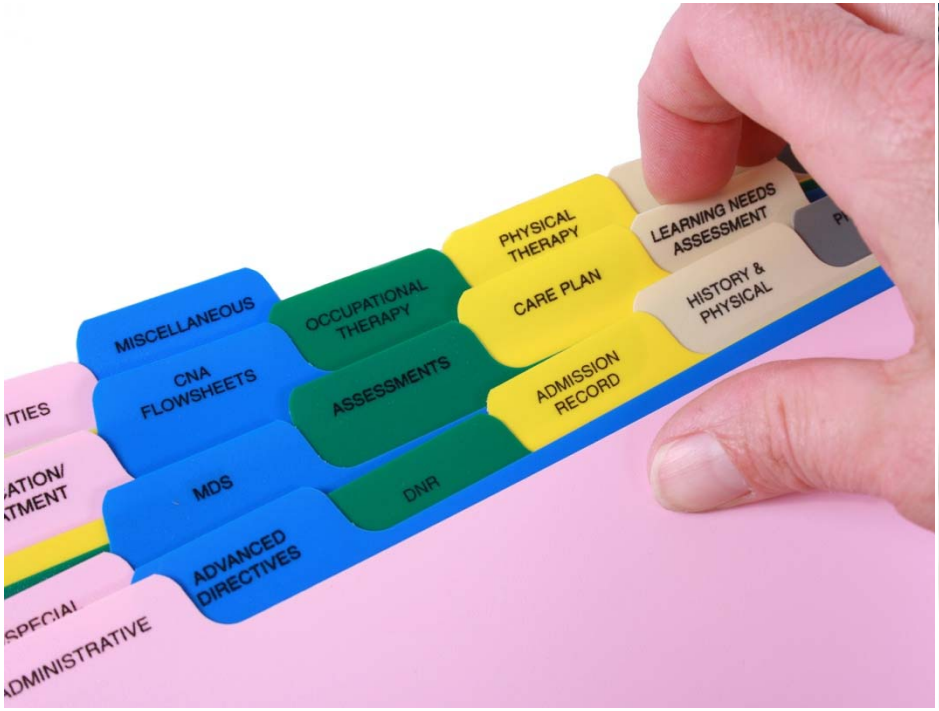
KCE REPORT 203

Federaal Kenniscentrum voor de Gezondheidszorg
Centre Fédéral d'Expertise des Soins de Santé
Belgian Health Care Knowledge Centre

A NATIONAL GUIDELINE FOR THE TREATMENT OF PRESSURE ULCERS



KCE REPORT 203
GOOD CLINICAL PRACTICE

Federaal Kenniscentrum voor de Gezondheidszorg
Centre Fédéral d'Expertise des Soins de Santé
Belgian Health Care Knowledge Centre

A NATIONAL GUIDELINE FOR THE TREATMENT OF PRESSURE ULCERS

DIMITRI BEECKMAN, CATHY MATHEÏ, AURÉLIE VAN LANCKER, GEERT VANWALLEGHEM, SABINE VAN HOUDT, LUC GRYSON, HILDE HEYMAN, CHRISTIAN THYSE, ADINDA TOPPETS, SABINE STORDEUR, KOEN VAN DEN HEEDE

COLOPHON

Title:	A national guideline for the treatment of pressure ulcers
Authors:	Dimitri Beeckman (UGent), Cathy Matheï (KULeuven), Aurélie Van Lancker (UGent), Geert Vanwalleghem (CNC vzw/ WCS/ AZ Delta), Sabine Van Houdt (KULeuven), Luc Gryson (CNC vzw), Hilde Heyman (WCS), Christian Thyse (AFISCeP.be), Adinda Toppets (UZLeuven), Sabine Stordeur (KCE), Koen Van den Heede (KCE)
External experts:	Diégo Backaert (Thuiszorg Groep Backaert); Hilde Beele (UZ Gent); Daniëlle Declercq (UMC Sint-Pieter); Anne Hermand (Cliniques uiversitaires Saint-Luc, Bruxelles); Aurore Lafosse (Cliniques universitaires Saint-Luc, Bruxelles); Dominique Putzeys (CIPIQ-s); Evelien Touriany (Militair Ziekenhuis Koningin Astrid); Dirk Van De Looverbosch (CRA Zorgbedrijf Antwerpen); Katrien Vanderwee (O.L.V. van Lourdes ziekenhuis Waregem).
Acknowledgements:	We thank Liz Avital (NCGC, UK), Katie Jones (NCGC, UK) and Julie Neilson (NCGC, UK) for the collaboration in the preparation of the evidence reports.
External validators:	Nicky Cullum (University of Manchester, United Kingdom); Bart Geurden (CEBAM); Sylvie Meaume (Hôpital Rothschild, France)
Other reported interests:	Dominique Putzeys and Dimitri Beeckman declared to have received funding for research related to the prevention and/or treatment of pressure ulcers. Diégo Backaert, Hilde Beele, Anne Hermand, Adinda Toppets, Geert Vanwalleghem, Dimitri Beeckman declared to have received a fee to lecture or reimbursement for training, travelling or participation to conferences related to the prevention and/or treatment of pressure ulcers

Publication date:	04 July 2013
Domain:	Good Clinical Practice (GCP)

MeSH: Pressure ulcer ; Practice Guidelines
NLM Classification: WR 598
Language: English
Format: Adobe® PDF™ (A4)
Legal depot: D/2013/10.273/30

How to refer to this document? Beeckman D, Matheï C, Van Lancker A, Vanwalleghem G, Van Houdt S, Gryson L, Heyman H, Thyse C, Toppets A, Stordeur S, Van Den Heede K. A national guideline for the treatment of pressure ulcers. Good Clinical Practice (GCP) Brussels: Belgian Health Care Knowledge Centre (KCE). 2013. KCE Reports 203. D/2013/10.273/30.

This document is available on the website of the Belgian Health Care Knowledge Centre.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF ABBREVIATIONS

ABBREVIATION	DEFINITION
AFM	Alternative Foam Mattress
AP	Alternating pressure
CDT	Clinical Decision Threshold
CI	Confidence Interval
CLP	Constant Low Pressure
CNC	Clinical Nursing Consulting
CPG	Clinical Practice Guideline
DMSO	Dimethyl sulfoxide
EPUAP	European Pressure Ulcer Advisory Panel
GDG	Guideline Development Group
HBOT	Hyperbaric Oxygen Therapy
IAD	Incontinence Associated Dermatitis
ICU	Intensive Care Unit
INAMI/RIZIV	Institut National d'Assurance Maladie-Invalidité - RijksInstituut voor Ziekte- en InvaliditeitsVerzekering
KCE	Belgian Healthcare Knowledge Centre
KUL	Katholieke Universiteit Leuven
LTC	Long term care
NBE	Non-blanchable eythema
NCGC	National Clinical Guideline Centre
NICE	National Institute for Health and Clinical Excellence
NPWT	Negative Pressure Wound Therapy
NPUAP	National Pressure Ulcer Advisory Panel
OIS	Optimal Information Size
PSST	Pressure Sore Status Tool
PICO	Population, Intervention, Comparison, Outcome
PU	Pressure ulcer

PUSH	Pressure Ulcer Scale for Healing
RCT	Randomized Controlled Trial
SFM	Standard Foam Mattress
UGENT	Universiteit Gent
WCS	VZW Wondzorgvereniging

SCIENTIFIC REPORT

1 INTRODUCTION

1.1 Background

A pressure ulcer can be defined as a localized injury of the skin and/or underlying tissue resulting from an internal response to an external mechanical load, applied to soft biological tissues, generally over a bony prominence. This external mechanical load can be a force perpendicular to the skin surface (pressure), a force parallel to the skin surface (shear), or a combination of pressure and shear.[1]

The aetiology of pressure ulcer development is multi-factorial. The role of individual factors, their importance and their interaction remain unknown.[2] Biomechanical research shows that a mechanical load will lead to (1) a reduced supply of oxygen in the tissue (leading to ischemia, including hypoxia, glucose depletion, and tissue acidification), (2) a reduced supply of nutrients, and (3) an accumulation of waste products.[2, 3] The role of other contributing factors, such as (1) direct cell deformation, (2) impaired lymphatic drainage, and (3) reperfusion damage is not yet fully understood.[3] Pressure ulcers most often develop over the sacrum, ischial tuberosities, trochanters, femoral condyles, malleoli, and heels.[4] Additionally, the National Pressure Ulcer Advisory Panel (NPUAP, USA) also recognizes the risk of pressure ulcer development beneath medical devices such as catheters, oxygen tubes, ventilator tubes, semi-rigid cervical collars.[1, 5]

The severity of a pressure ulcer varies from non-blanchable erythema of the intact skin to tissue destruction involving skin, subcutaneous fat, muscle and bone. Numerous tools have been developed to classify the severity of a pressure ulcer.[6, 7] In 1989, the National Pressure Ulcer Advisory Panel (NPUAP) developed a classification using four grades (Table 1). This classification was adopted by the European Pressure Ulcer Advisory Panel (EPUAP) in 1999 with some minor textual changes.[6] As part of a 2009 international guideline development process, NPUAP and EPUAP developed a common international classification system for pressure ulcers.[1]

In this classification system a pressure ulcer is defined as:

- Category I as a non-blanchable erythema of the intact skin;
- Category II as an abrasion or a blister;
- Category III as a superficial ulcer;
- Category IV as a deep ulcer.[1]

A Category II lesion should not be used to describe other superficial skin lesions such as skin tears, tape burns, incontinence associated dermatitis (IAD), maceration or excoriation.[1]

Table 1 – Classification of Pressure Ulcers according to NPUAP/EPUAP.

Category	Description
Category/Stage I Non-blanchable erythema	Intact skin with non-blanchable redness of a localized area usually over a bony prominence. Darkly pigmented skin may not have visible blanching; its colour may differ from the surrounding area. The area may be painful, firm, soft, warmer or cooler as compared to adjacent tissue. Category I may be difficult to detect in individuals with dark skin tones. May indicate “at risk” persons.
Category/Stage II Partial thickness skin loss	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-sanguineous filled blister. Presents as a shiny or dry shallow ulcer without slough or bruising. This category should not be used to describe skin tears, tape burns, incontinence associated dermatitis, maceration or excoriation.
Category/Stage III Full thickness skin loss	Full thickness skin loss. Subcutaneous fat may be visible but bone, tendon or muscle are not exposed. Slough may be present but does not obscure the depth of tissue loss. May include undermining and tunnelling. The depth of a Category/Stage III pressure ulcer varies by anatomical location. The bridge of the nose, ear, occiput and malleolus do not have (adipose) subcutaneous tissue and Category/Stage III ulcers can be shallow. In contrast, areas of significant adiposity can develop extremely deep Category/Stage III pressure ulcers. Bone/tendon is not visible or directly palpable.
Category/Stage IV Full thickness tissue loss	Full thickness tissue loss with exposed bone, tendon or muscle. Slough or eschar may be present. Often includes undermining and tunnelling. The depth of a Category/Stage IV pressure ulcer varies by anatomical location. The bridge of the nose, ear, occiput and malleolus do not have (adipose) subcutaneous tissue and these ulcers can be shallow. Category/Stage IV ulcers can extend into muscle and/or supporting structures (e.g., fascia, tendon or joint capsule) making osteomyelitis or osteitis likely to occur. Exposed bone/muscle is visible or directly palpable.

Source. European Pressure Ulcer Advisory PPUAP. Prevention and treatment of pressure ulcers: Clinical Practice Guideline. Washington (DC): 2009

1.2 Relevance of the guideline

In several European countries (Table 2), national prevalence studies had been conducted.[4, 8-11] The reported prevalence rates ranged from 8.9% to 18.1% in hospitals and from 6.4% to 31.4% in nursing homes. In Belgium, the prevalence of pressure ulcers had only been studied on a national level within the hospital setting (19 968 patients; 1 005 nursing units; 84 acute hospitals). Vanderwee et al. (2011)[4] reported a prevalence of 12.1% (Category I-IV). The comparison between countries remains difficult because of differences in pressure ulcer definitions, methods of data collection and patient population.[4]

Pressure ulcers are more likely to occur in sub-groups like spinal-cord injury patients[12], cachectic patients[13], patients treated in intensive care[14, 15] or geriatric units[15], patients with advanced incurable illness[16] and wheelchair bound patients.[17]

Pressure ulcers may cause pain and discomfort to the affected patients[16, 18], a prolonged and/or more frequent contact with the healthcare system[19-21] and their presence has been associated with an increased risk of mortality.[22, 23] In addition, the treatment of pressure ulcers is associated with considerable costs. Studies estimated the cost for treating pressure ulcers between 1% (the Netherlands)[24] and 4% (England)[25] of the total healthcare budget. A significant increase of the economic burden is expected because of the ageing population and an increase of patient comorbidities.

Table 2 – Prevalence of pressure ulcers in adults in a selection of European countries

Country	Setting	Study year	Prevalence (Grade I-IV)	Sample size (n)	Reference
Belgium	Hospitals	2008	12.1%	19 968	Vanderwee et al., 2011[4]
France	Hospitals	2004	8.9%	37 307	Barrois et al., 2008[8]
Germany	Hospitals	2004	9.0%	8 515	Tannen et al., 2008[11]
	Nursing Homes	2004	6.4%	2 531	Tannen et al., 2008[11]
Italy	Hospitals	2005	8.3%	1 097	Vanderwee et al., 2007a[15]
	Long- term care	2005	27.0%	571	Capon et al., 2007[9]
Portugal	Hospitals	2005	12.5%	786	Vanderwee et al., 2007a[15]
Sweden	Hospitals	2011	16.6%	16 466	Gunningberg et al., 2012[10]
	Nursing Homes	2011	14.5%	18 592	Gunningberg et al., 2012[10]
The Netherlands	Hospitals	2004	18.1%	10 237	Tannen et al., 2008[11]
	Nursing Homes	2004	31.4%	10 098	Tannen et al., 2008[11]

1.3 Scope

The aim of this study was to develop a clinical practice guideline (CPG) on the treatment of pressure ulcers in adults and children being admitted to hospitals, long-term care facilities (including nursing homes, rehabilitation facilities and long-term chronic care hospitals) and those receiving home care. The CPG will cover following topics:

- Nutrition for treatment;
- Devices for therapy (mattresses, overlays, beds, seatings, cushions);
- Debridement;
- Topical agents for treatment;
- Dressings for treatment;
- Indications for surgery;
- Systemic antimocrobial treatment;
- Electrotherapy;
- Light therapy;
- Hyperbaric oxygen therapy;
- Negative pressure wound therapy.

The recommendations are formulated in a generic way in order to be applicable to the majority of patients and settings. It may require adjustments and tailoring in specific conditions and for particular target groups.

The CPG will not cover management of incontinence associated dermatitis because of the unique nature and the specific aetiology of this skin disorder.[26] The guideline will be relevant to, but will not cover, other aspects of pressure ulcer risk assessment and prevention (e.g. identifying patients at risk of developing a pressure ulcer, the use of risk assessment scales, skin assessment, repositioning). Recommendations for these areas are included in the national guideline on the prevention of pressure ulcers that is published as a separate CPG.[27]

1.4 Remit of the guideline

1.4.1 Overall objectives

This guideline provides recommendations based on current scientific evidence for the treatment of patients with pressure ulcers. Clinicians are encouraged to interpret these recommendations in the context of the individual patient situation, values and preferences.

1.4.2 Target users of the guideline

This guideline is intended to be used by all care providers involved in the management of patients with pressure ulcers, including dermatologists, (plastic) surgeons, nurses, general practitioners, advanced practice nurses in wound care, dieticians. It could also be of particular interest for patients and their families, for hospital/nursing home managers and policy makers.

1.5 Statement of intent

Clinical Guidelines are designed to improve the quality of health care and decrease the use of unnecessary or harmful interventions. This guideline has been developed by clinicians, advanced practice nurses in wound care and researchers for use within the Belgian healthcare context. It provides advice regarding the care and management of patients with pressure ulcers.

The recommendations are not intended to indicate an exclusive course of action or to serve as a standard of care. Standards of care are determined on the basis of all clinical data available for an individual case and are subject to change as scientific knowledge and technology advance and patterns of care evolve. Variations, which take into account individual circumstances, clinical judgement and patient choice, may also be appropriate. The information in this guideline is not a substitute for proper diagnosis, treatment or the provision of advice by an appropriate health professional. It is advised, however, that significant deviations from the national guideline should be fully documented in the patient's file at the time the relevant decision is taken.

1.6 Funding and declaration of interest

The KCE is a federal institution which is financed for the largest part by INAMI/RIZIV, but also by the Federal Public Service of Health, food chain safety and environment, and Federal Public Service of social security. The Federal Public Service of Health, food chain safety and environment commissioned this guideline but did not have influence on the content of the guideline.

The development of clinical practice guidelines is part of the legal mission of the KCE. Although the development of the guidelines is paid by KCE budget, the sole mission of the KCE is providing scientifically valid information. The KCE has no interest in companies (commercial or not, e.g. hospital, university), associations (e.g. professional association, syndicate), individuals or organisations (e.g. lobby group) on which the guidelines could have a positive or negative impact (financial or other).

All clinicians involved in the Guideline Development Group (GDG) or the peer-review process completed a declaration of interest form. The information of possible conflicts of interest is published in the colophon of this report. All members of the KCE Expert Team make yearly declarations of interest and further details of these are available on request.

2 METHODOLOGY

2.1 Clinical questions

The clinical questions were the result of a scoping review of existing guidelines and consecutive discussions within the multidisciplinary research team (see Table 5) and the multidisciplinary expert panel (see also 1.1). The clinical questions were refined based on discussions with our international partner (see 2.2).

The CPG addresses the following clinical questions (for detailed protocols, see appendix 1-12):

1. **What are the most clinically effective nutritional interventions for the treatment of pressure ulcers?**

- Population: people of any age with existing pressure ulcers in any care setting;
- Intervention: nutritional interventions (supplementation or special diet) and hydration for treatment of pressure ulcers;
- Comparison: usual diet (including hospital diet); other supplementation; other special diet;
- Outcomes:
  - Critical outcomes for decision making: time to complete healing (time to event data), rate of complete healing (continuous data), rate of change in size and volume of ulcer (absolute and relative) (continuous data), reduction in size of ulcer and volume of ulcer, proportion of patients completely healed within trial period;
  - Important outcomes: wound-related pain, time in hospital or other health care setting (continuous data), patient acceptability e.g. measured by compliance and tolerance, side effects, health-related quality of life (continuous data or narratively summarised).

2. What are the most clinically effective pressure redistributing devices for the treatment of pressure ulcers?

- Population: people of any age with existing pressure ulcers in any care setting;
- Intervention:
  - Mattresses/overlays: standard foam mattresses, alternative foam mattresses/ overlays (e.g. convoluted foam, cubed foam), specialised foam mattresses, gel-filled mattresses/ overlays, fibre-filled mattresses/ overlays, air-filled mattresses/ overlays, water-filled mattresses/ overlays, bead-filled mattresses/ overlays, AP mattresses/ overlays (air-filled sacs which inflate and deflate), low-air-loss mattresses, operating-table overlays, sheepskins (synthetic/natural);
  - Beds: air-fluidised beds, low-air-loss beds – patients are supported on a series of air sacs through which warmed air passes, air flotation beds, bead-filled beds;
  - Seating: standard chair tilt in space, pressure relieving chairs;
  - Cushions: foam-filled cushions, gel-filled cushions, fluid-filled cushions, air/dry flotation cushions, alternating pressure cushions, tilt-in-space;
  - Wheelchair support surfaces;
  - Other: pillows, postural support, limb protectors: pads and cushions of different forms to protect bony prominences.
- Comparison: each other or no intervention.
- Outcomes:

Critical outcomes for decision making: time to complete healing (time to event data), rate of complete healing (continuous data), rate of change in size and volume of ulcer (absolute and relative) (continuous data), reduction in size of ulcer and volume of ulcer, proportion of patients completely healed within trial period;

Important outcomes: wound-related pain, time in hospital or other health care setting (continuous data), patient acceptability e.g. measured by compliance and tolerance, side effects, health-related quality of life (continuous data or narratively summarised).

3. What are the most clinically effective methods of debridement of non-viable tissue for treatment of pressure ulcers?

- Population: people of any age with existing pressure ulcers in any care setting;
- Intervention: debridement (sharp debridement, dressings which promote autolysis e.g. hydrogels and hydrocolloids, enzymatic, mechanical, maggot);
- Comparison: no debridement; comparison between debridement methods; other type of therapy for pressure ulcer treatment;
- Outcomes:
  - Critical outcomes for decision making: time to complete healing (time to event data), rate of complete healing (continuous data), rate of change in size and volume of ulcer (absolute and relative) (continuous data), reduction in size of ulcer and volume of ulcer, proportion of patients completely healed within trial period;
  - Important outcomes: wound-related pain, time in hospital or other health care setting (continuous data), patient acceptability e.g. measured by compliance and tolerance, side effects, health-related quality of life (continuous data or narratively summarised).

4. What are the most clinically effective topical agents for the treatment of pressure ulcers?

- Population: people of any age with existing pressure ulcers in any care setting;
- Intervention: topical agents (cleansers, moisturizers, protective agents, antiseptic agents, antibiotics, anti-inflammatory agents, anti-fungal agents);
- Comparison: no topical agent; comparison between topical agents; placebo; other type of therapy for pressure ulcer treatment;
- Outcomes:
  - Critical outcomes for decision making: time to complete healing (time to event data), rate of complete healing (continuous data), rate of change in size and volume of ulcer (absolute and relative) (continuous data), reduction in size of ulcer and volume of ulcer, proportion of patients completely healed within trial period;

- Important outcomes: wound-related pain, time in hospital or other health care setting (continuous data), patient acceptability e.g. measured by compliance and tolerance, side effects, health-related quality of life (continuous data or narratively summarised).

5. What are the most clinically effective dressings for the treatment of pressure ulcers?

- Population: people of any age with existing pressure ulcers in any care setting;
- Intervention: dressings (absorbing, impregnated, alginate, capillary, hydrocolloid, hydrofibre®, foam, collagen, hyaluronic acid, film, hydrogels);
- Comparison: no dressing; comparison between dressings; other type of therapy for pressure ulcer treatment;
- Outcomes:
  - Critical outcomes for decision making: time to complete healing (time to event data), rate of complete healing (continuous data), rate of change in size and volume of ulcer (absolute and relative) (continuous data), reduction in size of ulcer and volume of ulcer, proportion of patients completely healed within trial period;
  - Important outcomes: wound-related pain, time in hospital or other health care setting (continuous data), patient acceptability e.g. measured by compliance and tolerance, side effects, mortality (all cause) (dichotomous), health-related quality of life (continuous data or narratively summarised)

6. What are the indications for surgery for the treatment of pressure ulcers?

- Population: people of any age with existing pressure ulcers in any care setting;
- Intervention: surgery (flap reconstruction);
- Comparison: no surgery;
- Outcomes:
  - Critical outcomes for decision making: time to complete healing (time to event data), rate of complete healing (continuous data), rate of change in size and volume of ulcer (absolute and relative) (continuous data), reduction in size of ulcer and volume of ulcer, proportion of patients completely healed within trial period;
  - Important outcomes: wound-related pain, time in hospital or other health care setting (continuous data), patient acceptability e.g. measured by compliance and tolerance, side effects, mortality (all cause) (dichotomous), health-related quality of life (continuous data or narratively summarised).

7. What are the most clinically effective systemic agents for the treatment of pressure ulcers?

- Population: people of any age with existing pressure ulcers in any care setting;
- Intervention: systemic antimicrobials (systemic antibiotics, systemic antifungals);
- Comparison: no systemic antimicrobials; placebo; comparison between types of systemic antimicrobials; other type of therapy for pressure ulcer treatment;
- Outcomes:
  - Critical outcomes for decision making: time to complete healing (time to event data), rate of complete healing (continuous data), rate of change in size and volume of ulcer (absolute and relative) (continuous data), reduction in size of ulcer and volume of ulcer, proportion of patients completely healed within trial period;
  - Important outcomes: wound-related pain, time in hospital or other health care setting (continuous data), patient acceptability eg measured by compliance and tolerance, side effects, mortality (all cause) (dichotomous), health-related quality of life (continuous data or narratively summarised).

8. What is the clinical effectiveness of electrotherapy for the treatment of pressure ulcers?

- Population: people of any age with existing pressure ulcers in any care setting;
- Intervention: electrotherapy as treatment for people with pressure ulcers;
- Comparison: other type of therapy for pressure ulcer treatment;

- Outcomes:
  - Critical outcomes for decision making: time to complete healing (time to event data), rate of complete healing (continuous data), rate of change in size and volume of ulcer (absolute and relative) (continuous data), reduction in size of ulcer and volume of ulcer, proportion of patients completely healed within trial period;
  - Important outcomes: wound-related pain, time in hospital or other health care setting (continuous data), patient acceptability e.g. measured by compliance and tolerance, side effects, mortality (all cause) (dichotomous), health-related quality of life (continuous data or narratively summarised).

9. What is the effectiveness of light therapy for the treatment of pressure ulcers?

- Population: people of any age with existing pressure ulcers in any care setting;
- Intervention: light therapy (infrared, ultraviolet, laser, monochromatic, polarized light);
- Comparison: no therapy; comparison between light therapies; placebo; sham light therapy; other type of therapy for pressure ulcer treatment;
- Outcomes:
  - Critical outcomes for decision making: time to complete healing (time to event data), rate of complete healing (continuous data), rate of change in size and volume of ulcer (absolute and relative) (continuous data), reduction in size of ulcer and volume of ulcer, proportion of patients completely healed within trial period;
  - Important outcomes: wound-related pain, time in hospital or other health care setting (continuous data), patient acceptability e.g. measured by compliance and tolerance, side effects, mortality (all cause) (dichotomous), health-related quality of life (continuous data or narratively summarised).

10. What is the clinical effectiveness of hyperbaric oxygen therapy for the treatment of pressure ulcers?

- Population: people of any age with existing pressure ulcers in any care setting;
- Intervention: hyperbaric oxygen therapy as treatment for people with pressure ulcers;
- Comparison: Other type of therapy for pressure ulcer treatment;
- Outcomes:
  - Critical outcomes for decision making: time to complete healing (time to event data), rate of complete healing (continuous data), rate of change in size and volume of ulcer (absolute and relative) (continuous data), reduction in size of ulcer and volume of ulcer, proportion of patients completely healed within trial period;
  - Important outcomes: wound-related pain, time in hospital or other health care setting (continuous data), patient acceptability e.g. measured by compliance and tolerance, side effects, mortality (all cause) (dichotomous), health-related quality of life (continuous data or narratively summarised).

11. What is the clinical effectiveness of negative pressure wound therapy for the treatment of pressure ulcers?

- Population: people of any age with existing pressure ulcers in any care setting;
- Intervention: negative pressure wound therapy as treatment for people with pressure ulcers;
- Comparison: other type of therapy for pressure ulcer treatment;
- Outcomes:
  - Critical outcomes for decision making: time to complete healing (time to event data), rate of complete healing (continuous data), rate of change in size and volume of ulcer (absolute and relative) (continuous data), reduction in size of ulcer and volume of ulcer, proportion of patients completely healed within trial period;

- Important outcomes: wound-related pain, time in hospital or other health care setting (continuous data), patient acceptability eg measured by compliance and tolerance, side effects, mortality (all cause) (dichotomous), health-related quality of life (continuous data or narratively summarised).

12. What is the most clinically effective method for management of pressure ulcers of the heel?

- Population: people of any age with existing pressure ulcers in any care setting;
- Intervention: Interventions for management of heel ulcers: pressure-redistributing devices; repositioning; nutrition and hydration; electrotherapy; negative pressure wound therapy; hyperbaric oxygen therapy; debridement; topical agents; dressings.
- Comparison: each other or no intervention;
- Outcomes:
  - Critical outcomes for decision making: time to complete healing (time to event data), rate of complete healing (continuous data), rate of change in size and volume of ulcer (absolute and relative) (continuous data), reduction in size of ulcer and volume of ulcer, proportion of patients completely healed within trial period;
  - Important outcomes: wound-related pain, time in hospital or other health care setting (continuous data), patient acceptability e.g. measured by compliance and tolerance, side effects, health-related quality of life (continuous data or narratively summarised).

2.2 International collaboration

The National Clinical Guideline Centre[a] (NCGC) commissioned by The National Institute for Health and Clinical Excellence (NICE, United Kingdom) is currently producing a clinical guideline on the prevention and treatment of pressure ulcers to replace its existing guidelines.[28-30] The CPG will be developed de novo. The twelve research questions regarding treatment of pressure ulcers were in common with those of the KCE except for the research questions regarding the indications for surgery and light therapy which were covered only by KCE. The elaboration of the topics was divided between both organisations.

A collaboration agreement was set up between NCGC and KCE concerning following:

1. **Scope**: the collaboration concerned the search for evidence (search strategy + selection), quality appraisal, evidence tables and the development of the evidence reports. The formulation of evidence statements and recommendations was the responsibility of the two organisations separately.
2. **Form of cooperation**: one research question was elaborated both by KCE and NCGC (question 8), five research questions were elaborated by NCGC (questions 1, 2, 10, 11, 12), while the six other questions were elaborated by KCE (questions 3-7, 9).
3. **Cross-validation was done after each of the following steps**:
   - Development of the search strategy;
   - Selection of the literature;
   - Quality appraisal and elaboration of evidence tables;
   - Evidence report.

2.3 Literature review

2.3.1 Study design

For most questions, the search focused on high-quality systematic reviews (i.e. reviews matching the PICO's; extensive quality assessment; data available for GRADE input) on randomized controlled trials (RCTs) (see protocols in appendices 1-12 for more details). However, when RCTs were unavailable the search was expanded to observational studies (see protocols in appendices 1-12 for details).

[a] The National Clinical Guideline Centre (NCGC) is a multi-disciplinary health services research team funded by the National Institute for Health and Clinical Excellence (NICE). They produce evidence based clinical practice guidelines commissioned by NICE.

2.3.2 Databases and date limits

The following databases were included in the literature search (see appendices 1-12 for search strings):

- The Cochrane Database of systematic reviews (http://www.cochrane.org);
- Medline (http://www.ncbi.nlm.nih.gov/pubmed);
- Embase (http://www.embase.com/);
- CINAHL (http://www.cinahl.com).

The search was limited to articles published in English, French and Dutch for the evidence reports produced by KCE (Questions 3-7, 9) while for the evidence reports that were produced by NCGC (Questions 1, 2, 8, 10-12) searches were restricted to articles published in English. No date restriction was used.

All literature searches were done between September 2012 and April 2013. Search strategies were checked by reviewing the reference lists of relevant key papers and requesting the advice of the expert panel about additional papers.

2.3.3 Search strategy

A combination of appropriate MeSH terms and free text words was used (Appendices 1-12). The PICOs and the search strategy that correspond to research questions are documented in Appendices 1-12.

The identified studies were selected by one reviewer based on title and abstract. For all eligible studies, the full-text was retrieved. Studies were selected if relevant to the review question (PICO: population, intervention, comparison, outcome). A quality assurance check was performed by a second reviewer on 10% of the search results. In case no full-text was available, the study was not taken into account to develop the final recommendations.

2.3.4 Quality appraisal

A quality appraisal was done for each individual study and for each outcome. All critical appraisals were done by one researcher. The quality of the retrieved RCTs and observational studies was assessed using the corresponding checklists of the National Institute for Health and Clinical Excellence (NICE).[31]

2.4 Data extraction

For each primary study, data were extracted by one reviewer. Following study characteristics were tabulated using a standard template: reference, patient characteristics, intervention/comparison, outcome measures, effect size, comments. All evidence tables are reported in Appendices 1-12.

2.5 Analysis

A meta-analysis was done if possible using Revman-software (http://ims.cochrane.org/revman). The specific review strategies were defined in the study protocols (see appendices 1-12).

In general, studies were combined in a meta-analysis if the clinical (e.g. similar patient population, intervention, comparison, outcome) and statistical heterogeneity were acceptable. The unit of analysis was separated in studies measuring outcomes at the patient or ulcer level. The following groups were considered separately as strata (children and adults) or subgroups (different categories of pressure ulcers; different ulcer locations). In absence of appropriate data, forest plot(s) were generated for each outcome using single studies for didactic purposes.

Fixed-effects (Mantel-Haenszel) techniques were used to calculate risk ratios (relative risk) for the binary outcomes. The continuous outcomes were analysed using an inverse variance method for pooling weighted mean differences and where the studies had different scales, standardised mean differences were used. Statistical heterogeneity was assessed by considering the chi-squared test for significance at $p<0.1$ or an I-squared inconsistency statistic of >50% to indicate significant heterogeneity. In case of heterogeneity and a sufficient number of studies, sensitivity analyses were conducted based on risk of bias and pre-specified subgroup analyses were carried out as defined in the protocol. Assessments of potential differences in effect between subgroups were based on the chi-squared tests for heterogeneity statistics between subgroups. If no sensitivity analysis was found to completely resolve statistical heterogeneity then a random effects (DerSimonian and Laird) model was employed to provide a more conservative estimate of the effect.

The means and standard deviations of continuous outcomes were required for meta-analysis. However, in cases where standard deviations were not reported, the standard error was calculated if the p-values or 95% confidence intervals (CIs) were reported and meta-analysis was undertaken with the mean difference and standard error using the generic inverse variance method in Cochrane Review Manager (RevMan5) software. Where p-values were reported as "less than", a conservative approach was undertaken. For example, if p-value was reported as "p<0.001", the calculations for standard deviations were based on a p-value of 0.001.

2.6 Grading of evidence

For each recommendation, we provided its strength and the quality of the supporting evidence.[32] According to GRADE, we classified the quality of evidence into 4 categories: high, moderate, low, and very low (Table 3 and Table 4). The quality of evidence reflects the extent to which a guideline panel's confidence in an estimate of the effect was adequate to support a particular recommendation.

For RCTs, quality rating was initially considered to be of high level (Table 3). The rating was then downgraded if needed based on the judgement of the different quality elements. Each quality element considered to have serious or very serious risk of bias was rated down -1 or -2 points respectively. Judgement of the overall confidence in the effect estimate was also taken into account. We considered confidence in estimates as a continuum and the final rating of confidence could differ from that suggested by each separate domain.[33]

Observational studies were by default considered low level of evidence (Table 3 and Table 4). However, the level of evidence of observational studies with no threats to validity can be upgraded for a number of reasons:

1. Large magnitude of effects: The larger the magnitude of effect, the stronger becomes the evidence. As a rule of thumb, the following criteria were proposed by GRADE:
   a. Large, i.e. RR >2 or <0.5 (based on consistent evidence from at least 2 studies, with no plausible confounders): upgrade 1 level;
   b. Very large, i.e. RR >5 or <0.2 (based on direct evidence with no major threats to validity): upgrade 2 levels;
2. All plausible confounders: all plausible confounding from observational studies or randomized trials may be working to reduce the demonstrated effect or increase the effect if no effect was observed
3. Dose-response gradient: The presence of a dose-response gradient may increase our confidence in the findings of observational studies and thereby increase the quality of evidence.

The general principles used to downgrade the quality rating are summarized in Table 5. Decisions on downgrading with -1 or -2 points were based on the judgment of the assessors. Reasons for (no) downgrading were summarized in the GRADE profiles in Table 6.

Table 3 – A summary of the GRADE approach to grading the quality of evidence for each outcome.

Source of body of evidence	Initial rating of quality of a body of evidence	Factors that may decrease the quality	Factors that may increase the quality	Final quality of a body of evidence
Randomized trials	High	1. Risk of bias 2. Inconsistency 3. Indirectness 4. Imprecision 5. Publication bias	1. Large effect 2. Dose-response 3. All plausible residual confounding would reduce the demonstrated effect or would suggest a spurious effect if no effect was observed	High (⊕⊕⊕⊕) Moderate (⊕⊕⊕⊖) Low (⊕⊕⊖⊖) Very low (⊕⊖⊖⊖)
Observational studies	Low			

Source. Andrews J, Guyatt G, Oxman AD, Alderson P, Dahm P, Falck-Ytter Y, et al. GRADE guidelines: 15. Going from evidence to recommendations: the significance and presentation of recommendations. J Clin Epidemiol. 2013.

Table 4 – Levels of evidence according to the GRADE system.

Quality level	Definition	Methodological Quality of Supporting Evidence
High	We are very confident that the true effect lies close to that of the estimate of the effect	RCTs without important limitations or overwhelming evidence from observational studies
Moderate	We are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different	RCTs with important limitations (inconsistent results, methodological flaws, indirect, or imprecise) or exceptionally strong evidence from observational studies
Low	Our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect	RCTs with very important limitations or observational studies or case series
Very low	We have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of the effect	

Table 5 – Downgrading the quality rating of evidence using GRADE.

Quality element	Reasons for downgrading
Limitations	For each study reporting the selected outcome, possible risk of bias introduced by lack of allocation concealment, lack of blinding, lack of intention-to-treat analysis, loss of follow-up and selective outcome reporting were assessed. Additionally, other limitations such as stopping early for benefit and use of unvalidated outcome measures were taken into consideration. Level of evidence was downgraded if studies were of sufficiently poor quality. Downgrading was omitted if studies with low risk of bias were available that lead to similar conclusions as the studies with a high risk of bias.
Inconsistency	Downgrading the level of evidence for inconsistency of results was considered in the following situations: point estimates vary widely across studies, confidence intervals show minimal or no overlap, the statistical test for heterogeneity shows a low p-value or the I^2 is large. If large variability in magnitude of effect remained unexplained, the quality of evidence was rated down.
Indirectness	Quality rating was downgraded for indirectness in case the trial population or the applied intervention differed significantly from the population or intervention of interest. Also, the use of surrogate outcomes could lead to downgrading. A third reason for downgrading for indirectness occurred when the studied interventions were not tested in a head-to-head comparison.
Imprecision	Evaluation of the imprecision of results was primarily based on examination of the 95%CI. Quality was rated down if clinical action would differ if the upper versus the lower boundary of the 95%CI represented the truth. In general, 95%CIs around relative effects were used for evaluation, except when the event rate was low in spite of a large sample size. To examine the 95%CIs, the clinical decision threshold (CDT) was defined. When the 95%CI crossed this clinical decision threshold, the quality level was rated down. A relative risk reduction (RRR) of 25% was defined as CDT by default and adapted if deemed appropriate e.g. in case of a low risk intervention.
Reporting bias	Quality rating was downgraded for reporting bias if publication bias was suggested by analysis using funnel plots or searching of trial registries. Publication bias was also suspected if results came from small, positive industry-sponsored trials only.

2.7 Formulation of evidence statements

A subgroup of researchers (see Table 9) was responsible for systematic searches, retrieval and appraisal of the evidence and the writing of the evidence report (procedure used to draft evidence statements is described in appendix 13).

2.8 Formulation of recommendations

A second group within the research team drafted recommendations based on the retrieved evidence (Table 9) and assigned a grade of recommendation to each recommendation using the GRADE system (see tables 6 & 7).

A grade of recommendation was assigned to each recommendation using the GRADE system (Table 6). The strength of recommendations depends on a balance between all desirable and all undesirable effects of an intervention (i.e., net clinical benefit), quality of available evidence, values and preferences, and cost (resource utilization). Factors that influence the strength of a recommendation are reported in Table 7.

Table 6 – Strength of recommendations according to the GRADE system.

Grade	Definition
Strong	The desirable effects of an intervention clearly outweigh the undesirable effects *(the intervention is to be put into practice)*, or the undesirable effects of an intervention clearly outweigh the desirable effects *(the intervention is not to be put into practice)*
Weak	The desirable effects of an intervention probably outweigh the undesirable effects *(the intervention probably is to be put into practice)*, or the undesirable effects of an intervention probably outweigh the desirable effects *(the intervention probably is not to be put into practice)*

Table 7 – Factors that influence the strength of a recommendation.

Factor	Comment
Balance between desirable and undesirable effects	The larger the difference between the desirable and undesirable effects, the higher the likelihood that a strong recommendation is warranted. The narrower the gradient, the higher the likelihood that a weak recommendation is warranted
Quality of evidence	The higher the quality of evidence, the higher the likelihood that a strong recommendation is warranted
Values and preferences	The more values and preferences vary, or the greater the uncertainty in values and preferences, the higher the likelihood that a weak recommendation is warranted
Costs (resource allocation)	The higher the costs of an intervention—that is, the greater the resources consumed—the lower the likelihood that a strong recommendation is warranted

A strong recommendation implies that most patients would want the recommended course of action. A weak recommendation implies that the majority of informed patients would want the intervention, but many would not.[34] Specifically, a strong negative recommendation means the harms of the recommended approach clearly exceed the benefits whereas a weak negative recommendation implies that the majority of patients would not want the intervention, but many would. In the case of a weak recommendation, clinicians are especially required to spend adequate time with patients to discuss patients' values and preferences. Such an in-depth discussion is necessary for the patient to make the best decision. This may lead a significant proportion of patients to choose an alternative approach. Fully informed patients are in the best position to make decisions that are consistent with the best evidence and patients' values and preferences.

For policy-makers, a strong recommendation implies that variability in clinical practice between individuals or regions would likely be inappropriate whereas a weak recommendation implies that variability between individuals or regions may be appropriate, and use as a quality of care criterion is inappropriate.[34]

We offer the suggested interpretation of "strong" and "weak" recommendations in Table 8.[35]

Table 8 – Interpretation of strong and conditional (weak)* recommendations

Implications	Strong recommendation	Weak recommendation
For clinicians	Most individuals should receive the intervention. Adherence to this recommendation according to the guideline could be used as a quality criterion or performance indicator.	Recognize that different choices will be appropriate for individual patients and that you must help each patient arrive at a management decision consistent with his or her values and preferences. Decision aids may be useful helping individuals making decisions consistent with their values and preferences.
For policy makers	The recommendation can be adapted as policy in most situations.	Policy-making will require substantial debate and involvement of various stakeholders.

** the terms ''conditional'' and ''weak'' can be used synonymously*

Source. Fiocchi A, Schunemann HJ, Brozek J, Restani P, Beyer K, Troncone R, et al. Diagnosis and Rationale for Action Against Cow's Milk Allergy (DRACMA): a summary report. J Allergy Clin Immunol. 2010;126(6):1119-28 e12.

2.9 Formulation of best practices

Based on the evidence review, the research team (i.e. authors of this report) formulated recommendations. In addition best practices were formulated. The latter were not based on the evidence reviews but on two existing guidelines (i.e. EPUAP/NPUAP 2009[1] & NICE 2005[30]) that were retained after a comprehensive systematic search (see appendix 15 for details).

2.10 External review

2.10.1 Healthcare professionals

The draft of the evidence report, recommendations and best practices were circulated to the expert panel (table 10) prior to each face-to-face meeting. The expert panel that consisted of 1 home care nurse, 5 hospital nurses, 1 general practitioner and coordinating physician of a nursing home, 1 dermatologist and 1 plastic surgeon had the following tasks:

- To verify that the research is complete and that the interpretation of the evidence is correct;
- To assess the relevance of the conclusions and the selected studies in relation to the Belgian context;
- To verify the evidence statements;
- To participate in the drawing up of recommendations.

The expert panel met on 2 occasions: 12 March 2012 (review of topics and review protocols) and 18 April 2013 (review of evidence reports and recommendations/best practices).

All recommendations and best practices were reviewed by a panel of experts (i.e. 18/04/2013) using a formal procedure. Ten days before the final expert meeting, all experts received the recommendations and best practices. As a preparation of the meeting all invited experts were asked to score each recommendation on a 5-point Likert-scale, with a score of '1' indicating 'completely disagree', '2' indicating 'somewhat disagree', '3' indicating 'unsure', '4' indicating 'somewhat agree', and '5' indicating 'completely agree' (the experts were also able to answer 'not applicable' in case they were not familiar with the underlying evidence or rationale). In case an expert disagreed with the recommendation or Best practice (score '1' or '2'), (s)he was asked to provide appropriate evidence or rationale, respectively. All scores were then anonymized and summarized into a median score, minimum score, maximum score and % of 'agreement-scores' (score '4' and '5') to allow a targeted discussion (see appendix 16). The recommendations were then discussed during a face-to-face meeting

on 18/04/2013. Recommendations and best practices were only changed if important evidence or rationale supported this change. In appendix 13, an overview is provided of how the comments of the external experts were taken into account. Based on the discussion meeting a final draft of recommendations and best practices was prepared and circulated to the GDG for final approval.

This final draft was reviewed by an internal review of KCE-researchers (i.e. General Practitioner; Physiotherapist; Epidemiologist) to fine-tune the formulation of recommendations.

2.10.2 Patient representatives

Patients or patient representatives were not consulted during the development process of this guideline.

2.11 Final validation

As part of the standard KCE procedures, an external scientific validation of the report was conducted prior to its publication. Such validation process was done in June 6th 2013. The current guideline was reviewed prior to its publication by 3 independent validators (Bart Geurden, Sylvie Méaume, Nicky Cullum), making use of the AGREE II checklist. The validation process was chaired by CEBAM (i.e. Bart Geurden). The validation of the report results from a consensus or a voting process between the validators.

Table 9 – Research team and responsibilities

Researchers	Organisation	Area of expertise	Researchers team responsible for evidence reports[a]	Working group responsible for drafting recommendations	Guideline Development Group (GDG)
Dimitri Beeckman	UGent	Professor in Nursing Science	X		X
Cathy Matheï	KUL	Professor in General Medicine	X		X
Aurélie Van Lancker	UGent	Researcher	X		X
Sabine Van Houdt	KUL	Researcher	X		X
Geert Vanwalleghem	Clinical Nursing Consulting or CNC/WCS (VZW Wondzorgvereninging)	Clinical nurse specialist wound care – Hospital setting		X	X
Luc Gryson	CNC	Clinical nurse specialist wound care		X	X
Hilde Heyman	WCS	Clinical nurse specialist wound care – Nursing home setting		X	X
Christian Thyse	AFIScep.be	Clinical nurse specialist wound care		X	X
Adinda Toppets	UZLeuven	Clinical nurse specialist wound care		X	
Sabine Stordeur	KCE	KCE-senior expert	X	X	X
Koen Van den Heede	KCE	KCE-expert	X	X	X

[a] Evidence reports for clinical questions 2-5 were produced by NCGC (Liz Avital, Katie Jones, Julie Neilson)

Table 10 – External experts

Expert	Organisation	Area of expertise
Diégo Backaert	Thuiszorg Groep Backaert	Home care Nurse
Hilde Beele	UZ Gent	Dermatologist
Daniëlle Declercq	UMC Sint-Pieter	Clinical nurse specialist wound care – Hospital setting
Anne Hermand	Cliniques uiversitaires Saint-Luc, Bruxelles	Nurse – hospital setting
Aurore Lafosse	Cliniques universitaires Saint-Luc, Bruxelles	Plastic surgeon
Dominique Putzeys	CIPIQ-s	Clinical nurse specialist wound care – Hospital setting and home care
Evelien Touriany	Militair Ziekenhuis Koningin Astrid	Nurse and clinical nurse specialist wound care – Hospital setting
Dirk Van De Looverbosch	CRA Zorgbedrijf Antwerpen	General practitioner and coordinating physician of a nursing home
Katrien Vanderwee	O.L.V. van Lourdes ziekenhuis Waregem	Nurse, Hospital Hygiene and extensive research expertise in the area of prevention and treatment of pressure ulcers

3 CLINICAL RECOMMENDATIONS

3.1 Introduction

Based on the evidence reviews (indicating the level of evidence by GRADE), the research team formulated recommendations. In addition, best practices were formulated. The latter were not based on the evidence reviews but on two existing guidelines (i.e. EPUAP/NPUAP 20091 & NICE 2001) that were selected based on a systematic search and quality evaluation (using AGREE II) performed by three independent reviewers. All recommendations and best practices were reviewed by a panel of experts using a formal procedure. The sources of the best practices are referenced (i.e. NPUAP/EPUAP; NICE, Expert opinion).

In this chapter we will describe for each of the research questions a summary of the available evidence as well as the recommendations for clinical practice. In addition to the recommendations also best practices are described. The formulations of the latter are based on expert discussions with the recommendations included in existing guidelines as starting point.

Five sets of general 'Best practices' were formulated:

Tailoring pressure ulcer treatment for each individual

Best Practices

Pressure ulcer treatment should be a combined approach, tailored to individual needs and situations and should be based on the principles of shared decision making:

- **Treatment should take into account several factors such as the individual's medical condition, the overall plan of care and the individual's preferences. The needs of the individual and the context should be re-assessed regularly;**
- **An individual plan of care should be adopted based on assessment data, identified risk factors for delayed healing and individual goals and preferences. The plan is developed in interaction with the individual, informal caregivers and the healthcare professionals. The planned and agreed/refused actions are documented in the individual record and communicated to all relevant caregivers (also in case transition between care settings takes place).**

Holistic assessment and individual plan of care for patients with pressure ulcers

Best Practices

Patients with pressure ulcers should receive an holistic initial assessment including:

- **The individual's medical condition;**
- **The individual's preferences;**
- **Risk factors for development and deterioration of pressure ulcers (see prevention guideline{Beeckman, 2013 2896 /id});**
- **A focused physical examination that includes:**
  - **Factors that may affect healing (e.g., impaired perfusion, impaired sensation, systemic infection);**
  - **Vascular assessment in the case of extremity ulcers (e.g., physical examination, history of claudication, ankle-brachial index);**

Best Practices

- **Pain assessment (see below);**
- **Nutritional assessment (see below);**
- **Ulcer assessment (see below).**

Reassess on regular basis and document the findings

Patients with pressure ulcers should receive an initial and ongoing ulcer assessment. The aim of ulcer assessment is to establish the severity of the ulcer, to develop a treatment plan, to evaluate treatment interventions, to assess for complications and to communicate information about the pressure ulcer to the relevant members of the multidisciplinary team.

- **The ulcer assessment should include:**
  - **Cause of the ulcer (e.g. pressure ulcer due to nasogastric tube, oxygen mask, pressure on bony prominences);**
  - **Site/location;**
  - **Time since pressure ulcer occurence;**
  - **Stage or category;**
  - **Dimensions of ulcer and type of tissue;**
  - **Exudate amount and type;**
  - **Local signs of infection;**
  - **Pain;**
  - **Wound appearance (e.g. wound edges, undermining/tracking (sinus or fistula), necrotic tissue, presence/absence of granulation tissue, and epithelialisation);**
  - **Surrounding skin;**
  - **Odour;**
  - **Dressing appearance (exsudate saturation, color, adhesion, …).**
- **A structured approach for ulcer assessment and monitoring should be used. This structured approach could include:**
  - **The consistent use of uniform measurement methods of the dimensions of the pressure ulcer (i.e. wound length and width, depth, tunneling and undermining) to facilitate consistent follow-up over time. The deepest part of the wound should be measured using a sterile probe and care should be taken to avoid causing injury;**
  - **The assessment of healing signs such as decreasing amount of exudate, decreasing wound size and improvement in wound bed tissue;**
  - **The use of photographs to monitor pressure ulcer healing over time;**
  - **The use of a standardized classification system for the initial assessment of the pressure ulcer category(e.g. NPUAP/EPUAP Classification System);**

Best Practices

- **The regular assessment and monitoring (e.g. PUSH-tool; PSST; Sessing scale[b]), with the frequency depending on the condition of the wound and the result of the holistic assessment of the patient. With each dressing change, the pressure ulcer should be observed for developments that may indicate the need for a change in treatment (e.g., wound improvement, wound deterioration, more or less exudate, signs of infection or other complications);**
- **All assessments and actions should be documented and time stamped.**

Any relevant change in the wound characteristics should be documented, and the information should be made accessible and communicated to the members of the multidisciplinary team.

Primary and secondary prevention of pressure ulcers

Best Practices

Patients with a pressure ulcer should be considered at risk of developing additional pressure ulcers. Therefore the general principles of pressure ulcer prevention (see prevention guideline{Beeckman, 2013 2896 /id}: risk and skin assessment; repositioning) should be applied to:

- **Prevent the development of new pressure ulcers;**
- **Prevent the pressure ulcers to get worse;**
- **Support the healing process.**

With regard to nutrition and re-distributing devices, specific recommendations for the treatment of pressure ulcers are formulated (see below).

Pain assessment and management

Best Practices

Pain assessment and management are of utmost importance and have to be integrated in the general plan of care. The evidence about treatment of pain related to pressure ulcers has not been studied specifically for the purpose of this guideline. Therefore we refer to generally accepted pain assessment and treatment procedures.

[b] See for examples at the website of the Belgian Ministry of Public Health (FOD/SPF): http://www.health.belgium.be/eportal/Healthcare/healthcareprofessions/Nursingpractitioners/EvidenceBasedNursing/physiologicaldomain/integrityoftissues/cwcare-pressureulcers/19074612_NL

Educating and training of professional caregivers in pressure ulcer treatment

Best Practices

Training and education should be tailored both to the needs of individual caregivers and to the responsibilities of each specific group of professionals.

Consider following educational/training programme components :

- **Holistic assessment and individual patient planning;**
- **Ulcer assessment;**
- **Normal healing process;**
- **Pain assessment;**
- **Nutritional support;**
- **Recognising inflammation and infection signs;**
- **Exudates management;**
- **Local treatment options, methods for debridement and/or protection of tissue;**
- **Skin protection;**
- **Properties and effectiveness of different types of dressing;**
- **Positioning/repositioning;**
- **Properties and effectiveness of different types of support surfaces (e.g. mattresses, devices for heel elevation, seat cushions).**

3.2 Nutrition/hydration for treatment

3.2.1 Introduction

One of the international proposed approaches to treat pressure ulcers is to optimise hydrational and nutritional status of patient.[1] Nutritional interventions to treat pressure ulcers include providing additional nutrition and dietary supplements, including zinc and vitamin C. Therefore it was considered important for clinical practice to conduct a systematic review to summarize the best available evidence about nutritional interventions such as oral nutritional supplements and/or tube feeding in the prevention of pressure ulcers.

3.2.2 Review question

What are the most clinically effective nutritional interventions for the treatment of pressure ulcers?

3.2.3 Clinical evidence

No RCTs with interventions for hydration to treat pressure ulcers were found. For interventions for nutrition to treat pressure ulcers we found one Cochrane review[36] which included 4 randomised controlled trials (Taylor, 1974[37], Ter Riet, 1995[38], Chernoff, 1990[39], and Norris, 1971[40]). We have included these randomised controlled trials in the evidence review and have updated this Cochrane Review. Eight further randomised controlled trials were found (Desneves, 2005[41], Lee, 2006[42], Cereda, 2009[43], Van Anholt, 2010[44], Brewer, 1967[45], Benati, 2001[46] and Ohura, 2011[47]) and included. Another study found in the search looked specifically at the efficacy and safety of ornithine alpha ketogluatarate in heel pressure ulcers (Meaume, 2009[48]).

Most of the studies looked at different forms of supplementation in addition to the standard hospital diet versus the standard hospital diet alone. The

supplements differed in their composition therefore we did not meta-analyse these studies together. There were two studies looking at ascorbic acid versus placebo which we meta-analysed under that comparison, although the populations were still different (nursing home and surgical patients).

Studies with ulcers of all stages were analysed separately from those with stages 2 and upwards (classification system is stated, where reported) and studies where patients were nutritionally deficient or non-nutritionally deficient were also separated.

3.2.3.1 Quality of studies

In general the methodological quality of the included studies was poor. The majority of studies did not use an intention-to-treat analyses[37, 39-43, 45-47] and did not report in an a priory sample size calculation.[37, 39-47, 49] In addition, in all studies sequence generation and allocation concealment was not clearly described or was performed poorly. Blinding was possible in the majority of the studies due to the use of lookalike products.[37, 40, 41, 43, 45, 48, 49] In appendix 1 the level of evidence can be found per outcome after applying the GRADE-methodology. The evidence base for all outcomes has been rated as being of low to very low quality.

3.2.3.2 Evidence statements

500kcal, 34g protein, 6g arginine, 500mg vitamin C, 18mg zinc and standard hospital diet versus standard hospital diet

- One study (n=28) (elderly LTC patients) showed that 500kcal, 34g protein, 6g arginine, 500mg vit C, 18mg zinc and standard hospital diet may be more effective compared to standard hospital diet only at reducing the proportion of stage II to IV pressure ulcers (VERY LOW QUALITY).[43]
- One study (n=28) (elderly LTC patients) reported a mean percentage reduction in ulcers size (stage II to IV PUs) for 500kcal, 34g protein, 6g arginine, 500mg vit C, 18mg zinc and standard hospital diet and standard hospital diet only. The mean was 72% for 500kcal, 34g protein, 6g arginine, 500mg vit C, 18mg zinc and standard hospital diet and 45% for standard hospital diet only. A p-value of 0.05 was reported (VERY LOW QUALITY) .[43]
- One study (n=28) (elderly LTC patients) showed that 500kcal, 34g protein, 6g arginine, 500mg vit C, 18mg zinc and standard hospital diet may be more effective compared to standard hospital diet only for mean cm² reduction in ulcer size stage II to IV pressure ulcers (VERY LOW QUALITY) .[43]
- One study (n=28) (elderly LTC patients) showed that 500kcal, 34g protein, 6g arginine, 500mg vit C, 18mg zinc and standard hospital diet may be more effective compared to standard hospital diet only for mean reduction in PUSH score of stage II to IV pressure ulcers (VERY LOW QUALITY) .[43]

250kcal, 28.4g carbohydrates, 20g protein, 3g arginine, 7g fat, vitamins, minerals and standard hospital diet versus placebo and standard hospital diet

- One study (n=43) (elderly non-malnourished adults) reported mean reduction in PUSH score (stage III and IV PUs) for 250kcal, 28.4g carbohydrates, 20g protein, 3g arginine, 7g fat, vitamins, minerals and standard hospital diet versus placebo and standard hospital diet. The mean reduction was 6 for the 250kcal, 28.4g carbohydrates, 20g protein, 3g arginine, 7g fat, vitamins, minerals and standard hospital diet and 5.4 for the placebo and standard hospital diet. A p-value of 0.011 was reported (VERY LOW QUALITY).[50]
- One study (n=43) (elderly non-malnourished adults) reported mean cm²/week reduction in ulcer size (stage III and IV PUs) for 250kcal, 28.4g carbohydrates, 20g protein, 3g arginine, 7g fat, vitamins, minerals and standard hospital diet versus placebo and standard hospital diet. The rate was 8.4 cm²/week for the 250kcal, 28.4g carbohydrates, 20g protein, 3g arginine, 7g fat, vitamins, minerals and standard hospital diet and 8.75 cm²/week for the placebo and standard hospital diet. A p-value of 0.006 was reported (VERY LOW QUALITY). [50]
- One study (n=43) (elderly non-malnourished adults) showed that placebo and standard hospital diet is potentially more effective compared to 250kcal, 28.4g carbohydrates, 20g protein, 3g arginine, 7g fat, vitamins, minerals and standard hospital diet for incidence of treatment related adverse events (VERY LOW QUALITY).[50]

- One study (n=43) (elderly non-malnourished adults) showed that placebo and standard hospital diet may be more effective compared to 250kcal, 28.4g carbohydrates, 20g protein, 3g arginine, 7g fat, vitamins, minerals and standard hospital diet for incidence of diarrhoea (VERY LOW QUALITY). [50]
- One study (n=43) (elderly non-malnourished adults) showed there may be no difference between 250kcal, 28.4g carbohydrates, 20g protein, 3g arginine, 7g fat, vitamins, minerals and standard hospital diet and placebo and standard hospital diet for incidence of nausea, the direction of the effect of the estimate favours 250kcal, 28.4g carbohydrates, 20g protein, 3g arginine, 7g fat, vitamins, minerals and standard hospital diet (VERY LOW QUALITY). [50]
- One study (n=43) (elderly non-malnourished adults) showed that 250kcal, 28.4g carbohydrates, 20g protein, 3g arginine, 7g fat, vitamins, minerals and standard hospital diet may be more effective compared to placebo and standard hospital diet for incidence of vomiting (VERY LOW QUALITY). [50]

500kcal, 18g protein, 0g fat, 72mg vitamin C and 7.5mg zinc and standard hospital diet versus standard hospital diet

- One study (n=11) (elderly adults or patients with a spinal cord injury) showed that 500kcal, 18g protein, 0g fat, 72mg vitamin C and 7.5mg zinc and standard hospital diet may be more effective compared to standard hospital diet for PUSH score at week 3 of stage II to IV PUs (VERY LOW QUALITY).[41]

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) (elderly adults or patients with a spinal cord injury) showed that 500kcal, 21g protein, 0g fat, 500mg vitamin C, 30mg zinc and 9g arginine and standard hospital diet is clinically more effective compared to standard hospital diet for PUSH score at week 3 of stage II to IV PUs (VERY LOW QUALITY). [41]

500kcal, 18g protein, 0g fat, 72mg vitamin C and 7.5mg zinc and standard hospital diet versus 500kcal, 21g protein, 0g fat, 500mg vitamin C, 30mg zinc and 9g arginine and standard hospital diet

- One study (n=11) (elderly adults or patients with a spinal cord injury) showed that 500kcal, 18g protein, 0g fat, 72mg vitamin C and 7.5mg zinc and standard hospital diet is clinically more effective compared to 500kcal, 21g protein, 0g fat, 500mg vitamin C, 30mg zinc and 9g arginine and standard hospital diet for PUSH score at week 3 of stage II to IV PUs (VERY LOW QUALITY). [41]

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) (majority elderly, tube-fed patients) showed that 4.38g protein, 2.23g fat, 15.62g carbohydrate, minerals and vitamins (per 100ml) and standard hospital diet is potentially more effective compared standard hospital diet to reduce the proportion of stage II to IV PUs (VERY LOW QUALITY).[47]
- One study (n=50) (majority elderly, tube-fed patients) showed that 4.38g protein, 2.23g fat, 15.62g carbohydrate, minerals and vitamins (per 100ml) and standard hospital diet is clinically more effective compared standard hospital diet for mean reduction in ulcer size of stage II to IV PUs (LOW QUALITY). [47]
- One study (n=50) (majority elderly, tube-fed patients) showed that standard hospital diet may be more effective compared 4.38g protein, 2.23g fat, 15.62g carbohydrate, minerals and vitamins (per 100ml) and standard hospital diet to reduce the incidence of treatment related adverse events of stage II to IV PUs (VERY LOW QUALITY).[47]

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

- One study (n=12) (long-term, tube-fed institutionalised patients) showed that very high dietary formula (92 to 150gms/day) may be more effective compared to high dietary formula (57 to 90gms/day) to reduce the proportion of PUs (VERY LOW QUALITY).[39]
- One study (n=12) (long-term, tube-fed institutionalised patients) reported mean surface percentage reduction for very high dietary formula (92 to 150gms/day) and high dietary formula (57 to 90gms/day). The mean for very high dietary formula (92 to 150gms/day) is 73% and 42% for high dietary formula (57 to 90gms/day) (VERY LOW QUALITY).[39]

1000mg ascorbic acid (500mg twice daily) and standard hospital diet versus placebo and standard hospital diet

- Two studies (n=108) (patients from 11 nursing homes and 1 hospital, and surgical patients; most with nutritional deficiencies) showed there may be no difference between 1000mg ascorbic acid (500mg twice daily) and standard hospital diet versus placebo and standard hospital diet to reduce the proportion of PUs, the direction of the estimate of the effect favoured the placebo and standard treatment (VERY LOW QUALITY).[37, 38]
- One study (n=88) (patients from 11 nursing homes and 1 hospital; most with nutritional deficiencies) showed there may be no difference between 1000mg ascorbic acid (500mg twice daily) and standard hospital diet versus placebo and standard hospital diet for time to complete healing, the direction of the estimate of the effect favoured the 1000mg ascorbic acid (500mg twice daily) and standard hospital diet (VERY LOW QUALITY).[38]
- One study (n=20) (surgical patients) showed 1000mg ascorbic acid (500mg twice daily) and standard hospital diet is clinically more effective compared to placebo and standard treatment for mean percentage reduction in ulcer area (VERY LOW QUALITY).[37]
- One study (n=88) (patients from 11 nursing homes and 1 hospital; most with nutritional deficiencies) reported rate of mean cm²/week reduction in ulcer size for 1000mg ascorbic acid (500mg twice daily) and standard hospital diet versus placebo and standard hospital diet. The mean rate for 1000mg ascorbic acid (500mg twice daily) and standard hospital diet was 0.21 cm²/week and 0.27 cm²/week for placebo and standard hospital diet. An adjusted mean difference of -0.02 (95% CI: -0.20 to 0.16) was reported (VERY LOW QUALITY). [38]
- One study (n=20) (surgical patients) reported rate of mean cm²/week reduction in ulcer size for 1000mg ascorbic acid (500mg twice daily) and standard hospital diet versus placebo and standard hospital diet. The mean rate for 1000mg ascorbic acid (500mg twice daily) and standard hospital diet was 2.47 cm²/week and 1.45 cm²/week for placebo and standard hospital diet. No estimate of effect or precision could be derived (VERY LOW QUALITY). [37]
- One study (n=88) (patients from 11 nursing homes and 1 hospital; most with nutritional deficiencies) reported rate of mean ml/week reduction in ulcer size for 1000mg ascorbic acid (500mg twice daily) and standard hospital diet versus placebo and standard hospital diet. The mean rate for 1000mg ascorbic acid (500mg twice daily) and standard hospital diet was 0ml/week and 0.20ml/week for placebo and standard hospital diet. An adjusted mean difference of -0.66 (95% CI: -1.44 to 0.78) was reported (VERY LOW QUALITY). [38]
- One study (n=88) (patients from 11 nursing homes and 1 hospital; most with nutritional deficiencies) reported of percentage/week reduction in volume for 1000mg ascorbic acid (500mg twice daily) and standard hospital diet versus placebo and standard hospital diet. The rate for 1000mg ascorbic acid (500mg twice daily) and standard hospital diet was -3.39%/week and 16.71%/week for placebo and standard hospital diet. An adjusted mean difference of 35.33 (95% CI: 11.31 to 81.91) was reported (VERY LOW QUALITY). [38]
- One study (n=88) (patients from 11 nursing homes and 1 hospital; most with nutritional deficiencies) reported of rate of mean healing velocity for 1000mg ascorbic acid (500mg twice daily) and standard hospital diet versus placebo and standard hospital diet. The rate for 1000mg ascorbic acid (500mg twice daily) and standard hospital diet was 0.12 cm/week and 0.19 cm/week for placebo and standard hospital diet. An adjusted mean difference of -0.05 (95% CI: 0.148 to 0.048) was reported (VERY LOW QUALITY). [38]

Zinc sulfate versus placebo

- One study (n=13) (patients with a spinal cord injury) showed placebo may be more effective compared to zinc sulphate to reduce the proportion of PUs (VERY LOW QUALITY).[51]
- One study (n=20) (hospitalized patients with a chronic disease and geriatric problems) showed there may be no difference between zinc sulphate and placebo for mean reduction in ulcer volume (VERY LOW QUALITY).[40]

Concentrated, fortified, collagen protein hydrolysate versus placebo

- One study (n=71) (elderly adult and patients with a spinal cord injury) showed there is potentially no difference between concentrated, fortified, collagen protein hydrolysate and placebo for mean reduction in PUSH score, the direction of the estimate of the effect favoured the concentrated, fortified, collagen protein hydrolysate (VERY LOW QUALITY).[42]
- One study (n=71) (elderly adult and patients with a spinal cord injury) reported a percentage reduction in PUSH score for concentrated, fortified, collagen protein hydrolysate versus placebo. The reduction for concentrated, fortified, collagen protein was 60% and 40% for placebo. A p-value < 0.05 was reported (VERY LOW QUALITY).[42]

Ornithine alpha-ketoglutarate versus placebo

- One study (n=160) (elderly patients) showed there is potentially no difference between ornithine alpha-ketoglutarate and placebo for rate of complete healing of stage II and III heel PUs, the direction of the estimate of the effect favoured the ornithine alpha-ketoglutarate (VERY LOW QUALITY).[48]
- One study (n=160) (elderly patients) showed there is no difference between ornithine alpha-ketoglutarate and placebo for rate of complete healing of stage II and III heel PUs (VERY LOW QUALITY).[48]
- One study (n=160) (elderly patients) showed there is no difference between ornithine alpha-ketoglutarate and placebo for mean surface reduction of stage II and III heel PUs (VERY LOW QUALITY).[48]
- One study (n=160) (elderly patients) showed that ornithine alpha-ketoglutarate may be more effective compared to placebo for 90% reduction by week 6 of stage II and III heel PUs (VERY LOW QUALITY).[48]

3.2.4 Conclusion

- **There is evidence of very low quality based on 12 randomized controlled trials about nutritional interventions in the treatment of pressure ulcers.**
- **There is evidence that nutritional supplements may be more effective compared to standard hospital diet for the treatment of pressure ulcers.**
- **None of the studies reported harms as a result of the interventions.**
- **These results should be interpreted with caution because of the small sample sizes and the numerous methodological flaws in the included studies. In addition, in some studies it was unclear if patients were malnourished and there was insufficient information on the standard hospital diet.**

3.2.5 *Recommendations and best practices for clinical practice*

Best Practices

Monitoring of the nutritional status of patients with pressure ulcers should be part of a general assessment procedure and an ongoing process throughout an individual's episode of care. The initial assessment should include documentation of the following factors:

- **Current weight and height;**
- **Recent weight loss;**
- **Usual eating habits;**
- **(Recent changes in) eating habits and intake;**
- **The adequacy of total nutrient intake (food, fluid, oral supplements, enteral/parenteral feedings).**

The nutritional support for the treatment of patients with pressure ulcers should be based on:

- **A formal nutritional assessment (e.g. Mini-Nutritional Assessment);**
- **General medical condition;**
- **Patient preferences;**
- **Advice from a professional with specific competencies in nutritional carein order to provide sufficient calories, protein, fluid, micronutrients, particularly when dietary intake is poor or deficiencies are confirmed or suspected.**

Recommendation	Strength of Recommendation	Level of Evidence
A care professional with specific competencies in nutritional care may recommend nutritional interventions (e.g. nutritional supplements) for patients with pressure ulcers. **As clinical studies did not demonstrate the superiority of one nutritional intervention over another, we cannot recommend a specific complementary diet (type and quantity) with nutritional supplements.**	**Weak**	**Very Low**

3.3 Redistributing devices

3.3.1 Introduction

Pressure relieving and redistributing devices are widely accepted methods of trying to treat pressure ulcers. These devices include different types of mattresses, overlays, cushions and seating. These devices work by either reducing pressure, friction or shearing forces. NICE guidelines of 2005[30] recommended that people with pressure ulcers should have access to appropriate pressure relieving devices and strategies 24 hours a day. The cost of these devices can vary considerably.

Selection of devices may depend on patient mobility, skin observation, the severity and site of the pressure ulcer, patient weight, staff availability and skill and the general health and condition of patient. NICE (2005) recommended that decisions regarding choice of pressure-relieving support surfaces should be made by registered health care professionals.[30] It is also accepted that these devices should be used in conjunction with other treatment strategies such as repositioning and wound management.

There is a limited amount of published high-quality research in this area. There is a body of research which has been conducted by the manufacturers of these devices, however much of this research has not been published in peer review journals. The previous NICE guideline[30] recognized that there was a lack of conclusive research evidence and made recommendations from professional consensus.

3.3.2 Review question

What are the most clinically effective pressure redistributing devices for the treatment of pressure ulcers?

3.3.3 Clinical evidence

A Cochrane Review[52] for support surfaces for treating pressure ulcers was retrieved from the search and we used this as the basis for our review. It included 18 randomized controlled trials.[53-69] No further RCTs were found to update it.

Various types of devices were used to redistribute pressure, and the Cochrane categorised them as low-tech (non-powered) constant low pressure support surfaces, high-tech support surfaces and other support surfaces.[52]

The low-tech CLP support surfaces included:

- Standard foam mattresses;
- Alternative foam mattresses/overlays;
- Gel-filled mattresses/overlays;
- Fibre-filled mattresses/overlays;
- Air-filled mattresses/overlays;
- Water-filled mattresses/overlays;
- Bead-filled mattresses/overlays;
- Sheepskins.

The high-tech support surfaces included:

- Alternating-pressure mattresses/overlays;
- Air-fluidised beds;
- Low-air-loss beds.

The other support surfaces included:

- Turning beds/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.

3.3.3.1 Quality of studies

In general the methodological quality of the included studies was poor. The majority of studies were not blinded[54, 56, 57, 60-66, 70-72], had unclear sequence generation[54-56, 58, 59, 61, 63, 64, 66, 67, 70, 71], and did not use an intention-to-treat analyses.[54-58, 61, 64, 67, 68, 70] Eight studies had unclear allocation concealment.[54, 63, 64, 66, 67, 69-71] Only nine studies reported an a priory sample size calculation[53, 55, 56, 60-62, 65, 67, 68, 72], of which seven were underpowered.[53, 55, 56, 61, 62, 65, 67, 72] In appendix 2 the level of evidence can be found per outcome after applying the GRADE-methodology. The evidence base for all outcomes has been rated as being of moderate to very low quality.

3.3.3.2 *Evidence statements*

Low-tech constant pressure devices

- One study (n=120) (nursing home patients) showed there may be no difference between a water mattress and low-tech mattress to reduce the proportion of stage III PUs, the direction of the estimate of the effect favoured the low-tech mattress (VERY LOW QUALITY).[61]
- One study (n=120) (nursing home patients) reported percentage with pain (stage III PUs) for a water mattress and low-tech mattress. The percentage for the water mattress was 35.9% and 16.2% for the low-tech mattress. No estimate of effect or precision could be derived (VERY LOW QUALITY). [61]

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

- Two studies (n=133) (nursing home patients) showed that a low-air loss bed is potentially more effective compared to low-tech foam overlay to reduce the proportion of stage ≥ II PUs (VERY LOW QUALITY).[60, 63]
- One study (n=84) (nursing home patients) showed that a low-air loss bed is potentially more effective compared to low-tech foam overlay to reduce the proportion of stage ≥ II PUs (VERY LOW QUALITY).[60]
- One study (n=49) (nursing home patients) showed that there may be no difference between a low-air loss bed and a low-tech foam overlay to reduce the proportion of stage III and IV PUs, the direction of the estimate of the effect favoured the low-tech foam (VERY LOW QUALITY).[63]
- One study (n=49) (nursing home patients) showed there may be no difference between a low-air-loss bed and a low-tech foam overlay to reduce ulcer stage by one or more stages of stage ≥ II PUs, the direction of the estimate of the effect favoured the low-air-loss bed (VERY LOW QUALITY).[63]
- One study (n=84) (nursing home patients) reported rate of healing (stage ≥ II PUs) for low-air-loss bed and low-tech foam overlay. The rate for low-air-loss bed was 9.0 mm²/day and 2.5 mm²/day for low-tech foam overlay. A p-value of 0.0002 was reported (VERY LOW QUALITY).[60]
- One study (n=48) (hospitalized patient) showed a low-air-loss bed is potentially more effective compared to low-tech foam overlay for mean change in ulcer size of stage II Pus (VERY LOW QUALITY).[56]
- One study (n=29) (hospitalized patient) showed a low-air-loss bed is clinically more effective compared to low-tech foam overlay for mean change in ulcer size of stage III and IV Pus (VERY LOW QUALITY).[56]
- One study (n=39) (hospitalized patient) showed there is potentially no difference between a low-air-loss bed and a low-tech foam overlay for mean comfort scores, the direction of the estimate of the effect favoured the low-air-loss bed (LOW QUALITY).[56]

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

- One study (n=55) (acute care patients) reported a median change in ulcer area for low-air-loss bed and low-air-loss overlay. The median for low-air-loss bed was 3.9 cm² and 1.9 cm² for low-air-loss overlay. A p-value of 0.06 was reported (VERY LOW QUALITY).[70]
- One study (n=55) (acute care patients) reported a mean change in ulcer area for low-air-loss bed and low-air-loss overlay. The mean for low-air-loss bed was 10.2 cm² and 3.8 cm² for low-air-loss overlay. No estimate of effect or precision could be derived (VERY LOW QUALITY).[70]

Air-fluidised therapy versus standard/conventional therapies

- One study (n=65) (surgical patients) showed air-fluidised beds may be more effective compared to standard therapy to reduce the proportion with 50% reduction in ulcer area (VERY LOW QUALITY) .[53]
- One study (n=45) (community patients) showed air-fluidised beds are potentially more effective compared to standard therapy to improve healing of stage III and IV PUs (VERY LOW QUALITY).[69]
- One study (n=65) (surgical patients) showed air-fluidised beds are potentially more effective compared to standard therapy to improve healing of PUs (LOW QUALITY) [53]
- Two studies (n=100) (surgical and community patients) showed air-fluidised beds are potentially more effective compared to standard therapy to improve healing of PUs (LOW QUALITY).[53, 69]

- One study (n=not reported) (hospitalized patients) reported change in mean ulcer area (stage II and III) for air-fluidised beds and standard therapy. The change for air-fluidised beds was 1158 mm² and 2051 mm² for standard therapy. A p-value of 0.05 was reported (VERY LOW QUALITY).[64]
- One study (n=65) (surgical patients) reported a median change in ulcer area for air-fluidised beds and standard therapy. The median for air-fluidised beds was -1.2 cm² and 0.5 cm² for standard therapy. No estimate of effect or precision could be derived (VERY LOW QUALITY). [53]
- One study (n=18) (hospitalized patients) showed air-fluidised beds are potentially more effective compared to standard therapy for patient satisfaction (LOW QUALITY).[64]
- One study (n=27) (surgical patients) showed air-fluidised beds are potentially more effective compared to standard therapy for increase in comfort (VERY LOW QUALITY). [53]
- One study (n=27) (surgical patients) showed air-fluidised beds are potentially more effective compared to standard therapy for reduction in comfort (VERY LOW QUALITY).[53]
- One study (n=97) (community patients) showed there is no difference between air-fluidised beds and standard therapy for time in hospital (VERY LOW QUALITY). [69]
- One study (n=65) (surgical patients) reported median length of stay in hospital for air-fluidised beds and standard therapy. The median for air-fluidised beds was 16 days and 15 days for standard therapy. No estimate of effect or precision could be derived (VERY LOW QUALITY).[53]
- One study (n=65) (surgical patients) showed air-fluidised beds are potentially more effective compared to standard therapy for reduction in pain (VERY LOW QUALITY).[53]
- One study (n=65) (surgical patients) showed air-fluidised beds are potentially more effective compared to standard therapy for increase in pain (VERY LOW QUALITY).[53]

Alternating-pressure mattress compared to each other

- One study (n=30) (elderly patients) showed an alternating-pressure mattress (Nimbus) is potentially more effective compared to another alternating-pressure mattress (Pegasus Airwave) to reduce the proportion of patients with a stage ≥ 2 PUs (VERY LOW QUALITY).[57]
- One study (n=30) (elderly patients) showed an alternating-pressure mattress (Pegasus Airwave) may be more effective compared to another alternating-pressure mattress (Nimbus) to improve healing of stage ≥ 2 PUs (VERY LOW QUALITY).[57]
- One study (n=30) (elderly patients) showed an alternating-pressure mattress (Nimbus) may be more effective compared to another alternating-pressure mattress (Pegasus Airwave) to reduce the proportion of patients with a stage ≥ 2 PUs worsened (VERY LOW QUALITY).[57]
- One study (n=30) (elderly patients) reported median rate of reduction in ulcer size (stage ≥ 2) for two alternating-pressure mattresses. The median for an alternating-pressure mattress (Nimbus 1) was 0.089 cm²/day and 0.107 cm²/day for another alternating-pressure mattress (Pegasus Airwave). A p-value of 0.92 was reported (VERY LOW QUALITY).[57]
- One study (n=not reported) (elderly hospital patients) reported a median absolute reduction in ulcer area (stage ≥ 2) for one alternating-pressure mattress and another alternating-pressure mattress or alternating-pressure overlay. The median for an alternating-pressure mattress (Nimbus 3) was 0.12 cm²/day and 0.08 cm²/day for another alternating-pressure mattress (P. Biwave, P. Airwave, P. Cairwave or AlphaXCell) or alternating-pressure overlay (AlphaXCell or Quattro). A p-value of 0.57 was reported (VERY LOW QUALITY).[58]
- One study (n= not reported) (elderly hospital patients) reported a median relative reduction in ulcer area (stage ≥ 2) for one alternating-pressure mattress and another alternating-pressure mattress or alternating-pressure overlay. The median for an alternating-pressure mattress (Nimbus 3) was 2.44% and 1.34% for another alternating-pressure mattress (P. Biwave, P. Airwave, P. Cairwave or AlphaXCell)

or alternating-pressure overlay (AlphaXCell or Quattro). A p-value of 0.57 was reported (VERY LOW QUALITY).[58]

- One study (n= not reported) (nursing patients) reported a median absolute reduction in ulcer area (stage ≥ 2) for one alternating-pressure mattress and another alternating-pressure mattress or alternating-pressure overlay. The median for an alternating-pressure mattress (Nimbus 3) was 0.11 cm²/day and 0.05 cm²/day for another alternating-pressure mattress (P. Biwave, P. Airwave, P. Cairwave or AlphaXCell) or alternating-pressure overlay (AlphaXCell or Quattro). A p-value of 0.57 was reported (VERY LOW QUALITY).[58]
- One study (n= not reported) (nursing patients) reported a median relative reduction in ulcer area (stage ≥ 2) for one alternating-pressure mattress and another alternating-pressure mattress or alternating-pressure overlay. The median for an alternating-pressure mattress (Nimbus 3) was 1.57% and 0.99% for another alternating-pressure mattress (P. Biwave, P. Airwave, P. Cairwave or AlphaXCell) or alternating-pressure overlay (AlphaXCell or Quattro). A p-value of 0.57 was reported (VERY LOW QUALITY).[58]
- One study (n= not reported) (elderly patients) reported a median comfort scores (stage ≥ 2) for one alternating-pressure mattress and another alternating-pressure mattress or alternating-pressure overlay. The median for an alternating-pressure mattress (Nimbus 3) was 5 (very comfortable) and 4 (comfortable) for another alternating-pressure mattress (P. Biwave, P. Airwave, P. Cairwave or AlphaXCell) or alternating-pressure overlay (AlphaXCell or Quattro). A p-value of 0.006 was reported (VERY LOW QUALITY).[58]
- One study (n= not reported) (nursing patients) reported a median comfort score (stage ≥ 2) for one alternating-pressure mattress and another alternating-pressure mattress or alternating-pressure overlay. The median for an alternating-pressure mattress (Nimbus 3) was 5 (very comfortable) and 4 (comfortable) for another alternating-pressure mattress (P. Biwave, P. Airwave, P. Cairwave or AlphaXCell) or alternating-pressure overlay (AlphaXCell or Quattro). A p-value of 0.002 was reported (VERY LOW QUALITY).[58]
- One study (n=30) (elderly patients) reported a median comfort score (stage ≥ 2) for two alternating-pressure mattresses. The median for an alternating-pressure mattress (Nimbus 1) was 8/10 and 8/10 for another alternating-pressure mattress (Pegasus Airwave). No estimate of effect or precision could be derived (VERY LOW QUALITY).[57]

Alternating-pressure mattress overlay versus alternating-pressure mattress

- One study (n=113) (elderly patients) showed there may be no difference between an alternating-pressure mattress and alternating-pressure mattress overlay to reduce the proportion of stage ≥ 2 PUs, the direction of the estimate of the effect favoured the alternating-pressure mattress (VERY LOW QUALITY).[65]
- One study (n=113) (elderly patients) showed there is potentially be no difference between an alternating-pressure mattress and alternating-pressure mattress overlay for absolute change in surface area of stage ≥ 2 PUs, the direction of the estimate of the effect favoured the alternating-pressure mattress (VERY LOW QUALITY).[65]
- One study (n=113) (elderly patients) showed there is potentially be no difference between an alternating-pressure mattress and alternating-pressure mattress overlay for percentage change in surface area of stage ≥ 2 PUs, the direction of the estimate of the effect favoured the alternating-pressure mattress (VERY LOW QUALITY).[65]
- One study (n=158) (elderly patients) showed there is no difference between an alternating-pressure mattress and alternating-pressure mattress overlay to improve healing of stage I and II PUs (VERY LOW QUALITY).[68]
- One study (n=158) (elderly patients) showed there may be no difference between an alternating-pressure mattress and alternating-pressure mattress overlay to reduce the proportion of stage I and II PUs worsened, the direction of the estimate of the effect favoured the alternating-pressure overlay (LOW QUALITY).[68]
- One study (n=113) (elderly patients) reported median time to healing (stage ≥ 2) for alternating-pressure mattress and alternating-pressure mattress overlay. A median for alternating-pressure overlay and alternating-pressure mattress was 20 days. A p-value of 0.86 was reported (VERY LOW QUALITY).[65]

- One study (n=158) (elderly patients) reported median time to healing (stage ≥ 2) for alternating-pressure mattress and alternating-pressure mattress overlay. A median for alternating-pressure overlay was 22.17 days and 20.05 days for alternating-pressure mattress. A p-value of 0.86 was reported (VERY LOW QUALITY).[65]
- One study (n=1 971) (elderly patients) showed there is potentially no difference between an alternating-pressure mattress and alternating-pressure mattress overlay for patient acceptability, the direction of the estimate of the effect favoured the alternating-pressure overlay (LOW QUALITY).[65]
- One study (n=1 820) (elderly patients) showed there is potentially no difference between an alternating-pressure mattress and alternating-pressure mattress overlay to reduce the incidence of patients with negative comments on mattress motion, the direction of the estimate of the effect favoured the alternating-pressure mattress (VERY LOW QUALITY).[65]
- One study (n=1 820) (elderly patients) showed there is no difference between an alternating-pressure mattress and alternating-pressure mattress overlay to reduce the incidence of patients with positive comments on mattress motion (LOW QUALITY).[65]
- One study (n=1 820) (elderly patients) showed there is potentially no difference between an alternating-pressure mattress and alternating-pressure mattress overlay to reduce the incidence of patients with negative comments on getting into/out bed, the direction of the estimate of the effect favoured the alternating-pressure overlay (LOW QUALITY).[65]
- One study (n=1 820) (elderly patients) showed there is no difference between an alternating-pressure mattress and alternating-pressure mattress overlay to reduce the incidence of patients with negative comments on movement in bed (LOW QUALITY).[65]
- One study (n=1 820) (elderly patients) showed an alternating-pressure mattress is potentially more effective compared to an alternating-pressure mattress overlay to reduce the incidence of patients commenting on temperature as hot/warm (VERY LOW QUALITY).[65]
- One study (n=1 820) (elderly patients) showed an alternating-pressure mattress is potentially more effective compared to an alternating-pressure mattress overlay to reduce the incidence of patients commenting on temperature as sweaty/sticky (VERY LOW QUALITY).[65]
- One study (n=1 820) (elderly patients) showed there may be no difference between an alternating-pressure mattress and alternating-pressure mattress overlay to reduce the incidence of patients commenting on temperature as cool/cold, the direction of the estimate of the effect favoured either interventions (VERY LOW QUALITY).[65]
- One study (n=1 820) (elderly patients) showed there may be no difference between an alternating-pressure mattress and alternating-pressure mattress overlay to reduce the incidence of mattresses not working (properly), the direction of the estimate of the effect favoured the alternating-pressure mattress overlay (VERY LOW QUALITY).[65]
- One study (n=1 820) (elderly patients) showed an alternating-pressure mattress is potentially more effective compared to an alternating-pressure mattress overlay to reduce the incidence of patients reporting the mattress as hard to tuck sheet, sheets come off or gather, or mattress cover slips (VERY LOW QUALITY).[65]
- One study (n=1 820) (elderly patients) showed an alternating-pressure mattress is potentially more effective compared to an alternating-pressure mattress overlay to reduce the incidence of patients reporting the mattress as too high (VERY LOW QUALITY).[65]
- One study (n=1 820) (elderly patients) showed an alternating-pressure mattress may be more effective compared to an alternating-pressure mattress overlay to reduce the incidence of patients reporting the mattress as slippy (VERY LOW QUALITY).[65]
- One study (n=1 820) (elderly patients) showed an alternating-pressure mattress overlay may be more effective compared to an alternating-pressure mattress to reduce the incidence of patients reporting the mattress as too soft, edges soft or slope (VERY LOW QUALITY).[65]
- One study (n=1 820) (elderly patients) showed an alternating-pressure mattress may be more effective compared to an alternating-pressure

mattress overlay to reduce the incidence of patients reporting not able to use backrest (VERY LOW QUALITY).[65]

- One study (n=1 820) (elderly patients) showed an alternating-pressure mattress overlay is potentially more effective compared to an alternating-pressure mattress to reduce the incidence of mattress-related fall (VERY LOW QUALITY).[65]
- One study (n=1 820) (elderly patients) showed an alternating-pressure mattress overlay is potentially more effective compared to an alternating-pressure mattress to reduce the incidence of suspected mattress-related contact dermatitis (VERY LOW QUALITY).[65]
- One study (n=1 820) (elderly patients) showed an alternating-pressure mattress may be more effective compared to an alternating-pressure mattress overlay to reduce the incidence of mattress-related climb over or fall through the cot sides (VERY LOW QUALITY).[65]
- One study (n=1 820) (elderly patients) showed an alternating-pressure mattress overlay is potentially more effective compared to an alternating-pressure mattress to reduce the incidence of mattress deflation during transfer (VERY LOW QUALITY).[65]

Air-filled devices versus alternating-pressure mattress

- One study (n=60) (elderly patients) showed air-filled devices may be more effective compared to alternating-pressure mattresses to reduce the proportion of patients with a stage ≥ 2 PUs (VERY LOW QUALITY).[66]

Profiling bed versus foam mattress

- One study (n=14) (surgical and medical patients) showed profiling bed is clinically more effective compared to foam mattress to reduce the proportion with a stage I PUs (VERY LOW QUALITY).[62]

Constant force mattress versus low-air loss mattress

- One study (n=18) (long-term or sub-acute inpatients) showed constant force mattress is potentially more effective compared to low-air loss mattress for mean rate of closure in stage III and IV PUs (VERY LOW QUALITY).[54]

Alternating-pressure cushion versus dry flotation cushion

- One study (n=25) (elderly patients) showed dry flotation cushion may be more effective compared to alternating-pressure cushion to reduce the proportion of stage ≥ 2 PUs (VERY LOW QUALITY).[73]
- One study (n=25) (elderly patients) showed there is potentially no difference between alternating-pressure cushion and dry floatation cushion for rate of healing (cm^2/day) of stage ≥ 2 PUs, the direction of the estimate of the effect favoured the dry floatation cushion (VERY LOW QUALITY).[73]
- One study (n=25) (elderly patients) showed there may be no difference between alternating-pressure cushion and dry floatation cushion for rate of healing (cm^3/day) of stage ≥ 2 PUs, the direction of the estimate of the effect favoured the alternating-pressure cushion (VERY LOW QUALITY).[73]
- One study (n=25) (elderly patients) showed there is potentially no difference between alternating-pressure cushion and dry floatation cushion for change in ulcer area per day of stage ≥ 2 PUs, the direction of the estimate of the effect favoured the alternating-pressure cushion (VERY LOW QUALITY).[73]
- One study (n=25) (elderly patients) showed there may be no difference between alternating-pressure cushion and dry floatation cushion for change in ulcer volume per day of stage ≥ 2 PUs, the direction of the estimate of the effect favoured the dry floatation (VERY LOW QUALITY).[73]

Alternating-pressure mattress and cushion compared to each other

- One study (n=141) (elderly patients) showed there is no difference between alternating-pressure mattresses (Nimbus 3, Aura cushion and 4-hourly turning versus Pegasus Cairwave Therapy System, Proactive 2 seating cushion and 8-hourly turning) to reduce the proportion of stage ≥ 2 PUs (MODERATE QUALITY).[67]
- One study (n=112) (elderly patients) reported mean time in hospital of patients completing the trial (stage ≥ 2) for two alternating-pressure mattresses. The mean time for an alternating-pressure mattress (Nimbus 3, Aura cushion and 4-hourly turning) was 21.6 days and 21.7 days for another alternating-pressure mattress (Pegasus

Cairwave Therapy System, Proactive 2 seating cushion and 8-hourly turning). No estimate of effect or precision could be derived (VERY LOW QUALITY).[67]

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

- One study (n=44) (para- and tetraplegic patients) showed that wheelchair cushion equipped with individualised cyclic pressure relief protocol is potentially more effective compared to standard wheelchair cushion to improve healing of stage II and III PUs (LOW QUALITY).[71]
- One study (n=44) (para- and tetraplegic patients) showed that standard wheelchair cushion is potentially more effective compared to the wheelchair cushion equipped with individualised cyclic pressure relief protocol for rate of healing of stage II and III PUs (LOW QUALITY).[71]
- One study (n=44) (para- and tetraplegic patients) showed that wheelchair cushion equipped with individualised cyclic pressure relief protocol is potentially more effective compared to standard wheelchair cushion for PUSH score improvement of stage II and III PUs (LOW QUALITY).[71]
- One study (n=44) (para- and tetraplegic patients) showed that wheelchair cushion equipped with individualised cyclic pressure relief protocol is clinically more effective compared to standard wheelchair cushion for percentage reduction in ulcer area of stage II and III PUs (LOW QUALITY).[71]
- One study (n=44) (para- and tetraplegic patients) showed that wheelchair cushion equipped with individualised cyclic pressure relief protocol is potentially more effective compared to standard wheelchair cushion for percentage improvement of PUSH score of stage II and III PUs (LOW QUALITY).[71]

3.3.4 Conclusion

- **One small RCT of very low quality suggests there may be no difference between a water mattress and a low-tech mattress to reduce the proportion of pressure ulcers.**
- **Three small RCT's of low to very low quality suggest low-air loss beds are potentially more effective compared to low-tech overlays for the treatment of pressure ulcers.**
- **Two small RCT's of low to very low quality suggest air-fluidised beds are potentially more effective compared to standard care for the treatment of pressure ulcers.**
- **The evidence about competing alternating pressure mattresses did not show clear differences in effectiveness. Neither did the comparison between alternating pressure cushions with dry flotation cushions showed clear difference.**
- **Two RCT's of low to very low quality suggest there is no difference in effectiveness between an alternating pressure mattress and alternating pressure overlay.**
- **One very small RCT of very low quality suggests air-filled devices may be more effective compared to alternating pressure mattresses to reduce the proportion of pressure ulcer.**
- **One very small RCT of very low quality suggests profiling beds are clinically more effective compared to foam mattresses for the treatment of pressure ulcers.**
- **One very small RCT of very low quality suggests constant force mattresses are potentially more effective compared to air-loss mattresses for the treatment of pressure ulcers.**
- **One small RCT of low quality suggest that a wheelchair cushion equipped with an individualised cyclic pressure–relief protocol is potentially more effective compared to a standard wheelchair cushion for the treatment of pressure ulcers.**
- **None of the studies reported harms as a result of the interventions.**
- **All conclusions from the included studies were weakened due to the poor methodological quality of the trials.**

3.3.5 Recommendations and best practices for clinical practice

Recommendations	Strength of Recommendation	Level of Evidence
The use of pressure-redistributing devices (low-tech constant low pressure surfaces or high-tech support surfaces) is recommended for patients who have a pressure ulcer. Redistributing devices should be used in combination with regular repositioning.	**Strong**	**Very low**
As clinical studies did not demonstrate the superiority of one pressure redistributing device over another (e.g. air-fluidised therapy, alternating-pressure mattress), decisions about which pressure redistributing device to use should be based on an overall assessment of the patient, including wound evolution and offloading possibilities, level of risk, comfort and general health state.	**Weak**	**Very low**

Best practices

When pressure ulcers deteriorate or fail to heal, or when there is an increase in risk status:

- **The professional caregiver should consider changing the existing redistributing device with one that will reduce time of applied pressure and/or improve pressure redistribution and reduce shearing forces;**
- **Preventive interventions and local wound care should also be intensified;**
- **Before replacing the existing mattress, evaluate the effectiveness of previous and current prevention and treatment plans.**

3.4 Debridement

3.4.1 Introduction

Debridement refers to the removal of dead, damaged, or infected tissue to improve the healing potential of the remaining healthy tissue. It can be achieved by various techniques including **surgical, mechanical, autolytic, osmotic, enzymatic and maggot therapy**.

In this review **all methods were considered except the autolytic and osmotic methods** which are included in the dressings (see 3.6) and topical agents (see 3.5) reviews.

Autolysis uses the body's own enzymes and moisture to re-hydrate, soften and finally liquefy hard eschar and slough. The autolytic debridement process can be enhanced with the use of dressings such as hydrocolloids, hydrogels, and transparent films. They complement the body's natural debriding process by providing a moist environment, which promotes autolysis, while still acting to preserve living healthy tissue.

Osmotic debridement, on the other hand, is generally performed using hyperosmolar sugar- or honey-based preparations. Dextranomer is an example of a hydroscopic dressing which has a high absorptive capacity, is capable of removing bacteria, debris and absorbing wound exudate, thereby also facilitating autolytic debridement.[74]

RCT's about the clinical effectiveness of debridement in terms of pressure ulcer healing are limited and concern enzymatic therapies and hydrotherapy only. Enzymatic wound debridement consists of selective removal of non-vital tissue using proteolytic enzymes such as streptokinase, streptodornase, collagenases, papain/urea and fibrinolysin/DNAse.

Maggot therapy, also known as larvae therapy, is an alternative method of debridement. Sterile fly larvae of the sheep blowfly *Luciliasericata*

(Diptera: Calliphoridae) are used. The enzymes produced by maggots dissolve only dead tissue in human wounds and therefore healthy tissue remains undamaged.(Zarchi & Jemec, 2012) They feed on dead and infected tissue without touching 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. Maggot therapy may result in more rapid debridement and less pain than some other therapies. The main disadvantage is that some patients are averse to the use of maggots. Maggot therapy is classified as a medicinal product. No European agency has provided a license to use this method/medicine and as a consequence the products are not licensed anywhere in Europe. However, every single Member State makes its own legal arrangements for the import and use of unlicensed medicines, which is allowed by the European Directive on Medicinal Products (2001/83/EC). The Belgian authority doesn't permit to deliver larvae to users in Belgium.

3.4.2 Review question

What are the most clinically effective methods of debridement of non-viable tissue for treatment of pressure ulcers?

3.4.3 Clinical evidence

Ten records, seven randomized controlled trials[75-80] and three observational studies[81-83], were included in this review. One observational study was not taken into account due to limited information available to assess the clinical effectiveness.

3.4.3.1 Quality of studies

In general the methodological quality of the included studies was poor. Seven studies were randomized controlled trial studies.[75-80, 84] None of these studies reported on allocation concealment. Sequence generation was poor in five studies[77-80, 84] and an intention to treat analyses was not used in four studies.[163;207;209] Three performed blinding of outcome assessor.[169;208;210] No other form of blinding was applied. Only two studies did an a priory sample size calculation[80, 84], of which one was underpowered.[80] Three studies had an observational design. [81-83] In appendix 3 the level of evidence can be found per outcome after applying the GRADE-methodology. The evidence base for all outcomes has been rated being of as low to very low quality.

3.4.3.2 Evidence statements

Collagenase versus inactivated collagenase

- One study (n=28) showed that collagenase is potentially more effective compared to inactivated collagenase to reduce the proportion of pressure ulcers decreased in volume (VERY LOW QUALITY).[78]
- One study (n=28) showed that inactivated collagenase is potentially more effective compared to collagenase to reduce the proportion of pressure ulcers decreased in ulcer size (VERY LOW QUALITY).[78]
- One study (n=28) showed that there may be no difference between collagenase and inactivated collagenase to reduce the incidence of odour, the direction of the estimate of the effect favoured the inactivated collagenase (VERY LOW QUALITY).[78]
- One study (n=28) showed that inactivated collagenase may be more effective compared to collagenase to reduce the incidence of adverse events (VERY LOW QUALITY).[78]

Collagenase versus dextranomer

- One study (n=25) showed that dextranomer is potentially more effective compared to collagenase to improve healing of pressure ulcers (VERY LOW QUALITY).[79]
- One study (n=25) showed that dextranomer may be more effective compared to collagenase to reduce the proportion of pressure ulcers (VERY LOW QUALITY).[79]
- One study (n=13) showed that dextranomer may be more effective compared to collagenase to reduce the proportion of patients with a pressure ulcer (VERY LOW QUALITY).[79]
- One study (n=13) showed that dextranomer is potentially more effective compared to collagenase to improve healing of patients with a pressure ulcer (VERY LOW QUALITY).[79]

Collagenase versus sugar and egg white

- One study (n=20) showed that collagenase may be more effective compared to sugar and egg white to improve healing of pressure ulcers (VERY LOW QUALITY).[79]

- One study (n=20) showed that collagenase may be more effective compared to sugar and egg white to reduce the proportion of pressure ulcers (VERY LOW QUALITY).[79]
- One study (n=10) showed that collagenase may be more effective compared to sugar and egg white to reduce the proportion of patients with a pressure ulcer (VERY LOW QUALITY).[79]
- One study (n=10) showed that collagenase may be more effective compared to sugar and egg white to improve healing of patients with a pressure ulcer (VERY LOW QUALITY).[79]

Collagenase versus papain/urea

- One study (n=21) showed that papain/urea is potentially more effective compared to collagenase for percentage reduction in ulcer size (VERY LOW QUALITY).[75]
- One study (n=21) showed that papain/urea may be more effective compared to collagenase to reduce the incidence of adverse events (VERY LOW QUALITY).[75]

Collagenase versus fibrolysis/DNAse

- One study (n=135) showed that fibrinolysin/DNAse is potentially more effective compared to collagenase to reduce the incidence of adverse events (VERY LOW QUALITY).[80]
- One study (n=221) showed that fibrinolysin/DNAse is more effective compared to collagenase to reduce the incidence of serious adverse events (LOW QUALITY).[80]

Collagenase versus hydrocolloid

- One study (n=37) showed that there is potentially no difference between collagenase and a hydrocolloid to improve healing of pressure ulcers, the direction of the estimate of the effect favoured the collagenase (VERY LOW QUALITY).[77]
- Two studies (n=60) showed collagenase is potentially more effective compared to hydrocolloid to reduce the proportion of pressure ulcers(VERY LOW QUALITY).[77, 84]
- One study (n=37) showed that there is potentially no difference between collagenase and a hydrocolloid for mean cm² reduction in ulcer area, the direction of the estimate of the effect favoured the collagenase (VERY LOW QUALITY).[77]
- One study (n=37) showed that collagenase may be more effective compared to a hydrocolloid to reduce the incidence of adverse events (VERY LOW QUALITY).[77]
- One study (n=23) showed collagenase is potentially more effective compared to hydrocolloid for mean time to healing of stage IV heel pressure ulcers (VERY LOW QUALITY).[84]

Collagenase ointment: application every 24 hours versus every 48 hours

- One study (n=86) showed that collagenase every 24 hours may be more effective compared to collagenase every 48 hours to reduce the proportion of pressure ulcers (VERY LOW QUALITY).[76]
- One study (n=92) showed there may be no difference between collagenase every 24 hours and collagenase every 48 hours to reduce the incidence of adverse events, the direction of the estimate of the effect favoured either intervention (VERY LOW QUALITY).[76]

Maggot therapy versus conservative treatment

- One study (n=92) (inpatients) showed that maggot therapy is clinically more effective compared to conservative treatment for cm² change of surface area of stage III and IV pressure ulcers (VERY LOW QUALITY).[81]
- One study (n=92) (inpatients) showed that maggot therapy is clinically more effective compared to conservative treatment for change of surface area per week of stage III and IV pressure ulcers (VERY LOW QUALITY).[81]
- One study (n=92) (inpatients) showed that maggot therapy is potentially more effective compared to conservative treatment to improve healing of stage III and IV pressure ulcers (VERY LOW QUALITY).[81]
- One study (n=92) (inpatients) showed there is potentially no difference between maggot therapy and conservative treatment for healing rate of stage III and IV pressure ulcers, the direction of the estimate of the effect favoured either maggot therapy (VERY LOW QUALITY).[81]

- One study (n=92) (inpatients) showed that maggot therapy is potentially more effective compared to conservative treatment to reduce the proportion of stage III and IV pressure ulcers (VERY LOW QUALITY).[81]
- Two studies (n=110) (inpatients and patients with a spinal cord injury) showed there is potentially no difference between maggot therapy and conservative treatment for time to healing of pressure ulcers (VERY LOW QUALITY).[81, 83]

3.4.4 Conclusion

- **Six RCT's of very low quality do not offer evidence that shows either a positive or negative effect of any debridement method on the treatment of pressure ulcers. This does not necessarily apply to the methods enhancing the autolytic debridement which were not included in this review.**
- **The existing evidence based on two observational studies indicates maggot therapy to be more effective than conservative treatment in terms of change in wound surface and time to healing. However, results should be interpreted with caution since studies were of very low quality.**
- **None of the studies reported harms as a result of the interventions.**

3.4.5 Best practices for clinical practice

Best practices

Debride devitalized tissue within the wound bed or edge of pressure ulcers.

If debridement is considered, the choice of the method(s) (chemical, bioactive, surgical, autolytic, enzymatic, mechanical debridement) will be based on: the patient's condition; goals of care; ulcer/periulcer status; type, quantity, and location of necrotic tissue; care setting; availability of products for debridement and the available professional skills.

3.5 Topical agents

3.5.1 Introduction

Topical agents are widely used in pressure ulcer treatment. Nowadays, the use of topical agents has become a part of routine care in the treatment of pressure ulcers. This has led to the development of a variety of therapeutic agents for topical use. However, the efficacy of topical agents has not been clearly established. This systematic review was conducted to assess the comparative efficacy among different topical agents. For the purpose of this review, two main groups of topical agents were defined and agreed by the expert panel: non anti-bacterial agents (cleansers, moisturizers, and protective agents) and anti-bacterial agents (antiseptic agents, antibiotics, anti-inflammatory agents, and anti-fungal agents). The first group of topical agents aims to protect the broken skin or tissue for further breakdown or tissue damage. The second main group of topical agents aims to reduce bacterial contamination in order to prevent sepsis.

Table 11 – Categories of topical agents

	Saline	Phenytoin	Solcoseryl	Aloe vera	Petrolatum	Semelil	Zinc oxide	A&D ointment	Silver sulfazidine	Ethoxy-diaminoacridine	Oxy-quinoline	Iodophor such as (Povidone)-iodine	Resin salve	Nitrofurazone
Cleanser	X													
Moisturiser		X	X	X	X	X								
Protecting agent							X	X						
Antiseptic agent									X	X	X	X	X	X
Antibiotic agent									X				X	X
Anti-inflammatory agent												X	X	X
Antifungal agent												X	X	X

Source. References[85-95]

Table 12 – Definition of topical agents

Topical agent	Description
Saline	An isotonic solution of sodium chloride in distilled water
Phenytoin	Possible mechanisms of action of phenytoin on wound healing are as follows: (1) decrease in serum corticosteroid and (2) acceleration of assembly and presence of collagen and fibrin in the ulcer area, and stimulation of alkaline phosphatase secretion
Dialysate (Solcoseryl®)	Solcoseryl contains a free protein extract of calf blood that possesses metabolic function in the tissue. Solcoseryl contains mixture of biologically active substances such as aminoacids, irreplaceable microelements, glycolipids, nucleotides, nucleosides.
Petrolatum	Vaseline
Zinc oxide	A topical astringent and protectant
Streptokinase-streptodornase	A mixture of enzymes and hemolytic streptococci; used as proteolytic and fibrinolytic agent
Povidone-iodine	Povidone iodine is an antiseptic that is used to disinfect skin/wounds

Topical agent	Description
Cadexomer	A dry powder consisting of spherical microbeads that range in diameter from 100 to 315μm. Each microbead is a highly hydrophilic, three 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 as a preservative; sulfa antibiotics
Resin salve	Pure spruce resin
Chinese herbal medical ointment	(1) Rhizoma Coptidis, Cortex Phellodendri, Radix Scutellariae, Borneolum Syntheticum, Myrrha, Sesame Oil (2) Rhizoma Curcumae Longae, Radix et Rhizoma Rhei, Cortex Phellodendri, Rhizoma Atractylodis, Cortex Magnoliae Officinalis, Pericarpium Citri Reticulatae, Radix Glycyrrhizae, Rhizoma Arisaematis, Radix Angelicae Dahuricae, Radix Trichosanthis, Sesame Oil. (3) Crinis Carbonisatus, Tortoise plastron, Radix Angelicae Sinensis, Radix Rehmanniae Recens, Gypsum, Galamina, Yellow Wax, Sesame Oil Ointment formulation: Radix Scutellariae, Cortex Phellodendri, Borneolum Syntheticum, Radix Angelicae Sinensis, Radix et Rhizoma Rhei, Sanguis Draconis, Sesame Oil (4) Radix et Rhizoma Rhei (150 g), Rhizoma Polygoni Cuspidati (150 g), Natrii Sulfas (10 g), Borneolum Syntheticum (10 g), Fresh Aloe (200 g). (5) Radix Angelicae Sinensis, Radix Angelicae Dahuricae, White Wax, Radix Glycyrrhizae, Radix Lithospermi, Sanguis Draconis, Sesame Oil. (6) Rhizoma Coptidis, Cortex Phellodendri, Rhizoma Curcumae Longae, Radix Angelicae Sinensis, Radix Rehmanniae Recens, Sesame Oil. (7) Rhizoma Coptidis (350 g), Cortex Phellodendri (150 g), Radix Scutellariae (100 g), Rhizoma Polygoni Cuspidati (150 g), Radix Sanguisorbae (100 g), Sesame Oil (2000 g).
Growth factors	(1) Topical growth factor – Beta3 (2) Mouse nerve growth factor (3) Recombinant platelet-derived growth factor-BB (4) Granulo-macrophage/colony-stimulating factor (5) basic fibroblast growth factor (6) Interleukin 1-beta

Source. References[85-95]

3.5.2 Review question

What are the most clinically effective topical agents for the treatment of pressure ulcers?

3.5.3 Clinical evidence

A Cochrane review on wound cleansing for pressure ulcer by Moore and Cowan (2011)[96] and a meta-analysis[97] on traditional Chinese medicine were identified and used as reference for this review. The Cochrane review by Moore and Cowan (2011)[96] included three RCT's[98-100], of which two were excluded because they didn't meet the inclusion criteria of our review. One was excluded as it was a study on hydrotherapy[99] and will therefore be included in the debridement review. The other study did not separately reported on outcomes for patients with pressure ulcers.[100] The meta-analysis by Zhang et al. (2012) [97] included 10 RCT's, which were all included in this review.[101-110] Forty-seven randomized controlled trials were included in this review. [88-90, 93-95, 98, 101-137] The authors of the review on traditional Chinese medicine[97] meta-analysed different types of Chinese ointments (intervention) with different types of comparisons such as iodophor and saline. In this review only studies with the same intervention

and outcome were meta-analysed together and therefore results will be presented differently from the review of Zhang et al. (2012). [97]

Various types of topical agents are used to treat pressure ulcers (e.g. Table 11 and Table 12). In this review different types of topical agents are compared to each other or to placebo. Following categories were made:

- Cleansers: soap, water, detergent, and solvent;
- Moisturisers (emollients): glycerine, oil, cream and ointment;
- Protective agents: e.g. talc, zinc oxide;
- Antiseptic agents: alcohol, iodine solution, chlorhexidine, chlor oxydantia, peroxide, quaternary ammonium compounds, phenol, mercury, gentian violet, silver preparation;
- Antibiotics;
- Anti-inflammatory agents;
- Anti-fungal agents;
- Insulin;
- Growth factors.

3.5.3.1 Quality of studies

In general the methodological quality of the included studies was poor. In the majority of the studies, sequence generation [89, 93, 94, 98, 101-105, 108, 112-117, 119, 121-126, 128-133, 136-141] and allocation concealment [112, 113, 88, 89, 93, 94, 98, 101-104, 106-111, 114-117, 119-126, 128-134, 136-142] were not clearly described or performed poorly. The majority of the studies did not use an intention-to-treat analyses.[89, 93, 95, 98, 103, 107-111, 113, 115, 118-120, 123-125, 130, 132-134, 137, 138, 140] Information on the latter was not available for five studies.[101, 102, 104-106] In few studies (n=17), single- or double blinding was used. [88, 90, 93, 95, 111, 112, 114, 118-120, 123-125, 130-134, 137, 138, 140] Few studies (n=8), reported an a priory sample size [90, 95, 111, 117, 122, 128, 140, 141] calculation,[90, 95, 111, 117, 122, 128, 140, 141] of which five were underpowered. [90, 95, 111, 128, 141] Information on the latter was not available for ten studies.[101-110] In appendix 4 the level of evidence can be found per outcome after applying the GRADE-methodology. The evidence base for all outcomes has been rated as being of moderate to very low quality.

3.5.3.2 Evidence statements

Saline versus hydrocolloid dressing

- Three studies (n=126) (general population and patients with a spinal cord injury) showed that hydrocolloid may be more effective than saline at reducing the proportion of ≥ stage I PUs (VERY LOW QUALITY). [90, 122, 136]
- Two studies (n=71) (general population) showed that hydrocolloid may be more effective compared to saline to reduce the proportion of ≥ stage I PUs (VERY LOW QUALITY).[122, 136]
- One study (n=55) (patients with a spinal cord injury) showed that hydrocolloid is clinically more effective than saline to reduce the proportion of stage I and II PUs (MODERATE QUALITY). [90]
- Two studies (n=148) (general population and patients with a spinal cord injury) showed that a hydrocolloid is potentially more effective compared to saline to reduce the proportion of stage I to III PUs (all sites) (VERY LOW QUALITY). [90, 125]
- One study (n=87) (general population) showed that a hydrocolloid may be more effective compared to saline to reduce the proportion of stage II and III PUs (all sites) (VERY LOW QUALITY).[125]
- One study (n=61) (patients with a spinal cord injury) showed that a hydrocolloid is clinically more effective compared to saline to reduce the proportion of stage I to II PUs (all sites) (MODERATE QUALITY). [90]
- One study (n=61) (patients with a spinal cord injury) showed that a hydrocolloid is potentially more effective compared to saline to reduce the proportion of stage I PUs (all sites) (MODERATE QUALITY). [90]
- Two studies (n=96) (general population and patients with a spinal cord injury) showed that a hydrocolloid is potentially more effective compared to saline to reduce the proportion of stage II PUs (all sites) (LOW QUALITY).[90, 125]
- One study (n=59) (general population) showed that that a hydrocolloid is potentially more effective compared to saline to reduce the proportion of stage II PUs (all sites) (LOW QUALITY). [90]

- One study (n=37) (patients with a spinal cord injury) showed that that a hydrocolloid is potentially more effective compared to saline to reduce the proportion of stage II PUs (all sites) (MODERATE QUALITY). [90]
- One study (n=28) (general population) showed that there may be no difference between saline and a hydrocolloid to reduce the proportion of stage III PUs (all sites), the direction of the estimate of the effect favoured the hydrocolloid dressing (VERY LOW QUALITY). [125]
- One study (n=15) (patients with a spinal cord injury) showed that a hydrocolloid is potentually more effective compared to saline to reduce the proportion stage I and II PU's (sacral area) (VERY LOW QUALITY). [90]
- One study (n=91) (patients with a spinal cord injury) showed that a hydrocolloid is potentially more effective compared to saline to improve healing of stage I and II PUs (MODERATE QUALITY).[90]
- Two studies (n=148) (general population and patients with a spinal cord injury) showed there may be no difference between a hydrocolloid and saline to reduce the proportion of stage I to III ulcers worsening (all sites), the direction of the estimate of the effect favoured the hydrocolloid dressing (VERY LOW QUALITY). [90, 125]
- One study (n=87) (general population) showed that there may be no difference between saline and a hydrocolloid to reduce the proportion of PU worsening (stage II and III) (all sites), the direction of the estimate of the effect favoured the hydrocolloid dressing (VERY LOW QUALITY). [125]
- One study (n=61) (patients with a spinal cord injury) showed that a hydrocolloid is potentially more effective compared to saline to reduce the proportion of PU worsening (stage I) (all sites) (VERY LOW QUALITY).[90]
- One study (n=59) (general population) showed that there may be no difference between saline and a hydrocolloid to reduce the proportion of PU worsening (stage II) (all sites), the direction of the estimate of the effect favoured the hydrocolloid dressing (VERY LOW QUALITY). [125]
- One study (n=28) (general population) showed that there may be no difference between saline and a hydrocolloid to reduce the proportion of PU worsening (stage III) (all sites), the direction of the estimate of the effect favoured the hydrocolloid dressing (VERY LOW QUALITY). [125]
- One study (n=34) (general population) showed that there is potentially no difference between saline and a hydrocolloid for mean percentage reduction in ulcer area (stage II and III), the direction of the estimate of the effect favoured the hydrocolloid dressing (VERY LOW QUALITY).[113]
- One study (n=32) (general population) showed that saline is clinically more effective for mean percentage reduction in ulcer volume (stage III and IV) (LOW QUALITY).[122]
- One study (n=50) (long-term care patients) reported a median percentage reduction in ulcer area (stage 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).[112]
- One study (n=59) (general population) reported a median percentage reduction in ulcer size (stage II) 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). [125]
- One study (n=28) (general population) reported a median percentage reduction in ulcer size (stage III) 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). [125]
- One study (n=39) (long-term care patients) reported median days to healing (stage II and III) 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).[136]
- One study (n=50) (long-term care patients) reported a healing distribution function (stage not reported) for saline and a hydrocolloid. A p-value of 0.15 was reported (VERY LOW QUALITY).[112]

- One study (n=34) (general population) showed that saline is more effective compared to a hydrocolloid in terms of pain at dressing removal (LOW QUALITY). [113]
- One study (n=32) (general population) reported a median pain score during treatment (stage III and IV) 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).[122]
- One study (n=34) (general population) showed that saline is more effective compared to a hydrocolloid in terms of discomfort at dressing removal (LOW QUALITY). [113]
- One study (n=32) (general population) reported a median comfort score during treatment (stage III and IV) 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).[122]
- One study (n=34) (general population) showed that no difference between saline and a hydrocolloid to reduce the incidence of infections (LOW QUALITY). [113]
- One study (n=32) (general population) reported a median comfort score during treatment (stage III and IV) 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).[122]
- One study (n=100) (general population) showed that saline is more effective compared ot hydrocolloid to reduce the incidence of skin irritation (VERY LOW QUALITY). [125]

Saline versus hydrogel dressing

- One study (n=30) (general population) showed that there may be no difference between saline and hydrogel to reduce the proportion of stage II to IV PUs, the direction of the estimate of the effect favoured the saline (VERY LOW QUALITY).[140]
- One study (n=41) (general population) showed that there may be no difference between saline and hydrogel to reduce the proportion of ulcers worsening (stage II to IV), the direction of the estimate of the effect favoured the hydrogel (VERY LOW QUALITY).[140]
- One study (n=30) (general population) reported a percentage healing rate (stage II to IV) 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).[140]
- One study (n=30) (general population) showed that there may be no difference between saline and hydrogel for mean weeks to healing of stage II to IV PUs, the direction of the estimate of the effect favoured the hydrogel (VERY LOW QUALITY).[140]

Saline versus foam dressing

- Two studies (n=74) (general population) showed that a foam dressing is potentially more effective compared to saline to reduce the proportion of stage II and III PUs (VERY LOW QUALITY). [117, 128]
- One study (n=36) (general population) reported a median days to to healing of 50% of the patients (stage 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). [128]

Saline versus polyurethane film

- One study (n=19) (general population) showed that a polyurethane film may be more effective compared to saline to reduce the proportion of stage II and III PUs (VERY LOW QUALITY).[126]
- One study (n=19) (general population) showed that a polyurethane film may be more effective compared to saline to reduce the proportion of PU worsening (stage II and III PUs) (VERY LOW QUALITY).[126]
- One study (n=19) (general population) reported a mean percentage reduction in ulcer area (stage II to IV) for saline and polyurethane film. The mean for saline was 2.5% and 42.9% for hydrogel. No estimate of effect or precision could be derived (VERY LOW QUALITY).[126]

Saline versus dextranomer

- One study (n=30) (patients with a spinal cord injury) showed that dextranomer is clinically more effective to improve healing of stage II to IV PUs (LOW QUALITY).[121]

- One study (n=30) (patients with a spinal cord injury) showed no difference for incidence of adverse events between saline and dextranomer (LOW QUALITY).[121]

Phenytoin versus saline

- One study (n=55) (patients with a spinal cord injury) showed that phenytoin may be more effective compared to saline to reduce the proportion of stage I and II PUs (VERY LOW QUALITY).[90]
- One study (n=60) (patients with a spinal cord injury) showed that phenytoin may be more effective compared to saline to reduce the proportion of stage I and II PUs (VERY LOW QUALITY).[90]
- One study (n=20) (patients with a spinal cord injury) showed that saline is potentially more effective compared to phenytoin to reduce the proportion of stage I (VERY LOW QUALITY).[90]
- One study (n=40) (patients with a spinal cord injury) showed that phenytoin is potentially more effective compared to saline to reduce the proportion of stage II (VERY LOW QUALITY).[90]
- One study (n=13) (patients with a spinal cord injury) showed that there may be no difference between phenytoin and saline to reduce the proportion of stage I and II PUs in the sacral area, the direction of the estimate of the effect favoured the saline (VERY LOW QUALITY).[90]
- One study (n=60) (patients with a spinal cord injury) showed that there may be no difference between phenytoin and saline to improve healing of stage I and II PUs, the direction of the estimate of the effect favoured the phenytoin (VERY LOW QUALITY).[90]
- One study (n=60) (patients with a spinal cord injury) showed that phenytoin is potentially more effective compared to saline to reduce the proportion of PU worsening (stage I and II) (VERY LOW QUALITY).[90]
- One study (n=26) (patients with a spinal cord injury) showed that phenytoin is potentially more effective compared to saline for mean percentage reduction in ulcer size (stage II) (VERY LOW QUALITY).[134]
- One study (n=26) (patients with a spinal cord injury) showed that there may be no difference between phenytoin and saline for mean percentage reduction in ulcer volume (stage II) (VERY LOW QUALITY).[134]
- One study (n=26) (patients with a spinal cord injury) showed that phenytoin may be more effective compared to saline for mean percentage reduction in PUSH score (stage II) (VERY LOW QUALITY).[134]
- One study (n=30) (patients with a spinal cord injury) showed no difference for incidence of adverse events between saline and phenytoin (LOW QUALITY).[134]

Phenytoin versus hydrocolloid dressing

- One study (n=56) (patients with a spinal cord injury) showed that a hydrocolloid is potentially more effective compared to phenytoin to reduce the proportion of stage I and II PUs (LOW QUALITY).[90]
- One study (n=61) (patients with a spinal cord injury) showed that a hydrocolloid is potentially more effective compared to phenytoin to reduce the proportion of stage I and II PUs (LOW QUALITY).[90]
- One study (n=22) (patients with a spinal cord injury) showed that a hydrocolloid is potentially more effective compared to phenytoin to reduce the proportion of stage I PUs (LOW QUALITY).[90]
- One study (n=39) (patients with a spinal cord injury) showed that a hydrocolloid is potentially more effective compared to phenytoin to reduce the proportion of stage II PUs (LOW QUALITY).[90]
- One study (n=15) (patients with a spinal cord injury) showed that there may be no difference between phenytoin and a hydrocolloid to reduce the proportion of stage I and II PUs in the sacral area (VERY LOW QUALITY).[90]
- One study (n=61) (patients with a spinal cord injury) showed that a hydrocolloid is potentially more effective compared to phenytoin to improve healing stage I and II PUs (LOW QUALITY).[90]
- One study (n=61) (patients with a spinal cord injury) showed that there may be no difference between phenytoin and a hydrocolloid to reduce the proportion (stage I and II) (VERY LOW QUALITY).[90]

- One study (n=28) (nursing home patients) showed that phenytoin is potentially more effective compared to a hydrocolloid for mean days to healing (stage II) (LOW QUALITY).[130]
- One study (n=28) (nursing home patients) reported minimal pain in patients receiving phenytoin and a hydrocolloid dressing. No estimate of effect or precision could be derived (VERY LOW QUALITY).[130]
- One study (n=28) (nursing home patients) showed no difference between phenytoin and a hydrocolloid to reduce the incidence of adverse events (LOW QUALITY).[130]

Phenytoin versus triple antibiotics

- One study (n=26) (nursing home patients) showed that phenytoin is clinically more effective compared to triple antibiotics for mean days to healing (stage II) (LOW QUALITY).[130]
- One study (n=26) (nursing home patients) reported minimal pain in patients receiving phenytoin and triple antibiotics. No estimate of effect or precision could be derived (VERY LOW QUALITY).[130]
- One study (n=26) (nursing home patients) showed no difference between phenytoin and triple antibiotics to reduce the incidence of adverse events (LOW QUALITY).[130]

Aloe vera, silver chloride and decyl glucoside versus saline

- One study (number of patients not reported) (elderly patients) reported a mean percentage reduction in PSST score (stage II to IV) 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).[98]

Dialysate (Solcoseryl®) versus placebo

- One study (n=8) (patients with a spinal cord injury) showed that dialysate is potentially more effective compared to placebo for reducing mean ml in ulcer area (VERY LOW QUALITY).[93]
- One study (n=8) (patients with a spinal cord injury) reported mean percentage reduction in 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).[93]
- One study (n=8) (patients with a spinal cord injury) reported mean percentage reduction in 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).[93]
- One study (n=8) (patients with a spinal cord injury) showed that dialysate is potentially more effective compared to placebo for mean healing half-time (VERY LOW QUALITY).[93]
- One study (n=8) (patients with a spinal cord injury) showed no difference between dialysate and placebo to reduce the incidence of adverse events (LOW QUALITY).[93]

Petrolatum ointment (petrolatum plus additives) versus petrolatum (base component)

- One study (n=19) (elderly patients) showed that petrolatum ointment may be more effective compared to petrolatum (base component) to reduce the proportion of stage I and II PUs (VERY LOW QUALITY).[119]
- One study (n=11) (elderly patients) showed that petrolatum ointment may be more effective compared to petrolatum (base component) to reduce the proportion of stage I PUs (VERY LOW QUALITY).[119]
- One study (n=8) (elderly patients) showed that petrolatum ointment may be more effective compared to petrolatum (base component) to reduce the proportion of stage II PUs (VERY LOW QUALITY).[119]
- One study (n=19) (elderly patients) showed that petrolatum ointment is potentially more effective compared to petrolatum (base component) to improve healing of stage I and II PUs (VERY LOW QUALITY).[119]
- One study (n=11) (elderly patients) showed that petrolatum ointment may be more effective compared to petrolatum (base component) to improve healing of stage I PUs (VERY LOW QUALITY).[119]
- One study (n=8) (elderly patients) showed that petrolatum ointment may be more effective compared to petrolatum (base component) to improve healing of stage II PUs (VERY LOW QUALITY).[119]
- One study (n=19) (elderly patients) showed that there may be no difference between petrolatum ointment and petrolatum (base component) to reduce the proportion of PU stage I and II not changed,

the direction of the estimate of the effect favoured the petrolatum ointment (VERY LOW QUALITY).[119]

- One study (n=11) (elderly patients) showed that petrolatum ointment may be more effective compared to petrolatum (base component) to reduce the proportion of PU stage I not changed (VERY LOW QUALITY).[119]
- One study (n=8) (elderly patients) showed that petrolatum (base component) may be more effective compared to petrolatum ointment to reduce the proportion of PU stage I not changed (VERY LOW QUALITY).[119]
- One study (n=19) (elderly patients) showed that petrolatum ointment is clinically more effective compared to petrolatum (base component) to reduce the proportion of stage I and II PU worsening (LOW QUALITY).[119]
- One study (n=11) (elderly patients) showed that petrolatum ointment may be more effective compared to petrolatum (base component) to reduce the proportion of stage I PU worsening (VERY LOW QUALITY).[119]
- One study (n=8) (elderly patients) showed that petrolatum ointment is clinically more effective compared to petrolatum (base component) to reduce the proportion of stage II PU worsening (LOW QUALITY).[119]

Herbal extract (Semelil) versus standard treatment

- One study (n=18) (general population) showed that the herbal extract is clinically more effective compared to standard treatment to reduce the proportion of PUs healed for > 80% (LOW QUALITY).[94]
- One study (n=18) (general population) showed that the herbal extract may be more effective compared to standard treatment to reduce the proportion of PUs healed for 50-80% (VERY LOW QUALITY).[94]
- One study (n=18) (general population) showed that there is no difference between herbal extract and standard treatment for healing of PUs for 20-50% (VERY LOW QUALITY).[94]
- One study (n=18) (general population) showed that the herbal extract is clinically more effective compared to standard treatment to reduce the proportion of PUs healed for < 20% (LOW QUALITY).[94]
- One study (n=18) (general population) showed that the herbal extract is potentially more effective compared to standard treatment for mean cm^2 reduction in ulcer area (VERY LOW QUALITY).[94]
- One study (n=18) (general population) showed that the herbal extract is clinically more effective compared to standard treatment for mean percentage healing rate (LOW QUALITY).[94]
- One study (n=18) (general population) showed no difference between the herbal extract and standard treatment placebo to reduce the incidence of adverse events (LOW QUALITY).[94]

Zinc oxide versus streptokinase-streptodornase

- One study (n=28) (elderly patients) reported a median percentage reduction in 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).[111]
- One study (n=28) (elderly patients) showed that zinc oxide may be more effective compared to streptokinase-streptodornase to reduce the incidence of infections (VERY LOW QUALITY).[111]
- One study (n=28) (elderly patients) showed that zinc oxide may be more effective compared to streptokinase-streptodornase to reduce the incidence of skin reactions (VERY LOW QUALITY).[111]

Phenol versus A&D® Petrolatum based ointment

- One study (n=137) (palliative care patients) showed that phenol is potentially more effective compared to A&D® ointment to reduce the proportion of stage I and II PUs (VERY LOW QUALITY).[88]
- One study (n=69) (palliative care patients) showed that there may be no difference between phenol and A&D® ointment to reduce the proportion of stage I PUs, the direction of the estimate of the effect favoured the A&D ointment (VERY LOW QUALITY).[88]
- One study (n=68) (palliative care patients) showed that phenol is potentially more effective compared to A&D ointment to reduce the proportion of stage II PUs (VERY LOW QUALITY).[88]

- One study (n=69) (palliative care patients) showed that phenol is potentially more effective compared to A&D® ointment to improve healing of stage I PUs (VERY LOW QUALITY).[88]
- One study (n=68) (palliative care patients) showed that there may be no difference between phenol and A&D® ointment to improve healing of stage II PUs, the direction of the estimate of the effect favoured the phenol (VERY LOW QUALITY).[88]
- One study (n=69) (palliative care patients) showed that phenol may be more effective compared to A&D® ointment to reduce the proportion of stage I PUs not changed (VERY LOW QUALITY).[88]
- One study (n=68) (palliative care patients) showed that phenol is potentially more effective compared to A&D® ointment to reduce the proportion of stage II PUs not changed (VERY LOW QUALITY).[88]
- One study (n=69) (palliative care patients) showed that phenol may be more effective compared to A&D® ointment to reduce the proportion of stage I PUs worsened (VERY LOW QUALITY).[88]
- One study (n=68) (palliative care patients) showed that phenol may be more effective compared to A&D® ointment to reduce the proportion of stage II PUs worsened (VERY LOW QUALITY).[88]
- One study (n=137) (palliative care patients) showed that there is potentially no difference between phenol and A&D® ointment for mean days to complete healing (stage I and II PUs), the direction of the estimate of the effect favoured the phenol (VERY LOW QUALITY).[88]
- One study (n=69) (palliative care patients) showed that there is potentially no difference between phenol and A&D® ointment for mean days to complete healing (stage I PUs), the direction of the estimate of the effect favoured the phenol (VERY LOW QUALITY).[88]
- One study (n=68) (palliative care patients) showed that phenol is clinically more effective compared to A&D® ointment for mean days to complete healing (stage II PUs) (LOW QUALITY).[88]

Ethoxy-diaminoacridine plus nitrofuazone versus honey

- One study (n=50) (general populations) showed that honey is clinically more effective compared to ethoxy-diaminoacridine plus nitrofuazone to reduce the proportion of stage II and III PUs (VERY LOW QUALITY).[89]
- One study (n=50) (general populations) showed that honey is clinically more effective compared to ethoxy-diaminoacridine plus nitrofuazone for mean percentage reduction in PUSH score (stage II and III PUs) (VERY LOW QUALITY).[89]
- One study (n=50) (general populations) showed that honey is clinically more effective compared to ethoxy-diaminoacridine plus nitrofuazone for mean percentage reduction in ulcer size (stage II and III PUs) (VERY LOW QUALITY).[89]
- One study (n=50) (general populations) showed that there is no difference between honey and ethoxy-diaminoacridine plus nitrofuazone to reduce the incidence of adverse events (LOW QUALITY).[89]

Povidone-iodine versus hydrocolloid dressing

- One study (n=44) (general populations) showed that there may be no difference between povidone-iodine and hydrocolloid to reduce the proportion of stage I and II PUs, the direction of the estimate of the effect favoured the hydrocolloid (VERY LOW QUALITY).[116]
- 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).[116]
- One study (n=44) (general populations) showed that a hydrocolloid may be more effective compared to povidone-iodine for mean speed of healing (stage I and II PUs) (VERY LOW QUALITY).[116]
- One study (n=44) (general populations) showed that there povidone-iodine may be more effective compared to a hydrocolloid to reduce the incidence of hypergranulation (stage I and II PUs) (VERY LOW QUALITY).[116]

Povidone-iodine versus hydrogel dressing

- One study (n=49) (general populations) showed that hydrogel is potentially more effective compared to povidone-iodine for mean speed of healing (stage I to III PUs) (VERY LOW QUALITY).[115]

Cadexomer iodine versus standard treatment

- One study (n=34) (general populations) showed that cadexomer iodine is clinically more effective compared to standard treatment to reduce the proportion of deep and superficial PUs healed for 50% (LOW QUALITY).[123]
- One study (n=34) (general populations) showed that cadexomer iodine is clinically more effective compared to standard treatment for mean cm² reduction in ulcer area (LOW QUALITY).[123]
- One study (n=34) (general populations) showed that cadexomer iodine is clinically more effective compared to standard treatment for mean percentage reduction in ulcer area (LOW QUALITY).[123]

Povidone-iodine versus silver sulfazidine

- One study (n=26) (general populations) reported proportion of clinical response to treatment for povidone-iodine and silver sulfazidine. A p-value of p≤0.022 in favour of silver sulfazidine was reported (VERY LOW QUALITY).[118]
- One study (n=26) (general populations) mean values of bacterial levels for povidone-iodine and silver sulfazidine. A p-value of p<0.01 in favour of silver sulfazidine was reported (VERY LOW QUALITY).[118]

Silver sulfazidine cream versus silver dressing

- One study (n=40) (general populations) showed that there is potentially no difference between silver sulfazidine cream and a silver dressing for mean percentage reduction in ulcer area (stage IV PUs) (VERY LOW QUALITY).[142]
- One study (n=40) (general populations) reported percentage reduction in PUSH score (stage 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).[142]
- One study (n=40) (general populations) showed no difference between silver sulfazidine cream and a silver dressing to reduce the incidence of adverse events (LOW QUALITY).[142]

Resin salve versus hydrofibre®

- One study (n=22) (general populations) showed that resin salve is potentially more effective compared to a hydrofibre® to reduce the proportion of stage II to IV PUs (VERY LOW QUALITY).[95]
- One study (n=29) (general populations) showed that resin salve is potentially more effective compared to a hydrofibre® to reduce the proportion of stage II to IV PUs (VERY LOW QUALITY).[95]
- One study (n=29) (general populations) showed that there is potentially no difference between resin salve and a hydrofibre® to improve healing of stage II to IV PUs, the direction of the estimate of the effect favoured the resin salve (VERY LOW QUALITY).[95]
- One study (n=29) (general populations) showed that resin salve may be more effective compared to a hydrofibre® to reduce the proportion of stage II to IV PUs worsened (VERY LOW QUALITY).[95]
- 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).[95]
- 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).[95]
- 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).[95]
- One study (n=22) (general populations) showed that hydrofibre® may be more effective compared to resin salve to reduce the incidence of skin reactions (VERY LOW QUALITY).[95]

Antibiotic ointment versus foam dressing

- One study (n=44) (institutionalized elderly) showed that a foam dressing may be more effective compared to antibiotic ointment to reduce the proportion of stage II PUs (VERY LOW QUALITY).[137]
- One study (n=44) (institutionalized elderly) 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).[137]

FuChunSanYi Hao ointment (Chinese herbal medical ointment) versus iodophor

- One study (n=48) showed that FuChunSanYi Hao ointment is potentially more effective compared to iodophor to reduce the proportion of stage II to IV PUs (VERY LOW QUALITY).[108]
- One study (n=48) showed that FuChunSanYi Hao ointment may be more effective compared to iodophor to improve healing of stage II to IV PUs (VERY LOW QUALITY).[108]
- One study (n=48) showed that FuChunSanYi Hao ointment may be more effective compared to iodophor to reduce the proportion of stage II to IV PUs worsened (LOW QUALITY).[108]

RuYiZhuHuang ointment (Chinese herbal medical ointment) versus iodophor

- One study (n=248) showed that RuYiZhuHuang ointment is clinically more effective compared to iodophor to reduce the proportion of stage I to IV PUs (LOW QUALITY).[105-107]
- One study (n=248) showed that there is potentially no difference between RuYiZhuHuang ointment and iodophor to improve healing of stage I to IV PUs, the direction of the estimate of the effect favoured the RuYiZhuHuang ointment (VERY LOW QUALITY).[105-107]
- One study (n=248) showed that RuYiZhuHuang ointment is clinically more effective compared to iodophor to reduce the proportion of stage I to IV PUs worsened (LOW QUALITY).[105-107]

ShenJi ointment (Chinese herbal medical ointment) versus iodophor

- One study (n=44) showed that ShenJi ointment is clinically more effective compared to iodophor to reduce the proportion of stage III and IV PUs (LOW QUALITY).[110]
- One study (n=44) showed that ShenJi ointment is potentially more effective compared to iodophor to improve healing of stage I to IV PUs (VERY LOW QUALITY).[110]
- One study (n=44) showed that ShenJi ointment is potentially more effective compared to iodophor to reduce the proportion of stage I to IV PUs worsened (VERY LOW QUALITY).[110]

JiFuYuan ointment (Chinese herbal medical ointment) versus gentamicin

- One study (n=46) showed that JiFuYuan ointment is clinically more effective compared to gentamicin to reduce the proportion of stage II to IV PUs (LOW QUALITY).[101]
- One study (n=46) showed that JiFuYuan ointment is potentially more effective compared to gentamicin to improve healing of stage I to IV PUs (VERY LOW QUALITY).[101]
- One study (n=46) showed that JiFuYuan ointment is potentially more effective compared to gentamicin to reduce the proportion of stage I to IV PUs worsened (VERY LOW QUALITY).[101]

FuFangDaHuang Ding ointment (Chinese herbal medical ointment) versus chloramphenicol and sulfazidine silver powder

- One study (n=55) showed that FuFangDaHuang Ding ointment is potentially more effective compared to chloramphenicol and sulfazidine silver powder to reduce the proportion of PUs (VERY LOW QUALITY).[103]
- One study (n=55) showed that FuFangDaHuang Ding ointment is potentially more effective compared to chloramphenicol and sulfazidine silver powder to improve healing of PUs (VERY LOW QUALITY).[103]

- One study (n=55) showed that FuFangDaHuang Ding ointment is clinically more effective compared to chloramphenicol and sulfazidine silver powder to reduce the proportion of PUs worsened (LOW QUALITY).[103]

ShenJiHuHong ointment (Chinese herbal medical ointment) versus saline

- One study (n=35) showed that ShenJiHuHong ointment is clinically more effective compared to saline to reduce the proportion of stage III and IV PUs (LOW QUALITY).[102]
- One study (n=35) showed that ShenJiHuHong ointment is potentially more effective compared to saline to improve healing of stage III and IV PUs (VERY LOW QUALITY).[102]
- One study (n=35) showed that ShenJiHuHong ointment is clinically more effective compared to saline to reduce the proportion of stage III and IV PUs (LOW QUALITY).[102]

ShenJi ointment (Chinese herbal medical ointment) versus antibacterial

- One study (n=109) showed that ShenJi ointment is potentially more effective compared to antibacterial to reduce the proportion of stage III and IV PUs (VERY LOW QUALITY).[109]
- One study (n=109) showed that there is potentially no difference between ShenJi ointment and antibacterial to improve healing of stage III and IV PUs (VERY LOW QUALITY).[109]
- One study (n=109) showed that ShenJi ointment is potentially more effective compared to antibacterial to reduce the proportion of stage III and IV PUs (VERY LOW QUALITY).[109]

SanHuangZhang Yu TouSha ointment (Chinese herbal medical ointment) versus nitrofurazone

- One study (n=308) showed that SanHuangZhang Yu TouSha ointment is clincially more effective compared to nitrofurazone to reduce the proportion of PUs (LOW QUALITY).[104]
- One study (n=308) showed that SanHuangZhang Yu TouSha ointment is potentially more effective compared to nitrofurazone to improve healing of PUs (VERY LOW QUALITY).[104]
- One study (n=308) showed that SanHuangZhang Yu TouSha ointment is clincially more effective compared to nitrofurazone to reduce the proportion of PUs (LOW QUALITY).[104]

Insulin versus standard treatment

- One study (n=14) (nursing home patients) reported mean healing rate for insulin and standard treatment. A p-value of 0.05 in favour of insulin was reported (VERY LOW QUALITY).[141]

Growth factored versus placebo or another dose or another growth factor

- Seven studies (n=316) (general population and denervated patients) showed that different types of growth factors may be more effective compared to placebo to reduce the proportion of stage II and above PUs (VERY LOW QUALITY).[114, 120, 124, 127, 129, 131, 139]
- One study (n=14) (inpatients) showed that transforming growth factor-beta 3 may be more effective compared placebo to reduce the proportion of stage III and IV PUs (VERY LOW QUALITY).[114]
- One study (n=9) (inpatients) showed that there is no difference between transforming growth factor-beta 3 (1.0μg/cm) and placebo to reduce the proportion of stage III and IV PUs (LOW QUALITY).[114]
- One study (n=9) (inpatients) reported mean percentage reduction in 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).[114]
- 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).[114]
- One study (n=9) (inpatients) showed that transforming growth factor-beta 3 (2.5μg/cm) may be more effective compared to transforming growth factor-beta 3 (1.0μg/cm) to reduce the proportion of stage III and IV PUs (VERY LOW QUALITY).[114]

- 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).[114]
- 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).[114]
- One study (n=10) (inpatients) showed that transforming growth factor-beta 3 (2.5μg/cm) may be more effective compared to placebo to reduce the proportion of stage III and IV PUs (LOW QUALITY).[114]
- 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).[114]
- 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).[114]
- One study (n=36) (nursing home patients) showed that mouse nerve growth factors is more effective compared placebo to reduce the proportion of stage II and above PUs (foot ulcers) (MODERATE QUALITY).[120]
- One study (n=36) (nursing home patients) showed that mouse nerve growth factors is more effective compared placebo to improve healing by three or more stages of stage II and above PUs (foot ulcers) (MODERATE QUALITY).[120]
- One study (n=36) (nursing home patients) showed that mouse nerve growth factors is more effective compared placebo to improve healing by two stages of stage II and above PUs (foot ulcers) (MODERATE QUALITY).[120]
- One study (n=36) (nursing home patients) showed that mouse nerve growth factors is more effective compared placebo to improve healing by one stage of stage II and above PUs (foot ulcers) (MODERATE QUALITY).[120]
- One study (n=36) (nursing home patients) showed that there may be no difference between mouse nerve growth factors and placebo for mean mm² reduction in ulcer area (stage II and above PUs; foot ulcers), the direction of the estimate of the effect favoured the nerve growth factors (LOW QUALITY).[120]
- One study (n=36) (nursing home patients) showed that mouse nerve growth factors is clinically more effective compared to placebo for mean mm² reduction in ulcer area (adjusted for baseline ulcer area, location and duration) (stage II and above PUs; foot ulcers) (MODERATE QUALITY).[120]
- One study (n=36) (nursing home patients) showed that no difference between mouse nerve growth factors and placebo for the incidence of adverse events (MODERATE QUALITY).[120]
- Three studies (n=188) (general population and denervated patients) showed that recombinant platelet-derived growth factor may be more effective compared to placebo to reduce the proportion of stage III and IV PUs (VERY LOW QUALITY).[124, 129, 139]
- Two studies (n=50) (general population and denervated patients) showed that recombinant platelet-derived growth factor (100μg/ml) may be more effective compared to placebo to reduce the proportion of stage III and IV PUs (VERY LOW QUALITY).[124, 129, 139]
- 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).[124]

- One study (n=28) (general population) showed that recombinant platelet-derived growth factor (100μg/ml) may be more effective compared to recombinant platelet-derived growth factor (300μg/ml) to reduce the proportion of stage III and IV PUs (VERY LOW QUALITY).[124]
- 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).[124]
- One study (n=26) (general population) showed that recombinant platelet-derived growth factor (300μg/ml) may be more effective compared to placebo to reduce the proportion of stage III and IV PUs (VERY LOW QUALITY).[124]
- 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).[124]
- One study (n=54) (inpatients) showed that there is potentially no difference between basic fibroblast growth factor or granulocyte-macrophage colony-stimulating factor and placebo to reduce the proportion of stage III and IV PUs (VERY LOW QUALITY).[127]
- One study (n=27) (inpatients) showed that placebo may be more effective compared to granulocyte-macrophage colony-stimulating factor (2.0μg/cm²) to reduce the proportion of stage III and IV PUs (VERY LOW QUALITY).[127]
- One study (n=27) (inpatients) showed that placebo may be more effective compared to granulocyte-macrophage colony-stimulating factor (2.0μg/cm²) to reduce the proportion of stage III and IV PUs worsened (VERY LOW QUALITY).[127]
- One study (n=30) (inpatients) showed that there is potentially no difference between granulocyte-macrophage colony-stimulating factor (2.0μg/cm²) and placebo for mean percentage reduction in ulcer area (stage III and IV PUs) (VERY LOW QUALITY).[132]
- 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).[132]
- One study (n=28) (inpatients) showed that there may be no difference between granulocyte-macrophage colony-stimulating factor (2.0μg/cm²) and basic fibroblast growth factor (5.0μg/cm²) to reduce the proportion of stage III and IV Pus, the direction of the estimate of the effect favoured the basic fibroblast growth factor (5.0μg/cm²) (VERY LOW QUALITY).[127]
- One study (n=28) (inpatients) showed that granulocyte-macrophage colony-stimulating factor (2.0μg/cm²) may be more effective compared to basic fibroblast growth factor (5.0μg/cm²) to reduce the proportion of stage III and IV PUs worsened (VERY LOW QUALITY).[127]
- One study (n=30) (inpatients) showed that basic fibroblast growth factor (5.0μg/cm²) is potentially more effective comparted to granulocyte-macrophage colony-stimulating factor (2.0μg/cm²) for mean percentage reduction in ulcer area (stage III and IV PUs) (VERY LOW QUALITY).[132]
- 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).[132]

- One study (n=27) (inpatients) showed that there may be no difference between 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) to reduce the proportion of stage III and IV Pus, 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).[127]
- 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 effective compared to granulocyte-macrophage colony-stimulating factor (2.0μg/cm²) to reduce the proportion of stage III and IV PUs worsened (VERY LOW QUALITY).[127]
- One study (n=30) (inpatients) showed that granulocyte-macrophage colony-stimulating factor (2.0μg/cm²) and basic fibroblast growth factor (5.0μg/cm²) may be more effective comparted to granulocyte-macrophage colony-stimulating factor (2.0μg/cm²) for mean percentage reduction in ulcer area (stage III and IV PUs) (VERY LOW QUALITY).[132]
- 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 (5.0μg/cm²). No estimate of effect or precision could be derived (VERY LOW QUALITY).[132]
- One study (n=27) (inpatients) showed that there may be no difference between basic fibroblast growth factor (5.0μg/cm²) and placebo to reduce the proportion of stage III and IV Pus, the direction of the estimate of the effect favoured placebo (VERY LOW QUALITY).[127]
- One study (n=27) (inpatients) showed that placebo is potentially more effective compared to basic fibroblast growth factor (5.0μg/cm²) to reduce the proportion of stage III and IV PUs worsened (VERY LOW QUALITY).[127]
- One study (n=30) (inpatients) showed that there is potentially no difference between basic fibroblast growth factor (5.0μg/cm²) and placebo for mean percentage reduction in ulcer area (stage III and IV PUs), the direction of the estimate of the effect favoured the basic fibroblast growth factor (5.0μg/cm²) (VERY LOW QUALITY).[132]
- 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).[132]
- One study (n=27) (inpatients) showed that there may be no 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) to reduce the proportion of stage III and IV PUs, the direction of the estimate of the effect favoured basic fibroblast growth factor (5.0μg/cm²) (VERY LOW QUALITY).[127]
- 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 effective compared to basic fibroblast growth factor (5.0μg/cm²) to reduce the proportion of stage III and IV PUs worsened (VERY LOW QUALITY).[127]
- One study (n=31) (inpatients) showed that there is potentially no 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 ulcer area (stage III and IV PUs), the direction of the estimate of the effect favoured the basic fibroblast growth factor (5.0μg/cm²) (VERY LOW QUALITY).[132]

- 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 (2.0μg/cm²) and basic fibroblast growth factor (5.0μg/cm²). No estimate of effect or precision could be derived (VERY LOW QUALITY).[132]
- One study (n=26) (inpatients) showed that there may be no difference between basic fibroblast growth factor (5.0μg/cm²) and granulocyte-macrophage colony-stimulating factor (2.0μg/cm²) versus placebo to reduce the proportion of stage III and IV Pus, the direction of the estimate of the effect favoured placebo (VERY LOW QUALITY).[127]
- One study (n=26) (inpatients) showed that placebo may be more effective compared to granulocyte-macrophage colony-stimulating factor (2.0μg/cm²) and basic fibroblast growth factor (5.0μg/cm²) to reduce the proportion of stage III and IV PUs worsened (VERY LOW QUALITY).[127]
- One study (n=31) (inpatients) showed that there may be no 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 ulcer area (stage III and IV PUs), 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).[132]
- 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).[132]
- One study (n=62) (general population) showed that recombinant platelet-derived growth factor-BB (100μg/g) is clinically more effective compared to placebo to reduce the proportion of stage III and IV PUs (LOW QUALITY).[129]
- One study (n=62) (general population) showed that recombinant platelet-derived growth factor-BB (100μg/g) is potentially more effective compared to placebo to improve healing ≥90% of stage III and IV PUs (VERY LOW QUALITY).[129]
- 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).[129]
- One study (n=62) (general population) showed that placebo may be more effective compared to recombinant platelet-derived growth factor-BB (100μg/g) to reduce the incidence of osteomyelitis (stage III and IV PUs) (VERY LOW QUALITY).[129]
- One study (n=62) (general population) showed that recombinant platelet-derived growth factor-BB (100μg/g) may be more effective compared to placebo to reduce the incidence of infections (stage III and IV PUs) (VERY LOW QUALITY).[129]
- One study (n=62) (general population) showed that there is no difference between recombinant platelet-derived growth factor-BB (100μg/g) and placebo for reduction of incidence of sepsis (stage III and IV PUs) (LOW QUALITY).[129]
- One study (n=62) (general population) showed that there may be no 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 favoured either intervention (stage III and IV PUs) (VERY LOW QUALITY).[129]
- One study (n=63) (general population) showed that there may be no 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 proportion of stage III

and IV PUs, the direction of the estimate of the effect favoured recombinant platelet-derived growth factor-BB (100μg/g) (VERY LOW QUALITY).[129]

- One study (n=63) (general population) showed that there may be no 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 ≥90% of stage III and IV PUs, the direction of the estimate of the effect favoured recombinant platelet-derived growth factor-BB (300μg/g) alternated with placebo (VERY LOW QUALITY).[129]
- 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).[129]
- One study (n=63) (general population) showed that recombinant platelet-derived growth factor-BB (100μg/g) may be more effective compared to recombinant platelet-derived growth factor-BB (300μg/g) alternated with placebo to reduce the incidence of osteomyelitis (stage III and IV PUs) (VERY LOW QUALITY).[129]
- 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 to reduce the incidence of infections (stage III and IV PUs) (VERY LOW QUALITY).[129]
- One study (n=63) (general population) showed that recombinant platelet-derived growth factor-BB (100μg/g) may be more effective compared to recombinant platelet-derived growth factor-BB (300μg/g) alternated with placebo for reduction of incidence of sepsis (stage III and IV PUs) (LOW QUALITY).[129]
- One study (n=63) (general population) showed that recombinant platelet-derived growth factor-BB (100μg/g) may be more effective 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 (stage III and IV PUs) (VERY LOW QUALITY).[129]
- One study (n=61) (general population) showed that recombinant platelet-derived growth factor-BB (100μg/g) is potentially more effective compared to recombinant platelet-derived growth factor-BB (300μg/g) to reduce the proportion of stage III and IV PUs (VERY LOW QUALITY).[129]
- One study (n=61) (general population) showed that recombinant platelet-derived growth factor-BB (100μg/g) is potentially recombinant platelet-derived growth factor-BB (300μg/g) to improve healing ≥90% of stage III and IV PUs (VERY LOW QUALITY).[129]
- 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).[129]
- One study (n=61) (general population) showed that recombinant platelet-derived growth factor-BB (300μg/g) may be more effective compared to recombinant platelet-derived growth factor-BB (100μg/g) to reduce the incidence of osteomyelitis (stage III and IV PUs) (VERY LOW QUALITY).[129]
- One study (n=61) (general population) showed that recombinant platelet-derived growth factor-BB (100μg/g) may be more effective compared to recombinant platelet-derived growth factor-BB (300μg/g) to reduce the incidence of infections (stage III and IV PUs) (VERY LOW QUALITY).[129]
- One study (n=61) (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) for reduction of incidence of sepsis (stage III and IV PUs) (VERY LOW QUALITY).[129]

- One study (n=61) (general population) showed that there may be no 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 (stage III and IV PUs), the direction of the estimate of the effect favoured recombinant platelet-derived growth factor-BB (100μg/g) (VERY LOW QUALITY).[129]
- One study (n=63) (general population) showed that recombinant platelet-derived growth factor-BB (300μg/g) alternated with placebo may be more effective compared to placebo to reduce the proportion of stage III and IV PUs (VERY LOW QUALITY).[129]
- One study (n=63) (general population) showed that recombinant platelet-derived growth factor-BB (300μg/g) alternated with placebo may be more effective compared placebo to improve healing ≥90% of stage III and IV PUs (VERY LOW QUALITY).[129]
- 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).[129]
- One study (n=63) (general population) showed that placebo may be more effective compared to recombinant platelet-derived growth factor-BB (300μg/g) alternated with placebo to reduce the incidence of osteomyelitis (stage III and IV PUs) (VERY LOW QUALITY).[129]
- One study (n=63) (general population) showed that recombinant platelet-derived growth factor-BB (300μg/g) alternated with placebo may be more effective compared to placebo to reduce the incidence of infections (stage III and IV PUs) (VERY LOW QUALITY).[129]
- One study (n=63) (general population) showed that placebo may be more effective compared to recombinant platelet-derived growth factor-BB (300μg/g) alternated with placebo for reduction of incidence of sepsis (stage III and IV PUs) (VERY LOW QUALITY).[129]
- One study (n=63) (general population) showed that placebo may be more effective 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 (stage III and IV PUs) (VERY LOW QUALITY).[129]
- One study (n=62) (general population) showed that recombinant platelet-derived growth factor-BB (300μg/g) alternated with placebo may be more effective compared to recombinant platelet-derived growth factor-BB (300μg/g) to reduce the proportion of stage III and IV PUs (VERY LOW QUALITY).[129]
- One study (n=62) (general population) showed that recombinant platelet-derived growth factor-BB (300μg/g) alternated with placebo is potentially more effective compared recombinant platelet-derived growth factor-BB (300μg/g) to improve healing ≥90% of stage III and IV PUs (VERY LOW QUALITY).[129]
- 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).[129]
- One study (n=62) (general population) showed that recombinant platelet-derived growth factor-BB (300μg/g) may be more effective compared to recombinant platelet-derived growth factor-BB (300μg/g) alternated with placebo to reduce the incidence of osteomyelitis (stage III and IV PUs) (VERY LOW QUALITY).[129]
- One study (n=62) (general population) showed that recombinant platelet-derived growth factor-BB (300μg/g) alternated with placebo may be more effective compared to placebo to reduce the incidence of infections (stage III and IV PUs) (VERY LOW QUALITY).[129]
- One study (n=62) (general population) showed that recombinant platelet-derived growth factor-BB (300μg/g) alternated with placebo may be more effective compared to recombinant platelet-derived growth factor-BB (300μg/g) for reduction of incidence of sepsis (stage III and IV PUs) (VERY LOW QUALITY).[129]

- One study (n=62) (general population) showed that recombinant platelet-derived growth factor-BB (300μg/g) may be more effective 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 (stage III and IV PUs) (VERY LOW QUALITY).[129]
- One study (n=61) (general population) showed that recombinant platelet-derived growth factor-BB (300μg/g) may be more effective compared to placebo to reduce the proportion of stage III and IV PUs (VERY LOW QUALITY).[129]
- One study (n=61) (general population) showed that recombinant platelet-derived growth factor-BB (300μg/g) may be more effective compared to placebo to improve healing ≥90% of stage III and IV PUs (VERY LOW QUALITY).[129]
- 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).[129]
- One study (n=61) (general population) showed that recombinant platelet-derived growth factor-BB (300μg/g) may be more effective compared to placebo to reduce the incidence of osteomyelitis (stage III and IV PUs) (VERY LOW QUALITY).[129]
- One study (n=61) (general population) showed that recombinant platelet-derived growth factor-BB (300μg/g) may be more effective compared to placebo to reduce the incidence of infections (stage III and IV PUs) (VERY LOW QUALITY).[129]
- One study (n=61) (general population) showed that there is no 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 (stage III and IV PUs) (LOW QUALITY).[129]
- One study (n=61) (general population) showed that recombinant platelet-derived growth factor-BB (300μg/g) may be more effective compared placebo for reduction of incidence of adverse events other than osteomyelitis, sepsis and infections (stage III and IV PUs) (VERY LOW QUALITY).[129]
- One study (n=11) (denervated patients) showed that there is no difference between recombinant platelet-derived growth factor-BB (1.0μg/g) and placebo to reduce the proportion of stage III and IV PUs (LOW QUALITY).[139]
- One study (n=11) (denervated patients) showed that there is no difference between recombinant platelet-derived growth factor-BB (1.0μg/g) and placebo at reducing the incidence of infections (stage III and IV PUs) (LOW QUALITY).[139]
- One study (n=8) (denervated patients) showed that there is no difference between recombinant platelet-derived growth factor-BB (1.0μg/g) and recombinant platelet-derived growth factor-BB (10.0μg/g) to reduce the proportion of stage III and IV PUs (LOW QUALITY).[139]
- One study (n=8) (denervated patients) showed that there is no 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 (stage III and IV PUs) (LOW QUALITY).[139]
- One study (n=9) (denervated patients) showed that recombinant platelet-derived growth factor-BB (100.0μg/g) may be more effective compared to recombinant platelet-derived growth factor-BB (1.0μg/g) to reduce the proportion of stage III and IV PUs (VERY LOW QUALITY).[139]
- One study (n=9) (denervated patients) showed that there is no 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 (stage III and IV PUs) (LOW QUALITY).[139]
- One study (n=11) (denervated patients) showed that there is no difference between recombinant platelet-derived growth factor-BB (10.0μg/g) and placebo to reduce the proportion of stage III and IV PUs (LOW QUALITY).[139]

- One study (n=11) (denervated patients) showed that there is no difference between recombinant platelet-derived growth factor-BB (10.0μg/g) and placebo at reducing the incidence of infections (stage III and IV PUs) (LOW QUALITY).[139]
- One study (n=9) (denervated patients) showed that recombinant platelet-derived growth factor-BB (100.0μg/g) may be more effective compared to recombinant platelet-derived growth factor-BB (10.0μg/g) to reduce the proportion of stage III and IV PUs (VERY LOW QUALITY).[139]
- One study (n=9) (denervated patients) showed that there is no 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 (stage III and IV PUs) (LOW QUALITY).[139]
- One study (n=12) (denervated patients) showed that recombinant platelet-derived growth factor-BB (100.0μg/g) may be more effective compared to placebo to reduce the proportion of stage III and IV PUs (VERY LOW QUALITY).[139]
- One study (n=12) (denervated patients) showed that there is no difference between recombinant platelet-derived growth factor-BB (100.0μg/g) and placebo at reducing the incidence of infections (stage III and IV PUs) (LOW QUALITY).[139]
- One study (n=12) (denervated patients) showed that recombinant platelet-derived growth factor-BB (100.0μg/g) is clinically more effective compared to placebo for mean percentage reduction in ulcer depth (stage III and IV PUs) (LOW QUALITY).[139]
- One study (n=12) (denervated patients) showed that recombinant platelet-derived growth factor-BB (100.0μg/g) is clinically more effective compared to placebo for mean percentage reduction in ulcer volume (stage III and IV PUs) (LOW QUALITY).[139]
- One study (n=49) (denervated patients) showed that basic fibroblast growth factors (different schedules and doses) is potentially more effective compared to placebo to improve >70% healing is stage III and IV PUs (VERY LOW QUALITY).[133]
- One study (n=49) (denervated patients) 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).[133]
- One study (n=24) (denervated patients) showed no difference between interleukin 1 beta and placebo to reduce the proportion of stage III and IV PUs (LOW QUALITY).[131]
- One study (n=12) (denervated patients) showed no difference between interleukin 1 beta (0.01μg/cm²) and placebo to reduce the proportion of stage III and IV PUs (LOW QUALITY).[131]
- One study (n=12) (denervated patients) showed no difference between interleukin 1 beta (0.01μg/cm²) and interleukin 1 beta (0.1μg/cm²) to reduce the proportion of stage III and IV PUs (LOW QUALITY).[131]
- One study (n=12) (denervated patients) showed no difference between interleukin 1 beta (0.01μg/cm²) and interleukin 1 beta (1.0μg/cm²) to reduce the proportion of stage III and IV PUs (LOW QUALITY).[131]
- One study (n=12) (denervated patients) showed no difference between interleukin 1 beta (0.1μg/cm²) and placebo to reduce the proportion of stage III and IV PUs (LOW QUALITY).[131]
- One study (n=12) (denervated patients) showed no difference between interleukin 1 beta (0.1μg/cm²) and interleukin 1 beta (1.0μg/cm²) to reduce the proportion of stage III and IV PUs (LOW QUALITY).[131]
- One study (n=12) (denervated patients) showed no difference between interleukin 1 beta (1.0μg/cm²) and placebo to reduce the proportion of stage III and IV PUs (LOW QUALITY).[131]

3.5.4 Conclusion

- **Evidence suggests that hydrocolloids are potentially more effective compared to saline for healing of stage I and above pressure ulcers.**
- **One very small RCT of very low quality comparing saline and hydrogels for the treatment of stage II to IV pressure ulcers suggests there is no difference for healing of pressure ulcers.**
- **Two small RCT's of very low quality suggest that foam dressings are more effective compared to saline for healing of stage II and III pressure ulcers.**
- **One very small RCT of very low quality suggests that polyurethane film may be more effective compared to saline for healing of stage II and III pressure ulcers.**
- **One very small RCT of low quality suggests that dextranomer is more effective compared to saline for healing of stage II to IV pressure ulcers.**
- **Two very small RCT's of very low quality comparing phenytoin and saline for the treatment of stage I and II pressure ulcers is conflicting. For ulcers in the sacral area, evidence suggests there is no difference for healing of pressure ulcers.**
- **One small RCT of low quality comparing phenytoin and hydrocolloids for the treatment of stage I and II pressure ulcers is conflicting. For ulcers in the sacral area, evidence suggests there is no difference for healing of pressure ulcers.**
- **One very small RCT of low to very low quality suggests that phenytoin is more effective compared to triple antibiotics for days to healing of stage II pressure ulcers.**
- **One very small RCT of very low quality suggests honey is more effective compared to ethoxydiaminoacridine for healing of stage II and III pressure ulcers.**
- **One very small RCT of very low quality comparing povidone-iodine and hydrocolloids for the treatment of stage I and II pressure ulcers suggests there is no difference for healing of stage I and II pressure ulcers. The rate of healing may be more effective using hydrocolloids.**
- **One very small RCT of very low quality suggests hydrogel is potentially more effective compared to povidone-iodine for speed of healing of stage I and II pressure ulcers.**
- **One very small RCT of low quality suggests cadexomer is more effective compared to standard treatment for healing of pressure ulcers.**
- **One very small RCT of very low quality comparing silver dressings and silver cream for the treatment of stage II pressure ulcers suggests there is no difference for healing of stage IV pressure ulcers.**
- **One very small RCT of very low quality suggests resin salve is potentially be more effective compared to hydrofibre® for healing of stage II to IV pressure ulcers.**
- **One very small RCT of very low quality suggests foam dressings are potentially more effective compared to antibiotic ointments for healing of stage II pressure ulcers.**
- **Ten Chinese RCT's of low to very low quality suggest that Chinese herbal medical ointment are potentially more effective for healing of stage II to IV pressure ulcers. In Belgium, Chinese herbal medical ointments are not available for use in daily practice.**
- **Evidence of moderate to very low quality comparing growth factors to placebo, different doses or other growth factors for the treatment of stage II to IV pressure ulcers are conflicting regarding its effectiveness.**
- **None of the studies reported harms as a result of the interventions.**
- **All conclusions for the included studies were weakened due to the poor methodological quality of the trials and poor descripiton of type of ulcers such as excudate level.**

3.5.5 Recommendations for topical agents

These recommendations are grouped with recommendations for dressings under section 3.6.5.

3.6 Dressings

3.6.1 Introduction

A wound dressing aims to promote pressure ulcer healing and/or to prevent the wound from further breakdown. A dressing is designed to be in direct contact with the wound, generally aiming to maintain a moist wound bed, to support granulation/epithelialisation and to promote pressure healing and closure. The application of a dressing is generally considered to be a central component in pressure ulcer management. Dressing selection and application require specific skills and should be the result of a thorough and systematic assessment of the pressure ulcer. Dressing selection and frequency of application should be based on the type of tissue, the presence of a bacterial load (and infection), the wound exudate (amount, odour, consistency), the status of the wound edges, and the pain experienced by the patient. The choice for a specific dressing may change over time as the ulcer heals or deteriorates. A plethora of different dressing options is currently available.

The aim of this review was to describe the current evidence about the effectiveness of different dressings for pressure ulcer treatment and to provide recommendations for clinical practice. Following two groups of dressings were considered: basic dressings (dressings that may cover a wound but do not create an optimum healing environment) and modern dressings (dressings that aim to create the optimum wound healing environment). [30]

3.6.2 Review question

What are the most clinically effective dressings for the treatment of pressure ulcers?

3.6.3 Clinical evidence

Sixty-one randomized controlled trials were included in this review.[77, 79, 84, 89, 90, 95, 112, 113, 115-117, 121, 122, 125, 126, 128, 130, 135-138, 140, 142-180]

Various types of dressings are used to treat pressure ulcers. In this review different types of dressings are compared to each other or to placebo. Following categories were made:

- Basic dressings
  - Gauze dressings;
  - Paraffin gauze dressings;
  - Simple dressing pads.
- Active dressings
  - Hydrocolloid dressings;
  - Foam dressings;
  - Polyurethane film;
  - Hydrogel;
  - Alginate dressings;
  - Hydrofibre® dressings;
  - Collagen dressing;
  - Hyaluronic dressing;
  - Copolymer dressing;
  - Polyhexadine dressing;
  - Charcoal dressings;
  - Silver dressings;
  - Dextranomer;
  - Sugar;
  - Honey;
  - Skin replacement;
  - Platelet gel.

3.6.3.1 Quality of studies

In general the methodological quality of the included studies was poor. In the majority of the studies, sequence generation[77, 84, 89, 90, 112, 113, 115-117, 121, 122, 125, 126, 128, 130, 138, 142-165, 167, 168] and allocation concealment[77, 90, 112, 113, 115-117, 121, 122, 125, 128, 130, 135, 138, 140, 142-146, 148-155, 157-165, 169-177] were not clearly described or were performed poorly did not report on sequence

generation. The majority of the studies did not use an intention-to-treat analyses.[77, 113, 116, 122, 125, 128, 130, 145, 149, 150, 152-155, 157, 160, 163, 165, 167, 169, 170, 173, 175-177, 181] In few studies (n=10), the outcome assessor was blinded.[112, 136, 137, 146-148, 153, 156, 168, 169, 171, 180] No other form of blinding was applied in the studies. Few studies (n=17), reported an a priory sample size calculation [79, 89, 90, 115, 125, 126, 136, 140, 146, 147, 151, 153, 156, 159, 162, 169, 174, 178, 180], of which nine were underpowered.[89, 126, 136, 147, 151, 162, 169, 174, 178] In appendix 5 the level of evidence can be found per outcome after applying the GRADE-methodology. The evidence base for all outcomes has been rated as being of moderate to very low quality.

Table 13 – Definition dressing types

Dressing type	Description
Basic dressings	
Gauze	Comes in woven and non-woven form and are usually made of from cotton, viscose, polyester, or other suitable fibres. It is absorptive and permeable to water, water vapor, and oxygen.
Modern dressings	
Hydrocolloid	Contains an elastomeric, adhesive, and gelling forming agent, such as carboxymethylcellulose, pectin or gelatin. It is often combined with adhesives and a tackiness agent and applied to a polyurethane foam or film carrier to create an absorbent, self-adhesive, waterproof sheet.
Foam	Cellulose or polyurethane dressing that can be impregnated or coated with other materials and has certain absorptive properties.
Polyurethane	It is a transparent, semi-permeable, and non-absorptive, polymer-based adhesive film.
Hydrofibre®	It has highly absorbent, with gelling properties derived from 100% sodium carboxymethylcellulose hydrocolloid polymers.
Collagen	Collagen is the most abundant protein in the human body and is a major component of the extracellular matrix. The dressing can be derived from bovine, porcine or avian sources.
Hydrogel	It consists of insoluble polymers which have a hydrophilic nature. When mixed with aqueous solutions, they will absorb water.
Impregnated gauze	Gauze that is impregnated with some other product such as paraffin or other products.
Poly-hema	A biocompatible, hydrophilic gel that is permeable to tissue fluids and functions as a hydrogel.
Amino acid co-polymer	It is permeable to water vapour. It does not allow microbial proliferation after in vitro inoculation. It is impermeable to bacteria, and supposed to increase epithelisation. It is a skin substitute.
Alginate	These are derived from seaweed, usually prepared as the calcium salt of alginic acid. When in contact with serum, wound exudate or solutions containing the insoluble calcium alginate will partially convert to a soluble sodium salt, and produce a hydrophilic gel.
Charcoal	Activated carbon in dressing adsorbs bacteria and helps to reduce wound odor.
Dextranomer	It is a sterile, insoluble powder in the form of circular beads when dry. It is a long chain polysaccharide constructed in a three dimensional network of cross-linked dextran molecules. Dextranomer is highly hygroscopic due to its high hydroxyl group content and 1 g of it absorbs 4 ml of water and swells till it is saturated. The microorganisms and high molecular weight substances which get confined to the interspaces move at a faster rate due to capillary action.

Dressing type	Description
Protease modulating matrix	It consists of freeze-dried collagen and oxidised regenerated cellulose, which are brought on the market to bind and inactivates protease.
Silver dressing	The presence of silver ions should result in antimicrobial properties.
Sugar	Sugar is a highly osmotic product, which draws fluid out of the wound. Reducing fluid in the wound inhibits the growth of bacteria.
Honey	Honey's beneficial effects are thought to be due to the hydrogen peroxide production from the activity of the glucose oxidase enzyme. Honey is a highly osmotic product, which draws fluid out of the wound.
Platelet gel	Concentrated platelet, which should form granulation and more collagen fibers.
Hyaluronic acid	Hyaluronic acid is a natural substance widely distributed throughout our whole bodies. It is an important aspect of cartilage, synovial fluid (the lubricating fluid found between joints) and skin. Hyaluronic acid cannot be absorbed when applied topically, therefore sodium hyaluronate is added. Sodium hyaluronate is the salt of the hyaluronic acid and it has a much lower molecular size. Sodium hyaluronate can hold more than 1000 times its weight in water.

Source. References[6, 30, 86, 91, 92, 156, 167, 182]

3.6.3.2 *Evidence statements*

Hydrocolloid versus gauze

- Four studies (n=170) (general population and patients with a spinal cord injury) showed that hydrocolloid is potentially more effective compared to gauze dressings to reduce the proportion of ≥ stage I PUs (VERY LOW QUALITY).[90, 116, 122, 136]
- Three studies (n=115) (general population) showed that hydrocolloid is potentially more effective compared to gauze dressings to reduce the proportion of ≥ stage I PUs (VERY LOW QUALITY). [116, 122, 136]
- One study (n=55) (patients with a spinal cord injury) showed that hydrocolloid is clinically more effective compared to gauze dressings to reduce the proportion of ≥ stage I PUs (MODERATE QUALITY). [90]
- Four studies (n=273) (general population and patients with a spinal cord injury) showed that hydrocolloid is clinically more effective compared to gauze dressings to reduce the proportion of ≥ stage I PUs (LOW QUALITY).[90, 125, 153, 160]
- Three studies (n=212) (general population) showed that hydrocolloid is potentially more effective compared to gauze dressings to reduce the proportion of ≥ stage I PUs (VERY LOW QUALITY).).[125, 153, 160]
- One study (n=61) (patients with a spinal cord injury) showed that hydrocolloid is clinically more effective compared to gauze dressings to reduce the proportion of ≥ stage I PUs (MODERATE QUALITY). [90]
- One study (n=24) (patients with a spinal cord injury) showed that hydrocolloid is potentially more effective compared to gauze dressings to reduce the proportion of stage I PUs (LOW QUALITY). [90]
- Two studies (n=96) (general population and patients with a spinal cord injury) showed that hydrocolloid is potentially more effective compared to gauze dressings to reduce the proportion of stage II PUs (LOW QUALITY). [90, 125]
- One study (n=37) (patients with a spinal cord injury) showed that hydrocolloid is clinically more effective compared to gauze dressings to reduce the proportion of stage II PUs (MODERATE QUALITY). [90]
- One study (n=59) (general population) showed that hydrocolloid is potentially more effective compared to gauze dressings to reduce the proportion of stage II PUs (VERY LOW QUALITY).[125]
- One study (n=28) (general population) showed that hydrocolloid may be more effective compared to gauze dressings to reduce the proportion of stage III PUs (VERY LOW QUALITY). [125]
- One study (n=15) (patients with a spinal cord injury) showed that hydrocolloid is potentially more effective compared to gauze dressings to reduce the proportion of ≥ stage I PUs at the sacral area (LOW QUALITY). [90]
- One study (n=91) (patients with a spinal cord injury) showed that hydrocolloid is clinically more effective compared to gauze dressings to improve healing of stage I and II PUs (MODERATE QUALITY). [90]
- Two studies (n=148) (general population and patients with a spinal cord injury) showed that hydrocolloid may be more effective compared to gauze dressings to reduce the proportion of ≥ stage I PUs worsening (LOW QUALITY). [90, 125]
- One study (n=61) (patients with a spinal cord injury) showed that hydrocolloid is potentially more effective compared to gauze dressings to reduce the proportion of stage I and II PUs worsening (LOW QUALITY). [90]
- One study (n=87) (general population) showed that there may be no difference between a hydrocolloid and a gauze dressings to reduce the proportion of stage II and III PUs worsening, the direction of the estimate of the effect favoured either intervention (VERY LOW QUALITY). [125]
- One study (n=59) (general population) showed that there may be no difference between a hydrocolloid and a gauze dressings to reduce the proportion of stage II PUs worsening, the direction of the estimate of the effect favoured the hydrocolloid dressing (VERY LOW QUALITY). [125]
- One study (n=28) (general population) showed that there may be no difference between a hydrocolloid and a gauze dressings to reduce the proportion of stage III PUs worsening, the direction of the estimate of the effect favoured the gauze dressing (VERY LOW QUALITY). [125]

- Two studies (n=75) (general population) showed that there is potentially no difference between a hydrocolloid and a gauze dressings for mean percentage reduction in ulcer volume (stage II and III PUs), the direction of the estimate of the effect favoured the gauze dressing (VERY LOW QUALITY).[113, 164]
- One study (n=97) (inpatients) reported a mean cm² reduction in ulcer area (stage II and III PUs) for a hydrocolloid and a gauze dressing. The mean for hydrocolloid was 0.73 cm² and -0.67 cm² for gauze. No estimate of effect or precision could be derived (VERY LOW QUALITY).[153]
- One study (n=50) (long-term care patients) reported a mean percentage reduction in ulcer area for a hydrocolloid and a gauze dressing. The mean for hydrocolloid was 100% and 85.7% for gauze. No estimate of effect or precision could be derived (VERY LOW QUALITY).[112]
- One study (n=41) (in- and out-patients) reported a median percentage reduction in ulcer area (stage II and III) for a hydrocolloid and a gauze dressing. The mean for hydrocolloid was 7.4% and 7.0% for gauze. No estimate of effect or precision could be derived (VERY LOW QUALITY).[164]
- One study (n=59) (general population) reported a median percentage reduction in ulcer area (stage II PUs) for a hydrocolloid and a gauze dressing. The mean for hydrocolloid was 91% and 48% for gauze. A p-value of >0.05 was reported (VERY LOW QUALITY). [125]
- One study (n=59) (general population) reported a median percentage reduction in ulcer area (stage III PUs) for a hydrocolloid and a gauze dressing. The mean for hydrocolloid was 0.3% and 30% for gauze. A p-value of >0.05 was reported (VERY LOW QUALITY). [125]
- One study (n=32) (general population) showed that gauze is clinically more effective compared to hydrocolloid dressings for mean percentage reduction in volume (stage III and IV PUs) (LOW QUALITY).[122]
- One study (n=32) (general population) showed that there is potentially no difference between a hydrocolloid and a gauze dressings for mean healing speed (stage I and II PUs), the direction of the estimate of the effect favoured the hydrocolloid dressing (VERY LOW QUALITY).[116]
- One study (n=39) (long-term care patients) reported a median time to healing (stage II and III PUs) for a hydrocolloid and a gauze dressing. The median for hydrocolloid was 9 days and 11 days for gauze. No estimate of effect or precision could be derived (VERY LOW QUALITY).[136]
- One study (n=34) (inpatients) showed that a hydrocolloid may be more effective compared to a gauze dressing to reduce the incidence of infected patients (stage II and III PUs) (VERY LOW QUALITY).[113]
- One study (n=28) (inpatients) showed there is no difference between a hydrocolloid and a gauze dressing at reducing the incidence of infected ulcers (LOW QUALITY).[160]
- One study (n=44) (general population) showed that a gauze dressing may be more effective compared to a hydrocolloid at reducing incidence of hypergranulation (stage I and II PUs) (VERY LOW QUALITY).[116]
- One study (n=100) (general population) showed that a hydrocolloid is clinically more effective compared to a gauze dressing at reducing incidence of skin irritation (stage II and III PUs) (LOW QUALITY). [125]
- One study (n=34) (inpatients) showed that a hydrocolloid is clinically more effective compared to a gauze dressing at reducing the incidence of pain at dressing removal (stage II and III PUs) (LOW QUALITY).[113]
- One study (n=32) (general population) reported a median pain during treatment (stage III and IV PUs) for a hydrocolloid and a gauze dressing. The median for hydrocolloid was 2.0 (range 1-4) and 2.0 (range 1-3) for gauze. No estimate of effect or precision could be derived (VERY LOW QUALITY).[122]
- One study (n=32) (general population) reported a median odour during treatment (stage III and IV PUs) for a hydrocolloid and a gauze dressing. The median for hydrocolloid was 2.0 (range 1-4) and 2.0 (range 1-3) for gauze. No estimate of effect or precision could be derived (VERY LOW QUALITY).[122]

- One study (n=34) (inpatients) showed that a hydrocolloid is clinically more effective compared to a gauze dressing at reducing the incidence of discomfort at dressing removal (stage II and III PUs) (LOW QUALITY) [113]
- One study (n=32) (general population) reported a median comfort during treatment (stage III and IV PUs) for a hydrocolloid and a gauze dressing. The median for hydrocolloid was 4.0 (range 3-4) and 3.0 (range 2-4) for gauze. No estimate of effect or precision could be derived (VERY LOW QUALITY).[122]

Hydrocolloid versus foam

- Three studies (n=157) (general population) showed that there is potentially no difference between a hydrocolloid and a foam dressing to reduce the proportion of stage II and III PUs, the direction of the estimate of the effect favoured the hydrocolloid dressing (VERY LOW QUALITY).[135, 174, 181]
- One study (n=96) (community patients) showed that there is no difference between a hydrocolloid and a foam dressing to improve healing of stage II and III PUs (LOW QUALITY).[135]
- Two studies (n=156) (general population) showed that a foam dressing may be more effective compared to a hydrocolloid to reduce the proportion of stage II and III PUs not changed (VERY LOW QUALITY).[135, 181]
- Two studies (n=156) (general population) showed that a foam dressing may be more effective compared to a hydrocolloid to reduce the proportion of stage II and III PUs worsened (VERY LOW QUALITY).[135, 181]
- One study (n=39) (general population) showed that there is potentially no difference between a hydrocolloid and a foam dressing for mean percentage reduction in ulcer area (stage II and III PUs), the direction of the estimate of the effect favoured the hydrocolloid dressing (VERY LOW QUALITY).[174]
- One study (n=96) (community patients) showed that there is no difference between a hydrocolloid and a foam dressing at reducing the incidence of hypergranulation (stage II and III PUs) (LOW QUALITY).[135]
- One study (n=96) (community patients) showed that a foam dressing may be more effective compared to a hydrocolloid at reducing the incidence of bleeding (stage II and III PUs) (VERY LOW QUALITY).[135]
- One study (n=96) (community patients) showed that a foam dressing is potentially be more effective compared to a hydrocolloid at reducing the incidence of maceration (stage II and III PUs) (VERY LOW QUALITY).[135]
- One study (n=39) (general population) showed that a hydrocolloid is potentially more effective compared to a foam dressing at reducing the incidence of maceration (stage II and III PUs) (VERY LOW QUALITY).[174]
- One study (n=39) (general population) showed that there is potentially no difference between a hydrocolloid and a foam dressing at reducing the incidence of pain at the end of treatment (stage II and III PUs), the direction of the estimate of the effect favoured the foam dressing (VERY LOW QUALITY).[174]
- One study (n=39) (general population) showed that there is potentially no difference between a hydrocolloid and a foam dressing at reducing the incidence of odour at the end of treatment (stage II and III PUs), the direction of the estimate of the effect favoured the foam dressing (VERY LOW QUALITY).[174]
- Two studies (n=100) (general population) showed that a hydrocolloid may be more effective compared to a foam dressing to reduce the incidence of adverse events (unknown if dressing related) (VERY LOW QUALITY).[174, 181]

Hydrocolloid versus polyurethane film

- Three studies (n=122) (general population) showed there is potentially no difference between a hydrocolloid and a polyurethane film to reduce the proportion of stage II and III PUs, the direction of the estimate of the effect favoured the hydrocolloid dressing (VERY LOW QUALITY).[146, 147, 151]
- One study (n=28) (community patients) showed that there is no difference between a hydrocolloid and a polyurethane film to improve healing of stage II and III PUs (LOW QUALITY).[147]

- One study (n=72) (general population) reported a mean percentage reduction in ulcer area (stage II and III PUs) for a hydrocolloid and a polyurethane film. The mean for hydrocolloid was 23.8% and 26.7% for polyurethane. No estimate of effect or precision could be derived (VERY LOW QUALITY).[151]
- One study (n=22) (inpatients) reported a median time to healing (stage II and III PUs) for a hydrocolloid and a polyurethane film. The median for hydrocolloid was 12.69 days and 13.36 days for polyurethane. A p-value of >0.05 was reported (VERY LOW QUALITY).[146]
- One study (n=72) (general population) showed there is potentially no difference between a hydrocolloid and a polyurethane film for linear healing rate of stage II and III PUs, the direction of the estimate of the effect favoured the hydrocolloid dressing (VERY LOW QUALITY). [151]
- One study (n=72) (general population) showed that a hydrocolloid is potentially more effective compared to a polyurethane film for mean odour (stage II and III PUs) (VERY LOW QUALITY). [151]
- One study (n=72) (general population) showed that a hydrocolloid is potentially more effective compared to a polyurethane film for mean comfort (stage II and III PUs) (VERY LOW QUALITY). [151]
- One study (n=72) (general population) showed there is no difference between a hydrocolloid and a polyurethane film at reducing the incidence of adverse events (stage II and III PUs) (VERY LOW QUALITY). [151]
- Two studies (n=50) (general population) reported the incidence of patients with pain at dressing removal for a hydrocolloid and a polyurethane film. A p-value >0.05 was reported (VERY LOW QUALITY).[146, 147]
- Two studies (n=50) (general population) reported the incidence of patients with discomfort at dressing removal for a hydrocolloid and a polyurethane film. A p-value >0.05 was reported (VERY LOW QUALITY).[146, 147]

Hydrocolloid versus collagenase ointment

- Two studies (n=60) (general population) showed there may be no difference between a hydrocolloid and a collagenase ointment at reducing the proportion of ≥ stage II PUs, the direction of the estimate of the effect favoured the collagenase ointment (VERY LOW QUALITY).[159, 165]
- One study (n=37) (inpatients) showed there may be no difference between a hydrocolloid and a collagenase ointment at reducing the proportion of stage II and III PUs, the direction of the estimate of the effect favoured the collagenase ointment (VERY LOW QUALITY).[159]
- One study (n=33) (general population) showed that a collagenase ointment is potentially more effective compared to a hydrocolloid at reducing the proportion of stage IV heel PUs (VERY LOW QUALITY).[165]
- One study (n=37) (inpatients) showed there may be no difference between a hydrocolloid and a collagenase ointment for mean percentage reduction in ulcer area of stage III PUs, the direction of the estimate of the effect favoured the collagenase ointment (VERY LOW QUALITY).[159]
- One study (n=37) (inpatients) showed there is potentially no difference between a hydrocolloid and a collagenase ointment for mean cm^2 reduction in ulcer area of stage III PUs, the direction of the estimate of the effect favoured the collagenase ointment (VERY LOW QUALITY).[159]
- Two studies (n=88) (general population) showed that a collagen is potentially more effective compared to a hydrocolloid for mean time to healing of ≥ stage II PUs (VERY LOW QUALITY).[84, 89, 165]
- One study (n=33) (general population) showed that a collagenase ointment is potentially more effective compared to a hydrocolloid for mean time to healing of stage IV heel PUs (VERY LOW QUALITY).[165]
- One study (n=37) (inpatients) showed there may be no difference between a hydrocolloid and a collagenase ointment at reducing the incidence of adverse events of stage III PUs, the direction of the estimate of the effect favoured the collagen dressing (all sites) (VERY LOW QUALITY).[159]

Hydrocolloid versus collagen dressing

- One study (n=65) (inpatients) showed there may be no difference between a hydrocolloid and a collagen dressing at reducing the proportion of stage II and III PUs, the direction of the estimate of the effect favoured the collagen dressing (VERY LOW QUALITY).[89]
- One study (n=65) (inpatients) showed there is potentially no difference between a hydrocolloid and a collagen dressing for mean percentage reduction in ulcer area of stage II and III PUs, the direction of the estimate of the effect favoured the collagen dressing (LOW QUALITY).[89]
- One study (n=65) (inpatients) showed there is no difference between a hydrocolloid and a collagen dressing for mean healing speed of stage II and III PUs, the direction of the estimate of the effect favoured either intervention (MODERATE QUALITY).[89]
- One study (n=65) (inpatients) showed there is potentially no difference between a hydrocolloid and a collagen dressing for mean time to healing of stage II and III PUs (all sites), the direction of the estimate of the effect favoured the collagen dressing (VERY LOW QUALITY).[89]
- One study (n=65) (inpatients) showed there is no difference between a hydrocolloid and a collagen dressing at reducing the incidence of adverse events of stage II and III PUs (all sites) (LOW QUALITY).[89]

Hydrocolloid versus hydrogel

- One study (n=10) (community patients) showed there may be no difference between a hydrocolloid and a hydrogel to reduce the proportion of stage II and III PUs, the direction of the estimate of the effect favoured the either intervention (VERY LOW QUALITY).[163]
- One study (n=129) (general population) showed that hydrogel is potentially more effective compared to a hydrocolloid to reduce the proportion of stage I and II PUs (Enis and Sarmienti classification) (VERY LOW QUALITY).[154]
- One study (n=129) (general population) showed that hydrogel is potentially more effective compared to a hydrocolloid to reduce the proportion of stage I and II PUs not changed (Enis and Sarmienti classification) (VERY LOW QUALITY).[154]
- One study (n=129) (general population) showed that hydrogel is potentially more effective compared to a hydrocolloid to reduce the proportion of stage I and II PUs worsened (Enis and Sarmienti classification) (VERY LOW QUALITY).[154]
- One study (n=58) (general population) reported a mean percentage reduction in ulcer area (stage I according to Enis and Sarmienti classification) for a hydrocolloid and a hydrogel. The mean for hydrocolloid was 44% and 72% for hydrogel. A p-value of >0.05 was reported (VERY LOW QUALITY).[154]
- One study (n=71) (general population) showed that hydrogel is potentially more effective compared to a hydrocolloid for mean reduction in ulcer area of stage II PUs (Enis and Sarmienti classification) (VERY LOW QUALITY).[154]
- One study (n=41) (in- and out-patients) reported a median percentage reduction in ulcer area (stage II and III PUs) for a hydrocolloid and a hydrogel. The median for hydrocolloid was 7.4% and 5.6% for hydrogel. No estimate of effect or precision could be derived (VERY LOW QUALITY).[164]
- One study (n=10) (community patients) showed that a hydrocolloid may be more effective compared to hydrogel for mean healing rate of stage II and III PUs (VERY LOW QUALITY).[163]
- One study (n= not reported) (general population) reported healing rate (stage I and II PUs according to the Enis and Sarmienti classification) for a hydrocolloid and a hydrogel. The rate for hydrocolloid was 3.1% and 8.1% for hydrogel. No estimate of effect or precision could be derived (VERY LOW QUALITY).[154]
- One study (n=10) (community patients) reported median odour (stage II and III PUs) for a hydrocolloid and a hydrogel. The median for hydrocolloid was 2 and 2 for hydrogel. No estimate of effect or precision could be derived (VERY LOW QUALITY).[163]
- One study (n=10) (community patients) reported median comfort (stage II and III PUs) for a hydrocolloid and a hydrogel. The median for hydrocolloid was 3 and 4 for hydrogel. No estimate of effect or precision could be derived (VERY LOW QUALITY).[163]

Hydrocolloid versus impregnated gauze

- One study (n=11) (general population) showed that a hydrocolloid is potentially more effective compared to impregnated gauze dressing to reduce the proportion PUs (VERY LOW QUALITY).[180]
- One study (n=11) (general population) showed there may be a difference between a hydrocolloid and impregnated gauze dressing to improve healing of PUs (VERY LOW QUALITY).[180]

Hydrocolloid versus poly-hema dressing

- One study (n=43) (elderly patients) showed there may be no difference between a hydrocolloid and poly-hema dressing to reduce the proportion of stage II and III PUs, the direction of the estimate of the effect favoured the hydrocolloid dressing (VERY LOW QUALITY).[150]
- One study (n=43) (elderly patients) reported median time to healing (stage II and III PUs) for a hydrocolloid and a poly-hema. The median for hydrocolloid was 42 days and 32 days for hydrogel. A p-value of 0.56 was reported (VERY LOW QUALITY).[150]
- One study (n=43) (elderly patients) showed that a poly-hema is potentially more effective compared to a hydrocolloid for absolute rate of healing of stage II and III PUs (VERY LOW QUALITY).[150]
- One study (n=43) (elderly patients) showed that a poly-hema is potentially more effective compared to a hydrocolloid at reducing the incidence of adverse events of stage II and III PUs (VERY LOW QUALITY).[150]

Hydrocolloid versus co-polymer (amino acid)

- One study (n=168) (inpatients) showed that a co-polymer is potentially more effective compared to a hydrocolloid to reduce the proportion of stage II to IV PUs (VERY LOW QUALITY).[158]
- One study (n=168) (inpatients) reported median time to healing (stage II and III PUs) for a hydrocolloid and a co-polymer. The median for hydrocolloid was 38 days and 32 days for co-polymer. A p-value of 0.044 (adjusted for wound depth) was reported (VERY LOW QUALITY).[158]
- One study (n=168) (inpatients) showed there may be no difference between a hydrocolloid and a co-polymer at reducing the incidence of infections of stage II to IV PUs, the direction of the estimate of the effect favoured the hydrocolloid dressing (VERY LOW QUALITY).[158]

Hydrocolloid versus phenytoin cream

- One study (n=55) (patients with a spinal cord injury) showed that a hydrocolloid is clinically more effective compared to phenytoin cream to reduce the proportion of stage I and II PUs (MODERATE QUALITY).[90]
- One study (n=61) (patients with a spinal cord injury) showed that a hydrocolloid is potentially more effective compared to phenytoin cream to reduce the proportion of stage I and II PUs (LOW QUALITY).[90]
- One study (n=23) (patients with a spinal cord injury) showed that a hydrocolloid is potentially more effective compared to phenytoin cream to reduce the proportion of stage I PUs (LOW QUALITY).[90]
- One study (n=39) (patients with a spinal cord injury) showed that a hydrocolloid is potentially more effective compared to phenytoin cream to reduce the proportion of stage II PUs (LOW QUALITY).[90]
- One study (n=12) (patients with a spinal cord injury) showed that a hydrocolloid may be more effective compared to phenytoin cream to reduce the proportion of stage I and II PUs at the sacral area (VERY LOW QUALITY).[90]
- One study (n=61) (patients with a spinal cord injury) showed that a hydrocolloid is potentially more effective compared to phenytoin cream to improve healing of stage I and II PUs (LOW QUALITY).[90]
- One study (n=61) (patients with a spinal cord injury) showed there may be no difference between a hydrocolloid and phenytoin to reduce the proportion of stage I and II PUs worsened, the direction of the estimate of the effect favoured the hydrocolloid dressing (VERY LOW QUALITY).[90]

Hydrocolloid versus alginate dressing

- One study (n=110) (older inpatients) showed there may be no difference between a hydrocolloid and an alginate dressing to reduce the proportion of partially healed (40%) stage III and IV PUs, the direction of the estimate of the effect favoured the alginate dressing (VERY LOW QUALITY).[148]
- One study (n=110) (older inpatients) showed that alginate dressing is clinically more effective compared to a hydrocolloid for mean percentage reduction in ulcer area of stage III and IV PUs (LOW QUALITY).[148]
- One study (n=110) (older inpatients) showed that alginate dressing is clinically more effective compared to a hydrocolloid for mean cm² reduction in ulcer area of stage III and IV PUs (LOW QUALITY).[148]
- One study (n=110) (older inpatients) showed that a hydrocolloid may be more effective compared to an alginate dressing at reducing the incidence of infection of stage III and IV PUs (VERY LOW QUALITY).[148]
- One study (n=110) (older inpatients) showed that a hydrocolloid may be more effective compared to an alginate dressing at reducing the incidence of skin irritation of stage III and IV PUs (VERY LOW QUALITY).[148]
- One study (n=110) (older inpatients) showed that an alginate dressing may be more effective compared to a hydrocolloid at reducing the incidence of hypergranulation of stage III and IV PUs (VERY LOW QUALITY).[148]
- One study (n=110) (older inpatients) showed that a hydrocolloid may be more effective compared to an alginate dressing at reducing the incidence of maceration of stage III and IV PUs (VERY LOW QUALITY).[148]
- One study (n=110) (older inpatients) showed that a hydrocolloid may be more effective compared to an alginate dressing at reducing the incidence of bleeding of stage III and IV PUs (VERY LOW QUALITY).[148]
- One study (n=2201) (older inpatients) showed that there is no difference between a hydrocolloid and alginate dressing to reduce the incidence of pain at dressing removal (VERY LOW QUALITY).[148]
- One study (n=2201) (older inpatients) showed that a hydrocolloid is potentially more effective compared to an alginate dressing at reducing the incidence of strong odour at dressing removal (VERY LOW QUALITY).[148]
- One study (n=2201) (older inpatients) showed that a hydrocolloid is potentially more effective compared to an alginate dressing at reducing the incidence of mild odour at dressing removal (VERY LOW QUALITY).[148]

Hydrocolloid versus charcoal dressing

- One study (n=59) (inpatients) showed that a hydrocolloid may be more effective compared to a charcoal dressing to reduce the proportion of stage III and IV PUs worsened (VERY LOW QUALITY).[159]
- One study (n=59) (inpatients) reported a median percentage reduction in ulcer area (stage III and IV PUs) for a hydrocolloid and a charcoal dressing. The median for hydrocolloid was 18.5% and 26.9% for charcoal. No estimate of effect or precision could be derived (VERY LOW QUALITY).[159]
- One study (n=59) (inpatients) reported a median cm² reduction in ulcer area (stage III and IV PUs) for a hydrocolloid and a charcoal dressing. The median for hydrocolloid was 3.1 cm² and 4.3 cm² for charcoal. No estimate of effect or precision could be derived (VERY LOW QUALITY).[159]
- One study (n=59) (inpatients) showed that a charcoal may be more effective compared to a hydrocolloid at reducing the incidence of maceration of stage III and IV PUs (VERY LOW QUALITY).[159]
- One study (n=59) (inpatients) showed that a charcoal may be more effective compared to a hydrocolloid at reducing the incidence of infection of stage III and IV PUs (VERY LOW QUALITY).[159]
- One study (n=59) (inpatients) showed that a charcoal may be more effective compared to a hydrocolloid at reducing the incidence of hypergranulation of stage III and IV PUs (VERY LOW QUALITY).[159]

- One study (n=59) (inpatients) showed that a charcoal may be more effective compared to a hydrocolloid at reducing the incidence of skin irritation of stage III and IV PUs (VERY LOW QUALITY).[159]
- One study (n=59) (inpatients) showed there is no difference between a hydrocolloid and a charcoal dressing at reducing the incidence of bleeding of stage III and IV PUs (LOW QUALITY).[159]
- One study (n=59) (inpatients) showed that a hydrocolloid may be more effective compared to a charcoal at reducing the incidence of pruritus of stage III and IV PUs (VERY LOW QUALITY).[159]
- One study (n=59) (inpatients) showed there is no difference between a hydrocolloid and a charcoal dressing at reducing the incidence of wound pain of stage III and IV PUs (LOW QUALITY).[159]
- One study (n=59) (inpatients) showed there may be no difference between a hydrocolloid and a charcoal dressing at reducing the incidence of pain at dressing removal of stage III and IV PUs, the direction of the estimate of the effect favoured the hydrocolloid dressing (VERY LOW QUALITY).[159]

Hydrocolloid versus phenytoin ointment

- One study (n=28) (nursing home patients) showed that phenytoin ointment is potentially more effective compared to a hydrocolloid for mean time to healing of stage II PUs (VERY LOW QUALITY).[130]
- One study (n=28) (nursing home patients) showed there is no difference between a hydrocolloid and phenytoin ointment at reducing the incidence of adverse events of stage II PUs (LOW QUALITY).[130]

Hydrocolloid versus antibiotic ointment

- One study (n=24) (nursing home patients) showed that there may be no difference between a hydrocolloid and antibiotic ointment for mean time to healing of stage II PUs, the direction of the estimate of the effect favoured the hydrocolloid dressing (VERY LOW QUALITY).[130]
- One study (n=24) (nursing home patients) showed there is no difference between a hydrocolloid and phenytoin ointment at reducing the incidence of adverse events of stage II PUs (LOW QUALITY).[130]

Hydrocolloid: triangular shape versus oval shape

- One study (n=96) (inpatients) showed that a triangular shape hydrocolloid is potentially more effective compared to an oval shape hydrocolloid to reduce the proportion of stage II and III PUs (VERY LOW QUALITY).[155]
- One study (n=96) (inpatients) showed that a triangular shape hydrocolloid is potentially more effective compared to an oval shape hydrocolloid to improve healing of stage II and III PUs (VERY LOW QUALITY).[155]
- One study (n=96) (inpatients) showed that an oval shape hydrocolloid may be more effective compared to a triangular shape hydrocolloid to reduce the proportion of stage II and III PUs not changed (VERY LOW QUALITY).[155]
- One study (n=96) (inpatients) showed that a triangular shape hydrocolloid is clinically more effective compared to an oval shape hydrocolloid to reduce the proportion of stage II and III PUs worsened (LOW QUALITY).[155]
- One study (n=96) (inpatients) showed that a triangular shape hydrocolloid is clinically more effective compared to an oval shape hydrocolloid for mean percentage reduction in ulcer length of stage II and III PUs (LOW QUALITY).[155]
- One study (n=96) (inpatients) reported a mean percentage reduction in ulcer width (stage II and III PUs) for a triangular and oval shape hydrocolloid. The mean for triangular shape hydrocolloid was 28% and 24% for oval shape hydrocolloid. A p-value of >0.05 was reported (VERY LOW QUALITY).[155]
- One study (n=96) (inpatients) showed that a triangular shape hydrocolloid is clinically more effective compared to an oval shape hydrocolloid for mean pain at dressing change of stage II and III PUs (LOW QUALITY).[155]
- One study (n=96) (inpatients) showed that a triangular shape hydrocolloid is potentially more effective compared to an oval shape hydrocolloid at reducing the incidence of ulcer pain of stage II and III PUs (VERY LOW QUALITY).[155]

- One study (n=96) (inpatients) showed that a triangular shape hydrocolloid is potentially more effective compared to an oval shape hydrocolloid at reducing the incidence of adverse events of stage II and III PUs (VERY LOW QUALITY).[155]

Hydrocolloid: Comfeel® versus Comfeel®Plus

- One study (n=61) (general population) reported a percentage reduction in ulcer area (necrotic PUs) for Comfeel® and Comfeel®Plus. The reduction for Comfeel® was 44% and 49% for Comfeel®Plus. No estimate of effect or precision could be derived (VERY LOW QUALITY).[169]
- One study (n=61) (general population) showed that Comfeel® may be more effective compared to Comfeel®Plus at reducing the incidence of dressing intolerance of necrotic PUs(VERY LOW QUALITY).[169]
- One study (n=333) (general population) showed there is no difference between Comfeel® and Comfeel®Plus at reducing the incidence of comfort of the dressing of necrotic PUs (VERY LOW QUALITY).[169]

Hydrocolloid: SignaDress® versus Comfeel®Plus

- One study (n=35) (nursing home patients) showed that SignaDress® is potentially be more effective compared to Comfeel®Plus to reduce the proportion of stage II to IV PUs (VERY LOW QUALITY).[172]
- One study (n=35) (nursing home patients) reported a percentage reduction in ulcer area (stage II to IV PUs) for SignaDress® and Comfeel®Plus. The reduction for SignaDress® was 60% and 62% for Comfeel®Plus. A p-value of 0.01 was reported (VERY LOW QUALITY).[172]
- One study (n=35) (nursing home patients) reported percentage healing rate (stage II to IV PUs) for SignaDress® and Comfeel®Plus. The rate for SignaDress® was 33.8%/week and 7.0%/week for Comfeel®Plus. No estimate of effect or precision could be derived (VERY LOW QUALITY).[172]
- One study (n=35) (nursing home patients) showed is no difference between SingaDress® and Comfeel®Plus at reducing the incidence of adverse events of stage II to IV PUs (LOW QUALITY).[172]

Gauze versus foam

- Two studies (n=74) (general population) showed that a foam dressing is potentially more effective compared to a gauze dressing to reduce the proportion of stage II and III PUs (VERY LOW QUALITY).[117, 128]
- One study (n=36) (general population) reported median time to 50% healing (stage II PUs) for a gauze and a foam dressing. The median for gauze was 28 days and 28 days for foam. No estimate of effect or precision could be derived (VERY LOW QUALITY).[117, 128]

Gauze versus polyurethane film

- Two studies (n=53) (general population) showed that a polyurethane film is clinically more effective compared to a gauze dressing to reduce the proportion of PUs (all stages) (LOW QUALITY). [126, 173]
- One study (n=34) (community patients) showed that a polyurethane film is clinically more effective compared to a gauze dressing to reduce the proportion of stage II PUs (LOW QUALITY).[173]
- Two studies (n=53) (general population) showed that a polyurethane film is clinically more effective compared to a gauze dressing to reduce the proportion of PUs worsened (all stages) (LOW QUALITY).[126, 173]
- One study (n=34) (community patients) showed that a polyurethane film is clinically more effective compared to a gauze dressing to improve healing by decreasing in ulcer stage (stage II PUs) (LOW QUALITY).[173]
- One study (n=34) (community patients) showed that a polyurethane film is potentially more effective compared to a gauze dressing to improve healing by less increasing in ulcer stage (stage II PUs) (LOW QUALITY).[173]
- One study (n=19) (inpatients) reported a mean percentage reduction in ulcer area (stage I and II PUs according to Enis and Sarmiento classification) for a gauze and a polyurethane film. The mean for gauze was 2.5% and 42.9% for polyurethane. No estimate of effect or precision could be derived (VERY LOW QUALITY).[126]

- One study (n=34) (community patients) reported a median percentage reduction in ulcer area (stage II PUs) for a gauze and a polyurethane film. The median for gauze was 52% and 100% for polyurethane. No estimate of effect or precision could be derived (VERY LOW QUALITY).[173]
- One study (n=34) (community patients) showed there is potentially no difference between a gauze and a polyurethane film at reducing the incidence of maceration of stage II PUs (LOW QUALITY).[173]

Gauze versus hydrogel

- One study (n=30) (general population) showed there may be no difference between a gauze and a hydrogel to reduce the proportion of stage II to IV PUs, the direction of the estimate of the effect favoured the gauze dressing (VERY LOW QUALITY).[140]
- One study (n=41) (general population) showed there may be no difference between a gauze and a hydrogel to reduce the proportion of stage II to IV PUs worsened, the direction of the estimate of the effect favoured the hydrogel (VERY LOW QUALITY).[140]
- One study (n=40) (in- and out-patients) showed there is potentially no difference between a gauze and a hydrogel for mean percentage reduction in ulcer area of stage II and III PUs, the direction of the estimate of the effect favoured the hydrogel (VERY LOW QUALITY).[164]
- One study (n=27) (patients with a spinal cord injury) showed there may be no difference between a gauze and a hydrogel for mean healing rate of stage I to III PUs, the direction of the estimate of the effect favoured the gauze dressing (VERY LOW QUALITY).[115]
- One study (n=30) (general population) showed there may be no difference between a gauze and a hydrogel for mean time to healing of stage II to IV PUs, the direction of the estimate of the effect favoured the gauze dressing (VERY LOW QUALITY).[140]

Gauze versus dextranomer

- One study (n=30) (patients with a spinal cord injury) showed that dextranomer is clinically more effective compared to a gauze dressing to reduce the proportion of stage II to IV (according to Eltorai classification) (LOW QUALITY).[121]
- One study (n=30) (patients with a spinal cord injury) showed no difference between gauze and dextranomer dressing to reduce the proportion of stage II to IV (according to Eltorai classification) (LOW QUALITY).[121]

Gauze versus phenytoin cream

- One study (n=55) (patients with a spinal cord injury) showed there may be no difference between gauze and phenytoin cream to reduce the proportion of stage I and II PUs, the direction of the estimate of the effect favoured the phenytoin cream (VERY LOW QUALITY).[90]
- One study (n=60) (patients with a spinal cord injury) showed that phenytoin cream is potentially more effective compared to a gauze dressing to reduce the proportion of stage I and II PUs (VERY LOW QUALITY).[90]
- One study (n=40) (patients with a spinal cord injury) showed that phenytoin cream is potentially more effective compared to a gauze dressing to reduce the proportion of stage II PUs (VERY LOW QUALITY).[90]
- One study (n=20) (patients with a spinal cord injury) showed that a gauze dressing may be more effective compared to phenytoin cream to reduce the proportion of stage I PUs (VERY LOW QUALITY).[90]
- One study (n=13) (patients with a spinal cord injury) showed there may be no difference between gauze and phenytoin cream to reduce the proportion of stage I and II sacral PUs, the direction of the estimate of the effect favoured the gauze dressing (VERY LOW QUALITY).[90]
- One study (n=13) (patients with a spinal cord injury) showed there may be no difference between gauze and phenytoin cream to improve healing of stage I and II PUs, the direction of the estimate of the effect favoured the phenytoin cream (VERY LOW QUALITY).[90]
- One study (n=60) (patients with a spinal cord injury) showed that phenytoin cream is potentially more effective compared to a gauze dressing at reducing the proportion of stage I and II PUs worsened (VERY LOW QUALITY).[90]

Foam versus skin replacement (Dermagraft®)

- One study (n=34) (general population) showed there may be no difference between a foam dressing and skin replacement at reducing the proportion of stage III PUs, the direction of the estimate of the effect favoured the foam dressing (VERY LOW QUALITY).[138]
- One study (n=34) (general population) reported median percentage reduction in ulcer area of closed ulcers (stage III PUs) for a foam dressing and skin replacement. The median for foam was 33.5% and 49.5% for skin replacement. No estimate of effect or precision could be derived (VERY LOW QUALITY).[138]
- One study (n=34) (general population) reported median percentage reduction in ulcer area of unclosed ulcers (stage III PUs) for a foam dressing and skin replacement. The median for foam was 17.4% and 38.8% for skin replacement. No estimate of effect or precision could be derived (VERY LOW QUALITY).[138]
- One study (n=34) (general population) reported mean percentage reduction in ulcer volume (stage III PUs) for a foam dressing and skin replacement. The mean for foam was 4.1% and 18.7% for skin replacement. No estimate of effect or precision could be derived (VERY LOW QUALITY).[138]
- One study (n=34) (general population) reported median percentage reduction in ulcer volume (stage III PUs) for a foam dressing and skin replacement. The median for foam was 17.4% and 41.2% for skin replacement. No estimate of effect or precision could be derived (VERY LOW QUALITY).[138]
- One study (n=34) (general population) showed there may be no difference between a foam dressing and skin replacement at reducing the incidence of infection of stage III PUs, the direction of the estimate of the effect favoured the skin replacement (VERY LOW QUALITY).[138]
- One study (n=34) (general population) showed there is no difference between a foam dressing and skin replacement to reduce the incidence of adverse events of stage III PUs (LOW QUALITY).[138]

Foam versus antibiotic ointment

- One study (n=44) (long-term care patients) showed that a foam dressing is potentially more effective compared to antibiotic ointment at reducing the proportion of stage II PUs (VERY LOW QUALITY).[137]
- One study (n=44) (long-term care patients) reported mean PUSH score at end of treatment (stage II PUs) for a foam dressing and antibiotic ointment. The mean for foam was 3.24 and 1.61 for antibiotic ointment. A p-value of >0.05 was reported (VERY LOW QUALITY).[137]

Foam: Allevyn® versus Biatain®

- One study (n=32) (general population) showed Allevyn® is clinically more effective compared to Biatain® to reduce the proportion of stage II and III PUs (LOW QUALITY).[143]
- One study (n=32) (general population) reported median percentage reduction in ulcer area (stage II and III PUs) for Allevyn® and Biatain®. The median for Allevyn® was 38.2% and 45.8% for Biatain®. A p-value of >0.05 was reported (VERY LOW QUALITY).[143]
- One study (n=32) (general population) reported median percentage reduction in ulcer area (stage II and III PUs) for Allevyn® and Biatain®. The median for Allevyn® was 38.2% and 45.8% for Biatain®. A p-value of >0.05 was reported (VERY LOW QUALITY).[143]
- One study (n=32) (general population) reported mean pain score at dressing removal (stage II and III PUs) for Allevyn® and Biatain®. The mean for Allevyn® was 1.01 and 1.10 for Biatain®. A p-value >0.05 was reported (VERY LOW QUALITY).[143]
- One study (n=32) (general population) showed Allevyn® is potentially more effective compared to Biatain® for mean comfort at dressing removal of stage II and III PUs (VERY LOW QUALITY).[143]
- One study (n=32) (general population) showed Allevyn® is potentially more effective compared to Biatain® at reducing the incidence of adverse events of stage II and III PUs (VERY LOW QUALITY).[143]

Foam: Mepilex® versus Tielle®

- One study (n=38) (elderly patients) showed there may be no difference between a Mepilex® and a Tielle® to reduce the proportion of stage II PUs, the direction of the estimate of the effect favoured the Tielle® (VERY LOW QUALITY).[162]
- One study (n=38) (elderly patients) showed there is potentially no difference between a Mepilex® and a Tielle® to improve healing of stage II PUs, the direction of the estimate of the effect favoured the Tielle® (LOW QUALITY).[162]
- One study (n=38) (elderly patients) showed that Tiele® may be more effective compared to Mepilex® and a Tielle® to reduce the proportion of stage II PUs worsened (VERY LOW QUALITY).[162]
- One study (n=38) (elderly patients) showed that Mepilex® may be more effective compared to Tielle® at reducing the incidence of maceration of stage II PUs (VERY LOW QUALITY).[162]
- One study (n=38) (elderly patients) showed that Mepilex® may be more effective compared to Tielle® at reducing the incidence of odour of stage II PUs (VERY LOW QUALITY).[162]
- One study (n=38) (elderly patients) showed that Mepilex® may be more effective compared to Tielle® at reducing the incidence of adverse events of stage II PUs (VERY LOW QUALITY).[162]

Hydrogel versus foam

- One study (n=38) (palliative care patients) showed there is potentially no difference between a hydrogel and a foam dressing to reduce the proportion of stage II and III (Torrance classification), the direction of the estimate of the effect favoured the foam dressing (VERY LOW QUALITY).[176]
- One study (n=12) (palliative care patients) showed there is potentially no difference between a hydrogel and a foam dressing to reduce the proportion of stage II (Torrance classification), the direction of the estimate of the effect favoured either intervention (VERY LOW QUALITY).[176]
- One study (n=26) (palliative care patients) showed there may be no difference between a hydrogel and a foam dressing to reduce the proportion of stage III (Torrance classification), the direction of the estimate of the effect favoured the foam dressing (VERY LOW QUALITY).[176]
- One study (n=38) (palliative care patients) showed there no difference between a hydrogel and a foam dressing to improve healing of stage II and III (Torrance classification), the direction of the estimate of the effect favoured the foam dressing (LOW QUALITY).[176]
- One study (n=12) (palliative care patients) showed there is potentially no difference between a hydrogel and a foam dressing to improve healing of stage II (Torrance classification), the direction of the estimate of the effect favoured either intervention (VERY LOW QUALITY).[176]
- One study (n=26) (palliative care patients) showed there no difference between a hydrogel and a foam dressing to improve healing of stage III (Torrance classification), the direction of the estimate of the effect favoured the foam dressing (LOW QUALITY).[176]
- One study (n=12) (palliative care patients) showed that a foam dressing may be more effective compared to a hydrogel for mean healing rate of healed ulcers (stage II, Torrance classification) (VERY LOW QUALITY).[176]
- One study (n=26) (palliative care patients) showed that a foam dressing is potentially more effective compared to a hydrogel for mean healing rate of healed ulcers (stage III, Torrance classification) (VERY LOW QUALITY).[176]
- One study (n=26) (palliative care patients) showed that a foam dressing is potentially more effective compared to a hydrogel for mean healing rate of improved ulcers (stage III, Torrance classification) (VERY LOW QUALITY).[176]

Hydrogel versus dextranomer

- One study (n=135) (general population) reported median percentage reduction in ulcer area (stage I to IV PUs) for hydrogel and dextranomer. The median for hydrogel was 35% and 7% for dextranomer. A p-value of 0.03 was reported (VERY LOW QUALITY).[152]
- One study (n=135) (general population) showed that hydrogel may be more effective compared to dextranomer at reducing the incidence of pain at dressing removal of stage I to IV PUs (VERY LOW QUALITY).[152]

Hydrogel, foam dressing or transparent film versus different types of dressing

- One study (n=41) (community patients) showed that hydrogel, foam dressing or transparent film are potentially more effective compared to different types of dressing at reducing the proportion of stage II to IV PUs (VERY LOW QUALITY).[175]
- One study (n=41) (community patients) reported percentage healed per week (stage II to IV PUs) for hydrogel, foam dressing or transparent film and different types of dressing. A p-value of 0.15 (log-rank test) was reported (VERY LOW QUALITY).[175]
- One study (n=21) (community patients) showed that hydrogel, foam dressing or transparent film are potentially more effective compared to different types of dressing at reducing the proportion of patients reporting the application of the dressing as comfortable (VERY LOW QUALITY).[175]
- One study (n=21) (community patients) showed that hydrogel, foam dressing or transparent film may be more effective compared to different types of dressing at reducing the proportion of patients reporting discomfort at dressing removal (VERY LOW QUALITY).[175]
- One study (n=41) (community patients) showed there is no difference between a hydrogel and different types of dressing for mean percentage reduction in ulcer area of stage II to IV PUs (LOW QUALITY).[175]

Hydrogel: Sterigel® versus Intrasite®

- One study (n=47) (general population) reported mean percentage reduction in ulcer area at 14 days. The mean for Sterigel® was -82.3% and 7.45% for Intrasite®. No estimate of effect or precision could be derived (VERY LOW QUALITY).[145]
- One study (n=47) (general population) showed there is potentially no difference between Sterigel® and Intrasite® to reduce the incidence of intermittent pain at end of study of necrotic ulcers, the direction of the estimate of the effect favoured the Sterigel® (VERY LOW QUALITY).[145]
- One study (n=47) (general population) showed that Sterigel® is potentially more effective compared to Intrasite® to reduce the incidence of continuous pain at end of study of necrotic ulcers (VERY LOW QUALITY).[145]
- One study (n=47) (general population) showed there may be no difference between Sterigel® and Intrasite® to reduce the incidence of slight pain at dressing removal of necrotic ulcers, the direction of the estimate of the effect favoured the Sterigel® (VERY LOW QUALITY).[145]
- One study (n=47) (general population) showed that Sterigel® is potentially more effective compared to Intrasite® to reduce the incidence of severe pain at dressing removal of necrotic ulcers (VERY LOW QUALITY).[145]
- One study (n=47) (general population) showed that Sterigel® may be more effective compared to Intrasite® to reduce the incidence of maceration of necrotic ulcers (VERY LOW QUALITY).[145]

Protease modulating matrix versus impregnated gauze

- One study (n=80) (inpatients) showed that a protease modulating matrix is potentially more effective compared to an impregnated gauze at reducing the proportion of stage II to IV PUs (VERY LOW QUALITY).[167]
- One study (n=80) (inpatients) reported time to complete healing (stage II to IV PUs) for a protease modulating matrix and impregnated gauze. The time for protease modulating matrix was 6 to 15 days and

14 to 52 days for impregnated gauze. No estimate of effect or precision could be derived (VERY LOW QUALITY).[167]

- One study (n=80) (inpatients) showed that no difference between a protease modulating matrix and an impregnated gauze to reduce the incidence of adverse events of stage II to IV PUs (LOW QUALITY).[167]

Polyurethane film versus different types of dressings

- One study (n=64) (inpatients) showed there is potentially no difference between a polyurethane film and other different types of dressings for mean time to healing of stage II and III PUs, the direction of the estimate of the effect favoured the different types of dressings (VERY LOW QUALITY).[149]
- One study (n=64) (inpatients) showed there may be no difference between a polyurethane film and other different types of dressings for mean time to healing of stage II PUs, the direction of the estimate of the effect favoured the different types of dressings (VERY LOW QUALITY).[149]
- One study (n=64) (inpatients) showed there is potentially no difference between a polyurethane film and other different types of dressings for mean time to healing of stage III PUs, the direction of the estimate of the effect favoured the polyurethane dressing (VERY LOW QUALITY).[149]
- One study (n=64) (inpatients) showed there may be no difference between a polyurethane film and other different types of dressings for mean difference in PUSH score of stage II and III PUs, the direction of the estimate of the effect favoured the different types of dressings (VERY LOW QUALITY).[149]
- One study (n=64) (inpatients) showed there may be no difference between a polyurethane film and other different types of dressings to reduce the incidence of systemic worsening of stage II and III PUs, the direction of the estimate of the effect favoured the different types of dressings (VERY LOW QUALITY).[149]
- One study (n=64) (inpatients) showed that a polyurethane film is potentially more effective compared to other different types of dressings to reduce incidence of localized adverse events of stage II and III PUs (VERY LOW QUALITY).[149]

Alginate versus silver alginate

- One study (n=28) (elderly patients) showed that a silver alginate may be more effective compared to an alginate dressing to reduce the proportion of stage III and IV PUs worsened (VERY LOW QUALITY).[161]
- One study (n=28) (elderly patients) showed that a silver alginate may be more effective compared to an alginate dressing for mean percentage reduction in ulcer area of stage III and IV PUs (VERY LOW QUALITY).[161]
- One study (n=28) (elderly patients) showed there is potentially no difference between an alginate and a silver alginate dressing for absolute cm² decrease in ulcer area of stage III and IV PUs, the direction of the estimate of the effect favoured the silver alginate dressing (VERY LOW QUALITY).[161]
- One study (n=28) (elderly patients) showed that a silver alginate is potentially more effective compared to an alginate dressing for mean rate of healing of stage III and IV PUs (VERY LOW QUALITY).[161]
- One study (n=28) (elderly patients) showed that a silver alginate may be more effective compared to an alginate dressing to reduce the incidence of infection of stage III and IV PUs (VERY LOW QUALITY).[161]
- One study (n=24) (general population) reported a percentage reduction in infection score for alginate and silver alginate dressing. The reduction for alginate was 50 and 52 for silver alginate. No estimate of effect or precision could be derived (VERY LOW QUALITY).[178]
- One study (n=28) (elderly patients) showed there is potentially no difference between an alginate and a silver alginate dressing for mean mASEPSIS index at end of treatment of stage III and IV PUs, the direction of the estimate of the effect favoured the silver alginate dressing (VERY LOW QUALITY).[161]
- One study (n=28) (elderly patients) showed that an alginate may be more effective compared to a silver alginate dressing to reduce the incidence of poor acceptability and/or tolerability of stage III and IV PUs (VERY LOW QUALITY).[161]

Alginate versus dextranomer

- One study (n=92) (general population) showed that an alginate is potentially more effective compared to dextranomer to reduce the proportion of patients with > 75% reduction in ulcer area of stage III and IV PUs (VERY LOW QUALITY).[170]
- One study (n=92) (general population) showed there may be no difference between an alginate and dextranomer to reduce the proportion of patients with > 40% reduction in ulcer area of stage III and IV PUs, the direction of the estimate of the effect favoured the alginate dressing (VERY LOW QUALITY).[170]
- One study (n=92) (general population) showed that an alginate is clinically more effective compared to dextranomer to reduce the proportion of stage III and IV PUs stagnated or worsened (LOW QUALITY).[170]
- One study (n=92) (general population) showed there is potentially no difference between an alginate and dextranomer for mean rate of healing of patients improved > 40% of stage III and IV PUs, the direction of the estimate of the effect favoured the alginate dressing (VERY LOW QUALITY).[170]
- One study (n=92) (general population) showed that an alginate is potentially more effective compared to dextranomer for mean rate of healing of stage III and IV PUs (VERY LOW QUALITY).[170]
- One study (n=92) (general population) showed there may be no difference between an alginate and dextranomer to reduce the incidence of infection of stage III and IV PUs, the direction of the estimate of the effect favoured the alginate dressing (VERY LOW QUALITY).[170]
- One study (n=92) (general population) showed that an alginate may be more effective compared to dextranomer to reduce the incidence of hypergranulation of stage III and IV PUs (VERY LOW QUALITY).[170]
- One study (n=92) (general population) showed there may be no difference between an alginate and dextranomer to reduce the incidence of skin irritation of stage III and IV PUs, the direction of the estimate of the effect favoured the alginate dressing (VERY LOW QUALITY).[170]
- One study (n=92) (general population) showed that an alginate is potentially more effective compared to dextranomer to reduce the incidence of bleeding of stage III and IV PUs (VERY LOW QUALITY).[170]
- One study (n=92) (general population) showed that an alginate is clinically more effective compared to dextranomer to reduce the incidence of bleeding of stage III and IV PUs (LOW QUALITY).[170]
- One study (n=92) (general population) showed that an alginate may be more effective compared to dextranomer to reduce the incidence of pruritus of stage III and IV PUs (VERY LOW QUALITY).[170]

Silver versus different types of dressings

- One study (n=48) (general population) reported a mean percentage reduction in ulcer area (stage II and III PUs) for silver and other types of dressings. The mean for silver was 58.5% and 33.3% for other types of dressings. No estimate of effect or precision could be derived (VERY LOW QUALITY).[165]

Silver dressing versus silver cream

- One study (n=40) (in –and out-patients) showed there is potentially no difference between silver dressing and silver cream for mean percentage reduction in ulcer area of stage IV PUs, the direction of the estimate of the effect favoured the silver dressing (VERY LOW QUALITY).[142]
- One study (n=40) (in –and out-patients) reported a mean percentage reduction in PUSH score (stage IV PUs) for silver dressing and silver cream. The mean for silver dressing was 28.15 and 34.51 for silver cream. A p-value of 0.473 was reported (VERY LOW QUALITY).[142]
- One study (n=40) (in –and out-patients) showed there is no difference between silver dressing and silver cream to reduce the incidence of adverse events of stage IV PUs (LOW QUALITY).[142]

Sugar versus dextranomer

- One study (n=12) (long-term care patients) showed that dextranomer is potentially more effective compared to sugar at reducing the proportion of PUs (VERY LOW QUALITY).[79]

- One study (n=12) (long-term care patients) showed that dextranomer is clinically more effective compared to sugar to improve healing of PUs (LOW QUALITY).[79]
- One study (n=23) (long-term care patients) showed that dextranomer is potentially more effective compared to sugar at reducing the proportion of PUs (VERY LOW QUALITY).[79]
- One study (n=23) (long-term care patients) showed that dextranomer is clinically more effective compared to sugar to improve healing of PUs (LOW QUALITY).[79]

Sugar versus different types of topical agents

- One study (n=38) (geriatric patients) showed sugar is clinically more effective compared to different types of topical agents to reduce the proportion of PUs (LOW QUALITY).[168]
- One study (n=38) (geriatric patients) showed sugar is potentially more effective compared to different types of topical agents for mean healing index of PUs (LOW QUALITY).[168]

Honey versus ethoxydiaminoacridine and nitrofurazone

- One study (n=50) (inpatients) showed that honey is clinically more effective compared to ethoxydiaminoacridine and nitrofurazone to reduce the proportion of stage II and III PUs (LOW QUALITY).[89]
- One study (n=50) (inpatients) showed that honey is clinically more effective compared to ethoxydiaminoacridine and nitrofurazone for mean percentage reduction in ulcer area of stage II and III PUs (VERY LOW QUALITY).[89]
- One study (n=50) (inpatients) showed that honey is clinically more effective compared to ethoxydiaminoacridine and nitrofurazone for mean percentage reduction in PUSH score of stage II and III PUs (LOW QUALITY).[89]
- One study (n=50) (inpatients) showed there is no difference between honey and ethoxydiaminoacridine and nitrofurazone to reduce the incidence adverse events of stage II and III PUs (LOW QUALITY).[89]

Platelet gel versus other treatment

- One study (n=16) (patients with a spinal cord injury) showed there is no difference between platelet gel and another treatment to reduce the proportion of stage III to IV PUs (LOW QUALITY).[171]
- One study (n=16) (patients with a spinal cord injury) showed there is potentially no difference between platelet gel and another treatment to improve healing of stage III to IV PUs, the direction of the estimate of the effect favoured the platelet gel (VERY LOW QUALITY).[171]
- One study (n=16) (patients with a spinal cord injury) showed there is potentially no difference between platelet gel and another treatment for mean percentage reduction in ulcer volume of stage III to IV PUs, the direction of the estimate of the effect favoured the platelet gel (VERY LOW QUALITY).[171]

Hyaluronic acid versus sodium hyaluronate

- One study (n=20) (inpatients) showed that hyaluronic acid may be more effective compared to sodium hyaluronate for mean percentage reduction in ulcer area of stage I PUs (VERY LOW QUALITY).[156]
- One study (n=20) (inpatients) showed that hyaluronic acid may be more effective compared to sodium hyaluronate for mean percentage reduction in ulcer area of stage II PUs (VERY LOW QUALITY).[156]
- One study (n=20) (inpatients) reported a mean percentage reduction in ulcer area (stage III PUs) for hyaluronic acid and sodium hyaluronate. A p-value < 0.01 was reported (VERY LOW QUALITY).[156]
- One study (n=20) (inpatients) showed that hyaluronic acid may be more effective compared to sodium hyaluronate for time to 50% reduction in ulcer diameter of stage I PUs (VERY LOW QUALITY).[156]
- One study (n=20) (inpatients) showed that hyaluronic acid may be more effective compared to sodium hyaluronate for time to 50% reduction in ulcer diameter of stage II PUs (VERY LOW QUALITY).[156]
- One study (n=20) (inpatients) showed that hyaluronic acid may be more effective compared to sodium hyaluronate for time to 50% reduction in ulcer diameter of stage III PUs (VERY LOW QUALITY).[156]

Polyhexadine dressing versus polyhexadine swab

- One study (n=30) (in- and outpatients with MRSA) showed polyhexadine dressing is potentially more effective compared to polyhexadine swab to reduce the proportion of MRSA of stage II to IV PUs (LOW QUALITY).[179]
- One study (n=30) (in- and outpatients with MRSA) reported a percentage reduction in pain (stage II to IV PUs) for polyhexadine dressing and polyhexadine swab. The reduction for polyhexadine dressing was 82.4% and 52.6% for polyhexadine swab. No estimate of effect or precision could be derived (VERY LOW QUALITY).[179]

Hydrofibre® versus resin salve

- One study (n=22) (hospitalised patients) showed resin salve is potentially more effective compared to a hydrofibre® to reduce the proportion of stage II to IV PUs (LOW QUALITY).[95]
- One study (n=29) (hospitalised patients) showed resin salve is potentially more effective compared to a hydrofibre® to reduce the proportion of stage II to IV PUs (LOW QUALITY).[95]
- One study (n=29) (hospitalised patients) showed there is potentially no difference between a hydrofibre® and resin salve to improve healing of stage II to IV PUs, the direction of the estimate of the effect favoured the resin salve (VERY LOW QUALITY).[95]
- One study (n=29) (hospitalised patients) showed resin salve may be more effective compared to a hydrofibre® to reduce the proportion of stage II to IV PUs worsened (VERY LOW QUALITY).[95]
- One study (n=29) (hospitalised patients) reported a mean percentage reduction in ulcer width (stage II to IV PUs) for hydrofibre® and resin salve. The mean for hydrofibre® was 57.14% and 93.75% for resin salve. No estimate of effect or precision could be derived (VERY LOW QUALITY).[95]
- One study (n=29) (hospitalised patients) reported a mean percentage reduction in ulcer depth (stage II to IV PUs) for hydrofibre® and resin salve. The mean for hydrofibre® was -1.89% and 88.46% for resin salve. No estimate of effect or precision could be derived (VERY LOW QUALITY).[95]
- One study (n=29) (hospitalised patients) reported a speed of healing (stage II to IV PUs) for hydrofibre® and resin salve. A p-value of 0.013 in favour of resin salve was reported (VERY LOW QUALITY).[95]
- One study (n=37) (hospitalised patients) showed hydrofibre® may be more effective compared to a resin salve to reduce the incidence of allergic skin reaction of stage II to IV PUs worsened (VERY LOW QUALITY).[95]

Dextranomer versus chlorinated lime solution,

- One study (n=11) showed that dextranomer is potentially more effective compared to chlorinated lime for time to healing (VERY LOW QUALITY).[166]
- One study (n=?) reported pain (deep PUs) for chlorinated lime and dextranomer. Three patients in de chlorinated lime group and one patient in the dextranomer group reported pain. No estimate of effect or precision could be derived (VERY LOW QUALITY).[166]

3.6.4 Conclusion

- **Evidence based on 11 RCT's of moderate to very low quality suggests that hydrocolloids are potentially more effective compared to gauze dressings for healing of stage I and above pressure ulcers. Concerning stage II and III pressure ulcers, there is no difference for reduction in proportion of pressure ulcers worsened. Concerning stage I and II pressure ulcers, there is no difference for speed of healing of pressure ulcers.**
- **Evidence based on three RCT's of low to very low quality comparing hydrocolloids and foam dressings for the treatment of stage II and III pressure ulcers suggests there is no difference for healing of pressure ulcers. However, the evidence suggests that foam dressings are potentially more effective to reduce the proportion of pressure ulcers worsening.**
- **Evidence based on three RCT's of low to very low quality comparing hydrocolloids and polyurethane film for the treatment of stage II and III pressure ulcers suggests there is no difference in effectiveness.**
- **Evidence based on two RCT's of very low quality comparing hydrocolloids and collagenase ointment for the treatment of stage II to IV pressure ulcers suggests there is no difference for healing of pressure ulcers. Evidence for stage IV pressure ulcers to the heel suggests collagenase ointment are potentially more effective compared to hydrocolloids for healing and time to healing of pressure ulcers.**
- **Evidence based on one small RCT of moderate to very low quality comparing hydrocolloids and collagen dressings for the treatment of stage II and III pressure ulcers suggests there is no difference for healing of pressure ulcers.**
- **Evidence based on three RCT's of very low quality comparing hydrocolloids and hydrogels for the treatment of stage II and III pressure ulcers are conflicting for healing of pressure ulcers. The rate of healing may be more effective using hydrocolloids.**
- **One very small RCT of very low quality suggests hydrocolloids are potentially more effective compared to impregnated gauze for healing of pressure ulcers.**
- **One very small RCT of very low quality comparing hydrocolloids and poly-hema for the treatment of stage II and III pressure ulcers suggests there is no difference for healing of pressure ulcers. The rate of healing is potentially be more effective using poly-hema.**
- **One RCT of very low quality suggests co-polymer are potentially more effective compared to hydrocolloids for the healing of stage II to IV pressure ulcers.**
- **One very small RCT of moderate to very low quality suggests hydrocolloids are more effective compared to phenytoin cream for the healing of stage I and II pressure ulcers.**
- **One RCT of low to very low quality suggests alginate are more effective compared to hydrocolloids for the improving stage III and IV pressure ulcers.**
- **Two small RCT's of very low quality suggest foam dressings are potentially more effective compared to gauze dressings for the healing of stage II and III pressure ulcers.**
- **Two very small RCT's of low to very low quality suggest polyurethane film are more effective compared to gauze dressings for the healing of stage II and III pressure ulcers.**
- **Three small RCT's of very low quality comparing gauze dressings and hydrogel for the treatment of stage II to IV pressure ulcers suggest there is no difference for healing and rate of healing of pressure ulcers.**
- **One very small RCT of low quality suggests dextranomer is more effective compared to gauze dressings for the healing of stage III and IV pressure ulcers.**
- **Evidence based on one RCT of very low quality comparing foam dressings and skin replacement for the treatment of stage I and I pressure ulcers are conflicting. For sacral ulcers evidence suggests there is no difference.**

- One very small RCT of very low quality suggests foam dressings are potentially more effective compared to antibiotic ointments for healing of stage II pressure ulcers.
- One very small RCT of low to very low quality comparing hydrogel and foam dressings for the treatment of stage II pressure ulcers suggests there is no difference for healing of pressure ulcers. The rate of healing is potentially be more effective using foam dressings.
- One small RCT of low to very low quality suggests protease modulating matrix are potentially more effective compared to impregnated dressings for healing of stage II to IV pressure ulcers.
- One very small RCT of very low quality comparing polyurethane film and different dressings for the treatment of stage II to IV pressure ulcers suggests there is no difference for healing of pressure ulcers.
- Two very small RCT of very low quality suggests silver alginate dressings may be more effective compared to alginate dressings for healing of stage III and IV pressure ulcers.
- One very small RCT of very low quality suggests alginate dressings are potentially more effective compared to dextranomer for healing and rate of stage III and IV pressure ulcers.
- One very small RCT of very low quality comparing silver dressings and silver cream for the treatment of stage II pressure ulcers suggests there is no difference for healing of stage IV pressure ulcers.
- One very small RCT of low to very low quality suggests dextranomer is potentially more effective compared to sugar for healing of pressure ulcers.
- One very small RCT of low quality suggests sugar is potentially more effective compared to topical agents for healing of pressure ulcers.
- One very small RCT of low to very low quality suggests honey is more effective compared to ethoxydiaminoacridine for healing of stage II and III pressure ulcers.
- One very small RCT of low to very low quality comparing platelet gel and other treatments for the treatment of stage II pressure ulcers suggests there is no difference for healing of stage II to IV pressure ulcers.
- One very small RCT of very low quality suggests hyaluronic acid may be more effective compared to sodium hyalutonate for healing of stage I and II pressure ulcers.
- One very small RCT of low to very low quality suggests resin salve is potentially be more effective compared to hydrofibre® for healing of stage II to IV pressure ulcers.
- One very small RCT of very low quality suggests dextranomer is potentially be more effective compared to chlorinated lime for healing of deep pressure ulcers.
- None of the studies reported harms as a result of the interventions.
- All conclusions for the included studies were weakened due to the poor methodological quality of the trials and poor descripiton of type of ulcers such as excudate level.

3.6.5 *Recommendation for topical agents and dressings*

Recommendation	Strength of Recommendation	Level of Evidence
Consider improving wound healing environment by using modern dressings and topical agents (e.g. hydrocolloids, hydrogels, hydrofibres, foams, alginates, silver dressings) instead of basic dressing types (e.g. gauze, paraffin gauze and simple dressing pads). **As clinical studies did not demonstrate the superiority of one type of modern dressing and topical agent over another, decisions about which type of modern dressing/topical agent to use should be based on:** o **Ulcer assessment (condition of wound: tissue, exudate, depth, degree of infection, odor, pain, wound edges and wound environment);** o **General skin assessment;** o **Treatment objective;** o **Dressing characteristics;** o **Previous positive effect of particular dressing/topical agent;** o **Manufacturer's indications for use and contraindications;** o **Risk of adverse events;** o **Patient preferences (lifestyle, abilities and comfort).**	**Weak**	**Very low**

3.7 Indications for surgery

3.7.1 Introduction

Surgery has been indicated for closure of pressure ulcers for almost a century. It may, for instance, be indicated when conservative measures have failed to heal the pressure ulcer or to achieve a more robust repair than could be achieved by conservative treatment. It is believed that stage III and IV pressure ulcers may be a relative indication for surgery to allow early and timely mobilization of patients, to reduce pain and also to shorten the input- intensive period of nursing care. Surgery can be divided into emergency (drainage or abscess); urgent (debridement of necrotic escar) or elective (further debridement followed by closure) surgery. Methods of wound closure can be divided into:

- Direct closure of the wound margins;
- Skin grafting;
- Preservation of the walls of the ulcer to conserve tissue;
- Followed by direct closure or flap closure over this retained tissue;
- Radical excision of the walls of the pressure ulcer followed by flap closure.

It is currently unclear how clinicians reach decisions about which technique to use. This review aims to identify for which indications surgery is effective.[30]

3.7.2 Review question

What are the indications for surgery for the treatment of pressure ulcers?

3.7.3 Clinical evidence

We conducted a search for RCTs and observational studies (with control groups) to determine indications for surgery for the closure of pressure ulcers but none were found.

3.7.4 Conclusion

The lack of any controlled studies means that reporting on the effectiveness of surgical interventions in the closure of existing pressure ulcers is not possible.

3.7.5 Best practices for clinical practice

Studying the clinical effectiveness of the different surgical techniques that are used in the closure of pressure ulcers was beyond the scope of this guideline. In this guideline it was studied for which indications surgery can be considered.

Best Practices

Referral for the surgical treatment of pressure ulcers should be based on:

- **Level of risk (anaesthesia and surgical intervention);**
- **Recurrence;**
- **Patient preferences (lifestyle, abilities and comfort);**
- **Ulcer assessment (e.g. anatomical site, staging);**
- **General skin assessment;**
- **General health status;**
- **Competing care needs;**
- **Assessment of psychosocial risk factors of recurrence;**
- **Previous success of surgical techniques;**
- **Failure of previous conservative management interventions.**

3.8 Systemic agents

3.8.1 Introduction

The role of microorganisms in the aetiology and persistence of chronic wounds 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 recommendations in terms of indications for antibiotic therapy are diverse and based on expert opinion or experiences with wounds of other aetiologies. Some guidelines recommend against systemic antibiotics for pressure ulcers with only clinical signs of local infection while others feel that some local infections also may require treatment with systemic antibiotics, especially when the clinician takes into account the virulence of the organism and the host defences.[1, 183] This review aimed to study the

clinical effectiveness of systemic agents for the treatment of pressure ulcers.

3.8.2 Review question

What are the most clinically effective systemic agents for the treatment of pressure ulcers?

3.8.3 Clinical evidence

We conducted a search for randomized controlled trials and observational studies (with control groups) on systemic agents for the treatment of pressure ulcers but none were found.

3.8.4 Conclusion

No studies could be identified to determine the effectiveness of systemic agents for the treatment of pressure ulcers.

3.8.5 Best practice for clinical practice

Best practice

In the presence of systemic and/or local clinical signs of infection in the patient with a pressure ulcer, systemic anti-microbial therapy will be considered by the treating physician.

3.9 Electrotherapy

3.9.1 Introduction

Electrical stimulation has been used for decades as a treatment for chronic wounds however its role in pressure ulcer healing is unclear. It is hypothesized that electrical stimulation influences the migratory, proliferative and synthetic functions of fibroblasts and also results in increased expression of growth factors. There are several types of electric treatment modalities including low-voltage direct current, high voltage pulsed direct current, low voltage alternating current and pulsed electromagnetic field. All have different administration regimens and equipment required. Electromagnetic therapy is distinct from most other forms of electrotherapy in that it is a field effect, and not a direct electrical effect of form of radiation. The aim of this review is to study the effectiveness of electrotherapy in the treatment of pressure ulcers.(National Institute for Health and Clinical Excellence, 2005) Electromagnetism is out of scope of this CPG.

3.9.2 Review question

What is the clinical effectiveness of electrotherapy for the treatment of pressure ulcers?

3.9.3 Clinical evidence

We searched for randomized trials comparing the effectiveness of electrotherapy versus placebo or usual care for treatment of patients with pressure ulcers. Fourteen randomized trials were identified.[184-197]

Various types of electrical stimulation were included as were different populations. We included one study which compared different types of electrical stimulation (which also compared these to a control group).[188] Another trial looked at different durations of electrotherapy compared to placebo.[186] We separated studies that reported ulcers (where one patient could have more than one ulcer) from those who reported patients. One study included a mixed population of children and adults (aged 14 to 88) but did not report the results separately.[190] The studies had varying time periods (4 weeks to 5 months), we meta-analyzed them together and no significant heterogeneity was found. We used change from baseline scores rather than final values to get the reduction in ulcer size. We reported outcomes such as size of ulcer separately from other outcomes, as the data was continuous and there was a probability that the data was skewed but this was not counter-acted with log transformation within the studies. It should be emphasized that this data should be interpreted with caution. It should also be noted that many of the studies had very small sample sizes.

3.9.3.1 Quality of studies

In general the methodological quality of the included studies was poor. The majority of studies did not use an intention-to-treat analyses.[184, 187-189, 191-195, 197] Eight studies had unclear allocation concealment.[185-188, 191, 192, 194-196] In addition, power calculation was only done in four studies.[185, 188, 191, 192] Moreover, one of these studies had a sample size lower than the desired power.[185] The ten remaining studies had a small sample size.[184, 186, 187, 189, 190, 193-197] In appendix 7 the level of evidence can be found per outcome after applying the GRADE-methodology. The evidence base for all outcomes has been rated as being of low or very low quality.

3.9.3.2 *Evidence statements*

Electrotherapy versus control (placebo or usual care)

- Five studies (n=188) (general population and patients with a spinal cord injury) showed that there may be no difference between electrotherapy and control reduce the proportion of patients with a PUs, the direction of the estimate of the effect favoured electrotherapy (VERY LOW QUALITY).[185, 187, 190, 192, 193]
- One study (n=74) (general population) showed electrotherapy is clinically more effective compared to control to reduce the proportion stage II and III PUs (VERY LOW QUALITY).[197]
- One study (n=74) (general population) showed electrotherapy is clinically more effective compared to control to improve healing of stage II and III PUs > 80% (LOW QUALITY).[197]
- One study (n=29) (patients with a spinal cord injury) showed electrotherapy is potentially more effective compared to improve healing of stage II and III PUs > 50% (LOW QUALITY).[193]
- One study (n=34) (patients with a spinal cord injury) showed electrotherapy is potentially more effective compared to control to improve PWAT score of II to IV PUs (LOW QUALITY).[193]
- One study (n=34) (patients with a spinal cord injury) showed that there may be no difference between electrotherapy and control to improve PSST score of II to IV PUs, the direction of the estimate of the effect favoured either intervention (LOW QUALITY).[193]
- One study (n=16) (geriatric patients) showed electrotherapy is potentially more effective compared to control to decrease of PUs (VERY LOW QUALITY).[187]
- Two studies (n=50) (general population and patients with a spinal cord injury) showed there may be no difference between electrotherapy and control for increase of PUs, the direction of the estimate of the effect electrotherapy (LOW QUALITY).[187, 193]
- One study (n=16) (geriatric patients) showed electrotherapy is potentially more effective compared to control for increase of PUs (VERY LOW QUALITY).[187]
- One study (n=34) (patients with a spinal cord injury) showed electrotherapy may be more effective compared to control for increase of PUs (VERY LOW QUALITY).[193]
- One study (n=34) (general population) showed electrotherapy is clinically more effective compared to control for increase of PUs (VERY LOW QUALITY).[197]
- Two studies (n=84) (surgery patients and patients with a spinal cord injury) showed electrotherapy is clinically more effective compared to control for mean percentage reduction in ulcer area of stage II to IV PUs (LOW QUALITY).[189, 193]
- One study (n=40) (general population) showed electrotherapy is potentially more effective compared to control for mean percentage reduction in ulcer area (VERY LOW QUALITY).[191]
- One study (n=17) (patients with a spinal cord injury) reported a median percentage reduction in ulcer area (stage II to IV) for electrotherapy and control. The median for electrotherapy was 80% and 52% for control. A p-value of 0.05 was reported (VERY LOW QUALITY).[192]
- One study (n=16) (general population) showed electrotherapy is clinically more effective compared to control for rate of healing of stage IV PUs (VERY LOW QUALITY).[196]
- Two studies (n=123) (general population and patients with a spinal cord injury) showed there is potentially no difference between electrotherapy and control for rate of healing, the direction of the estimate of the effect favoured control (VERY LOW QUALITY).[188, 191]
- One study (n=12) (male patients with a spinal cord injury) showed electrotherapy is clinically more effective compared to control for rate of healing (LOW QUALITY).[195]
- One study (n=109) (patients with a spinal cord injury) showed electrotherapy is potentially more effective compared to control for rate of healing (exponential fitting) (VERY LOW QUALITY).[194]
- One study (n=109) (patients with a spinal cord injury) showed that there is potentially no difference between electrotherapy and control for rate of healing (linear fitting), the direction of the estimate of the effect favoured electrotherapy (VERY LOW QUALITY).[194]

- One study (n=40) (patients with a spinal cord injury) showed electrotherapy is potentially more effective compared to control for rate of healing (exponential fitting, crossover group) (VERY LOW QUALITY).[194]
- One study (n=40) (patients with a spinal cord injury) showed electrotherapy is potentially more effective compared to control for rate of healing (linear fitting, crossover group) (VERY LOW QUALITY).[194]
- One study (n=19) (geriatric patients) showed electrotherapy is clinically more effective compared to control for time to complete healing of stage III PUs (VERY LOW QUALITY).[185]
- One study (n=63) (geriatric patients) showed there is potentially no difference between electrotherapy and control for speed of healing of stage III PUs, the direction of the estimate of the effect favoured control (VERY LOW QUALITY).[185]
- One study (n=34) reported mean compliance to treatment (stage II to IV) for electrotherapy. A mean of 3.0 (SD 1.5)h/day were reported.. No estimate of effect or precision could be derived (VERY LOW QUALITY).[193]
- One study (n=40) (general patients) reported percentage of ulcers with uncomfortable sensation when current turned on (stage II to IV) for electrotherapy and control. The percentage for electrotherapy was 13.6% and 4.2% for control. No estimate of effect or precision could be derived (VERY LOW QUALITY).[191]
- One study (n=50) (surgical patients) showed electrotherapy is potentially more effective compared to control for mean percentage reduction in ulcer length (LOW QUALITY).[189]
- One study (n=50) (surgical patients) showed electrotherapy is clinically more effective compared to control for mean percentage reduction in ulcer width (LOW QUALITY).[189]
- One study (n=50) (surgical patients) showed electrotherapy is clinically more effective compared to control for mean percentage reduction in cavity volume (LOW QUALITY).[189]
- One study (n=50) (surgical patients) showed there is potentially no difference between electrotherapy and control for mean percentage reduction in granulation tissue, the direction of the estimate of the effect electrotherapy (VERY LOW QUALITY).[189]
- Two studies (n=108) (surgical patients) showed electrotherapy is potentially more effective compared to control for relative change in Gillman parameter (VERY LOW QUALITY).[189]

Asymmetric biphasic electrostimulation at 100us versus control

- One study (n=92) (patients with a spinal cord injury) showed asymmetric biphasic electrostimulation at 100us is potentially more effective compared to control for mean percentage reduction in ulcer area per week (VERY LOW QUALITY).[188]

Symmetric biphasic electrostimulation at 300 usec versus control

- One study (n=83) (patients with a spinal cord injury) showed control is potentially more effective compared to symmetric biphasic electrostimulation at 300us for mean percentage reduction in ulcer area per week (VERY LOW QUALITY).[188]

Microcurrent versus control

- One study (n=67) (patients with a spinal cord injury) showed control is potentially more effective compared to microcurrent for mean percentage reduction in ulcer area per week (VERY LOW QUALITY).[188]

Asymmetric biphasic electrostimulation at 100us versus symmetric biphasic electrostimulation at 300 usec

- One study (n=125) (patients with a spinal cord injury) showed asymmetric biphasic electrostimulation at 100us is clinically more effective compared to symmetric biphasic electrostimulation at 300us for mean percentage reduction in ulcer area per week (VERY LOW QUALITY).[188]

Asymmetric biphasic electrostimulation at 100us versus microcurrent

- One study (n=109) (patients with a spinal cord injury) showed asymmetric biphasic electrostimulation at 100us is clinically more effective compared to microcurrent for mean percentage reduction in ulcer area per week (VERY LOW QUALITY).[188]

Symmetric biphasic electrostimulation at 300 usec versus microcurrent

- One study (n=100) (patients with a spinal cord injury) showed asymmetric biphasic electrostimulation at 100us is clinically more effective compared to microcurrent for mean percentage reduction in ulcer area per week (VERY LOW QUALITY).[188]

Electrotherapy versus control for hard to heal ulcers (grade III and IV)

- Three studies (n=105) (general population and patients with a spinal cord injury) showed that there may be no difference between electrotherapy and control to reduce the proportion of patients with a stage III to IV PUs, the direction of the estimate of the effect favoured electrotherapy (VERY LOW QUALITY).[185, 192, 193]
- One study (n=46) (geriatric patients) showed control is clinically more effective compared to control for absolute reduction in ulcer size at end of treatment (LOW QUALITY).[185]
- One study (n=46) (geriatric patients) showed that there is potentially no difference between electrotherapy and control for absolute reduction in ulcer size at end of follow-up, the direction of the estimate of the effect favoured control (VERY LOW QUALITY).[185]
- One study (n=16) (general population) showed electrotherapy is clinically more effective compared to control for rate of healing of stage IV PUs (LOW QUALITY).[196]
- One study (n=19) (geriatric patients) showed electrotherapy is clinically more effective compared to control for time to complete healing (VERY LOW QUALITY).[185]
- One study (n=63) (geriatric patients) showed that there is potentially no difference between electrotherapy and control for speed of healing(VERY LOW QUALITY).[185]

3.9.4 Conclusion

- **Evidence based on 12 RCT's of low to very low quality indicates that the effectiveness of electrotherapy is conflicting, but suggests that there may be no difference between electrotherapy and the control interventions (e.g. usual care) studied for the treatment of pressure ulcers. All results should be interpreted with caution because evidence is based on low to very low quality studies and sample sizes were small. In addition, it was unclear if ulcers were debrided prior to the electrotherapy.**
- **None of the studies reported harms as a result of the interventions.**

3.10 Hyperbaric oxygen therapy

3.10.1 Introduction

Hyperbaric Oxygen Therapy (HBOT) is the administration of oxygen at pressures greater than normal atmospheric pressure for therapeutic reasons. It is defined by the Undersea and Hyperbaric Medical Society as 'a treatment in which a patient breathes 100% oxygen while inside a treatment chamber at a pressure higher than sea level pressure (i.e. more than 1 atmosphere absolute).

The treatment is performed in pressure chambers of various sizes, ranging from monoplace chambers for one patient only, to multiplace or multi-compartment treatment chambers in which several patients can sit and where hospital beds or even an entire intensive care setting can be installed and where health workers can attend to the patients. HBOT is used for various indications of which a restricted number of indications have been accepted by the two main scientific hyperbaric societies (i.e. 'European Committee for Hyperbaric Medicine' or the North-American 'Undersea and Hyperbaric Medical Society'): e.g. air or gas embolism; Carbon Monoxide poisoning; necrotising soft tissue infections. The use for other indications is mainly experimental. When applied under optimal circumstances, hyperbaric therapy is generally safe.[198] In this review we study the clinical effectiveness of HBOT as a treatment for pressure ulcers.

3.10.2 Review question

What is the clinical effectiveness of hyperbaric oxygen therapy for the treatment of pressure ulcers?

3.10.3 Clinical evidence

We conducted a search for randomized controlled trials of hyperbaric oxygen therapy for the treatment of pressure ulcers but none were found. We then conducted a search for hyperbaric oxygen 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)[199] but no randomized controlled trials were identified.

3.10.4 Conclusion

No studies could be identified to determine the effectiveness of hyperbaric oxygen for the treatment of pressure ulcers.

3.11 Negative pressure wound therapy

3.11.1 Introduction

Negative pressure wound therapy (NPWT) (Syn. vacuum-assisted wound closure, topical negative pressure, sub-atmospheric pressure) was pioneered in the late eighties. A pressure below the atmospheric pressure (i.e. a relative vacuum) is used to create suction, which drains the wound and influences the shape and growth of the surface tissues in a way that promotes healing. By draining the fluid from the wound, the substrate for growth of micro-organisms is removed, leading to a reduction of the microbial load. Negative pressure may also accelerate granulation tissue formation and improve blood flow in the tissue at the wound edges. Above this, the mechanical stimulation of cells by tensile forces may also play a role, by increasing cell proliferation and protein synthesis. During the procedure, a sterile foam dressing is cut to fit the shape and size of the wound. This foam is placed into the wound bed and held in place with an overlying airtight adhesive polyurethane drape secured to surrounding normal skin. A non-collapsible drain tube is embedded in the foam dressing and included under the adhesive drape with a mesentery technique used to maximize the seal obtained. The tube is connected to a vacuum source, and fluid is drawn from the wound through the foam into a disposable canister. The device can be programmed to provide varying degrees of pressure (usually a sub-atmospheric pressure in a range of -25 to -200 mmHg) either continuously or intermittently. The foam dressing collapses and its open cell nature allows equal levels of sub-atmospheric pressure to be transmitted to all surfaces in contact with the foam.[200] This technology is increasingly used in the treatment of chronic wounds. This review aimed to study the clinical effectiveness of NPWT in the treatment of pressure ulcers.

3.11.2 Review question

What is the clinical effectiveness of negative pressure wound therapy for the treatment of pressure ulcers?

3.11.3 Clinical evidence

One Cochrane review was identified (Ubbink 2008)[201] for negative pressure wound therapy for treating chronic wounds. We used this as a basis for the review, focusing only on the pressure ulcer studies included in the Cochrane review. No further studies were identified since the 2008 Cochrane review.

Two studies with pressure ulcers were included in the Cochrane review[202, 203]. Ford 2002 [202] included 28 patients with stage III or IV ulcers and compared NPWT to modern wound dressings (wound gel products) and followed up for 3-10 weeks. Wanner 2003 [203] included 22 paraplegic or tetraplegic patients with grade 2 or above pressure ulcers of the pelvic region and compared NPWT to wet-to-dry/wet-to-wet gauze dressings with Ringer's solution.

3.11.3.1 Quality of studies

In general the methodological quality of both included studies was very poor. None of the studies used use an intention-to-treat analyses and allocation concealment was unclear. In addition, power calculation was not done. There was no blinding except for outcome assessor in one study. [202] In appendix 10 the level of evidence can be found per outcome after applying the GRADE-methodology. The evidence base for all outcomes has been rated as being of very low quality.

3.11.3.2 Evidence statements

NPWT versus wet-to-dry/wet-to-wet gauze

- One study (n=22) (paraplegic and tretraplegic patients) showed there may be no difference between NPWT and gauze for time to 50% of initial wound volume of stage III and IV pelvic PUs, the direction of the estimate of the effect favoured the NPWT (VERY LOW QUALITY). [203]
- One study (n=22) (paraplegic and tretraplegic patients) reported mean percentage reduction in volume (stage III and IV pelvic PUs) for NPWT and gauze. The reduction for NPWT was 53% and 65% for gauze. A p-value of 0.9 was reported (VERY LOW QUALITY). [203]
- One study (n=22) (paraplegic and tretraplegic patients) reported mean ml reduction in volume (stage III and IV pelvic PUs) for NPWT and gauze. The reduction for NPWT was 26.5ml and 27.3ml for gauze. No estimate of effect or precision could be derived (VERY LOW QUALITY). [203]

NPWT versus wound gel products

- One study (n=35) (inpatients) showed wound gel products may be more effective compared to NPWT to reduce the proportion of stage III and IV PUs (VERY LOW QUALITY). [202]
- One study (n=35) (inpatients) reported mean percentage reduction in ulcer volume (stage III and IV PUs) for NPWT and wound gel products. The reduction for NPWT was 1.8% and 42.1% for wound gel products. A p-value of 0.46 was reported (VERY LOW QUALITY). [202]

3.11.4 Conclusion

Two very small RCT's of very low quality about the effectiveness of negative pressure wound therapy for the treatment of pressure ulcers could be identified. No conclusive statements can be made on the effectiveness of negative pressure wound therapy for the treatment of pressure ulcers.

3.12 Light therapy

3.12.1 Introduction

Light therapy (infrared, ultraviolet, laser, monochromatic, polarized light) is a therapeutic method which claims to regulate the biological behavior of cells.[204] The effects of light therapy are expected to accelerate wound healing, to support cellular and extracellular matrix proliferation (including fibroblasts, collagen production and granulation tissue formation), to reduce the inflammatory response, to relief pain, and to regulate the release of bioactive substances.[205, 206] This review aims to report on the effectiveness of light therapy for the treatment of pressure ulcers and guide clinicians in their decision making about the application of this method in clinical practice.

3.12.2 Review question

What is the effectiveness of light therapy for the treatment of pressure ulcers?

3.12.3 Clinical evidence

Ten randomized controlled trials were included in this review. [207-216]

Various types of light therapy are used to treat pressure ulcers. In this review different types of light therapy were compared to control or each other:

- Laser therapy: any therapy using light delivered by a laser device;
- Monochromatic infrared light: infrared light at one wavelength;
- Polarized light: light can be polarized (vibration of light is going in the same direction) or unpolarized (vibration of light is going in all directions).
- Low level laser therapy: therapy by laser used at a very low energy level per cm² or time-unit.
- Multiwave length light: intense pulsed light (broad spectrum lights) with multiple wavelengths;
- Ultraviolet therapy: light therapy using radiation in the ultraviolet range.

Table 14 – Types of light therapy

Laser therapy	Any therapy using intense beaming of light
Monochromatic infrared light	Infrared light at one wavelength
Polarized light	Light can be polarized (vibration of light is going in the same direction) or unpolarized (vibration of light is going in all directions)
Low level laser therapy	Therapy by laser used at a very low energy level per cm² or time-unit.
Multiwave length light	Intense pulsed light (broad spectrum lights) with multiple wavelengths
Ultraviolet therapy	Light therapy using radiation in the ultraviolet range

3.12.3.1 Quality of studies

In general the methodological quality of the included studies was poor. None of the studies reported on allocation concealment. In the majority of studies sequence generation was not clearly described or was performed poorly,[208-210, 212-214, 216] and intention-to-treat analyses was not used.[207-210, 212-214, 216] Only four studies reported an a priory sample size calculation[207, 208, 211, 214], of which two were underpowered.[207, 211] All studies were single- or double blinded, except for one study.[213] In appendix 11 the level of evidence can be found per outcome after applying the GRADE-methodology. The evidence base for all outcomes has been rated as being of low to very low quality.

3.12.3.2 Evidence statements

Light therapy versus control (placebo, sham therapy, or standard care)

- Two studies (n=95) (nursing home patients and patients with a spinal cord injury) showed that light therapy is potentially more effective compared to standard care to reduce the proportion of PUs (VERY LOW QUALITY).[211, 214]
- One study (n=79) (nursing home patients) showed that light therapy is potentially more effective compared to standard care to reduce the proportion of stage III PUs (VERY LOW QUALITY).[211]
- One study (n=16) (patients with a spinal cord injury) showed that light therapy may be more effective compared to standard care to reduce the proportion of PUs (VERY LOW QUALITY).[214]
- One study (n=not reported) (hospitalized patients) reported proportion of PUs completely healed (stage II PUs) for light therapy and standard care. A p-value < 0.05 was reported (VERY LOW QUALITY).[213]
- Two studies (n=228) (geriatric patients and patients with a spinal cord injury) showed there is potentially no difference between light therapy and control (placebo or sham therapy) to reduce the proportion of stage II to IV PUs, the direction of the estimate of the effect favoured the light therapy (VERY LOW QUALITY).[207, 215]
- One study (n=164) (geriatric patients) showed there is potentially no difference between light therapy and placebo to reduce the proportion of stage II and III PUs, the direction of the estimate of the effect favoured the light therapy (VERY LOW QUALITY).[207]
- One study (n=64) (patients with a spinal cord injury) showed there may be no difference between light therapy and placebo to reduce the proportion of stage II and III PUs, the direction of the estimate of the effect favoured the light therapy (VERY LOW QUALITY).[215]
- One study (n=164) (geriatric patients) showed there is potentially no difference between light therapy and placebo for > 90% healing of stage II and III PUs, the direction of the estimate of the effect favoured the light therapy (VERY LOW QUALITY).[207]
- One study (n=59) (hospitalized patients) showed that light therapy is potentially more effective compared to standard care for > 50% healing after 2 weeks of stage II and III PUs (VERY LOW QUALITY).[213]
- One study (n=59) (hospitalized patients) showed that light therapy is potentially more effective compared to standard care for > 50% healing after 3 weeks of stage II and III PUs (VERY LOW QUALITY).[213]

- One study (n=16) (patients with a spinal cord injury) showed there may be no difference between light therapy and standard care to improve healing of PUs, the direction of the estimate of the effect favoured the light therapy (VERY LOW QUALITY).[214]
- One study (n=16) (patients with a spinal cord injury) showed there may be no difference between light therapy and standard care to reduce the proportion of PUs not changed, the direction of the estimate of the effect favoured either intervention (VERY LOW QUALITY).[214]
- Three studies (n=111) (nursing home patients and patients with a spinal cord injury) showed that standard care may be more effective compared to light therapy to reduce the proportion of stage III PUs worsened (VERY LOW QUALITY).[210, 211, 214]
- Two studies (n=95) (nursing home patients) showed that there may be no difference between light therapy and standard to reduce the proportion stage III PUs worsened, the direction of the estimate of the effect favoured the standard care(VERY LOW QUALITY).[210, 211]
- One study (n=16) (patients with a spinal cord injury) showed that light therapy may be more effective compared to standard care to reduce the proportion of PUs worsened (VERY LOW QUALITY).[214]
- One study (n=64) (patients with a spinal cord injury) showed that light therapy may be more effective compared to sham therapy to reduce the proportion of stage II to IV PUs not changed or worsened (VERY LOW QUALITY).[215]
- One study (n=81) (nursing home patients) showed that light therapy may be more effective compared to standard care to reduce the proportion of stage III PU which developed to a stage IV PU (VERY LOW QUALITY).[211]
- One study (n=?) (patients with a spinal cord injury) reported proportion of ulcer decreased in stage (stage III PUs) for light therapy and standard care. Only the proportion of the light therapy group was reported. No estimate of effect or precision could be derived (VERY LOW QUALITY).[214]
- One study (n=?) (patients with a spinal cord injury) reported proportion of ulcers of unchanged stage for light therapy and standard care. Only the proportion of the light therapy group was reported. No estimate of effect or precision could be derived (VERY LOW QUALITY).[214]
- One study (n=9) (patients with a spinal cord injury) showed that light therapy may be more effective compared to sham therapy for proportion of stage III and IV PUs reduced to a stage I after three weeks (VERY LOW QUALITY).[215]
- One study (n=9) (patients with a spinal cord injury) showed that light therapy is more effective compared to sham therapy for proportion of stage III and IV PUs reduced to a stage II after two weeks (VERY LOW QUALITY).[215]
- One study (n=9) (patients with a spinal cord injury) showed that light therapy may be more effective compared to sham therapy for proportion of stage III and IV PUs reduced to a stage II after three weeks (VERY LOW QUALITY).[215]
- One study (n=163) (geriatric patients) showed there is no difference between light therapy and placebo for mean percentage reduction in ulcer area of stage II PUs (LOW QUALITY).[208]
- One study (n=40) (general population) reported a mean percentage reduction in ulcer area for light therapy and standard care. The mean for light therapy was 28.5% and -20% for standard care. No estimate of effect or precision could be derived (VERY LOW QUALITY).[209]
- One study (n=164) (geriatric patients) reported reduction in ulcer area (stage II and III) for light therapy and placebo. A p-value of 0.12 was reported (VERY LOW QUALITY).[207]
- One study (n=163) (geriatric patients) reported a median percentage reduction in ulcer area (stage II) for light therapy and placebo. The median for light therapy was 100% and 100% for placebo. No estimate of effect or precision could be derived (LOW QUALITY).[208]
- One study (n=16) (nursing home patients) reported a median percentage reduction in ulcer area (stage III) for light therapy and standard care. The median for light therapy was 83% and 95% for standard care. No estimate of effect or precision could be derived (LOW QUALITY).[210]

- One study (n=40) (general population) showed that light therapy is potentially more effective compared to standard care for mean cm² ulcer area at end of treatment (VERY LOW QUALITY).[209]
- One study (n=79) (nursing home patients) showed there is potentially no difference between light therapy and standard care for absolute reduction in ulcer area of stage III PUs, the direction of the estimate of the effect favoured the standard care (LOW QUALITY).[211]
- One study (n=79) (nursing home patients) showed there is potentially no difference between light therapy and standard care for relative percentage reduction in ulcer area of stage III PUs, the direction of the estimate of the effect favoured the standard care (LOW QUALITY).[211]
- One study (n=40) (general population) reported a mean percentage reduction PUSH score for light therapy and standard care. The mean for light therapy was 31% and -13.4% for standard care. No estimate of effect or precision could be derived (VERY LOW QUALITY).[209]
- One study (n=40) (general population) showed that light therapy is clinically more effective compared to standard care for mean PUSH score at end of treatment (LOW QUALITY).[209]
- One study (n=64) (patients with a spinal cord injury) showed there may be no difference between light therapy and sham therapy for proportion of stage II to IV PUs with a lower PSST score, the direction of the estimate of the effect favoured the sham therapy (VERY LOW QUALITY).[215]
- One study (n=9) (patients with a spinal cord injury) showed that light therapy is potentially more effective compared to sham therapy for PSST score of stage III and IV PUs at end of study (LOW QUALITY).[215]
- One study (n=9) (patients with a spinal cord injury) showed there may be no difference between light therapy and sham therapy for PSST score of stage III and IV PUs at end of treatment, the direction of the estimate of the effect favoured the light therapy (VERY LOW QUALITY).[215]
- One study (n=9) (patients with a spinal cord injury) reported a mean percentage reduction PSST score at end of treatment (stage III and IV) for light therapy and sham therapy. The mean for light therapy was 32.2% and 12.9% for sham therapy. No estimate of effect or precision could be derived (VERY LOW QUALITY).[215]
- One study (n=9) (patients with a spinal cord injury) reported a mean percentage reduction PSST score at end of study (stage III and IV) for light therapy and sham therapy. The mean for light therapy was 37.8% and 19.4% for sham therapy. No estimate of effect or precision could be derived (VERY LOW QUALITY).[215]
- One study (n=40) (general population) showed that light therapy is clinically more effective compared to standard care for mean rank of PU at end of treatment (LOW QUALITY).[209]
- One study (n=40) (general population) reported a mean percentage reduction in rank of PU for light therapy and standard care. The mean for light therapy was 19.6% and -4.9% for standard care. No estimate of effect or precision could be derived (VERY LOW QUALITY).[209]
- One study (n=9) (patients with a spinal cord injury) reported a mean percentage reduction in PU stage at end of treatment (stage III and IV) for light therapy and sham therapy. The mean for light therapy was 17.9% and 12.5% for sham therapy. No estimate of effect or precision could be derived (VERY LOW QUALITY).[215]
- One study (n=9) (patients with a spinal cord injury) reported a mean percentage reduction in PU stage at end of study (stage III and IV) for light therapy and sham therapy. The mean for light therapy was 35.7% and 25% for sham therapy. No estimate of effect or precision could be derived (VERY LOW QUALITY).[215]
- One study (n=164) (geriatric patients) reported a time to complete healing (stage II and III) for light therapy and placebo. A p-value of 0.93 was reported (VERY LOW QUALITY).[207]
- One study (n=165) (geriatric patients) reported a time to complete healing (stage II) for light therapy and placebo. A p-value of 0.58 was reported (VERY LOW QUALITY).[208]
- Two studies (n=80) (general population and patients with a spinal cord injury) there may be no difference between light therapy and sham therapy for time to complete healing, the direction of the estimate of the effect favoured the light therapy (VERY LOW QUALITY).[215, 216]

- One study (n=16) (general population) showed light therapy is potentially more effective compared to sham therapy for time to complete healing of superficial PUs (VERY LOW QUALITY).[216]
- One study (n=16) (general population) showed light therapy is potentially more effective compared to sham therapy for time to complete healing (age and initial area as covariates) of superficial PUs (VERY LOW QUALITY).[216]
- One study (n=64) (patients with a spinal cord injury) showed there is potentially no difference between light therapy and sham therapy for time to complete healing of stage II to IV PUs (VERY LOW QUALITY).[215]
- One study (n=59) (hospitalized patients) reported time to 90% reduction in ulcer area (stage II and III) for light therapy and standard care . The time for light therapy was 5 weeks and 9 weeks for control. No estimate of effect or precision could be derived (VERY LOW QUALITY).[213]
- One study (n=164) (geriatric patients) reported time of reduction in ulcer area (stage II and III) for light therapy and placebo. A p-value < 0.0001 was reported (VERY LOW QUALITY).[207]
- One study (n=9) (patients with a spinal cord injury) showed light therapy is potentially more effective compared to sham therapy for time for stage III and IV PUs to reach a stage II (LOW QUALITY).[215]
- One study (n=163) (geriatric patients) reported mean healing rate (stage II) for light therapy and placebo. The mean for light therapy was 15.1%/week and 10.9%/week for control. No estimate of effect or precision could be derived (VERY LOW QUALITY).[208]
- One study (n=12) (patients with a spinal cord injury) showed there may be no difference between light therapy and standard care for mean healing rate, the direction of the estimate of the effect favoured the standard care (VERY LOW QUALITY).[212]
- One study (n=59) (hospitalized patients) reported healing rate per week (stage II and III) for light therapy and standard care. The rate for light therapy was 0.298 and 0.2 for standard care. A p-value < 0.05 was reported (VERY LOW QUALITY).[213]
- One study (n=?) (hospitalized patients) reported healing rate per week (stage II) for light therapy and standard care. The rate for light therapy was 0.317 and 0.204 for standard care. A p-value < 0.05 was reported (VERY LOW QUALITY).[213]
- One study (n=59) (hospitalized patients) reported constant healing rate (stage II and III) for light therapy and standard care. The rate for light therapy was 5.3%/day and 3.4%/day for standard care. No estimate of effect or precision could be derived (VERY LOW QUALITY).[213]
- One study (n=?) (hospitalized patients) reported constant healing rate (stage II) for light therapy and standard care. The rate for light therapy was 5.9%/day and 3.4%/day for standard care. No estimate of effect or precision could be derived (VERY LOW QUALITY).[213]
- One study (n=16) (patients with a spinal cord injury) reported minimum reduction of 50% in ulcer size for light therapy and standard care. A p-value of 0.007 was reported (VERY LOW QUALITY).[214]
- One study (n=64) (patients with a spinal cord injury) showed light therapy may be more effective compared to sham therapy to reduce the incidence of hypergranulation in stage II to IV PUs (VERY LOW QUALITY).[215]
- Three studies (n=260) (geriatric and nursing home patients) showed there may be no difference between light therapy and control (placebo or standard care) to reduce the incidence of adverse events in stage II and III PUs (VERY LOW QUALITY).[208, 210, 211]

Laser therapy versus ultrasound/ultraviolet-C

- One study (n=12) (patients with a spinal cord injury) showed ultrasound/ultraviolet-C is potentially more effective compared to laser therapy for mean healing rate per week (VERY LOW QUALITY).[212]

Ultrasound/ultraviolet-C versus standard care

- One study (n=12) (patients with a spinal cord injury) showed ultrasound/ultraviolet-C is potentially more effective compared to standard care for mean healing rate per week (VERY LOW QUALITY).[212]

3.12.4 Conclusions

- **Evidence on the effectiveness of light therapy for the treatment of pressure ulcers based on 10 RCT's of low to very low quality is unclear with mixed results. As such, no general conclusion can be drawn.**
- **None of the studies reported harms as a result of the interventions.**
- **The most common weaknesses were the absence of allocation concealment, sequence generation and/or blinding, no use of an intention to treat analysis, and small sample sizes.**

3.13 Recommendation for adjuvant therapies

This recommendation is based on the evidence reports of electrotherapy, hyperbaric oxygen therapy, light therapy and negative pressure wound therapy.

Recommendation	Strength of Recommendation	Level of Evidence
As clinical studies failed to demonstrate the clinical effectiveness of negative pressure wound therapy, electrotherapy, light therapy, hyperbaric oxygen therapy, we cannot recommend any of these technologies as routine treatments for pressure ulcers.	Weak	Low to Very Low

3.14 Treatment of heel ulcers

3.14.1 Introduction

The treatment of heel ulcers may deserve specific scrutiny since they may represent a distinct clinical entity in terms of risk and responses to treatment. After all, feet are distinct from other body sites for the reasons such as a different composition of the skin (e.g. relative high number of collagen and elastic fibres); the high number of elderly with neuropathy of the lower limbs and the high frequency of circulation problems of the lower limbs.[52] Therefore this review aimed to study the clinical effectiveness of interventions specific for the treatment of heel pressure ulcers.

3.14.2 Review question

What is the most clinically effective method for management of pressure ulcers of the heel?

3.14.3 Clinical evidence

A Cochrane Review (McGinnis 2011)[52] was found for pressure-relieving devices for treating heel pressure ulcers, plus one study (Russell 2000)[67] which looked at two different types of mattress. One study looked at topical agents – nerve growth factors compared to placebo (Landi 2003)[120], this is reported in the topical agents review and reported feet and heel ulcers. As this present review focuses on heel ulcers, only one outcome was extricable from the study (reduction in ulcer area) as all other outcomes related to foot and heel ulcers. One study[84] looked at collagenase-containing ointment compared to hydrocolloid dressing to treat pressure ulcers. Meaume (2009)[48] looked at ornithine alpha-ketoglutarate, an amino acid salt, compared to placebo as a supplement to treat heel pressure ulcers.

No randomized controlled trials were identified regarding repositioning, electrotherapy, NPWT, HBOT, debridement, antimicrobials, antibiotics, skin massage/rubbing.

3.14.3.1 Quality of studies

In general the methodological quality of the included studies was variable. Allocation concealment and sequence generation was unclear in two studies[67, 84]. In three studies the use of intention-to-treat analyses was not clear[67, 84, 120]. Three studies[48, 67, 84] reported an a priory sample size calculation, of which one was underpowered[67]. All studies were single- or double blinded, except for one study.[84] In appendix 12 the level of evidence can be found per outcome after applying the GRADE-methodology. The evidence base for all outcomes has been rated as being of low to very low quality.

3.14.3.2 Evidence statements

Nimbus system (1 in 2 alternating cycle) versus cairewave system (1 in 3 alternating cycle)

- One study (n=113) (care for the elderly units) showed that a nimbus system is potentially more effective compared to a cairwave system to increase the proportion of patients with completely healed heel pressure ulcers (LOW QUALITY).[67]

Nerve growth versus placebo

- One study (n=36) (nursing home patients) showed nerve growth factor is clinically more effective compared to placebo in reducing the area of heel pressure ulcers (LOW QUALITY).[120]

Hydrocolloid dressing versus collagen dressing

- One study (n=23) (female inpatients with grade IV pressure ulcers) showed that a collagen dressing is potentially more effective compared to a hydrocolloid dressing to increase the proportion of patients with completely healed heel pressure ulcers (VERY LOW QUALITY).[84]
- One study (n=24) (female inpatients with grade IV pressure ulcers) showed collagen dressings are clinically more effective compared to hydrocolloid dressings in reducing the time to heal heel pressure ulcers. (VERY LOW QUALITY)[84]

Ornithine alpha-ketogluterate versus placebo

- One study (n=160) (elderly inpatients with grade II or IIIg pressure ulcers) showed no clinical difference in the rate of complete healing of heel pressure ulcers between patients that received 10 sachets of ornithine alpha-ketoglutarate compared to placebo (VERY LOW QUALITY). [48]
- One study (n=160) (elderly inpatients with grade II or IIIg pressure ulcers) showed that ornithine alpha-ketogluterate is potentially more effective in reducing the size of pressure ulcers of the heels compared to placebo (VERY LOW QUALITY). [48]
- One study (n=160) (elderly inpatients with grade II or IIIg pressure ulcers) showed that there is potentially no difference between ornithine alpha-ketogluterate and placebo in the reduction of the mean surface area of heel ulcers (VERY LOW QUALITY). [48]
- One study (n=160) (elderly inpatients with grade II or IIIg pressure ulcers) showed that ornithine alpha-ketogluterate is potentially more effective in reducing the size of pressure ulcers of the heels with 90% at week 6 compared to placebo (VERY LOW QUALITY). [48]

3.14.4 Conclusions

- **One RCT of low quality compared the effectiveness of two different types of alternating mattresses in the treatment of heel pressure ulcers. No conclusions about the relative effectiveness of pressure relieving devices for healing pressure ulcers of the heel could be drawn on this evidence.**
- **One very small RCT of low quality showed that nerve growth factor is clinically more effective than placebo in reducing the heel pressure ulcer area. Given the very small sample size and lack of well designed studies that replicate this finding there is insufficient evidence to direct clinical practice.**
- **One very small RCT of very low quality compared the effectiveness of two different dressing types in the treatment of heel pressure ulcers. There are indications that collagenase dressings are more effective compared to hydrocolloid dressing in the treatment of heel pressure ulcers. However, given the very small sample size and the methodological limitations, no robust conclusions can be drawn on this evidence to direct clinical practice.**
- **One RCT of low quality compared the effectiveness of a nutritional supplement (i.e. Ornithine alpha-ketogluterate) with placebo in the treatment of heel pressure ulcers. No conclusions about the relative effectiveness of nutritional supplements for healing pressure ulcers of the heel can be drawn on this evidence.**
- **None of the studies reported harms as a result of the interventions.**

3.14.5 Best practices for the treatment of heel ulcers

Best Practices
Heels with pressure ulcers should be offloaded maximally. The choice of devices to offload the heel could be informed by factors such as cost, ease of use, patient comfort, patient preferences, anatomical position of the ulcer site.
For bedridden patients or patients sitting in a chair in backward position with the feet up, heel-protection devices should offload the heel completely. This can be done by distributing the weight of the leg along the calf without putting pressure on the Achilles tendon. The knee should be in slight flexion and supported.

4 DISCUSSION

4.1 Summary of findings and coherence with other recent reviews

4.1.1 Introduction

Despite current advances in medicine, surgery and nursing care, pressure ulcers remain a major cause of morbidity and mortality. A considerably **high prevalence** of pressure ulcers remains in all healthcare settings. Depending on the setting **clinicians have a plethora of options at their disposal to treat pressure ulcers**. Pressure ulcer management involves a comprehensive care plan with consideration of all factors contributing to and affecting the ulcer and the patient. Pressure ulcer management is highly demanding in terms of resources and product costs. The economical impact of pressure ulcer treatment is highly variable. This variability is linked with pressure ulcer severity (the more severe, the longer the time to heal), product costs and resource input. The development of a clinical practice guideline supporting clinicians in their decision making on the best available evidence is important. The challenges of pressure ulcer management are not limited to clinical decisions. Besides, financial, emotional, psychosocial, regulatory, and medico-legal aspects should be taken into account.

A large discrepancy exists between the relevance of this topic and the **availability of methodologically sound clinical studies with a focus on pressure ulcer treatment**. In general, the included studies (Randomized Controlled Trials) for all of the topics being studied are largely under-powered and have common methodological flaws such as: lack of allocation concealment; lack of baseline comparability; lack of blind – or independently verified – outcome assessment; poor description of standard care and co-interventions. Given these major methodological limitations, the results of the studies should be interpreted with caution. In the paragraphs below we aim to summarize the most important results, study limitations and research recommendations.

4.1.2 Nutrition

The studies about nutritional supplementation for pressure ulcer treatment mainly focused on the effect of a standard hospital diet with addition of nutritional supplements versus a standard hospital diet alone. Because of the significant heterogeneity in terms of patient population (e.g. surgical patients, critically ill, nursing home residents), nutritional composition (e.g. type, dose, duration), outcome measurements and follow-up period, they could not be meta-analysed.

The evidence included 12 RCT's of very low quality. The most frequent shortcomings were: small sample sizes, absence of intention-to-treat analyses, a priori sample size calculation, unclear sequence generation and allocation concealment. In addition, in some studies it remained unclear if patients were malnourished and/or there was insufficient information on the standard hospital diet.

There is evidence that the addition of nutritional supplements to standard hospital diet may be more effective compared to standard hospital diet alone for the treatment of pressure ulcers. However, clinical studies did not demonstrate the superiority of one nutritional supplementation over another.

Further research with large patient numbers and a sound methodology is required to procure evidence for the impact of nutritional supplementation on pressure ulcers healing. Consideration should be given as to the constituents of the supplement and method of application as well as to the baseline nutritional status of the included patients.[30, 36]

4.1.3 Redistributing devices

Pressure relieving and redistributing devices include different types of mattresses, overlays and cushions. Their effect is focused on reducing pressure and shearing forces.

The evidence base included 18 RCT's of very low quality. Since most RCT's were underpowered there is a great risk of failing to detect clinically and statistically significant differences. In addition, the majority of studies is weakened by methodological shortcomings (no blinding, unclear sequence generation, no intention-to-treat analysis). In addition 8 studies had unclear allocation concealment and only 9 studies reported an a priori sample size calculation.

There is no conclusive or reliable evidence to suggest the superiority of either 'high-tech' support surfaces or 'low-tech' continuous low pressure support surfaces over another for pressure ulcer treatment.[217] This lack of high quality evidence to determine the relative effects of pressure relieving devices for healing pressure ulcers is striking in light of the frequency of pressure ulcer occurrence and the overabundance of types of redistributing devices (with highly variable cost) that have been commercialized.[217]

As such, there is an urgent need for independent, well designed, sufficiently powered, multi-centred, randomized, controlled trials to compare the clinical effectiveness of different types of pressure relieving devices for pressure ulcer treatment. In particular, this research should compare different devices categories:

- 'High tech' alternating pressure devices with 'lower-tech' alternatives (such as different types of foam mattresses);
- 'High tech' alternating pressure devices with other 'high-tech' equipment (such as low-air-loss therapy and air-fluidised beds);
- 'High tech' alternating pressure mattresses (mattress replacement systems) with alternating pressure overlays.[217]

4.1.4 Debridement

Debridement can be defined as the removal of dead damaged, or infected tissue to improve healing of the remaining healthy tissue. This can be achieved by various techniques. This report focused on **surgical, mechanical, enzymatic methods and the application of maggot therapy**.

The evidence regarding the clinical effectiveness of debridement for pressure ulcer treatment is based on seven RCT's and two observational studies of very low quality. Besides small sample sizes, serious methodological issues were identified in most studies. These issues included the lack of allocation concealment, sequence generation and intention-to-treat analyses.

No study about surgical debridement meeting the inclusion criteria was found. The other debridement methods (collagenase, dextranomer, sugar, egg white, papain/urea, fibrolysis DNAse, hydrocolloid) were evaluated in studies with very small sample sizes, leading to unclear and uncertain

results. To date, it is impossible to draw a conclusion about the clinical effectiveness of the different debridement methods. The three observational studies indicated a higher effectiveness compared to conservative treatment in terms of change in wound surface and time to heal. Nevertheless, given the poor methodological quality of these studies no clear conclusions can be drawn. Maggot therapy can currently not be used in Belgium due to legislation restrictions.

Sufficiently powered RCT's studying the clinical effectiveness of different debridement methods on objective outcome measures (e.g. time to complete wound healing) are required to enable better guidance of clinical practice. In particular, attention should be given to a complete and thorough description about the concurrent treatments including secondary dressings as well as to a blinded assessment of outcomes.

4.1.5 Topical agents

Nowadays, the use of topical agents has become a part of routine care in the treatment of pressure ulcers. Various types of topical agents are used to treat pressure ulcers. For the purpose of this study, two main groups were defined: non anti-bacterial and anti-bacterial agents. The development of these categories is artificial and complex. The categories were developed based on expert opinion, literature and reports of the authors of the included studies.

The evidence included 47 RCT's of moderate to very low quality. Since most RCT's were underpowered there is a great risk of failing to detect clinically and statistically significant differences. In addition, the majority of the studies had unclear sequence generation and allocation concealment, and absence of intention-to-treat analysis, and a priori sample size calculation. Few studies were single- or double blinded. In addition, the rationale for the choice of the 'comparator treatment' in the control arm was not clear in the included studies. Besides, the description of the clinical appearance of the pressure ulcers (exudate level, infection, wound edges, surrounding skin) was lacking in most of the studies.

Clinical studies did not demonstrate the superiority of one type of topical agent over another. As such there is an urgent need for well designed, sufficiently powered, multi-centred, randomized, controlled trials to compare the clinical effectiveness of different types of topical agents to treat pressure ulcers. In particular, attention should be given to a complete and thorough description of the intervention, and clinical appearance of the pressure ulcer. Finally, the topical agent that is subject of the study should be compared with a clinically relevant comparator (e.g. alternative topical agent or dressing used for same indications).

4.1.6 Dressings

A wound dressing aims to promote pressure ulcer healing and/or to prevent the wound from further breakdown. A dressing is designed to be in direct contact with the wound, generally aiming to maintain a moist wound bed, to support granulation/epithelialisation and to promote pressure healing and closure. A plethora of different dressing options is currently available. Following categories were made: basic dressings (e.g. gauze, paraffin gauze and simple dressing pads) and modern dressings (e.g. hydrocolloids, hydrogels, foams, films, alginates). The categorisation of dressings is complex and artificial. No clear guidance and consensus is available in the literature. In this review the categorisation was made based on expert opinion, literature and reports of the authors of the included studies.

The evidence included 61 RCT's of moderate to very low quality. Since most RCT's were underpowered there is a great risk of failing to detect clinically and statistically significant differences. In addition, the majority of the studies had unclear sequence generation and allocation concealment, absence of intention-to-treat analysis, and a priori sample size calculation. In few studies the outcome assessor was blinded. In addition, the rationale for the choice of the 'comparator treatment' in the control arm was not clear in the included studies. Besides, the description of the clinical appearance of the pressure ulcers (exudate level, infection, wound edges, surrounding skin) was lacking in most of the studies.

Clinical studies indicate that modern dressings are potentially more effective than basic dressings but do not illustrate the clinical superiority of a particular modern dressing type. As such there is an urgent need for well designed, sufficiently powered, multi-centred, randomized, controlled trials to compare the clinical effectiveness of different types of modern dressings to treat pressure ulcers. In particular, attention should be given to a complete and thorough description of the intervention and type of pressure ulcers based on category/grade, exudates level, infection status. Finally, the dressing that is subject of the study should be compared with a

clinically relevant comparator (e.g. alternative topical agent or dressing used for same indications).

4.1.7 Indications for surgery

Surgery has been indicated to close a pressure ulcer for almost a century. It may, for instance, be indicated for full- thickness pressure ulcers when conservative measures have failed to heal the pressure ulcer or to achieve a more robust repair than could be achieved by conservative treatment. It is currently unclear how clinicians reach decisions about when to debride and which technique to use. Despite the history of surgery as an intervention to close a pressure ulcer, evidence about its effectiveness is absent. There is a need for controlled clinical studies instead of the currently published case reports, case series and retrospective chart reviews. Research needs to focus on the effectiveness of different types of surgery and surgery compared to conventional treatments.[30]

4.1.8 Systemic agents

It is unclear how clinicians decide to prescribe systemic agents in the treatment of pressure ulcers. Some clinicians prescribe systemic agents for patients with pressure ulcers on the basis of clinical signs of local infection. Nevertheless, this review did not offer additional guidance due to the absence of controlled studies. This review stresses therefore the need to set up RCT's about the effectiveness of systemic agents in the treatment of pressure ulcers with local signs of infection. In particular, attention should be given to a clear description of the indications for choosing the systematic antibiotic as intervention and referral should be made to existing guidelines.

4.1.9 Electrotherapy

Electrical stimulation is used for its potential effect in pressure ulcer healing, i.e. its influence on the migratory, proliferative and synthetic functions of fibroblasts and also on the increasing expression of growth factors. Electric treatment modalities include low-voltage direct current, high voltage pulsed direct current, low voltage alternating current and pulsed electromagnetic field. Pulsed electromagnetic field stimulation was out of scope of this review.

Fourteen RCT's were included. In general studies were largely underpowered and of poor methodological quality. Frequent methodological flaws were lack of intention-to-treat analysis, unclear allocation concealment and lack of a priori power calculation.

The evidence on the effectiveness of electrotherapy is conflicting. However the meta-analysis of five studies (n=188) comparing electrotherapy with a control treatment (usual care or placebo) suggests that there may be no difference between electrotherapy and the control interventions (e.g. usual care) for the treatment of pressure ulcers.

There is a need for independent, well-designed, adequately powered multicentre RCT's to evaluate the contribution of electrotherapy to the healing of pressure ulcers. It is recommended that studies clearly describe the frequency and duration of treatment, location of wounds and any treatment(s) applied concurrently with electrotherapy. It is recommended that standard care with electrotherapy as adjuvant therapy is compared to standard care alone (or with sham therapy).[30]

4.1.10 Hyperbaric oxygen therapy

Hyperbaric oxygen therapy is the administration of oxygen at pressures greater than normal atmospheric pressure. It is used for many indications, such as air or gas embolism; Carbon Monoxide poisoning; necrotising soft tissue infections. However, no RCT's were found on the effectiveness of the use of Hyperbaric oxygen therapy as an adjuvant therapy in the treatment of pressure ulcers stressing the need for RCT's in this area.

4.1.11 Negative pressure wound therapy

With this therapy, a pressure below the atmospheric pressure (i.e. a relative vacuum) is used to create suction, which drains the wound and influences the shape and growth of the surface tissues in a way that promotes healing. Although clinical experts indicated that negative pressure wound therapy is an increasingly popular treatment for pressure ulcers (mainly category/stage III and IV pressure ulcers), we found only two very small RCT's of very low quality. None of the studies used an intention-to-treat analysis and allocation concealment was unclear. In addition, a priori power calculation was not done. There was no blinding except for outcome assessor in one study. No conclusive statements can be made on the effectiveness of negative pressure wound therapy for the treatment of pressure ulcers.

There is a need for well designed, adequately powered RCTs to evaluate the effects of negative pressure wound therapy on pressure ulcer healing.

In order to determine whether negative pressure wound therapy improves the healing of pressure ulcers, a comparison between negative pressure wound therapy and a control dressing identical to that used in negative pressure wound therapy is required. Perhaps more clinically relevant would be RCT's which compare negative pressure wound therapy with dressings that would be commonly used alternatives to negative pressure wound therapy and for which there is good evidence of effect available. Such RCT's should preferably be conducted independently of the manufacturer.[218]

4.1.12 Light therapy

Light therapy (infrared, ultraviolet, laser, monochromatic, polarized light) is a therapeutic method which claims to regulate the biological behavior of cells. Evidence on the effectiveness of light therapy for the treatment of pressure ulcers is based on 10 RCT's of low to very low quality. Most studies were underpowered and had methodological flaws such as lack of allocation concealment, unclear description or poorly performed sequence generation and absence of intention-to-treat analyses. Results on its effectiveness were mixed. As such there is insufficient evidence in this review to give a clear direction for practice. Given the small sample sizes and methodological shortcomings of the included studies replication in larger, well designed studies preferably independent from the manufacturers is required.

4.1.13 Heel ulcer treatment

Evidence on the treatment of heel ulcers is very limited. We found: one small RCT of low quality that compared the effectiveness of two different types of alternating mattresses; one very small RCT of low quality that compared nerve growth factor with a placebo; one very small RCT of very low quality that compared the effectiveness of two different dressing types and one RCT of low quality that compared the effectiveness of the administration of a nutritional supplement (i.e. Ornithine alpha-ketogluterate) compared with placebo. Given the limited, fragmented and poor quality evidence no conclusions that can direct clinical practice about the treatment of heel pressure ulcers can be drawn.

Clearly further well-designed trials for the specific treatment options of heel pressure ulcers are needed. Consideration needs to be given to the population studied. These need to include elderly, vascular, diabetic and orthopaedic patients in all settings.[52]

4.2 Absence of evidence is not the same as evidence of absence

Based on the evidence reviews we cannot formulate specific recommendations on, for instance the type of mattresses, type of modern dressing, or which nutritional supplements should be used. However, it should be stressed that **absence of evidence is not the same as evidence for absence of clinical effectiveness**.[219] In general, the topics of this guideline are largely understudied and the (few) published studies are generally underpowered to illustrate clinical effectiveness (or rule out harm).

It is clear that vigorous research efforts are needed to improve the body of knowledge concerning the treatment of pressure ulcers. For each of the topics under study there is a need for more independent, well designed multi-centre studies.

4.3 How to use this guideline

There is a plethora of treatment options but limited high quality evidence to give a clear direction for clinical practice. Nevertheless it can be concluded that pressure ulcer treatment requires a patient tailored multi-factorial approach including a holistic assessment, a structured ulcer assessment and follow up (e.g. photographs and ulcer assessment tools), and an individual plan of care that is agreed upon within the multidisciplinary team. This individualized care plan includes aspects of wound care (e.g. wound cleansing, debridement, dressings, surgical wound closure), symptom management (e.g. pain management), primary and secondary prevention interventions (e.g. redistributing devices and repositioning) as well as systemic interventions that promote wound healing (e.g. nutritional support).

As such this guideline should be considered as a starting point for organizations to develop a comprehensive policy that targets all caregivers concerned. This includes the development of organization specific protocols and procedures that take into account local circumstances. The wound care associations (e.g. CNC, WCS, Afiscep) and organisations of healthcare professions can support the implementation of this guideline in

daily practice by including it on their websites and in their educational activities. Some authors[220] suggest that healthcare organizations should invest in multidisciplinary wound care teams that are responsible for supporting clinicians and organizations in making practice informed choices. Examples of activities that organizations could employ with the support of a multidisciplinary wound care team are: the development of a wound care module in the (electronic) patient record, the organization of multidisciplinary continuous education, clinical bedside or remote (e.g. photographs) wound care consultation, follow-up of investment on patient outcomes.

4.4 Guideline update

The KCE processes foresee that the relevance of an update would be yearly assessed for each published guideline by the authors. Decisions are made on the basis of new scientific publications on a specific topic (e.g. Cochrane reviews, RCTs on medications or interventions). Potential interest for groups of health practitioners is also considered in this process.

This appraisal leads to a decision on whether to update or not a guideline or specific parts of it to ensure the recommendations stay in line with the latest scientific developments.

5 REFERENCES

1. European Pressure Ulcer Advisory PPUAP. Prevention and treatment of pressure ulcers: Clinical Practice Guideline. Washington (DC): 2009.
2. Gawlitta D, Oomens CW, Bader DL, Baaijens FP, Bouten CV. Temporal differences in the influence of ischemic factors and deformation on the metabolism of engineered skeletal muscle. J.Appl.Physiol. 2007;103(2):464-73.
3. Loerakker S, Stekelenburg A, Strijkers GJ, Rijpkema JJ, Baaijens FP, Bader DL, et al. Temporal effects of mechanical loading on deformation-induced damage in skeletal muscle tissue. Ann.Biomed.Eng. 2010;38(8):2577-87.
4. Vanderwee K, Defloor T, Beeckman D, Demarre L, Verhaeghe S, Van DT, et al. Assessing the adequacy of pressure ulcer prevention in hospitals: a nationwide prevalence survey. BMJ Quality & Safety. 2011;20(3):260-7.
5. Black JM, Cuddigan JE, Walko MA, Didier LA, Lander MJ, Kelpe MR. Medical device related pressure ulcers in hospitalized patients. Int.Wound.J. 2010;7(5):358-65.
6. Beeckman D, Schoonhoven L, Fletcher J, Furtado K, Gunningberg L, Heyman H, et al. EPUAP classification system for pressure ulcers: European reliability study. Journal of advanced nursing. 2007;60(6):682-91.
7. Dealy C, Lindholm C. Pressure Ulcer Classification. Romanelli MCMCD, et al., editor. London: European Pressure Ulcer Advisory Panel & Springler-Verlag; 2012.
8. Barrois B, Labalette C, Rousseau P, Corbin A, Colin D, Allaert F, et al. A national prevalence study of pressure ulcers in French hospital inpatients. J.Wound.Care. 2008;17(9):373-9.
9. Capon A, Pavoni N, Mastromattei A, Di LD. Pressure ulcer risk in long-term units: prevalence and associated factors. Journal of advanced nursing. 2007;58(3):263-72.
10. Gunningberg L, Hommel A, Baath C, Idvall E. The first national pressure ulcer prevalence survey in county council and

municipality settings in Sweden. Journal of Evaluation in Clinical Practice. 2012.

11. Tannen A, Dassen T, Halfens R. Differences in prevalence of pressure ulcers between the Netherlands and Germany--associations between risk, prevention and occurrence of pressure ulcers in hospitals and nursing homes. Journal of Clinical Nursing. 2008;17(9):1237-44.
12. Alderden J, Whitney JD, Taylor SM, Zaratkiewicz S. Risk profile characteristics associated with outcomes of hospital-acquired pressure ulcers: a retrospective review. Crit Care Nurse. 2011;31(4):30-43.
13. Kottner J, Gefen A, Lahmann N. Weight and pressure ulcer occurrence: a secondary data analysis. International Journal of Nursing Studies. 2011;48(11):1339-48.
14. Shahin ES, Dassen T, Halfens RJ. Pressure ulcer prevalence and incidence in intensive care patients: a literature review. Nurs.Crit Care. 2008;13(2):71-9.
15. Vanderwee K, Clark M, Dealey C, Gunningberg L, Defloor T. Pressure ulcer prevalence in Europe: a pilot study. J Eval Clin Pract. 2007;13(2):227-35.
16. Gorecki C, Closs SJ, Nixon J, Briggs M. Patient-reported pressure ulcer pain: a mixed-methods systematic review. J.Pain Symptom.Manage. 2011;42(3):443-59.
17. Brienza D, Kelsey S, Karg P, Allegretti A, Olson M, chmeler M, et al. A randomized clinical trial on preventing pressure ulcers with wheelchair seat cushions. Journal of the American Geriatrics Society. 2010;58(12):2308-14.
18. Hopkins A, Dealey C, Bale S, Defloor T, Worboys F. Patient stories of living with a pressure ulcer. Journal of advanced nursing. 2006;56(4):345-53.
19. Allman RM, Goode PS, Burst N, Bartolucci AA, Thomas DR. Pressure ulcers, hospital complications, and disease severity: impact on hospital costs and length of stay. Adv.Wound.Care. 1999;12(1):22-30.
20. Graves N, Birrell F, Whitby M. Effect of pressure ulcers on length of hospital stay. Infection Control and Hospital Epidemiology. 2005;26(3):293-7.
21. Theisen S, Drabik A, Stock S. Pressure ulcers in older hospitalised patients and its impact on length of stay: a retrospective observational study. Journal of Clinical Nursing. 2012;21(3-4):380-7.
22. Bo M, Massaia M, Raspo S, Bosco F, Cena P, Molaschi M, et al. Predictive factors of in-hospital mortality in older patients admitted to a medical intensive care unit. Journal of the American Geriatrics Society. 2003;51(4):529-33.
23. Redelings MD, Lee NE, Sorvillo F. Pressure ulcers: more lethal than we thought? Adv.Skin Wound.Care. 2005;18(7):367-72.
24. Severens JL, Habraken JM, Duivenvoorden S, Frederiks CM. The cost of illness of pressure ulcers in The Netherlands. Adv.Skin Wound.Care. 2002;15(2):72-7.
25. Bennett RG, Baran PJ, DeVone LV, Bacetti H, Kristo B, Tayback M, et al. Low airloss hydrotherapy versus standard care for incontinent hospitalized patients. Journal of the American Geriatrics Society. 1998;46(5):569-76.
26. Gray M, Beeckman D, Bliss DZ, Fader M, Logan S, Junkin J, et al. Incontinence-associated dermatitis: a comprehensive review and update. J.Wound.Ostomy.Continence.Nurs. 2012;39(1):61-74.
27. Beeckman D, Mathe‹ C, Van Lancker A, Van Houdt S, Vanwalleghem G, Gryson L, et al. A national guideline for the prevention of pressure ulcers. Brussels: Belgian Healthcare Knowledge Centre (KCE); 2013. KCE reports 193C D/2013/10.273/97
28. National Institute for H, Clinical E. Guidelines on pressure ulcer risk management and prevention - guideline. London: National Institute for Clinical Excellence; 2001.
29. National Institute for H, Clinical E. Pressure relieving devices: the use of pressure relieving devices for the prevention of pressure ulcers in primary and secondary care. London: National Institute for Clinical Excellence; 2003.

30. National Institute for H, Clinical E. Pressure ulcers: The management of pressure ulcers in primary and secondary care. London: National Institute for Clinical Excellence; 2005.
31. National Institute for H, Clinical E. The guidelines manual. London: National Institute for Health and Clinical Excellence; 2009.
32. Balshem H, Helfand M, Schunemann HJ, Oxman AD, Kunz R, Brozek J, et al. GRADE guidelines: 3. Rating the quality of evidence. Journal of Clinical Epidemiology. 2011;64(4):401-6.
33. Guyatt G, Oxman AD, Sultan S, Brozek J, Glasziou P, Alonso-Coello P, et al. GRADE guidelines: 11. Making an overall rating of confidence in effect estimates for a single outcome and for all outcomes. J Clin Epidemiol. 2013;66(2):151-7.
34. Andrews J, Guyatt G, Oxman AD, Alderson P, Dahm P, Falck-Ytter Y, et al. GRADE guidelines: 15. Going from evidence to recommendations: the significance and presentation of recommendations. J Clin Epidemiol. 2013.
35. Fiocchi A, Schunemann HJ, Brozek J, Restani P, Beyer K, Troncone R, et al. Diagnosis and Rationale for Action Against Cow's Milk Allergy (DRACMA): a summary report. J Allergy Clin Immunol. 2010;126(6):1119-28 e12.
36. Langer G, Schloemer G, Knerr A, Kuss O, Behrens J. Nutritional interventions for preventing and treating pressure ulcers. Cochrane database of systematic reviews (Online). 2003;Issue 4:CD003216.
37. Taylor TV, Rimmer S, Day B, Butcher J, Dymock IW. Ascorbic acid supplementation in the treatment of pressure-sores. Lancet. 1974;2(7880):544-6.
38. ter Riet G, Kessels AG, Knipschild PG. Randomized clinical trial of ascorbic acid in the treatment of pressure ulcers. Journal of Clinical Epidemiology. 1995;48(12):1453-60.
39. Chernoff RS, Milton KY, Lipschitz DA. The effect of a very high-protein liquid formula on decubitus ulcers healing in long-term tube-fed institutionalized patients. Journal of the American Dietetic Association. 1990;90:A-130.
40. Norris J, Reynolds R. The effect of oral zinc sulphate therapy in decubitus ulcers. Journal of Americal Geriatrics Society. 1971;19:793-7.
41. Desneves KJ, Todorovic BE, Cassar A, Crowe TC. Treatment with supplementary arginine, vitamin C and zinc in patients with pressure ulcers: a randomised controlled trial. Clinical Nutrition. 2005;24(6):979-87.
42. Lee SK, Posthauer ME, Dorner B, Redovian V, Maloney MJ. Pressure ulcer healing with a concentrated, fortified, collagen protein hydrolysate supplement: a randomized controlled trial. Advances in skin and wound care. 2006;19(2):92-6.
43. Cereda E, Gini A, Pedrolli C, Vanotti A. Disease-specific, versus standard, nutritional support for the treatment of pressure ulcers in institutionalized older adults: a randomized controlled trial. Journal of the American Geriatrics Society. 2009;57(8):1395-402.
44. Van Anholt RD, Sobotka L, Meijer EP, Heyman H, Groen HW, Topinkovÿ E, et al. Specific nutritional support accelerates pressure ulcer healing and reduces wound care intensity in non-malnourished patients. Nutrition. 2010;26(9):867-72.
45. Brewer RD, Jr., Mihaldzic N, Dietz A. The effect of oral zinc sulfate on the healing of decubitus ulcers in spinal cord injured patients. Proc Annu Clin Spinal.Cord.Inj Conf. 1967;16:70-2.
46. Benati G, Delvecchio S, Cilla D, Pedone V. Impact on pressure ulcer healing of an arginine-enriched nutritional solution in patients with severe cognitive impairment. Archives of Gerontology and Geriatrics.Supplement. 2001;7:43-7.
47. Ohura T, Nakajo T, Okada S, Omura K, Adachi K. Evaluation of effects of nutrition intervention on healing of pressure ulcers and nutritional states (randomized controlled trial). Wound Repair and Regeneration. 2011;19(3):330-6.
48. Meaume S, Kerihuel JC, Constans T, Teot L, Lerebours E, Kern J, et al. Efficacy and safety of ornithine alpha-ketoglutarate in heel pressure ulcers in elderly patients: results of a randomized controlled trial. journal of nutrition, health and aging. 2009;13(7):623-30.

49. Terris DD, Woo C, Jarczok MN, Ho CH. Comparison of in-person and digital photograph assessment of stage III and IV pressure ulcers among veterans with spinal cord injuries. Journal of Rehabilitation Research and Development. 2011;48(3):215-24.
50. Van Anholt RD, Sobotka L, Meijer EP, Schols JM. An arginine- and micronutrient-enriched nutritional supplement accelerates pressure ulcer healing and reduces wound care in non-malnourished patients. EWMA Journal. 2010;10(2):45, Abstract.
51. Brewer S, Desneves K, Pearce L, Mills K, Dunn L, Brown D, et al. Effect of an arginine-containing nutritional supplement on pressure ulcer healing in community spinal patients. Journal of Wound Care. 2010;19(7):311-6.
52. McGinnis E, Stubbs N. Pressure-relieving devices for treating heel pressure ulcers. Cochrane.Database.Syst.Rev. 2011(9):CD005485.
53. Allman RM, Keruly JC, Smith CR. Air-fluidized beds or conventional therapy for pressure sores. Annals of Internal Medicine. 1987;107(5):641-8.
54. Branom R, Rappl LM. "Constant force technology" versus low-air-loss therapy in the treatment of pressure ulcers. Ostomy/Wound Management. 2001;47(9):38-46.
55. Clark M. A randomised controlled trial comparing the healing of pressure sores upon two pressure-redistributing seat cushions. Proceedings of the 7th European European Conference on Advances in Wound Management. 1998:122-5.
56. Day A, Leonard F. Seeking quality care for patients with pressure ulcers. Decubitus. 1993;6(1):32-43.
57. Devine B. Alternating pressure air mattresses in the management of established pressure sores. Journal of tissue viability. 1995;5(3):94-8.
58. Evans D, Land L, Geary A. A clinical evaluation of the Nimbus 3 alternating pressure mattress replacement system. Journal of Wound Care. 2000;9(4):181-6.
59. Ewing MR, Garrow C, Presley TA, Ashley C, Kisella NM. Further experiences in the use of sheep skins as an aid in nursing. Australian Nurses Journal. 1964:215-9.
60. Ferrell BA, Osterweil D, Christenson P. A randomized trial of low-air-loss beds for treatment of pressure ulcers. JAMA. 1993;269(4):494-7.
61. Groen HW, Groenier KH, Schuling J. Comparative study of a foam mattress and a water mattress. Journal of Wound Care. 1999;8(7):333-5.
62. Keogh A, Dealey C. Profiling beds versus standard hospital beds: effects on pressure ulcer incidence outcomes. Journal of Wound Care. 2001;10(2):15-9.
63. Mulder GD, Taro N, Seeley J, Andrews K. A study of pressure ulcer response to low air loss beds vs. conventional treatment. Journal of Geriatric Dermatology. 1994;2(3):87-91.
64. Munro BH, Brown L, Heitman BB. Pressure ulcers: one bed or another? Geriatric Nursing. 1989;10(4):190-2.
65. Nixon J, Cranny G, Iglesias C, Nelson EA, Hawkins K, Phillips A, et al. Randomised, controlled trial of alternating pressure mattresses compared with alternating pressure overlays for the prevention of pressure ulcers: PRESSURE (pressure relieving support surfaces) trial. BMJ. 2006;332(7555):1413.
66. Osterbrink J, Mayer H, Schroder G. Clinical evaluation of the effectiveness of a multimodal static pressure relieving device. European Wound Management Association Conference. 2005;Thur14:00-15:30;V26-6:73.
67. Russell L, Reynolds TM, Carr J, Evans A, Holmes M. Randomised controlled trial of two pressure-relieving systems. Journal of Wound Care. 2000;9(2):52-5.
68. Russell L, Reynolds TM, Towns A, Worth W, Greenman A, Turner R. Randomized comparison trial of the RIK and the Nimbus 3 mattresses. British Journal of Nursing. 2003;12(4):254, 6-, 9.
69. Strauss MJ, Gong J, Gary BD, Kalsbeek WD, Spear S. The cost of home air-fluidized therapy for pressure sores. A randomized controlled trial. Journal of Family Practice. 1991;33(1):52-9.

70. Caley L, Jones S, Freer J, Muller JS. Two types of low air loss therapy. In; 1994.
71. Makhsous M, Lin F, Knaus E, Zeigler M, Rowles DM, Gittler M, et al. Promote pressure ulcer healing in individuals with spinal cord injury using an individualized cyclic pressure-relief protocol. Advances in skin and wound care. 2009;22(11):514-21.
72. Nixon J, Nelson EA, Cranny G, Iglesias CP, Hawkins K, Cullum NA, et al. Pressure relieving support surfaces: a randomised evaluation. Health Technology Assessment. 2006;10(22):1-163.
73. Clark M. Repositioning to prevent pressure sores--what is the evidence? Nursing Standard. 1998;13(3):58-64.
74. Madhok BM, Vowden K, Vowden P. New techniques for wound debridement. Int Wound J. 2013;doi: 10.1111/iwj.12045.
75. Alvarez OM, Fernandez-Obregon A, Rogers RS, Bergamo L, Masso J, Black M. Chemical debridement of pressure ulcers: A prospective, randomized, comparative trial of collagenase and papain/urea formulations. Wounds. 2000;12(2):15-25.
76. Burgos A, Gimenez J, Moreno E, Campos J, Ardanaz J, Talaero C, et al. Collagenase ointment application at 24- versus 48-hour intervals in the treatment of pressure ulcers. A randomised multicentre study. Clinical Drug Investigation. 2000;19(6):399-407.
77. Burgos A, Gimenez J, Moreno E, Lamberto E, Utrera M, Urraca EM, et al. Cost, efficacy, efficiency and tolerability of collagenase ointment versus hydrocolloid occlusive dressing in the treatment of pressure ulcers: a comparative, randomised, multicentre study. Clinical Drug Investigation. 2000;19(5):357-65.
78. Lee JK, Ambrus JL. Collagenous therapy for decubitus ulcers. Geriatrics. 1975;30(5):91-8.
79. Parish LC, Collins E. Decubitus ulcers: a comparative study. Cutis. 1979;23(1):106-10.
80. Püllen R, Popp R, Volkers P, F□sgen I. Prospective randomized double-blind study of the wound debriding effects of collagenase and fibrinolysin/deoxyribonuclease in pressure ulcers. Age and Ageing. 2002;31(2):126-30.
81. Sherman RA. Maggot versus conservative debridement therapy for the treatment of pressure ulcers. Wound Repair and Regeneration. 2002;10(4):208-14.
82. Sherman RA, Wyle F, Vulpe M. Maggot therapy for treating pressure ulcers in spinal cord injury patients. The Journal of Spinal Cord Medicine. 1995;18(2):71-4.
83. Wang SY, Wang JN, Lv DC, Diao YP, Zhang Z. Clinical research on the bio-debridement effect of maggot therapy for treatment of chronically infected lesions. Orthopaedic surgery. 2010;2(3):201-6.
84. Muller E, van Leen MWF, Bergemann R. Economic evaluation of collagenase-containing ointment and hydrocolloid dressing in the treatment of pressure ulcers. Pharmacoeconomics. 2001;19(12):1209-16.
85. Barr JE. Principles of wound cleansing. Ostomy.Wound.Manage. 1995;41(7A Suppl):15S-21S.
86. Belgisch Centrum voor Farmacotherapeutische I. Belgisch Centrum voor Farmacotherapeutische Informatie; 2013.
87. Fernandez R, Griffiths R. Water for wound cleansing. Cochrane.Database.Syst.Rev. 2012;2:CD003861.
88. Gerding GA, Browning JS. Oxyquinoline-containing ointment vs. standard therapy for stage I and stage II skin lesions. Dermatology nursing / Dermatology Nurses' Association. 1992;4(5):389-98.
89. Günes UY, Eser I. Effectiveness of a honey dressing for healing pressure ulcers. Journal of Wound, Ostomy and Continence Nursing. 2007;34(2):184-90.
90. Hollisaz MT, Khedmat H, Yari F. A randomized clinical trial comparing hydrocolloid, phenytoin and simple dressings for the treatment of pressure ulcers [ISRCTN33429693]. BMC Dermatology. 2004;4(1):18-26.
91. Joint Formulary C. British national formulary. London: British Medical Association and Royal Pharmaceutical Society; 2011.
92. Joint Formulary C. Britisch National Formulary. London: Pharmeutical press; 2013.
93. Knudsen L, Solvhoj L, Christensen B. The use of a haemodialysate in the treatment of decubital ulcer: A double-blind

randomized clinical study. Current Therapeutic Research - Clinical and Experimental. 1982;32(3):498-504.

94. Shamimi NK, Karimian R, Nasli E, Kamali K, Chaman R, Farhadi M, et al. Topical application of Semelil (ANGIPARSø in treatment of pressure ulcers: a randomized clinical trial. Daru. 2008;16(Supplement 1):54-7.

95. Sipponen A, Jokinen JJ, Sipponen P, Papp A, Sarna S, Lohi J. Beneficial effect of resin salve in treatment of severe pressure ulcers: A prospective, randomized and controlled multicentre trial. British Journal of Dermatology. 2008;158(5):1055-62.

96. Moore ZE, Cowman S, Moore ZEH. Wound cleansing for pressure ulcers. Cochrane Database of Systematic Reviews. 2005(4):CD004983.

97. Zhang QH, Sun ZR, Yue JH, Ren X, Qiu LB, Lv XL, et al. Traditional Chinese medicine for pressure ulcer: A meta-analysis. International wound journal. 2012;doi: 10.1111/j.1742-481X.2012.00969.x.

98. Bellingeri A, Attolini R, Fioretti C, Scalise A, Forma O, Traspedini P, et al. Evaluation of the effectiveness of a centre to cleanse skin lesions. Multicentric open, controlled and randomised study. Minerva Medica. 2004;95:1-9.

99. Burke DT, Ho CHK, Saucier MA, Stewart G. Effects of hydrotherapy on pressure ulcer healing. American Journal of Physical Medicine and Rehabilitation. 1998;77(5):394-8.

100. Griffiths RD, Fernandez RS, Ussia CA. Is tap water a safe alternative to normal saline for wound irrigation in the community setting. Journal of Wound Care. 2001;10(10):407-11.

101. Bao HY. The effect of JiFu FuYuan ointment on patients with bedsores. Journal of Changzhi Medical College. 2006;20:308-9.

102. Chen PY, Sui DS. The effect of ShenJiYuHong ointment on 18 patients with pressure ulcers. Journal of Chinese Medicine. 2008;40:45-7.

103. Jing L. The effect of Fufang Dahuang Ding on patients with bedsores. Journal of External Therapy of Traditional Chinese Medicine. 2005;14:18-9.

104. Li XC, Wang JF. The clinical observation of SanHuangZhangYuYouSha on patients with bedsores. China Medical Herald. 2008;5:159.

105. Li XF, Gong SZ, Lu JE, Zhang WH, Xu HP. Comparison of effects of RuYiZhuHuang ointment and conventional treatment on pressed wound. Liaoning Journal of Traditional Chinese Medicine. 2007;34:1286-7.

106. Li XF, Gong SZ, Lu JE, Zhang WH, Xu HY. The clinical study of RuYi ZhuHuang ointment on patients with III stage of pressure sores. J.Nurs.Training. 2007;22:1646-7.

107. Luo KH, Huang SI, Li JH. The clinical observation of RuYi JinHuang ointment on patients with I and ? stage of pressure ulcers. Journal of Human College of Traditional Chinese Medicine. 1998;18:45-6.

108. Tao XF, Ren YQ. The effect of FuChunSan YiHao ointment on the pressure ulcers. Journal of Traditional Chinese Medicine and Pharmacy. 2008;5:88.

109. Zhang YIWXY, Wang ZHDXD. Study of the basic fibroblast growth factor in decubitus tissue treating with QuFu Shengji ointment. Clin Med China. 2010;26:388-91.

110. Zhao JM. The clinical observation of Shenli ointment on patients with III and IV stage of pressure ulcers. Med Res Edu. 2010;27:65-6.

111. Agren MS, Stromberg HE. Topical treatment of pressure ulcers. A randomized comparative trial of Varidase and zinc oxide. Scandinavian Journal of Plastic and Reconstructive Surgery. 1985;19(1):97-100.

112. Alm A, Hornmark AM, Fall PA, Linder L, Bergstrand B, Ehrnebo M, et al. Care of pressure sores: a controlled study of the use of a hydrocolloid dressing compared with wet saline gauze compresses. Acta Derm Venereol Suppl (Stockh). 1989;149:1-10.

113. Chang KW, Alsagoff S, Ong KT, Sim PH. Pressure ulcers--randomised controlled trial comparing hydrocolloid and saline gauze dressings. The Medical journal of Malaysia. 1998;53(4):428-31.

114. Hirshberg J, Coleman J, Marchant B, Rees RS. TGF-beta3 in the treatment of pressure ulcers: a preliminary report. Advances in skin & wound care. 2001;14:91-5.
115. Kaya AZ, Turani N, Akyuz M. The effectiveness of a hydrogel dressing compared with standard management of pressure ulcers. Journal of Wound Care. 2005;14(1):42-4.
116. Kim YC, Shin JC, Park CI, Oh SH, Choi SM, Kim YS. Efficacy of hydrocolloid occlusive dressing technique in decubitus ulcer treatment: a comparative study. Yonsei Medical Journal. 1996;37(3):181-5.
117. Kraft MR, Lawson LL, Pohlmann B, Reid-Lokos C, Barder L. A comparison of epi-lock and saline dressings in the treatment of pressure ulcers. Decubitus. 1993;6(6):42-8.
118. Kucan JO, Robson MC, Heggers JP. Comparison of silver sulfadiazine, povidone-iodine and physiologic saline in the treatment of chronic pressure ulcers. Journal of the American Geriatrics Society. 1981;29(5):232-5.
119. Kuflik A, Stillo JV, Sanders D, Roland K, Sweeney T, Lemke PM. Petrolatum versus Resurfix ointment in the treatment of pressure ulcers. Ostomy/Wound Management. 2001;47(2):52-6.
120. Landi F, Aloe L, Russo A, Cesari M, Onder G, Bonini S, et al. Topical Treatment of Pressure Ulcers with Nerve Growth Factor: A Randomized Clinical Trial. Annals of Internal Medicine. 2003;139(8):635-42.
121. Ljungberg S. Comparison of dextranomer paste and saline dressings for management of decubital ulcers. Clinical Therapeutics. 1998;20(4):737-43.
122. Matzen S, Peschardt A, Alsbjorn B. A new amorphous hydrocolloid for the treatment of pressure sores: A randomised controlled study. Scandinavian Journal of Plastic and Reconstructive Surgery and Hand Surgery. 1999;33(1):13-5.
123. Moberg S, Hoffman L, Grennert ML, Holst A. A randomized trial of cadexomer iodine in decubitus ulcers. Journal of the American Geriatrics Society. 1983;31(8):462-5.
124. Mustoe TA, Cutler NR, Allman RM, Goode PS, Deuel TF, Prause JA, et al. A phase II study to evaluate recombinant platelet-derived growth factor- BB in the treatment of stage 3 and 4 pressure ulcers. Archives of Surgery. 1994;129(2):213-9.
125. Neill KM, Conforti C, Kedas A, Burris JF. Pressure sore response to a new hydrocolloid dressing. Wounds: A Compendium of Clinical Research & Practice. 1989;1(3):173-85.
126. Oleske DM, Smith XP, White P, Pottage J, Donovan MI. A randomized clinical trial of two dressing methods for the treatment of low-grade pressure ulcers. Journal of Enterostomal Therapy. 1986;13(3):90-8.
127. Payne WG, Ochs DE, Meltzer DD, Hill DP, Mannari RJ, Robson LE, et al. Long-term outcome study of growth factor-treated pressure ulcers. American Journal of Surgery. 2001;181(1):81-6.
128. Payne WG, Posnett J, Alvarez O, Brown-Etris M, Jameson G, Wolcott R, et al. A prospective, randomized clinical trial to assess the cost-effectiveness of a modern foam dressing versus a traditional saline gauze dressing in the treatment of stage II pressure ulcers. Ostomy/Wound Management. 2009;55(2):50-5.
129. Rees RS, Robson MC, Smiell JM, Perry BH. Becaplermin gel in the treatment of pressure ulcers: A phase II randomized, double-blind, placebo-controlled study. Wound Repair and Regeneration. 1999;7(3):141-7.
130. Rhodes RS, Heyneman CA, Culbertson VL, Wilson SE, Phatak HM. Topical phenytoin treatment of stage II decubitus ulcers in the elderly. The Annals of pharmacotherapy. 2001;35(6):675-81.
131. Robson MC, Abdullah A, Burns BF, Phillips LG, Garrison L, Cowan W, et al. Safety and effect of topical recombinant human interleukin-1 beta in the management of pressure sores. Wound Repair and Regeneration. 1994;2(3):177-81.
132. Robson MC, Hill DP, Smith PD, Wang X, Meyer-Siegler K, Ko F, et al. Sequential cytokine therapy for pressure ulcers: clinical and mechanistic response. Annals of Surgery. 2000;231(4):600-11.
133. Robson MC, Phillips LG, Lawrence WT, Bishop JB, Youngerman JS, Hayward PG, et al. The safety and effect of topically applied

recombinant basic fibroblast growth factor on the healing of chronic pressure sores. Annals of Surgery. 1992;216:401-6.

134. Subbanna PK, Margaret Shanti FX, George J, Tharion G, Neelakantan N, Durai S, et al. Topical phenytoin solution for treating pressure ulcers: a prospective, randomized, double-blind clinical trial. Spinal Cord. 2007;45(11):739-43.

135. Thomas S, Banks V, Bale S, Fear-Price M, Hagelstein S, Harding KG, et al. A comparison of two dressings in the management of chronic wounds. Journal of Wound Care. 1997;6(8):383-6.

136. Xakellis GC, Chrischilles EA. Hydrocolloid versus saline-gauze dressings in treating pressure ulcers: a cost-effectiveness analysis. Archives of Physical Medicine and Rehabilitation. 1992;73(5):463-.

137. Yastrub DJ. Relationship between type of treatment and degree of wound healing among institutionalized geriatric patients with stage II pressure ulcers. Care Management Journals. 2004;5(4):213-8.

138. Payne WG, Wright TE, Ochs D, Mannari RJ, Robson MC, Edington H, et al. An exploratory study of dermal replacement therapy in the treatment of stage III pressure ulcers. The Journal of Applied Research. 2004;4(1):12-23.

139. Robson MC, Phillips LG, Thomason A, Altrock BW, Pence PC, Heggers JP, et al. Recombinant human platelet-derived growth factor-BB for the treatment of chronic pressure ulcers. Annals of Plastic Surgery. 1992;29:193-201.

140. Thomas DR, Goode PS, LaMaster K, Tennyson T. Acemannan hydrogel dressing versus saline dressing for pressure ulcers. A randomized, controlled trial. Advances in Wound Care. 1998;11(6):273-6.

141. Van Ort SR, Gerber RM. Topical application of insulin in the treatment of decubitus ulcers: a pilot study. Nursing Research. 1976;25(1):9-12.

142. Chuangsuwanich A, Charnsanti O, Lohsiriwat V, Kangwanpoom C, Thong-In N. The efficacy of silver mesh dressing compared with silver sulfadiazine cream for the treatment of pressure ulcers. Journal of the Medical Association of Thailand = Chotmaihet thangphaet. 2011;94(5):559-65.

143. Amione P, Ricci E, Topo F, Izzo L, Pirovano R, Rega V, et al. Comparison of Allevyn Adhesive and Biatain Adhesive in the management of pressure ulcers. Journal of Wound Care. 2005;14(8):365-70.

144. Bale S, Banks V, Haglestein S, Harding KG. A comparison of two amorphous hydrogels in the debridement of pressure sores. Journal of Wound Care. 1998;7(2):65-8.

145. Bale S, Hagelstein S, Banks V, Harding KG. Costs of dressings in the community. Journal of Wound Care. 1998;7(7):327-30.

146. Banks V, Bale S, Harding K. The use of two dressings for moderatly exuding pressure sores. Journal of Wound Care. 1994;3(3):132-4.

147. Banks V, Bale S, Harding K. Comparing two dressings for exuding pressure sores in community patients. Journal of Wound Care. 1994;3(4):175-8.

148. Belmin J, Meaume S, Rabus MT, Bohbot S. Sequential treatment with calcium alginate dressings and hydrocolloid dressings accelerates pressure ulcer healing in older subjects: A multicenter randomized trial of sequential versus nonsequential treatment with hydrocolloid dressings alone. Journal of the American Geriatrics Society. 2002;50(2):269-74.

149. Bito S, Mizuhara A, Oonishi S, Takeuchi K, Suzuki M, Akiyama K, et al. Randomised controlled trial evaluating the efficacy of wrap therapy for wound healing acceleration in patients with NPUAP stage II and III pressure ulcer. BMJ. 2012;2:1-8.

150. Brod M, McHenry E, Plasse TF, Fedorczyk D, Trout JR. A randomized comparison of poly-hema and hydrocolloid dressings for treatment of pressure sores. Archives of Dermatology. 1990;126(7):969-70.

151. Brown-Etris M, Milne C, Orsted H, Gates JL, Netsch D, Punchello M, et al. A prospective, randomized, multisite clinical evaluation of a transparent absorbent acrylic dressing and a hydrocolloid dressing in the management of Stage II and shallow Stage III pressure ulcers. Advances in skin and wound care. 2008;21(4):169-74.

152. Colin D, Kurring PA, Quinlan D, Yvon C. The clinical investigation of an amorphous hydrogel compared with a dextranomer paste dressing in the management of sloughy pressure sores. Proceedings of the 5th European Conference on Advances in Wound Management. 1996:22-5.

153. Colwell J, Foreman M, Trotter J. A comparison of the efficacy and cost-effectiveness of two methods of managing pressure ulcers. Decubitus. 1993;6:28-36.

154. Darkovich SL, Brown-Etris M, Spencer M. Biofilm hydrogel dressing: a clinical evaluation in the treatment of pressure sores. Ostomy/Wound Management. 1990;29:47-60.

155. Day A, Dombranski S, Farkas C, Foster C, Godin J, Moody M, et al. Managing sacral pressure ulcers with hydrocolloid dressings: results of a controlled, clinical study. Ostomy/Wound Management. 1995;41(2):52-65.

156. Felzani G, Spoletini I, Convento A, Di LB, Rossi P, Miceli M, et al. Effect of lysine hyaluronate on the healing of decubitus ulcers in rehabilitation patients. Advances in Therapy. 2011;28(5):439-45.

157. Graumlich JF, Blough LS, McLaughlin RG, Milbrandt JC, Calderon CL, Agha SA, et al. Healing pressure ulcers with collagen or hydrocolloid: a randomized, controlled trial. Journal of the American Geriatrics Society. 2003;51(2):147-54.

158. Hondé, C, Derks C, Tudor D. Local treatment of pressure sores in the elderly: Amino acid copolymer membrane versus hydrocolloid dressing. Journal of the American Geriatrics Society. 1994;42(11):1180-3.

159. Kerihuel JC. Effect of activated charcoal dressings on healing outcomes of chronic wounds. Journal of Wound Care. 2010;19(5):208-15.

160. Kordestani S, Shahrezaee M, Tahmasebi MN, Hajimahmodi H, Haji GD, Abyaneh MS. A randomised controlled trial on the effectiveness of an advanced wound dressing used in Iran. Journal of Wound Care. 2008;17(7):323-7.

161. Meaume S, Vallet D, Morere MN, Teot L, Morere MN. Evaluation of a silver-releasing hydroalginate dressing in chronic wounds with signs of local infection.[Erratum appears in J Wound Care. 2005 Nov;14(10):479]. Journal of Wound Care. 2005;14(9):411-9.

162. Meaume S, Van De Looverbosch D, Heyman H, Romanelli M, Ciangherotti A, Charpin S. A study to compare a new self-adherent soft silicone dressing with a self-adherent polymer dressing in stage II pressure ulcers. Ostomy/Wound Management. 2003;49(9):44-51.

163. Motta G, Dunham L, Dye T, Mentz J, O'Connell-Gifford E, Smith E. Clinical efficacy and cost-effectiveness of a new synthetic polymer sheet wound dressing. Ostomy/Wound Management. 1999;45(10):41-9.

164. Mulder GD, Altman M, Seeley JE, Tintle T. Prospective randomized study of the efficacy of hydrogel, hydrocolloid, and saline solutionâ€"moistened dressings on the management of pressure ulcers. Wound Repair and Regeneration. 1993;1(4):213-8.

165. Münter KC, Beele H, Russell L, Crespi A, Gr"chenig E, Basse P, et al. Effect of a sustained silver-releasing dressing on ulcers with delayed healing: the CONTOP study. Journal of Wound Care. 2006;15(5):199-206.

166. Nasar MA, Morley R. Cost effectiveness in treating deep pressure sores and ulcers. Practitioner. 1982;226(1364):307-10.

167. Nisi G, Brandi C, Grimaldi L, Calabro M, D'Aniello C. Use of a protease-modulating matrix in the treatment of pressure sores. Chirurgia Italiana. 2005;57(4):465-8.

168. Rhodes B, Daltrey D, Chattwood JG. The treatment of pressure sores in geriatric patients: a trial of sterculia powder. Nursing Times. 1979;75(9):365-8.

169. Routkovsky-Norval C, Meaume S, Goldfarb JM, Le PC, Preauchat A. Randomized comparative study of two hydrocolloid dressings in the treatment of decubitus ulcers. Revue de Geriatrie. 1996;21(3):213-8.

170. Sayag J, Meaume S, Bohbot S. Healing properties of calcium alginate dressings. Journal of Wound Care. 1996;5(8):357-62.

171. Scevola S, Nicoletti G, Brenta F, Isernia P, Maestri M, Faga A. Allogenic platelet gel in the treatment of pressure sores: A pilot study. International wound journal. 2010;7(3):184-90.

172. Seaman S, Herbster S, Muglia J, Murray M, Rick C. Simplifying modern wound management for nonprofessional caregivers. Ostomy/Wound Management. 2000;46(8):18-27.

173. Sebern MD. Pressure ulcer management in home health care: efficacy and cost-effectiveness of moisture vapor permeable dressing. Archives of Physical Medicine and Rehabilitation. 1986;67(10):726-9.

174. Seeley J, Jensen JL, Hutcherson J. A randomized clinical study comparing a hydrocellular dressing to a hydrocolloid dressing in the management of pressure ulcers. Ostomy/Wound Management. 1999;45(6):39-47.

175. Small N, Mulder M, Mackenzie MJ, Nel M. A comparative analysis of pressure sore treatment modalities in community settings. Curationis. 2002;25(1):74-82.

176. Sopata M, Luczak J, Ciupinska M. Effect of bacteriological status on pressure ulcer healing in patients with advanced cancer. Journal of Wound Care. 2002;11(3):107-10.

177. Thomas DR, Diebold MR, Eggemeyer LM. A controlled, randomized, comparative study of a radiant heat bandage on the healing of stage 3-4 pressure ulcers: A pilot study. Journal of American Medical Directors Association. 2005;6(1):46-9.

178. Trial C, Darbas H, Lavigne JP, Sotto A, Simoneau G, Tillet Y, et al. Assessment of the antimicrobial effectiveness of a new silver alginate wound dressing: a RCT. Journal of Wound Care. 2010;19(1):20-6.

179. Wild T, Bruckner M, Payrich M, Schwarz C, Eberlein T, Andriessen A. Eradication of methicillin-resistant Staphylococcus aureus in pressure ulcers comparing a polyhexanide-containing cellulose dressing with polyhexanide swabs in a prospective randomized study. Advances in skin and wound care. 2012;25(1):17-22.

180. Winter A, Hewitt H. Testing a hydrocolloid. Nursing Times. 1990;86(50):59-62.

181. Bale S, Squires D, Varnon T, Walker A, Benbow M, Harding KG. A comparison of two dressings in pressure sore management. Journal of Wound Care. 1997;6(10):463-6.

182. Colin D, Kurring PA, Yvon C. Managing sloughy pressure sores. Journal of Wound Care. 1996;5(10):444-6.

183. Australian Wound Management A. Clinical Practice Guidelines for the Prediction and Prevention of Pressure Ulcers. West Leederville WA: Cambridge Publishing; 2001.

184. Adegoke BO, Badmos KA. Acceleration of pressure ulcer healing in spinal cord injured patients using interrupted direct current. African Journal of Medicine and Medical Sciences. 2001;30(3):195-7.

185. Adunsky A, Ohry A, Group D. Decubitus direct current treatment (DDCT) of pressure ulcers: results of a randomized double-blinded placebo controlled study. Archives of Gerontology and Geriatrics. 2005;41(3):261-9.

186. Ahmad ET. High-voltage pulsed galvanic stimulation: effect of treatment duration on healing of chronic pressure ulcers. Annals of burns and fire disasters. 2008;21(3):124-8.

187. Asbjornsen G, Hernaes B, Molvaer G. The effect of transcutaneous electrical nerve stimulation on pressure sores in geriatric patients. Journal of Clinical and Experimental Gerontology. 1990;12(4):209-14.

188. Baker LL, Rubayi S, Villar F, Demuth SK. Effect of electrical stimulation waveform on healing of ulcers in human beings with spinal cord injury. Wound Repair and Regeneration. 1996;4(1):21-8.

189. Franek A, Kostur R, Polak A, Taradaj J, Szlachta Z, Blaszczak E, et al. Using high-voltage electrical stimulation in the treatment of recalcitrant pressure ulcers: results of a randomized, controlled clinical study. Ostomy/Wound Management. 2012;58(3):30-44.

190. Franek A, Kostur R, Taradaj J, Blaszczak E, Szlachta Z, Dolibog P. Effect of high voltage monophasic stimulation on pressure ulcer healing: results from a randomized controlled trial. Wounds: A Compendium of Clinical Research and Practice. 2011;23(1):15-23.

191. Gentzkow GD, Pollack VP, Kloth LC, Stubbs HA. Improved healing of pressure ulcers using Dermapulse, a new electrical stimulation device. Wounds: A Compendium of Clinical Research and Practice. 1991;3(5):158-70.

192. Griffin JW, Tooms RE, Mendius RA, Clifft JK, Vander Zwaag R, el-Zeky F. Efficacy of high voltage pulsed current for healing of pressure ulcers in patients with spinal cord injury. Physical Therapy. 1991;71(6):433-4.

193. Houghton PE, Campbell KE, Fraser CH, Harris C, Keast DH, Potter PJ, et al. Electrical stimulation therapy increases rate of healing of pressure ulcers in community-dwelling people with spinal cord injury. Archives of Physical Medicine and Rehabilitation. 2010;91(5):669-78.

194. Jercinovic A, Karba R, Vodovnik L, Stefanovska A, Kroselj P, Turk R, et al. Low frequency pulsed current and pressure ulcer healing. IEEE Transactions on Rehabilitation Engineering. 1994;2(4):225-33.

195. Karba R, Benko H, Savrin R, Vodovnik L. Combination of occlusive dressings and electrical stimulation in pressure ulcer treatment. Medical Science Research. 1995;23(10):671-3.

196. Kloth LC, Feedar JA. Acceleration of wound healing with high voltage, monophasic, pulsed current Phys Ther 1989 Aug;69(8):702. Physical Therapy. 1988;68(4):503-8.

197. Wood JM, Evans PE, Schallreuter KU, Jacobson WE, Sufit R, Newman J, et al. A multicenter study on the use of pulsed low-intensity direct current for healing chronic stage II and stage III decubitus ulcers. Archives of Dermatology. 1993;129(8):999-1009.

198. De Laet C, Obyn C, Ramaekers D, Van De Sande S, Neyt M. Hyperbaric Oxygen Therapy: a Rapid Assessment. Health Technology Assessment (HTA). Brussels: Belgian Health Care Knowledge Centre (KCE); 2008. KCE Reports 74C (D/2008/10.273/15)

199. Kranke P, Bennett MH, Martyn-St JM, Schnabel A, Debus SE. Hyperbaric oxygen therapy for chronic wounds. Cochrane Database of Systematic Reviews. 2012;Issue 4:CD004123.

200. Vlayen J, Camberlin C, Ramaekers D. Vacu□mgeassisteerde Wondbehandeling: een Rapid Assessment. . Brussel: Federaal Kenniscentrum voor de Gezondheidszorg(KCE) 2007. KCE reports 61A (D2007/10.273/30)

201. Ubbink DT, Westerbos SJI, Evans D, Land L, Vermeulen H. Topical negative pressure for treating chronic wounds. Cochrane Database of Systematic Reviews. 2008;Issue 3:CD001898.

202. Ford CN, Reinhard ER, Yeh D, Syrek D, De Las Morenas A, Bergman SB, et al. Interim analysis of a prospective, randomized trial of vacuum-assisted closure versus the healthpoint system in the management of pressure ulcers. Annals of Plastic Surgery. 2002;49(1):55-61.

203. Wanner MB, Schwarzl F, Strub B, Zaech GA, Pierer G. Vacuum-assisted wound closure for cheaper and more comfortable healing of pressure sores: a prospective study. Scandinavian Journal of Plastic and Reconstructive Surgery and Hand Surgery. 2003;37(1):28-33.

204. Prindeze NJ, Moffatt LT, Shupp JW. Mechanisms of action for light therapy: a review of molecular interactions. Exp.Biol Med (Maywood.). 2012;237(11):1241-8.

205. Jahangiri NY, abani M, tankhah N, shemian SJ, bari K. A combination of 670 nm and 810 nm diode lasers for wound healing acceleration in diabetic rats. Photomed.Laser Surg. 2010;28(5):621-7.

206. Rodrigo SM, Cunha A, Pozza DH, Blaya DS, Moraes JF, Weber JB, et al. Analysis of the systemic effect of red and infrared laser therapy on wound repair. Photomed.Laser Surg. 2009;27(6):929-35.

207. Dehlin O, Elmst†hl S, Gottrup F. Monochromatic phototherapy in elderly patients: a new way of treating chronic pressure ulcers? Aging clinical and experimental research. 2003;15(3):259-63.

208. Dehlin O, Elmst†hl S, Gottrup F. Monochromatic phototherapy: effective treatment for grade II chronic pressure ulcers in elderly patients. Aging clinical and experimental research. 2007;19(6):478-83.

209. Durovic A, Maric D, Brdareski Z, Jevtic M, Durdevic S. The effects of polarized light therapy in pressure ulcer healing. Vojnosanitetski pregled. 2008;65(12):906-12.
210. Lucas C, Coenen CHM, Haan RJ. The effect of low level laser therapy (LLLT) on stage III decubitus ulcers (pressure sores); A prospective randomised single blind, multicentre pilot study. Lasers in Medical Science. 2000;15:94-100.
211. Lucas C, Gemert MJ, Haan RJ. Efficacy of low-level laser therapy in the management of stage III decubitus ulcers: a prospective, observer-blinded multicentre randomised clinical trial. Lasers in Medical Science. 2003;18:72-7.
212. Nussbaum EL, Biemann I, Mustard B. Comparison of ultrasound/ultraviolet-C and laser for treatment of pressure ulcers in patients with spinal cord injury. Physical Therapy. 1994;74(9):812-23.
213. Schubert V. Effects of phototherapy on pressure ulcer healing in elderly patients after a falling trauma. A prospective, randomized, controlled study. Photodermatology, Photoimmunology and Photomedicine. 2001;17(1):32-8.
214. Shojaei H, Sokhangoei Y, Soroush MR. Low level laser therapy in the treatment of pressure ulcers in spinal cord handicapped veterans living in Tehran. Iranian Journal of Medical Sciences. 2008;33(1):44-8.
215. Taly AB, Sivaraman-Nair KP, Murali T, John A. Efficacy of multiwavelength light therapy in the treatment of pressure ulcers in subjects with disorders of the spinal cord: A randomized double-blind controlled trial. Archives of Physical Medicine and Rehabilitation. 2004;85:1657-61.
216. Wills EE, Anderson TW, Beattie BL, Scott A. A randomized placebo-controlled trial of ultraviolet light in the treatment of superficial pressure sores. Journal of American Geriatrtics Society. 1983;31(3):131-3.
217. McInnes E, Dumville JC, Jammali-Blasi A, Bell-Syer SE. Support surfaces for treating pressure ulcers. Cochrane Database Syst Rev. 2011(12):CD009490.
218. Ubbink DT, Westerbos SJ, Nelson EA, Vermeulen H. A systematic review of topical negative pressure therapy for acute and chronic wounds. British Journal of Surgery. 2008;95(6):685-92.
219. Altman DGB, J.M. Absence of evidence is not evidence of absence. BMJ. 1995;311(7003).
220. van Mierlo-Van den Broek PAHDL, H.E.W. Verkenning Wondbehandeling in Nederland. Nijmegen, Nederland: UMC, St Radboud; 2012.