentage reduction in ulcer depth for resin salve and hydrofibre. The mean for resin salve was 88.46% and -1.89% for hydrofibre. No estimate of effect or precision could be derived (very low quality).
- One study (n=29) (general populations) reported speed of healing for resin salve and hydrofibre. The log-rank-test revealed a p-value 0.013, which favoured resin salve (very low quality).
- One study (n=22) (general populations) showed there may be no clinical difference between hydrofibre and resin salve to reduce the incidence of skin reactions, the direction of the estimate of effect favours hydrofibre (very low quality).
- One study (n=29) (general populations) showed hydrofibre may be more clinically harmful than resin salve for mortality (all-cause) (very low quality).
- No evidence was found for the following outcomes:
  - Time to complete healing of pressure ulcers
  - Pain (wound-related)
  - Time in hospital
  - Acceptability of treatment
  - Side effects
  - Health-related quality of life

10.1.5.1.20 Antibiotic ointment versus foam dressing

- One study (n=44) (institutionalised elderly adults) showed that a foam dressing may be more clinically effective compared to antibiotic ointment for proportion of people with pressure ulcers completely healed (grade 2) (very low quality).
- One study (n=44) (institutionalized elderly adults) reported mean PUSH score for antibiotic ointment and a foam dressing. The mean score was 1.61 for the antibiotic ointment and 3.24 for foam dressing. A p-value > 0.05 was reported (very low quality).
- No evidence was found for the following outcomes:
  - Time to complete healing of pressure ulcers
  - Rate of reduction in size or volume of pressure ulcers
  - Reduction in size or volume of pressure ulcers
  - Pain (wound-related)
  - Time in hospital
  - Acceptability of treatment
  - Side effects
  - Mortality (all-cause)

10.1.5.1.21 Insulin versus standard treatment

- One study (n=14) (people in a nursing home) reported mean healing rate for insulin and standard treatment. A p-value of 0.05 in favour of insulin was reported (very low quality).
- One study (n=12) showed there is no clinical difference between insulin and standard treatment for mortality (all-cause), the direction of the estimate of effect could favour either intervention (low quality).
- No evidence was found for the following outcomes:
  - Proportion of people with pressure ulcers completely healed
  - Time to complete healing
  - Reduction in size or volume of pressure ulcers
  - Pain (wound-related)
  - Time in hospital
  - Acceptability of treatment
  - Side effects
  - Health-related quality of life

10.1.5.1.22 Growth factor versus placebo

- Six studies (n=316) (general population and denervated people) showed that different types of growth factors may be more clinically effective compared to placebo for proportion of people with pressure ulcers completely healed (grade 2 and above) (very low quality).
- One study (n=14) showed that TGFβ3 may be more clinically effective compared to placebo for proportion of people completely healed (grade 3 to 4) (very low quality).
- One study (n=36) (people in a nursing home with foot ulcers) showed that mNGF is more clinically effective than placebo for proportion of people with pressure ulcers completely healed (grade 2 and above) (moderate quality).
- One study (n=188) showed that there may be no clinical difference between rPDFG-BB compared to placebo for the proportion of people completely healed (grade 3 and 4) (very low quality).
- One study (n=54) showed that there may be no clinical difference between bFGF or GM-CSF compared to placebo for proportion of people completely healed (grade 3 and 4) (very low quality).
- One study (n=24) showed that there is no clinical difference between rIL-1β compared to placebo for proportion of people completely healed (grade 3 and 4) (low quality).
- No evidence was found for the following outcomes:
  - Mortality (all-cause)
  - Time to complete healing of pressure ulcers
  - Rate of reduction in size or volume of pressure ulcers
  - Reduction in size or volume of pressure ulcers
  - Pain (wound-related)
  - Time in hospital
  - Acceptability of treatment
  - Side effects
  - Health-related quality of life

10.1.5.1.23 Transforming growth factor-beta 3 (1.0µg/cm) versus placebo

- One study (n=9) (inpatients) showed that there is no clinical difference between transforming growth factor-beta 3 (1.0µg/cm) and placebo for proportion of people with pressure ulcers completely healed (grade 3 and 4) (low quality).
- One study (n=9) (inpatients) reported mean percentage reduction in pressure ulcer area for transforming growth factor-beta 3 (1.0µg/cm) and placebo. The mean for transforming growth factor-beta 3 (1.0µg/cm) was 70% and 30% for placebo. No estimate of effect or precision could be derived (very low quality).
- One study (n=9) (inpatients) reported mean percentage reduction in ulcer volume for transforming growth factor-beta 3 (1.0µg/cm) and placebo. The mean for transforming growth factor-beta 3 (1.0µg/cm) was 75% and 20% for placebo. No estimate of effect or precision could be derived (very low quality)

  One study (n=14) (inpatients) showed that transforming growth factor-beta 3 (1.0µg/cm) may be more clinically effective when compared to placebo for reduction in mortality (all-cause) (grade 3 and 4) (very low quality)
- No evidence was found for the following outcomes:
  - Time to complete healing of pressure ulcers
  - Rate of reduction in size or volume of pressure ulcers
  - Pain (wound-related)
  - Time in hospital
  - Acceptability of treatment
  - Side effects
  - Health-related quality of life

10.1.5.1.24 Transforming growth factor-beta 3 (2.5µgm/cm) versus transforming growth factor- beta 3 (1.0µg/cm)

- One study (n=9) (inpatients) showed that transforming growth factor-beta 3 (2.5µg/cm) may be more clinically effective compared to transforming growth factor-beta 3 (1.0µg/cm) for proportion of people with pressure ulcers completely healed (grade 3 and 4) (very low quality).
- One study (n=9) (inpatients) reported mean percentage reduction in ulcer area for transforming growth factor-beta 3 (1.0µg/cm) and transforming growth factor-beta 3 (2.5µg/cm). The mean for transforming growth factor-beta 3 (1.0µg/cm) was 70% and 60% for transforming growth factor-beta 3 (2.5µg/cm). No estimate of effect or precision could be derived (very low quality).
- One study (n=9) (inpatients) reported mean percentage reduction in ulcer volume for transforming growth factor-beta 3 (1.0µg/cm) and transforming growth factor-beta 3 (2.5µg/cm). The mean for transforming growth factor-beta 3 (1.0µg/cm) was 75% and 60% for transforming growth factor-beta 3 (2.5µg/cm). No estimate of effect or precision could be derived (very low quality).
- One study (n=9) (inpatients) showed that transforming growth factor-beta 3 (2.5µg/cm) may be more clinically effective compared to transforming growth factor-beta 3 (1.0µg/cm) for mortality (all-cause)(very low quality).
- No evidence was found for the following outcomes:
  - Time to complete healing of pressure ulcers
  - Rate of reduction in size or volume of pressure ulcers
  - Pain (wound-related)
  - Time in hospital

- Acceptability of treatment
- Side effects
- Health-related quality of life

10.1.5.1.25 Transforming growth factor-beta 3 (2.5µg/cm) versus placebo

- One study (n=10) (inpatients) showed that transforming growth factor-beta 3 (2.5µg/cm) may be more clinically effective compared to placebo for proportion of people with pressure ulcers completely healed (grade 3 and 4) (low quality).
- One study (n=10) (inpatients) reported mean percentage reduction in ulcer area for transforming growth factor-beta 3 (2.5µg/cm) and placebo. The mean for transforming growth factor-beta 3 (2.5µg/cm) was 60% and 30% for placebo. No estimate of effect or precision could be derived (very low quality).
- One study (n=10) (inpatients) reported mean percentage reduction in ulcer volume for transforming growth factor-beta 3 (2.5µg/cm) and placebo. The mean for transforming growth factor-beta 3 (2.5µg/cm) was 60% and 20% for placebo. No estimate of effect or precision could be derived (very low quality).
- One study (n=10) (inpatients) showed that transforming growth factor-beta 3 (2.5µg/cm) may be more clinically effective compared to placebo for mortality (all-cause) (very low quality).
- No evidence was found for the following outcomes:
  - Time to complete healing of pressure ulcers
  - Rate of reduction in size or volume of pressure ulcers
  - Pain (wound-related)
  - Time in hospital
  - Acceptability of treatment
  - Side effects
  - Health-related quality of life

10.1.5.1.26 Mouse nerve growth factor (2.5 S murine) versus placebo

- One study (n=36) (people in a nursing home) showed that mouse nerve growth factors is potentially more clinically effective compared to placebo for proportion of people with pressure ulcers completely healed (grade 2 and above) (foot ulcers) (moderate quality).
- One study (n=36) (people in a nursing home) showed that mouse nerve growth factors is more clinically effective compared to placebo to improve healing by 3 or more grade of pressure ulcers (grade 2 and above) (foot ulcers) (moderate quality).
- One study (n=36) (people in a nursing home) showed that mouse nerve growth factors is more clinically effective compared to placebo to improve healing by 2 grade of pressure ulcers (grade 2 and above) (foot ulcers) (moderate quality).
- One study (n=36) (people in a nursing home) showed that mouse nerve growth factors is more clinically effective compared to placebo to improve healing by 1 grade of pressure ulcers (grade 2 and above) (foot ulcers) (moderate quality).
- One study (n=36) (people in a nursing home) showed that there may be no clinical difference between mouse nerve growth factors and placebo for mean mm^2 reduction in pressure ulcer area (grade 2 and above pressure ulcers)(foot ulcers), the direction of the estimate of the effect favoured the nerve growth factors (low quality).
- One study (n=36) (people in a nursing home) showed that mouse nerve growth factors is more clinically effective compared to placebo for mean mm^2 reduction in pressure ulcer area (adjusted

for baseline ulcer area, location and duration) (grade 2 and above pressure ulcers) (foot ulcers) (moderate quality).

- One study (n=36) (people in a nursing home) showed that no clinical difference between mouse nerve growth factors and placebo for the incidence of adverse events (moderate quality).
- One study (n=36) (people in a nursing home) showed that there may be no clinical difference between mouse nerve growth factors and placebo for the mortality (all-cause), the direction of the estimate of effect could favour the mouse nerve growth factors (moderate quality).
- No evidence was found for the following outcomes:
  - Time to complete healing of pressure ulcers
  - Rate of reduction in size or volume of pressure ulcers
  - Pain (wound-related)
  - Time in hospital
  - Acceptability of treatment
  - Health-related quality of life

10.1.5.1.27 Recombinant platelet-derived growth factor 100µ/ml versus placebo

- Two studies (n=50) (general population and denervated people) showed that recombinant platelet-derived growth factor (100µg/ml) may be more clinically effective compared to placebo for proportion of people with pressure ulcers completely healed (grade 3 and 4) (very low quality).
- One study (n=30) (general population) reported ulcer volume at end of treatment (adjusted for initial volume) for recombinant platelet-derived growth factor (100µg/ml) and placebo. The volume was 1.75g for the recombinant platelet-derived growth factor (100µg/ml) and 3.5 g for placebo. No estimate of effect or precision could be derived (very low quality).
- One study (n=50) (general population and denervated people) showed there is no clinical difference between recombinant platelet-derived growth factor and placebo for mortality (all-cause) (very low quality).
- No evidence was found for the following outcomes:
  - Time to complete healing of pressure ulcers
  - Rate of reduction in size or volume of pressure ulcers
  - Reduction in size or volume of pressure ulcers
  - Pain (wound-related)
  - Time in hospital
  - Acceptability of treatment
  - Side effects
  - Health-related quality of life

10.1.5.1.28 Recombinant platelet-derived growth factor 100µg/ml versus recombinant platelet-derived growth factor 300µg/ml

- One study (n=28) (general population) showed that recombinant platelet-derived growth factor (100µg/ml) may be more clinically effective compared to recombinant platelet-derived growth factor (300µg/ml) for proportion of people with pressure ulcers completely healed (grade 3 and 4) (very low quality).
- One study (n=28) (general population) reported ulcer volume at end of treatment (adjusted for initial volume) for recombinant platelet-derived growth factor (100µg/ml) and recombinant

platelet-derived growth factor (300µg/ml). The volume was 1.75g for the recombinant platelet-derived growth factor (100µg/ml) and 2.0g for recombinant platelet-derived growth factor (300µg/ml). No estimate of effect or precision could be derived (very low quality).

10.1.5.1.29 Recombinant platelet-derived growth factor 300µg/ml versus placebo

- One study (n=26) (general population) showed that recombinant platelet-derived growth factor (300µg/ml) may be more clinically effective compared to placebo for proportion of people with pressure ulcers completely healed (grade 3 and 4) (very low quality).
- One study (n=30) (general population) reported ulcer volume at end of treatment (adjusted for initial volume) for recombinant platelet-derived growth factor (300µg/ml) and placebo. The volume was 2.0g for the recombinant platelet-derived growth factor (300µg/ml) and 3.5g for placebo. No estimate of effect or precision could be derived (very low quality).

10.1.5.1.30 Basic fibroblast growth factor or granulocyte-macrophage colony-stimulating factor versus placebo

- One study (n=54) (inpatients) showed that there is potentially no clinical difference between basic fibroblast growth factor or granulocyte-macrophage colony-stimulating factor and placebo for complete healing of pressure ulcers (grade 3 and 4) (very low quality).

10.1.5.1.31 Granulocyte-macrophage colony-stimulating factor 2.0µg/cm^2 versus placebo

- One study (n=27) (inpatients) showed that placebo may be more clinically effective compared to granulocyte-macrophage colony-stimulating factor (2.0µg/cm²) for proportion of people with pressure ulcers completely healed (grade 3 and 4) (very low quality).
- One study (n=27) (inpatients) showed that placebo may be more clinically effective compared to granulocyte-macrophage colony-stimulating factor (2.0µg/cm²) to reduce pressure ulcers (grade 3 and 4) worsening (very low quality).
- One study (n=30) (inpatients) showed that there is potentially no clinical difference between granulocyte-macrophage colony-stimulating factor (2.0µg/cm²) and placebo for mean percentage reduction in pressure ulcer area (grade 3 and 4 pressure ulcers) (very low quality).
- One study (n=30) (inpatients) reported median percentage reduction in ulcer area for granulocyte-macrophage colony-stimulating factor (2.0µg/cm²) and placebo. The median for granulocyte-macrophage colony-stimulating factor (2.0µg/cm²) was 70% and 72% for placebo. No estimate of effect or precision could be derived (very low quality).
- One study (n=30) (inpatients) reported no clinical difference between granulocyte-macrophage colony-stimulating factor (2.0 µg/cm²) and placebo for mortality (all-cause) (low quality).
- No evidence was found for the following outcomes:
  - Time to complete healing of pressure ulcers
  - Rate of reduction in size or volume of pressure ulcers
  - Reduction in size or volume of pressure ulcers
  - Pain (wound-related)
  - Time in hospital
  - Acceptability of treatment
  - Side effects
  - Health-related quality of life

10.1.5.1.32 Basic fibroblast growth factor (5.0µg/cm²) versus granulocyte-macrophage colony-stimulating factor (2.0µg/cm²)

- One study (n=28) (inpatients) showed that there basic fibroblast growth factor (5.0µg/cm²) may be more clinically effective for the proportion of people with pressure ulcers completely healed compared to granulocyte-macrophage colony-stimulating factor (2.0µg/cm²) (grade 3 and 4), (very low quality).
- One study (n=28) (inpatients) showed that granulocyte-macrophage colony-stimulating factor (2.0µg/cm²) may be more clinically effective compared to basic fibroblast growth factor (5.0µg/cm²) to reduce pressure ulcers (grade 3 and 4) worsening (very low quality).
- One study (n=30) (inpatients) showed that basic fibroblast growth factor (5.0µg/cm²) is potentially more clinically effective compared to granulocyte-macrophage colony-stimulating factor (2.0µg/cm²) for mean percentage reduction in pressure ulcer area (grade 3 and 4 pressure ulcers) (very low quality).
- One study (n=30) (inpatients) reported median percentage reduction in ulcer area for granulocyte-macrophage colony-stimulating factor (2.0µg/cm²) and basic fibroblast growth factor (5.0µg/cm²). The median for granulocyte-macrophage colony-stimulating factor (2.0µg/cm²) was 70% and 79% for basic fibroblast growth factor (5.0µg/cm²). No estimate of effect or precision could be derived (very low quality).
- One study (n=28) (inpatients) showed that there is no clinical difference between granulocyte-macrophage colony-stimulating factor (2.0µg/cm²) and basic fibroblast growth factor (5.0µg/cm²) for mortality (all-cause) (low quality).
- No evidence was found for the following outcomes:
  - Time to complete healing of pressure ulcers
  - Rate of reduction in size or volume of pressure ulcers
  - Reduction in size or volume of pressure ulcers
  - Pain (wound-related)
  - Time in hospital
  - Acceptability of treatment
  - Side effects
  - Mortality
  - Health-related quality of life

10.1.5.1.33 Granulocyte-macrophage colony-stimulating factor (2.0µg/cm²) and basic fibroblast growth factor (5.0µg/cm²) versus granulocyte-macrophage colony-stimulating factor (2.0µg/cm²)

- One study (n=27) (inpatients) showed that granulocyte-macrophage colony-stimulating factor (2.0µg/cm²) and basic fibroblast growth factor (5.0µg/cm²) may be more clinically effective for proportion of people with pressure ulcers completely healed compared to granulocyte-macrophage colony-stimulating factor (2.0µg/cm²) (grade 3 and 4), the direction of the estimate of the effect favoured the granulocyte-macrophage colony-stimulating factor (2.0µg/cm²) and basic fibroblast growth factor (5.0µg/cm²) (very low quality).
- One study (n=27) (inpatients) showed that granulocyte-macrophage colony-stimulating factor (2.0µg/cm²) and basic fibroblast growth factor (5.0µg/cm²) may be more clinically effective compared to granulocyte-macrophage colony-stimulating factor (2.0µg/cm²) to reduce pressure ulcers (grade 3 and 4) worsening (very low quality).
- One study (n=30) (inpatients) showed there may be no clinical difference between granulocyte-macrophage colony-stimulating factor (2.0µg/cm²) and basic fibroblast growth factor (5.0µg/cm²) compared to granulocyte-macrophage colony-stimulating factor (2.0µg/cm²) for mean percentage

reduction in pressure ulcer area (grade 3 and 4 pressure ulcers), the direction of the estimate of effect could favour either granulocyte-macrophage colony-stimulating factor (2.0µg/cm²) (very low quality).

- One study (n=30) (inpatients) reported median percentage reduction in ulcer area for granulocyte-macrophage colony-stimulating factor (2.0µg/cm²) versus granulocyte-macrophage colony-stimulating factor (2.0µg/cm²) and basic fibroblast growth factor (5.0µg/cm²). The median for granulocyte-macrophage colony-stimulating factor (2.0µg/cm²) was 70% and 73% granulocyte-macrophage colony-stimulating factor (2.0µg/cm²) and basic fibroblast growth factor (5.0?g/cm²). No estimate of effect or precision could be derived (very low quality).
- One study (n=30) (inpatients) showed there is no clinical difference between granulocyte-macrophage colony-stimulating factor (2.0µg/cm²) and basic fibroblast growth factor (5.0µg/cm²) compared to granulocyte-macrophage colony-stimulating factor (2.0µg/cm²) for mortality (all-cause), the direction of the estimate of effect could favour either intervention (very low quality).
- No evidence was found for the following outcomes:
  - Time to complete healing of pressure ulcers
  - Rate of reduction in size or volume of pressure ulcers
  - Pain (wound-related)
  - Time in hospital
  - Acceptability of treatment
  - Side effects
  - Health-related quality of life

10.1.5.1.34 Basic fibroblast growth factor (5.0µg/cm²) versus placebo

- One study (n=27) (inpatients) showed that there may be no clinical difference between basic fibroblast growth factor (5.0µg/cm²) and placebo for proportion of people with pressure ulcers completely healed (grade 3 and 4), the direction of the estimate of the effect favoured placebo (very low quality).
- One study (n=27) (inpatients) showed that placebo is potentially more clinically effective compared to basic fibroblast growth factor (5.0µg/cm²) to reduce pressure ulcer (grade 3 and 4) worsening (very low quality).
- One study (n=30) (inpatients) showed that there is potentially no clinical difference between basic fibroblast growth factor (5.0µg/cm²) and placebo for mean percentage reduction in pressure ulcer area (grade 3 and 4 pressure ulcers), the direction of the estimate of the effect favoured the basic fibroblast growth factor (5.0µg/cm²) (very low quality).
- One study (n=30) (inpatients) reported median percentage reduction in ulcer area for basic fibroblast growth factor (5.0µg/cm²) and placebo. The median for basic fibroblast growth factor (5.0µg/cm²) was 79% and 72% placebo. No estimate of effect or precision could be derived (very low quality).
- One study (n=30) (inpatients) showed that there is no clinical difference between basic fibroblast growth factor (5.0µg/cm²) and placebo for mortality (all-cause), the direction of the estimate of the effect could favour either intervention (low quality).
- No evidence was found for the following outcomes:
  - Time to complete healing of pressure ulcers
  - Rate of reduction in size or volume of pressure ulcers
  - Pain (wound-related)
  - Time in hospital
  - Acceptability of treatment

- Side effects
- Health-related quality of life

10.1.5.1.35 Basic fibroblast growth factor (5.0µg/cm²) versus granulocyte-macrophage colony-stimulating factor (2.0µg/cm²) and basic fibroblast growth factor (5.0µg/cm²)

- One study (n=27) (inpatients) showed that there may be no clinical difference between basic fibroblast growth factor (5.0µg/cm²) versus granulocyte-macrophage colony-stimulating factor (2.0µg/cm²) and basic fibroblast growth factor (5.0µg/cm²) for proportion of people with pressure ulcers completely healed (grade 3 and 4), the direction of the estimate of the effect favoured basic fibroblast growth factor (5.0µg/cm²) (very low quality).
- One study (n=27) (inpatients) showed that granulocyte-macrophage colony-stimulating factor (2.0µg/cm²) and basic fibroblast growth factor (5.0µg/cm²) may be more clinically effective compared to basic fibroblast growth factor (5.0µg/cm²) to reduce pressure ulcers (grade 3 and 4) worsening (very low quality).
- One study (n=31) (inpatients) showed that there is potentially no clinical difference between basic fibroblast growth factor (5.0µg/cm²) versus granulocyte-macrophage colony-stimulating factor (2.0µg/cm²) and basic fibroblast growth factor (5.0µg/cm²) for mean percentage reduction in pressure ulcer area (grade 3 and 4 pressure ulcers), the direction of the estimate of the effect favoured the basic fibroblast growth factor (5.0µg/cm²) (very low quality).
- One study (n=31) (inpatients) reported median percentage reduction in ulcer area for basic fibroblast growth factor (5.0µg/cm²) versus granulocyte-macrophage colony-stimulating factor (2.0µg/cm²) and basic fibroblast growth factor (5.0µg/cm²). The median for basic fibroblast growth factor (5.0µg/cm²) was 79% and 73% granulocyte-macrophage colony-stimulating factor (2.0?g/cm²) and basic fibroblast growth factor (5.0µg/cm²). No estimate of effect or precision could be derived (very low quality).
- One study (n=31) (inpatients) showed no clinical difference between basic fibroblast growth factor (5.0µg/cm²) versus granulocyte-macrophage colony-stimulating factor (2.0µg/cm²) and basic fibroblast growth factor (5.0µg/cm²) for mortality (all-cause) (low quality).
- No evidence was found for the following outcomes:
  - Time to complete healing of pressure ulcers
  - Rate of reduction in size or volume of pressure ulcers
  - Pain (wound-related)
  - Time in hospital
  - Acceptability of treatment
  - Side effects
  - Health-related quality of life

10.1.5.1.36 Basic fibroblast growth factor (5.0µg/cm²) and granulocyte-macrophage colony-stimulating factor (2.0µg/cm²) versus placebo

- One study (n=26) (inpatients) showed that there may be no clinical difference between basic fibroblast growth factor (5.0µg/cm²) and granulocyte-macrophage colony-stimulating factor (2.0µg/cm²) versus placebo for proportion of people with pressure ulcers completely healed (grade 3 and 4), the direction of the estimate of the effect favoured placebo (very low quality).
- One study (n=26) (inpatients) showed that placebo may be more clinically effective compared to granulocyte-macrophage colony-stimulating factor (2.0µg/cm²) and basic fibroblast growth factor (5.0µg/cm²) to reduce pressure ulcers (grade 3 and 4) worsening (very low quality).

- One study (n=31) (inpatients) showed that there may be no clinical difference between basic fibroblast growth factor (5.0µg/cm²) and granulocyte-macrophage colony-stimulating factor (2.0µg/cm²) versus placebo for mean percentage reduction in pressure ulcer area (grade 3 and 4 pressure ulcers), the direction of the estimate of the effect favoured the basic fibroblast growth factor (5.0µg/cm²) and granulocyte-macrophage colony-stimulating factor (2.0µg/cm²) (very low quality).
- One study (n=31) (inpatients) reported median percentage reduction in ulcer area for basic fibroblast growth factor (5.0µg/cm²) and granulocyte-macrophage colony-stimulating factor (2.0µg/cm²) versus placebo. The median for basic fibroblast growth factor (5.0µg/cm²) and granulocyte-macrophage colony-stimulating factor (2.0µg/cm²) was 73% and 72% for placebo. No estimate of effect or precision could be derived (very low quality).
- One study (n=31) (inpatients) showed that there may be no clinical difference between basic fibroblast growth factor (5.0µg/cm²) and granulocyte-macrophage colony-stimulating factor (2.0µg/cm²) versus placebo for mortality (all-cause) (low quality).
- No evidence was found for the following outcomes:
  - Time to complete healing of pressure ulcers
  - Rate of reduction in size or volume of pressure ulcers
  - Pain (wound-related)
  - Time in hospital
  - Acceptability of treatment
  - Side effects
  - Health-related quality of life

10.1.5.1.37 Recombinant platelet-derived growth factor-BB (100µg/g) versus placebo

- One study (n=62) (general population) showed that recombinant platelet-derived growth factor-BB (100µg/g) is more clinically effective compared to placebo for proportion of people with pressure ulcers completely healed (grade 3 and 4) (low quality).
- One study (n=62) (general population) showed that recombinant platelet-derived growth factor-BB (100µg/g) is potentially more clinically effective compared to placebo to improve healing ?90% pressure ulcers (grade 3 and 4) (very low quality).
- One study (n=62) (general population) reported median percentage reduction in ulcer volume for recombinant platelet-derived growth factor-BB (100µg/g) and placebo. The median for recombinant platelet-derived growth factor-BB (100µg/g) was 99.6% and 99.1% for placebo. A p-value of 0.013 was reported (very low quality).
- One study (n=62) (general population) showed that there may be no clinical difference between recombinant platelet-derived growth factor-BB (100µg/g) and placebo to reduce the incidence of osteomyelitis (grade 3 and 4 pressure ulcers) (very low quality).
- One study (n=62) (general population) showed that there may be no clinical difference between recombinant platelet-derived growth factor-BB (100µg/g) and placebo to reduce the incidence of infections (grade 3 and 4 pressure ulcers) (very low quality).
- One study (n=62) (general population) showed that there is no clinical difference between recombinant platelet-derived growth factor-BB (100µg/g) and placebo for reduction of incidence of sepsis (grade 3 and 4 pressure ulcers) (low quality).
- One study (n=62) (general population) showed that there may be no clinical difference between recombinant platelet-derived growth factor-BB (100µg/g) and placebo for reduction of incidence of adverse events other than osteomyelitis, sepsis and infections, the direction of the estimate of the effect could favour either intervention (grade 3 and 4 pressure ulcers) (very low quality).

- One study (n=62) (general population) showed no clinical difference between platelet-derived growth factor-BB (100µg/g) and placebo for mortality (all-cause) (low quality).
- No evidence was found for the following outcomes:
  - Time to complete healing of pressure ulcers
  - Rate of reduction in size or volume of pressure ulcers
  - Pain (wound-related)
  - Time in hospital
  - Acceptability of treatment
  - Side effects
  - Health-related quality of life

10.1.5.1.38 Recombinant platelet-derived growth factor-BB (100µg/g) versus recombinant platelet-derived growth factor-BB (300µg/g) alternated with placebo

- One study (n=63) (general population) showed that there may be no clinical difference between recombinant platelet-derived growth factor-BB (100µg/g) and recombinant platelet-derived growth factor-BB (300µg/g) alternated with placebo for proportion of people with pressure ulcers completely healed (grade 3 and 4 pressure ulcers), the direction of the estimate of the effect favoured recombinant platelet-derived growth factor-BB (100µg/g) (very low quality).
- One study (n=63) (general population) showed that there may be no clinical difference between recombinant platelet-derived growth factor-BB (100µg/g) and recombinant platelet-derived growth factor-BB (300µg/g) alternated with placebo to improve healing of 90% of pressure ulcers grade III and IV, the direction of the estimate of the effect favoured recombinant platelet-derived growth factor-BB (300µg/g) alternated with placebo (very low quality).
- One study (n=63) (general population) reported median percentage reduction in ulcer volume for recombinant platelet-derived growth factor-BB (100µg/g) and recombinant platelet-derived growth factor-BB (300µg/g) alternated with placebo. The median for recombinant platelet-derived growth factor-BB (100µg/g) was 99.6% and 99.7% for recombinant platelet-derived growth factor-BB (300µg/g) alternated with placebo. No estimate of effect or precision could be derived (very low quality).
- One study (n=63) (general population) showed that there may be no clinical difference between recombinant platelet-derived growth factor-BB (100µg/g) and recombinant platelet-derived growth factor-BB (300µg/g) alternated with placebo to reduce the incidence of osteomyelitis (grade 3 and 4 pressure ulcers) (very low quality).
- One study (n=63) (general population) showed that there is no clinical difference between recombinant platelet-derived growth factor-BB (100µg/g) and recombinant platelet-derived growth factor-BB (300µg/g) alternated with placebo to reduce the incidence of infections (grade 3 and 4 pressure ulcers) (low quality).
- One study (n=63) (general population) showed that there may be no clinical difference between recombinant platelet-derived growth factor-BB (100µg/g) and recombinant platelet-derived growth factor-BB (300µg/g) alternated with placebo for reduction of incidence of sepsis (grade 3 and 4 pressure ulcers) (very low quality).
- One study (n=63) (general population) showed there may be no clinical difference between recombinant platelet-derived growth factor-BB (100µg/g) and recombinant platelet-derived growth factor-BB (300µg/g) alternated with placebo for reduction of incidence of adverse events other than osteomyelitis, sepsis and infections (grade 3 and 4 pressure ulcers), the direction of the estimate of effect favours recombinant platelet-derived growth factor-BB (100µg/g) and recombinant platelet-derived growth factor-BB (300µg/g) (very low quality).

- One study (n=63) (general population) showed that there is no difference between recombinant platelet-derived growth factor-BB (100µg/g) and recombinant platelet-derived growth factor-BB (300µg/g) alternated with placebo for mortality (all-cause) (low quality).
- No evidence was found for the following outcomes:
  - Time to complete healing of pressure ulcers
  - Rate of reduction in size or volume of pressure ulcers
  - Pain (wound-related)
  - Time in hospital
  - Acceptability of treatment
  - Side effects
  - Health-related quality of life

10.1.5.1.39 Recombinant platelet-derived growth factor-BB (100µg/g) versus recombinant platelet-derived growth factor-BB (300µg/g)

- One study (n=61) (general population) showed that recombinant platelet-derived growth factor-BB (100µg/g) is potentially more clinically effective compared to recombinant platelet-derived growth factor-BB (300µg/g) for proportion of people with pressure ulcers completely healed (grade 3 and 4) (very low quality).
- One study (n=61) (general population) showed that recombinant platelet-derived growth factor-BB (100µg/g) is potentially more clinically effective than recombinant platelet-derived growth factor-BB (300µg/g) to improve healing of 90% of pressure ulcers (grade 3 and 4) (very low quality).
- One study (n=61) (general population) reported median percentage reduction in ulcer volume for recombinant platelet-derived growth factor-BB (100µg/g) and recombinant platelet-derived growth factor-BB (300µg/g). The median for recombinant platelet-derived growth factor-BB (100µg/g) was 99.6% and 98.6% for recombinant platelet-derived growth factor-BB (300µg/g). No estimate of effect or precision could be derived (very low quality).
- One study (n=61) (general population) showed there may be no clinical difference between recombinant platelet-derived growth factor-BB (300?g/g) and recombinant platelet-derived growth factor-BB (100µg/g) to reduce the incidence of osteomyelitis (grade 3 and 4 pressure ulcers) (very low quality).
- One study (n=61) (general population) showed that there may be no clinical difference between recombinant platelet-derived growth factor-BB (100?g/g) compared to recombinant platelet-derived growth factor-BB (300µg/g) to reduce the incidence of infections (grade 3 and 4 pressure ulcers) (very low quality).
- One study (n=61) (general population) showed that there is no clinical difference between recombinant platelet-derived growth factor-BB (100µg/g) and recombinant platelet-derived growth factor-BB (300µg/g) for reduction of incidence of sepsis (grade 3 and 4 pressure ulcers) (very low quality).
- One study (n=61) (general population) showed that there may be no clinical difference between recombinant platelet-derived growth factor-BB (100µg/g) and recombinant platelet-derived growth factor-BB (300µg/g) for reduction of incidence of adverse events other than osteomyelitis, sepsis and infections (grade III and IV pressure ulcers), the direction of the estimate of the effect favoured recombinant platelet-derived growth factor-BB (100µg/g) (very low quality).
- One study (n=61) (general population) showed no clinical difference between recombinant platelet-derived growth factor-BB (100µg/g) and recombinant platelet-derived growth factor-BB (300µg/g) for mortality (all-cause), the direction of the estimate of effect could favour either intervention (low quality).

- No evidence was found for the following outcomes:
  - Time to complete healing of pressure ulcers
  - Rate of reduction in size or volume of pressure ulcers
  - Pain (wound-related)
  - Time in hospital
  - Acceptability of treatment
  - Health-related quality of life

10.1.5.1.40 Recombinant platelet-derived growth factor-BB (300µg/g) alternated with placebo versus placebo

- One study (n=63) (general population) showed that recombinant platelet-derived growth factor-BB (300µg/g) alternated with placebo is more clinically effective compared to placebo for proportion of people with pressure ulcers completely healed (grade 3 and 4) (low quality).
- One study (n=63) (general population) showed that recombinant platelet-derived growth factor-BB (300µg/g) alternated with placebo is potentially more clinically effective compared placebo to improve healing of 90% of pressure ulcers (grade 3 and 4) (very low quality).
- One study (n=63) (general population) reported median percentage reduction in ulcer volume for recombinant platelet-derived growth factor-BB (300µg/g) alternated with placebo and placebo. The median for recombinant platelet-derived growth factor-BB (300µg/g) alternated with placebo was 99.7% and 99.1% for placebo. A p-value of 0.011 was reported (very low quality).
- One study (n=63) (general population) showed there may be no clinical difference between recombinant platelet-derived growth factor-BB (300µg/g) alternated with placebo compared to placebo to reduce the incidence of osteomyelitis (grade 3 and 4 pressure ulcers) (very low quality).
- One study (n=63) (general population) showed there may be no clinical difference between recombinant platelet-derived growth factor-BB (300µg/g) alternated with placebo compared to placebo to reduce the incidence of infections (grade 3 and 4 pressure ulcers) (very low quality).
- One study (n=63) (general population) showed there may be no clinical difference between recombinant platelet-derived growth factor-BB (300µg/g) alternated with placebo and placebo for reduction of incidence of sepsis (grade 3 and 4 pressure ulcers) (very low quality).
- One study (n=63) (general population) showed there may be no clinical difference between recombinant platelet-derived growth factor-BB (300µg/g) alternated with placebo compared to placebo for reduction of incidence of adverse events other than osteomyelitis, sepsis and infections (grade 3 and 4 pressure ulcers) (very low quality).
- One study (n=63) (general population) showed no clinical difference between recombinant platelet-derived growth factor-BB (300µg/g) and placebo for mortality (all-cause), the direction of the estimate of effect could favour either intervention (low quality).
- No evidence was found for the following outcomes:
  - Time to complete healing of pressure ulcers
  - Rate of reduction in size or volume of pressure ulcers
  - Pain (wound-related)
  - Time in hospital
  - Acceptability of treatment
  - Health-related quality of life

10.1.5.1.41 Recombinant platelet-derived growth factor-BB (300µg/g) alternated with placebo versus recombinant platelet-derived growth factor-BB (300µg/g)

- One study (n=62) (general population) showed that recombinant platelet-derived growth factor-BB (300µg/g) alternated with placebo may be more clinically effective compared to recombinant platelet-derived growth factor-BB (300µg/g) for proportion of people with pressure ulcers completely healed (grade 3 and 4) (very low quality).
- One study (n=62) (general population) showed that recombinant platelet-derived growth factor-BB (300µg/g) alternated with placebo is potentially more clinically effective compared recombinant platelet-derived growth factor-BB (300µg/g) to improve healing of 90% of pressure ulcers (grade 3 and 4) (very low quality).
- One study (n=62) (general population) reported median percentage reduction in ulcer volume for recombinant platelet-derived growth factor-BB (300µg/g) alternated with placebo and recombinant platelet-derived growth factor-BB (300µg/g). The median for recombinant platelet-derived growth factor-BB (300µg/g) alternated with placebo was 99.7% and 98.6% for recombinant platelet-derived growth factor-BB (300µg/g). No estimate of effect or precision could be derived (very low quality).
- One study (n=62) (general population) showed there may be no clinical difference between recombinant platelet-derived growth factor-BB (300µg/g) compared to recombinant platelet-derived growth factor-BB (300µg/g) alternated with placebo to reduce the incidence of osteomyelitis (grade 3 and 4 pressure ulcers) (very low quality).
- One study (n=62) (general population) showed there may be no clinical difference between recombinant platelet-derived growth factor-BB (300µg/g) alternated with placebo compared to placebo to reduce the incidence of infections (grade 3 and 4 pressure ulcers) (very low quality).
- One study (n=62) (general population) showed there may be no clinical difference between that recombinant platelet-derived growth factor-BB (300µg/g) alternated with placebo compared to recombinant platelet-derived growth factor-BB (300µg/g) for reduction of incidence of sepsis (grade 3 and 4 pressure ulcers) (very low quality).
- One study (n=62) (general population) showed there may be no clinical difference between recombinant platelet-derived growth factor-BB (300µg/g) compared to recombinant platelet-derived growth factor-BB (300µg/g) alternated with placebo for reduction of incidence of adverse events other than osteomyelitis, sepsis and infections (grade 3 and 4 pressure ulcers) (very low quality).
- One study (n=62) (general population) showed no clinical difference between recombinant platelet-derived growth factor-BB (300µg/g) and recombinant platelet-derived growth factor-BB (300µg/g) for mortality (all-cause), the direction of the estimate of effect could favour either intervention (low quality).
- No evidence was found for the following outcomes:
  - Time to complete healing of pressure ulcers
  - Rate of reduction in size or volume of pressure ulcers
  - Pain (wound-related)
  - Time in hospital
  - Acceptability of treatment
  - Health-related quality of life

10.1.5.1.42 Recombinant platelet-derived growth factor-BB (300µg/g) versus placebo

- One study (n=61) (general population) showed there may be no clinical difference between recombinant platelet-derived growth factor-BB (300µg/g) compared to placebo for proportion of people with pressure ulcers completely healed (grade 3 and 4) (very low quality).

- One study (n=61) (general population) showed that recombinant platelet-derived growth factor-BB (300µg/g) may be more clinically effective compared to placebo to improve healing of 90% of pressure ulcers (grade 3 and 4) (very low quality).
- One study (n=61) (general population) reported median percentage reduction in ulcer volume for recombinant platelet-derived growth factor-BB (300µg/g) and placebo. The median for recombinant platelet-derived growth factor-BB (300µg/g) was 98.6% and 99.1% for placebo. No estimate of effect or precision could be derived (very low quality).
- One study (n=61) (general population) showed there may be no clinical difference between recombinant platelet-derived growth factor-BB (300µg/g) compared to placebo to reduce the incidence of osteomyelitis (grade 3 and 4 pressure ulcers) (very low quality).
- One study (n=61) (general population) showed that there may be no clinical difference between recombinant platelet-derived growth factor-BB (300µg/g) and recombinant platelet-derived growth factor-BB (300µg/g) for reduction of incidence of infections (grade 3 and 4 pressure ulcers), the direction of the estimate of effect favours placebo (very low quality).
- One study (n=61) (general population) showed that there is no clinical difference between recombinant platelet-derived growth factor-BB (300µg/g) and recombinant platelet-derived growth factor-BB (300µg/g) for reduction of incidence of sepsis (grade 3 and 4 pressure ulcers) (low quality).
- One study (n=61) (general population) showed there may be no clinical difference between recombinant platelet-derived growth factor-BB (300µg/g) and placebo for reduction of incidence of adverse events other than osteomyelitis, sepsis and infections (grade 3 and 4 pressure ulcers), the direction of the estimate of effect favours placebo (very low quality).
- One study (n=61) (general population) showed there may be no clinical difference between recombinant platelet-derived growth factor-BB (300µg/g) and placebo for mortality (all-cause) (low quality).
- No evidence was found for the following outcomes:
  - Time to complete healing of pressure ulcers
  - Rate of reduction in size or volume of pressure ulcers
  - Pain (wound-related)
  - Time in hospital
  - Acceptability of treatment
  - Health-related quality of life

10.1.5.1.43 Recombinant platelet-derived growth factor-BB (1.0µg/g) versus placebo

- One study (n=11) (denervated people) showed that there is no clinical difference between recombinant platelet-derived growth factor-BB (1.0µg/g) and placebo for proportion of people with pressure ulcers completely healed (grade 3 and 4) (low quality).
- One study (n=11) (denervated people) showed that there is no clinical difference between recombinant platelet-derived growth factor-BB (1.0µg/g) and placebo at reducing the incidence of infections (grade 3 and 4 pressure ulcers) (low quality).
- One study (n=11) (denervated people) showed that there is no clinical difference between recombinant platelet-derived growth factor-BB (1.0µg/g) and placebo for mortality (all-cause), the direction of the estimate of effect could favour either intervention (low quality).

10.1.5.1.44 Recombinant platelet-derived growth factor-BB (1.0µg/g) versus recombinant platelet-derived growth factor-BB (10.0µg/g)

- One study (n=8) (denervated people) showed that there is no clinical difference between recombinant platelet-derived growth factor-BB (1.0µg/g) and recombinant platelet-derived growth factor-BB (10.0µg/g) for the proportion of people with pressure ulcers completely healed (grade 3 and 4) , the direction of the estimate of effect could favour either intervention (low quality).
- One study (n=8) (denervated people) showed that there is no clinical difference between recombinant platelet-derived growth factor-BB (1.0µg/g) and recombinant platelet-derived growth factor-BB (10.0µg/g) at reducing the incidence of infections (grade 3 and 4 pressure ulcers) , the direction of the estimate of effect could favour either intervention (low quality).
- One study (n=8) (denervated people) showed that there is no clinical difference between recombinant platelet-derived growth factor-BB (1.0µg/g) and recombinant platelet-derived growth factor-BB (10.0µg/g) for mortality (all-cause) , the direction of the estimate of effect could favour either intervention (low quality).
- No evidence was found for the following outcomes:
  - Time to complete healing of pressure ulcers
  - Rate of reduction in size or volume of pressure ulcers
  - Pain (wound-related)
  - Time in hospital
  - Acceptability of treatment
  - Health-related quality of life

10.1.5.1.45 Recombinant platelet-derived growth factor-BB (100.0µg/g) versus recombinant platelet-derived growth factor-BB (1.0µg/g)

- One study (n=9) (denervated people) showed that recombinant platelet-derived growth factor-BB (100.0µg/g) may be more clinically effective compared to recombinant platelet-derived growth factor-BB (1.0µg/g) for proportion of people with pressure ulcers completely healed (grade 3 and 4) (very low quality).
- One study (n=9) (denervated people) showed that there is no clinical difference between recombinant platelet-derived growth factor-BB (1.0µg/g) and recombinant platelet-derived growth factor-BB (100.0µg/g) at reducing the incidence of infections (grade 3 and 4 pressure ulcers) , the direction of the estimate of effect could favour either intervention (low quality).
- One study (n=9) (denervated people) showed that there is no clinical difference between recombinant platelet-derived growth factor-BB (1.0µg/g) and recombinant platelet-derived growth factor-BB (100.0µg/g) for mortality (all-cause) , the direction of the estimate of effect could favour either intervention (low quality).
- No evidence was found for the following outcomes:
  - Time to complete healing of pressure ulcers
  - Rate of reduction in size or volume of pressure ulcers
  - Pain (wound-related)
  - Time in hospital
  - Acceptability of treatment
  - Health-related quality of life

10.1.5.1.46 Recombinant platelet-derived growth factor-BB (10.0µg/g) versus placebo

- One study (n=11) (denervated people) showed that there is no clinical difference between recombinant platelet-derived growth factor-BB (10.0µg/g) and placebo for the proportion of people with pressure ulcers completely healed (grade 3 and 4), the direction of the estimate of effect could favour either intervention (low quality).
- One study (n=11) (denervated people) showed that there is no clinical difference between recombinant platelet-derived growth factor-BB (10.0µg/g) and placebo at reducing the incidence of infections (grade 3 and 4 pressure ulcers), the direction of the estimate of effect could favour either intervention (low quality).
- One study (n=11) (denervated people) showed that there is no clinical difference between recombinant platelet-derived growth factor-BB (10.0µg/g) and placebo for mortality (all-cause) , the direction of the estimate of effect could favour either intervention (low quality).
- No evidence was found for the following outcomes:
  - Time to complete healing of pressure ulcers
  - Rate of reduction in size or volume of pressure ulcers
  - Reduction in size or volume of pressure ulcers
  - Pain (wound-related)
  - Time in hospital
  - Acceptability of treatment
  - Health-related quality of life

10.1.5.1.47 Recombinant platelet-derived growth factor-BB (100.0µg/g) versus recombinant platelet-derived growth factor-BB (10.0µg/g)

- One study (n=9) (denervated people) showed that recombinant platelet-derived growth factor-BB (100.0µg/g) may be more clinically effective compared to recombinant platelet-derived growth factor-BB (10.0µg/g) for the proportion of people with pressure ulcers completely healed (grade 3 and 4) (very low quality).
- One study (n=9) (denervated people) showed that there is no clinical difference between recombinant platelet-derived growth factor-BB (10.0µg/g) and recombinant platelet-derived growth factor-BB (100.0µg/g) at reducing the incidence of infections (grade 3 and 4 pressure ulcers), the direction of the estimate of effect could favour either intervention (low quality).
- One study (n=9) (denervated people) showed that there is no clinical difference between recombinant platelet-derived growth factor-BB (10.0µg/g) and recombinant platelet-derived growth factor-BB (100.0µg/g) for mortality (all-cause), the direction of the estimate of effect could favour either intervention (low quality).
- No evidence was found for the following outcomes:
  - Time to complete healing of pressure ulcers
  - Rate of reduction in size or volume of pressure ulcers
  - Reduction in size or volume of pressure ulcers
  - Pain (wound-related)
  - Time in hospital
  - Acceptability of treatment
  - Health-related quality of life

10.1.5.1.48 Recombinant platelet-derived growth factor-BB (100.0µg/g) versus placebo

- One study (n=12) (denervated people) showed that recombinant platelet-derived growth factor-BB (100.0µg/g) may be more effective compared to placebo for the proportion of people with pressure ulcers completely healed (grade 3 and 4) (very low quality).
- One study (n=12) (denervated people) showed that recombinant platelet-derived growth factor-BB (100.0µg/g) is clinically more effective compared to placebo for mean percentage reduction in pressure ulcer depth (grade 3 and 4 pressure ulcers) (low quality).
- One study (n=12) (denervated people) showed that recombinant platelet-derived growth factor-BB (100.0µg/g) is clinically more effective compared to placebo for mean percentage reduction in pressure ulcer volume (grade 3 and 4 pressure ulcers) (low quality).
- One study (n=12) (denervated people) showed that there is no clinical difference between recombinant platelet-derived growth factor-BB (100.0µg/g) and placebo at reducing the incidence of infections (grade 3 and 4 pressure ulcers), the direction of the estimate of effect could favour either intervention (low quality).
- One study (n=12) (denervated people) showed that there is no clinical difference between recombinant platelet-derived growth factor-BB (100.0µg/g) and placebo for mortality (all-cause), the direction of the estimate of effect could favour either intervention (low quality).
- No evidence was found for the following outcomes:
  - Time to complete healing of pressure ulcers
  - Rate of reduction in size or volume of pressure ulcers
  - Reduction in size or volume of pressure ulcers
  - Pain (wound-related)
  - Time in hospital
  - Acceptability of treatment
  - Health-related quality of life

10.1.5.1.49 Basic fibroblast growth factors (different schedules and doses) versus placebo

- One study (n=49) (denervated people) showed that basic fibroblast growth factors (different schedules and doses) is potentially more effective compared to placebo to improve >70% healing of pressure ulcers (grade 3 and 4) (very low quality).
- One study (n=49) (denervated people) reported mean percentage reduction in ulcer volume for basic fibroblast growth factors (different schedules and doses) and placebo. The mean was 69% for basic fibroblast growth factors (different schedules and doses) and 59% for placebo. No estimate of effect or precision could be derived (very low quality).
- One study (n=49) (denervated people) showed no clinical difference between basic fibroblast growth factors (different schedules and doses) and placebo for mortality (all-cause), the direction of the estimate of effect could favour either intervention (low quality).
- No evidence was found for the following outcomes:
  - Time to complete healing of pressure ulcers
  - Rate of reduction in size or volume of pressure ulcers
  - Reduction in size or volume of pressure ulcers
  - Pain (wound-related)
  - Time in hospital
  - Acceptability of treatment
  - Health-related quality of life

10.1.5.1.50 Interleukin 1 beta versus placebo

- One study (n=24) (denervated people) showed no clinical difference between interleukin 1 beta and placebo for the proportion of people with pressure ulcers completely healed (grade 3 and 4), the direction of the estimate of effect could favour either intervention (low quality).
- One study (n=24) (denervated people) showed no clinical difference between interleukin 1 beta and placebo for mortality (all-cause), the direction of the estimate of effect could favour either intervention (low quality).
- No evidence was found for the following outcomes:
  - Time to complete healing of pressure ulcers
  - Rate of reduction in size or volume of pressure ulcers
  - Reduction in size or volume of pressure ulcers
  - Pain (wound-related)
  - Time in hospital
  - Acceptability of treatment
  - Health-related quality of life

10.1.5.1.51 Interleukin 1 beta (0.01µg/cm²) versus placebo

- One study (n=12) (denervated people) showed no clinical difference between interleukin 1 beta (0.01µg/cm²) and placebo for the proportion of people with pressure ulcers completely healed (grade 3 and 4), the direction of the estimate of effect could favour either intervention (low quality).
- One study (n=12) (denervated people) showed no clinical difference between interleukin 1 beta (0.01µg/cm²) and placebo for mortality (all-cause), the direction of the estimate of effect could favour either intervention (low quality).
- No evidence was found for the following outcomes:
  - Time to complete healing of pressure ulcers
  - Rate of reduction in size or volume of pressure ulcers
  - Pain (wound-related)
  - Time in hospital
  - Acceptability of treatment
  - Health-related quality of life

10.1.5.1.52 Interleukin 1 beta (0.01µg/cm²) versus interleukin 1 beta (0.1µg/cm²)

- One study (n=12) (denervated people) showed no clinical difference between interleukin 1 beta (0.01µg/cm²) and interleukin 1 beta (0.1µg/cm²) for the proportion of people with pressure ulcers completely healed (grade 3 and 4), the direction of the estimate of effect could favour either intervention (low quality).
- One study (n=12) (denervated people) showed no clinical difference between interleukin 1 beta (0.01µg/cm²) and interleukin 1 beta (0.1µg/cm²) for mortality (all-cause) , the direction of the estimate of effect could favour either intervention (low quality).
- No evidence was found for the following outcomes:
  - Proportion of people with pressure ulcers completely healed
  - Time to complete healing of pressure ulcers
  - Rate of reduction in size or volume of pressure ulcers
  - Pain (wound-related)

- Time in hospital
- Acceptability of treatment
- Side effects
- Health-related quality of life

10.1.5.1.53 Interleukin 1 beta (0.01µg/cm²) versus interleukin 1 beta (1.0µg/cm²)

- One study (n=12) (denervated people) showed no clinical difference between interleukin 1 beta (0.01µg/cm²) and interleukin 1 beta (1.0µg/cm²) for the proportion of people with pressure ulcers completely healed (grade 3 and 4), the direction of the estimate of effect could favour either intervention (low quality).
- One study (n=12) (denervated people) showed no clinical difference between interleukin 1 beta (0.01µg/cm²) and interleukin 1 beta (1.0µg/cm²) for mortality (all-cause), the direction of the estimate of effect could favour either intervention (low quality).
- No evidence was found for the following outcomes:
  - Time to complete healing of pressure ulcers
  - Rate of reduction in size or volume of pressure ulcers
  - Reduction in size or volume of pressure ulcers
  - Pain (wound-related)
  - Time in hospital
  - Acceptability of treatment
  - Side effects
  - Health-related quality of life

10.1.5.1.54 Interleukin 1 beta (0.1µg/cm²) versus placebo

- One study (n=12) (denervated people) showed no clinical difference between interleukin 1 beta (0.1µg/cm²) and placebo for the proportion of people with pressure ulcers completely healed (grade 3 and 4), the direction of the estimate of effect could favour either intervention (low quality).
- One study (n=12) (denervated people) showed no clinical difference between interleukin 1 beta (0.1µg/cm²) and placebo for mortality (all-cause), the direction of the estimate of effect could favour either intervention (low quality).
- No evidence was found for the following outcomes:
  - Time to complete healing of pressure ulcers
  - Rate of reduction in size or volume of pressure ulcers
  - Reduction in size or volume of pressure ulcers
  - Pain (wound-related)
  - Time in hospital
  - Acceptability of treatment
  - Side effects
  - Health-related quality of life

10.1.5.1.55 Interleukin 1 beta (0.1µg/cm²) versus interleukin 1 beta (1.0µg/cm²)

- One study (n=12) (denervated people) showed no clinical difference between interleukin 1 beta (0.1µg/cm²) and interleukin 1 beta (1.0µg/cm²) for the proportion of people with pressure ulcers

completely healed (grade 3 and 4), the direction of the estimate of effect could favour either intervention (low quality).

- One study (n=12) (denervated people) showed no clinical difference between interleukin 1 beta (0.1µg/cm²) and interleukin 1 beta (1.0µg/cm²) for mortality (all-cause), the direction of the estimate of effect could favour either intervention (low quality).
- No evidence was found for the following outcomes:
  - Time to complete healing of pressure ulcers
  - Rate of reduction in size or volume of pressure ulcers
  - Reduction in size or volume of pressure ulcers
  - Pain (wound-related)
  - Time in hospital
  - Acceptability of treatment
  - Side effects
  - Health-related quality of life

10.1.5.1.56 Interleukin 1 beta (1.0µg/cm²) versus placebo

- One study (n=12) (denervated people) showed no clinical difference between interleukin 1 beta (1.0µg/cm²) and placebo for the proportion of people with pressure ulcers completely healed (grade 3 and 4), the direction of the estimate of effect could favour either intervention (low quality).
- One study (n=12) (denervated people) showed no clinical difference between interleukin 1 beta (1.0µg/cm²) and placebo for mortality (all-cause), the direction of the estimate of effect could favour either intervention (low quality).
- No evidence was found for the following outcomes:
  - Time to complete healing of pressure ulcers
  - Rate of reduction in size or volume of pressure ulcers
  - Reduction in size or volume of pressure ulcers
  - Pain (wound-related)
  - Time in hospital
  - Acceptability of treatment
  - Side effects
  - Health-related quality of life

10.1.5.2 Economic (adults)

- One cost-effectiveness analysis found that polyurethane self-adhesive foam dressing dominated saline soaked gauze, providing an increase in pressure ulcer free days, and ulcers healed at day 28, at a lower cost. This study was partially applicable with minor limitations.

10.1.5.3 Clinical (neonates, infants, children and young people)

No evidence was identified.

10.1.5.4 Economic (neonates, infants, children and young people)

No evidence was identified.

10.2 Recommendations and link to evidence

10.2.1 Adults

Recommendations	40. Do not routinely use topical antiseptics or antimicrobials to treat a pressure ulcer in adults.
Relative values of different outcomes	The GDG identified that the proportion of people with pressure ulcers completely healed, time to complete healing, reduction in size and rate of reduction in size and volume of pressure ulcers were the most critical outcomes to inform decision making. It was also recognised that it was important to consider quality of life for this question.
Trade off between clinical benefits and harms	The evidence does not support the use of saline-soaked gauze. Some evidence suggested a benefit of hydrocolloid dressing on grade 1-2 pressure ulcers when compared to saline-soaked gauze, and no difference or a possible benefit of saline-soaked gauze for grade 3-4. The GDG felt this mirrored clinical practice and that people often use hydrocolloid dressings on grade 1 and 2 pressure ulcers. It was not necessarily appropriate to use hydrocolloid dressings on more severe pressure ulcers as the dressing would not cover the wound. The GDG also noted that saline-soaked gauze was not used within the UK regularly but is used in Europe and the US. The group who had the hydrocolloid dressing experienced more pain and discomfort on removal of dressing and greater skin irritation. There was no difference in infection rates. Saline-soaked gauze was also not clinically beneficial when compared to other dressings. There was no clinical difference between hydrogel dressings and saline-soaked gauze for the proportion of people completely healed, people worsened and mean weeks to healing. There was however higher mortality in this group. Foam dressing was more clinically beneficial than saline-soaked gauze for the proportion of people complete healing of pressure ulcers. Polyurethane dressing was more clinically beneficial than saline-soaked gauze for the proportion of pressure ulcers completely healed, reduction of pressure ulcers worsened, mean percentage reduction in pressure ulcer area. Dextranomer powder was of clinical benefit when compared to saline-soaked gauze for the proportion of pressure ulcers improved but there was no difference in the number of adverse events. There was no clinically important benefit for isotonic saline solution when compared to aloe vera, silver chloride and decyl glucoside for mean percentage Pressure Sore Status Tool (PSST). The GDG expressed concern as to whether this outcome represented healing. The evidence was favourable for phenytoin ointment when compared to other topical agents (saline solution and triple antibiotics ointment), but was not as favourable when compared to a hydrocolloid dressing. Phenytoin cream was clinically beneficial when compared to saline-soaked gauze for the proportion of pressure ulcers completely healed, proportion of pressure ulcers improved and reduction in the number of pressure ulcers worsened. There was no difference for the proportion of people with treatment-related adverse events. Phenytoin was of benefit when compared to triple antibiotic ointment for mean days to healing but there was no difference for pain and treatment-related adverse events. There was a clinical benefit for foam dressing compared to phenytoin cream for the proportion of people completely healed (yet unsure of clinical benefit for mean Pressure ulcer Scale for Healing (PUSH) score) when compared to antibiotic ointment. Hydrocolloid dressing was of clinical benefit for the proportion of people completely healed when compared to phenytoin cream. There was no difference for pain, treatment-related adverse events and proportion of people whose pressure ulcers had worsened. Overall however, the GDG did not consider that there was sufficient evidence to

	demonstrate a benefit of the use of phenytoin and therefore, chose not to make a recommendation on its use for the treatment of pressure ulcers. Resin salve was favourable in comparison to hydrofibre dressings. There was a clinical benefit for resin salve for the proportion of people completely healed, improved, reduction in pressure ulcers worsened, mean percentage reduction in pressure ulcer width, depth, speed of healing and for less allergic skin reaction. There was no strong evidence to favour iodine solutions (povidone-iodine and cadexomer iodine solutions). Povidone-iodine solution was not as beneficial as hydrocolloid dressing. There was no clinical benefit of povidone-iodine when compared to hydrogel dressings and cadexomer iodine showed unclear results when compared to standard treatment (which was a range of different comparators including saline dressings, enzyme-based debriding agents, and nonadhesive dressing). There was no clinical benefit for hydrocolloid dressing compared to povidone-iodone for people completely healed and no clinical benefit of povidone-iodone for mean speed of healing. There was a clinical benefit for the proportion of pressure ulcers reduced by 50 percent, which is an uncommon outcome. There was also a mean percentage reduction in pressure ulcer area but there was no clinical benefit for the mean cm2 reduction in pressure ulcer area for cadexomer iodine compared to standard treatment. Standard treatment was individualised to each person and included saline dressings, enzyme-based debriding agents, and non-adhesive dressings. Povidone-iodine had no clinical benefit when compared to hydrogel dressings. Some benefits were shown for dialysate versus placebo (jelly and ointment) but this study was extremely small (under 10 participants) and was compared to placebo. There was no clinical difference found between insulin and standard treatment but this was also a small study with few relevant outcomes which was compared to standard treatment. Oxyquinoline ointment was of clinical benefit for the proportion of pressure ulcers completely healed, improved and for reducing the amount of pressure ulcers worsened for people in palliative care s with grade 2 and 3 pressure ulcers when compared to vitamin A and D cream. The GDG were unsure as to whether vitamin A and D cream was a valid comparator. Petrolatum ointment compared to base component was deemed not relevant by the GDG as it contained products which were unlicensed in the UK. One study compared honey to ethoxy-diaminoacridine and nitrofurzaone dressing but the GDG stated that ethoxy-diaminoacridine and nitrofurzaone dressing is not used in clinical practice in the UK and could not be found in the BNF. There was no strong evidence to recommend silver sulfazidine cream over silver dressing. In addition the GDG did not regard this as a relevant comparison. The GDG considered the evidence on growth factors. There was some evidence to suggest their benefit but the GDG felt that more information was needed and therefore further research was required. The GDG noted that most growth factors are used for research but are not generally used in clinical practice. It was noted that it is likely that growth factors have a greater effect on highly debrided wounds but they are very expensive. No evidence was identified on skin protectants, cleansers and moisturisers. The GDG felt that there was no convincing evidence to support a recommendation to suggest the use of 1 topical agent over another or against placebo. The evidence was not strong enough to suggest the effectiveness of topical agents and therefore the choice of agent would be down to local resources and cost. There was no conclusive

	evidence towards saline-soaked gauze or hydrocolloid dressing. There is some cross-over to the dressings review but the topical agents review focuses on the topical agent which is applied or in gauze. In addition the GDG recognised that there were many confounders and biases. The GDG noted that phenytoin cream is used topically for venous leg ulcers, and although it is not routinely used for pressure ulcers, it could be effective. The GDG felt that there was limited evidence available across a broad range of products and as such, it was not appropriate to develop a recommendation in favour of using 1 product. Furthermore, the GDG did not feel that topical agents were likely to be significant additional benefits to the use of topical agents compared to the use of dressings, which were likely to have further benefits for example, in promoting autolytic debridement. Additionally, it is likely that topical agents would need to be used in combination with a dressing. The GDG did not think that the addition of a topical agent to a dressing would provide any further clinical benefit. The GDG therefore developed a recommendation that topical antiseptics and antibiotics should not be routinely used to treat pressure ulcers, acknowledging that there may be specific situations in which the use of these agents may be beneficial.
Economic considerations	One economic evaluation was included which compared saline soaked gauze to polyurethane self-adhesive foam dressing. The polyurethane self-adhesive foam dressing was found to dominate saline soaked gauze. This study was based in the US, therefore applicability to the UK is limited. No economic evaluations were found which compared topical agents to no topical agents, or to dressings. The GDG felt that there was no convincing clinical evidence for the use of topical agents, and noted that use of such topical agents will have resource implications. Therefore, based on current evidence, the use of topical agents is considered unlikely to be cost-effective.
Quality of evidence	Overall the evidence was limited. Most studies looked at different interventions and comparisons and studies were small. Most of the studies had very serious risk of bias, and a few had serious risk of bias. Most of the results where there was an event had serious to very serious limitations. Therefore the overall grading was very low or low. The comparison which had the most studies was saline-soaked gauze compared to hydrocolloid dressing, however when this was meta-analysed there was a lot of heterogeneity and thus the results were analysed separately. This was done according to pre-defined subgroups, such as people with spinal cord injury. Imprecision was serious to very serious for all outcomes except for people with spinal cord injuries. The results forpeople with spinal cord injury had no imprecision or slight imprecision (just crossed the minimally important difference) therefore we have more confidence in these results. The proportion of pressure ulcers completely healed, opposed to the proportion of people with pressure ulcers completely healed, had no imprecision for grade 2 pressure ulcers. The proportion of people with pain, discomfort or skin irritation at dressing removal had no imprecision. The other comparisons were all small studies. Where there was an event there was serious to very serious imprecision and in most cases a very serious risk of bias. In the study of phenytoin versus saline-soaked gauze in people with spinal cord injury there was a serious risk of bias. Saline versus dextranomer had no serious imprecision and very serious risk of bias even though it was a very small study. Cadexomer iodine showed a benefit compared to standard treatment. There was no serious imprecision but there was a very wide confidence interval that nearly crossed the minimally important difference and a very serious risk of bias.

	Phenytoin did not show benefits compared to hydrocolloid and this study had serious to very serious imprecision where there was an event and had a serious risk of bias for the majority of outcomes. Resin salve showed a benefit compared to hydrofibre for complete healing of pressure ulcers, speed of healing and reduction in mortality but no clinical difference for improvement or worsening of pressure ulcers and skin reactions. Antibiotic ointment compared to foam dressing outcomes showed foam dressing more clinically effective than the antibiotic ointment for complete healing of pressure ulcers and reduction in PUSH score. The type of support surface was not reported in many of the studies. In order for there to be an accurate account of the benefit of the topical agent the surfaces need to be comparable. In addition the application of a topical agent can result in the patient being repositioned which may bias the benefits shown in studies for topical agents.
Other considerations	There is some overlap between the dressings review and the topical agents review as many of the comparators were dressings. Some consideration should be given to the number and frequency of dressing changes, as the topical creams will not require this. Dressings which include iodine may have evidence, this will be considered in the dressings review as this review is focused on the use of solutions. Studies looking at saline were included in the topical agent review as well as the dressings review. Although cleansing of pressure ulcers has not been included in the guideline, saline was included in this review as the studies were focused on treatment as opposed to cleansing.

10.2.2 Neonates, infants, children and young people

Recommendations	**41. Do not routinely use topical antiseptics or antimicrobials to treat a pressure ulcer in neonates, infants, children and young people.**
Relative values of different outcomes	The GDG identified that the proportion of people with pressure ulcers completely healed, time to complete healing, reduction in size and volume and rate of reduction in size and volume of pressure ulcers were the most critical outcomes to inform decision making. It was also recognised that it was important to consider quality of life for this question.
Trade off between clinical benefits and harms	The GDG used 1 statement from the Delphi consensus panel to develop the recommendation 'Healthcare professionals should not routinely use topical antimicrobial dressings (for example, silver or iodine) for the treatment of pressure ulcers in infants, children and young people.' The statement was included in Round 1 of the Delphi consensus survey and did not reach consensus. Qualitative responses gathered during Round 1 of the survey noted that the treatment of a pressure ulcer should be tailored to the needs of the individual. Comments suggested that topical antiseptics and antimicrobials may have a role in some pressure ulcers showing signs of infection. The GDG discussed the comments received on this statement and amended it to reflect that, although topical antimicrobials may be used in some situations for the treatment of infected pressure ulcers, it was likely that systemic antibiotics would be used for the majority of these situations. However, there may be instances were infected pressure ulcers are treated topically and the statement has been clarified to reflect this. The GDG also noted that certain antimicrobials (for example, iodine) were not

	necessarily appropriate for use in these populations and this would be highlighted when developing the recommendation. The amended statement 'Healthcare professionals should not routinely use topical antimicrobials for infected pressure ulcers in neonates, infants, children and young people.' was therefore developed and included in Round 2 of the survey, where it reached consensus agreement. The GDG subsequently discussed the agreed statement and developed a recommendation to reflect this.
Economic considerations	The GDG felt that there was limited clinical benefit to be gained from the use of topical agents in most cases, and noted that use of topical agents will have resource implications. Therefore, based on current evidence, use of topical agents is considered unlikely to be cost-effective for treatment of the majority of pressure ulcers.
Quality of evidence	No RCTs or cohort studies were identified for neonates, infants, children or young people. Formal consensus using a modified Delphi was therefore used to develop the recommendation. To inform the recommendation, the GDG used 1 statement which was included in Round 1 of the Delphi consensus survey and reached 64% consensus agreement. The latter statement was therefore included in Round 2 of the survey, where it reached 86% consensus agreement. Further details can be found in Appendix N.
Other considerations	The GDG noted that Chatper 10 covers the use of iodine dressings in neonates.

11 Dressings

For the promotion of pressure ulcer healing, it is recognised that a moist healing environment is needed which can be stimulated by the use of an appropriate dressing. In order for healing to take place at an optimum rate, all dressing materials used should ensure that the pressure ulcer remains moist with exudate but does not become macerated. It also needs to be free from clinical infection, excessive slough or devitalised tissue, toxic chemical and fibres. To achieve this, there are a number of dressings which fall broadly into 3 groups:

- passive materials which may cover and simply protect the pressure ulcer
- interactive materials, that have the ability to both create and maintain a moist healing environment if used as per manufacturer's instructions
- active materials that because of their mechanism of action have the ability to facilitate a change in composition of the pressure ulcer healing fluid whilst the product is in use. (Thomas 2010).

A number of considerations are also needed when choosing the most appropriate dressing such as the anatomical location of the pressure ulcer, its condition and that of the surrounding skin, the aim of treatment and influence of any relevant aetiological factors.

The choice of dressings is vast and thus the GDG were interested in identifying the most clinically and cost effective dressings for the management of pressure ulcers.

11.1 Review question: What are the most clinically and cost effective dressings for the treatment of pressure ulcers?

For full details see review protocol in Appendix A.

11.1.1 Clinical evidence (adults)

Sixty-two randomised trials were included in this review. [4,7,10,16-19,24,28,31,32,35,41,43,45,46,49,50,58,69,74,81,82,87,90,93,96,98,106,110,115,116,122,124,125,127] Evidence from the included studies is summarised in the clinical GRADE evidence profiles (Table 146). All forest plots and study evidence tables are presented in Appendix Dand Appendix G.

Various types of dressings are used to treat pressure ulcers. A definition of the different dressings is provided in Table 145.

In this review different types of dressings are compared to each other, or to placebo. The following categories were considered, with further information provided in Table 145:

- Passive dressings
- Gauze dressings
- Impregnated gauze dressings
- Charcoal dressings
- Active dressings
- Hydrocolloid dressings
- Foam dressings
- Polyurethane dressings
- Hydrogel
- Alginate dressings

- Hydrofibre dressings
- Capillary dressings
- Collagen dressing
- Hyaluronic dressing
- Copolymer dressing
- Antibacterial dressings
- Silver dressings
- Dextranomer
- Sugar
- Honey
- Other dressings
- Skin replacement
- Growth factors
- Platelet gel

No randomised trials were identified for capillary dressing in the treatment of pressure ulcers.

Summary of included studies

Study	Intervention	Population	Outcome	Follow-up
Agren 1985[4]	Gauze dressing premedicated with zinc Streptokinase-streptodornase ointment	Geriatric adultswith necrotic pressure ulcers	• Reduction in ulcer area • Side effects	8 weeks of treatment
Alm 1989[7]	Hydrocolloid dressing Wet saline gauze dressing	People in jong-term care with pressure ulcers	• Reduction in ulcer area • Side effects	6 weeks of treatment and additional 3 and 6 weeks of follow-up
Amione 2005[10]	Foam dressing (Allevyn) Foam dressing (Biatain)	People with a grade 2 or 3 pressure ulcer (EPUAP classification)	• Proportion of people completely healed • Reduction in ulcer area • Side effects	7 dressings with a maximum of 6 weeks of treatment
Bale 1997[17]	Hydrocolloid dressing Foam dressing	People with a stage 2 or 3 pressure ulcer (Stirling classification)	• Proportion of people completely healed	30 days of treatment or until complete healing
Bale 1998[16]	Hydrogel (Sterigel) Hydrogel (Intrasite)	People with necrotic pressure ulcers	• Wound pain • Side effects	4 weeks of treatment or until complete debridement
Banks 1994a[18]	Hydrocolloid dressing Polyurethane dressing	Inpatients with a grade 2 or 3 pressure ulcer.	• Proportion of people completely healed • Proportion of people improved • Time to healing • Side effects	6 weeks of treatment or until complete healing
Banks 1994b[19]	Hydrocolloid dressing Polyurethane dressing	People in the community with a grade 2 or 3 pressure ulcer.	• Proportion of people completely healed • Proportion of people improved • Side effects	6 weeks of treatment or until complete healing
Belmin 2002[24]	Hydrocolloid dressing Alginate dressing	Inpatients aged 65 years and older with a grade 3 or 4 pressure ulcer (Yarkony's classification)	• Proportion of people with at least 40% healing • Reduction in ulcer area • Side effects	8 weeks of treatment

Study	Intervention	Population	Outcome	Follow-up
Bito 2012[28]	Wrap therapy (polyurethane dressing) Standard care	Inpatients aged 50 years and older with a stage 2 or 3 pressure ulcer (NPUAP classification)	• Time to healing • Difference in PUSH score • Side effects	12 weeks of treatment or until complete healing
Brod 1990[31]	Hydrocolloid dressing Poly-hema	Elderly peoplewith a grade 2 or 3 pressure ulcer	• Proportion of people completely healed • Time to healing • Rate of healing • Side effects	6 weeks of treatment
Brown-Etris 2006[32]	Hydrocolloid dressing Polyurethane dressing	People with a stage 3 or shallow 3pressure ulcer	• Proportion of people completely healed • Reduction in ulcer area • Rate of healing • Side effects	56 days of treatment or until complete healing
Burgos 2000[35]	Hydrocolloid dressing Collagenase ointment	Inpatients with a stage 3 pressure ulcer	• Proportion of people completely healed • Reduction in ulcer area • Side effects	12 weeks of treatment or until complete healing
Chang 1998[41]	Hydrocolloid dressing Wet saline gauze dressing	Inpatients with a stage 2 or 3 pressure ulcer	• Reduction in ulcer area • Side effects	8 weeks of treatment or until complete healing
Chuansuwanich 2011[43]	Silver dressing Silver sulfadiazine cream	In- and outpatients with a stage 3 or 4 pressure ulcer (NPUAP classification)	• Rate of healing • Reduction in PUSH score • Side effects	8 weeks of treatment
Colin 1996[45]	Hydrogel Dextranomer	People with a grade 1, 2, 3 or 4 pressure ulcer (according to AHCRQ and International Association of Enterostomal Therapy)	• Reduction in ulcer area • Side effects	21 days of treatment or until complete healing
Colwell 1993[46]	Hydrocolloid dressing Moist gauze dressing	Inpatients with a stage 2 or 3 pressure ulcer	• Proportion of people completely healed	Minimum 8 days of treatment (range: 6-56 days)

Study	Intervention	Population	Outcome	Follow-up
			• Reduction in ulcer area	
Darkovich 1990[49]	Hydrocolloid dressing Hydrogel	People with a stage 1 or 2pressure ulcer (Enis and Sarmienti classification - equivalent to stage 2 or 3 in the NPUAP system)	• Proportion of ulcers completely healed • Proportion of ulcers improved • Proportion of ulcers not changed • Proportion of ulcers worsened • Reduction in ulcer area • Rate of healing	60 days of treatment or until complete healing, discharge or no change based on clinical judgement
Day 1995[50]	Hydrocolloid dressing: triangular shape versus oval shape	Inpatients with a stage 2 or 3 sacral pressure ulcer (NPUAP classification)	• Proportion of people completely healed • Proportion of people improved • Proportion of people not changed • Proportion of people worsened • Reduction in ulcer length • Side effects	6 dressings or until complete healing
Felzani 2011[58]	Hyaluronic acid Sodium hyaluronate	Inpatients with a stage 1, 2 or 3 pressure ulcer (NPUAP classification)	• Reduction in ulcer area • Time to 50% healing	15 days of treatment
Graumlich 2003[69]	Hydrocolloid dressing Collagen dressing	People with a stage 2 or 3 pressure ulcer (NPUAP classification)	• Proportion of people completely healed • Time to healing • Reduction in ulcer area • Side effects	8 weeks of treatment with a median follow-up of 35 days
Günes 2007[74]	Honey dressing Ethoxydiaminoacridine and nitrofurazone dressing	Inpatients with a stage 2 or 3 pressure ulcer (AHCRQ classification)	• Proportion of ulcers completely healed • Reduction in ulcer area • Reduction in PUSH score • Side effects	5 weeks or until complete healing
Hollisaz	Hydrocolloid dressing	People with a spinal cord injury	• Proportion of ulcers completely	8 weeks of treatment

Study	Intervention	Population	Outcome	Follow-up
2004[81]	Gauze dressing Phenytoin cream	and a stage 1 or 2 pressure ulcer (Shea classification)	healed • Proportion of ulcers improved • Proportion of ulcers worsened • Proportion of people completely healed	
Hondé 2004[82]	Hydrocolloid dressing Amino acid copolymer dressing	Inpatients aged 65 years or older with a grade 2, 3 or 4 pressure ulcer (NPUAP classification)	• Proportion of people completely healed • Time to healing • Side effects	8 weeks of treatment or until complete healing
Kaya 2005[87]	Hydrogel Povidone-iodine gauze dressing	Inpatients with a spinal cord injury and grade 1, 2 or 3 pressure ulcer (NPUAP classification)	• Rate of healing	Not reported
Kerihuel 2010[90]	Hydrocolloid dressing Charcoal dressing	Inpatients with a stage 2c or 4 pressure ulcer (Yarkoni classification)	• Proportion of people worsened • Reduction in ulcer area • Wound pain • Side effects	4 weeks of treatment
Kim 1996[93]	Hydrocolloid dressing Povidone gauze dressing	People with a stage 1 or 2 pressure ulcer (NPUAP classification)	• Proportion of people completely healed • Rate of healing • Side effects	Mean duration was 18.9 (8.2) days in group 1 and 24.3 (11.2) days in group 2
Kordestani 2008[96]	Hydrocolloid dressing Gauze dressing	Inpatients with a pressure ulcer (NPUAP classification) – no stage reported	• Proportion of ulcers completely healed • Side effects	21 days of treatment and 3 months of follow-up
Kraft 1993[98]	Foam dressing Saline moistened gauze dressing	Male veterans with a stage 2 or 3 pressure ulcer (Enterstomal Therapy definition)	• Proportion of people completely healed	24 days of treatment
Ljungberg 2009[106]	Saline gauze dressing Dextranomer	Male adults with a spinal cord injury and exudative pressure ulcers (Eltorai classification)	• Proportion of ulcers improved • Side effects	14 days of treatment

Study	Intervention	Population	Outcome	Follow-up
Matzen 1999[110]	Hydrocolloid dressing Saline gauze dressing	People with a stage 3 or 4 pressure ulcer (Lowthian classification)	• Proportion of people completely healed • Reduction in ulcer volume • Side effects	12 weeks of treatment or until complete healing
Meaume 2003[116]	Foam dressing (Mepilex®) Foam dressing (Tielle®)	People aged 65 years or older with a stage 2 pressure ulcer (NPUAP classification)	• Proportion of people completely healed • Proportion of people improved • Proportion of people worsened • Side effects	8 weeks of treatment or until complete healing
Meaume 2005[115]	Alginate dressing Silver alginate dressing	People aged 65 years or older with a stage III or IV pressure ulcer (NPUAP classification)	• People aged 65 years or older with a stage 3 or 4 pressure ulcer (NPUAP classification)	4 weeks of treatment
Motta 1999[122]	Hydrocolloid dressing Hydrogel	People receiving home care with a stage 2 or 3 pressure ulcer	• Proportion of people completely healed • Rate of healing • Reduction in ulcer area • Side effects	8 weeks of treatment
Mulder 1993[124]	Hydrocolloid dressing Hydrogel	In- and outpatients with a stage 2 or 3 pressure ulcer	• Reduction in ulcer area • Side effects	8 weeks of treatment or until complete healing
Müller 2001[125]	Hydrocolloid dressing Collagenase ointment	Female inpatients with a grade 4 heel pressure ulcer	• Proportion of people completely healed • Time to healing	Maximum 16 weeks
Münter 2006[127]	Silver foam dressing Different types of dressings	People with a grade 2 or 3 pressure ulcer (EPUAP classification)	• People with a grade 2 or 3 pressure ulcer (EPUAP classification)	4 weeks of treatment
Nasar 1982[129]	Dextranomer Chlorinated lime solution	Elderly people with a deep pressure ulcer	• Time to healing (defined as granulation and less than 25% of original ulcer area) • Pain	Until healing

Study	Intervention	Population	Outcome	Follow-up
Neill 1989[133]	Hydrocolloid dressing Saline gauze dressing	People with a grade 2 or 3 pressure ulcer (Shea classification)	• Proportion of ulcers completely healed • Proportion of people worsened • Reduction in ulcer area • Side effects	8 weeks of treatment
Nisi 2005[135]	Protease modulating matrix Vaseline soaked gauze dressing	Inpatients with a stage 2, 3 or 4 pressure ulcer (NPUAP classification)	• Proportion of people completely healed • Time to healing • Side effects	Treatment time not reported. 6 months of follow-up.
Oleske 1986[144]	Polyurethane dressing Saline gauze dressing	Inpatients with a stage 1 or 2 pressure ulcer (Enis and Sarmiento classification)	• Proportion of ulcers completely healed • Proportion of ulcers worsened • Reduction in ulcer area	10 days of treatment
Parish 1979[146]	Dextranomer Sugar and eggs white	Long-term care people with a pressure ulcer	• Proportion of ulcers completely healed • Proportion of people completely healed • Proportion of ulcers improved • Proportion of people improved • Side effects	4 weeks of treatment. Some patients were treated longer.
Payne 2004[149]	Skin replacement Saline moistened gauze dressing	People with a grade 3 pressure ulcer	• Proportion of people completely healed • Reduction in ulcer area • Reduction in ulcer volume • Side effects	Maximum 24 weeks of treatment and up to 2 weeks of follow-up
Payne 2009[148]	Collagen and foam dressing Foam dressing	People with a stage 2pressure ulcer (NPUAP classification)	• Proportion of people completely healed • Time to healing	4 weeks of treatment or until complete healing
Piatkowski	Collagen and foam dressing	People with stagnating pressure	• Proportion of people completely	3weeks.

Study	Intervention	Population	Outcome	Follow-up
2012	Foam dressing	ulcers, of at least 4 weeks' duration	healed	
Rhodes 1979[154]	Sugar Different types of topical agents	Geriatric adults with a pressure ulcer – stage not reported	• Proportion of ulcers completely healed • Mean healing index	Not reported
Rhodes 2001[155]	Hydrocolloid dressing Phenytoin ointment Antibiotic ointment	People in a nursing home with a stage 2 pressure ulcer (AHCPR classification)	• Time to healing • Side effects	Not reported
Sayag 1996[165]	Alginate dressing Dextranomer	People with a grade 3 or 4 pressure ulcer (Yarkony classification)	• Proportion of people healed more than 75% • Proportion of people healed more than 40%Proportion of people stagnated or worsened • Reduction in ulcer area • Side effects	Maximum 8 weeks
Scevola 2010[166]	Allogeneic platelet gel Different types of dressings	People with a spinal cord injury and a grade 3 or 4 pressure ulcer (NPUAP classification)	• Proportion of ulcers completely healed • Proportion of ulcers improved • Reduction in ulcer area	8 weeks of treatment and up to 4 weeks of follow-up
Seaman 2000[170]	Hydrocolloid dressing (SignaDress®) Hydrocolloid dressing (Comfeel®Plus)	People in a nursing home with a stage 2, 3 or 4 pressure ulcer (AHCPR classification)	• People in a nursing home with a stage 2, 3 or 4 pressure ulcer (AHCPR classification)	5 dressing changes or until complete healing
Sebern 1989[171]	Polyurethane dressing Gauze dressing	People receiving home care with a grade 2 or 3 pressure ulcer (Shea classification)	• Proportion of ulcers completely healed • Proportion of ulcers not changed • Proportion of ulcers worsened • Proportion of ulcers decreased in pressure ulcer grade • Proportion of ulcers increased in pressure ulcer grade	5 dressing changes or until complete healing

Study	Intervention	Population	Outcome	Follow-up
			• Reduction in ulcer area	
Seeley 1999[172]	Hydrocolloid dressing Foam dressing	People with a stage2 or 3 pressure ulcer (AHCPR classification)	• Proportion of people completely healed • Reduction in ulcer area • Side effects	8 weeks of treatment
Sipponen 2008[176]	Hydrofibre dressing Resin salve	People in hospital with a grade 2 to 4 pressure ulcer (EPUAP classification)	• Proportion of people completely healed • Proportion of ulcers completely healed • Proportion of ulcers improved • Proportion of ulcers worsened • Mean percentage reduction in ulcer width • Mean percentage reduction in ulcer depth • Speed of healing (days) • Side effects	6 months
Small 2002[177]	Hydrogel Different types of dressings	People in the community with a stage 2, 3 or 4 pressure ulcer (Stirling classification)	• Proportion of people completely healed • Reduction in ulcer area • Side effects	6 weeks of treatment or until complete healing, withdrawal or occurrence of adverse events
Sopata 2002[179]	Foam dressing Hydrogel	People receiving palliative care with a grade 2 or 3 pressure ulcer (Torrance classification)	• Proportion of ulcers completely healed • Proportion of ulcers improved • Rate of healing	8 weeks of treatment or until complete healing
Thomas 1997[192]	Hydrocolloid dressing Foam dressing	People in the community with a grade 2 or 3 pressure ulcer (Stirling classification)	• Proportion of people completely healed • Proportion of people improved • Proportion of people not changed	6 weeks of treatment

Study	Intervention	Population	Outcome	Follow-up
			• Proportion of people worsened • Reduction in ulcer area • Side effects	
Thomas 1998[190]	Hydrogel Saline soaked gauze dressing	People with a stage 2, 3 or 4 pressure ulcer	• Proportion of people completely healed • Proportion of people worsened • Reduction in ulcer area • Time to healing	10 weeks of treatment or until complete healing
Thomas 2005[189,195]	Hydrocolloid dressing Radiant heat dressing	People with a stage 3 or 4pressure ulcer	• Proportion of people completely healed	12 weeks of treatment
Trial 2010	Alginate dressing Silver alginate dressing	People with a pressure ulcer – stage not reported	• Decrease in infection score	15 days of treatment
Winter 1990[207]	Hydrocolloid dressing Paraffin gauze dressing	People with a pressure ulcer – stage not reported	• Proportion of people completely healed • Proportion of people improved • Proportion of people not changed	12 weeks of treatment
Xakellis 1992[209]	Hydrocolloid dressing Saline wet-to-moist gauze dressing	People in long term care with a stage 2 or 3 (Shea classification)	• Proportion of people completely healed • Time to healing	6 months of treatment
Yastrub 2004[211]	Foam dressing Antibiotic ointment	People in long term care with a stage 2 pressure ulcer (AHCPR classification)	• Proportion of people improved • PUSH score	4 weeks of treatment

Table 145: Types of dressings

Dressing type	Usual Presentation	Prime Treatment Objectives
Hydrocolloid dressing	Hydrocolloid layer bonded to a film membrane or foam pad, Semi-permeable to water vapour and oxygen	• Protection • Rehydration of tissues • Promote autolysis • Absorption (moderate) • Optimise the local wound healing environment
Gauze dressing	Cotton - plain weave Ideally should be non-filamented	• Temporary covering • Absorption (minimal) • Padding agent
Foam dressing	Hydrophillic polyurethane foam with or without a plastic film backing. Adhesive and non- adhesive versions	• Protection • Absorption (moderate) • Optimise the local wound healing environment
Polyurethane film membrane dressing	Vapour permeable (to water vapour and oxygen but impermeable to water and micro- organisms) sheets with or without a combined central island pad	• Protection • Minimise risk of infection (Barrier to micro-organisms) • Optimise the local wound healing environment (superficial wounds) • Can also be used as a secondary dressing to secure another interactive dressing in place for example alginates
Collagen dressing	Collagen, silver and oxidised regenerated cellulose matrix sheets (needs to be covered by a secondary dressing)	• Rebalancing the wound environment • Protease modulating matrix dressings used to control the activity of proteolytic enzymes such as MMP's • Stimulate healing
Hydrogel	Amorphous hydrogel (water donating) available in tubes or sheets of a fixed structure	• Rehydration of tissues • Promote autolysis

Dressing type	Usual Presentation	Prime Treatment Objectives
		• Stimulate healing
Alginate	Non-woven or fibrous, non-occlusive, made up of calcium alginate or a combination of calcium alginate and sodium alginate – derived form brown seaweed If has no integral backing sheet, needs to be covered by a secondary dressing	• Fill lesions – sinus or cavity • Absorption • Removal of slough and /or cellular debris from the wound bed • Assists with Heamostasis (should not be prime reason for use) • Stimulate healing
Charcoal dressing	Activated charcoal contained with another dressing material such as viscose rayon / foam / alginate	• Odour absorbing • Fluid absorption • (minimal)
Silver alginate	An alginate (see above) impregnated with Silver	• Anti-microbial effect • Fill lesions – sinus or cavity • Absorption • Removal of slough and /or cellular debris from the wound bed • Assists with Heamostasis (should not be prime reason for use) • Stimulate healing
Silver dressing	Three layer dressing consisting of a polyester core between low adherent silver coated high density polyethylene mesh	• Anti-microbial effect • Minimise risk of infection (Barrier to micro-organisms) • Absorption (moderate) • Stimulate healing
Sugar	Needs to made up as a paste (usually in pharmacy). Always requires a secondary dressing	• Increase osmolarity of wound bed • Antimicrobial effect • Stimulate healing
Hydrofibre dressing	Soft non-woven pad containing hydrocolloid fibres, resemble alginate dressings	• Fill lesions – sinus or cavity • Absorption (moderate)

Dressing type	Usual Presentation	Prime Treatment Objectives
		• Removal of slough and /or cellular debris from the wound bed • Assists with Heamostasis (should not be prime reason for use) • Stimulate healing

Table 146: Clinical evidence profile: hydrocolloid dressing versus gauze dressing

Quality assessment							No of patients/ulcers		Effect			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Hydrocolloid dressing**	**Gauze dressing**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
Proportion of people with pressure ulcers completely healed – general population and people with a spinal cord injury (meta-analysed) – all grade (grade 1 and above) – NPUAP, Shea, Lowthian classification[m81,93,110,209]												
4	Randomised trials	Very serious[a,b]	Very serious[c]	No serious indirectness	Serious[d]	None	62/89 (69.7%)	40/81 (49.4%)	RR 1.38 (0.81 to 2.35)	188 more per 1000 (from 94 more to 667 more)	Very low	Critical
							-	53.7%		204 more per 1000 (from 102 more to 725 more)		
Proportion of people with pressure ulcers completely healed - general population (analysed separately by population due to heterogeneity) – all grade (grade 1 and above) - NPUAP, Shea, Lowthian classification[m 93,110,209]												
3	Randomised trials	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[d]	None	42/61 (68.9%)	32/54 (59.3%)	RR 1.07 (0.77 to 1.48)	41 more per 1000 (from 136 fewer to 284 more)	Very low	Critical
							-	77.8%		54 more per 1000 (from 179 fewer to 373 more)		
Proportion of people with pressure ulcers completely healed - people s with spinal cord injury (analysed separately by population due to heterogeneity) – all grade (grade 1 and above) – Shea classification[81]												
1	Randomised trial	Serious[b]	No serious inconsistency	No serious indirectness	No serious imprecision	None	20/28 (71.4%)	8/27 (29.6%)	RR 2.41 (1.29 to 4.51)	418 more per 1000 (from 86 more to 1000	Moderate	Critical

Quality assessment							No of patients/ulcers		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Hydrocolloid dressing**	**Gauze dressing**	**Relative (95% CI)**	**Absolute**		
										more)		
							-	29.6%		417 more per 1000 (from 86 more to 1000 more)		
Proportion of pressure ulcers completely healed (all sites) - general population and people with a spinal cord injury (meta-analysed) – all grade (grade 1 and above) – NPUAP, Shea classification[n 46,81,96,133]												
4	Randomised trials	Very serious[a,b]	No serious inconsistency	No serious indirectness	No serious imprecision	None	61/137 (44.5%)	23/136 (16.9%)	RR 2.53 (1.7 to 3.78)	259 more per 1000 (from 118 more to 470 more)	Low	Critical
							-	24.4%		373 more per 1000 (from 171 more to 678 more)		
Proportion of pressure ulcers completely healed (all sites) - general population (analysed separately by grade due to heterogeneity) – all grade (grade 1 and above) - NPUAP, Shea classification[n 46,96,133]												
3	Randomised trials	Very serious[a]	Serious[e]	No serious indirectness	Serious[d]	None	38/106 (35.8%)	15/106 (14.2%)	RR 2.46 (1.01 to 5.96)	207 more per 1000 (from 1 more to 702 more)	Very low	Critical
							-	22.2%		324 more per 1000 (from 2 more to 1000 more)		

Quality assessment							No of patients/ulcers		Effect			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Hydrocolloid dressing**	**Gauze dressing**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
Proportion of pressure ulcers completely healed (all sites) - people with a spinal cord injury (analysed separately by grade due to heterogeneity) –all grade (grade 1 and 2)- Shea classification[81]												
1	Randomised trial	Serious[b]	No serious inconsistency	No serious indirectness	No serious imprecision	None	23/31 (74.2%)	8/30 (26.7%)	RR 2.78 (1.48 to 5.22)	475 more per 1000 (from 128 more to 1000 more)	Moderate	Critical
							-	26.7%		475 more per 1000 (from 128 more to 1000 more)		
Proportion of pressure ulcers completely healed (all sites) – general population and people with a spinal cord injury (meta-analysed grade 2 and above) – (grade 2 and 3) – Shea classification[81,133]												
2	Randomised trials	Very serious[a,b]	Serious[f]	No serious indirectness	Serious[d]	None	23/43 (53.5%)	12/53 (22.6%)	RR 2.42 (0.97 to 6.00)	322 more per 1000 (from 7 fewer to 1000 more)	Very low	Critical
							-	21.1%		300 more per 1000 (from 6 fewer to 1000 more)		
Proportion of pressure ulcers completely healed (all sites) - people with a spinal cord injury (analysed separately due to heterogeneity) – grade 2 and above – Shea classification[81]												
1	Randomised	Serious[b]	No serious	No serious	No serious	None	12/18	3/19	RR 4.22	508 more	Moderate	Critical

Quality assessment							No of patients/ulcers		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Hydrocolloid dressing**	**Gauze dressing**	**Relative (95% CI)**	**Absolute**		
	trial		inconsistency	indirectness	imprecision		(66.7%)	(15.8%)	(1.42 to 12.54)	per 1000 (from 66 more to 1000 more)		
							-	15.8%		509 more per 1000 (from 66 more to 1000 more)		
Proportion of pressure ulcers completely healed (all sites) - general population (analysed seperately due to heterogeneity) – grade 2 and above (analysed separately due to heterogeneity) – Shea classification[133]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[d]	None	11/25 (44%)	9/34 (26.5%)	RR 1.66 (0.81 to 3.39)	175 more per 1000 (from 50 fewer to 633 more)	Very low	Critical
							-	26.5%		175 more per 1000 (from 50 fewer to 633 more)		
Proportion of pressure ulcers completely healed (all sites) - general population (analysed separately due to heterogeneity) – grade 3 (analysed separately due to heterogeneity) – Shea classification[133]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[g]	None	2/17 (11.8%)	1/11 (9.1%)	RR 1.29 (0.13 to 12.62)	26 more per 1000 (from 79 fewer to 1000 more)	Very low	Critical
							-	9.1%		26 more		

Quality assessment							No of patients/ulcers		Effect			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Hydrocolloid dressing**	**Gauze dressing**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
										per 1000 (from 79 fewer to 1000 more)		
Proportion of pressure ulcers completely healed (sacral) - people with a spinal cord injury – grade 1 and 2 (analysed separately due to heterogeneity) – Shea classification[133]												
1	Randomised trial	Serious[b]	No serious inconsistency	No serious indirectness	Serious[d]	None	0/7 (0%)	4/8 (50%)	Peto OR 0.09 (0.01 to 0.84)	417 fewer per 1000 (from 43 fewer to 490 fewer)	Low	Critical
							-	50%		417 fewer per 1000 (from 43 fewer to 490 fewer)		
Proportion of pressure ulcers improved - people with a spinal cord injury – all grade (grade 1 and 2) – Shea classification[133]												
1	Randomised trial	Serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	27/31 (87.1%)	29/60 (48.3%)	RR 1.8 (1.34 to 2.42)	387 more per 1000 (from 164 more to 686 more)	Moderate	Critical
							-	48.3%		386 more per 1000 (from 164 more to 686 more)		
Proportion of pressure ulcers worsened– general pressure ulceration and people with a spinal cord injury (meta-analysed) – all grade (grade 1 to 3) - Shea classification[81,133]												
2	Randomised	Very	Very serious[c]	No serious	Very	None	16/73	24/75	RR 0.53 (0.12 to	150 fewer per 1000	Very low	Critical

Quality assessment							No of patients/ulcers		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Hydrocolloid dressing**	**Gauze dressing**	**Relative (95% CI)**	**Absolute**		
	trials	serious[a,b]		indirectness	serious[g]		(21.9%)	(32%)	2.46)	(from 282 fewer to 467 more)		
							-	31.7%		149 fewer per 1000 (from 279 fewer to 463 more)		
Proportion of pressure ulcers worsened - people with a spinal cord injury (analysed separately due to pressure ulceration)– all grade (grade 1 and 2) - Shea classification [81]												
1	Randomised trial	Serious[b]	No serious inconsistency	No serious indirectness	Serious[d]	None	2/31 (6.5%)	9/30 (30%)	RR 0.22 (0.05 to 0.91)	234 fewer per 1000 (from 27 fewer to 285 fewer)	Low	Critical
							-	30%		234 fewer per 1000 (from 27 fewer to 285 fewer)		
Proportion of pressure ulcers worsened - general pressure ulceration (analysed separately due to pressure ulceration) – all grade (grade 2 and 3) - Shea classification[133]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[g]	None	14/42 (33.3%)	15/45 (33.3%)	RR 1 (0.55 to 1.81)	0 fewer per 1000 (from 150 fewer to 270 more)	Very low	Critical
							-	33.3%		0 fewer per 1000 (from 150		

Quality assessment							No of patients/ulcers		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Hydrocolloid dressing**	**Gauze dressing**	**Relative (95% CI)**	**Absolute**		
										fewer to 270 more)		
Proportion of pressure ulcers worsened - general pressure ulceration – grade 2 (analysed separately due to heterogeneity)- Shea classification[133]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[g]	None	7/25 (28%)	11/34 (32.4%)	RR 0.87 (0.39 to 1.92)	42 fewer per 1000 (from 197 fewer to 298 more)	Very low	Critical
							-	32.4%		42 fewer per 1000 (from 198 fewer to 298 more)		
Proportion of pressure ulcers worsened - general pressure ulceration – grade 3 (analysed separately due to heterogeneity) - Shea classification[133]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[g]	None	7/17 (41.2%)	4/11 (36.4%)	RR 1.13 (0.43 to 2.98)	47 more per 1000 (from 207 fewer to 720 more)	Very low	Critical
							-	36.4%		47 more per 1000 (from 207 fewer to 721 more)		
Mean percentage reduction in pressure ulcer area – general pressure ulceration – all grade (grade 2 and 3) – classification system not reported[41,123]												
2	Randomised trials	Very serious[a,h,0]	No serious inconsistency	No serious indirectness	Serious[d]	None	18.65 (n=38)	46.73 (n=37)	-	MD 0.34 higher (14.71 lower to 15.38 higher)	Very low	Critical

Quality assessment							No of patients/ulcers		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Hydrocolloid dressing**	**Gauze dressing**	**Relative (95% CI)**	**Absolute**		
Mean cm² reduction in pressure ulcer area – inpatients – all grade (grade 2 and 3) – classification system not reported[46]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[j]	None	0.73 (n=48)	-0.67 (n=49)	-	Not pooled	Very low	Critical
Median percentage reduction in pressure ulcer area– people in long-term care– all grade – classification system not reported[7]												
1	Randomised trial	Very serious[k]	No serious inconsistency	No serious indirectness	Very serious[l]	None	100 (n=28)	85.7 (n=21)	-	Not pooled	Very low	Critical
Median percentage reduction in pressure ulcer area– in-and out patients – grade 2 and 3 - classification system not reported[124]												
1	Randomised trial	Very serious[h]	No serious inconsistency	No serious indirectness	Very serious[j]	None	7.4 (n=21)	7.0 (n=20)	-	Not pooled	Very low	Critical
Median percentage reduction in pressure ulcer area - general pressure ulceration – grade 2 – Shea classification[133]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[j]	None	91 (n=25)	48 (n=34)	p>0.05	Not pooled	Very low	Critical
Median percentage reduction in pressure ulcer area - general pressure ulceration – grade 3 – Shea classification[133]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[i]	None	0.3 (n=17)	30 (n=11)	p>0.05	Not pooled	Very low	Critical
Mean percentage reduction in pressure ulcer volume – general pressure ulceration – all grade (grade 3 and 4) – Lowthian classification[110]												
1	Randomised trial	Very serious[a,p]	No serious inconsistency	No serious indirectness	No serious imprecision	None	26 (SD 20)	64 (SD 16)	-	MD 38 higher (50.49 to 25.51 lower)	Low	Critical
Mean healing speed of pressure ulcers (mm²/day) – general pressure ulceration – all grade (grade 1 and 2) - NPUAP classification[93]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[d]	None	9.1 (SD 5.4)	7.9 (SD 4.7)	-	MD 1.2 higher (1.8 lower to 4.2 higher)	Very low	Critical

Quality assessment							No of patients/ulcers		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Hydrocolloid dressing**	**Gauze dressing**	**Relative (95% CI)**	**Absolute**		
Median time to healing of pressure ulcers (days) – people in long-term care– all grade (grade 2 and 3) – Shea classification[209]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[i]	None	9 (n=18)	11 (n=21)	-	Not pooled	Very low	Critical
Proportion of people with an infection – inpatients – all grade (grade 2 and 3) – no classification reported[41]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[g]	None	0/17 (0%)	1/17 (0%)	OR 0.14 (0.00 to 6.82)	50 fewer per 1000 (from 59 fewer to 240 more)	Very low	Important
							-	0%		50 fewer per 1000 (from 59 fewer to 240 more)		
Proportion of infected pressure ulcers – inpatients – no grade reported – NPUAP classification[96]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	0/16 (0%)	0/12 (0%)	not pooled	Not pooled	Low	Important
							-	0%		Not pooled		
Proportion of people with hypergranulation - general pressure ulceration – all grade (grade 1 and 2) - NPUAPclassification[93]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[g]	None	3/26 (11.5%)	0/18 (0%)	OR 5.9 (0.56 to 62.29)	120 more (from 30 fewer to 260 more)	Very low	Important
							-	0%		120 more (from 30 fewer to 260 more)		
Proportion of people with skin irritation – general pressure ulceration – all grade (grade 2 and 3) – Shea classification[133]												
1	Randomised	Very	No serious	No serious	No serious	None	0/50	9/50	OR 0.11	156 fewer	Low	Important

Quality assessment							No of patients/ulcers		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Hydrocolloid dressing**	**Gauze dressing**	**Relative (95% CI)**	**Absolute**		
	trial	serious[a]	inconsistency	indirectness	imprecision		(0%)	(18%)	(0.03 to 0.44)	per 1000 (from 92 fewer to 173 fewer)		
							-	18%		156 fewer per 1000 (from 92 fewer to 173 fewer)		
Proportion of people with pain at dressing removal - inpatients – all grade (grade 2 and 3) – classification system not reported[41]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	0/17 (0%)	7/17 (41.2%)	OR 0.09 (0.02 to 0.45)	352 fewer per 1000 (from 172 fewer to 398 fewer)	Low	Important
							-	41.2%		353 fewer per 1000 (from 172 fewer to 398 fewer)		
Median pain score during treatment (scoring system not reported) - general pressure ulceration – all grade (grade 3 and 4) – Lowthian classification[110]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[i]	None	2.0 (range: 1-3) (n=17)	2.0 (range: 1-3) (n=15)	-	Not pooled	Very low	Important
Median odour score during treatment (scoring system not reported) - general pressure ulceration – all grade (grade 3 and 4) – Lowthian classification[110]												
1	Randomised	Very	No serious	No serious	Very	None	2.0	2.0	-	Not	Very low	Important

Quality assessment							No of patients/ulcers		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Hydrocolloid dressing**	**Gauze dressing**	**Relative (95% CI)**	**Absolute**		
	trial	serious[a]	inconsistency	indirectness	serious[i]		(range: 1-4) (n=17)	(range: 1-3) (n=15)		pooled		
Proportion of people with discomfort - inpatients – all grade (grade 2 and 3) – classification system not reported[41]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	0/17 (0%)	9/17 (52.9%)	Peto OR 0.07 (0.02 to 0.32)	456 fewer per 1000 (from 265 fewer to 507 fewer)	Low	Important
							-	52.9%		456 fewer per 1000 (from 265 fewer to 507 fewer)		
Median comfort score during treatment (scoring system not reported) – general pressure ulceration – all grade (grade 3 and 4) – Lowthian classification[110]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[i]	None	4.0 (range: 3-4) (n=17)	3.0 (range: 2-4) (n=15)	-	Not pooled	Very low	Important
Mortality (all cause)[96,110,209]												
6	Randomised trials	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[d]	None	2/119 (1.7%)	14/150 (9.3%)	RR 0.24 (0.07 to 0.89)	71 fewer per 1000 (from 10 fewer to 87 more)	Very low	Important
							-	3.3%		25 fewer per 1000 (from 4 fewer to		

Quality assessment							No of patients/ulcers		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Hydrocolloid dressing	Gauze dressing	Relative (95% CI)	Absolute		
										31 fewer)		
Time to complete healing of pressure ulcers												
0	-	-	-	-	-	-	-	-	-	-	-	-
Rate of healing of pressure ulcers												
0	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
0	-	-	-	-	-	-	-	-	-	-	-	-

(a) Kim (1996), Matzen (1999), Xakellis (1992), Colwell (1993), Kordestani (2008), Neill (1989), Chang (1998)[41,46,93,96,110,133,209] did not report or there was insufficient information on sequence generation, allocation concealment and no blinding. Matzen (1999)[110]: drop out 10% differential or higher than event rate for proportion completely healed. Colwell (1993):[46] Drop out is more than 10% higher than event rate for proportion completely healed. Kordestani (2008):[96] Drop out is more than 10% higher than event rate for proportion completely healed for proportion of infected ulcers.

(b) Hollisaz (2004):[81] only blinding of outcome assessor.

(c) Different pressure ulcerations and high heterogeneity (> 50%) and p-value < 0.1.

(d) The confidence interval crossed 1 MID point.

(e) Heterogeneity > 50%.

(f) Different pressure ulcerations and high heterogeneity (> 50%) but p-value > 0.1.

(g) The confidence interval crossed both MID points.

(h) Mulder (1993):[124] no report on allocation concealment or blinding.

(i) No standard deviations were reported and the study used a small sample size.

(j) No standard deviation was reported and it was unknown if sample size was sufficient.

(k) Alm (1989):[7] no report on sequence generation; allocation concealment by stratification according to Norton score; only blinding of outcome assessor.

(l) No standard deviation was reported and the number of participants completed per group was unclear.

(m) Kim (1996):[93] NPUAP classification; Matzen (1999):[110] Lowthian classificatio.; Xakellis (1992) and Hollisaz (2004):[81,209] Shea classification.

(n) Kordestani (2008)[96]: NPUAP classification; Colwell (1993):[46] no classification reported; Neill (1989) and Hollisaz (2004):[81] Shea classification.

(o) Chang (1998)[41]: standard deviation was calculated based on the available raw data. Mulder (1993): no transformation of data.

(p) Matzen (1999):[110] no log-transformation of data was carried out.

Table 147: Clinical evidence profile: hydrocolloid dressing versus foam dressing

Quality assessment	No of patients	Effect	Quality	Importance

No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Hydrocolloid dressing	Foam dressing	Relative (95% CI)	Absolute		
Proportion of people with pressure ulcers completely healed – general pressure ulceration – all grade (grade 2 and 3) – Stirling and AHCPR classification[g 17,172,192]												
3	Randomised trials	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	None	29/77 (37.7%)	25/80 (31.3%)	RR 1.24 (0.81 to 1.9)	75 more per 1000 (from 59 fewer to 281 more)	Very low	Critical
								40%		96 more per 1000 (from 76 fewer to 360 more)		
Proportion of people with pressure ulcers improved – people in the community – all grade (grade 2 and 3) – Stirling classification[192]												
1	Randomised trial	Very serious[c]	No serious inconsistency	No serious indirectness	No serious imprecision	None	39/48 (81.3%)	39/48 (81.3%)	RR 1 (0.83 to 1.21)	0 fewer per 1000 (from 138 fewer to 171 more)	Low	Critical
								81.3%		0 fewer per 1000 (from 138 fewer to 171 more)		
Proportion of people with pressure ulcers not changed - general pressure ulceration – all grade (grade 2 and 3) – Stirling classification[17,192]												
2	Randomised trials	Very serious[a, c]	No serious inconsistency	No serious indirectness	Very serious[d]	None	5/79 (6.3%)	2/77 (2.6%)	RR 2.17 (0.50 to 9.33)	30 more per 1000 (from 13 fewer to 216 more)	Very low	Critical
								4.2%		49 more per 1000 (from 21 fewer to 350 more)		
Proportion of people with pressure ulcers worsened - general pressure ulceration – all grade (grade 2 and 3) – Stirling classification[17,192]												

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Hydrocolloid dressing**	**Foam dressing**	**Relative (95% CI)**	**Absolute**		
2	Randomised trials	Very serious[a, c]	No serious inconsistency	No serious indirectness	Very serious[d]	None	9/79 (11.4%)	6/77 (7.8%)	RR 1.48 (0.56 to 3.94)	37 more per 1000 (from 34 fewer to 229 more)	Very low	Critical
								10.4%		50 more per 1000 (from 46 fewer to 306 more)		
Mean percentage reduction in pressure ulcer area – general pressure ulceration – all grade (grade 2 and 3) - AHCPR classification[172]												
1	Randomised trial	Very serious[c, h]	No serious inconsistency	No serious indirectness	Serious[b]	None	52 (SD 6.06)	50 (SD 6.06)	-	MD 2.0 higher (1.81 lower to 5.81 higher)	Very low	Critical
Proportion of people with hypergranulation – people in the community – all grade (grade 2 and 3) – Stirling classification[192]												
1	Randomised trial	Very serious[c]	No serious inconsistency	No serious indirectness	No serious imprecision	None	0/49 (0%)	0/50 (0%)	not pooled	0 more (from 4 fewer to 4 more)	Low	Important
								0%		0 more (from 4 fewer to 4 more)		
Proportion of people with bleeding - people in the community – all grade (grade 2 and 3) – Stirling classification[192]												
1	Randomised	Very	No serious	No serious	Very serious[d]	None	2/49	0/50	Peto OR	4 more	Very	Important

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Hydrocolloid dressing**	**Foam dressing**	**Relative (95% CI)**	**Absolute**		
	trial	serious[c]	inconsistency	indirectness			(4.1%)	(0%)	7.7 (0.47 to 124.89)	(from 3 fewer to 11 more)	low	
								0%		4 more (from 3 fewer to 11 more)		
Proportion of people with maceration - people in the community – all grade (grade 2 and 3) – Stirling classification[192]												
1	Randomised trial	Very serious[c]	No serious inconsistency	No serious indirectness	Serious[b]	None	4/49 (8.2%)	0/50 (0%)	Peto OR 8.04 (1.1 to 58.85)	8 more (from 0 fewer to 170 more)	Very low	Important
								0%		8 more (from 0 fewer to 170 more)		
Proportion of people with inflammation or maceration – general population – all grade (grade 2 and 3) - AHCPR classification[172]												
1	Randomised trial	Very serious[e]	No serious inconsistency	No serious indirectness	Serious[b]	None	6/19 (31.6%)	12/20 (60%)	RR 0.53 (0.25 to 1.12)	282 fewer per 1000 (from 450 fewer to 72 more)	Very low	Important
								60%		282 fewer per 1000 (from 450 fewer to 72 more)		

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Hydrocolloid dressing**	**Foam dressing**	**Relative (95% CI)**	**Absolute**		
Mean pain score at end of treatment (scale 0 no pain - 3 severe pain) – general population – all grade (grade 2 and 3) - AHCPR classification[172]												
1	Randomised trial	Very serious[e]	No serious inconsistency	No serious indirectness	Serious[b]	None	0.47 (SD 0.9)	0.15 (SD 0.8)	-	MD 0.32 higher (0.22 lower to 0.86 higher)	Very low	Important
Mean odour score at end of treatment (scale 0 no odour - 3 severe odour) – general population – all grade (grade 2 and 3) - AHCPR classification[172]												
1	Randomised trial	Very serious[e]	No serious inconsistency	No serious indirectness	Serious[b]	None	0.47 (SD 0.8)	0.16 (SD 0.5)	-	MD 0.31 higher (0.11 lower to 0.73 higher)	Very low	Important
Proportion of people with adverse events (unknown if dressing related) – general population – all grade (grade 2 and 3) – Stirling and AHCPR classification[g17,172]												
2	Randomised trials	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[d]	None	5/51 (9.8%)	8/49 (16.3%)	RR 0.61 (0.22 to 1.71)	64 fewer per 1000 (from 127 fewer to 116 more)	Very low	Important
								17.7%		69 fewer per 1000 (from 138 fewer to 126 more)		
Mortality (all-cause)[17]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[d]	None	2/31 (6.5%)	6/29 (20.7%)	RR 0.31 (0.07 to 1.42)	143 fewer per 1000 (from 192 fewer to 87 more)	Very low	Important

Time in hospital or NHS care

Quality assessment							No of patients		Effect			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Hydrocolloid dressing**	**Foam dressing**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
								20.7%		143 fewer per 1000 (from 193 fewer to 87 more)		
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Patient acceptability												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) Bale (1997):[17] did not report on sequence generation, allocation concealment and blinding; Seeley (1999)did not report allocation concealment by stratification according to initial ulcer size and no blinding; Thomas (1997): [192]did not report on sequence generation and there was no blinding.

(b) The confidence interval crossed 1 MID point.

(c) Thomas (1997):[192] did not report on sequence generation and there was no blinding.

(d) The confidence interval crossed both MID points.

(e) Seeley (1999):[172] allocation concealment by stratification according to initial ulcer size and no blinding.

(f) No standard deviation was reported and the study used a small sample size.

(g) Bale (1997) and Thomas (1997): [192]Stirling classification; Seeley (1999):[172] AHCPR classification.

(h) Seeley (1999):[172] no log-transformation of data was carried out.

Table 148: Clinical evidence profile profile: hydrocolloid dressing versus polyurethane dressing

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Hydrocolloid dressing	Polyurethane dressing	Relative (95% CI)	Absolute	Quality	Importance
Proportion of people with pressure ulcers completely healed – general population (meta-analysed) – all grade (grade 2 and 3) – classification system not reported[18,19,32]												
3	Randomised trials	Very serious[a]	Serious[b]	No serious indirectness	Serious[c]	None	43/59 (72.9%)	43/63 (68.3%)	RR 1.07 (0.87 to 1.33)	48 more per 1000 (from 89 fewer to 225 more)	Very low	Critical
							-	66.7%		47 more per 1000 (from 87 fewer to 220 more)		
Proportion of people with pressure ulcers improved – people in the community (analysed separately due to heterogeneity)– all grade (grade 2 and 3) – classification system not reported[19]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	10/10 (100%)	18/18 (100%)	RR 1 (0.86 to 1.16)	0 fewer per 1000 (from 140 fewer to 160 more)	Low	Critical
							-	100%		0 fewer per 1000 (from 140 fewer to 160 more)		
Mean percentage reduction in pressure ulcer area - general population (analysed separately due to heterogeneity) – all grade (grade 2 and 3) – classification system not reported[32]												

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Hydrocolloid dressing	Polyurethane dressing	Relative (95% CI)	Absolute	Quality	Importance
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[d]	None	23.8 (n=37)	26.7 (n=35)	-	Not pooled	Very low	Critical
Median time to healing of pressure ulcers (days) – inpatients - all grade (grade 2 and 3) – classification system not reported[19]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[e]	None	12.69 (n=12)	13.36 (n=10)	p > 0.05	Not pooled	Very low	Critical
Linear healing rate of pressure ulcers (cm/week) - general population – all grade (grade 2 and 3) – classification system not reported[32]												
1	Randomised trial	Very serious[a,h]	No serious inconsistency	No serious indirectness	Serious[c]	None	0.12 (n=37)	0.10 (n=35)	-	MD 0.02 higher (0.06 lower to 0.1 higher)	Very low	Critical
Mean odour score (1 very poor - 5 very good) - general population – all grade (grade 2 and 3) – classification system not reported[32]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[c]	None	4.8 (SD 0.39)	5 (SD 0.14)	-	MD 0.2 lower (0.33 to 0.07 lower)	Very low	Important
Mean comfort score (1 very poor - 5 very good) - general population – all grade (grade 2 and 3) – classification system not reported[32]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[c]	None	4.4 (SD 0.66)	4.8 (SD 0.34)	-	MD 0.4 lower (0.64 to 0.16 lower)	Very low	Important
Proportion of people with adverse events - general population – all grade (grade 2 and 3) – classification system not reported[32]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	0/37 (0%)	0/35 (0%)	Not pooled	Not pooled	Low	Important
							-	0%		Not		

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Hydrocolloid dressing	Polyurethane dressing	Relative (95% CI)	Absolute	Quality	Importance
										pooled		
Proportion of people with pain at dressing removal - general population– all grades (grade 2 and 3) – classification system not reported[18,19]												
2	Randomised trials	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[f]	None	-	-	p < 0.005	Not pooled	Very low	Important
							-	0%		Not pooled		
Proportion of people with discomfort at dressing removal – general population – all grades (grade 2 and 3) – classification system not reported[18,19]												
2	Randomised trials	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[g]	None	-	-	p > 0.05	Not pooled	Very low	Important
							-	0%		Not pooled		
Mortality (all-cause) [18,19]												
2	Randomised trials	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[i]	None	2/36 (5.6%)	1/33 (3%[19])	RR 2 (0.2 to 20.33)	30 more per 1000 (from 24 fewer to 586 more)	Very low	Important
							-	2.5%		25 more per 1000 (from 20 fewer to 483 more)		
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital or NHS care												

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Hydrocolloid dressing	Polyurethane dressing	Relative (95% CI)	Absolute	Quality	Importance
-	-	-	-	-	-	-	-	-	-	-	-	-
Patient acceptability												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) No report on sequence generation, allocation concealment and no blinding.
(b) Heterogeneity > 50%; p-value of 0.1.
(c) Confidence interval crossed 1MID point.
(d) No standard deviation; unknown if sample size was sufficient.
(e) No standard deviation; small sample size.
(f) Only p-values and a figure are reported. Both studies showed more pain in the hydrocolloid group compared to the polyurethane group.
(g) Only p-values and a figure are reported. Both studies showed more discomfort in the hydrocolloid group compared to the polyurethane group.
(h) Brown-Etris (2006):[32] no log-transformation of data.
(i) Confidence interval crossed both MID points.

Table 149: Clinical evidence profile: hydrocolloid dressing versus collagenase ointment

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Hydrocolloid dressing	Collagenase	Relative (95% CI)	Absolute	Quality	Importance
Proportion of people with pressure ulcers completely healed – general population – all grades (grade 2 and above) – no system classification reported[35,125]												
2	Randomised trials	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	10/30 (33.3%)	14/30 (46.7%)	RR 0.75 (0.45 to 1.26)	117 fewer per 1000 (from 257 fewer to 121 more)	Very low	Critical
							-	54.2%		135 fewer per 1000 (from 298 fewer to 141 more)		

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Hydrocolloid dressing**	**Collagenase**	**Relative (95% CI)**	**Absolute**		
Mean percentage reduction in pressure ulcer area – inpatients – all grades (grade 3) - classification system not reported[35]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	73.7 (SD=92.4)	83.3 (SD=92.4)	-	MD 9.6 lower (69.17 lower to 49.97 higher)	Very low	Critical
Mean cm² reduction in pressure ulcer area – inpatients – all grades (grade 3) - classification system not reported[35]												
1	Randomised trial	Very serious[a, d]	No serious inconsistency	No serious indirectness	Serious[c]	None	6.2 (SD 9.8)	9.1 (SD 12.7)	-	MD 2.9 lower (10.24 lower to 4.44 higher)	Very low	Critical
Mean time to pressure ulcer healing (weeks) – general population - all grades (grade 4) – classification system not reported[125]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	14 (SD 4.6)	10 (SD 4.6)	-	MD 4 higher (0.24 to 7.76 higher)	Very low	Critical
Proportion of people with adverse events[e] – inpatients – all grades (grade 3) - classification system not reported[35]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	2/19 (10.5%)	1/18 (5.6%)	RR 1.89 (0.19 to 19.13)	49 more per 1000 (from 45 fewer to 1000 more)	Very low	Important
							-	5.6%		50 more per 1000 (from 45 fewer to 1000 more)		
Mortality (all-cause)[35,125]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	1/31 (3.2%)	3/30 (10%)	RR 0.32 (0.04 to 2.76)	68 fewer per 1000 (from 96 fewer to 176 more)	Very low	Important
								8.3%		56 fewer per 1000 (from 80		

Rate of reduction in size of pressure ulcers												
Quality assessment							**No of patients**		**Effect**			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Hydrocolloid dressing**	**Collagenase**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
										fewer to 146 more)		
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital or NHS care												
-	-	-	-	-	-	-	-	-	-	-	-	-
Patient acceptability												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) Burgos (2000a): no allocation concealment and only blinding of assessor; Müller (2001): no report on sequence generation, allocation concealment and no blinding.
(b) Confidence interval crossed both MID points.
(c) Confidence interval crossed 1 MID point.
(d) Burgos (2000a): no allocation concealment and only blinding of assessor; no log-transformation of data.
(e) Hydrocolloid group: 1 participant had erythema and exudate and 1participant had exudate and intense odour. Collagenase group: 1 participant had dermatitis.

Table 150: Clinical evidence profile: hydrocolloid dressing versus collagen

Quality assessment							**No of patients**		**Effect**			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Hydrocolloid dressing**	**Collagen**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
Proportion of people with pressure ulcers completely healed – inpatients – all grades (grade 2 and 3) - NPUAP classification[69]												
1	Randomised trial	Serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	15/30 (50%)	18/35 (51.4%)	RR 0.97 (0.6 to	15 fewer per 1000 (from	Very low	Critical

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Hydrocolloid dressing	Collagen	Relative (95% CI)	Absolute	Quality	Importance
									1.57)	206 fewer to 293 more)		
							-	51.4%		15 fewer per 1000 (from 206 fewer to 293 more)		
Mean percentage reduction in pressure ulcer area – inpatients – all grades (grade 2 and 3) - NPUAP classification[69]												
1	Randomised trial	Serious[a]	No serious inconsistency	No serious indirectness	Serious[c]	None	9 (SD=73.98)	33 (SD=73.98)	-	MD 24 lower (60.08 lower to 12.08 higher)	Low	Critical
Mean healing speed of pressure ulcers (mm²/day) – inpatients – all grades (grade 2 and 3) - NPUAP classification[69]												
1	Randomised trial	Serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	6 (SD 16)	6 (SD 19)	-	MD 0 higher (8.23 lower to 8.23 higher)	Moderate	Critical
Mean time to healing of pressure ulcers (weeks) – inpatients – all grades (grade 2 and 3) - NPUAP classification[69]												
1	Randomised trial	Serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	6 (SD 2.68)	6 (SD 2.68)	-	MD 1 higher (0.36 lower to	Very low	Critical

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Hydrocolloid dressing	Collagen	Relative (95% CI)	Absolute	Quality	Importance
										2.36 higher)		
Proportion of people with adverse events – inpatients – all grades (grade 2 and 3) - NPUAP classification[69]												
1	Randomised trial	Very serious[d]	No serious inconsistency	No serious indirectness	No serious imprecision	None	0/30 (0%)	0/35 (0%)	not pooled	Not pooled	Low	Important
							-	0%		Not pooled		
Mortality (all-cause)[69]												
1	Randomised trial	Serious[a]	No serious inconsistency	No serious indirectness	Very Serious[b]	None	2/30 (6.7%)	3/35 (8.6%)	RR 0.78 (0.14 to 4.35)	19 fewer per 1000 (from 74 fewer to 287 more)	Very low	Important
							-	8.6%		19 fewer per 1000 (from 74 fewer to 288 more)		
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital or NHS care												
-	-	-	-	-	-	-	-	-	-	-	-	-
Patient acceptability												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Hydrocolloid dressing	Collagen	Relative (95% CI)	Absolute	Quality	Importance
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) Only blinding of outcome assessor.
(b) Confidence interval crossed both MID points.
(c) Confidence interval crossed 1 MID point.
(d) Only blinding of outcome assessor; drop out is more than 10% higher than event rate.

Table 151: Clinical evidence profile: hydrocolloid dressing versus hydrogel

Quality assessment							No of patients/ulcers		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Hydrocolloid dressing	Hydrogel	Relative (95% CI)	Absolute	Quality	Importance
Proportion of people with pressure ulcers completely healed – people in the community – all grades (grade 2 and 3) – classification system not reported (but described as partial thickness wounds which is equivalent to stage II and III in the NPUAP classification system) [122]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[c,b]	None	2/5 (40%)	2/5 (40%)	RR 1 (0.22 to 4.56)	0 fewer per 1000 (from 312 fewer to 1000 more)	Very low	Critical
							-	40%		0 fewer per 1000 (from 312 fewer to 1000 more)		
Proportion of pressure ulcers completely healed (all sites) – general population - all grades (grade 1 and 2) – Enis and Sarmienti classification (equivalent to grade 2 and 3 in the NPUAP classification system)[49]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[c]	None	12/67 (17.9%)	24/62 (38.7%)	RR 0.46 (0.25 to	209 fewer per 1000 (from 62	Very low	Critical

Quality assessment							No of patients/ulcers		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Hydrocolloid dressing**	**Hydrogel**	**Relative (95% CI)**	**Absolute**		
									0.84)	fewer to 290 fewer)		
							-	38.7%		209 fewer per 1000 (from 62 fewer to 290 fewer)		
Proportion of pressure ulcers not changed – general population - all grades (grade 1 and 2) – Enis and Sarmienti classification (equivalent to stage II and III in the NPUAP classification system)[49]												
1	Randomised trial	Very serious[b]	No serious inconsistency	No serious indirectness	Very serious[b]	None	8/67 (11.9%)	5/62 (8.1%)	RR 1.48 (0.51 to 4.28)	39 more per 1000 (from 40 fewer to 265 more)	Very low	Critical
							-	8.1%		39 more per 1000 (from 40 fewer to 266 more)		
Proportion of pressure ulcers worsened– general population - all grades (grade 1 and 2) – Enis and Sarmienti classification (equivalent to stage II and III in the NPUAP classification system)[49]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[c]	None	7/67 (10.4%)	1/62 (1.6%)	RR 6.48 (0.82 to 51.16)	88 more per 1000 (from 3 fewer to 809 more)	Very low	Critical
							-	1.6%		88 more per 1000 (from 3 fewer to 803 more)		
Mean percentage reduction in pressure ulcer area– general population – grade 1 - Enis and Sarmienti classification (equivalent to stage II and III in the NPUAP classification system) [49]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[d]	None	44 (n=31)	72 (n=27)	p > 0.05	Not pooled	Very low	Critical
Mean percentage reduction in pressure ulcer area– general population – grade 2 - Enis and Sarmienti classification (equivalent to stage II and III in the NPUAP classification system) [49]												

Quality assessment							No of patients/ulcers		Effect			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Hydrocolloid dressing**	**Hydrogel**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
1	Randomised trial	Very serious[a, i]	No serious inconsistency	No serious indirectness	Very serious[c,e]	None	34 (SD 47.7)	64 (SD 47.7)	-	MD 30 lower (52.19 to 7.81 lower)	Very low	Critical
Median percentage reduction in pressure ulcer area– in –and outpatients – all grades (grade 2 and 3) – classification system not reported[124]												
1	Randomised trial	Very serious[f]	No serious inconsistency	No serious indirectness	Very serious[d]	None	7.4 (n=21)	5.6 (n=20)	-	Not pooled	Very low	Critical
Mean healing rate of pressure ulcers (cm/day) – people in the community – all grades (grade 2 and 3) – classification system not reported[122]												
1	Randomised trial	Very serious[a, i]	No serious inconsistency	No serious indirectness	Very serious[b]	None	0.35 (SD 0.43)	0.15 (SD 0.22)	-	MD 0.2 higher (0.22 lower to 0.62 higher)	Very low	Critical
Healing rate of pressure ulcers (%/day) – general population - all grades (grade 1 and 2) – Enis and Sarmienti classification[49]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[g]	None	3.1 (n=?)	8.1 (n=?)	-	Not pooled	Very low	Critical
Median odour score during treatment – people in the community – all grades (grade 2 and 3) – classification system not reported[122]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[h]	None	2 (n=5)	2 (n=5)	-	Not pooled	Very low	Important
Median comfort score during treatment – people in the community – all grades (grade 2 and 3) – classification system not reported[122]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[h]	None	3 (n=5)	4 (n=5)	-	Not pooled	Very low	Important
Mortality (all-cause)[122]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious	None	0/5 (0%)	0/5 (0%)	Not pooled	Not pooled	Low	Important
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-

Quality assessment							No of patients/ulcers		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Hydrocolloid dressing	Hydrogel	Relative (95% CI)	Absolute	Quality	Importance
Time in hospital or NHS care												
-	-	-	-	-	-	-	-	-	-	-	-	-
Patient acceptability												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) No report on sequence generation, allocation concealment and no blinding.
(b) The confidence interval crossed both MID points.
(c) The confidence interval crossed 1 MID point.
(d) No standard deviation was reported; unknown if sample size was insufficient.
(e) The standard deviation was calculated on a p-value <0.01 (less precise).
(f) Mulder (1993) did not report on allocation concealment and no blinding was reported.
(g) No standard deviation was reported and it is unknown how many ulcers were included in analysis.
(h) No standard deviation was reported and the study used a very small sample size.
(i) No log-transformation of data was carried out.

Table 152: Clinical evidence profile: hydrocolloid dressing versus impregnated gauze

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Hydrocolloid dressing	Impregnated gauze	Relative (95% CI)	Absolute	Quality	Importance
Proportion of people with pressure ulcers completely healed – general population – grade and classification system not reported[207]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	5/6 (83.3%)	3/5 (60%)	RR 1.39 (0.62 to 3.09)	234 more per 1000 (from 228 fewer to 1000	Very low	Critical

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Hydrocolloid dressing	Impregnated gauze	Relative (95% CI)	Absolute	Quality	Importance
										more)		
							-	60%		234 more per 1000 (from 228 fewer to 1000 more)		
Proportion of people with pressure ulcers improved – general population – grade and classification system not reported[207]												
1	Randomised trial	Very serious[a,c]	No serious inconsistency	No serious indirectness	Very serious[b]	None	6/6 (100%)	5/5 (100%)	RR 1 (0.73 to 1.37)	0 fewer per 1000 (from 270 fewer to 370 more)	Very low	Critical
							-	100%		0 fewer per 1000 (from 270 fewer to 370 more)		
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate of change in size of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Hydrocolloid dressing	Impregnated gauze	Relative (95% CI)	Absolute	Quality	Importance
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital or NHS care												
Patient acceptability												
-	-	-	-	-	-	-	-	-	-	-	-	-
Side effects												
-	-	-	-	-	-	-	-	-	-	-	-	-
Mortality (all-cause)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) No report on sequence generation, allocation concealment and no blinding was reported.
(b) The confidence interval crossed both MID points.
(c) The drop out is more than 10% higher than event rate.

Table 153: Clinical evidence profile: hydrocolloid dressing versus poly-hema dressing

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Hydrocolloid dressing	Poly-hema dressing	Relative (95% CI)	Absolute	Quality	Importance
Proportion of people with pressure ulcers completely healed – elderly people – all grades (grade 2 and 3) – classification system not reported[31]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	10/16 (62.5%)	14/27 (51.9%)	RR 1.21 (0.71 to 2.04)	109 more per 1000 (from 150	Very low	Critical

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Hydrocolloid dressing	Poly-hema dressing	Relative (95% CI)	Absolute	Quality	Importance
										fewer to 539 more)		
							-	51.9%		109 more per 1000 (from 151 fewer to 540 more)		
Median time to healing of pressure ulcers (days) – elderly people – all grades (grade 2 and 3) – classification system not reported[31]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[c]	None	42 (n=16)	32 (n=27)	p=0.56	Not pooled	Very low	Critical
Absolute rate of healing of pressure ulcers (cm²/week) – elderly people – all grades (grade 2 and 3) – classification system not reported[31]												
1	Randomised trial	Very serious[a, g]	No serious inconsistency	No serious indirectness	Serious[d]	None	0.10 (SD 0.085)	0.18 (SD 0.085)	-	MD 0.08 lower (0.13 to 0.03 lower)	Very low	Critical
Proportion of people with adverse events – elderly people – all grades (grade 2 and 3) – classification system not reported[31]												
1	Randomised trial	Very serious[a, f]	No serious inconsistency	No serious indirectness	Very serious[b]	None	1/16 (6.3%)	0/27 (0%)	Peto OR 14.69 (0.25 to 847.55)	6 more (from 8 fewer to 210 more)	Very low	Important
							-	0%		6 more (from 8 fewer to 210		

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Hydrocolloid dressing	Poly-hema dressing	Relative (95% CI)	Absolute	Quality	Importance
										more)		
Mortality (all-cause) [31]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	1/16 (6.3%)	2/27 (7.4%)	RR 0.84 (0.08 to 8.58)	12 fewer per 1000 (from 68 fewer to 561 more)	Very low	Important
							-	-				
Reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital or NHS care												
-	-	-	-	-	-	-	-	-	-	-	-	-
Patient acceptability												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) Allocation concealment was stratified according to lesion stage and only blinding of the outcome assessor was reported.
(b) The confidence interval crossed both MID points.
(c) No standard deviation was reported and the study used a small sample size.
(d) The confidence interval crossed 1 MID point.
(e) It was unknown if adverse events were dressing related.
(f) The drop out is more than 10% higher than event rate.
(g) No log-transformation of data was carried out.

Table 154: Clinical evidence profile: hydrocolloid dressing versus co-polymer (amino acid) dressing

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Hydrocolloid dressing	Copolymer (amino acid)	Relative (95% CI)	Absolute		
Proportion of people with pressure ulcers completely healed – inpatients – all grades (grade 2, 3 or 4) – NPUAP classification[82]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	None	23/88 (26.1%)	31/80 (38.8%)	RR 0.67 (0.43 to 1.05)	128 fewer per 1000 (from 221 fewer to 19 more)	Very low	Critical
							-	38.8%		128 fewer per 1000 (from 221 fewer to 19 more)		
Median time to pressure ulcer healing (days) – inpatients – all grades (grade 2, 3 or 4) – NPUAP classification[82]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[c]	None	38 (range: 13-59) (n=88)	32 (range:11-63) (n=80)	p=0.044 (adjusted for wound depth)	Not pooled	Very low	Critical
Proportion of people with an infection – inpatients – all grades (grade 2, 3 or 4) – NPUAP classification[82]												
1	Randomised trial	Very serious[a,e]	No serious inconsistency	No serious indirectness	Very serious[d]	None	6/88 (6.8%)	6/80 (7.5%)	RR 0.91 (0.31 to 2.7)	7 fewer per 1000 (from 52 fewer to 128 more)	Very low	Important
							-	7.5%		7 fewer		

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Hydrocolloid dressing	Copolymer (amino acid)	Relative (95% CI)	Absolute	Quality	Importance
										per 1000 (from 52 fewer to 128 more)		
Rate of change in size in pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital or NHS care												
-	-	-	-	-	-	-	-	-	-	-	-	-
Patient acceptability												
-	-	-	-	-	-	-	-	-	-	-	-	-
Mortality (all-cause)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) No report on allocation concealment or blinding.
(b) The confidence interval crossed 1 MID point.
(c) No standard deviation was reported.
(d) The confidence interval crossed both MID points.
(e) The drop out is more than 10% higher than event rate.

Table 155: Clinical evidence profile: hydrocolloid dressing versus phenytoin cream

Quality assessment							No of patients/ulcers		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Hydrocolloid dressing	Phenytoin cream	Relative (95% CI)	Absolute	Quality	Importance
Proportion of people with pressure ulcers completely healed – people with a spinal cord injury – all grades (grade 1 and 2) – Shea classification[81]												
1	Randomised trial	Serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	20/28 (71.4%)	8/27 (29.6%)	RR 2.41 (1.29 to 4.51)	418 more per 1000 (from 86 more to 1000 more)	Moderate	Critical
							-	29.6%		417 more per 1000 (from 86 more to 1000 more)		
Proportion of pressure ulcers completely healed – people with a spinal cord injury – all grades (grade 1 and 2) – Shea classification[81]												
1	Randomised trial	Serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	None	23/31 (74.2%)	12/30 (40%)	RR 1.85 (1.14 to 3.01)	340 more per 1000 (from 56 more to 804 more)	Low	Critical
							-	40%		340 more per 1000 (from 56 more to 804 more)		
Proportion of pressure ulcers improved – people with a spinal cord injury – all grades (grade 1 and 2) – Shea classification[81]												

Quality assessment							No of patients/ulcers		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Hydrocolloid dressing**	**Phenytoin cream**	**Relative (95% CI)**	**Absolute**		
1	Randomised trial	Serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	None	27/31 (87.1%)	16/30 (53.3%)	RR 1.63 (1.14 to 2.34)	336 more per 1000 (from 75 more to 715 more)	Low	Critical
							-	53.3%		336 more per 1000 (from 75 more to 714 more)		
Proportion of pressure ulcers worsened– people with a spinal cord injury – all grades (grade 1 and 2) – Shea classification[81]												
1	Randomised trial	Serious[a]	No serious inconsistency	No serious indirectness	Very serious[c]	None	2/31 (6.5%)	2/30 (6.7%)	RR 0.97 (0.15 to 6.44)	2 fewer per 1000 (from 57 fewer to 363 more)	Very low	Critical
							-	6.7%		2 fewer per 1000 (from 57 fewer to 364 more)		
Mortality (all-cause) [81]												
1	Randomised trial	Serious[a]	No serious inconsistency	No serious indirectness	No serious	None	0/28 (0%)	0/28 (0%)	Not pooled	Not pooled	Moderate	Important
Time to complete healing of pressure ulcers												

Quality assessment							No of patients/ulcers		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Hydrocolloid dressing	Phenytoin cream	Relative (95% CI)	Absolute	Quality	Importance
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate of change in size of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital or NHS care												
-	-	-	-	-	-	-	-	-	-	-	-	-
Patient acceptability												
-	-	-	-	-	-	-	-	-	-	-	-	-
Side effects												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) Only blinding of outcome assessor was reported.
(b) The confidence interval crossed 1 MID point.
(c) The confidence interval crossed both MID points.

Table 156: Clinical evidence profile: hydrocolloid dressing versus alginate dressing

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Hydrocolloid dressing	Alginate dressing	Relative (95% CI)	Absolute	Quality	Importance
Proportion of people with pressure ulcers partially (40%) healed – older inpatients – all grades (grade 3 and 4) – Yarkony classification[24]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	None	31/53 (58.5%)	43/57 (75.4%)	RR 0.78 (0.59 to 1.02)	166 fewer per 1000 (from 309 fewer to 15 more)	Very low	Critical
							-	75.4%		166 fewer per 1000 (from 309 fewer to 15 more)		
Mean percentage reduction in pressure ulcer area – older inpatients – all grades (grade 3 and 4) – Yarkony classification[24]												
1	Randomised trial	Very serious[a,e]	No serious inconsistency	No serious indirectness	No serious imprecision	None	42.6 (SD 49.1)	69.1 (SD 33.9)	-	MD 26.5 lower (42.38 to 10.62 lower)	Low	Critical
Mean cm² reduction in pressure ulcer area – older inpatients – all grades (grade 3 and 4) – Yarkony classification[24]												
1	Randomised trial	Very serious[a,e]	No serious inconsistency	No serious indirectness	No serious imprecision	None	5.2 (SD 7.2)	9.7 (SD 7.1)	-	MD 4.5 lower (7.17 to 1.83 lower)	Very low	Critical
Proportion of people with an infection – older inpatients – all grades (grade 3 and 4) – Yarkony classification[24]												
1	Randomised trial	Very serious[a,d]	No serious inconsistency	No serious indirectness	Very serious[c]	None	0/53 (0%)	1/57 (1.8%)	Peto OR 0.15 (0	15 fewer per 1000	Very low	Important

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Hydrocolloid dressing	Alginate dressing	Relative (95% CI)	Absolute		
									to 7.34)	(from 18 fewer to 98 more)		
							-	1.8%		15 fewer per 1000 (from 18 fewer to 101 more)		
Proportion of people with skin irritation – older inpatients – all grades (grade 3 and 4) – Yarkony classification[24]												
1	Randomised trial	Very serious[a,d]	No serious inconsistency	No serious indirectness	Very serious[c]	None	0/53 (0%)	2/57 (3.5%)	Peto OR 0.14 (0.01 to 2.31)	30 fewer per 1000 (from 35 fewer to 46 more)	Very low	Important
							-	3.5%		30 fewer per 1000 (from 35 fewer to 46 more)		
Proportion of people with hypergranulation – older inpatients – all grades (grade 3 and 4) – Yarkony classification[24]												
1	Randomised trial	Very serious[a,d]	No serious inconsistency	No serious indirectness	Very serious[c]	None	5/53 (9.4%)	1/57 (1.8%)	RR 5.38 (0.65 to 44.54)	77 more per 1000 (from 6 fewer to 764 more)	Very low	Important
							-	1.8%		79 more per 1000 (from 6 fewer to 784		

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Hydrocolloid dressing	Alginate dressing	Relative (95% CI)	Absolute		
										more)		
Proportion of people with maceration – older inpatients – all grades (grade 3 and 4) – Yarkony classification[24]												
1	Randomised trial	Very serious[a,d]	No serious inconsistency	No serious indirectness	Very serious[c]	None	0/53 (0%)	1/57 (1.8%)	Peto OR 0.15 (0 to 7.34)	15 fewer per 1000 (from 18 fewer to 98 more)	Very low	Important
							-	1.8%		15 fewer per 1000 (from 18 fewer to 101 more)		
Proportion of people with bleeding – older inpatients – all grades (grade 3 and 4) – Yarkony classification[24]												
1	Randomised trial	Very serious[a,d]	No serious inconsistency	No serious indirectness	Very serious[c]	None	0/53 (0%)	1/57 (1.8%)	Peto OR 0.15 (0 to 7.34)	15 fewer per 1000 (from 18 fewer to 98 more)	Very low	Important
							-	1.8%		15 fewer per 1000 (from 18 fewer to 101 more)		
Incidence of pain at dressing removal – older inpatients – all grades (grade 3 and 4) – Yarkony classification[24]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	411/1314 (31.3%)	316/887 (35.6%)	RR 0.88 (0.78 to 0.99)	43 fewer per 1000 (from 4 fewer to 78 fewer)	Very low	Important

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Hydrocolloid dressing**	**Alginate dressing**	**Relative (95% CI)**	**Absolute**		
							-	35.6%		43 fewer per 1000 (from 4 fewer to 78 fewer)		
Incidence of strong odour at dressing removal – older inpatients – all grades (grade 3 and 4) – Yarkony classification[24]												
1	Randomised trials	Very serious[a,d]	No serious inconsistency	No serious indirectness	Serious[b]	None	173/1314 (13.2%)	178/887 (20.1%)	RR 0.66 (0.54 to 0.79)	68 fewer per 1000 (from 42 fewer to 92 fewer)	Very low	Important
							-	20.1%		68 fewer per 1000 (from 42 fewer to 92 fewer)		
Incidence of mild odour at dressing removal – older inpatients – all grades (grade 3 and 4) – Yarkony classification[24]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	None	382/1314 (40.7%)	361/887 (40.7%)	RR 0.71 (0.64 to 0.80)	118 fewer per 1000 (from 81 fewer to 147 fewer)	Very low	Important
								40.7%		118 fewer per 1000 (from 81 fewer to 147 fewer)		
Mortality (all-cause) [24]												

Quality assessment							No of patients		Effect			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Hydrocolloid dressing**	**Alginate dressing**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[c]	None	11/57 (19.3%)	8/53 (15.1%)	RR 1.28 (0.56 to 2.93)	42 more per 1000 (from 66 fewer to 291 more)	Very low	Important
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Proportion of people with pressure ulcers completely healed												
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate of change in size of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital or NHS care												
-	-	-	-	-	-	-	-	-	-	-	-	-
Patient acceptability												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) Sequence generation was by block of 4 participants; allocation was balanced by centre; only blinding of outcome assessor.
(b) The confidence interval crossed 1 MID point.
(c) The confidence interval crossed both MID points.
(d) The drop out is more than 10% higher than event rate.
(e) No log-transformation of data was carried out.

Table 157: Clinical evidence profile: hydrocolloid dressing versus charcoal dressing

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Hydrocolloid dressing	Charcoal dressing	Relative (95% CI)	Absolute	Quality	Importance
Proportion of people with pressure ulcers worsened – inpatients – all grades (grade 2c and 4) – Yarkoni classification[90]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	1/30 (3.3%)	0/29 (0%)	Peto OR 7.15 (0.14 to 360.38)	3 more (from 6 fewer to 120 more)	Very low	Critical
							-	0%		3 more (from 6 fewer to 120 more)		
Median percentage reduction in pressure ulcer area– inpatients – all grades (grade 2c and 4) – Yarkoni classification[90]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[c]	None	18.5 (range:100 to -260.9) (n=31)	26.9 (range: 82 to -97.9) (n=29)	-	Not pooled	Very low	Critical
Median cm² reduction in pressure ulcer area – inpatients – all grades (grade 2c and 4) – Yarkoni classification[90]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[c]	None	3.1 (range: 24.1 to -46.0) (n=31)	4.3 (range: 31.2 to -13.8) (n=29)	-	Not pooled	Very low	Critical
Proportion of people with maceration – inpatients – all grades (grade 2c and 4) – Yarkoni classification[90]												
1	Randomised trial	Very serious[a,e]	No serious inconsistency	No serious indirectness	Very serious[b]	None	2/30 (6.7%)	0/29 (0%)	Peto OR 7.4 (0.45 to	7 more (from 4 fewer to	Very low	Important

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Hydrocolloid dressing	Charcoal dressing	Relative (95% CI)	Absolute	Quality	Importance
									121.22)	170 more)		
							-	0%		7 more (from 4 fewer to 170 more)		
Proportion of people with an infection – inpatients – all grades (grade 2c and 4) – Yarkoni classification[90]												
1	Randomised trial	Very serious[a,e]	No serious inconsistency	No serious indirectness	Very serious[d]	None	2/30 (6.7%)	1/29 (3.4%)	RR 1.93 (0.19 to 20.18)	32 more per 1000 (from 28 fewer to 661 more)	Very low	Important
							-	3.5%		33 more per 1000 (from 28 fewer to 671 more)		
Proportion of people with hypergranulation – inpatients – all grades (grade 2c and 4) – Yarkoni classification[90]												
1	Randomised trial	Very serious[a,e]	No serious inconsistency	No serious indirectness	Very serious[d]	None	1/30 (3.3%)	0/29 (0%)	Peto OR 7.15 (0.14 to 360.38)	3 more (from 6 fewer to 120 more)	Very low	Important

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Hydrocolloid dressing	Charcoal dressing	Relative (95% CI)	Absolute	Quality	Importance
							-	0%		3 more (from 6 fewer to 120 more)		
Proportion of people with skin irritation and eczema – inpatients – all grades (grade 2c and 4) – Yarkoni classification[90]												
1	Randomised trial	Very serious[a,e]	No serious inconsistency	No serious indirectness	Very serious[d]	None	1/30 (3.3%)	0/29 (0%)	Peto OR 7.15 (0.14 to 360.38)	3 more (from 6 fewer to 120 more)	Very low	Important
							-	0%		3 more (from 6 fewer to 120 more)		
Proportion of people with bleeding – inpatients – all grades (grade 2c and 4) – Yarkoni classification[90]												
1	Randomised trial	Very serious[a,e]	No serious inconsistency	No serious indirectness	No serious imprecision	None	0/30 (0%)	0/29 (0%)	not pooled	0 more (from 6 fewer to 6 more)	Low	Important
							-	0%		0 more (from 6 fewer to 6 more)		
Proportion of people with pruritus – inpatients – all grades (grade 2c and 4) – Yarkoni classification[90]												

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Hydrocolloid dressing**	**Charcoal dressing**	**Relative (95% CI)**	**Absolute**		
1	Randomised trial	Very serious[a,e]	No serious inconsistency	No serious indirectness	Very serious[d]	None	0/30 (0%)	1/29 (3.4%)	Peto OR 0.13 (0 to 6.59)	30 fewer per 1000 (from 34 fewer to 156 more)	Very low	Important
							-	3.5%		30 fewer per 1000 (from 35 fewer to 158 more)		
Proportion of people with wound pain – inpatients – all grades (grade 2c and 4) – Yarkoni classification[90]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	0/30 (0%)	0/29 (0%)	Not pooled	0 more (from 6 fewer to 6 more)	Low	Important
							-	0%		0 more (from 6 fewer to 6 more)		
Proportion of people with pain at dressing removal – inpatients – all grades (grade 2c and 4) – Yarkoni classification[90]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[d]	None	19/30 (63.3%)	19/29 (65.5%)	RR 0.97 (0.66 to 1.41)	20 fewer per 1000 (from 223 fewer to 269 more)	Very low	Important

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Hydrocolloid dressing	Charcoal dressing	Relative (95% CI)	Absolute	Quality	Importance
							-	65.5%		20 fewer per 1000 (from 223 fewer to 269 more)		
Mortality (all-cause)[90]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious imprecision[d]	None	2/31 (6.5%)	1/29 (3.4%)	RR 1.87 (0.18 to 19.55)	30 more per 1000 (from 28 fewer to 640 more)	Very low	Important
							-	3.5%		30 more per 1000 (from 29 fewer to 649 more)		
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Proportion of people with pressure ulcers completely healed												
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate of change in size of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Patient acceptability												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) No report on sequence generation and only blinding of outcome assessor.
(b) The confidence interval crossed both MID points.
(c) No standard deviation was reported and it was unknown if sample size was sufficient.
(d) The confidence interval crossed both MID points.
(e) The drop out is more than 10% higher than event rate.

Table 158: Clinical evidence profile: hydrocolloid dressing versus phenytoin ointment

Quality assessment							No of patients		Effect			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Hydrocolloid dressing**	**Phenytoin ointment**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
Mean time to healing of pressure ulcers (days) – people in a nursing home – all grades (grade 2) – AHCPR classification[155]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	None	51.8 (SD 19.6)	35.3 (SD 14.3)	-	MD 16.5 higher (3.62 to 29.38 higher)	Very low	Critical
Proportion of people with adverse events – people in a nursing home – all grades (grade 2) – AHCPR classification[155]												
1	Randomised trial	Very serious[a,c]	No serious inconsistency	No serious indirectness	No serious imprecision	None	0/13 (0%)	0/15 (0%)	Not pooled	0 more (from 130 fewer to 130 more)	Low	Important
							-	0%		0 more (from 130 fewer to 130 more)		
Mortality (all-cause) [155]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[d]	None	2/16 (12.5%)	2/18 (11.1%)	RR 1.13 (0.18 to 7.09)	13 more per 1000 (from 91 fewer to 677	Very low	Important

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Hydrocolloid dressing	Phenytoin ointment	Relative (95% CI)	Absolute	Quality	Importance
										more)		
							-	11.1%		13 more per 1000 (from 91 fewer to 676 more)		
Proportion of people with pressure ulcers completely healed												
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate of change in size of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Reduction in size and volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital or NHS care												
-	-	-	-	-	-	-	-	-	-	-	-	-
Patient acceptability												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) No report on sequence generation, allocation concealment or blinding.
(b) The confidence interval crossed 1 MID point.
(c) The drop out is more than 10% higher than event rate.
(d) The confidence interval crossed both MID points.

Table 159: Clinical evidence profile: hydrocolloid dressing versus antibiotic ointment

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Hydrocolloid dressing	Antibiotic ointment	Relative (95% CI)	Absolute	Quality	Importance
Mean time to healing of pressure ulcers (days) – people in a nursing home – all grades (grade 2) – AHCPR classification[155]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	51.8 (SD 19.6)	53.8 (SD 8.5)	-	MD 2 lower (13.78 lower to 9.78 higher)	Very low	Critical
Proportion of people with adverse events – people in a nursing home – all grades (grade 2) – AHCPR classification[155]												
1	Randomised trial	Very serious[a,c]	No serious inconsistency	No serious indirectness	No serious imprecision	None	0/13 (0%)	0/11 (0%)	Not pooled	0 more (from 150 fewer to 150 more)	Low	Important
							-	0%		0 more (from 150 fewer to 150 more)		
Proportion of people with pressure ulcers completely healed												
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate of change in size of pressure ulcer												
-	-	-	-	-	-	-	-	-	-	-	-	-
Reduction in size and volume of pressure ulcer												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital or NHS care												
-	-	-	-	-	-	-	-	-	-	-	-	-

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Hydrocolloid dressing	Antibiotic ointment	Relative (95% CI)	Absolute	Quality	Importance
Patient acceptability												
-	-	-	-	-	-	-	-	-	-	-	-	-
Mortality (all cause)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) No report on sequence generation, allocation concealment or blinding.
(b) The confidence interval crossed both MID points.
(c) The drop out is more than 10% higher than event rate.

Table 160: Clinical evidence profile: hydrocolloid dressing: triangular shape versus oval shape

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Hydrocolloid dressing: triangular shape	Hydrocolloid dressing: oval shape	Relative (95% CI)	Absolute	Quality	Importance
Proportion of people with pressure ulcers completely healed – inpatients – all grades (grade 2 and 3) – NPUAP classification[50]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	None	17/47 (36.2%)	11/49 (22.4%)	RR 1.61 (0.85 to 3.07)	137 more per 1000 (from 34 fewer to 465 more)	Very low	Critical
							-	22.5%		137 more per 1000 (from 34		

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Hydrocolloid dressing: triangular shape	Hydrocolloid dressing: oval shape	Relative (95% CI)	Absolute	Quality	Importance
										fewer to 466 more)		
Proportion of people with pressure ulcers improved – inpatients – all grades (grade 2 and 3) – NPUAP classification[50]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	None	41/47 (87.2%)	31/49 (63.3%)	RR 1.38 (1.08 to 1.75)	240 more per 1000 (from 51 more to 474 more)	Very low	Critical
							-	63.3%		241 more per 1000 (from 51 more to 475 more)		
Proportion of people with pressure ulcers not changed – inpatients – all grades (grade 2 and 3) – NPUAP classification[50]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[c]	None	4/47 (8.5%)	3/49 (6.1%)	RR 1.39 (0.33 to 5.88)	24 more per 1000 (from 41 fewer to 299 more)	Very low	Critical
							-	6.1%		24 more per 1000 (from 41 fewer to 298		

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Hydrocolloid dressing: triangular shape	Hydrocolloid dressing: oval shape	Relative (95% CI)	Absolute	Quality	Importance
										more)		
Proportion of people with pressure ulcers worsened – inpatients – all grades (grade 2 and 3) – NPUAP classification[50]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	2/47 (4.3%)	15/49 (30.6%)	RR 0.14 (0.03 to 0.58)	263 fewer per 1000 (from 129 fewer to 297 fewer)	Low	Critical
							-	91.8%		789 fewer per 1000 (from 386 fewer to 890 fewer)		
Mean percentage reduction in pressure ulcer length – inpatients – all grades (grade 2 and 3) – NPUAP classification[50]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	32 (SD 34.15)	17 (SD 34.15)	-	MD 15 higher (1.33 to 28.67 higher)	Low	Critical
Mean percentage reduction in pressure ulcer width – inpatients – all grades (grade 2 and 3) – NPUAP classification[50]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[d]	None	28 (n=47)	24 (n=49)	p > 0.05	Not pooled	Very low	Critical
Mean pain at dressing change – inpatients – all grades (grade 2 and 3) – NPUAP classification[50]												
1	Randomised	Very	No serious	No serious	No serious	None	2.1	4.3	-	MD 2.2	Low	Important

Quality assessment							No of patients		Effect			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Hydrocolloid dressing: triangular shape**	**Hydrocolloid dressing: oval shape**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
	trial	serious[a]	inconsistency	indirectness	imprecision		(SD 2.1)	(SD 1.75)		lower (2.97 to 1.43 lower)		
Proportion of people with ulcer pain – inpatients – all grades (grade 2 and 3) – NPUAP classification[50]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	None	8/47 (17%)	15/49 (30.6%)	RR 0.56 (0.26 to 1.19)	135 fewer per 1000 (from 227 fewer to 58 more)	Very low	Important
							-	30.6%		135 fewer per 1000 (from 226 fewer to 58 more)		
Proportion of people with adverse events – inpatients – all grades (grade 2 and 3) – NPUAPclassification[50]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	None	0/47 (0%)	4/49 (8.2%)	OR 0.13 (0.02 to 0.97)	70 fewer per 1000 (from 2 fewer to 80 fewer)	Very low	Important
							-	8.2%		71 fewer per 1000 (from 2 fewer to		

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Hydrocolloid dressing: triangular shape	Hydrocolloid dressing: oval shape	Relative (95% CI)	Absolute	Quality	Importance
										80 fewer)		
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate of change in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital or NHS care												
-	-	-	-	-	-	-	-	-	-	-	-	-
Patient acceptability												
-	-	-	-	-	-	-	-	-	-	-	-	-
Mortality (all-cause)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) Randomised schedule and no report on allocation concealment and no blinding was reported. no log-transformation of data was carried out.
(b) The confidence interval crossed 1 MID point.
(c) The confidence interval crossed both MID points.
(d) No standard deviation was reported and it was unknown if sample size was sufficient.
(e) Oval group: increase in necrotic tissue, wound size and depth, inflammation of surrounding skin, severe pain upon dressing removal, and bleeding.

Table 161: Clinical evidence profile: hydrocolloid dressing (SignaDress) versus hydrocolloid dressing (ComfeelPlus)

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Hydrocolloids : SingaDress	Hydrocolloids : ComfeelPlus	Relative (95% CI)	Absolute	Quality	Importance
Proportion of people with pressure ulcers completely healed – people in a nursing home – all grades (grade 2 to 4) – AHCPR classification[170]												
1	Randomised trial	Very serious[a, d]	No serious inconsistency	No serious indirectness	Serious[b]	None	6/17 (35.3%)	1/18 (5.6%)	RR 6.35 (0.85 to 47.44)	297 more per 1000 (from 8 fewer to 1000 more)	Very low	Critical
							-	5.6%		300 more per 1000 (from 8 fewer to 1000 more)		
Percentage reduction in pressure ulcer area – people in a nursing home – all grades (grade 2 to 4) – AHCPR classification[170]												
1	Randomised trial	Very serious[a, e]	No serious inconsistency	No serious indirectness	Very serious[c]	None	60 (n=17)	22 (n=18)	p=0.01	Not pooled	Very low	Critical
Healing rate of pressure ulcers (%/week) – people in a nursing home – all grades (grade 2 to 4) – AHCPR classification[170]												
1	Randomised trial	Serious[a]	No serious inconsistency	No serious indirectness	Very serious[c]	None	33.8 (n=17)	7.0 (n=18)	-	Not pooled	Very low	Critical
Proportion of people with adverse events – people in a nursing home – all grades (grade 2 to 4) – AHCPR classification[170]												
1	Randomised trial	Very serious[a, d]	No serious inconsistency	No serious indirectness	No serious imprecision	None	0/17 (0%)	0/18 (0%)	Not pooled	0 (from 100 fewer to 100 more)	Low	Important
							-	0%		0 (from 100 fewer to 100		

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Hydrocolloids : SingaDress	Hydrocolloids : ComfeelPlus	Relative (95% CI)	Absolute	Quality	Importance
										more)		
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital or NHS care												
-	-	-	-	-	-	-	-	-	-	-	-	-
Patient acceptability												
-	-	-	-	-	-	-	-	-	-	-	-	-
Mortality (all-cause)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) The authors did not reportreport on blinding.
(b) The confidence interval crossed 1 MID point.
(c) No standard deviation was reported and the study used a small sample size.
(d) The drop out is more than 10% higher than event rate.
(e) No log-transformation of data was carried out.

Table 162: Clinical evidence profile: gauze dressing versus foam dressing

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Gauze dressing	Foam dressing	Relative (95% CI)	Absolute		
Proportion of people with pressure ulcers completely healed – general population – all grades (grade 2 and 3) – Enterostomal Therapy and NPUAP classification[d98,148]												
2	Randomised trials	Very serious[a,e]	No serious inconsistency	No serious indirectness	Serious[b]	None	9/30 (30%)	20/44 (45.5%)	RR 0.64 (0.34 to 1.22)	164 fewer per 1000 (from 300 fewer to 100 more)	Very low	Critical
							-	45.8%		165 fewer per 1000 (from 302 fewer to 101 more)		
Median time to 50% healing of pressure ulcers (days) – general population – grade 2 – NPUAP classification[148]												
1	Randomised trials1	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[c]	None	28 (n=16)	28 (n=20)	-	Not pooled	Very low	Critical
Mortality (all-cause) [98,148]												
2	Randomised trials	Very serious[a,e]	No serious inconsistency	No serious indirectness	Very serious[c]	None	4/30 (13.3%)	3/44 (6.8%)	RR 1.76 (0.49 to 6.34)	52 more per 1000 (from 35 fewer to 364 more)	Very low	Important
							-	7.5%		57 more per 1000 (from 38 fewer to 401		

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Gauze dressing	Foam dressing	Relative (95% CI)	Absolute	Quality	Importance
										more)		
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate of change in size of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Reduction in size and volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital or NHS care												
-	-	-	-	-	-	-	-	-	-	-	-	-
Patient acceptability												
-	-	-	-	-	-	-	-	-	-	-	-	-
Side effects												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) No report on sequence generation, allocation concealment ro blinding
(b) The confidence interval crossed 1 MID point
(c) No standard deviation was reported and the study used a ; small sample size
(d) Kraft (2003): Enterostomal therapy classification; Payne (2009): NPUAP classification
(e) Kraft (1993): Drop out is more than 10% higher than event rate

Table 163: Clinical evidence profile: gauze dressing versus polyurethane dressing

Quality assessment							No of patients/ulcers		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Gauze dressing	Polyurethane dressing	Relative (95% CI)	Absolute		
Proportion of pressure ulcers completely healed – general population – all grades – Enis and Sarmiento and Shea classification[f 144,171]												
2	Randomised trials	Very serious[a,b]	No serious inconsistency	No serious indirectness	No serious imprecision	None	0/22 (0%)	15/31 (48.4%)	Peto OR 0.08 (0.02 to 0.31)	414 fewer per 1000 (from 259 fewer to 465 fewer)	Low	Critical
							-	37.4%		328 fewer per 1000 (from 218 fewer to 362 fewer)		
Proportion of pressure ulcers completely healed – people in the community – grade 2 – Shea classification[171]												
1	Randomised trial	Very serious[b]	No serious inconsistency	No serious indirectness	No serious imprecision	None	0/12 (0%)	14/22 (63.6%)	Peto OR 0.08 (0.02 to 0.32)	514 fewer per 1000 (from 277 fewer to 603 fewer)	Low	Critical
							-	63.6%		513 fewer per 1000 (from 277		

Quality assessment							No of patients/ulcers		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Gauze dressing**	**Polyurethane dressing**	**Relative (95% CI)**	**Absolute**		
										fewer to 02 fewer)		
Proportion of pressure ulcers worsened – general population – Enis and Sarmiento and Shea classification[f144,171]												
2	Randomised trials	Very serious[a,b]	No serious inconsistency	No serious indirectness	No serious imprecision	None	9/22 (40.9%)	4/31 (12.9%)	RR 3.46 (1.26 to 9.49)	317 more per 1000 (from 34 more to 1000 more)	Low	Critical
							-	12.4%		305 more per 1000 (from 32 more to 1000 more)		
Proportion of pressure ulcers decreased in ulcer stage– people in the community– grade 2 – Shea classification[171]												
1	Randomised trial	Very serious[b]	No serious inconsistency	No serious indirectness	No serious imprecision	None	0/12 (0%)	16/22 (72.7%)	Peto OR 0.06 (0.01 to 0.24)	589 fewer per 1000 (from 337 fewer to 701 fewer)	Low	Critical
							-	72.7%		589 fewer per 1000 (from 337 fewer to 701 fewer)		

Quality assessment							No of patients/ulcers		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Gauze dressing**	**Polyurethane dressing**	**Relative (95% CI)**	**Absolute**		
Proportion of pressure ulcers increased in ulcer stage – people in the community –grade 2 – Shea classification[171]												
1	Randomised trial	Very serious[b]	No serious inconsistency	No serious indirectness	Serious[c]	None	5/12 (41.7%)	1/22 (4.5%)	RR 9.17 (1.21 to 69.69)	371 more per 1000 (from 10 more to 1000 more)	Very low	Critical
							-	4.6%		376 more per 1000 (from 10 more to 1000 more)		
Mean percentage reduction in pressure ulcer area – inpatients – all grades (grade 1 and 2) – Enis and Sarmiento classification[144]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[d]	None	2.5 (n=10)	42.9 (n=9)	-	Not pooled	Very low	Critical
Median percentage reduction in pressure ulcer area– people in the community – grade 2 – Shea classification[171]												
1	Randomised trial	Very serious[b]	No serious inconsistency	No serious indirectness	Very serious[e]	None	52 (n=22)	100 (n=22)	-	Not pooled	Very low	Critical
Median percentage reduction in pressure ulcer area– people in the community – grade 3 – Shea classification[171]												
1	Randomised trial	Very serious[b]	No serious inconsistency	No serious indirectness	Very serious[d]	None	44 (n=15)	67 (n=15)	-	Not pooled	Very low	Critical
Proportion of people with maceration – people in the community – Shea classification[171]												
1	Randomised trial	Very serious[b]	No serious inconsistency	No serious indirectness	Serious[c]	None	10/12 (83.3%)	17/22 (77.3%)	RR 1.08 (0.77 to 1.51)	62 more per 1000 (from 178 fewer to 394	Very low	Important

Quality assessment							No of patients/ulcers		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Gauze dressing	Polyurethane dressing	Relative (95% CI)	Absolute	Quality	Importance
										more)		
							-	77.3%		62 more per 1000 (from 178 fewer to 394 more)		
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate of change in size of pressure ulcer												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital or NHS care												
-	-	-	-	-	-	-	-	-	-	-	-	-
Patient acceptability												
-	-	-	-	-	-	-	-	-	-	-	-	-
Mortality (all-cause)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) Olekse (1986) did not report report on sequence generation, allocation concealment or blinding. No log-transformation of data was carried out.
(b) Sebern (1989) did not report on allocation concealment or blinding.
(c) The confidence interval crossed 1 MID point
(d) No standard deviation was reported and there was a small sample size.
(e) No standard deviation was reported and it was unknown if sample size was sufficient.
(f) Oleske (1986): Enis and Sarmiento classification; Sebern (1989): Shea classification

Table 164: Clinical evidence profile: gauze dressing versus hydrogel

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Gauze dressing	Hydrogel dressing	Relative (95% CI)	Absolute	Quality	Importance
Proportion of people with pressure ulcers completely healed – general pressure ulceration – all grades (grade 2 to 4) – classification system not reported[190]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	9/14 (64.3%)	10/16 (62.5%)	RR 1.03 (0.6 to 1.77)	19 more per 1000 (from 250 fewer to 481 more)	Very low	Critical
							-	62.5%		19 more per 1000 (from 250 fewer to 481 more)		
Proportion of people with pressure ulcers worsened – general pressure ulcerlation – all grades (grade 2 to 4) – classification system not reported[190]												
1	Randomised trial	Very serious[a,f]	No serious inconsistency	No serious indirectness	Very serious[b]	None	1/19 (5.3%)	1/22 (4.5%)	RR 1.16 (0.08 to 17.28)	7 more per 1000 (from 42 fewer to 740 more)	Very low	Critical
							-	4.6%		7 more per 1000 (from 42 fewer to 749 more)		
Mean percentage reduction in pressure ulcer area – In- and outpatients – grade 2 and 3 – classification system not reported[124]												
1	Randomised trial	Very serious[c]	No serious inconsistency	No serious indirectness	Serious[d]	None	5.1 (SD 14.8)	8 (SD 14.8)	-	MD 2.9 lower (12.07 lower to 6.27 higher)	Very low	Critical
Mean healing rate of pressure ulcers (cm^2/day) – people with a spinal cord injury – all grades (grade 2 to 4) – NPUAP classification[87]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	0.12 (SD 0.16)	0.09 (SD 0.05)	-	MD 3 higher (5.58 lower to 11.58 higher)	Very low	Critical
Mean time to healing of pressure ulcers (weeks) – general population – all grades (grade 2 to 4) – classification system not reported[190]												

Quality assessment							No of patients		Effect			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Gauze dressing**	**Hydrogel dressing**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	5.2 (SD 2.4)	5.3 (SD 2.3)	-	MD 0.1 lower (1.79 lower to 1.59 higher)	Very low	Critical
Mortality (all-cause) [190]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	2/14 (14.3%)	4/16 (25%)	RR 0.57 (0.12 to 2.66)	108 fewer per 1000 (from 220 fewer to 415 more)	Very low	Critical
							-	25%		108 fewer per 1000 (from 220 fewer to 415 more)		
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital or NHS care												
-	-	-	-	-	-	-	-	-	-	-	-	-
Patient acceptability												
-	-	-	-	-	-	-	-	-	-	-	-	-
Side effects												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) No report on sequence generation, allocation concealment or blinding. No log-transformation of data was carried out.
(b) The confidence interval crossed both MID points.
(c) Mulder (1993) did not report on allocation concealment or blinding.
(d) The confidence interval crossed 1 MID point.
(e) No standard deviation was reported and the study used a small sample size.

(f) The drop out is more than 10% higher than event rate

Table 165: Clinical evidence profile: gauze dressing versus dextranomer

Quality assessment							No of patients/ulcers		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Gauze dressing	Dextranomer dressing	Relative (95% CI)	Absolute		
Proportion of pressure ulcers improved – people with a spinal cord injury – all grades (grade 2 to 4) – Eltorai classification[106]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	2/15 (13.3%)	11/15 (73.3%)	RR 0.18 (0.05 to 0.68)	601 fewer per 1000 (from 235 fewer to 697 fewer)	Low	Critical
							-	73.3%		601 fewer per 1000 (from 235 fewer to 696 fewer)		
Proportion of people with adverse events - people with a spinal cord injury – all grades (grade 2 to 4) – Eltorai classification[106]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	0/15 (0%)	0/15 (0%)	Not pooled	0 more (from 120 fewer to 120 more)	Low	Important
							-	0%		0 more (from 120 fewer to 120 more)		
Proportion of people with pressure ulcers completely healed												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate of change in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-

Quality assessment							No of patients/ulcers		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Gauze dressing	Dextranomer dressing	Relative (95% CI)	Absolute	Quality	Importance
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital or NHS care												
-	-	-	-	-	-	-	-	-	-	-	-	-
Patient acceptability												
-	-	-	-	-	-	-	-	-	-	-	-	-
Mortality (all cause)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) Ljungberg (2009) did not report on sequence generation, allocation concealment or blinding.
(b) Sebern (2009) did not report on sequence generation, allocation concealment or blinding.

Table 166: Clinical evidence profile: gauze dressing versus phenytoin cream

Quality assessment							No of patients/ulcers		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Gauze dressing	Phenytoin cream	Relative (95% CI)	Absolute	Quality	Importance
Proportion of people with pressure ulcers completely healed – people with a spinal cord injury – all grades (grade 1 and 2) – NPUAP classification[81]												
1	Randomised trial	Serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	8/27 (29.6%)	11/28 (39.3%)	RR 0.75 (0.36 to 1.58)	98 fewer per 1000 (from 251 fewer to 228 more)	Very low	Critical
							-	39.3%		98 fewer per 1000 (from 252 fewer to		

Quality assessment							No of patients/ulcers		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Gauze dressing**	**Phenytoin cream**	**Relative (95% CI)**	**Absolute**		
										228 more)		
Proportion of pressure ulcers completely healed (all sites) – people with a spinal cord injury – all grades (grade 1 and 2) – NPUAP classification[81]												
1	Randomised trial	Serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	8/30 (26.7%)	12/30 (40%)	RR 0.67 (0.32 to 1.39)	132 fewer per 1000 (from 272 fewer to 156 more)	Very low	Critical
							-	40%		132 fewer per 1000 (from 272 fewer to 156 more)		
Proportion of pressure ulcers improved – people with a spinal cord injury – all grades (grade 1 and 2) – NPUAP classification[81]												
1	Randomised trial	Serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	13/30 (43.3%)	16/30 (53.3%)	RR 0.81 (0.48 to 1.38)	101 fewer per 1000 (from 277 fewer to 203 more)	Very low	Critical
							-	53.3%		101 fewer per 1000 (from 277 fewer to 203 more)		
Proportion of pressure ulcers worsened – people with a spinal cord injury – all grades (grade 1 and 2) – NPUAP classification[81]												
1	Randomised trial	Serious[a]	No serious inconsistency	No serious indirectness	Serious[c]	None	9/30 (30%)	2/30 (6.7%)	RR 4.5 (1.06 to 19.11)	233 more per 1000 (from 4 more to 1000 more)	Low	Critical
							-	6.7%		235 more per 1000		

Quality assessment							No of patients/ulcers		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Gauze dressing**	**Phenytoin cream**	**Relative (95% CI)**	**Absolute**		
										(from 4 more to 1000 more)		
Mortality (all-cause) [81]												
1	Randomised trial	Serious[a]	No serious inconsistency	No serious indirectness	No serious	None	0/27 (0%)	0/28 (0%)	Not pooled	Not pooled	Moderate	Important
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate of change in size of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital or NHS care												
-	-	-	-	-	-	-	-	-	-	-	-	-
Patient acceptability												
-	-	-	-	-	-	-	-	-	-	-	-	-
Side effects												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) Only blinding of outcome assessor was conducted.
(b) The confidence interval crossed both MID points.
(c) The confidence interval crossed 1 MID point.

Table 167: Clinical evidence profile: foam dressing versus skin replacement

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Foam dressing	skin replacement	Relative (95% CI)	Absolute	Quality	Importance
Proportion of people with pressure ulcers completely healed – general pressure ulceration – all grades (grade 3) – classification system not reported[149]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	2/16 (12.5%)	2/18 (11.1%)	RR 1.13 (0.18 to 7.09)	13 more per 1000 (from 91 fewer to 677 more)	Very low	Critical
							-	11.1%		13 more per 1000 (from 91 fewer to 676 more)		
Median percentage reduction in pressure ulcer area (closed ulcers) – general pressure ulceration – all grades (grade 3) – classification system not reported[149]												
1	Randomised trial	Very serious[a,e]	No serious inconsistency	No serious indirectness	Very serious[c]	None	33.5 (range:-77.5-100) (n=16)	49.5 (range: -81.7-100) (n=18)	-	Not pooled	Very low	Critical
Median percentage reduction in pressure ulcer area (unclosed ulcers) – general pressure ulceration – all grades (grade 3) – classification system not reported[149]												
1	Randomised trial	Very serious[a,e]	No serious inconsistency	No serious indirectness	Very serious[c]	None	17.4 (range: -434.5-100) (n=16)	38.8 (range:-201.7-100) (n=18)	-	Not pooled	Very low	Critical
Mean percentage reduction in pressure ulcer volume – general pressure ulceration – all grades (grade 3) – classification system not reported[149]												
1	Randomised trial	Very serious[a,e]	No serious inconsistency	No serious indirectness	Very serious[c]	None	4.1 (n=16)	18.7 (n=18)	-	Not pooled	Very low	Critical
Median percentage reduction in pressure ulcer volume – general pressure ulceration – all grades (grade 3) – classification system not reported[149]												

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Foam dressing**	**skin replacement**	**Relative (95% CI)**	**Absolute**		
1	Randomised trial	Very serious[a,e]	No serious inconsistency	No serious indirectness	Very serious[c]	None	17.4 (n=16)	41.2 (n=18)	-	Not pooled	Very low	Critical
Proportion of people with infection – general pressure ulceration – all grades (grade 3) – classification system not reported[149]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	3/16 (18.8%)	3/18 (16.7%)	RR 1.13 (0.26 to 4.8)	22 more per 1000 (from 123 fewer to 633 more)	Very low	Important
							-	16.7%		22 more per 1000 (from 124 fewer to 635 more)		
Proportion of people with adverse events – general pressure ulceration – all grades (grade 3) – classification system not reported[149]												
1	Randomised trials	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	0/16 (0%)	0/18 (0%)	Not pooled	0 more (from 110 fewer to 110 more)	Low	Important
							-	0%		0 more (from 110 fewer to 110 more)		
Time to complete healing of pressure ulcers												

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Foam dressing	skin replacement	Relative (95% CI)	Absolute	Quality	Importance
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate of change in size of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital or NHS care												
-	-	-	-	-	-	-	-	-	-	-	-	-
Patient acceptability												
-	-	-	-	-	-	-	-	-	-	-	-	-
Mortality (all-cause)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) Single blinding (no additional information) was carried out.
(b) The confidence interval crossed both MID points.
(c) No standard deviation was reported and the study used a small sample size.
(d) The drop out is more than 10% higher than event rate.
(e) No log-transformation of data was carried out.

Table 168: Clinical evidence profile: foam dressing versus antibiotic ointment

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Foam dressing	Antibiotic ointment	Relative (95% CI)	Absolute	Quality	Importance
Proportion of people with pressure ulcers completely healed – people in long term care – all grades (grade 2) – AHCPR classification[211]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	None	18/21 (85.7%)	15/23 (65.2%)	RR 1.31 (0.93 to 1.86)	202 more per 1000 (from 46 fewer to 561 more)	Very low	Critical
							-	65.2%		202 more per 1000 (from 46 fewer to 561 more)		
Mean PUSH score at end of treatment – people in long term care – all grades (grade 2) – AHCPR classification[211]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[c]	None	3.24 (n=19)	1.61 (n=23)	p > 0.05	Not pooled	Very low	Critical
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate of change in size of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital or NHS care												
-	-	-	-	-	-	-	-	-	-	-	-	-
Patient acceptability												
-	-	-	-	-	-	-	-	-	-	-	-	-
Side effects												
-	-	-	-	-	-	-	-	-	-	-	-	-
Mortality (all-cause)												

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Foam dressing	Antibiotic ointment	Relative (95% CI)	Absolute	Quality	Importance
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) No report on sequence generation, allocation concealment or blinding; no log-transformation of data was carried out.
(b) The confidence interval crossed 1 MID point.
(c) No standard deviation was reported and there was a small sample size.

Table 169: Clinical evidence profile: foam dressing: Allevyn® versus Biatain®

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Allevyn	Biatain	Relative (95% CI)	Absolute	Quality	Importance
Proportion of people with pressure ulcer completely healed – general pressure ulceration – all grades (grade 2 and 3) – NPUAP classification[10]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	11/14 (78.6%)	5/18 (27.8%)	RR 2.83 (1.28 to 6.25)	508 more per 1000 (from 78 more to 1000 more)	Low	Critical
							-	27.8%		509 more per 1000 (from 78 more to 1000 more)		
Median percentage reduction in pressure ulcer area – general pressure ulceration – all grades (grade 2 and 3) – NPUAP classification[10]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	38.2 (range: -97.6-99.4) (n=14)	45.8 (range: -56.9-90.0) (n=18)	p > 0.05	Not pooled	Very low	Critical

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Allevyn	Biatain	Relative (95% CI)	Absolute		
Mean pain score at dressing removal (1: none - 4 severe) – general pressure ulceration – all grades (grade 2 and 3) – NPUAP classification[10]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	1.01 (range: 1.00-1.17) (n=14)	1.10 (range: -1.00-2.17) (n=18)	p > 0.05	Not pooled	Very low	Important
Mean comfort score at dressing removal (1: none - 4 severe) – general pressure ulceration – all grades (grade 2 and 3) – NPUAP classification[10]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[c]	None	1.84 (SD 0.26)	2.11 (SD 0.26)	-	MD 0.27 lower (0.45 to 0.09 lower)	Very low	Important
Proportion of people with dressing related adverse events – general pressure ulceration – all grades (grade 2 and 3) – NPUAP classification[10]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[d]	None	1/14 (7.1%)	4/18 (22.2%)	RR 0.32 (0.04 to 2.57)	151 fewer per 1000 (from 213 fewer to 349 more)	Very low	Important
							-	22.2%		151 fewer per 1000 (from 213 fewer to 349 more)		
Mortality (all-cause) [10]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[d]	None	0/14 (0%)	1/18 (5.6%)	Peto OR 0.17 (0 to 8.79)	46 fewer per 1000 (from 56 fewer to 285 more)	Very low	Important
							-	5.6%		46 fewer per 1000 (from 56		

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Allevyn	Biatain	Relative (95% CI)	Absolute	Quality	Importance
										fewer to 287 more)		
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate of change in size of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital or NHS care												
-	-	-	-	-	-	-	-	-	-	-	-	-
Patient acceptability												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) No report on sequence generation or blinding. Allocation according to baseline exudate level and treatment centre; no log-transformation of data was carried out.
(b) No standard deviation was reported and the study used a small sample size.
(c) The confidence interval crossed 1 MID point.
(d) The confidence interval crossed both MID points

Table 170: Clinical evidence profile: foam dressing (Mepilex) versus foam dressing (Tielle)

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Mepilex	Tielle	Relative (95% CI)	Absolute	Quality	Importance
Proportion of people with pressure ulcers completely healed – elderly people – all grades (grade 2) – NPUAP classification[116]												
1	Randomised trial	Serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	8/18 (44.4%)	10/20 (50%)	RR 0.89 (0.45 to 1.75)	55 fewer per 1000 (from 275 fewer to 375 more)	Very low	Critical

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Mepilex	Tielle	Relative (95% CI)	Absolute	Quality	Importance
							-	50%		55 fewer per 1000 (from 275 fewer to 375 more)		
Proportion of people with pressure ulcers improved – elderly people – all grades (grade 2) – NPUAP classification[116]												
1	Randomised trial	Serious[a]	No serious inconsistency	No serious indirectness	Serious[c]	None	15/18 (83.3%)	19/20 (95%)	RR 0.88 (0.7 to 1.1)	114 fewer per 1000 (from 285 fewer to 95 more)	Low	Critical
							-	95%		114 fewer per 1000 (from 285 fewer to 95 more)		
Proportion of people with pressure ulcers worsened – elderly people – all grades (grade 2) – NPUAP classification[116]												
1	Randomised trial	Serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	2/18 (11.1%)	1/20 (5%)	RR 2.22 (0.22 to 22.49)	61 more per 1000 (from 39 fewer to 1000 more)	Very low	Critical
							-	5%		61 more per 1000 (from 39 fewer to 1000 more)		
Proportion of people with maceration – elderly people – all grades (grade 2) – NPUAP classification[116]												
1	Randomised trial	Serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	0/18 (0%)	3/20 (15%)	OR 0.13 (0.01 to 1.38)	128 fewer per 1000 (from 148 fewer to 46 more)	Very low	Important
							-	15%		128 fewer per 1000 (from 148 fewer to 46 more)		

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Mepilex	Tielle	Relative (95% CI)	Absolute		
Proportion of people reporting odour – elderly people – all grades (grade 2) – NPUAP classification[116]												
1	Randomised trial	Serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	0/18 (0%)	3/20 (15%)	OR 0.13 (0.01 to 1.38)	128 fewer per 1000 (from 148 fewer to 46 more)	Very low	Important
							-	15%		128 fewer per 1000 (from 148 fewer to 46 more)		
Proportion of people with adverse events[d] – elderly people – all grades (grade 2) – NPUAP classification[116]												
1	Randomised trial	Serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	1/18 (5.6%)	3/20 (15%)	RR 0.37 (0.04 to 3.25)	95 fewer per 1000 (from 144 fewer to 338 more)	Very low	Important
							-	15%		95 fewer per 1000 (from 144 fewer to 338 more)		
Mortality (all-cause) [116]												
1	Randomised trial	Serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	1/18 (5.6%)	1/20 (5%)	RR 1.11 (0.07 to 16.49)	6 more per 1000 (from 47 fewer to 775 more)	Very low	Important
							-	5%		6 more per 1000 (from 47 fewer to 775 more)		
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate of healing												

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Mepilex	Tielle	Relative (95% CI)	Absolute	Quality	Importance
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate of change in size of ulcer												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital or NHS care												
-	-	-	-	-	-	-	-	-	-	-	-	-
Patient acceptability												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) No blinding reported.
(b) The confidence interval crossed both MID points.
(c) The confidence interval crossed 1 MID point.
(d) Mepilex group: hyperganulation; Tielle group: hypergranulation, new ulcer, and redness and irritation.

Table 171: Clinical evidence profile: hydrogel (aquagel) versus polyurethane foam (lyofoam) dressing

Quality assessment							No of ulcers		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Hydrogel dressing	Foam dressing	Relative (95% CI)	Absolute	Quality	Importance
Proportion of pressure ulcers completely healed – people in palliative care– all grades (grade 2 and 3) – Torrance classification[179]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	None	15/20 (75%)	15/18 (83.3%)	RR 0.9 (0.65 to 1.25)	83 fewer per 1000 (from 292 fewer to 208 more)	Very low	Critical
							-	83.3%		83 fewer per		

Quality assessment							No of ulcers		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Hydrogel dressing	Foam dressing	Relative (95% CI)	Absolute	Quality	Importance
										1000 (from 292 fewer to 208 more)		
Proportion of pressure ulcers improved - people in palliative care – all grades (grade 2 and 3) – Torrance classification[179]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	19/20 (95%)	18/18 (100%)	RR 0.95 (0.83 to 1.1)	50 fewer per 1000 (from 170 fewer to 100 more)	Low	Critical
							-	100%		50 fewer per 1000 (from 170 fewer to 100 more)		
Mean healing rate healed pressure ulcers (cm²/day) - people in palliative care – grade 2 – Torrance classification[179]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[c]	None	0.67 (SD 0.37)	1.23 (SD 1.33)	-	MD 0.56 lower (1.66 lower to 0.54 higher)	Very low	Critical
Mean healing rate healed pressure ulcers (cm²/day) - people in palliative care – grade 3 – Torrance classification[179]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	None	0.31 (SD 0.21)	0.44 (SD 0.27)	-	MD 0.13 lower (0.32 lower to 0.06 higher)	Very low	Critical
Mean healing rate improved ulcers (cm²/day) - people in palliative care – grade 3 – Torrance classification[179]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	None	0.27 (SD 0.11)	0.7 (SD 0.63)	-	MD 0.43 lower (0.79 to 0.07 lower)	Very low	Critical
Mortality (all-cause)[179]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[c]	None	3/17 (17.6%)	2/17 (11.8%)	RR 1.5 (0.29 to	59 more per 1000 (from 84 fewer to 808	Very low	Important

Quality assessment							No of ulcers		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Hydrogel dressing	Foam dressing	Relative (95% CI)	Absolute	Quality	Importance
									7.87)	more)		
							-	11.8%		59 more per 1000 (from 84 fewer to 811 more)		
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital or NHS care												
-	-	-	-	-	-	-	-	-	-	-	-	-
Patient acceptability												
-	-	-	-	-	-	-	-	-	-	-	-	-
Side effects												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) No report on allocation concealment and no blinding; no log-transformation of data.
(b) The confidence interval crossed 1 MID point
(c) The confidence interval crossed both MID points.

Table 172: Clinical evidence profile: hydrogel versus dextranomer

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Hydrogel dressing	Dextranomer	Relative (95% CI)	Absolute	Quality	Importance
Median percentage reduction in pressure ulcer area – general pressure ulceration – all grades (grade 1 to 4) – AHCPR and International Association of Enterostomal Therapy classification[45]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	None	35 (n=67)	7 (n=68)	p=0.03	Not pooled	Very low	Critical
Proportion of people with pain at dressing application – general pressure ulceration - all grades (grade 1 to 4) – AHCPR and International Association of Enterostomal Therapy classification[45]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[c]	None	0/67 (0%)	1/68 (1.5%)	Peto OR 0.14 (0 to 6.92)	13 fewer per 1000 (from 15 fewer to 79 more)	Very low	Important
							-	1.5%		13 fewer per 1000 (from 15 fewer to 80 more)		
Mortality (all-cause) [45]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[c]	None	2/67 (3%)	2/68 (2.9%)	RR 1.01 (0.15 to 7)	0 more per 1000 (from 25 fewer to 176 more)	Very low	Important
							-	2.9%		0 more per 1000 (from 25 fewer to 174 more)		
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Hydrogel dressing	Dextranomer	Relative (95% CI)	Absolute	Quality	Importance
Proportion of people with pressure ulcers completely healed												
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate of change in size of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Reduction in size and volume of pressure ulcer												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital or NHS care												
-	-	-	-	-	-	-	-	-	-	-	-	-
Patient acceptability												
-	-	-	-	-	-	-	-	-	-	-	-	-
Side effects												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) The authors did not report on sequence generation, allocation concealment or blinding.
(b) No standard deviation was reported.
(c) The confidence interval crossed both MID points

Table 173: Clinical evidence profile: hydrogel, foam dressing or transparent film versus different types of dressings

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Hydrogel dressings	Different types of dressings	Relative (95% CI)	Absolute	Quality	Importance
Proportion of people with pressure ulcers completely healed – people in the community – all grades (grade 2 to 4) – Stirling classification[177]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	None	15/23 (65.2%)	9/18 (50%)	RR 1.3 (0.75 to	150 more per 1000	Very low	Critical

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Hydrogel dressings	Different types of dressings	Relative (95% CI)	Absolute	Quality	Importance
									2.26)	(from 125 fewer to 630 more)		
							-	50%		150 more per 1000 (from 125 fewer to 630 more)		
Percentage healed per week – people in the community – all grades (grade 2 to 4) – Stirling classification[177]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	None	n=28	n=30	p=0.15 (log-rank test)		Very low	Critical
Proportion of people reporting the application of the dressing as comfortable – people in the community – all grades (grade 2 to 4) – Stirling classification[177]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	None	14/14 (100%)	6/7 (85.7%)	RR 1.19 (0.84 to 1.68)	163 more per 1000 (from 137 fewer to 583 more)	Very low	Important
							-	85.7%		163 more per 1000 (from 137 fewer to 583 more)		
Proportion of people reporting discomfort at dressing removal – people in the community – all grades (grade 2 to 4) – Stirling classification[177]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[c]	None	0/14 (0%)	1/7 (14.3%)	Peto OR 0.05 (0.00 to 3.18)	135 fewer per 1000 (143 fewer to 204 more)	Very low	Important
							-	14.3%		135 fewer		

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Hydrogel dressings	Different types of dressings	Relative (95% CI)	Absolute	Quality	Importance
										per 1000 (143 fewer to 204 more)		
Proportion of people with adverse events – people in the community – all grades (grade 2 to 4) – Stirling classification[177]												
1	Randomised trial	Very serious[a, d]	No serious inconsistency	No serious indirectness	No serious imprecision	None	0/28 (0%)	0/30 (0%)	Not pooled	0 more (from 6 fewer to 6 more)	Low	Important
							-	0%		0 more (from 6 fewer to 6 more)		
Mortality (all-cause)[177]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[c]	None	3/28 (10.7%)	7/30 (23.3%)	RR 0.46 (0.13 to 1.6)	126 fewer per 1000 (from 203 fewer to 140 more)	Very low	Important
							-	23.3%		126 fewer per 1000 (from 203 fewer to 140 more)		
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate of change in size of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Hydrogel dressings	Different types of dressings	Relative (95% CI)	Absolute	Quality	Importance
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital or NHS care												
-	-	-	-	-	-	-	-	-	-	-	-	-
Patient acceptability												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) Allocation according to pressure ulcer stage and blinding was not reported.
(b) The confidence interval crossed 1 MID point.
(c) The confidence interval crossed both MID points.
(d) The drop out is more than 10% higher than event rate.

Table 174: Clinical evidence profile: hydrogel (Sterigel) versus hydrogel (Intrasite)

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Sterigel	Intrasite	Relative (95% CI)	Absolute	Quality	Importance
Mean percentage reduction in pressure ulcer area – general pressure ulceration – necrotic pressure ulcers – classification not reported[15]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[d]	None	-82.3	7.45	Not pooled	Not pooled	Very low	Critical
Proportion of people with intermittent pressure ulcer pain at end of study[e] – general pressure ulceration – necrotic pressure ulcers – classification not reported[15]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	None	13/24 (54.2%)	16/23 (69.6%)	RR 0.78 (0.49 to 1.23)	153 fewer per 1000 (from 355 fewer to 160 more)	Very low	Important
							-	69.6%		153 fewer		

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Sterigel	Intrasite	Relative (95% CI)	Absolute	Quality	Importance
										per 1000 (from 355 fewer to 160 more)		
Proportion of people with continuous pressure ulcer pain at end of study[f] – general pressure ulceration – necrotic pressure ulcers – classification not reported[15]												
1	Randomised trial	Very serious[a,g]	No serious inconsistency	No serious indirectness	Very serious[c]	None	1/24 (4.2%)	2/23 (8.7%)	RR 0.48 (0.05 to 4.93)	45 fewer per 1000 (from 83 fewer to 342 more)	Very low	Important
							-	8.7%		45 fewer per 1000 (from 83 fewer to 342 more)		
Proportion of people with slight pain at dressing removal – general pressure ulceration – necrotic pressure ulcers – classification not reported[15]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[c]	None	5/22 (22.7%)	6/20 (30%)	RR 0.76 (0.27 to 2.1)	72 fewer per 1000 (from 219 fewer to 330 more)	Very low	Important
							-	30%		72 fewer per 1000 (from 219 fewer to 330 more)		
Proportion of people with severe pain at dressing removal – general pressure ulceration – necrotic pressure ulcers – classification not reported[15]												
1	Randomised trial	Very serious[a,g]	No serious inconsistency	No serious indirectness	Very serious[c]	None	0/22 (0%)	1/20 (5%)	Peto OR 0.12 (0 to 6.2)	44 fewer per 1000 (from 50 fewer to	Very low	Important

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Sterigel	Intrasite	Relative (95% CI)	Absolute		
										196 more)		
							-	5%		44 fewer per 1000 (from 50 fewer to 196 more)		
Proportion of people with discomfort – general pressure ulceration – necrotic pressure ulcers – classification not reported[15]												
1	Randomised trial	Very serious[a,g]	No serious inconsistency	No serious indirectness	Very serious[c]	None	0/22 (0%)	1/20 (5%)	Peto OR 0.12 (0 to 6.2)	44 fewer per 1000 (from 50 fewer to 196 more)	Very low	Important
							-	5%		44 fewer per 1000 (from 50 fewer to 196 more)		
Proportion of people with maceration – general pressure ulceration – necrotic pressure ulcers – classification not reported[15]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[c]	None	8/21 (38.1%)	9/17 (52.9%)	RR 0.72 (0.36 to 1.46)	148 fewer per 1000 (from 339 fewer to 244 more)	Very low	Important
							-	52.9%		148 fewer per 1000 (from 339 fewer to 243 more)		
Mortality (all-cause)[15]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[c]	None	3/26 (11.5%)	4/24 (16.7%)	RR 0.69 (0.17 to	52 fewer per 1000	Very low	Important

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Sterigel	Intrasite	Relative (95% CI)	Absolute	Quality	Importance
									2.78)	(from 138 fewer to 297 more)		
							-	16.7%		52 fewer per 1000 (from 139 fewer to 297 more)		
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Proportion of people with complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate of change in size of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital or NHS care												
-	-	-	-	-	-	-	-	-	-	-	-	-
Patient acceptability												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) The authors did not report on allocation concealment and only blinding of outcome assessor; no log-transformation of data was carried out.
(b) The confidence interval crossed 1 MID point.
(c) The confidence interval crossed both MID points.
(d) Reduction was calculated based on reported baseline value and value at 14 days. No p-value or SD could be derived.

(e) At start of the study 17/24 and 18/23 reported intermittent pain.
(f) At start of the study 3/24 and 2/23 reported continuous pain
(g) The drop out is more than 10% higher than event rate.

Table 175: Clinical evidence profile: protease modulating matrix versus impregnated gauze dressing

Quality assessment							No of patients		Effect			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Collagen dressing**	**Impregnated gauze dressing**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
Proportion of people completely healed – inpatients – all grades (grade 2 to 4) – NPUAP classification[135]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	None	36/40 (90%)	28/40 (70%)	RR 1.29 (1.02 to 1.61)	203 more per 1000 (from 14 more to 427 more)	Very low	Critical
							-	70%		203 more per 1000 (from 14 more to 427 more)		
Time to complete healing of pressure ulcers (days) – inpatients – all grades (grade 2 to 4) – NPUAP classification[135]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[c]	None	6-15 (n=40)	14-52 (n=40)	-	Not pooled	Very low	Critical
Proportion of people with adverse events – inpatients – all grades (grade 2 to 4) – NPUAP classification[135]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	0/40 (0%)	0/40 (0%)	Not pooled	Not pooled	Low	Important
Mortality (all-cause) [135]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	0/40 (0%)	0/40 (0%)	Not pooled	Not pooled	Low	Important

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Collagen dressing	Impregnated gauze dressing	Relative (95% CI)	Absolute	Quality	Importance
Rate of change in size of pressure ulcer												
0	-	-	-	-	-	-	-	-	-	-	-	-
Reduction in size or volume of pressure ulcer												
0	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
0	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital or NHS care												
0	-	-	-	-	-	-	-	-	-	-	-	-
Patient acceptability												
0	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
0	-	-	-	-	-	-	-	-	-	-	-	-

(a) The authors did not report on sequence generation, allocation concealment or blinding.
(b) The confidence interval crossed 1 MID point.
(c) Only range values were reported.

Table 176: Clinical evidence profile: polyurethane dressing versus different types of dressing

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Polyurethane dressing	Different types of dressings	Relative (95% CI)	Absolute	Quality	Importance
Mean time to healing of pressure ulcers (days)– inpatients – all grades (grade 2 and 3) – NPUAP classification[28]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	None	59.8 (SD 29.4)	57.5 (SD 33.5)	-	MD 2.3 higher	Very low	Critical

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Polyurethane dressing**	**Different types of dressings**	**Relative (95% CI)**	**Absolute**		
										(13.31 lower to 17.91 higher)		
Mean difference in PUSH score – inpatients – all grades (grade 2 and 3) – NPUAP classification[28]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	0.9 (SD 1.3)	1.1 (SD 2.1)	-	MD 0.2 lower (1.08 lower to 0.68 higher)	Low	Critical
Proportion of people with systemic worsening – inpatients – all grades (grade 2 and 3) – NPUAP classification[28]												
1	Randomised trial	Very serious[a, d]	No serious inconsistency	No serious indirectness	Very serious[c]	None	4/35 (11.4%)	3/29 (10.3%)	RR 1.1 (0.27 to 4.54)	10 more per 1000 (from 76 fewer to 366 more)	Very low	Important
							-	10.3%		10 more per 1000 (from 75 fewer to 365 more)		
Proportion of people with localized adverse events – inpatients – all grades (grade 2 and 3) – NPUAP classification[28]												
1	Randomised trial	Very serious[a, d]	No serious inconsistency	No serious indirectness	Very serious[c]	None	6/35 (17.1%)	7/29 (24.1%)	RR 0.71 (0.27 to 1.88)	70 fewer per 1000 (from 176 fewer to 212 more)	Very low	Important
							-	24.1%		70 fewer		

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Polyurethane dressing	Different types of dressings	Relative (95% CI)	Absolute	Quality	Importance
										per 1000 (from 176 fewer to 212 more)		
Mortality (all-cause) [28]												
1	Randomised trial	Very serious[a, d]	No serious inconsistency	No serious indirectness	Very serious[c]	None	2/35 (5.7%)	2/31 (6.5%)	RR 0.89 (0.13 to 5.92)	7 fewer per 1000 (from 56 fewer to 317 more)	Very low	Important
							-	6.5%		7 fewer per 1000 (from 57 fewer to 320 more)		
Proportion of people with pressure ulcers completely healed												
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate of change in size of pressure ulcer												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital or NHS care												
-	-	-	-	-	-	-	-	-	-	-	-	-
Patent acceptability												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) No report on sequence generation and only blinding of outcome assessor was reported; no log-transformation of data was carried out.

(b) The confidence interval crossed 1 MID point.
(c) The confidence interval crossed both MID points.
(d) The drop out is more than 10% higher than event rate.

Table 177: Clinical evidence profile: alginate dressing versus silver alginate dressing

Quality assessment							No of patients		Effect			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Alginate dressing**	**Silver alginate dressing**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
Proportion of people with pressure ulcers worsened – elderly people – all grades (grade 3 and 4) – NPUAP classification[112]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	4/15 (26.7%)	2/13 (15.4%)	RR 1.73 (0.38 to 7.98)	112 more per 1000 (from 95 fewer to 1000 more)	Very low	Critical
							-	15.4%		112 more per 1000 (from 95 fewer to 1000 more)		
Mean percentage reduction in pressure ulcer area – elderly people – all grades (grade 3 and 4) – NPUAP classification[112]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	13.9 (SD 50.3)	31.6 (SD 38.1)	-	MD 17.7 lower (50.52 lower to 15.12 higher)	Very low	Critical
Absolute cm² decrease in pressure ulcer area – elderly people – all grades (grade 3 and 4) – NPUAP classification[112]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[c]	None	0.8 (SD 10)	7.2 (SD 9)	-	MD 6.4 lower (13.44 lower to 0.64 higher)	Very low	Critical
Mean rate of healing of pressure ulcers (cm²/day) – elderly people – all grades (grade 3 and 4) – NPUAP classification[112]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[c]	None	0.03 (SD 0.36)	0.26 (SD 0.32)	-	MD 0.23 lower (0.48 lower to 0.02	Very low	Critical

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Alginate dressing	Silver alginate dressing	Relative (95% CI)	Absolute	Quality	Importance
										higher)		
Proportion of people with infection – elderly people – all grades (grade 3 and 4) – NPUAP classification[112]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	2/15 (13.3%)	1/13 (7.7%)	RR 1.73 (0.18 to 16.99)	56 more per 1000 (from 63 fewer to 1000 more)	Very low	Important
							-	7.7%		56 more per 1000 (from 63 fewer to 1000 more)		
Percentage reduction in infection score – generalpressure ulceration – grade and classification system not reported[195]												
1	Randomised trial	Very serious[d]	No serious inconsistency	No serious indirectness	Very serious[e]	None	50 (n=13)	52 (n=11)	-	Not pooled	Very low	Important
Mean mASEPSIS index at end of treatment – elderly people – grade 3 and 4 – NPUAP classification[112]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[c]	None	115.3 (SD 80.2)	81.8 (SD 45.1)	-	MD 33.5 higher (13.92 lower to 80.92 higher)	Very low	Important
Proportion of people with poor acceptability and/or tolerability – elderly people – grade 3 and 4 – NPUAP classification[112]												
1	Randomised trial	Very serious[a,f]	No serious inconsistency	No serious indirectness	Very serious[b]	None	0/15 (0%)	1/13 (7.7%)	OR 0.12 (0 to 5.91)	67 fewer per 1000 (from 77 fewer to 253 more)	Very low	Important
							-	7.7%		67 fewer per 1000 (from 77 fewer to 253 more)		
Mortality (all-cause)[112]												
1	Randomised	Very	No serious	No serious	No serious	None	0/48	0/51	Not pooled	Not pooled	Low	Important

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Alginate dressing	Silver alginate dressing	Relative (95% CI)	Absolute	Quality	Importance
	trial	serious[a]	inconsistency	indirectness			(0%)	(0%)				
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Proportion of people with complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital or NHS care												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) Meaume (2006) did not report allocation according to wound type and no report on blinding was reported.
(b) The confidence interval crossed both MID points
(c) The confidence interval crossed 1 MID point.
(d) Trial (2010) did not report on sequence generation and blinding.
(e) No standard deviation was reported and the study had a small sample size.
(f) The drop out is more than 10% higher than event rate.

Table 178: Clinical evidence profile: alginate dressing versus dextranomer

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Alginate dressing	Detraxomer	Relative (95% CI)	Absolute	Quality	Importance
Proportion of people with more than 75% reduction in pressure ulcer area – general pressure ulceration – all grades (grade 3 and 4) – Yarkony classification[165]												
1	Randomised trial	Very serious[a, d]	No serious inconsistency	No serious indirectness	Serious[b]	None	15/47 (31.9%)	6/45 (13.3%)	RR 2.39 (1.02 to 5.62)	185 more per 1000 (from 3 more to 616 more)	Very low	Critical
							-	13.3%		185 more per 1000 (from 3 more to 614 more)		
Proportion of people with more than 40% reduction in pressure ulcer area – general pressure ulceration – all grades (grade 3 and 4) – Yarkony classification[165]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	None	35/47 (74.5%)	19/45 (42.2%)	RR 1.76 (1.21 to 2.58)	321 more per 1000 (from 89 more to 667 more)	Very low	Critical
							-	42.2%		321 more per 1000 (from 89 more to 667 more)		
Proportion of people with pressure ulcers worsened or stagnated – general pressure ulceration – all grades (grade 3 and 4) – Yarkony classification[165]												
1	Randomised trial	Very serious[a, d]	No serious inconsistency	No serious indirectness	No serious imprecision	None	2/47 (4.3%)	15/45 (33.3%)	RR 0.13 (0.03 to 0.53)	290 fewer per 1000 (from 157 fewer to 323 fewer)	Low	Critical
							-	33.3%		290 fewer per 1000		

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Alginate dressing	Detraxomer	Relative (95% CI)	Absolute	Quality	Importance
										(from 157 fewer to 323 fewer)		
Mean rate of healing in people improved more than 40% (cm²/week) – general pressure ulceration – all grades (grade 3 and 4) – Yarkony classification[165]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	None	3.55 (SD 2.18)	2.15 (SD 3.6)	-	MD 1.4 higher (0.18 to 2.62 higher)	Very low	Critical
Mean rate of healing of pressure ulcers (cm²/week) – general pressure ulceration – all grades (grade 3 and 4) – Yarkony classification[165]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	None	2.39 (SD 3.54)	0.27 (SD 3.21)	-	MD 2.12 higher (0.74 to 3.5 higher)	Very low	Critical
Proportion of people with infection – general pressure ulceration – all grades (grade 3 and 4) – Yarkony classification[165]												
1	Randomised trial	Very serious[a, d]	No serious inconsistency	No serious indirectness	Very serious[c]	None	2/47 (4.3%)	2/45 (4.4%)	RR 0.96 (0.14 to 6.51)	2 fewer per 1000 (from 38 fewer to 245 more)	Very low	Important
							-	4.4%		2 fewer per 1000 (from 38 fewer to 242 more)		
Proportion of people with hypergranulation – general pressure ulceration – all grades (grade 3 and 4) – Yarkony classification[165]												
1	Randomised trial	Very serious[a, d]	No serious inconsistency	No serious indirectness	Very serious[c]	None	1/47 (2.1%)	3/45 (6.7%)	RR 0.32 (0.03 to 2.96)	45 fewer per 1000 (from 65 fewer to 131 more)	Very low	Important
							-	6.7%		46 fewer per 1000 (from 65		

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Alginate dressing**	**Detraxomer**	**Relative (95% CI)**	**Absolute**		
										fewer to 131 more)		
Proportion of people with skin irritation – general pressure ulceration – all grades (grade 3 and 4) – Yarkony classification[165]												
1	Randomised trial	Very serious[a, d]	No serious inconsistency	No serious indirectness	Very serious[c]	None	1/47 (2.1%)	1/45 (2.2%)	RR 0.96 (0.06 to 14.85)	1 fewer per 1000 (from 21 fewer to 308 more)	Very low	Important
								2.2%		1 fewer per 1000 (from 21 fewer to 305 more)		
Proportion of people with bleeding – general pressure ulceration – all grades (grade 3 and 4) – Yarkony classification[165]												
1	Randomised trial	Very serious[a, d]	No serious inconsistency	No serious indirectness	Serious[b]	None	0/47 (0%)	3/45 (6.7%)	Peto OR 0.12 (0.01 to 1.22)	58 fewer per 1000 (from 66 fewer to 13 more)	Very low	Important
							-	6.7%		58 fewer per 1000 (from 66 fewer to 14 more)		
Proportion of people with pain – general pressure ulceration – all grades (grade 3 and 4) – Yarkony classification[165]												
1	Randomised trial	Very serious[a, d]	No serious inconsistency	No serious indirectness	No serious imprecision	None	0/47 (0%)	5/45 (11.1%)	Peto OR 0.12 (0.02 to 0.71)	96 fewer per 1000 (from 30 fewer to 109 fewer)	Low	Important
							-	11.1%		96 fewer per 1000		

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Alginate dressing	Detraxomer	Relative (95% CI)	Absolute	Quality	Importance
										(from 30 fewer to 109 fewer)		
Proportion of people with pruritus – general pressure ulceration – all grades (grade 3 and 4) – Yarkony classification[165]												
1	Randomised trial	Very serious[a, d]	No serious inconsistency	No serious indirectness	Very serious[c]	None	0/47 (0%)	1/45 (2.2%)	Peto OR 0.13 (0 to 6.53)	19 fewer per 1000 (from 22 fewer to 107 more)	Very low	Important
							-	2.2%		19 fewer per 1000 (from 22 fewer to 106 more)		
Mortality (all-cause) [165]												
1	Randomised trial	Very serious[a, d]	No serious inconsistency	No serious indirectness	Very serious[c]	None	5/47 (10.6%)	6/45 (13.3%)	RR 0.8 (0.26 to 2.43)	27 fewer per 1000 (from 99 fewer to 191 more)	Very low	Important
							-	13.3%		27 fewer per 1000 (from 98 fewer to 190 more)		
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Proportion of patients with pressure ulcers completely healed												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital or NHS care												

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Alginate dressing	Detraxomer	Relative (95% CI)	Absolute	Quality	Importance
-	-	-	-	-	-	-	-	-	-	-	-	-
Patient acceptability												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) Sayag (1996) did not report sequence generation and blinding; no log-transformation of data was carried out.
(b) The confidence interval crossed 1 MID point.
(c) The confidence interval crossed both MID points.
(d) The drop out is more than 10% higher than event rate.

Table 179: Clinical evidence profile: silver dressing versus different types of dressings

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Silver dressing	Different types of dressings	Relative (95% CI)	Absolute	Quality	Importance
Mean percentage reduction in pressure ulcer area – general pressure ulceration – all grades (grade 2 and 3) – NPUAP classification[127]												
1	Randomised trial	Serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	58.5 (n=24)	33.3 (n=24)	-	Not pooled	Very low	Critical
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Proportion of people with complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate of change in size of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Silver dressing	Different types of dressings	Relative (95% CI)	Absolute	Quality	Importance
Time in hospital or NHS care												
-	-	-	-	-	-	-	-	-	-	-	-	-
Patient acceptability												
-	-	-	-	-	-	-	-	-	-	-	-	-
Side effects												
-	-	-	-	-	-	-	-	-	-	-	-	-
Mortality (all-cause)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) The authors did not report on blinding.
(b) No standard deviation was reported and it was unknown if sample size was sufficient as sample size calculation was based on the inclusion of different types of wounds..

Table 180: Clinical evidence profile: silver dressing versus silver cream

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Silver dressing	Silver cream	Relative (95% CI)	Absolute	Quality	Importance
Mean percentage reduction in pressure ulcer area – in- and outpatients – all grades (grade 4) – NPUAP classification[43]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	36.95 (SD 56.13)	25.06 (SD 56.13)	-	MD 11.89 higher (22.9 lower to 46.68 higher)	Very low	Critical
Percentage reduction in PUSH score – in- and outpatients – all grades (grade 4) – NPUAP classification[43]												

Quality assessment							No of patients		Effect			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Silver dressing**	**Silver cream**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[c]	None	28.15 (n=20)	34.51 (n=20)	p=0.473	Not pooled	Very low	Critical
Proportion of people with adverse events – in- and outpatients – all grades (grade 4) – NPUAP classification[43]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	0/20 (0%)	0/20 (0%)	Not pooled	0 more (from 9 fewer to 9 more)	Low	Important
Mortality (all-cause)[43]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	0/20 (0%)	0/20 (0%)	Not pooled	0 more (from 9 fewer to 9 more)	Low	Important
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Proportion of people with complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate of change in size of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital or NHS care												
-	-	-	-	-	-	-	-	-	-	-	-	-
Patient acceptability												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) The authors did not report on allocation concealment or blinding.
(b) The confidence interval crossed both MID points.

(c) No standard deviation was reported and there was a small sample size.

Table 181: Clinical evidence profile: sugar versus dextranomer

Quality assessment							No of patients/ulcers		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Sugar	Dextranomer	Relative (95% CI)	Absolute		
Proportion of people with pressure ulcers completely healed – people in long term care – grade and classification system not reported[146]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	None	0/5 (0%)	4/7 (57.1%)	Peto OR 0.09 (0.01 to 0.97)	464 fewer per 1000 (from 7 fewer to 558 fewer)	Very low	Critical
							-	57.1%		464 fewer per 1000 (from 7 fewer to 558 fewer)		
Proportion of pressure ulcers completely healed – people in long term care – grade and classification system not reported[146]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	None	0/9 (0%)	6/14 (42.9%)	Peto OR 0.12 (0.02 to 0.77)	346 fewer per 1000 (from 62 fewer to 414 fewer)	Very low	Critical
							-	42.9%		346 fewer per 1000 (from 63 fewer to 414 fewer)		
Proportion of people with pressure ulcers improved – people in long term care – grade and classification system not reported[146]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	0/5 (0%)	7/7 (100%)	Peto OR 0.02 (0 to 0.21)	2 more (from 0 more to 210 more)	Low	Critical
							-	100%		2 more		

Quality assessment							No of patients/ulcers		Effect			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Sugar**	**Dextranomer**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
										(from 0 more to 210 more)		
Proportion of pressure ulcers improved -– people in long term care – grade and classification system not reported[146]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	0/9 (0%)	12/14 (85.7%)	Peto OR 0.04 (0.01 to 0.19)	664 fewer per 1000 (from 324 fewer to 801 fewer)	Low	Critical
							-	85.7%		664 fewer per 1000 (from 325 fewer to 800 fewer)		
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate of change in size of pressure ulcer												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital or NHS care												
-	-	-	-	-	-	-	-	-	-	-	-	-
Patient acceptability												
-	-	-	-	-	-	-	-	-	-	-	-	-
Side effects												
-	-	-	-	-	-	-	-	-	-	-	-	-
Mortality (all-cause)												
-	-	-	-	-	-	-	-	-	-	-	-	-

Quality assessment							No of patients/ulcers		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Sugar	Dextranomer	Relative (95% CI)	Absolute	Quality	Importance
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) No sequence generation or allocation concealment was reported and blinding failed.
(b) The confidence interval crossed 1MID point.

Table 182: Clinical evidence profile: sugar versus different types of topical agents

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Sugar	Different types of topical agents	Relative (95% CI)	Absolute	Quality	Importance
Proportion of people with pressure ulcers completely healed – geriatric adults – grade and classification system not reported[154]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	16/17 (94.1%)	9/21 (42.9%)	RR 2.2 (1.32 to 3.65)	514 more per 1000 (from 137 more to 1000 more)	Low	Critical
							-	42.9%		515 more per 1000 (from 137 more to 1000 more)		
Mean healing index – geriatric adults – grade and classification system not reported[154]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	None	16.8 (SD 39.65)	-3.8 (SD 39.65)	-	MD 20.6 higher (4.75 lower to 45.95 higher)	Very low	Critical
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate of change in size of pressure ulcers												

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Sugar	Different types of topical agents	Relative (95% CI)	Absolute	Quality	Importance
-	-	-	-	-	-	-	-	-	-	-	-	-
Reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital or NHS care												
-	-	-	-	-	-	-	-	-	-	-	-	-
Patient acceptability												
-	-	-	-	-	-	-	-	-	-	-	-	-
Side effects												
-	-	-	-	-	-	-	-	-	-	-	-	-
Mortality (all-cause)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) The authors did not report on allocation concealment or blinding.
(b) The confidence interval crossed 1 MID point.

Table 183: Clinical evidence profile: honey versus ethoxydiaminoacridine and nitrofurazone

Quality assessment							No of patients/ulcers		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Honey	Ethoxydiamino-acridine and nitrofurazone	Relative (95% CI)	Absolute	Quality	Importance
Proportion of pressure ulcers completely healed – inpatients – all grades (grade 2 and 3) – AHCPR classification[74]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	5/25 (33.3%)	0/25 (0%)	Peto OR 8.83 (1.42 to 54.99)	200 more per 1000 (from 30 more to 370 more)	Low	Critical
								0%		200 more per 1000 (from 30 more to 370 more)		
Mean percentage reduction in pressure ulcer area – inpatients – all grades (grade 2 and 3) – AHCPR classification[74]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	None	56 (SD 28.92)	13 (SD 28.92)	-	MD 43 higher (24.49 to 61.51 higher)	Very low	Critical
Mean percentage decrease in PUSH score – inpatients – all grades (grade 2 and 3) – AHCPR classification[74]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	12.62 (SD 2.15)	6.55 (SD 2.14)	-	MD 6.07 higher (4.40 to 7.74 higher)	Low	Critical
Proportion of people with adverse events – inpatients – all grades (grade 2 and 3) – AHCPR classification[74]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	0/15 (0%)	0/11 (0%)	Not pooled	0 more (from 140 fewer to 140 more)	Low	Important

Quality assessment							No of patients/ulcers		Effect			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Honey**	**Ethoxydiamino-acridine and nitrofurazone**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
							-	0%		0 more (from 140 fewer to 140 more)		
Mortality (all-cause) [74]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[c]	None	0/15 (0%)	1/12 (8.3%)	OR 0.11 (0 to 5.44)	73 fewer per 1000 (from 83 fewer to 248 more)	Very low	Important
							-	8.3%		73 fewer per 1000 (from 83 fewer to 247 more)		
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate of change in size of pressure ulcer												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital or NHS care												
-	-	-	-	-	-	-	-	-	-	-	-	-
Patient acceptability												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) The authors did not report on sequence generation, allocation concealment and no blinding; no log-transformation of data was carried out.
(b) SD calculated on a p-value < 0.001 (less precise).
(c) The confidence interval crossed both MID points.

Table 184: Clinical evidence profile: platelet gel versus other treatment

Quality assessment							No of ulcers		Effect			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Platelet gel**	**Other treatment**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
Proportion of pressure ulcers completely healed – people with a spinal cord injury – all grades (grade 3 and 4) – NPUAP classification[166]												
1	Randomised trial	Very serious[a,c]	No serious inconsistency	No serious indirectness	No serious imprecision	None	0/8 (0%)	0/8 (0%)	Not pooled	0 more (from 210 fewer to 210 more)	Low	Critical
							-	0%		0 more (from 210 fewer to 210 more)		
Proportion of pressure ulcers improved – people with a spinal cord injury – all grades (grade 3 and 4) – NPUAP classification[166]												
1	Randomised trial	Very serious[a,c]	No serious inconsistency	No serious indirectness	Serious[b]	None	8/8 (100%)	7/8 (87.5%)	RR 1.13 (0.81 to 1.58)	114 more per 1000 (from 166 fewer to 508 more)	Very low	Critical
							-	87.5%		114 more per 1000 (from 166 fewer to 508 more)		
Mean percentage reduction in pressure ulcer volume – people with a spinal cord injury – all grades (grade 3 and 4) – NPUAP classification[166]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	None	55 (SD 22.9)	17.2 (SD 98.1)	-	MD 37.8 higher (32.01 lower to 107.61 higher)	Very low	Critical
Time to complete healing of pressure ulcers												

Quality assessment							No of ulcers		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Platelet gel	Other treatment	Relative (95% CI)	Absolute	Quality	Importance
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate of change in size of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital or NHS care												
-	-	-	-	-	-	-	-	-	-	-	-	-
Patient acceptability												
-	-	-	-	-	-	-	-	-	-	-	-	-
Side effects												
-	-	-	-	-	-	-	-	-	-	-	-	-
Mortality (all-cause)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) The authors did not report on sequence generation, allocation concealment or blinding.
(b) The confidence interval crossed 1 MID point.
(c) The drop out is more than 10% higher than event rate.

Table 185: Clinical evidence profile: hyaluronic acid versus sodium hyaluronic

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Hyaluronic acid	Sodium hyaluronate	Relative (95% CI)	Absolute	Quality	Importance
Mean percentage reduction in pressure ulcer area– inpatients – grade 1– NPUAP classification[58]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	90 (SD 21.29)	70 (SD 21.29)	-	MD 20 higher (1.34 to 38.66 higher)	Very low	Critical
Mean percentage reduction in pressure ulcer area– inpatients – grade 2 – NPUAP classification[58]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[c]	None	70 (SD 26.28)	40 (SD 26.28)	-	MD 30 higher (6.96 to 53.04 higher)	Very low	Critical
Mean percentage reduction in pressure ulcer area– inpatients – grade 3 – NPUAP classification[58]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[d]	None	(n=7)	(n=7)	p<0.01	Not pooled	Very low	Critical
Time to 50% reduction in pressure ulcer diameter (days)– inpatients – grade 1– NPUAP classification[58]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	9 (SD 6.39)	15 (SD 6.39)	-	MD 6 lower (11.6 to 0.4 lower)	Very low	Critical
Time to 50% reduction in pressure ulcer diameter (days)– inpatients – grade 2 – NPUAP classification[58]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	9.5 (SD 5.85)	15 (SD 5.85)	-	MD 5.5 lower (10.63 to 0.37 lower)	Very low	Critical
Time to 50% reduction in pressure ulcer diameter (days)– inpatients – grade 3 – NPUAP classification[58]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	12.9 (SD 6.71)	19.2 (SD 6.71)	-	MD 6.3 lower (13.33 lower to 0.73 higher)	Very low	Critical
Time to complete healing of pressure ulcers												

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Hyaluronic acid	Sodium hyaluronate	Relative (95% CI)	Absolute	Quality	Importance
-	-	-	-	-	-	-	-	-	-	-	-	-
Proportion of people with pressure ulcers completely healed												
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate of change in size of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital or NHS care												
-	-	-	-	-	-	-	-	-	-	-	-	-
Patient acceptability												
-	-	-	-	-	-	-	-	-	-	-	-	-
Side effects												
-	-	-	-	-	-	-	-	-	-	-	-	-
Mortality (all-cause)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) The authors did not report on sequence generation and allocation concealment and blinding of nurse, outcome assessor and statistician, blinding of participant not reported; no log-transformation of data.
(b) The confidence interval crossed 1 MID point; SD calculated on a p-value < 0.05 (less precise).
(c) The confidence interval crossed 1 MID point; SD calculated on a p-value < 0.02 (less precise).
(d) Only p-value were reported.

Table 186: Clinical evidence profile: zinc gauze dressing versus streptokinase-streptodornase ointment

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Zinc gauze	Streptokinase-streptodornase (ointment)	Relative (95% CI)	Absolute	Quality	Importance
Median percentage reduction in pressure ulcer area – geriatric adults – necrotic pressure ulcers – classification system not reported[4]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	2.4 (n=14)	-18.7 (n=14)	-	Not pooled	Very low	Critical
Proportion of people with skin reaction – geriatric adults– necrotic pressure ulcers – classification system not reported[4]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[c]	None	0/14 (0%)	1/14 (7.1%)	OR 0.14 (0 to 6.82)	61 fewer per 1000 (from 71 fewer to 273 more)	Very low	Important
							-	7.1%		60 fewer per 1000 (from 71 fewer to 272 more)		
Proportion of people with infection – geriatric adults – necrotic pressure ulcers – classification system not reported[4]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[c]	None	0/14 (0%)	1/14 (7.1%)	OR 0.14 (0 to 6.82)	61 fewer per 1000 (from 71 fewer to 273 more)	Very low	Important
							-	7.1%		60 fewer per 1000 (from 71 fewer to 272 more)		
Mortality (all-cause) [4]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious	None	0/14 (0%)	0/14 (0%)	Not pooled	Not pooled	Low	Important

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Zinc gauze	Streptokinase-streptodornase (ointment)	Relative (95% CI)	Absolute	Quality	Importance
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Proportion of people with pressure ulcers completely healed												
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate of change in size of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital or NHS care												
-	-	-	-	-	-	-	-	-	-	-	-	-
Patient acceptability												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) Sequence generation by pairs, no report on allocation concealment and only blinding of outcome assessor; no log-transformation of data was carried out.
(b) No standard deviation was reported and the study used a small sample size.
(c) The confidence interval crossed both MID points.

Table 187: Clinical evidence profile: hydrofibre dressing versus resin salve

Quality assessment							No of patients/ulcers		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Hydrofibre	Resin salve	Relative (95% CI)	Absolute	Quality	Importance
Proportion of people with pressure ulcers completely healed – people in hospital – all grades (grade 2 to 4) – EPUAP classification[176]												
1	Randomised trial	Serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	None	4/9 (44.4%)	12/13 (92.3%)	RR 0.48 (0.23 to 1.02)	480 fewer per 1000 (from 711 fewer to 18 more)	Low	Critical
							-	92.3%		480 fewer per 1000 (from 711 fewer to 18 more)		
Proportion of pressure ulcers completely healed – people in hospital – all grades (grade 2 to 4) – EPUAP classification[176]												
1	Randomised trial	Serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	None	4/11 (36.4%)	17/18 (94.4%)	RR 0.39 (0.17 to 0.85)	576 fewer per 1000 (from 142 fewer to 784 fewer)	Low	Critical
							-	94.4%		576 fewer per 1000 (from 142 fewer to 784 fewer)		
Proportion of pressure ulcers improved – people in hospital – all grades (grade 2 to 4) – EPUAP classification[176]												
1	Randomised trial	Serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	None	10/11 (90.9%)	18/18 (100%)	RR 0.9 (0.72 to 1.13)	100 fewer per 1000 (from 280 fewer to 130 more)	Low	Critical
							-	100%		100 fewer per 1000		

Quality assessment							No of patients/ulcers		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Hydrofibre	Resin salve	Relative (95% CI)	Absolute	Quality	Importance
										(from 280 fewer to 130 more)		
Proportion of pressure ulcers worsened – people in hospital – all grades (grade 2 to 4) – EPUAP classification[176]												
1	Randomised trial	Very serious[a,f]	No serious inconsistency	No serious indirectness	Very serious[c]	None	1/11 (9.1%)	0/18 (0%)	OR 13.96 (0.25 to 792.93)	90 more per 1000 (from 110 fewer to 290 more)	Very low	Critical
							-	0%		90 more per 1000 (from 110 fewer to 290 more)		
Mean percentage reduction in pressure ulcer width – people in hospital – all grades (grade 2 to 4) – EPUAP classification[176]												
1	Randomised trial	Very serious[a,g]	No serious inconsistency	No serious indirectness	Very serious[d]	None	57.14 (n=11)	93.75 (n=18)	-	Not pooled	Very low	Critical
Mean percentage reduction in pressure ulcer depth – people in hospital – all grades (grade 2 to 4) – EPUAP classification[176]												
1	Randomised trial	Very serious[a,g]	No serious inconsistency	No serious indirectness	Very serious[d]	None	-1.89 (n=11)	88.46 (n=18)	-	Not pooled	Very low	Critical
Speed of healing of pressure ulcers (days) (log-rank-test) – people in hospital – all grades (grade 2 to 4) – EPUAP classification[176]												
1	Randomised trial	Serious[a]	No serious inconsistency	No serious indirectness	Very serious[e]	None	(n=11)	n=18)	p=0.013 (favour resin salve)	Not pooled	Very low	Critical
Proportion of people with allergic skin reaction – people in hospital – all grades (grade 2 to 4) – EPUAP classification[176]												
1	Randomised trial	Very serious[a,f]	No serious inconsistency	No serious indirectness	Very serious[c]	None	0/16 (0%)	1/21 (4.8%)	Peto OR 0.17 (0 to 8.97)	39 fewer per 1000 (from 48 fewer to	Very low	Important

Quality assessment							No of patients/ulcers		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Hydrofibre	Resin salve	Relative (95% CI)	Absolute	Quality	Importance
										262 more)		
							-	4.8%		40 fewer per 1000 (from 48 fewer to 263 more)		
Mortality (all-cause) [176]												
1	Randomised trial	Very serious[a,f]	No serious inconsistency	No serious indirectness	Very serious[c]	None	4/16 (25%)	3/21 (14.3%)	RR 1.75 (0.45 to 6.74)	107 more per 1000 (from 79 fewer to 820 more)	Very low	Important
							-	14.3%		107 more per 1000 (from 79 fewer to 821 more)		
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital or NHS care												
-	-	-	-	-	-	-	-	-	-	-	-	-
Patient acceptability												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) The authors did not report blinding; no intention-to-treat analysis was carried out.
(b) The confidence interval crossed 1 MID point.

(c) The confidence interval crossed both MID points.
(d) No standard deviation was reported and the study used a small sample size.
(e) No values, only p-value and the study used a small sample size.
(f) The drop out is more than 10% higher than event rate.
(g) No log-transformation was carried out.

Table 188: Clinical evidence profile: dextranomer versus chlorinated lime solution

Quality assessment							No of patients		Effect			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Dextranomer**	**Chlorinated lime solution**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
Time to healing (defined as granulating and less than 25% of original ulcer area) (days) – elderly adults – grade not reported – classification system not reported[129]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	None	39.3 (SD 17.67)	61.8 (SD 13.86)	-	MD 22.5 lower (41.14 to 3.86 lower)	Very low	Critical
Proportion of people with pain[129]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[c]	None	1/?	3/?	Not pooled	Not pooled	Very low	Important
							-	-		Not pooled		
Mortality (all-cause) [129]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[d]	None	1/8 (12.5%)	0/8 (0%)	Peto OR 7.39 (0.15 to 372.38)	1/8 (12.5%)	Very low	Important
							-	0%		-		
Proportion of people with pressure ulcers completely healed												
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate of change in size of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Dextranomer	Chlorinated lime solution	Relative (95% CI)	Absolute	Quality	Importance
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital or NHS care												
-	-	-	-	-	-	-	-	-	-	-	-	-
Patient acceptability												
-	-	-	-	-	-	-	-	-	-	-	-	-
Side effects												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) The authors did not report on allocation concealment, sequence generation, and no blinding; no intention to treat analysis was carried out.
(b) The confidence interval crossed 1 MID point.
(c) It was unclear how many participants were included in each group.
(d) The confidence interval crossed both MID points. There were a limited number of events.

Table 189: Clinical evidence profile: collagen and foam versus foam dressing

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Collagen and foam	Foam	Relative (95% CI)	Absolute	Quality	Importance
Proportion of people with pressure ulcers completely healed - stagnating pressure ulcers, of at least 4 weeks duration - classification system not reported[151]												
1	Randomised trial	Very serious [a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	4/5 (80%)	5/5 (100%)	RR 0.82 (0.49 to 1.38)	180 fewer per 1000 (from 510 fewer to 380 more)	Very low	Critical
							-	100%		180 fewer per 1000 (from 510 fewer to		

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Collagen and foam	Foam	Relative (95% CI)	Absolute	Quality	Importance
										380 more)		
Mortality (all-cause) [151]												
1	Randomised trial	Very serious [a]	No serious inconsistency	No serious indirectness	No serious	None	0/5 (0%)	0/5 (0%)	Not pooled	Not pooled	Low	Important
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate of change in size of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital or NHS care												
-	-	-	-	-	-	-	-	-	-	-	-	-
Patient acceptability												
-	-	-	-	-	-	-	-	-	-	-	-	-
Side effects												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) There was a very small sample size. The author did not report details of allocation concealment or blinding.
(b) The confidence interval crossed both MID points.

11.1.2 Economic evidence (adults)

Published literature

Eleven studies were included with relevant comparisons.[27,36,62,69,92,113,122,125,143,148,206] These are summarised in the economic evidence profiles below(Table 190 - Table 196). See also the study selection flow chart in Appendix D and study evidence tables in Appendix H.

Two studies that met the inclusion criteria were selectively excluded[75,91] – these are summarised in Appendix H, with reasons for exclusion given.

Unit costs

Relevant unit costs were provided to aid consideration of cost effectiveness. See Appendix P..

Table 190: Economic evidence profile: hydrocolloid dressing versus. collagen dressing

Study	Applicability	Limitations	Other comments	Incremental cost	Incremental effects	Cost effectiveness	Uncertainty
Burgos 2000[36] (Spain)	Partially applicable[a]	Potentially serious limitations[b]	Within trial analysis of a collagen dressing compared to a hydrocolloid dressing, based on analysis of individual level resource use with unit costs applied.	-£46	Patients healed: RR 0.95 (CI 0.22-4.10) Mean percentage reduction in ulcer area MD: -9.6 (CI -69.17-49.97) Mean cm2 reduction in ulcer area MD: -2.9 (CI -10.24 – 4.44)	Collagen is both more expensive and more effective than hydrocolloid	None reported
Graumlich 2003[69] (US)	Partially applicable[c]	Potentially serious limitations[d]	Within trial analysis of a collagen dressing compared to a hydrocolloid dressing, based on analysis of individual level resource use with unit costs applied.	-£260	Patients healed: RR 0.97 (CI 0.60-1.57) Mean percentage reduction in ulcer area MD: -24.00 (CI -60.08-	Collagen is both more expensive and more effective than hydrocolloid	It is stated that sensitivity analyses did not reveal likely conditions under which collagen would be cheaper than hydrocolloid; results are not presented.

Study	Applicability	Limitations	Other comments	Incremental cost	Incremental effects	Cost effectiveness	Uncertainty
					12.08) Mean time to healing (weeks) MD 1.00 (CI -0.36-2.36) Mean healing speed (mm2/day) MD: 0.00 (CI -8.23-8.23)		
Müller 2001[125] (Netherlands)	Partially applicable[e]	Potentially serious limitations[f]	Within trial analysis of a collagen dressing compared to a hydrocolloid dressing for heel ulcers, based on analysis of individual level resource use with unit costs applied.	£25	Proportion of patients healed: -29% (p <0.005)	Collagen dominates hydrocolloid	No useful sensitivity analyses reported.

(a) Study based in Spain, quality of life not considered, costs based on 1998 values
(b) no analysis of uncertainty reported, unit costs are based on prices faced by patients and could be substantially different to those faced by hospitals, differential costs past 12 weeks not included due to time horizon
(c) Study based in US, quality of life not considered, costs year not reported
(d) No consideration of quality of life, analysis of uncertainty results are not reported, it is not clear whether unit costs are nationally representative, differential costs past 8 weeks not included due to time horizon
(e) Study based in the Netherlands, quality of life not considered, costs based on 1998 values
(f) Small study, no unit cost source reported, no consideration of quality of life, no useful analysis of uncertainty reported

Table 191: Economic evidence profile: hydrocolloid dressings versus saline gauze

Study	Applicability	Limitations	Other comments	Costs	Effects	Cost effectiveness	Uncertainty
Kerstein	Partially	Potentially	Decision analytic model to	Intvn 1: £703	Patients	DuoDERM	None reported

Study	Applicability	Limitations	Other comments	Costs	Effects	Cost effectiveness	Uncertainty
2001[92] (US)	applicable[a]	serious limitaions[b]	compare saline gauze (intvn 1), Comfeel dressing (intvn 2), and DuoDERM dressing (intvn 3). The model is based on proportion of patients healed, and takes into account the probability of debridement and infection.	Intvn 2: £384 Intvn 3: £353	healed at 12 weeks: Intvn 1: 51% Intvn 2: 48% Intvn 3: 61%	dressing dominates Comfeel dressing and saline gauze.	
Meaume 2002[113] (Europe)	Partially applicable[c]	Potentially serious limitaions[d]	Decision analytic model to compare saline gauze (intvn 1), Comfeel dressing (intvn 2), and DuoDERM dressing (intvn 3). The model is based on proportion of patients healed, and takes into account the probability of debridement and infection.	Intvn 1: £1,651 Intvn 2: £516 Intvn 3: £500	Patients healed at 12 weeks: Intvn 1: 51% Intvn 2: 48% Intvn 3: 61%	DuoDERM dressing dominates Comfeel dressing and saline gauze.	None reported

(a) The analysis is based in the US; quality of life is not considered
(b) No analysis of uncertainty reported, average ratios presented, no cohort characteristics provided. There is also a potential conflict of interest as the study is carried out by manufacturer of the DuoDERM dressing. Differential costs past 12 weeks note included due to time horizon
(c) The analysis is based in Europe (based a variety of countries, costs calculated in Euros); quality of life is not considered.
(d) No analysis of uncertainty reported, average ratios presented, no cohort characteristics provided. Source of funding not reported. Differential costs past 12 weeks not included due to time horizon.

Table 192: Economic evidence profile: hydrocolloid dressing versus hydrogel dressing

Study	Applicability	Limitations	Other comments	Incremental cost	Effects	Cost effectiveness	Uncertainty
Motta 1999[122] (US)	Partially applicable[a]	Potentially serious limitations[b]	Within trial analysis of a hydrocolloid dressing compared to a polymer hydrogel dressing, based on analysis of individual level resource use with unit costs applied	-£22	Patients healed: RR 1 (CI 0.22-4.56) Mean healing rate (cm/day)	Number of patients healed equal, so lower cost of hydrogel indicates hydrogel is cost-effective.	None reported

Study	Applicability	Limitations	Other comments	Incremental cost	Effects	Cost effectiveness	Uncertainty
					MD: 0.2 (CI -0.22-0.62)		

(a) US healthcare system, quality of life not considered, cost year not reported
(b) Small pilot study with only ten patients, no unit cost source reported, no analysis of uncertainty reported. Differential costs past 8 weeks not included due to time horizon restriction.

Table 193: Economic evidence profile: hydrogel dressing versus collagenase dressing

Study	Applicability	Limitations	Other comments	Incremental cost	Incremental effects	Cost effectiveness	Uncertainty
Waycaster 2013[206] (US)	Partially applicable[a]	Potentially serious limitations[b]	Markov model based on a single RCT. Three states: inflamed wound, healing wound, healed wound. Hydrogel dressings are compared to collagenase dressings.	£2,297	Days spent with pressure ulcer: 99	Collagenase dressings dominate hydrogel dressings: lower costs and fewer days spent with pressure ulcer.	Parameters were varied by +/- 20%. Collagenese dressings remained dominant in all scenarios. Frequency of dressing change was varied from twice daily to every 3 days – this variable had the greatest influence on the results.

(a) US healthcare system, quality of life not considered
(b) Based on single RCT. The study does not fully describe cost sources or resource usage. No consideration is given to quality of life. Analysis of uncertainty is incomplete.

Table 194: Economic evidence profile: gauze versus impregnated gauze versus calcium alginate versus hydroactive wound dressing

Study	Applicability	Limitations	Other comments	Costs	Effects	Cost effectiveness	Uncertainty
Bergermann 1999[27](Germany)	Partially applicable[a]	Potentially serious limitations[b]	A model comparing gauze, ointment impregnated gauze, calcium alginate, and a hydroactive wound dressing (in combination with enzymatic wound cleaning) in the treatment of four sizes of PU: 5cm x 8 cm, 8cm x 12 cm, 10cm x	Total costs (per patient, median) for 12x20cm ulcer: Intvn 1: £3,813 Intvn 2: £1,501 Intvn 3: £1,677	None	Intervention 4 has the lowest cost.	Results were not sensitive to changes in personnel cost per minute, time required for changing a wound dressing or total number of wound dressing changes.

Study	Applicability	Limitations	Other comments	Costs	Effects	Cost effectiveness	Uncertainty
			15cm, 12cm x 20cm. Cost-comparison only.	Intvn 4: £592			

(a) Based in Germany, quality of life not considered, health outcomes not considered (assumed equivalent)

(b) Unclear whether unit costs are nationally representative, efficacy is assumed the same, it is assumed (not based on evidence) that treatment with hydroactive wound dressing reduces inpatient stay by 10%

Table 195: Economic evidence profile: advanced dressings versus traditional/simple dressings

Study	Applicability	Limitations	Other comments	Incremental cost	Incremental effects	Cost effectiveness	Uncertainty
Ohura 2004[143] (Japan)	Partially applicable[a]	Potentially serious limitations[b]	Within study analysis (prospective cohort study) of a variety of modern wound dressings compared to a traditional dressing, based on analysis of individual level resource use with unit costs applied	-£0.32	Reduction in PSST score: 4.2	Modern dressings dominate traditional wound care, with reduced costs and greater reduction in PSST score	No sensitivity analysis reported
Foglia 2012[62] (Italy)	Partially applicable[c]	Potentially serious limitations[d]	Within trial analysis with analysis of individual level resource use. Observational study in which advanced dressings were compared to simple saline dressings.	-£78	Reduction in ulcer size 6%	Advanced dressings dominated simple dressings, with a reduction in cost and greater reduction in ulcer size.	Deterministic analyses revealed that when using min and max values for personnel costs, transport expenses and material costs, the cost savings from the use of advanced dressings were between 27-29%. Bootstrapping methods and Monte Carlo simulation were also carried out; the use of advanced dressings was cost

Study	Applicability	Limitations	Other comments	Incremental cost	Incremental effects	Cost effectiveness	Uncertainty
							saving in all scenarios.

(a) Japanese healthcare system, quality of life not considered
(b) No analysis of uncertainty reported, unclear whether unit costs are nationally representative, dfferential costs past 12 weeks not included due to time horizon (healing is not recorded and effectiveness is based on PSST score only), not a randomised study (no significant differences in age, size of ulcer or PSST score at baseline).
(c) The analysis is based in Italy; quality of life is not considered
(d) Based on single observational study. The study does not fully describe the relevant comparators, or the cost sources. Only the costs were subject to sensitivity analysis. Differential costs past 30 days not included due to time horizon restriction.

Table 196: Economic evidence profile: saline soaked gauze verses polyurethane self-adhesive foam dressing

Study	Applicability	Limitations	Other comments	Incremental cost	Incremental effects	Cost effectiveness	Uncertainty
Payne 2009[148] (US)	Partially applicable[a]	Minor limitaions[b]	Within trial analysis with analysis of individual level resource use. Patients randomised to receive saline soaked gauze or polyurethane self-adhesive foam dressing.	-£301	Pressure ulcer free days: 2.4 Ulcers healed by day 28: 12%	Polyurethane self-adhesive foam dressing dominates saline soaked gauze	Costs for patients who dropped out were included only up until the point of withdrawal in a deterministic sensitivity analysis (in the base case analysis costs were included up until the 28 day horizon even if the patient withdrew). The foam dressing remained dominant compared to saline soaked gauze.

(a) The analysis is based in the US; quality of life is not considered

All resource use and health outcomes are obtained from within the trial rather than via a systematic procedure. The cost of the saline soaked gauze is calculated to be the same cost as the foam dressing. Exploration of uncertainty is inadequate. Differential costs past 28 days not included due to time horizon.

11.1.3 Clinical evidence (neonates, infants, children and young people)

No RCTs or cohort studies were identified. Recommendations were developed using a modified Delphi consensus technique. Further details can be found in Appendix N.

11.1.4 Economic evidence (neonates, infants, children and young people)

No relevant economic evaluations were identified. The GDG considered relevant unit costs (see Appendix P).

11.1.5 Evidence statements

11.1.5.1 Clinical (adults)

11.1.5.1.1 Hydrocolloid dressing versus gauze dressing

- Four studies (n=170) (general population and people with spinal cord injury) showed a hydrocolloid dressing is potentially more clinically effective at increasing the proportion of people with pressure ulcers completely healed (all grades) when compared to a gauze dressing (very low quality).
- Three studies (n=115) (general population) showed there is potentially no clinical difference between a hydrocolloid dressing and gauze dressing for increasing the proportion of people with pressure ulcers completely healed (all grades) (very low quality).
- One study (n=55) (people with spinal cord injury) showed a hydrocolloid dressing is more clinically effective at increasing the proportion of people with pressure ulcers completely healed (all grades) when compared to a gauze dressing (moderate quality).
- Four studies (n=273) (general population and people with spinal cord injury) showed a hydrocolloid dressing is more clinically effective at increasing the proportion of pressure ulcers completely healed (all sites, all grades) when compared to a gauze dressing (low quality).
- Three studies (n=212) (general population) showed a hydrocolloid dressing is potentially more clinically effective at increasing the proportion of pressure ulcers completely healed (all sites, all grades) when compared to a gauze dressing (very low quality).
- One study (n=61) (people with spinal cord injury) showed a hydrocolloid dressing is more clinically effective at increasing the proportion of pressure ulcers completely healed (all sites, all grades) when compared to a gauze dressing (moderate quality).
- Two studies (n=96) (general population and people with spinal cord injury) showed a hydrocolloid dressing is potentially more clinically effective at increasing the proportion of people with pressure ulcers completely healed (all sites, grade 2 and above) when compared to a gauze dressing (very low quality).
- One study (n=37) (people with spinal cord injury) showed a hydrocolloid dressing is more clinically effective at increasing the proportion of people with pressure ulcers completely healed (all sites, grade 2 and above) when compared to a gauze dressing (moderate quality).
- One study (n=59) (general population) showed a hydrocolloid dressing is potentially more clinically effective at increasing the proportion of people with pressure ulcers completely healed (all sites, grade 2 and above) when compared to a gauze dressing (very low quality).
- One study (n=28) (general population) showed there may be no clinical difference between a hydrocolloid dressing and a gauze dressing for the proportion of people with pressure ulcers completely healed (all sites, grade 3), but the direction of the estimate of effect favoured the hydrocolloid dressing (very low quality).

- One study (n=15) (people with spinal cord injury) showed a gauze dressing is potentially more clinically effective at increasing the proportion of people with pressure ulcers completely healed (sacral, grade 1 and 2) when compared to a hydrocolloid dressing (low quality).
- One study (n=91) (people with spinal cord injury) showed a hydrocolloid dressing is more clinically effective at increasing the proportion of people with pressure ulcers improved (all grades) when compared to a gauze dressing (moderate quality).
- Two studies (n=148) (general population and people with spinal cord injury) showed there may be a clinical benefit for a hydrocolloid dressing compared to a gauze dressing at reducing the proportion of people with pressure ulcers worsened (all grades) (very low quality).
- One study (n=61) (people with spinal cord injury) showed a hydrocolloid dressing is potentially more clinically effective at reducing the proportion of people with pressure ulcers worsened (all grades) when compared to a gauze dressing (low quality).
- One study (n=87) (general population) showed there may be no clinical difference between a hydrocolloid dressing and a gauze dressing 2 for the proportion of people with pressure ulcers worsened (all grades), but the direction of the estimate of effect could favour either intervention (very low quality).
- One study (n=59) (general population) showed there may be no clinical difference between a hydrocolloid dressing and a gauze dressing for the proportion of people with pressure ulcers worsened (grade 2) but the direction of the estimate of effect favoured the hydrocolloid dressing (very low quality).
- One study (n=28) (general population) showed there may be no clinical difference between a hydrocolloid dressing and a gauze dressing for the proportion of people with pressure ulcers worsened (grade 3) but the direction of the estimate of effect favoured the gauze dressing (very low quality).
- Two studies (n=75) (general population) showed there is potentially no clinical difference between a hydrocolloid dressing and a gauze dressing for mean percentage reduction in ulcer area (all grades), the direction of the estimate of effect favoured the gauze dressing (very low quality).
- One study (n=97) (in-patients) showed there may be a clinical benefit for a gauze dressing compared to a hydrocolloid dressing for the mean cm2 reduction in ulcer area (all grades). No estimate of precision could be derived (very low quality).
- One study (n=49) (people in long term care) reported medians for a hydrocolloid dressing and a gauze dressing for percentage reduction in pressure ulcer area (all grades). The median reduction for the hydrocolloid dressing was 100% and 85.7% for the gauze dressing. No estimate of effect or precision could be derived (very low quality).
- One study (n=41) (in- and out-patients) reported medians for a hydrocolloid dressing and a gauze dressing for percentage reduction in pressure ulcer area (grade 2 and 3). The median reduction for the hydrocolloid dressing was 7.4% and 7.0% for the gauze dressing. No estimate of effect or precision could be derived (very low quality).
- One study (n=59) (general population) reported medians for a hydrocolloid dressing and a gauze dressing for percentage reduction in pressure ulcer area (grade 2). The median reduction for the hydrocolloid dressing was 91% and 48% for the gauze dressing. No estimate of effect or precision could be derived (very low quality).
- One study (n=28) (general population) reported medians for a hydrocolloid dressing and a gauze dressing for percentage reduction in pressure ulcer area (grade 3). The median reduction for the hydrocolloid dressing was 0.3% and 30% for the gauze dressing. No estimate of effect or precision could be derived (very low quality).

- One study (n=32) (general population) showed a gauze dressing is more clinically effective for mean percentage reduction in pressure ulcer volume (all grades) when compared to a hydrocolloid dressing (low quality).
- One study (n=32) (general population) showed there is potentially no clinical difference between a hydrocolloid dressing and a gauze dressing for mean healing speed of pressure ulcers (all grades), the direction of the estimate of effect favoured the hydrocolloid dressing (very low quality).
- One study (n=39) (people in long term care) reported medians for a hydrocolloid dressing and a gauze dressing for time to healing of pressure ulcer area (all grades). The median reduction for the hydrocolloid dressing was 9 days and 11 days for the gauze dressing. No estimate of effect or precision could be derived (very low quality).
- One study (n=34) (in-patients) showed there may be no clinical difference between a hydrocolloid dressing and a gauze dressing for the proportion of people with an infection, but the direction of the estimate of effect favoured hydrocolloid dressing (very low quality).
- One study (n=28) (general population) showed there is no clinical difference between a hydrocolloid dressing and a gauze dressing for the proportion of people with infected pressure ulcers, the estimate of effect could favour either intervention (low quality).
- One study (n=44) (general population) showed there may be a clinical benefit for a hydrocolloid dressing compared to a gauze dressing for a higher proportion of people with hypergranulation (very low quality).
- One study (n=100) (general population) showed a hydrocolloid dressing is more clinically effective for reducing the proportion of people with skin irritation when compared to a gauze dressing (low quality).
- One study (n=34) (in-patients) showed a hydrocolloid dressing is more clinically effective for reducing the proportion of people with pain at dressing removal when compared to a gauze dressing (low quality).
- One study (n=32) (general population) showed there may be no clinical difference between a hydrocolloid dressing and a gauze dressing for median pain score during treatment, but the direction of the estimate of effect could favour either intervention. No estimate of precision could be derived (very low quality).
- One study (n=32) (general population) showed there may be no clinical difference between a hydrocolloid dressing and a gauze dressing for median odour score during treatment, but the direction of the estimate of effect could favour either intervention. No estimate of precision could be derived (very low quality).
- One study (n=34) (in-patients)showed there is potentially a clinical benefit for a hydrocolloid dressing compared to a gauze dressing for reducing the proportion of people with discomfort (low quality).
- One study (n=32) (general population) reported medians comfort score during treatment for a hydrocolloid dressing and a gauze dressing. The median for the hydrocolloid dressing was 4.0 (range 3-4) and 3.0 (range 2-4) for the gauze dressing. No estimate of effect or precision could be derived (very low quality).
- Six studies (n=269) showed there is potentially no clinical difference between a hydrocolloid dressing and gauze dressing for reducing all-cause mortality, the estimate of effect favours the hydrocolloid dressing (very low quality).
- No evidence was found for the following outcomes:
  - Time to complete healing
  - Time in hospital or NHS care
  - Health-related quality of life

11.1.5.1.2 Hydrocolloid dressing versus foam dressing

- Three studies (n=157) (general population) showed a hydrocolloid dressing is potentially more clinically effective at increasing the proportion of people with pressure ulcers completely healed (all grades) when compared to a foam dressing (very low quality).
- One study (n=96) (community patients) showed there is no clinical difference of a hydrocolloid dressing for proportion of people with pressure ulcers improved (all grades) when compared with a foam dressing, the estimate of effect favoured either intervention (very low quality).
- Two studies (n=156) (general population) showed there may be no clinical difference between a hydrocolloid dressing and a foam dressing for proportion of people with pressure ulcers not changed (all grades), but the direction of the estimate of effect favoured the foam dressing (very low quality).
- Two studies (n=156) (general population) showed there may be no clinical difference between a hydrocolloid dressing and a foam dressing for proportion of people with pressure ulcers worsened (all grades), but the direction of the estimate of effect favoured the foam dressing (very low quality).
- One study (n=39) (general population) showed there is potentially no clinical difference between a hydrocolloid dressing and a foam dressing for mean reduction in pressure ulcer area, the direction of the estimate of effect favoured the hydrocolloid dressing (very low quality).
- One study (n=99) (people in the community) showed there is no clinical difference between a hydrocolloid dressing and a foam dressing for proportion of people with hypergranulation, the direction of the estimate of effect could favour either intervention (low quality).
- One study (n=99) (people in the community) showed there may be no clinical difference between a hydrocolloid dressing and a foam dressing for proportion of people with bleeding, but the direction of the estimate of effect could favour either intervention (very low quality).
- One study (n=99) (people in the community) showed there is potentially no clinical difference between a foam dressing and a hydrocolloid dressing for lower proportion of people with maceration, the direction of the estimate of effect favours either intervention (very low quality).
- One study (n=39) (general population) showed a hydrocolloid dressing is potentially more clinically effective at reducing the proportion of people with inflammation or maceration when compared to a foam dressing (very low quality).
- One study (n = 39) (general population) showed there is potentially no clinical difference between a hydrocolloid dressing and a foam dressing for mean pain score at the end of treatment, the direction of the estimate of effect favoured the foam dressing (very low quality).
- One study (n = 39) (general population) showed there is potentially no clinical difference between a hydrocolloid dressing and a foam dressing for mean odour score at the end of treatment, the direction of the estimate of effect favoured the foam dressing (very low quality).
- Two studies (n=100) (general population) showed there may be no clinical difference between a hydrocolloid dressing and a foam dressing for reducing the proportion of people with adverse events, the direction of the estimate of effect favoured the hydrocolloid dressing (very low quality).
- One study (n=60) showed there may be a clinical benefit for a hydrocolloid dressing compared to a foam dressing for reducing all-cause mortality (very low quality).
- No evidence was found for the following outcomes:
  - Time to complete healing
  - Rate of reduction in size of ulcers
  - Time in hospital or NHS care
  - Patient acceptability
  - Health-related quality of life

11.1.5.1.3 Hydrocolloid dressing versus polyurethane dressing

- One study (n=122) (general population) showed there is potentially no clinical difference between a hydrocolloid dressing and a polyurethane dressing for increasing the proportion of people with pressure ulcers completely healed (all grades), the direction of the estimate of effect favoured the hydrocolloid dressing (very low quality).
- One study (n=28) (people in the community) showed there is no clinical difference between a hydrocolloid dressing and a polyurethane dressing for increasing the proportion of people with pressure ulcers improved (all grades), the direction of the estimate of effect favoured the hydrocolloid dressing(low quality).
- One study (n=72) (general population) reported mean percentage reduction in pressure ulcer area (all grades) for a hydrocolloid dressing and a polyurethane dressing. The mean for the hydrocolloid dressing was 23.8% and 26.7% for the polyurethane dressing. No estimate of effect or precision could be derived (very low quality).
- One study (n=22) (in-patients) reported median time to healing of pressure ulcers (all grades) for a hydrocolloid dressing and a polyurethane dressing. The median for the hydrocolloid dressing was 12.69 days and 13.36 days for the polyurethane dressing. No estimate of effect or precision could be derived (very low quality).
- One study (n=72) (general population) showed there is potentially no clinical difference between a hydrocolloid dressing and a polyurethane dressing for linear healing rate of pressure ulcer (all grades), the direction of the estimate of effect favoured the hydrocolloid dressing (very low quality).
- One study (n=72) (general population) showed there is potentially no clinical difference between a hydrocolloid dressing and a polyurethane dressing for mean odour score, the direction of the estimate of effect favoured the polyurethane dressing (very low quality).
- One study (n=72) (general population) showed there is potentially no clinical difference between a hydrocolloid dressing and a polyurethane dressing for mean comfort score, the direction of the estimate of effect favoured the polyurethane dressing (very low quality).
- One study (n=72) (general population) showed there is no clinical difference between a hydrocolloid dressing and a polyurethane dressing for proportion of people with adverse events, the direction of the estimate of effect could have favoured either intervention (low quality).
- One study (n=69) (general population) reported a significant difference between a hydrocolloid dressing and a polyurethane dressing for proportion of people with pain at dressing removal. The clinical importance is unknown (very low quality).
- One study (n=69) (general population) reported no significant difference between a hydrocolloid dressing and a polyurethane dressing for proportion of people with discomfort at dressing removal. The clinical importance is unknown (very low quality).
  One study (n=69) (general population) showed there may be no clinical difference between a polyurethane dressing and a hydrocolloid dressing for reducing all-cause mortality (very low quality).
- No evidence was found for the following outcomes:
  - Time to complete healing
  - Time in hospital or NHS care
  - Health-related quality of life
  - Patient acceptability

11.1.5.1.4 Hydrocolloid dressing versus collagenase ointment

- Two studies (n=60) (general population) showed a collagenase ointment may be more clinically effective at increasing the proportion of people with pressure ulcers (grade 2 and above) completely healed when compared to a hydrocolloid dressing (very low quality).
- One study (n=60) (in-patients) showed there may be a clinical benefit for a collagenase ointment compared to a hydrocolloid dressing for mean percentage reduction in pressure ulcer area (very low quality).
- One study (n=60) (in-patients) showed there is potentially a clinical benefit for a collagenase ointment compared to a hydrocolloid dressing for mean cm^2 reduction in pressure ulcer area (very low quality).
- One study (n=33) (general population) showed there may be a clinical benefit for a collagenase ointment compared to a hydrocolloid dressing for reducing the mean time to pressure ulcer healing (grade 4) (very low quality).
- One study (n=37) (in-patients) showed there may be no clinical difference between a collagenase ointment and a hydrocolloid dressing for proportion of people with adverse events, but the direction of the estimate of effect favoured collagenase (very low quality).
- Two studies (n=88) (general population) showed a collagenase ointment is potentially more clinically effective for reducing the mean time to pressure ulcer healing (grade 2 and above) when compared to a hydrocolloid dressing (very low quality).
- One study (n=61) (population) showed there may be a clinical benefit for a hydrocolloid dressing compared to a collagenase ointment for reducing all-cause mortality (very low quality).
- No evidence was found for the following outcomes:
  - Rate of reduction in size of ulcers
  - Pain (wound-related)
  - Time in hospital or NHS care
  - Patient acceptability
  - Health-related quality of life

11.1.5.1.5 Hydrocolloid dressing versus collagen

- One study (n=65) (in-patients) showed there may be no clinical difference between collagen and a hydrocolloid dressing for increasing the proportion of people with pressure ulcers completely healed (grade 2 and 3), the direction of the estimate of effect favoured collagen (very low quality).
- One study (n=65) (in-patients) showed collagen is potentially more clinically effective at increasing the mean percentage reduction in pressure ulcer area (grade 2 and 3) when compared to a hydrocolloid dressing (low quality).
- One study (n=65) (in-patients) showed there is no clinical difference between collagen and hydrocolloid dressing for mean healing speed of pressure ulcers , the direction of the estimate of effect favoured either intervention(moderate quality).
- One study (n=65) (in-patients) showed there may be no clinical difference between collagen and a hydrocolloid dressing for reducing the mean time to pressure ulcer healing (grade 2 and 3), the direction of the estimate of effect favoured either intervention (very low quality).
- One study (n=65) (in-patients) showed there is no clinical difference between a hydrocolloid dressing and collagen for the proportion of people with adverse events, the direction of the estimate of effect favoured either intervention (low quality).

- One study (n=65) (in-patients) showed there may be no clinical difference between a hydrocolloid dressing and collagen for all-cause mortality, but the direction of the estimate of effect favoured the hydrocolloid dressing (very low quality).
- No evidence was found for the following outcomes:
  - Pain (wound-related)
  - Time in hospital or NHS care
  - Patient acceptability
  - Health-related quality of life

11.1.5.1.6 Hydrocolloid dressing versus hydrogel

- One study (n=10) (people in the community) showed there may be no clinical difference between a hydrocolloid dressing and hydrogel for increasing the proportion of people with pressure ulcers completely healed (grade 2 and 3), but the direction of the estimate of effect could favour either intervention (very low quality).
- One study (n=129) (general population) showed hydrogel is potentially more clinically effective at increasing the proportion of people with pressure ulcers completely healed (grade 2 and 3) when compared to a hydrocolloid dressing (very low quality).
- One study (n=129) (general population) showed there may be a clinical benefit of hydrogel dressing for proportion of people with pressure ulcers not changed (grade 2 and 3) when compared to hydrocolloid dressing (very low quality).
- One study (n=129) (general population) showed hydrogel is potentially more clinically effective at reducing the proportion of people with pressure ulcers worsened (grade 2 and 3) when compared to a hydrocolloid dressing (very low quality).
- One study (n=58) (general population) showed there may be a clinical benefit for hydrogel compared to a hydrocolloid dressing for increasing the mean percentage reduction in pressure ulcer area (grade 1). No estimate of precision could be derived (very low quality).
- One study (n=71) (general population) showed there may be a clinical benefit for hydrogel compared to a hydrocolloid dressing for increasing the mean percentage reduction in pressure ulcer area (grade 2) (very low quality).
- One study (n=41) (in- and out-patients) reported median percentage reduction in pressure ulcer area for a hydrocolloid dressing and hydrogel. The median for the hydrocolloid dressing was 7.4% and 5.6 for hydrogel. No estimate of effect or precision could be derived (very low quality).
- One study (n=10) (people in the community) showed there may be no clinical difference between a hydrocolloid dressing and hydrogel for mean healing rate of pressure ulcers (grade 2 and 3), but the direction of the estimate of effect favoured hydrogel (very low quality).
- One study (n=129) (general population) reported healing rate of pressure ulcers (grade 2 and 3) for a hydrocolloid dressing and hydrogel. The rate for the hydrocolloid dressing was 3.1%/day and 8.1%/day for hydrogel. No estimate of effect or precision could be derived (very low quality).
- One study (n=10) (people in the community) reported median odour score during treatment for a hydrocolloid dressing and hydrogel. The median for the hydrocolloid dressing was 2 and 2 for hydrogel. No estimate of effect or precision could be derived (very low quality).
- One study (n=10) (people in the community) reported median comfort score during treatment for a hydrocolloid dressing and hydrogel. The median for the hydrocolloid dressing was 3 and 4 for hydrogel. No estimate of effect or precision could be derived (very low quality).
- One study (n=10) (people in the community) showed there is no clinical difference between a hydrocolloid dressing and hydrogel for all-cause mortality (low quality).
- No evidence was found for the following outcomes:

- Time to complete healing
- Pain (wound-related)
- Time in hospital or NHS care
- Health-related quality of life

11.1.5.1.7 Hydrocolloid dressing versus impregnated gauze

- One study (n=11) (general population) showed there may be a clinical benefit for a hydrocolloid dressing compared to impregnated gauze for increasing the proportion of people with pressure ulcers completely healed (grade unknown) (very low quality).
- One study (n=11) (general population) showed there may be no clinical difference between a hydrocolloid dressing and impregnated gauze for increasing the proportion of people with pressure ulcers improved (grade unknown), but the direction of the estimate of effect could favour either intervention (very low quality).
- No evidence was found for the following outcomes:
  - Time to complete healing
  - Rate of reduction in size of ulcers
  - Reduction in size and/or volume of ulcer.
  - Pain (wound-related)
  - Time in hospital or NHS care
  - Patient acceptability
  - Side effects
  - Mortality (all cause)
  - Health-related quality of life

11.1.5.1.8 Hydrocolloid dressing versus poly-hema dressing

- One study (n=43) (elderly people) showed there may be a clinical benefit for a hydrocolloid dressing compared to a poly-hema dressing for increasing the proportion of people with pressure ulcers completely healed (grade 2 and 3) (very low quality).
- One study (n=42) (elderly people) reported median time to healing of pressure ulcers (grade 2 and 3) for a hydrocolloid dressing and a poly-hema dressing. The median for the hydrocolloid dressing was 42 days and 32 days for a poly-hema dressing. No estimate of effect or precision could be derived (very low quality).
- One study (n=42) (elderly people) showed there is potentially no clinical difference between a hydrocolloid dressing and a poly-hema dressing for absolute rate of healing of pressure ulcers (grade 2 and 3), the direction of the estimate of effect favoured the poly-hema dressing (very low quality).
- One study (n=42) (elderly population) showed there may be no clinical difference between a hydrocolloid dressing and a poly-hema dressing for proportion of people with adverse events, but the direction of the estimate of effect favoured poly-hema dressing (very low quality).
- One study (n=42) (elderly population) showed there may be no clinical difference between a hydrocolloid dressing and a poly-hema dressing for all-cause mortality, but the direction of the estimate of effect favoured the hydrocolloid dressing (very low quality).
- No evidence was found for the following outcomes:
  - Reduction in size and/or volume of ulcer.
  - Pain (wound-related)
  - Time in hospital or NHS care

- Patient acceptability
- Mortality (all cause)
- Health-related quality of life

11.1.5.1.9 Hydrocolloid dressing versus co-polymer (amino acid) dressing

- One study (n=168) (in-patients) showed a co-polymer (amino acid) dressing is potentially more clinically effective at increasing the proportion of people with pressure ulcers completely healed (grade 2 and above) when compared to a hydrocolloid dressing (very low quality).
- One study (n=168) (in-patients) reported median time to pressure ulcer healing (grade 2 and above) for a hydrocolloid dressing and a co-polymer (amino acid) dressing. The median for the hydrocolloid dressing was 38 days (range 13-59 days) and 32 days (range 11-63 days) for a co-polymer (amino acid) dressing. No estimate of effect or precision could be derived (very low quality).
- One study (n=168) (in-patients) showed there may be no clinical difference between a hydrocolloid dressing and a co-polymer (amino acid) dressing for the proportion of people with an infection, but the direction of the estimate of effect favoured the hydrocolloid dressing (very low quality).
- No evidence was found for the following outcomes:
  - Rate of reduction in size of ulcers
  - Reduction in size and/or volume of ulcer.
  - Pain (wound-related)
  - Time in hospital or NHS care
  - Patient acceptability
  - Mortality (all cause)
  - Health-related quality of life

11.1.5.1.10 Hydrocolloid dressing versus phenytoin cream

- One study (n=55) (people with a spinal cord injury) showed a hydrocolloid dressing is more clinically effective at increasing the proportion of people with pressure ulcers completely healed (grade 1 and 2) when compared to phenytoin cream (moderate quality).
- One study (n=61) (people with a spinal cord injury) showed a hydrocolloid dressing is potentially more clinically effective at increasing the proportion of pressure ulcers completely healed (grade 1 and 2) when compared to phenytoin cream (low quality).
- One study (n=61) (people with a spinal cord injury) showed a hydrocolloid dressing is potentially more clinically effective at increasing the proportion of pressure ulcers completely healed (grade 2) when compared to phenytoin cream (low quality).
- One study (n=61) (people with a spinal cord injury) showed a hydrocolloid dressing is potentially more clinically effective at increasing the proportion of pressure ulcers improved (grade 1 and 2) when compared to phenytoin cream (low quality).
- One study (n=61) (people with a spinal cord injury) showed there may be no clinical difference between a hydrocolloid dressing and phenytoin cream at reducing the proportion of people with pressure ulcers worsened (grade 1 and 2), but the direction of the estimate of effect favoured phenytoin cream (very low quality).
- One study (n=56) (people with a spinal cord injury) showed there is no clinical difference between a hydrocolloid dressing and phenytoin cream for all-cause mortality (moderate quality).
- No evidence was found for the following outcomes:

- Time to complete healing
- Rate of reduction in size of ulcers
- Reduction in size and/or volume of ulcer.
- Pain (wound-related)
- Time in hospital or NHS care
- Patient acceptability
- Side effects
- Health-related quality of life

11.1.5.1.11 Hydrocolloid dressing versus alginate dressing

- One study (n=110) (older in-patients) showed an alginate dressing is potentially more clinically effective at increasing the proportion of people with pressure ulcers partially (40%) healed (grade 3 and 4) when compared to a hydrocolloid dressing (very low quality).
- One study (n=110) (older in-patients) showed an alginate dressing is more clinically effective for reducing the mean percentage pressure ulcer area (grade 3 and 4) when compared to a hydrocolloid dressing (low quality).
- One study (n=110) (older in-patients) showed an alginate dressing is more clinically effective for reducing the mean cm2 pressure ulcer area (grade 3 and 4) when compared to a hydrocolloid dressing (very low quality).
- One study (n=110) (older in-patients) showed there may be no clinical difference between an alginate dressing and a hydrocolloid dressing for proportion of people with an infection, but the direction of the estimate of effect favoured the hydrocolloid dressing (very low quality).
- One study (n=110) (older in-patients) showed there may be no clinical difference between an alginate dressing and a hydrocolloid dressing for proportion of people with skin irritation, but the direction of the estimate of effect favoured the hydrocolloid dressing (very low quality).
- One study (n=110) (older in-patients) showed there may be no clinical difference between alginate dressing and hydrocolloid for hypergranulation (very low quality).
- One study (n=110) (older in-patients) showed there may be no clinical difference between an alginate dressing and a hydrocolloid dressing for proportion of people with maceration, but the direction of the estimate of effect favoured the hydrocolloid dressing (very low quality).
- One study (n=110) (older in-patients) showed there may be no clinical difference between an alginate dressing and a hydrocolloid dressing for proportion of people with bleeding, but the direction of the estimate of effect favoured the hydrocolloid dressing (very low quality).
- One study (n=2201) (older in-patients) showed no clinical difference between a hydrocolloid dressing and alginate dressing for pain at dressing removal, but the estimate of effect favoured the hydrocolloid dressing(very low quality).
- One study (n=2201) (older in-patients) showed there is potentially no clinical difference between a hydrocolloid dressing and alginate dressing for lower proportion of people with strong odour, but the direction of estimate of effect favoured the hydrocolloid dressing(very low quality).
- One study (n=2201) (older in-patients) showed a hydrocolloid dressing is potentially more clinically effective for lower proportion of people with mild odour at dressing removal when compared to an alginate dressing (very low quality).
- One study (n=110) (older in-patients) showed there may no clinical difference between an alginate dressing and a hydrocolloid dressing for reducing all-cause mortality, but the direction of estimate of effect favoured the alginate dressing (very low quality).
- No evidence was found for the following outcomes:
  - Time to complete healing

- Rate of reduction in size of ulcers
- Proportion of completely healed within trial period
- Pain (wound-related)
- Time in hospital or NHS care
- Patient acceptability
- Health-related quality of life

11.1.5.1.12 Hydrocolloid dressing versus charcoal dressing

- One study (n=59) (in-patients) showed there may be no clinical difference between a hydrocolloid dressing and a charcoal dressing for proportion of people with pressures ulcers worsened (grade 2c and 4), but the direction of the estimate of effect favoured the charcoal dressing (very low quality).
- One study (n=60) (in-patients) reported median percentage reduction in pressure ulcer area for a hydrocolloid dressing and a charcoal dressing. The median for a hydrocolloid dressing was 18.5% (range 100% to -260.9%) and 26.9% (range 82% to -97.9%) for a charcoal dressing. No estimate of effect or precision could be derived (very low quality).
- One study (n=60) (in-patients) reported median reduction in pressure ulcer area (cm2) for a hydrocolloid dressing and a charcoal dressing. The median for a hydrocolloid dressing was 3.1cm2 (range 24cm^2 to -46.0cm^2) and 4.3cm^2 (range 31.2 cm2 to -13.8cm^2) for a charcoal dressing. No estimate of effect or precision could be derived (very low quality).
- One study (n=59) (in-patients) showed there may be no clinical difference between a charcoal dressing and a hydrocolloid dressing for lowering the proportion of people with maceration, but the direction of the estimate of effect favoured the charcoal dressing (very low quality).
- One study (n=59) (in-patients) showed there may be no clinical difference between a charcoal dressing and a hydrocolloid dressing for proportion of people with an infection, but the direction of the estimate of effect favoured the charcoal dressing (very low quality).
- One study (n=59) (in-patients) showed there may be no clinical difference between a charcoal dressing and a hydrocolloid dressing for proportion of people with hypergranulation, but the direction of the estimate of effect favoured the charcoal dressing (very low quality).
- One study (n=59) (in-patients) showed there may be no clinical difference between a charcoal dressing and a hydrocolloid dressing for proportion of people with skin irritation and eczema, but the direction of the estimate of effect could favour either intervention (very low quality).
- One study (n=59) (in-patients) showed there is no clinical difference between a charcoal dressing and a hydrocolloid dressing for proportion of people with bleeding (low quality).
- One study (n=59) (in-patients) showed there may be no clinical difference between a charcoal dressing and a hydrocolloid dressing for proportion of people with pruritus, but the direction of the estimate of effect favoured the charcoal dressing (very low quality).
- One study (n=59) (in-patients) showed there is no clinical difference between a charcoal dressing and a hydrocolloid dressing for proportion of people with wound pain (low quality).
- One study (n=59) (in-patients) showed there may be no clinical difference between a charcoal dressing and a hydrocolloid dressing for proportion of people with pain at dressing removal, but the direction of the estimate of effect favoured the charcoal dressing (very low quality).
- One study (n=60) (in-patients) showed there may be no clinical difference between a charcoal dressing and a hydrocolloid dressing for all-cause mortality, but the direction of the estimate of effect favoured the charcoal dressing (very low quality).
- No evidence was found for the following outcomes:
  - Time to complete healing
  - Rate of reduction in size of ulcers

- Proportion of completely healed within trial period
- Time in hospital or NHS care
- Patient acceptability
- Health-related quality of life

11.1.5.1.13 Hydrocolloid dressing versus phenytoin ointment

- One study (n=28) (people in a nursing home) showed phenytoin ointment is potentially more clinically effective at reducing the mean time to healing of pressure ulcers (grade 2) when compared to a hydrocolloid dressing (very low quality).
- One study (n=28) (people in a nursing home) showed there is no clinical difference between a hydrocolloid dressing and phenytoin ointment for proportion of people with adverse events (low quality).
- One study (n=34) (people in a nursing home) showed there may be no clinical difference between a hydrocolloid dressing and phenytoin ointment for all-cause mortality, but the direction of the estimate of effect favoured phenytoin ointment (very low quality).
- No evidence was found for the following outcomes:
  - Rate of reduction in size of ulcers
  - Reduction in size and/or volume of ulcer.
  - Proportion of completely healed within trial period
  - Pain (wound-related)
  - Time in hospital or NHS care
  - Patient acceptability
  - Health-related quality of life

11.1.5.1.14 Hydrocolloid dressing versus antibiotic ointment

- One study (n=24) (people in a nursing home) showed there may be no clinical difference between a hydrocolloid dressing and antibiotic ointment for mean time to healing of pressure ulcers, but the direction of the estimate of effect favoured hydrocolloid dressing (very low quality).
- One study (n=24) (people in a nursing home) showed there is no clinical difference between a hydrocolloid dressing and antibiotic ointment for proportion of people with adverse events (low quality).
- No evidence was found for the following outcomes:
  - Rate of reduction in size of ulcers
  - Reduction in size and/or volume of ulcer.
  - Proportion of completely healed within trial period
  - Pain (wound-related)
  - Time in hospital or NHS care
  - Patient acceptability
  - Health-related quality of life
  - All-cause mortality

11.1.5.1.15 Hydrocolloid dressing: triangular shape versus oval shape

- One study (n=96) (in-patients) showed a triangular shaped hydrocolloid dressing is potentially more clinically effective at increasing the proportion of people with pressure ulcers completely healed (grade 2 and 3) when compared to an oval shaped hydrocolloid dressing (very low quality).

- One study (n=96) (in-patients) showed a triangular shaped hydrocolloid dressing is potentially more clinically effective at increasing the proportion of people with pressure ulcers improved (grade 2 and 3) when compared to an oval shaped hydrocolloid dressing (very low quality).
- One study (n=96) (in-patients) showed there may be no clinical difference between a triangular shaped hydrocolloid dressing and an oval shaped hydrocolloid dressing for the proportion of people with pressure ulcers unchanged (grade 2 and 3), but the direction of the estimate of effect could favour either intervention (very low quality).
- One study (n=96) (in-patients) showed a triangular shaped hydrocolloid dressing is more clinically effective at reducing the proportion of people with pressure ulcers worsened (grade 2 and 3) when compared to an oval shaped hydrocolloid dressing (low quality).
- One study (n=96) (in-patients) showed a triangular shaped hydrocolloid dressing is more clinically effective for mean percentage reduction in pressure ulcer length when compared to an oval shaped hydrocolloid dressing (low quality).
- One study (n=96) (in-patients) showed there may be no clinical difference between a triangular shaped hydrocolloid dressing and an oval shaped hydrocolloid dressing for mean percentage reduction in pressure ulcer width. No estimate of precision could be derived (very low quality).
- One study (n=96) (in-patients) reported mean pain at dressing change for a triangular shaped hydrocolloid dressing a triangular shaped hydrocolloid dressing (2.1 SD 2.1) and an oval shaped hydrocolloid dressing (4.3 SD 1.75). The clinical importance is unknown (low quality).
- One study (n=96) (in-patients) showed a triangular shaped hydrocolloid dressing is potentially more clinically effective for a lower proportion of people with ulcer pain when compared to an oval shaped hydrocolloid dressing (very low quality).
- One study (n=96) (in-patients) showed there is potentially no clinical difference between a triangular shaped hydrocolloid dressing and an oval shaped hydrocolloid dressing for lowering the proportion of people with adverse events (very low quality).
- No evidence was found for the following outcomes:
  - Time to complete healing
  - Rate of reduction in size of ulcers
  - Time in hospital or NHS care
  - Patient acceptability
  - Mortality (all cause)
  - Health-related quality of life

11.1.5.1.16 Hydrocolloid dressing: Comfeel versus ComfeelPlus

- One study (n=61) (general population with necrotic pressure ulcers) showed there may be no clinical difference between a Comfeel hydrocolloid dressing and a Comfeel Plus hydrocolloid dressing for percentage reduction in pressure ulcer area, but the direction of the estimate of effect could favour either intervention (very low quality).
- One study (n=61) (general population with necrotic pressure ulcers) showed there may be no clinical difference between a Comfeel hydrocolloid dressing and a Comfeel Plus hydrocolloid dressing for proportion of people with dressing intolerance, but the direction of the estimate of effect could favour either intervention (very low quality).
- One study (n=333) (general population with necrotic pressure ulcers) showed there is no clinical difference between a Comfeel Plus hydrocolloid dressing and a Comfeel hydrocolloid dressing for proportion of people reporting the dressing as good to excellent for comfort at dressing change, the direction of the estimate of effect favoured the Comfeel®Plus hydrocolloid dressing (low quality).

- One study (n=61) (general population with necrotic pressure ulcers) showed there is no clinical difference between a ComfeelPlus hydrocolloid dressing and a Comfeel hydrocolloid dressing for all-cause mortality (low quality).
- No evidence was found for the following outcomes:
  - Time to complete healing
  - Rate of reduction in size of ulcers
  - Proportion of completely healed within trial period
  - Pain (wound-related)
  - Time in hospital or NHS care
  - Side effects
  - Health-related quality of life

11.1.5.1.17 Hydrocolloid dressing: SignaDress versus Comfeel®Plus

- One study (n=35) (people in a nursing home) showed a SignaDress hydrocolloid dressing is potentially more clinically effective at increasing the proportion of people with pressure ulcers completely healed (grade 2 to 4) when compared to a Comfeel Plus hydrocolloid dressing (low quality).
- One study (n=35) (people in a nursing home) showed there may be a clinical benefit for a SignaDress hydrocolloid dressing compared to a Comfeel Plus hydrocolloid dressing for percentage reduction in pressure ulcer area (grade 2 to 4). No estimate of precision could be derived (very low quality).
- One study (n=35) (people in a nursing home) showed there may be a clinical benefit for a SignaDress hydrocolloid dressing compared to a Comfeel Plus hydrocolloid dressing for increasing the healing rate of pressure ulcers (grade 2 to 4). No estimate of precision could be derived (very low quality).
- One study (n=35) (people in a nursing home) showed there is no clinical difference between a SignaDress hydrocolloid dressing and a Comfeel Plus hydrocolloid dressing for proportion of people with adverse events (low quality).
- No evidence was found for the following outcomes:
  - Time to complete healing
  - Pain (wound-related)
  - Time in hospital or NHS care
  - Patient acceptability
  - Mortality (all cause)
  - Health-related quality of life

11.1.5.1.18 Gauze dressing versus foam dressing

- Two studies (n=74) (general population) showed a foam dressing is potentially more clinically effective at reducing the proportion of people with pressure ulcers completely healed (grade 2and 3) when compared to a gauze dressing (very low quality).
- One study (n=36) (general population) showed there may be no clinical difference between a foam dressing and a gauze dressing for median time to 50% healing of pressure ulcers. No estimate of precision could be derived (very low quality).
- Two studies (n=74) (general population) showed there may be a clinical benefit for a foam dressing compared to a gauze dressing for reducing all-cause mortality (very low quality).

- No evidence was found for the following outcomes:
  - Time to complete healing
  - Rate of reduction in size of ulcers
  - Reduction in size and/or volume of ulcer.
  - Pain (wound-related)
  - Time in hospital or NHS care
  - Patient acceptability
  - Side effects
  - Health-related quality of life

11.1.5.1.19 Gauze dressing versus polyurethane dressing

- Two studies (n=53) (general population) showed a polyurethane dressing is more clinically effective at increasing the proportion of pressure ulcers completely healed (all grades) when compared to a gauze dressing (low quality).
- One study (n=34) (people in the community) showed a polyurethane dressing is more clinically effective at increasing the proportion of pressure ulcers completely healed (grade 2) when compared to a gauze dressing (low quality).
- Two studies (n=53) (general population) showed a polyurethane dressing is more clinically effective at reducing the proportion of pressure ulcers worsened (all grades) when compared to a gauze dressing (low quality).
- One study (n=34) (people in the community) showed a polyurethane dressing is more clinically effective at increasing the proportion of pressure ulcers decreased in ulcer stage when compared to a gauze dressing (low quality).
- One study (n=34) (people in the community) showed a polyurethane dressing is potentially more clinically effective at reducing the proportion of ulcers increased in ulcer stage when compared to a gauze dressing (very low quality).
- One study (n=19) (in-patients) showed there may be a clinical benefit for a polyurethane dressing compared to a gauze dressing for mean percentage reduction in pressure ulcer area (grade 1 and 2). No estimate of precision could be derived (very low quality).
- One study (n=44) (people in the community) showed there may be a clinical benefit for a polyurethane dressing compared to a gauze dressing for median percentage reduction in pressure ulcer area (grade 2). No estimate of precision could be derived (very low quality).
- One study (n=30) (people in the community) showed there may be a clinical benefit for a polyurethane dressing compared to a gauze dressing for median percentage reduction in pressure ulcer area (grade 3). No estimate of precision could be derived (very low quality).
- One study (n=34) (people in the community) showed there is potentially no clinical difference between a polyurethane dressing and a gauze dressing for proportion of people with maceration, the direction of the estimate of effect favoured the polyurethane dressing (very low quality).
- No evidence was found for the following outcomes:
  - Time to complete healing
  - Rate of reduction in size of ulcers
  - Pain (wound-related)
  - Time in hospital or NHS care
  - Patient acceptability
  - Mortality (all cause)
  - Health-related quality of life

11.1.5.1.20 Gauze dressing versus hydrogel

- One study (n=30) (general population) showed there is potentially no clinical difference between a gauze dressing and hydrogel for increasing the proportion of people with pressure ulcers completely healed (grade 2 to 4), the direction of the estimate of effect favoured the gauze dressing (very low quality).
- One study (n=41) (general population) showed there may be no clinical difference between a gauze dressing and hydrogel for reducing the proportion of people with pressure ulcers worsened (grade 2 to 4), but the direction of the estimate of effect favoured hydrogel dressing (very low quality).
- One study (n=40) (in- and out-patients) showed there is potentially no clinical difference between a gauze dressing and hydrogel for mean percentage reduction in pressure ulcer area (grade 2 and 3), the direction of the estimate of effect favoured the hydrogel (very low quality).
- One study (n=30) (general population) showed there may be no clinical difference between a gauze dressing and hydrogel for increasing the percentage rate of pressure ulcer healing, but the direction of the estimate of effect favoured hydrogel dressing (very low quality).
- One study (n=27) (people with a spinal cord injury) showed there may be no clinical difference between a gauze dressing and hydrogel for mean healing rate of pressure ulcers (grade 2 to 4), but the direction of the estimate of effect favoured gauze dressing (very low quality).
- One study (n=30) (general population) showed there may be no clinical difference between a gauze dressing and hydrogel for increasing the mean time to healing of pressure ulcers (grade 2 to 4), but the direction of the estimate of effect favoured either intervention (very low quality).
- One study (n=30) (general population) showed there may be a clinical benefit for a gauze dressing compared to hydrogel for reducing all-cause mortality (very low quality).
- No evidence was found for the following outcomes:
  - Pain (wound-related)
  - Time in hospital or NHS care
  - Patient acceptability
  - Side effects
  - Health-related quality of life

11.1.5.1.21 Gauze dressing versus dextranomer

- One study (n=30) (people with a spinal cord injury) showed dextranomer is more clinically effective at increasing the proportion of pressure ulcers improved (grade 2 to 4) when compared to a gauze dressing (low quality).
- One study (n=30) (people with a spinal cord injury) showed there is no clinical difference between a gauze dressing and dextranomer for proportion of people with adverse events (low quality).
- No evidence was found for the following outcomes:
  - Time to complete healing
  - Rate of reduction in size of ulcers
  - Proportion of completely healed within trial period
  - Pain (wound-related)
  - Time in hospital or NHS care
  - Patient acceptability
  - Mortality (all cause)

- Health-related quality of life

11.1.5.1.22 Gauze dressing versus phenytoin cream

- One study (n=55) (people with a spinal cord injury) showed there may be a clinical benefit for phenytoin cream compared to a gauze dressing for increasing the proportion of people with pressure ulcers completely healed (grade 1 and 2)(very low quality).
- One study (n=60) (people with a spinal cord injury) showed there may be a clinical benefit for phenytoin cream compared to a gauze dressing for increasing the proportion of pressure ulcers completely healed (grade 1 and 2) (very low quality).
- One study (n=60) (people with a spinal cord injury) showed phenytoin cream is potentially more clinically effective for increasing the proportion of pressure ulcers completely healed when compared to a gauze dressing (grade 2) (low quality).
- One study (n=60) (people with a spinal cord injury) showed there may be a clinical benefit for phenytoin cream compared to a gauze dressing for increasing the proportion of pressure ulcers improved (grade 1 and 2) (very low quality).
- One study (n=60) (people with a spinal cord injury) showed there is potentially a clinical benefit for phenytoin cream compared to a gauze dressing for reducing the proportion of pressure ulcers worsened (grade 1 and 2) (low quality).
- One study (n=55) (people with a spinal cord injury) showed there is no clinical difference between phenytoin cream and a gauze dressing for all-cause mortality (moderate quality).
- No evidence was found for the following outcomes:
  - Time to complete healing
  - Rate of reduction in size of ulcers
  - Pain (wound-related)
  - Time in hospital or NHS care
  - Patient acceptability
  - Side effects
  - Health-related quality of life

11.1.5.1.23 Foam dressing versus skin replacement

- One study (n=34) (general population) showed there may be no clinical difference between a foam dressing and skin replacement for increasing the proportion of people with pressure ulcers completely healed (grade 3), but the direction of the estimate of effect favoured the foam dressing (very low quality).
- One study (n=34) (general population) reported medians for percentage reduction in pressure ulcer area (closed ulcers). The median for a foam dressing was 33.5% (range -77.5 to 100%) and 49.5% (range -81.7 to 100%) for the skin replacement. No estimate of effect or precision could be derived (very low quality).
- One study (n=34) (general population) reported medians for percentage reduction in pressure ulcer area (unclosed ulcers). The median for a foam dressing was 17.4.5% (range -434.5 to 100%) and 38.8% (range -201.7 to 100%) for the skin replacement. No estimate of effect or precision could be derived (very low quality).
- One study (n=34) (general population) showed there may be a clinical benefit for skin replacement compared to a foam dressing for mean percentage reduction in pressure ulcer volume. No estimate of precision could be derived (very low quality).

- One study (n=34) (general population) reported medians for percentage reduction in pressure ulcer volume. The median for a foam dressing was 17.4% and 41.2% for the skin replacement. No estimate of effect or precision could be derived (very low quality).
- One study (n=34) (general population) showed there may be no clinical difference between skin replacement and a foam dressing for proportion of people with infection, but the direction of the estimate of effect favoured skin replacement (very low quality).
- One study (n=34) (general population) showed there is no clinical difference between a foam dressing and skin replacement for proportion of people with adverse events (low quality).
- No evidence was found for the following outcomes:
  - Time to complete healing
  - Rate of reduction in size of ulcers
  - Pain (wound-related)
  - Time in hospital or NHS care
  - Patient acceptability
  - Mortality (all cause)
  - Health-related quality of life

11.1.5.1.24 Foam dressing versus antibiotic ointment

- One study (n=44) (people in long term care) showed a foam dressing is potentially more clinically effective at increasing the proportion of people with pressure ulcers completely healed when compared to antibiotic ointment (very low quality).
- One study (n=42) (people in long-term care) reported means for PUSH score at end of treatment for a foam dressing and antibiotic ointment. The mean for a foam dressing was 3.24 and 1.61 for antibiotic ointment. No estimate of effect or precision could be derived (very low quality).
- No evidence was found for the following outcomes:
  - Time to complete healing
  - Rate of reduction in size of ulcers
  - Pain (wound-related)
  - Time in hospital or NHS care
  - Patient acceptability
  - Side effects
  - Mortality (all cause)
  - Health-related quality of life

11.1.5.1.25 Foam dressing: Allevyn versus Biatain®

- One study (n=32) (general population) showed Allevyn is more clinically effective at increasing the proportion of people with pressure ulcers completely healed (grade 2 and 3) when compared to Biatain® (low quality).
- One study (n=32) (general population) reported median percentage reduction in pressure ulcer area for Allevyn and Biatain. The median for Allevyn was 38.2% range -97.6 to 99.4%) and 45.8% (range -56.9-90.0%) for Biatain. No estimate of effect or precision could be derived (very low quality).
- One study (n=32) (general population) showed there may be no clinical difference between Allevyn and Biatain for mean pain score at dressing removal, but the direction of the estimate of effect favoured Allevyn (very low quality).

- One study (n=32) (general population) showed there is potentially no clinical difference between Allevyn and Biatain for mean comfort score at dressing removal, the direction of the estimate of effect favoured Biatain (very low quality).
- One study (n=32) (general population) showed there may be a clinical benefit for Allevyn compared to Biatain for reducing the proportion of people with dressing related adverse events (very low quality).
- One study (n=32) (general population) showed there may be no clinical difference between Allevyn and Biatain for all-cause mortality, but the direction of the estimate of effect favoured Allevyn (very low quality).
- No evidence was found for the following outcomes:
  - Time to complete healing
  - Rate of reduction in size of ulcers
  - Time in hospital or NHS care
  - Patient acceptability
  - Health-related quality of life

11.1.5.1.26 Foam dressing: Mepilex versus Tielle

- One study (n=38) (elderly adults) showed there may be no clinical difference between Mepilex and Tielle® for increasing the proportion of people with pressure ulcers completely healed (grade 2), but the direction of the estimate of effect favoured Tielle (very low quality).
- One study (n=38) (elderly adults) showed Tielle is potentially more clinically effective at increasing the proportion of people with pressure ulcers improved (grade 2) when compared to Mepilex (low quality).
- One study (n=38) (elderly adults) showed there may be no clinical difference between Tielle and Mepilex for reducing the proportion of people with pressure ulcers worsened (grade 2), the direction of the estimate of effect favoured Tielle (very low quality).
- One study (n=38) (elderly adults) showed there may be a clinical benefit for Mepilex compared to Tielle for a lower proportion of people with maceration (very low quality).
- One study (n=38) (elderly adults) showed there may be a clinical benefit for Mepilex compared to Tielle for a lower proportion of people reporting odour (very low quality).
- One study (n=38) (elderly adults) showed there may be a clinical benefit for Mepilex compared to Tielle for a lower proportion of people with adverse events (very low quALITY).
- One study (n=38) (elderly adults) showed there may be no clinical difference between Mepilex and Tielle for all-cause mortality, but the direction of the estimate of effect could favour either Tielle (very low quality).
- No evidence was found for the following outcomes:
  - Time to complete healing of pressure ulcers
  - Rate of healing of pressure ulcers
  - Rate of reduction in size or volume of pressure ulcers
  - Time in hospital or NHS care
  - Patient acceptability
  - Health-related quality of life

11.1.5.1.27 Hydrogel (aquagel) versus polyurethane foam (lyofoam) dressing

- One study (n=38) (people in palliative care) showed a polyurethane foam dressing is potentially more clinically effective for increasing the proportion of pressure ulcers completely healed (grade 2 and 3) when compared to a hydrogel dressing (very low quality).
- One study (n=38) (people in palliative care) showed no clinical difference between a polyurethane foam dressing and a hydrogel dressing for the proportion of pressure ulcers improved (grade 2 and 3) (low quality).
- One study (n=12) (people in palliative care) showed there may be no clinical difference between a polyurethane foam dressing and hydrogel for mean healing rate for healed pressure ulcers (grade 2), but the direction of the estimate of effect favoured the foam dressing (very low quality).
- One study (n=26) (people in palliative care) showed there is potentially no clinical difference between a polyurethane foam dressing and hydrogel for mean healing rate for healed pressure ulcers (grade 3), the direction of the estimate of effect favoured the polyurethane foam dressing (very low quality).
- One study (n=26) (people in palliative care) showed there is potentially no clinical difference between a polyurethane foam dressing and hydrogel for mean healing rate for improved pressure ulcers (grade3), the direction of the estimate of effect favoured the polyurethane foam dressing (very low quality).
- One study (n=34) (people in palliative care) showed there may be no clinical difference between a polyurethane foam dressing and hydrogel for all-cause mortality, but the direction of the estimate of effect favoured the foam dressing (very low quality).
- No evidence was found for the following outcomes:
  - Time to complete healing
  - Pain (wound-related)
  - Time in hospital or NHS care
  - Patient acceptability
  - Side effects
  - Health-related quality of life

11.1.5.1.28 Hydrogel dressing versus dextranomer dressing

- One study (n=135) (general population) reported medians for percentage reduction in pressure ulcer area for a hydrogel dressing and a dextranomer dressing. The median for hydrogel dressing was 35% and 7% for dextranomer dressing. No estimate of effect or precision could be derived (very low quality).
- One study (n=135) (general population) showed there may be no clinical difference between hydrogel dressing and dextranomer dressing for proportion of people with pain at dressing application, but the direction of the estimate of effect favoured the hydrogel dressing (very low quality).
- One study (n=34) (people in palliative care) showed there may be no clinical difference between polyurethane foam dressing and hydrogel dressing for all-cause mortality, but the direction of the estimate of effect could favour either intervention (very low quality).
- No evidence was found for the following outcomes:
  - Time to complete healing
  - Rate of reduction in size or volume of pressure ulcers
  - Proportion of completely healed within trial period
  - Time in hospital or NHS care
  - Patient acceptability

- Side effects

Hydrogel, foam dressing or transparent film versus different types of dressings

- One study (n=41) (people in the community) showed there is potentially a clinical benefit of hydrogel, foam dressing or transparent film for proportion of people with pressure ulcers completely healed (grade 2 to 4) when compared to different types of dressing (very low quality).
- One study (n=58) (people in the community) reported that there was no significant difference in the percentage of pressure ulcers healed per week (grade 2 to 4)when hydrogel, foam dressing or transparent film was compared with different types of dressing. No estimate of effect or precision could be derived (very low quality).
- One study (n=21) (people in the community) showed there is potentially a clinical benefit of hydrogel, foam dressing or transparent film for proportion of people reporting the application of the dressing as comfortablewhen compared to different types of dressings (very low quality).
- One study (n=21) (people in the community) showed there may difference clinical benefit of hydrogel, foam or transparent film for proportion of people reporting discomfort at dressing removal when compared to different types of dressings (very low quality).
- One study (n=58) (people in the community) showed there is no clinical difference between hydrogel, foam or transparent film and different types of dressing for proportion of people with adverse events (low quality).
- One study (n=58) (people in the community) showed there may be a clinical benefit for hydrogel, foam or transparent film compared to different types of dressing for reducing all-cause mortality (very low quality).
- No evidence was found for the following outcomes:
  - Time to complete healing
  - Rate of reduction in size of ulcers
  - Pain (wound-related)
  - Time in hospital or NHS care
  - Patient acceptability
  - Health-related quality of life

11.1.5.1.29 Hydrogel: Sterigel versus Intrasite

- One study (n=47) (general population with necrotic pressure ulcers) showed Intrasite is potentially more clinically effective for mean percentage reduction in pressure ulcer area when compared to Sterigel. No estimate of precision could be derived (very low quality).
- One study (n=47) (general population with necrotic pressure ulcers) showed Sterigel is potentially more clinically effective at for reducing the proportion of people with intermittent pressure ulcer pain at the end of the study when compared to Intrasite (very low quality).
- One study (n=47) (general population with necrotic pressure ulcers) showed there may be no clinical difference between Sterigel and Intrasite for reducing the proportion of people with continuous pressure ulcer pain at the end of the study, but the direction of the estimate of effect could favour Sterigel (very low quality).
- One study (n=42) (general population with necrotic pressure ulcers) showed there may no clinical difference between Sterigel and Intrasite® for a lower proportion of people with slight pain at dressing removal, the direction of the estikmate of effect favoured Sterigel® (very low quality).
- One study (n=42) (general population with necrotic pressure ulcers) showed there may be no clinical difference between Sterigel and Intrasite for a lower proportion of people with severe pain at dressing removal, but the direction of the estimate of effect could favour Sterigel (very low quality).

- One study (n=42) (general population with necrotic pressure ulcers) showed there may be no clinical difference between Sterigel and Intrasite for a lower proportion of people with discomfort, but the direction of the estimate of effect could favour Sterigel (very low quality).
- One study (n=42) (general population with necrotic pressure ulcers) showed there may be a clinical benefit of Sterigel for a lower proportion of people with maceration when compared to Intrasite® (very low quality).
- One study (n=50) (general population with necrotic pressure ulcers) showed there may be no clinical difference between Sterigel and Intrasite for reducing all-cause mortality, the direction of the estimate of effect favoured Sterigel® (very low quality).
- No evidence was found for the following outcomes:
  - Time to complete healing
  - Rate of reduction in size or volume of pressure ulcers
  - Proportion of pressure ulcers completely healed
  - Pain (wound-related)
  - Time in hospital or NHS care
  - Patient acceptability
  - Health-related quality of life

11.1.5.1.30 Protease modulating matrix versus impregnated gauze dressing

- One study (n=80) (in-patients) showed a protease modulating matrix is potentially more clinically effective at increasing the proportion of people completely healed (grade 2 to 4) when compared to an impregnated gauze dressing (very low quality).
  One study (n=80) (in-patients) reported time to complete healing of pressure ulcers (grade 2 to 4) for a protease modulating matrix and an impregnated gauze dressing. The time to complete healing for the protease modulating matrix was 6-15 days and 14-52 days for the an impregnated gauze dressing. No estimate of effect or precision could be derived (very low quality).
- One study (n=80) (in-patients) showed there is no clinical difference between a protease modulating matrix and an impregnated gauze dressing for proportion of people with adverse events (low quality).
- One study (n=80) (in-patients) showed there is no clinical difference between a protease modulating matrix and an impregnated gauze dressing for all-cause mortality (low quality).
- No evidence was found for the following outcomes:
  - Rate of reduction in size of ulcers
  - Reduction in size and/or volume of ulcer.
  - Pain (wound-related)
  - Time in hospital or NHS care
  - Patient acceptability
  - Health-related quality of life

11.1.5.1.31 Polyurethane dressing versus different types of dressing

- One study (n=64) (in-patients) showed there is potentially no clinical difference between a polyurethane dressing and different types of dressings for mean time to healing of pressure ulcers (grade 2 and 3), the direction of the estimate of effect favoured different types of dressings (very low quality).
- One study (n=64) (in-patients) showed there is no clinical difference between a polyurethane dressing and different types of dressing for reduction in PUSH tool, the direction of the estimate of effect favoured the polyurethane dressing (low quality).

- One study (n=64) (in-patients) showed there may be no clinical difference between a polyurethane dressing and different types of dressings for proportion of people with systematic worsening, but the direction of the estimate of effect favoured the different types of dressing (very low quality).
- One study (n=64) (in-patients) showed there may be no clinical difference between a polyurethane dressing and different types of dressing for reducing the proportion of people with localised adverse events, the direction of the estimate of effect favoured the polyurethane dressing (very low quality).
- One study (n=64) (in-patients) showed there may be no clinical difference between a polyurethane dressing and different types of dressings for all-cause mortality, but the direction of the estimate of effect favouredthe polyurethane dressing(very low quality).
- No evidence was found for the following outcomes:
  - Rate of reduction in size of ulcers
  - Proportion of completely healed within trial period
  - Pain (wound-related)
  - Time in hospital or NHS care
  - Patient acceptability
  - Health-related quality of life

11.1.5.1.32 Alginate dressing versus silver alginate dressing

- One study (n=28) (elderly people) showed there may be a clinical benefit for a silver alginate dressing compared to an alginate dressing for reducing the proportion of people with pressure ulcers worsened (grade 3 and 4) (very low quality).
- One study (n=28) (elderly people) showed there may be a clinical benefit for a silver alginate dressing compared to an alginate dressing for mean percentage reduction in pressure ulcer area (grade 3 and 4) (very low quality).
- One study (n=28) (elderly people) showed a silver alginate dressing is potentially more clinically effective for absolute decrease in pressure ulcer area (grade 3 and 4) when compared to an alginate dressing (very low quality).
- One study (n=28) (elderly people) showed there is potentially no clinical difference between a silver alginate dressing and an alginate dressing for mean rate of healing of pressure ulcers, the direction of the estimate of effect favoured the silver alginate dressing (very low quality).
- One study (n=28) (elderly people) showed there may be no clinical difference between a silver alginate dressing and an alginate dressing for proportion of people with infection, but the direction of the estimate of effect favoured the silver alginate dressing (very low quality).
- One study (n=24) (elderly people) showed there may be no clinical difference between a silver alginate dressing and an alginate dressing for percentage reduction in infection score, but the direction of the estimate of effect could favour either intervention. No estimate of precision could be derived (very low quality).
- One study (n=28) (elderly people) reported mean mASEPSIS index at the end of treatment for a silver alginate dressing and an alginate dressing. The index for a silver alginate dressing was 115.3 and 81.8 for an alginate dressing. The clinical importance is unknown (very low quality).
- One study (n=28) (elderly people) showed there may be no clinical difference between a silver alginate dressing and (grade 3 and 4) an alginate dressing for proportion of people with poor acceptability and/or tolerability, but the direction of the estimate of effect favoured the silver alginate dressing (very low quality).
- One study (n=99) (elderly people) showed there is no clinical difference between a silver alginate dressing and an alginate dressing for all-cause mortality (low quality).

- No evidence was found for the following outcomes:
  - Proportion of completely healed within trial period
  - Time to complete healing
  - Pain (wound-related)
  - Time in hospital or NHS care
  - Health-related quality of life

11.1.5.1.33 Alginate dressing versus dextranomer

- One study (n=92) (general population) showed an alginate dressing is potentially more clinically effective for increasing the proportion of people with more than 75% reducing in pressure ulcer area (grade 3 and 4) when compared to dextranomer (very low quality).
- One study (n=92) (general population) showed an alginate dressing is potentially more clinically effective for increasing the proportion of people with more than 40% reducing in pressure ulcer area (grade 3 and 4) when compared to dextranomer (very low quality).
- One study (n=92) (general population) showed an alginate dressing is more clinically effective at reducing the proportion of people with pressure ulcers worsened or stagnated (grade 3 and 4) when compared to dextranomer (low quality).
- One study (n=92) (general population) showed an alginate dressing is potentially more clinically effective for increasing the mean rate of healing of pressure ulcers in people improved more than 40% (grade 3 and 4) when compared to dextranomer (very low quality).
- One study (n=92) (general population) showed an alginate dressing is potentially more clinically effective for increasing the mean rate of healing of pressure ulcers (grade 3 and 4) when compared to dextranomer (very low quality).
- One study (n=92) (general population) showed there may be no clinical difference between an alginate dressing and dextranomer for the proportion of people with infection, but the direction of the estimate of effect favoured the alginate dressing (very low quality).
- One study (n=92) (general population) showed there may be no clinical difference between an alginate dressing and dextranomer for the proportion of people with hypergranulation, but the direction of the estimate of effect favoured the dextranomer dressing (very low quality).
- One study (n=92) (general population) showed there may be no clinical difference between an alginate dressing and dextranomer for the proportion of people with skin irritation, but the direction of the estimate of effect favoured the alginate dressing (very low quality).
- One study (n=92) (general population) showed there is potentially no clinical difference between an alginate dressing and dextranomer for the proportion of people with bleeding, the direction of the estimate of effect favoured the alginate dressing (very low quality).
- One study (n=92) (general population) showed an alginate dressing is more clinically effective for a lower proportion of people with pain when compared to dextranomer (low quality).
- One study (n=92) (general population) showed there may be no clinical difference between an alginate dressing and dextranomer for the proportion of people with pruritus, but the direction of the estimate of effect favoured the alginate dressing (very low quality).
- One study (n=92) (general population) showed there may be no clinical difference between an alginate dressing and dextranomer for all-cause mortality, but the direction of the estimate of effect could favoured the alginate dressing (very low quality).
- No evidence was found for the following outcomes:
  - Time to complete healing
  - Proportion of completely healed within trial period

- Time in hospital or NHS care
- Patient acceptability
- Health-related quality of life

11.1.5.1.34 Silver dressing versus different types of dressings

- One study (n=48) (general population) showed there may be a clinical benefit for a silver dressing compared to different types of dressings for mean percentage reduction in pressure ulcer area. No estimate of precision could be derived (very low quality).

11.1.5.1.35 Silver dressing versus silver cream

- One study (n=40) (in- and out-patients) showed there may be a clinical benefit for a silver dressing compared to a silver cream for mean percentage reduction in pressure ulcer area (very low quality).
- One study (n=40) (in- and out-patients) showed there may be a clinical benefit for a silver cream compared to a silver dressing for percentage reduction in PUSH score. No estimate of precision could be derived (very low quality).
- One study (n=40) (in- and out-patients) showed there is no clinical difference of a silver dressing and a silver cream for proportion of people with adverse events (low quality).
- One study (n=40) (in- and out-patients) showed there is no clinical difference between a silver dressing and a silver cream for all-cause mortality (low quality).
- No evidence was found for the following outcomes:
  - Time to complete healing
  - Rate of reduction in size of ulcers
  - Proportion of completely healed within trial period
  - Pain (wound-related)
  - Time in hospital or NHS care
  - Patient acceptability
  - Health-related quality of life

11.1.5.1.36 Sugar versus dextranomer

- One study (n=12) (people in long term care) showed dextranomer is potentially more clinically effective for increasing the proportion of people with pressure ulcers completely healed (grade unknown) when compared to sugar (very low quality).
- One study (n=12) (people in long term care) showed no clinical difference between dextranomer and sugar for increasing the proportion of people with pressure ulcers improved, the direction of the estimate of effect favoured sugar(low quality).
- One study (n=23) (people in long term care) showed dextranomer is potentially more clinically effective for increasing the proportion of pressure ulcers completely healed (grade unknown) when compared to sugar (very low quality).
- One study (n=23) (people in long term care) showed dextranomer is more clinically effective for increasing the proportion of pressure ulcers improved when compared to sugar (low quality).
- No evidence was found for the following outcomes:
  - Time to complete healing
  - Rate of reduction in size of ulcers

- Pain (wound-related)
- Time in hospital or NHS care
- Patient acceptability
- Side effects
- Mortality (all cause)
- Health-related quality of life

11.1.5.1.37 Sugar versus different types of topical agents

- One study (n=38) (geriatric adults) showed sugar is more clinically effective at increasing the proportion of people with pressure ulcers completely healed (grade not reported) when compared to different types of topical agents (low quality).
- One study (n=38) (geriatric adults) showed sugar is potentially more clinically effective at improving mean healing index when compared to different types of topical agents (very low quality).
- No evidence was found for the following outcomes:
  - Time to complete healing
  - Rate of reduction in size of ulcers
  - Reduction in size and/or volume of ulcer.
  - Pain (wound-related)
  - Time in hospital or NHS care
  - Patient acceptability
  - Side effects
  - Mortality (all cause)
  - Health-related quality of life

11.1.5.1.38 Honey versus ethoxydiaminoacridine and nitrofurazone

- One study (n=50) (in-patients) showed honey is more clinically effective at increasing the proportion of pressure ulcers completely healed (grade 2 and 3) when compared to ethoxydiaminoacridine and nitrofurazone (low quality).
- One study (n=26) (in-patients) showed honey is potentially more clinically effective for mean percentage reduction in pressure ulcer area (grade 2 and 3) when compared to ethoxydiaminoacridine and nitrofurazone (very low quality).
- One study (n=26) (in-patients) showed honey is more clinically effective for mean percentage decrease in PUSH score when compared to ethoxydiaminoacridine and nitrofurazone ((grade 2 and 3) (grade 2 and 3) (grade 2 and 3) (low quality).
- One study (n=26) (in-patients) showed there is no clinical difference between honey and ethoxydiaminoacridine and nitrofurazone for proportion of people with adverse events (low quality).
- One study (n=27) (in-patients) showed there may be no clinical difference between honey and ethoxydiaminoacridine and nitrofurazone for all-cause mortality, but the direction of the estimate of effect favoured honey (very low quality).
- No evidence was found for the following outcomes:
  - Time to complete healing
  - Rate of reduction in size of ulcers
  - Pain (wound-related)
  - Time in hospital or NHS care

- Patient acceptability
- Health-related quality of life

11.1.5.1.39 Platelet gel versus other treatment

- One study (n=16) (people with a spinal cord injury) showed there is no clinical difference between platelet gel and other treatment for proportion of pressure ulcers completely healed (grade 3 and 4) (low quality).
- One study (n=16) (people with a spinal cord injury) showed there is potentially no clinical difference between platelet gel and other treatment for proportion of pressure ulcers improved (grade 3 and 4), the direction of the estimate of effect favoured platelet gel (very low quality).
- One study (n=16) (people with a spinal cord injury) showed platelet gel is potentially more clinically effective at mean percentage reduction in pressure ulcer volume (grade 3 and 4) when compared to other treatment (very low quality).
- No evidence was found for the following outcomes:
  - Time to complete healing
  - Rate of reduction in size of ulcers
  - Pain (wound-related)
  - Time in hospital or NHS care
  - Patient acceptability
  - Side effects
  - Mortality (all cause)
  - Health-related quality of life

11.1.5.1.40 Hyaluronic acid versus sodium hyaluronic

- One study (n=20) (in-patients) showed there may be a clinical benefit for hyaluronic acid compared to sodium hyaluronic for mean percentage reduction in pressure ulcer area (grade 1) (very low quality).
- One study (n=20) (in-patients) showed there may be a clinical benefit for hyaluronic acid compared to sodium hyaluronic for mean percentage reduction in pressure ulcer area (grade 2) (very low quality).
- One study (n=14) (in-patients) showed there may be a clinical benefit for hyaluronic acid compared to sodium hyaluronic for mean percentage reduction in pressure ulcer area (grade 3) No estimate of precision could be derived (very low quality).
- One study (n=20) (in-patients) showed there may be a clinical benefit for hyaluronic acid compared to sodium hyaluronic for time to 50% reduction in pressure ulcer diameter (grade 1) (very low quality).
- One study (n=20) (in-patients) showed there may be a clinical benefit for hyaluronic acid compared to sodium hyaluronic for time to 50% reduction in pressure ulcer diameter (grade 2) (very low quality).
- One study (n=14) (in-patients) showed there may be a clinical benefit for hyaluronic acid compared to sodium hyaluronic for time to 50% reduction in pressure ulcer diameter (grade 3) (very low quality).
- No evidence was found for the following outcomes:
  - Time to complete healing
  - Rate of reduction in size of ulcers

- Proportion of completely healed within trial period
- Pain (wound-related)
- Time in hospital or NHS care
- Patient acceptability
- Side effects
- Mortality (all cause)
- Health-related quality of life

11.1.5.1.41 Zinc gauze dressing versus streptokinase-streptodornase ointment

- One study (n=28) (geriatric adults with necrotic pressure ulcers) reported medians for percentage reduction in pressure ulcer area for a zinc gauze dressing and a streptokinase-streptodornase ointment. The median for a zinc gauze dressing was 2.4% and -18.7% for a streptokinase-streptodornase ointment. No estimate of effect or precision could be derived (very low quality).
- One study (n=28) (geriatric adults with necrotic pressure ulcers) showed there may be no clinical difference between a zinc gauze dressing and a streptokinase-streptodornase ointment for proportion of people with skin reaction, but the direction of the estimate of effect favoured the zinc gauze dressing (very low quality).
- One study (n=28) (geriatric adults with necrotic pressure ulcers) showed there may be no clinical difference between a zinc gauze dressing and a streptokinase-streptodornase ointment for proportion of people with infection, but the direction of the estimate of effect favoured the zinc gauze dressing (very low quality).
- One study (n=28) (geriatric adults with necrotic pressure ulcers) showed there is no clinical difference between a zinc gauze dressing and a streptokinase-streptodornase ointment for all-cause mortality (low quality).
- No evidence was found for the following outcomes:
  - Time to complete healing
  - Rate of reduction in size of ulcers
  - Proportion of completely healed within trial period
  - Pain (wound-related)
  - Time in hospital or NHS care
  - Patient acceptability
  - Health-related quality of life

11.1.5.1.42 Hydrofibre dressing versus resin salve

- One study (n=22) (people in hospital) showed a resin salve is potentially more clinically effective at increasing the proportion of people with pressure ulcers completely healed (grade 2 to 4) when compared to a hydrofibre dressing (low quality).
- One study (n=29) (people in hospital) showed a resin salve is potentially more clinically effective at increasing the proportion of pressure ulcers completely healed (grade 2 to 4) when compared to a hydrofibre dressing (low quality).
- One study (n=29) (people in hospital) showed a resin salve is potentially more clinically effective at increasing the proportion of pressure ulcers improved (grade 2 to 4) when compared to a hydrofibre dressing (low quality).
- One study (n=29) (people in hospital) showed there may be clinical harm for a hydrofibre dressing for the proportion of pressure ulcers worsened when compared to resin salve (very low quality).
- One study (n=29) (people in hospital) showed there may be a clinical benefit for a resin salve compared to a hydrofibre dressing for mean percentage reduction in pressure ulcer width (grade 2 to 4). No estimate of precision could be derived (very low quality).

- One study (n=29) (people in hospital) showed there may be a clinical benefit for a resin salve compared to a hydrofibre dressing for mean percentage reduction in pressure ulcer depth (grade 2 to 4). No estimate of precision could be derived (very low quality).
- One study (n=29) (people in hospital) reported that the speed of healing of pressure ulcers was significantly faster with a resin salve when compared with a hydrofibre dressing. No estimate of effect or precision could be derived (very low quality).
- One study (n=37) (people in hospital) showed there may be no clinical difference between a resin salve and a hydrofibre dressing for proportion of people with allergic skin reaction, but the direction of the estimate of effect favoured the hydrofibre dressing (very low quality).
- One study (n=37) (people in hospital) showed there may be a clinical benefit of resin salve for the for all-cause mortality, when compared to a hydrofibre dressing (very low quality).
- No evidence was found for the following outcomes:
  - Time to complete healing
  - Pain (wound-related)
  - Time in hospital or NHS care
  - Patient acceptability
  - Health-related quality of life

11.1.5.1.43 Dextranomer versus chlorinated lime solution

- One study (n=16) (elderly adults) showed dextranomer is potentially more clinically effective at reducing the time to healing (defined as granulating and less than 25% of original ulcer area) when compared to a chlorinated lime solution (very low quality).
- One study (n=16) (elderly adults) showed there may be no clinical difference between a dextranomer and a chlorinated lime solution for all-cause mortality, the direction of the estimate of effect favoured the intervention (very low quality).
- No evidence was found for the following outcomes:
  - Rate of reduction in size of ulcers
  - Reduction in size and/or volume of ulcer.
  - Proportion of completely healed within trial period
  - Pain (wound-related)
  - Time in hospital or NHS care
  - Patient acceptability
  - Side effects
  - Health-related quality of life

11.1.5.1.44 Collagen and foam versus foam dressing

- One study (n=10) (stagnating pressure ulcers of at least 4 weeks duration) showed there may be no clinical difference between collagen and foam, and a foam dressing for increasing the proportion of people with pressure ulcers completely healed, but the direction of the estimate of effect could favour the foam dressing (very low quality).
- One study (n=10) (stagnating pressure ulcers of at least 4 weeks duration) showed there is no clinical difference between collagen and foam, and a foam dressing for all-cause mortality (low quality).
- No evidence was found for the following outcomes:
  - Time to complete healing

- Rate of reduction in size of ulcers
- Reduction in size and/or volume of ulcer.
- Pain (wound-related)
- Time in hospital or NHS care
- Patient acceptability
- Side effects
- Health-related quality of life

11.1.5.2 Economic (adults)

- Two cost-consequence analyses found collagen is likely to be more expensive and more effective than hydrocolloid for healing people with pressure ulcers; 1 additional cost-effectiveness analysis found that collagen is likely to dominate hydrocolloid (collagen is less costly and more effective) in the treatment of heel pressure ulcers. All 3 studies were partially applicable with potentially serious limitations.
- Two cost-effectiveness analyses found DuoDERM hydrocolloid dressings are likely to dominate Comfeel hydrocolloid dressings and saline gauze; both studies reported the Comfeel dressing to be less effective and less costly than the saline gauze. Both studies were partially applicable with potentially serious limitations.
- One cost-consequence analysis found that hydrogel dressings are likely to be less costly than hydrocolloid dressings (effectiveness was assumed equal). This study was assed to be partially applicable with potentially serious limitations.
- One cost-consequence analysis found collagenase dressings dominate hydrogel dressings, with lower costs and fewer days spent with a pressure ulcer. This study was assessed to be partially applicable with potentially serious limitations.
- One cost comparison found a hydroactive wound dressing, in combination with enzymatic wound cleaning, to be less costly than gauze, impregnated gauze, and calcium alginate. This study was assessed to be partially applicable with potentially serious limitations.
- One cost-effectiveness analysis found modern dressings are likely to dominate traditional wound care (modern dressings are less costly and more effective than traditional care); an additional cost-effectiveness analysis found advanced dressings are likely to dominate simple dressings. Both studies were assessed as partially applicable with potentially serious limitations.
- One cost-consequence analysis found that polyurethane self-adhesive foam dressing is likely to dominate saline soaked gauze. This analysis was partially applicable and had minor limitations.

11.1.5.3 Clinical (neonates, infants, children and young people)

No evidence was identified.

11.1.5.4 Economic (neonates, infants, children and young people)

No relevant evidence was identified.

11.1.6 Recommendations and link to evidence

11.1.6.1 Adults

Recommendations	**42. Consider using a dressing for adults that promotes a warm, moist wound healing environment to treat grade 2, 3 and 4 pressure ulcers.** **43. Discuss with adults with a pressure ulcer and, if appropriate, their family or carers, what type of dressing should be used, taking into account:** • **pain and tolerance** • **position of the ulcer** • **amount of exudate** • **frequency of dressing change**
Relative values of different outcomes	The GDG identified that the proportion of people with pressure ulcers completely healed, time to complete healing, reduction in size and volume and rate of reduction in size and volume of pressure ulcers were the most critical outcomes to inform decision making. It was acknowledged that pain experienced during dressing change was important from a patient perspective and that the frequency of dressing change should be considered.
Trade off between clinical benefits and harms	The majority of studies were compared against hydrocolloid dressing, as the GDG felt this is often considered the gold standard and that it has been available for a long time. The results were mixed for the benefits of hydrocolloid. There was a clinical benefit of hydrocolloid dressing over foam dressing and phenytoin cream for proportion of people completely healed, also for improvement in pressure ulcers when compared to phenytoin cream. However there was no difference for pressure ulcers worsened. When hydrocolloid dressing was compared to phenytoin ointment in a small study the phenytoin ointment was more clinically beneficial for reducing the mean time to healing but there was no difference for adverse events and mortality. There was no clinical difference between a collagen dressing when compared to a hydrocolloid dressing for people completely healed, mean healing speed, time to healing, adverse events or mortality but there was a clinical benefit of collagen for the mean percentage reduction in ulcer area. Hydrogel dressings were more clinically beneficial than hydrocolloid dressings for the proportion of people with pressure ulcers completely healed in 1 study (Darkovich 1990) but no difference in proportion of pressure ulcers completely healed in another very small (Motta, 1999)[122] study (grade 2 and 3). For reduction in size and for reduction of worsened pressures ulcers, hydrogel was more beneficial but there was uncertainty in any difference in healing rate. There was no clinical difference in odour score, comfort or mortality rate. The GDG discussed that in clinical practice hydrogel dressings and hydrocolloid dressings were not necessarily an appropriate comparison as there would be different clinical indications for each dressing. It would also be determined by what form the dressing takes for example, sheet or film. Alginate dressing was more clinically beneficial than hydrocolloid dressing for the proportion of people partially healed (40%) and reduction in pressure ulcer area. There was no clinical difference in infection, skin irritation, maceration, bleeding, pain at dressing removal, odour, hypergranulation and mortality. The GDG thought that alginate dressings and hydrocolloid dressings was not a relevant comparison as they are used in clinical practice for different clinical indications.

	There was no clinical benefit of hydrocolloid dressing for time to healing or for adverse events when compared to antibiotic ointment, nor for any outcomes for hydrocolloid dressing compared to polyurethane dressing. The GDG noted that this may be due to the fact that the results would be dependent upon the grade of pressure ulcer. There was a clinical benefit for resin salve dressing compared to hydrofibre dressing for the proportion of people completely healed, improved, worsened, mean percentage reduction in ulcer width and depth and mortality. There was an unclear benefit for speed of healing but it favoured the hydrofibre dressing. There was a clinical benefit of foam dressing for the proportion of ulcers completely healed in a palliative care setting when compared to a hydrogel dressing. There were no other clinical differences between foam dressings and hydrogel dressings. More pressure ulcers worsened with an alginate dressing than with a silver alginate dressing and there was a clinical benefit for silver alginate dressing for reduction in pressure ulcer area. There were no clinical differences for rate of healing of pressure ulcers, poor acceptability and/or tolerability, infection and mortality between alginate and silver alginate dressings. Dextranomer, sugar, hyaluronic acid and poly-hema were judged to have little relevance by the GDG as they are not in use in current clinical practice in the UK. Furthermore, the GDG thought that the comparison of silver dressing compared to silver cream was not relevant to the review as silver is the same constituent and this was therefore not a comparison of dressings. Where different hydrocolloid dressings were compared this was not regarded as relevant to the review as again it was not comparing different types of dressing (with different functions). This also applied to different foam dressings. The GDG felt that where interventions were compared to a variety of dressings or other treatments this was not useful to informing the recommendation. Where comparisons included debriding or topical agents these studies were included in the debridement and topical agent reviews. Charcoal dressing was compared to hydrocolloid dressing but the GDG suggested that charcoal dressings are mainly used for odour control and that this comparison was therefore not appropriate, particularly given that odour was not an outcome considered by the study. One study compared honey to ethyocydiaminoacridine and nitrofurzaone but the GDG noted that ethyocydiaminoacridine and nitrofurazone is not used in clinical practice and is not listed in the BNF. The GDG did not feel that the evidence allowed for a recommendation to be made about the use of a specific type of dressing. This was due to the lack and quality of evidence, as well as the importance of considering the function of the dressing and specific patient factors. The GDG emphasised that the effectiveness of each dressing would be dependent upon the type of pressure ulcer. The GDG therefore chose to recommend a dressing which promotes the optimum healing environment, rather than a specific type of dressing. To inform this decision, a second recommendation was developed to highlight the patient factors which should be considered in choosing the most appropriate dressing.
Economic considerations	Eleven economic studies were included, however the majority of these provided only pairwise comparisons, and none were conducted inside the UK. The existing economic evidence was considered to be only partially informative in determining the cost-effectiveness of various dressings. The GDG did not feel that the evidence was strong enough to identify a cost-effective type of dressing.

	The GDG considered UK relevant unit costs, but noted that the major resource implications come from the frequency that each dressing requires changing. This is likely to be dependent on a range of factors, such as location of the ulcer, the amount of exudate, and patient acceptability. The frequency of dressing change can also have a substantial impact on quality of life. The GDG therefore agreed that the dressing which was deemed more effective when taking these factors into account would be most likely to be cost-effective.
Quality of evidence	Overall, the quality of evidence was graded low to very low. Most of the studies had very serious limitations. In the studies where a clinical effect was found most of the results had serious to very serious imprecision, thus indicating a lot of uncertainty in the results. The GDG noted that there were some problems with the comparisons in studies, such as non-clinically relevant comparisons and dressings not used in current clinical practice. Therefore these comparisons have not been focused upon. Having reviewed the evidence and taken into consideration the above listed limiting factors the recommendation was developed by informal consensus of the GDG.
Other considerations	The GDG felt it was important to consider the following factors when choosing a dressing. Such factors include; the adhesiveness of a dressing (ease of removal), the nature of the wound, ease of use of the dressing, amount of exudate, amount of pain at dressing change, protection of surrounding skin, irritation caused by the adhesive, infection, odour, and absorption. In addition, it was noted that the wound can deteriorate because of dressing changes and this is specific issue with regards to sacral ulcers that are likely to become frequently soiled. The frequency of dressing changes was also noted as have an impact on the healing of a wound and can be detrimental to the effectiveness of the dressing. The patient members of the GDG stated that tolerability of the dressing and dressing change were important factors, as were odour and skin irritation. Discussion also focused on the need to consider who has the responsibility for choosing the type of dressing used, and who is responsible for dressing changes. It was felt that this should be a healthcare professional with appropriate knowledge and experience of the use of dressings. The GDG highlighted that when a pressure ulcer is not improving it was important to consider other factors such as pressure redistribution and nutrition to facilitate healing. It was also important to recognise when a certain dressing is not appropriate and consideration should be given to using a different type of dressing. The GDG felt that different shapes of dressing may be needed for different pressure ulcer sites.

Recommendations	**44.Do not offer gauze dressings to treat pressure ulcers in adults.**
Relative values of different outcomes	The GDG identified that the proportion of people with pressure ulcers completely healed, time to complete healing, reduction in size and volume and rate of reduction in size and volume of pressure ulcers were the most critical outcomes to inform decision making. It was acknowledged that pain at dressing change was important from a patient perspective and that the frequency of dressing change should be considered.
Trade off between clinical benefits and harms	Evidence showed there was a clinical benefit for hydrocolloid dressing compared to gauze dressing for the proportion of people with pressure ulcers completely healed, and improved. There was heterogeneity in the results so the results were analysed in their pre-defined subgroups, which showed a more profound benefit for those with

	spinal cord injury than the general population, although most results showing hydrocolloid to be more beneficial. There was no difference for the proportion of pressure ulcers which worsened for the general population but hydrocolloid dressing was more clinically beneficial than gauze dressing for reducing pressure ulcers worsened. There was a clinical benefit for gauze dressing for the reduction in size and volume of pressure ulcers. There was a clinical harm for gauze dressing for skin irritation, pain at dressing removal and discomfort. There was also a clinical benefit of hydrocolloid dressing compared to impregnated gauze dressing for proportion of completely healed, but there was no difference for people improved. There was a clinical benefit for hydrocolloid dressing compared to foam dressing for the proportion of people completely healed. Foam dressing showed more harm for the proportion of people with inflammation or maceration but other outcomes showed no clinically beneficial results. There was a clinical benefit of foam dressing when compared to gauze dressing for the proportion of people completely healed and reduced mortality. Polyurethane dressing was clinically beneficial when compared to gauze dressing for: the proportion of pressure ulcers completely healed, worsened, decreased in size, increased in ulcer grade. There was no clinical benefit for polyurethane dressing for proportion with maceration. There was a clinical benefit of phenytoin cream when compared to gauze dressing for people completely healed, for the proportion of ulcers improved and for a lower proportion of people with worsening of pressure ulcers. There was no clinical benefit for hydrogel dressing or gauze dressing for any outcomes except there may be a benefit for gauze dressing for reducing all-cause mortality. Dextranomer dressing was more clinically beneficial than gauze dressing but the GDG judged it to have little relevance as it is not used in current clinical practice in the UK. The GDG did not think that this was a relevant comparison. Overall there was little clinical benefit of gauze dressing. There are adverse events associated with gauze dressings which the GDG identified as important such as increased pain at dressing removal, skin irritation and discomfort. The GDG stated that gauze is rarely used in clinical practice due to the fact that there are more effective dressings available. It is for these reasons that the above recommendation has been made.
Economic considerations	The GDG considered 3 economic analyses which included gauze dressing as a comparator. None of these studies found gauze dressing to be cost effective (comparators included calcium alginate, hydroactive wound dressings, and hydrocolloid dressings).
Quality of evidence	Overall, the quality of evidence was graded low to very low. Most of the studies had very serious limitations. Where there was a clinical effect, most of the results had serious to very serious imprecision indicating a lot of uncertainty in these results. No serious imprecision was found for gauze versus hydrocolloid dressings or gauze versus polyurethane dressings. The GDG noted that there were some problems with the studies, such as non-clinically relevant comparisons and dressings not used in current clinical practice. Therefore these comparisons have not been focused upon.
Other considerations	The GDG were concerned about the use of gauze dressings as they often dry out and on removal can remove healing skin. Such removal can also cause pain to the individual.

11.1.6.2 Neonates, infants, children and young people

Recommendations	**45.Do not use iodine dressings to treat pressure ulcers in neonates.**

Relative values of different outcomes	The GDG identified that the proportion of people with pressure ulcers completely healed, time to complete healing, reduction in size and volume and rate of reduction in size and volume of pressure ulcers were the most critical outcomes to inform decision making. It was acknowledged that pain at dressing change was important from a patient perspective and that the frequency of dressing change should be considered.
Trade-off between clinical benefits and harms	The GDG used 1 statement from the Delphi consensus panel to develop the recommendation. The statement was 'Healthcare professionals should not use iodine dressings for the treatment of pressure ulcers in neonates.' The statement was accepted by the Delphi consensus panel in Round 1 of the survey. Further detail on the Delphi consensus survey can be found in Appendix N. The statement was included in Round 1 of the Delphi consensus. Qualitative responses gathered from panel members suggested that there was a risk of toxicity from the use of iodine in neonates. The GDG discussed the statement and agreed that a recommendation should be made. The GDG agreed that the risk of toxicity from the use of iodine dressings in neonates meant that these dressings should not be used in this population and a recommendation was developed to reflect this.
Economic considerations	The primary concern is safety for the neonates; iodine dressings are not advised in this population, therefore cost-effectiveness is not considered.
Quality of evidence	No RCTs or cohort studies were identified for neonates, infants, children or young people. Formal consensus using a modified Delphi was therefore used to develop the recommendation. To inform the recommendation, the GDG used 1 statement which was included in Round 1 of the Delphi consensus survey and reached 86% consensus agreement. Further details can be found in Appendix N.
Other considerations	Comments from the Delphi consensus panel suggested that iodine dressings should be used only with extreme caution in infants and children, where other dressings were not appropriate.

Recommendations	**46. Consider using a dressing that promotes a warm, moist healing environment to treat grade 2, 3 and 4 pressure ulcers in neonates, infants, children and young people.**
Relative values of different outcomes	The GDG identified that the proportion of people with pressure ulcers completely healed, time to complete healing, reduction in size and volume and rate of reduction in size and volume of pressure ulcers were the most critical outcomes to inform decision making. It was acknowledged that pain at dressing change was important from an individual perspective and that the frequency of dressing change should be considered.
Trade-off between clinical benefits and harms	The GDG used 1 statement from the Delphi consensus panel to develop the recommendation. The statement 'Healthcare professionals should treat all pressure ulcers with wound dressings which promote a warm, moist wound healing environment' was not accepted during Round 1 of the Delphi consensus survey and was therefore amended for Round 2 of the survey. The GDG discussed comments from panel members which suggested that the use of such dressings would not be appropriate for Grade 1 ulcers and only for some Grade 2 ulcers. Comments also highlighted that different dressings would be required depending upon the clinical condition of the neonate, infant, child or young person. As such, the statement was amended to reflect that such a dressing should be considered, rather than used for all ulcers. The statement was also amended to reflect that this may be used for

	Grade 2, 3 or 4 ulcers only. The statement was accepted by the Delphi consensus panel in Round 2 of the survey. Further detail on the Delphi consensus survey can be found in Appendix N. The GDG discussed the comments and agreed that a recommendation should be developed to support the use of a dressing which promotes a warm, moist healing environment, rather than a specific type of dressing. Comments gathered from the panel in Round 2 of the Delphi consensus survey suggested that the use of any dressings should be part of an individualised management plan.
Economic considerations	The GDG considered UK relevant unit costs, but noted that the major resource implications come from the frequency that each dressing requires changing. This is likely to be dependent on a range of factors, such as location of the ulcer, the amount of exudate, and patient acceptability. The frequency of dressing change can also have a substantial impact on quality of life. In the absence of evidence the GDG did not feel that 1 cost-effective type of dressing could be identified, but agreed that the dressing which was deemed more effective when taking these factors (for example, location of the ulcer, the amount of exudate, and patient acceptability) into account would be most likely to be cost-effective.
Quality of evidence	No RCTs or cohort studies were identified for neonates, infants, children or young people. Formal consensus using a modified Delphi was therefore used to develop the recommendation. To inform the recommendation, the GDG used 1 statement which was included in Round 1 of the Delphi consensus survey and reached 74% consensus agreement. The statement was therefore amended and included in Round 2 of the Delphi consensus survey where it reached 87% consensus. Further details can be found in Appendix N.
Other considerations	There were no other considerations.

Recommendations	**47. Consider using topical antimicrobial dressings to treat pressure ulcers where clinically indicated in neonates, infants, children and young people, for example, where there is spreading cellulitis** **48. Do not offer gauze dressings to treat pressure ulcers in neonates, infants, children and young people.**
Relative values of different outcomes	The GDG identified that the proportion of people with pressure ulcers completely healed, time to complete healing, reduction in size and volume and rate of reduction in size and volume of pressure ulcers were the most critical outcomes to inform decision making. It was acknowledged that pain at dressing change was important from a patient perspective and that the frequency of dressing change should be considered.
Trade-off between clinical benefits and harms	The GDG used 1 statement from the Delphi consensus survey to develop the recommendation on topical antimicrobial dressings. The statement 'Healthcare professionals should not routinely use topical antimicrobial dressings (for example silver or iodine) for the treatment of pressure ulcers in infants, children and young people.' was included in Round 1 of the Delphi consensus process and was not accepted. The statement was subsequently amended by the GDG for inclusion in Round 2 of the survey. The GDG noted that the majority of comments received during Round 1 were based upon the use of silver and iodine dressings. The statement was therefore amended to remove these examples, as it was agreed that they were not appropriate examples. The statement was also amended to suggest

	that there may be situations in which topical antimicrobial dressings are appropriate and that these may be considered when treating neonates, infants, children and young people, depending upon the clinical condition. The amended statement 'Healthcare professionals should consider using topical antimicrobial dressings for the treatment of pressure ulcers in infants, children and young people, where clinically indicated' was therefore included in Round 2 of the Delphi consensus survey, where it was accepted. The GDG agreed that a recommendation should be developed to highlighted that topical antimicrobial dressings should be considered in these populations where clinically indicated. Comments from the Delphi consensus panel highlighted that the choice of topical antimicrobial should be considered carefully in neonates, infants and children and that silver and iodine dressings were unlikely to be appropriate in people of these ages. Comments also emphasised that of topical antimicrobials should not be used routinely and the GDG therefore felt that a recommendation to 'consider' using these dressings would be appropriate.
Economic considerations	The GDG noted that in some scenarios topical antimicrobials will be required for the treatment of pressure ulcers. In such cases they are required for healing, therefore the small upfront cost is expected to be off-set by reductions in future treatment costs and improvements in quality of life. These dressings will not require substantial additional resource over the use of a dressing which promotes a warm, moist healing environment, as recommended in Chapter 10. The GDG agreed that the use of topical antimicrobial dressings is highly likely to be cost-effective, but only where clinically indicated.
Quality of evidence	No RCTs or cohort studies were identified for neonates, infants, children or young people. Formal consensus using a modified Delphi was therefore used to develop the recommendation. To inform the recommendation, the GDG used 1 statement which was included in Round 1 of the Delphi consensus survey and reached 65% consensus agreement. An amended statement was therefore included in Round 2 of the survey where it reached 79% consensus and was accepted. Further details can be found in Appendix N.
Other considerations	Recommendation X covers the use of iodine dressings in neonates.

Recommendations	**49. Do not offer gauze dressings to treat pressure ulcers in neonates, infants, children and young people.**
Relative values of different outcomes	The GDG identified that the proportion of people with pressure ulcers completely healed, time to complete healing, reduction in size and volume and rate of reduction in size and volume of pressure ulcers were the most critical outcomes to inform decision making. It was acknowledged that pain at dressing change was important from an individual perspective and that the frequency of dressing change should be considered.
Trade-off between clinical benefits and harms	During discussion of the Delphi consensus survey and development of the recommendations, the GDG highlighted that it was inappropriate to use gauze dressings to treat pressure ulcers and subsequently developed a corresponding recommendation using informal consensus.
Economic considerations	Gauze dressings are not considered to be effective in the treatment of pressure ulcers, therefore they are not considered to be cost-effective.

Quality of evidence	No RCTs or cohort studies were identified for neonates, infants, children or young people. Formal consensus using a modified Delphi was therefore used to develop the recommendation. The recommendation was based upon informal consensus of the GDG.
Other considerations	There were no other considerations.

12 Management of heel pressure ulcers

Heel pressure ulcers are localised injury to the heel as result of pressure sometimes in association with other factors. The heel is at the back of the foot, extending from the Achilles tendon around the plantar surface, it covers the apex of the calcaneum bone. It is a common site for pressure ulcer development, particularly in people who are supine or semi-recumbent with immobility. In this position, bone and tendon can be involved as there is little underlying connective tissue.

The lower limb can be subject to disease processes such as ischaemia, oedema, structural changes (due to fractures or bone disorders) and neuropathy, all of which affect the development and healing of heel pressure ulcers.

In light of these anatomical and pathological differences of the heel, the GDG wished to consider whether there are specific management considerations for heel pressure ulcers.

12.1 Review question: What is the most clinically and cost-effective method for management of pressure ulcers of the heel?

For full details see review protocol in Appendix C.

12.1.1 Clinical evidence (adults)

Five studies were included in the review and 1 Cochrane Review was found.[101,111,114,125,161] Evidence from these are summarised in the clinical GRADE evidence profile below (Table 197). See also the study selection flow chart in Appendix D, forest plots in Appendix I, study evidence tables in Appendix G and exclusion list in Appendix J.

A Cochrane Review (McGinnis 2011)[111] was found for pressure-relieving devices for treating heel pressure ulcers, 1 study was found (Russell 2000)[161] which looked at 2 different types of mattress. One study looked at topical agents – nerve growth factors compared to placebo (Landi 2003), this is reported in the topical agents review and reported feet and heel ulcers. As this present review focuses on heel ulcers, only 1 outcome was extricable from the study (reduction in ulcer area) as all other outcomes related to foot and heel ulcers. One study (Muller 2001) looked at collagenase-containing ointment compared to hydrocolloid dressing to treat pressure ulcers. Meaume (2009) looked at ornithine alpha-ketoglutarate, an amino acid salt, compared to placebo as a supplement to treat heel pressure ulcers.

No randomised trials were identified regarding repositioning, electrotherapy, NPWT, HBOT, debridement, antimicrobials, antibiotics, skin massage or rubbing.

Summary of included studies

Study	Intervention/comparator	Population	Outcome	Study length
Landi 2003[101]	Nerve growth factor Placebo	People in a nursing home with a stage 2 to 5 foot pressure ulcer (Yarkony classification)	• Reduction in ulcer area	Six weeks of treatment or until complete healing
Meaume 2009[114]	10g sachet of ornithine alpha-ketoglutarate versus 1 sachet of placebo	Elderly people (geriatrics, internal medicine, physical medicine and rehabilitation, trauma, plastic surgery, cardiology, neurology and dermatology settings) who had pressure ulcers of the heel of stage 2 or 3 (NPUAP classification)	• % reduction in pressure ulcer surface area; more than 90% reduction by week 6; rate of complete healing (cm^2/day); all-cause mortality	6 weeks
Muller 2001[125]	Hydrocolloid dressing Collagen dressing	Female inpatients with a grade 4 heel pressure ulcer	• Proportion of people completely healed • Time to healing	Maximum 16 weeks
Russell 2000[161]	2 types of alternating cell mattress systems with pressure-relieving cushions: Huntleigh Nimbus 3 with Aura cushion and 4-hourly turning versus Pegasus Cairwave Therapy System with Proactive 2 seating cushion and 8-hourly turning.	People from care of the elderly units with pressure ulcer of grade 2 or above (Torrance classification system). Average age 83.9 and 84.6 years in the 2 groups.	• Ulcer healing at 12 and 18 months	18-month follow-up

Table 197: Clinical evidence profile: Nimbus system versus Cairwave system

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Nimbus system	Cairwave system	Relative (95% CI)	Absolute	Quality	Importance
Proportion of people with heel pressure ulcers completely healed – grade 2 and above heel pressure ulcers (Torrance)[161]												
1	Randomised trial	Serious[a]	No serious inconsistency	no serious indirectness	Serious[b]	None	24/55 (43.6%)	17/58 (29.3%)	RR 1.49 (0.9 to 2.45)	144 more per 1000 (from 29 fewer to 425 more)	Low	Critical
							-	29.3%		144 more per 1000 (from 29 fewer to 425 more)		
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate of reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital												
-	-	-	-	-	-	-	-	-	-	-	-	-
Acceptability of treatment												
-	-	-	-	-	-	-	-	-	-	-	-	-
Side effects												
-	-	-	-	-	-	-	-	-	-	-	-	-
Mortality												
-	-	-	-	-	-	-	-	-	-	-	-	-

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Nimbus system	Cairwave system	Relative (95% CI)	Absolute	Quality	Importance
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) No details of randomisation method were provided by the authors and there were unclear methods of allocation concealment.
(b) The confidence interval crossed 1 MID point.

Table 198: Clinical evidence profile: nerve growth factor versus placebo

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Nerve growth factor	Placebo	Relative (95% CI)	Absolute	Quality	Importance
Reduction in heel ulcer area (mm^2) (better indicated by higher values) – grade 2-4 heel pressure ulcers (Yarkony)[101]												
1	Randomised trial	Serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	None	623 (SD 451) n=18	485 (SD 384) n=18	-	MD 138 higher (135.64 lower to 411.64 higher)	Low	Critical
Proportion of people with pressure ulcers completely healed												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time to complete healing of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate of reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital												

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Nerve growth factor	Placebo	Relative (95% CI)	Absolute	Quality	Importance
-	-	-	-	-	-	-	-	-	-	-	-	-
Acceptability of treatment												
-	-	-	-	-	-	-	-	-	-	-	-	-
Side effects												
-	-	-	-	-	-	-	-	-	-	-	-	-
Mortality												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) Allocation according to age group, sex and ulcer area and blinding of nurses and outcome assessor but no blinding of patient.
(b) The confidence internval crosses 1 MID point.

Table 199: Clinical evidence profile: hydrocolloid dressing versus collagen dressing

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Hydrocolloid dressing	Collagen dressing	Relative (95% CI)	Absolute	Quality	Importance
Proportion of people with heel pressure ulcers completely healed – general population – grade 4 heel pressure ulcers – classification system not reported[125]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	None	7/11 (63.6%)	11/12 (91.7%)	RR 0.69 (0.43 to 1.12)	284 fewer per 1000 (from 522 fewer to 110 more)	Very low	Critical
							-	91.7%		284 fewer per 1000 (from 523 fewer to		

Quality assessment							No of patients		Effect			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Hydrocolloid dressing**	**Collagen dressing**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
										110 more)		
Mean time to healing of heel pressure ulcers (weeks) – general population – grade 4 heel pressure ulcers – classification system not reported[125]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[c]	None	14 (SD 4.6)	10 (SD 4.6)	-	MD 4 higher (0.24 to 7.76 higher)	Very low	Critical
Time to complete healing of pressure ulcers (time to event data)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Rate of reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Reduction in size or volume of pressure ulcers												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital												
-	-	-	-	-	-	-	-	-	-	-	-	-
Acceptability of treatment												
-	-	-	-	-	-	-	-	-	-	-	-	-
Side effects												
-												
Mortality												
-												
Health-related quality of life												
-												

(a) Müller (2001) did not report on sequence generation, allocation concealment or blinding.
(b) The confidence interval crossed 1 MID point.

(c) The confidence interval crossed both MID points.

Table 200: Clinical evidence profile: ornithine alpha-ketoglutarate versus placebo

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	10g Ornithine alpha-ketoglutarate	Placebo	Relative (95% CI)	Absolute	Quality	Importance
Rate of complete healing of heel pressure ulcers (cm2/day) – elderly people – grade 2 or 3 heel pressure ulcers (NPUAP) (unclear if nutritionally deficient)[114]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	None	0.07 (s.d 0.11) n= 85	0.04 (s.d 0.08) n= 75	MD 0.03 higher (0 to 0.06 higher)	-	Very low	Critical
Mean % reduction in heel pressure ulcer size – elderly people – grade 2 or 3 heel pressure ulcers (NPUAP) (unclear if nutritionally deficient) [114]												
1	Randomised trial	Very serious[a]	No serious inconsistency	No serious indirectness	No serious	None[f]	59.5 (s.d 71.4) n= 85	54 (s.d 69) n= 75	MD 5.5 higher (16.28 lower to 27.28 higher)	-	Low	Critical
Mean surface area reduction (cm^2) – elderly people – grade 2 or 3 heel pressure ulcers (NPUAP) (unclear if nutritionally deficient) [114]												
1	Randomised trials	Very serious[a]	No serious inconsistency	No serious indirectness	No serious	None[f]	2.3 (s.d 4.2) n= 85	1.7 (s.d 1.7) n= 75	MD 0.6 higher (0.37 lower to 1.57 higher)	-	Low	Critical
90% reduction by week 6 – elderly people – grade 2 or 3 heel pressure ulcers (NPUAP) (unclear if nutritionally deficient) [114]												
1	Randomised trials	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	None	23.4% n=85	13% n=75	OR 0.49 (CI 0.16 to 14.6)[e]	-	Very low	Critical
All-cause mortality – elderly people – grade 2 or 3 heel pressure ulcers (NPUAP) (unclear if nutritionally deficient) [114]												

Quality assessment							No of patients		Effect			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**10g Ornithine alpha-ketoglutarate**	**Placebo**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
1	Randomised trials	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[c]	None	5/89 (5.6%)	3/76 (3.9%)	RR 1.42 (0.35 to 5.76)	17 more per 1000 (from 26 fewer to 188 more)	Very low	Important
							-	4%		17 more per 1000 (from 26 fewer to 190 more)		
Proportion of people with pressure ulcers completely healed												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time to complete healing												
-	-	-	-	-	-	-	-	-	-	-	-	-
Pain (wound-related)												
-	-	-	-	-	-	-	-	-	-	-	-	-
Time in hospital												
-	-	-	-	-	-	-	-	-	-	-	-	-
Acceptability of treatment												
-	-	-	-	-	-	-	-	-	-	-	-	-
Side effects												
-	-	-	-	-	-	-	-	-	-	-	-	-
Mortality												
-	-	-	-	-	-	-	-	-	-	-	-	-
Health-related quality of life												
-	-	-	-	-	-	-	-	-	-	-	-	-

(a) There was a very high drop-out in both arms. Due to problems in recruitment the study was opened up to other centres so some centres had 2 participants and randomisation was balanced by blocks of four. There were baseline differences. The missing data were higher than the event rate.
(b) The confidence interval crossed 1 MID point.
(c) The confidence interval crossed both MID points.
(d) Value reported by study
(e) Odds ratio reported by study.

ANCOVA used. Non-parametric tests detected between-group differences (p=0.044) which were confirmed by parametric tests after log-transformation to normalise distribution (p=0.027 for group comparisons).

12.1.2 Economic evidence (adults)

Published literature

One study was included with a relevant comparison.[125] This is summarised in the economic evidence profiles below(Table 201). See also the study selection flow chart in Appendix D and study evidence tables in Appendix H.

Table 201: Economic evidence profile: hydrocolloid dressing versus collagen dressing

Study	Applicability	Limitations	Other comments	Incremental cost	Incremental effects	Cost effectiveness	Uncertainty
Müller 2001[125] (Netherlands)	Partially applicable[a]	Potentially serious limitations[b]	Within trial analysis of a collagen dressing compared to a hydrocolloid dressing for heel ulcers, based on analysis of individual level resource use with unit costs applied.	£25	Pressure ulcers healed: -0.29 (p <0.005)	Collagen dominates hydrocolloid	No useful sensitivity analyses reported.

(a) Study based in the Netherlands, quality of life not considered, costs based on 1998 values
(b) Small study, no unit cost source reported, no consideration of quality of life, no useful analysis of uncertainty reported

12.1.3 Clinical evidence (neonates, infants, children and young people)

No RCTs or cohort studies were identified. Recommendations were developed using a modified Delphi consensus technique. Further details can be found in Appendix N.

12.1.4 Economic evidence (neonates, infants, children and young people)

No economic evidence was identified.

12.1.5 Evidence statements

12.1.5.1 Clinical (adults)

12.1.5.1.1 Alternating pressure mattress (Nimbus system) versus alternating pressure mattress (Cairwave system)

- One study (n=113) showed the nimbus system is potentially more clinically effective than the cairwave system for complete healing of heel pressure ulcers (grade 2 and above pressure ulcers) (low quality).
- No evidence was found for the following outcomes:
  - Time to complete healing (time to event data)
  - Rate of healing
  - Rate of change in size of ulcer
  - Reduction in size of ulcer and volume of ulcer
  - Pain (wound-related)
  - Time in hospital or NHS care
  - Patient acceptability
  - Side effects
  - Mortality (all cause)
  - Health-related quality of life

12.1.5.1.2 Nerve growth factor versus placebo

- One study (n=36) showed that nerve growth factor is potentially more clinically effective at reducing the size of the heel ulcer area when compared to placebo (low quality).
- No evidence was found for the following outcomes:
  - Time to complete healing (time to event data)
  - Rate of healing
  - Rate of change in size of ulcer
  - Proportion of people completely healed
  - Pain (wound-related)
  - Time in hospital or NHS care
  - Patient acceptability
  - Side effects
  - Mortality (all cause)
  - Health-related quality of life

12.1.5.1.3 Hydrocolloid dressing versus collagen dressing

- One study (n= 23) showed that a collagen dressing is potentially more clinically effective than a hydrocolloid dressing for complete healing of heel pressure ulcers (grade 4 pressure ulcers) (very low quality).
- One study (n=24) showed a collagen dressing may be more clinically effective than a hydrocolloid dressing for reducing the time to healing of heel pressure ulcers (grade 4 pressure ulcers) (very low quality).
- No evidence was found for the following outcomes:
  - Time to complete healing (time to event data)
  - Rate of healing
  - Rate of change in size of ulcer
  - Reduction in size of ulcer and volume of ulcer.
  - Pain (wound-related)
  - Time in hospital or NHS care (continuous data)
  - Patient acceptability
  - Side effects
  - Mortality (all cause)
  - Health-related quality of life

12.1.5.1.4 Ornithine alpha-ketoglutarate versus placebo

- One study (n=160) showed there is potentially no clinical difference between ornithine alpha-ketoglutarate and placebo for rate of complete healing of heel pressure ulcers (grade 2 or 3 pressure ulcers), but the direction of the estimate of effect favoured ornithine alpha-ketoglutarate (very low quality).
- One study (n=160) showed a clinical benefit of ornithine alpha-ketoglutarate mean reduction in size (%) when compared to placebo (low quality).
- One study (n=160) showed no clinical difference between ornithine alpha-ketoglutarate and placebo for mean reduction in size (cm^2) but the direction of the estimate of effect favoured ornithine alpha-ketoglutarate (low quality).
- One study (n=160) showeda clinical benefit of ornithine alpha-ketoglutarate for 90% reduction in heel pressure ulcers compared to placebo (very low quality).
- One study (n=165) showed there may be no clinical difference between ornithine alpha-ketoglutarate and placebo for mortality, but the direction of the estimate of effect favoured the placebo (very low quality).
- No evidence was found for the following outcomes:
  - Time to complete healing (time to event data)
  - Rate of change in size of ulcer
  - Proportion of people completely healed
  - Pain (wound-related)
  - Time in hospital or NHS care (continuous data)
  - Patient acceptability
  - Side effects
  - Health-related quality of life

12.1.5.2 Economic (adults)

- One cost-effectiveness analysis found that collagen is likely to dominate hydrocolloid (collagen is less costly and more effective) in the treatment of heel pressure ulcers. This study was assessed to be partially applicable with potentially serious limitations.

12.1.5.3 Clinical (neonates, infants, children and young people)

No evidence was identified.

12.1.5.4 Economic (neonantes, infants, children and young people)

No evidence was identified.

12.2 Recommendations and link to evidence

12.2.1 Adults

Recommendations	**50. Discuss with adults with a heel pressure ulcer and, if appropriate, their family or carers, a strategy to offload heel pressure as part of their individualised care plan.**
Relative values of different outcomes	The GDG identified that the proportion of people with pressure ulcers completely healed, time to complete healing, reduction in size and volume and rate of reduction in size and volume of pressure ulcers were the most critical outcomes to inform decision making.
Trade off between clinical benefits and harms	There was limited evidence from 4 studies, which included widely varying management techniques for the management of heel pressure ulcers. One study included 2 types of alternating pressure mattresses with pressure-relieving cushions and found 1 alternating pressure mattress (NIMBUS system) was more clinically beneficial than another alternating pressure mattress (CAREWAVE system) for complete healing of grade 2 and above heel pressure ulcers. There was, however, a difference in repositioning between the 2 arms which could confound results. One study looked at topical nerve growth factor (2.5S murine nerve growth factor) which was more clinically beneficial than placebo for the reduction in heel pressure ulcer area for grade 2 and above heel pressure ulcers. Another study on dressings identified that collagen dressing was more clinically beneficial for complete healing of heel pressure ulcers than hydrocolloid dressing. A final study found that a nutritional supplement, ornithine alpha-ketoglutarate, was clinically more beneficial than placebo for the percentage reduction in heel pressure ulcer size and 90% reduction in heel pressure ulcers. The GDG considered this information and noted that the management of heel ulcers had not been excluded from the other recommendations which had been drafted on ulcer management. Therefore it was decided that no individual recommendations relating to the management of heel ulcers using the interventions included in the guideline were needed. However, the GDG felt that it was important to highlight that people who had a heel pressure ulcer should be provided with a heel elevation strategy to ensure that pressure is relieved from the heel. No evidence to support a specific strategy was identified.
Economic considerations	One economic analysis was identified for this question however this looked at dressings rather than heel elevation strategies.

	Once a heel pressure ulcer has developed, pressure must be relieved from the heels. The GDG acknowledged that there may be resource implications associated with a heel elevation strategy, but asserted that pressure must be relieved immediately to prevent further pressure damage. Further pressure damage would lead to reductions in quality of life and escalated treatment costs.
Quality of evidence	There was little evidence on the management of heel pressure ulcers. The evidence available was graded low to very low due to serious or very serious imprecision and study limitations. There were no interventions specifically aimed at managing heel pressure ulcers.
Other considerations	Heel ulcers are often found in association with peripheral arterial disease and recommendations on the management of peripheral arterial disease can be found in NICE clinical guideline147 'Lower limb peripheral arterial disease'. For recommendations on the prevention of heel pressure ulcers please see part 1 'Prevention of pressure ulcers'.

12.2.2 Neonates, infants, children and young people

Recommendations	**51. Discuss with the parents or carers of neonates and infants and with children and young people (and their parents or carers if appropriate) a strategy to offload heel pressure as part of their individualised care plan to manage their heel pressure ulcer, taking into account differences in size, mobility, pain and tolerance.**
Relative values of different outcomes	The GDG identified that the proportion of people with pressure ulcers completely healed, time to complete healing, reduction in size and volume and rate of reduction in size and volume of pressure ulcers were the most critical outcomes to inform decision making.
Trade off between clinical benefits and harms	The GDG used 1 statement from the Delphi consensus panel to develop the recommendation, 'Healthcare professionals should treat heel pressure ulcers in neonates, infants, children and young people in line with treatments for adults.' The statement was not accepted during Round 1 of the Delphi consensus survey. The GDG therefore discussed treatment of heel pressure ulcers. Comments received during Round 1 had highlighted that although treatment in children was likely to be similar to adults, there may be differences arising from variation in size, mobility and tolerability and the statement was amended to reflect this. The statement 'Healthcare professionals should treat heel pressure ulcers in neonates, infants, children and young people in line with treatment for adults, taking in account differences in size, mobility and tolerability.' was therefore included in round 2 of the survey. The statement was accepted. Qualitative responses gathered during round 2 of the survey highlighted that there was limited evidence relating to neonates, infants, children and young people and supported the statement. The GDG therefore chose to develop a recommendation highlighting that the treatment of heel pressure ulcers in neonates, infants, children and young people was likely to be similar to adults and was likely to focus on pressure redistribution using appropriate strategies.
Economic considerations	The GDG agreed that the cost-effective strategies for the treatment of heel pressure ulcers were likely to be similar to those identified for adults. Additional considerations of size, mobility and pain tolerance will allow more effective, efficient treatment, and mean economic and clinical benefits can be realised as early as

	possible.
Quality of evidence	No RCTs or cohort studies were identified for neonates, infants, children or young people. Formal consensus using a modified Delphi was therefore used to develop the recommendation. To inform the recommendation, the GDG used 1 statement which was included in Round 1 of the Delphi consensus survey and reached 43% consensus agreement. The latter statement was therefore included in Round 2 of the survey, where it reached 84% consensus agreement. Further details can be found in Appendix N.
Other considerations	The GDG noted that in neonates, infants, children and young people there were specific at risk sites which should be considered, for example the head and scalp, in addition to heels.

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14 Acronyms and abbreviations

ACA	Available case analysis
APAM	Alternative pressure air mattress
AUC	Area under the curve
CBA	Cost benefit analysis
CCA	Cost consequences analysis
CEA	Cost effectiveness analysis
CUA	Cost utility analysis
CI	Confidence interval
CLP	Continuous low pressure
CLP	Continuous low pressure
DMSO	Dimethyl sulfoxide
EPUAP	European pressure ulcer advisory panel
GDG	Guideline Development Group
GRADE	Grading of Recommendations Assessment, Development and Evaluation
HBOT	Hyperbaric oxygen therapy
HR	Hazard ratio
ICER	Incremental cost effectiveness ratio
ICU	Intensive care unit
IDL	Indentation load deflection
INB	Incremental net benefit
IQR	Inter quartile range
ISO	Inflated static overlay
ITT	Intention to treat
LALDM	Low air loss dynamic mattress
MID	Minimal important difference
MSO	Microfluid static overlay
NBE	Non-blanchable erythema
NCGC	National Clinical Guideiline Centre
NHS	National health service
NICE	National Institute for Health and Care Excellence
NNT	Number needed to treat
NPV	Negative predictive value
NPWT	Negative pressure wound therapy
OR	Odds ratio
PPV	Positive predictive value
PUM	Poly-urethane mattress
QALY	Quality adjusted life year
RCT	Randomised controlled trial
ROC	Receiver operator curve
RR	Relative risk
SD	Standard deviation
SFC	Standard foam cushion

SFM	Standard foam mattress
SHM	Standard hospital mattress

15 Glossary

Abstract	Summary of a study, which may be published alone or as an introduction to a full scientific paper.
Algorithm (in guidelines)	A flow chart of the clinical decision pathway described in the guideline, where decision points are represented with boxes, linked with arrows.
Allocation concealment	The process used to prevent advance knowledge of group assignment in an RCT. The allocation process should be impervious to any influence by the individual making the allocation, by being administered by someone who is not responsible for recruiting participants.
Applicability	How well the results of a study or NICE evidence review can answer a clinical question or be applied to the population being considered.
Arm (of a clinical study)	Subsection of individuals within a study who receive 1 particular intervention, for example placebo arm
Association	Statistical relationship between two or more events, characteristics or other variables. The relationship may or may not be causal.
Autolysis	Autolysis is the disintegration of devitalised cells or tissues by natural enzymes. During autolytic debridement, the process may be facilitated by the use of a dressing.
Baseline	The initial set of measurements at the beginning of a study (after run-in period where applicable), with which subsequent results are compared.
Bias	Influences on a study that can make the results look better or worse than they really are. (Bias can even make it look as if a treatment works when it does not.) Bias can occur by chance, deliberately or as a result of systematic errors in the design and execution of a study. It can also occur at different stages in the research process, for example, during the collection, analysis, interpretation, publication or review of research data. For examples see selection bias, performance bias, information bias, confounding factor, and publication bias.
Blanchable erythema	See erythema
Blinding	A way to prevent researchers, doctors and patients in a clinical trial from knowing which study group each patient is in so they cannot influence the results. The best way to do this is by sorting patients into study groups randomly. The purpose of 'blinding' or 'masking' is to protect against bias. A single-blinded study is 1 in which patients do not know which study group they are in (for example whether they are taking the experimental drug or a placebo). A double-blinded study is 1 in which neither patients nor the researchers/doctors know which study group the patients are in. A triple blind study is 1 in which neither the patients, clinicians or the people carrying out the statistical analysis know which treatment patients received.
Carer (caregiver)	Someone who looks after family, partners or friends in need of help because they are ill, frail or have a disability.
Categorisation	The process of determining the severity of the pressure ulcer in order to guide management.
Child	Person aged between 1 to 13 years
Clinical efficacy	The extent to which an intervention is active when studied under controlled research conditions.
Clinical effectiveness	How well a specific test or treatment works when used in the 'real world' (for example, when used by a doctor with a patient at home), rather than in a carefully controlled clinical trial. Trials that assess clinical effectiveness are sometimes called management trials. Clinical effectiveness is not the same as efficacy.

Clinician	A healthcare professional who provides patient care. For example, a doctor, nurse or physiotherapist.
Cochrane Review	The Cochrane Library consists of a regularly updated collection of evidence-based medicine databases including the Cochrane Database of Systematic Reviews (reviews of randomised trials prepared by the Cochrane Collaboration).
Cohort study	A study with two or more groups of people - cohorts - with similar characteristics. One group receives a treatment, is exposed to a risk factor or has a particular symptom and the other group does not. The study follows their progress over time and records what happens. See also observational study.
Comorbidity	A disease or condition that someone has in addition to the health problem being studied or treated.
Comparability	Similarity of the groups in characteristics likely to affect the study results (such as health status or age).
Confidence interval (CI)	There is always some uncertainty in research. This is because a small group of patients is studied to predict the effects of a treatment on the wider population. The confidence interval is a way of expressing how certain we are about the findings from a study, using statistics. It gives a range of results that is likely to include the 'true' value for the population. The CI is usually stated as '95% CI', which means that the range of values has a 95 in a 100 chance of including the 'true' value. For example, a study may state that 'based on our sample findings, we are 95% certain that the 'true' population blood pressure is not higher than 150 and not lower than 110'. In such a case the 95% CI would be 110 to 150. A wide confidence interval indicates a lack of certainty about the true effect of the test or treatment - often because a small group of patients has been studied. A narrow confidence interval indicates a more precise estimate (for example, if a large number of patients have been studied).
Confounding factor	Something that influences a study and can result in misleading findings if it is not understood or appropriately dealt with. For example, a study of heart disease may look at a group of people that exercises regularly and a group that does not exercise. If the ages of the people in the two groups are different, then any difference in heart disease rates between the two groups could be because of age rather than exercise. Therefore age is a confounding factor.
Consensus methods	Techniques used to reach agreement on a particular issue. Consensus methods may be used to develop NICE guidance if there is not enough good quality research evidence to give a clear answer to a question. Formal consensus methods include Delphi and nominal group techniques.
Control group	A group of people in a study who do not receive the treatment or test being studied. Instead, they may receive the standard treatment (sometimes called 'usual care') or a dummy treatment (placebo). The results for the control group are compared with those for a group receiving the treatment being tested. The aim is to check for any differences. Ideally, the people in the control group should be as similar as possible to those in the treatment group, to make it as easy as possible to detect any effects due to the treatment.
Cost–benefit analysis (CBA)	Cost-benefit analysis is 1 of the tools used to carry out an economic evaluation. The costs and benefits are measured using the same monetary units (for example, pounds sterling) to see whether the benefits exceed the costs.
Cost–consequences analysis	Cost-consequence analysis is 1 of the tools used to carry out an economic

(CCA)	evaluation. This compares the costs (such as treatment and hospital care) and the consequences (such as health outcomes) of a test or treatment with a suitable alternative. Unlike cost-benefit analysis or cost-effectiveness analysis, it does not attempt to summarise outcomes in a single measure (like the quality-adjusted life year) or in financial terms. Instead, outcomes are shown in their natural units (some of which may be monetary) and it is left to decision-makers to determine whether, overall, the treatment is worth carrying out.
Cost-effectiveness analysis (CEA)	Cost-effectiveness analysis is 1 of the tools used to carry out an economic evaluation. The benefits are expressed in non-monetary terms related to health, such as symptom-free days, heart attacks avoided, deaths avoided or life years gained (that is, the number of years by which life is extended as a result of the intervention).
Cost-effectiveness model	An explicit mathematical framework, which is used to represent clinical decision problems and incorporate evidence from a variety of sources in order to estimate the costs and health outcomes.
Cost–utility analysis (CUA)	Cost-utility analysis is 1 of the tools used to carry out an economic evaluation. The benefits are assessed in terms of both quality and duration of life, and expressed as quality-adjusted life years (QALYs). See also utility.
Debridement	The process of removal of devitalised (dead or dying) tissue from an ulcer. Types of debridement include: Autolytic: the removal of devitalised tissue by the body's own mechanisms Mechanical: the removal of devitalised tissue by physical forces such as with scissors or scalpels. Larval: the use of maggots to remove devitalised tissue
Decision analysis	An explicit quantitative approach to decision-making under uncertainty, based on evidence from research. This evidence is translated into probabilities, and then into diagrams or decision trees which direct the clinician through a succession of possible scenarios, actions and outcomes.
Diascopy	A test, used to identify non-blanchable erythema, by putting pressure on the surface of the skin and observing colour changes. Pressure may be placed on the skin using a transparent disk or a finger.
Discounting	Costs and perhaps benefits incurred today have a higher value than costs and benefits occurring in the future. Discounting health benefits reflects individual preference for benefits to be experienced in the present rather than the future. Discounting costs reflects individual preference for costs to be experienced in the future rather than the present.
Dominance	A health economics term. When comparing tests or treatments, an option that is both less effective and costs more is said to be 'dominated' by the alternative.
Dressings	Materials applied to a wound for a variety of reasons, including protection, absorption, and hydration.
Drop-out	A participant who withdraws from a trial before the end.
Economic evaluation	An economic evaluation is used to assess the cost effectiveness of healthcare interventions (that is, to compare the costs and benefits of a healthcare intervention to assess whether it is worth doing). The aim of an economic evaluation is to maximise the level of benefits - health effects - relative to the resources available. It should be used to inform and support the decision-making process; it is not supposed to replace the judgement of healthcare professionals. There are several types of economic evaluation: cost-benefit analysis, cost-consequence analysis, cost-effectiveness analysis, cost-minimisation analysis and cost-utility analysis. They use similar methods to define and evaluate costs, but differ in the way they estimate the benefits of a

	particular drug, programme or intervention.
Effect (as in effect measure, treatment effect, estimate of effect, effect size)	A measure that shows the magnitude of the outcome in 1 group compared with that in a control group. For example, if the absolute risk reduction is shown to be 5% and it is the outcome of interest, the effect size is 5%. The effect size is usually tested, using statistics, to find out how likely it is that the effect is a result of the treatment and has not just happened by chance (that is, to see if it is statistically significant).
Effectiveness	How beneficial a test or treatment is under usual or everyday conditions, compared with doing nothing or opting for another type of care.
Efficacy	How beneficial a test, treatment or public health intervention is under ideal conditions (for example, in a laboratory), compared with doing nothing or opting for another type of care.
Electrotherapy	The use of an electrical current, delivered in various ways, to stimulate wound healing.
Epidemiological study	The study of a disease within a population, defining its incidence and prevalence and examining the roles of external influences (for example, infection, diet) and interventions.
Erythema	Redness of the skin due to dilation of superficial capillaries. Erythema is blanchable when the area turns white or pale temporarily with the application of pressure. Non-blanchable erythema retains redness on the application of pressure.
EQ-5D (EuroQol 5 dimensions)	A standardised instrument used to measure health-related quality of life. It provides a single index value for health status.
Evidence	Information on which a decision or guidance is based. Evidence is obtained from a range of sources including randomised trials, observational studies, expert opinion (of clinical professionals or patients).
Exclusion criteria (literature review)	Explicit standards used to decide which studies should be excluded from consideration as potential sources of evidence.
Exclusion criteria (clinical study)	Criteria that define who is not eligible to participate in a clinical study.
Extended dominance	If Option A is both more clinically effective than Option B and has a lower cost per unit of effect, when both are compared with a do-nothing alternative then Option A is said to have extended dominance over Option B. Option A is therefore more cost effective and should be preferred, other things remaining equal.
Extrapolation	An assumption that the results of studies of a specific population will also hold true for another population with similar characteristics.
Follow-up	Observation over a period of time of an individual, group or initially defined population whose appropriate characteristics have been assessed in order to observe changes in health status or health-related variables.
Generalisability	The extent to which the results of a study hold true for groups that did not participate in the research. See also external validity.
Gold standard	A method, procedure or measurement that is widely accepted as being the best available to test for or treat a disease.
GRADE, GRADE Profile	A system developed by the GRADE (Grading of Recommendations Assessment, Development and Evaluation) Working Group to address the shortcomings of present grading systems in healthcare. The GRADE system uses a common, sensible and transparent approach to grading the quality of evidence. The results of applying the GRADE system to clinical trial data are displayed in a table known as a GRADE profile.

Harms	Adverse effects of an intervention.
Health economics	Study or analysis of the cost of using and distributing healthcare resources.
Health-related quality of life (HRQoL)	A measure of the effects of an illness to see how it affects someone's day-to-day life.
Heel devices	Equipment or materials with known pressure redistributing/alleviating properties to minimise the effects of pressure on the heel.
Heterogeneity or Lack of homogeneity	The term is used in meta-analyses and systematic reviews to describe when the results of a test or treatment (or estimates of its effect) differ significantly in different studies. Such differences may occur as a result of differences in the populations studied, the outcome measures used or because of different definitions of the variables involved. It is the opposite of homogeneity.
High specification foam mattress	Mattresses made of high density foam or visco-elastic foam which conforms to the body contours resulting in superior pressure reduction to the standard hospital foam mattress.
High risk	Neonates, infants, children and young people considered to be at high risk of developing a pressure ulcer will usually have more than 1 risk factor (for example, significantly limited mobility, risk of nutritional deficiency, inability to reposition themselves, a neurological condition, significant cognitive impairment) identified during risk assessment with or without a validated scale. Those with a history of pressure ulcers are also considered to be at high risk.
Hydration	The provision of an adequate fluid intake to meet all bodily needs and replace any losses.
Hyperbaric oxygen therapy	The use of above atmospheric pressure to increase the oxygen supply to the wound bed and possibly promote wound healing.
Imprecision	Results are imprecise when studies include relatively few patients and few events and thus have wide confidence intervals around the estimate of effect.
Inclusion criteria (literature review)	Explicit criteria used to decide which studies should be considered as potential sources of evidence.
Infant	Person under 1 year of age
Incremental analysis	The analysis of additional costs and additional clinical outcomes with different interventions.
Incremental cost	The extra cost linked to using 1 test or treatment rather than another. Or the additional cost of doing a test or providing a treatment more frequently.
Incremental cost-effectiveness ratio (ICER)	The difference in the mean costs in the population of interest divided by the differences in the mean outcomes in the population of interest for 1 treatment compared with another.
Incremental net benefit (INB)	The value (usually in monetary terms) of an intervention net of its cost compared with a comparator intervention. The INB can be calculated for a given cost-effectiveness (willingness to pay) threshold. If the threshold is £20,000 per QALY gained then the INB is calculated as: (£20,000 x QALYs gained) – Incremental cost.
Indirectness	The available evidence is different to the review question being addressed, in terms of PICO (population, intervention, comparison and outcome).
Intention to treat analysis (ITT)	An assessment of the people taking part in a clinical trial, based on the group they were initially (and randomly) allocated to. This is regardless of whether or not they dropped out, fully complied with the treatment or switched to an alternative treatment. Intention-to-treat analyses are often used to assess clinical effectiveness because they mirror actual practice: that is, not everyone complies with treatment and the treatment people

	receive may be changed according to how they respond to it.
Intervention	In medical terms this could be a drug treatment, surgical procedure, diagnostic or psychological therapy. Examples of public health interventions could include action to help someone to be physically active or to eat a more healthy diet.
Intraoperative	The period of time during a surgical procedure.
Kappa statistic	A statistical measure of inter-rater agreement that takes into account the agreement occurring by chance.
Length of stay	The total number of days a participant stays in hospital.
Licence	See 'Product licence'.
Life years gained	Mean average years of life gained per person as a result of the intervention compared with an alternative intervention.
Likelihood ratio	The likelihood ratio combines information about the sensitivity and specificity. It tells you how much a positive or negative result changes the likelihood that a patient would have the disease. The likelihood ratio of a positive test result (LR+) is sensitivity divided by (1 minus specificity).
Long-term care	Residential care in a home that may include skilled nursing care and help with everyday activities. This includes nursing homes and residential homes.
Markov model	A method for estimating long-term costs and effects for recurrent or chronic conditions, based on health states and the probability of transition between them within a given time period (cycle).
Mattress overlay	An overlay which lies on top of the base mattress and may have pressure reducing, pressure redistributing or pressure relieving properties.
Meta-analysis	A method often used in systematic reviews. Results from several studies of the same test or treatment are combined to estimate the overall effect of the treatment.
Moisture lesion	A moisture lesion can be defined as localised injury to the skin initiated by the effects of moisture.
Multivariate model	A statistical model for analysis of the relationship between two or more predictor (independent) variables and the outcome (dependent) variable.
Negative predictive value (NPV)	In screening or diagnostic tests: A measure of the usefulness of a screening or diagnostic test. It is the proportion of those with a negative test result who do not have the disease, and can be interpreted as the probability that a negative test result is correct.
Negative pressure wound therapy (NPWT)	The use of negative pressure with the aim of promoting wound healing by enhancing nutrient and oxygen delivery, removal of wound exudate, promotion of granulation tissue, promotion of angiongenesis, and the removal of wound inhibitory factors.
Neonate	A baby under 4 weeks of age
Non-blanchable erythema	See erythema
Number needed to treat (NNT)	The average number of patients who need to be treated to get a positive outcome. For example, if the NNT is four, then 4 patients would have to be treated to ensure 1 of them gets better. The closer the NNT is to 1, the better the treatment. For example, if you give a stroke prevention drug to 20 people before 1 stroke is prevented, the number needed to treat is 20. See also number needed to harm, absolute risk reduction.
Nutrition	The provision of all essential food components (including macro and micro nutrients) to maintain current body function and growth whilst also meeting any additional needs associated with promoting pressure ulcer healing and other metabolic stresses.
Observational study	Individuals or groups are observed or certain factors are measured. No

	attempt is made to affect the outcome. For example, an observational study of a disease or treatment would allow 'nature' or usual medical care to take its course. Changes or differences in 1 characteristic (for example, whether or not people received a specific treatment or intervention) are studied without intervening. There is a greater risk of selection bias than in experimental studies.
Odds ratio	Odds are a way to represent how likely it is that something will happen (the probability). An odds ratio compares the probability of something in 1 group with the probability of the same thing in another. An odds ratio of 1 between two groups would show that the probability of the event (for example a person developing a disease, or a treatment working) is the same for both. An odds ratio greater than 1 means the event is more likely in the first group. An odds ratio less than 1 means that the event is less likely in the first group. Sometimes probability can be compared across more than two groups - in this case, 1 of the groups is chosen as the 'reference category', and the odds ratio is calculated for each group compared with the reference category. For example, to compare the risk of dying from lung cancer for non-smokers, occasional smokers and regular smokers, non-smokers could be used as the reference category. Odds ratios would be worked out for occasional smokers compared with non-smokers and for regular smokers compared with non-smokers. See also confidence interval, relative risk, risk ratio.
Opportunity cost	The loss of other health care programmes displaced by investment in or introduction of another intervention. This may be best measured by the health benefits that could have been achieved had the money been spent on the next best alternative healthcare intervention.
Outcome	The impact that a test, treatment, policy, programme or other intervention has on a person, group or population. Outcomes from interventions to improve the public's health could include changes in knowledge and behaviour related to health, societal changes (for example, a reduction in crime rates) and a change in people's health and wellbeing or health status. In clinical terms, outcomes could include the number of patients who fully recover from an illness or the number of hospital admissions, and an improvement or deterioration in someone's health, functional ability, symptoms or situation. Researchers should decide what outcomes to measure before a study begins.
P-value	The p value is a statistical measure that indicates whether or not an effect is statistically significant. For example, if a study comparing two treatments found that 1 seems more effective than the other, the p value is the probability of obtaining these results by chance. By convention, if the p value is below 0.05 (that is, there is less than a 5% probability that the results occurred by chance) it is considered that there probably is a real difference between treatments. If the p value is 0.001 or less (less than a 1% probability that the results occurred by chance), the result is seen as highly significant. If the p value shows that there is likely to be a difference between treatments, the confidence interval describes how big the difference in effect might be.
Perioperative	The period from admission through surgery until discharge, encompassing the pre-operative and post-operative periods.
Placebo	A fake (or dummy) treatment given to participants in the control group of a clinical trial. It is indistinguishable from the actual treatment (which is given to participants in the experimental group). The aim is to determine what effect the experimental treatment has had - over and above any placebo effect caused because someone has received (or thinks they have received)

	care or attention.
Polypharmacy	The use or prescription of multiple medications.
Positive predictive value (PPV)	In screening or diagnostic tests: A measure of the usefulness of a screening or diagnostic test. It is the proportion of those with a positive test result who have the disease, and can be interpreted as the probability that a positive test result is correct.
Postoperative	Pertaining to the period after patients leave the operating theatre, following surgery.
Power (statistical)	The ability to demonstrate an association when 1 exists. Power is related to sample size; the larger the sample size, the greater the power and the lower the risk that a possible association could be missed.
Preoperative	The period before surgery commences.
Pressure redistributing devices	The use of a support surface to distribute weight over the contact areas of the human body. This term replaces prior terminology of pressure reduction and pressure relief surfaces.
Pressure ulcer	A pressure ulcer is a localized injury to the skin and/or underlying tissue 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 is yet to be elucidated. This term replaces prior terminology pressure sore or bed sore.
Prevention	To keep something from happening. Interventions before the initial onset of a condition through the reduction of risk factors and the enhancement of protective factors in a targeted population
Primary care	Healthcare delivered outside hospitals. It includes a range of services provided by GPs, nurses, health visitors, midwives and other healthcare professionals and allied health professionals such as dentists, pharmacists and opticians.
Primary outcome	The outcome of greatest importance, usually the 1 in a study that the power calculation is based on.
Prognosis	A probable course or outcome of a disease. Prognostic factors are patient or disease characteristics that influence the course. Good prognosis is associated with low rate of undesirable outcomes; poor prognosis is associated with a high rate of undesirable outcomes.
Prospective study	A research study in which the health or other characteristic of participants is monitored (or 'followed up') for a period of time, with events recorded as they happen. This contrasts with retrospective studies.
Publication bias	Publication bias occurs when researchers publish the results of studies showing that a treatment works well and don't publish those showing it did not have any effect. If this happens, analysis of the published results will not give an accurate idea of how well the treatment works. This type of bias can be assessed by a funnel plot.
Quality of life	See ‘Health-related quality of life’.
Quality-adjusted life year (QALY)	A measure of the state of health of a person or group in which the benefits, in terms of length of life, are adjusted to reflect the quality of life. One QALY is equal to 1 year of life in perfect health. QALYS are calculated by estimating the years of life remaining for a patient following a particular treatment or intervention and weighting each year with a quality of life score (on a zero to 1 scale). It is often measured in terms of the person's ability to perform the activities of daily life, freedom from pain and mental disturbance.
Randomisation	Assigning participants in a research study to different groups without taking any similarities or differences between them into account. For example, it

	could involve using a random numbers table or a computer-generated random sequence. It means that each individual (or each group in the case of cluster randomisation) has the same chance of receiving each intervention.
Randomised controlled trial (RCT)	A study in which a number of similar people are randomly assigned to two (or more) groups to test a specific drug or treatment. One group (the experimental group) receives the treatment being tested, the other (the comparison or control group) receives an alternative treatment, a dummy treatment (placebo) or no treatment at all. The groups are followed up to see how effective the experimental treatment was. Outcomes are measured at specific times and any difference in response between the groups is assessed statistically. This method is also used to reduce bias.
RCT	See 'Randomised controlled trial'.
Receiver operated characteristic (ROC) curve	A graphical method of assessing the accuracy of a diagnostic test. Sensitivity is plotted against 1 minus specificity. A perfect test will have a positive, vertical linear slope starting at the origin. A good test will be somewhere close to this ideal.
Reference standard	The test that is considered to be the best available method to establish the presence or absence of the outcome – this may not be the 1 that is routinely used in practice.
Relative risk (RR)	The ratio of the risk of disease or death among those exposed to certain conditions compared with the risk for those who are not exposed to the same conditions (for example, the risk of people who smoke getting lung cancer compared with the risk for people who do not smoke). If both groups face the same level of risk, the relative risk is 1. If the first group had a relative risk of 2, subjects in that group would be twice as likely to have the event happen. A relative risk of less than 1 means the outcome is less likely in the first group. Relative risk is sometimes referred to as risk ratio.
Reporting bias	See 'Publication bias'.
Resource implication	The likely impact in terms of finance, workforce or other NHS resources.
Retrospective study	A research study that focuses on the past and present. The study examines past exposure to suspected risk factors for the disease or condition. Unlike prospective studies, it does not cover events that occur after the study group is selected.
Review question	In guideline development, this term refers to the questions about treatment and care that are formulated to guide the development of evidence-based recommendations.
Risk assessment	A method of assessing the likelihood of developing pressure ulcers.
Risk assessment tools	Tools used to assess the likelihood of developing pressure ulcers, which can be used in combination with clinical judgement. A validated risk assessment tool has been co-oborated within the population it is designed for.
Secondary outcome	An outcome used to evaluate additional effects of the intervention deemed a priori as being less important than the primary outcomes.
Selection bias	Selection bias occurs if: a) The characteristics of the people selected for a study differ from the wider population from which they have been drawn, or b) There are differences between groups of participants in a study in terms of how likely they are to get better.
Sensitivity	How well a test detects the thing it is testing for. If a diagnostic test for a disease has high sensitivity, it is likely to pick up all cases of the disease in people who have it (that is, give a 'true positive'

	result). But if a test is too sensitive it will sometimes also give a positive result in people who don't have the disease (that is, give a 'false positive'). For example, if a test were developed to detect if a woman is 6 months pregnant, a very sensitive test would detect everyone who was 6 months pregnant, but would probably also include those who are 5 and 7 months pregnant. If the same test were more specific (sometimes referred to as having higher specificity), it would detect only those who are 6 months pregnant, and someone who was 5 months pregnant would get a negative result (a 'true negative'). But it would probably also miss some people who were 6 months pregnant (that is, give a 'false negative'). Breast screening is a 'real-life' example. The number of women who are recalled for a second breast screening test is relatively high because the test is very sensitive. If it were made more specific, people who don't have the disease would be less likely to be called back for a second test but more women who have the disease would be missed.
Sensitivity analysis	A means of representing uncertainty in the results of economic evaluations. Uncertainty may arise from missing data, imprecise estimates or methodological controversy. Sensitivity analysis also allows for exploring the generalisability of results to other settings. The analysis is repeated using different assumptions to examine the effect on the results. One-way simple sensitivity analysis (univariate analysis): each parameter is varied individually in order to isolate the consequences of each parameter on the results of the study. Multi-way simple sensitivity analysis (scenario analysis): two or more parameters are varied at the same time and the overall effect on the results is evaluated. Threshold sensitivity analysis: the critical value of parameters above or below which the conclusions of the study will change are identified. Probabilistic sensitivity analysis: probability distributions are assigned to the uncertain parameters and are incorporated into evaluation models based on decision analytical techniques (for example, Monte Carlo simulation).
Shear	The pressure caused when layers of skin are caused to slide over 1 another. This can happen when a person slides down a bed or is pulled up in bed. Stress caused by shear can contribute to the development of a pressure ulcer.
Significance (statistical)	A result is deemed statistically significant if the probability of the result occurring by chance is less than 1 in 20 ($p<0.05$).
Skin assessment	Methods used to assess skin status to identify potential risk of pressure ulcer development, or early signs of pressure damage. This may include the use of diascopy or the measurement of skin temperature.
Skin massage	Rubbing or kneading of parts of the skin, with the aim of reducing pressure ulceration.
Specificity	The proportion of true negatives that are correctly identified as such. For example in diagnostic testing the specificity is the proportion of non-cases correctly diagnosed as non-cases. See related term ‘Sensitivity’. In terms of literature searching a highly specific search is generally narrow and aimed at picking up the key papers in a field and avoiding a wide range of papers.
Stakeholder	An organisation with an interest in a topic that NICE is developing a clinical guideline or piece of public health guidance on. Organisations that register as stakeholders can comment on the draft scope and the draft guidance. Stakeholders may be:

	• manufacturers of drugs or equipment • national patient and carer organisations • NHS organisations • organisations representing healthcare professionals.
Systematic review	A review in which evidence from scientific studies has been identified, appraised and synthesised in a methodical way according to predetermined criteria. It may include a meta-analysis.
Systemic antimicrobials	An agent, that acts directly on a microorganism to destroy bacteria and prevent the development of new bacteria, viruses and fungi colonies, that is ingested by an individual as a means of treatment. These may include antiseptics, antiviral, antibiotic and antibacterial agents.
Time horizon	The time span over which costs and health outcomes are considered in a decision analysis or economic evaluation.
Topical antimicrobials	An agent, that acts directly on a microorganism to destroy the bacteria, viruses or fungi and prevent the development of new bacterial colonies, that is applied to the body's surface as a means of prevention/treatment of infection. These may include antiseptics, antibiotics and antibacterial agents.
Treatment allocation	Assigning a participant to a particular arm of a trial.
Ulcer assessment	Methods used to determine the area, depth and volume of a pressure ulcer.
Univariate	Analysis which separately explores each variable in a data set.
Utility	In health economics, a 'utility' is the measure of the preference or value that an individual or society places upon a particular health state. It is generally a number between zero (representing death) and 1 (perfect health). The most widely used measure of benefit in cost-utility analysis is the quality-adjusted life year, but other measures include disability-adjusted life years (DALYs) and healthy year equivalents (HYEs).
Young person	Person aged 13-18.

Appendices

Appendices A-O can be found in separate documents.