The management of pressure ulcers in primary and secondary care
A Clinical Practice Guideline

17 December 2004
1st Draft Consultation

This guideline has been developed by the Royal College of Nursing and the National Institute for Clinical Excellence
Guideline. Funding for the Health Economics analysis for this Guideline was received from the National Institute for Clinical Excellence (NICE), and this work was undertaken by the Centre for Health Economic (CHE) at the University of York. The RCN is host to the National Collaborating Centre for Nursing and Supportive Care (NCC-NSC) which receives partnership support from the: Centre for Evidence-Based Nursing; Centre for Statistics in Medicine; Clinical Effectiveness Forum for Allied Health Professionals, College of Health; Health Care Libraries (University of Oxford); Health Economics Research Centre, and UK Cochrane Centre.

This guideline should be read in conjunction with the NICE guideline for risk assessment and prevention of pressure ulcers (beds, mattresses and support surfaces), NICE 2003 and is a further addition to clinical guidelines forming the Wound Care Suite.
Disclaimer

Clinical guidelines have been defined as ‘systematically’ developed statements that are designed to assist clinicians, patients and carers in making decisions about appropriate treatments for specific conditions and aspects of care.

As with all clinical guidelines, recommendations may not be appropriate for use in all circumstances. Decisions to adopt any particular recommendations must be made by the practitioners in the light of:

- Available resources
- Local services, policies and protocols
- The patient’s circumstances and wishes
- Available personnel and support surfaces
- Clinical experience of the practitioner
- Knowledge of more recent research findings

It is important for all healthcare professionals when implementing evidence-based guidance that they understand the local context in which they work and existing quality improvement structures.

Where the term ‘carer’ is used in this Guideline this refers to unpaid carers as opposed to paid carers such as care workers.
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Luton and Dunstable Hospital NHS Trust
Mid Staffordshire General Hospitals NHS Trust
National Nurses Nutrition Group
North Middlesex University Hospital NHS Trust
Northumberland Care Trust
Nottingham City PCT
Nuffield Orthopaedic Centre NHS Trust
Princess Alexandra Hospital NHS Trust
Rotherham Primary Care Trust
Royal Liverpool Children's NHS Trust
Royal National Orthopaedic Hospital NHS Trust
Sheffield Teaching Hospitals NHS Trust
South Birmingham Primary Care Trust
South Devon Healthcare Trust
South Essex Partnership NHS Trust
South West Kent PCT
Surrey & Sussex NHS Trust
Tameside and Glossop Acute Services NHS Trust
The Dudley Group of Hospitals NHS Trust
The Medway NHS Trust
The Royal West Sussex Trust
Trafford Primary Care Trusts
University College London Hospitals NHS Trust
Vale of Aylesbury PCT
West Norfolk PCT
West of Cornwall Primary Care Trust
African & Caribbean Diabetes Association
Help the Aged
Help the Hospices
L’Arche UK
Limbless Association
Marie Curie Cancer Care
National Council for Disabled People, Black, Minority and Ethnic Community (Equalities)
Relatives and Residents Association
Sue Ryder Care
All Wales Senior Nurses Advisory Group (Mental Health)
Association of Surgeons of Great Britain and Ireland
British Association for Parenteral & Enteral Nutrition (BAPEN)
British Association of Dermatologists, The
British Dietetic Association
British Geriatrics Society
British Healthcare Trades Association
British Psychological Society, The
British Society for Antimicrobial Chemotherapy
British Society of Rehabilitation Medicine
Chartered Society of Physiotherapy
College of Occupational Therapists
Community District Nurses Association
Faculty of Public Health
Health Protection Agency

Royal College of Nursing and National Institute for Clinical Excellence
Hospital Infection Society
National Association of Theatre Nurses
Nightingale Care Beds Ltd
Nuffield Hospitals Acute Care
Royal Association of Disability and Rehabilitation
Royal College of General Practitioners
Royal College of General Practitioners Wales
Royal College of Nursing (RCN)
Royal College of Paediatrics and Child Health
Royal College of Physicians of London
Royal College of Surgeons of England
Royal Pharmaceutical Society of Great Britain
Skin Care Campaign
Society of Chiropodists & Podiatrists
Southern Alliance of Tissue Viability Nurses
Spinal Injuries Association
Stoke Mandeville NHS Trust
The National Association of Assistants in Surgical Practice
The Royal Society of Medicine
Tissue Viability Nurses Association
Tissue Viability Nurses Forum (South)
Tissue Viability Society (UK)
Wound Care Society
British National Formulary (BNF)
Department of Health
Healthcare Commission
Medicines and Healthcare Products Regulatory Agency (MHRA)
National Institute for Clinical Excellence
National Patient Safety Agency
National Public Health Service – Wales
NHS Modernisation Agency, The
NHS Quality Improvement Scotland
Scottish Intercollegiate Guidelines Network (SIGN)
Welsh Assembly Government (formerly National Assembly for Wales)

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Abbreviations

Technical terms

ARR  absolute relative risk
ARr  absolute risk reduction
BMI  body mass index
CI   confidence intervals
DH   Department of Health
GDG  Guideline Development Group
GRP  Guideline Review Panel
HTA  health technology assessment
NNT  number needed to treat
OR   odds ratio
QALY quality-adjusted life year
RCT  randomised controlled trial
RR   relative risk (risk ratio)
RD   risk difference
SEM  standard error of the mean
PU   pressure ulcer

Organizations

CHE  Centre for Health Economics, University of York
CRD  Centre for Reviews and Disseminations, University of York
CWG  Cochrane Wounds Group
DH   Department of Health
MHRA Medicines and Healthcare Products Regulatory Agency
NCC-NSC National Collaborating Centre for Nursing and Supportive Care
NICE National Institute for Clinical Excellence
RCN  Royal College of Nursing
UKC  UK Cochrane
### General Glossary

<table>
<thead>
<tr>
<th>Term</th>
<th>Definition</th>
</tr>
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<tbody>
<tr>
<td><strong>Absolute risk reduction</strong></td>
<td>The difference between the observed event rates (proportions of individuals with the outcome of interest) in the 2 groups.</td>
</tr>
<tr>
<td><strong>Bias</strong></td>
<td>Influences on a study that can lead to invalid conclusions about a treatment or intervention. This may result from flaws in the design of a study or in the analysis of results and may result in either an underestimate or an overestimate of the effect. Bias can occur at different stages in the research process, for example in the collection, analysis, interpretation, publication or review of the research.</td>
</tr>
<tr>
<td><strong>Case-control study</strong></td>
<td>A study in which the effects of an exposure in a group of patients (cases) who have a particular condition is compared with the effects of the exposure in a similar group of people who do not have the clinical condition (the latter is called the control group).</td>
</tr>
<tr>
<td><strong>Case report</strong></td>
<td>Detailed report on one patient (case), usually covering the course of that person’s disease and response to treatment.</td>
</tr>
<tr>
<td><strong>Case series</strong></td>
<td>Description of several cases of a given disease or condition, usually covering the course of that disease and response to treatment. There is no comparison (control) group of patients.</td>
</tr>
<tr>
<td><strong>Carer</strong></td>
<td>An individual who provides unpaid care as opposed to paid carers (for example care workers).</td>
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<tr>
<td><strong>Cohort</strong></td>
<td>A group of people sharing some common characteristics (e.g. patients with the same disease or condition), followed up in a research study for a specified period of time.</td>
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<tr>
<td><strong>Clinical effectiveness</strong></td>
<td>The extent to which an intervention (for example a support surface or treatment) produces health benefits (that is more good than harm).</td>
</tr>
</tbody>
</table>
Cochrane Collaboration
An international organisation in which people retrieve, appraise and review available evidence of the effect of interventions in health care. The Cochrane Database of Systematic Reviews contains regularly updated reviews on a variety of issues. The Cochrane library contains the Central Register of Controlled Trials (CENTRAL) and a number of other databases which are regularly updated and is available as CD-Rom or on the internet (www.cochranelibrary.com).

Cohort study
An observations study that takes a group (cohort) of patients and follows their progress over time in order to measure outcomes such as disease or mortality rates and makes comparisons according to the treatments or interventions that patients receive. Thus within the study group, subgroups of patients are identified and these groups are compared to with respect to outcome for example comparing mortality between groups that did or did not receive treatment. Cohorts can be assembled in the present and follow into the future (a concurrent or prospective cohort study) or identified from past record and follow forward from that time up to the present (a historical or retrospective cohort study). Patients are not randomly allocated to subgroups; these may be quite different in their characteristics and therefore adjustments must be made when analysing the results to ensure that the comparison between groups is as fair as possible.

Co-interventions
Interventions/treatments etc other than the treatment under study that are applied differently to the treatment and control groups.

Co-morbidity
Co-existence of a disease or diseases in a study population in addition to the condition that is the subject of study.

Confidence intervals
A way of expressing certainty about the findings from a study or group of studies using statistical techniques. A confidence interval describes a range of possible effects (of a treatment or intervention) that is consistent with the results of a study or group of studies. A wide confidence interval indicates a lack of certainty or precision about the true size of the clinical effect and is seen in studies with too few patients. Where they are narrow these indicates precision and are found in studies with larger patient samples. It is usual to interpret a
‘95% CI’ as the range of effects within which we are 95% confident that the true effect lies.

Cost–benefit analysis  A type of economic evaluation where both costs and benefits of healthcare treatments are measured in the same monetary units. If benefits exceed cost, the evaluation would recommend the treatment.

Cost effectiveness  A type of economic evaluation that assesses the additional costs and benefits of doing something. In cost-effectiveness analysis, the cost and benefit of different treatments are compared. When a new treatment is compared with the current care, its additional costs divided by its additional benefit is called the cost-effectiveness ratio. Benefits are measured in natural units, for example cost per additional pressure ulcer healed or prevented.

Cost–utility analysis  A special form of cost-effectiveness analysis where benefit is measured in quality adjusted life years. A treatment is assessed in terms of its ability to extend or improve the quality of life.

Cost impact  The total cost to the person, the NHS or to society.

Discounting  The process of converting future pounds and future health outcomes to their present value.

Debridement  The removal of dead (devitalised) tissue, cell debris or foreign material from the wound.

Dead Tissue  Dead tissue can present in a variety of forms. Dead (necrotic) tissue varies in appearance according to moisture content. When dry it presents as black eschar (hard leather like material). If moisture content rises the eschar becomes brown, then yellow before breaking down to slough (yellow/grey fibrous tissue with a gelatinous surface attached to the wound bed).

Double blind study  A study in which neither the subject (patient) nor the observer (investigator or clinician) is aware of which treatment or intervention the subject is receiving. The purpose of blinding is to protect against bias.
<table>
<thead>
<tr>
<th>Economic evaluation</th>
<th>Comparative analysis of alternative courses of action in terms of both their costs and consequences.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Effectiveness</td>
<td>The extent to which interventions achieve health improvements in real practice settings.</td>
</tr>
<tr>
<td>Efficacy</td>
<td>The extent to which medical interventions achieve health improvements under ideal circumstances.</td>
</tr>
<tr>
<td>Epidemiological study</td>
<td>A study which looks at how a disease or clinical condition is distributed across geographical areas</td>
</tr>
<tr>
<td>Evidence based</td>
<td>The process of systematically finding, appraising and using research findings as the basis for clinical decisions.</td>
</tr>
<tr>
<td>Evidence-based clinical practice</td>
<td>Evidence-based clinical practice involves making decisions about the care of individual patients based on the best available research evidence rather than on personal opinion or common practice (which may not always be evidence based). Evidence-based clinical practice involves integrating individual clinical expertise and patient preferences with the best available evidence from research.</td>
</tr>
<tr>
<td>Evidence table</td>
<td>A table with information extracted from research papers usually summarising the results of a collection of studies. Together this information represents the supporting evidence for a recommendation in a guideline.</td>
</tr>
<tr>
<td>Experimental study</td>
<td>A research study designed to test whether a treatment or intervention has an effect on the course or outcome of a condition or disease, where the conditions of testing are to some extent under the control of the investigator. Controlled trials and randomised controlled trials are examples of experimental studies.</td>
</tr>
<tr>
<td>Extrinsic</td>
<td>Factors which are external to the individual.</td>
</tr>
<tr>
<td>Follow-up</td>
<td>Observation over a period of time of an individual, group or population whose relevant characteristics have been assessed in order to observe changes in health status or health-related variables.</td>
</tr>
</tbody>
</table>
Gold standard
A method, procedure or measurement that is widely accepted as being the best available.

Health professional
Includes nurses, allied health professionals and doctors.

Health economics
A field of economics that examines the benefits of healthcare interventions (for example medicines) compared with their financial costs.

Health technology assessment
The process by which evidence on the clinical effectiveness and the costs and benefits of using a technology in clinical practice is systematically evaluated.

Heterogeneity
Or lack of homogeneity. The term is used in meta-analysis and systematic review when the results or estimates of effects of treatment from separate studies seem to be very different, in terms of size of treatment effects, adverse treatment effects. Such results may occur as a result of differences between studies in terms of the patient population, outcome measures, definitions of variables or duration of follow-up.

Homogeneity
This means that the results of the studies in a systematic review or meta-analysis are similar and there is no evidence of heterogeneity. Results are usually regarded as homogenous when the differences between studies are those which can reasonably be expected between studies.

Incidence
The number of new cases of illness commencing, or of persons falling ill during a specified time period in a given population.

Intervention
Healthcare action intended to benefit the patient, for example drug treatment, dressings, physiological therapy.

Intrinsic
Factors which present within the individual.

Logistic regression model
A data analysis technique to derive an equation to predict the probability of an event given one or more predictor variables. This model assumes that the natural logarithm of
the odds for the event (the logit) is a linear sum of weighted values of the predictor variable. The weights are derived from data using the method of maximum likelihood.

**Meta-analysis**
A statistical method of summarising the results from a group of similar studies.

**Number needed to treat**
The number of patients who need to be treated to prevent one event.

**Odds ratio**
Odds in favour of being exposed in subjects with the target disorder divided by the odds in favour of being exposed in control subjects (without the target disorder).

**Predictive validity**
A risk assessment tool would have high predictive validity if the predictions it makes of pressure ulcer development in a sample became true (i.e. it has both high sensitivity and specificity).

**Prevalence**
The proportion of persons with a particular disease within a given population at a given time.

**Quality adjusted life expectancy**
Life expectancy using quality adjusted life years rather than nominal life years

**Quality adjusted life years**
A measure of health outcome which assigns to each time period a weight, ranging from 0–1, corresponding to the health-related quality of life during that period, where a weight of 1 corresponds to optimal health, and a weight of 0 corresponds to a health state judged as equivalent to death; these are then aggregated across time periods.

**Randomised controlled trial**
A clinical trial in which the treatments are randomly assigned to subjects. The random allocation eliminates bias in the assignment of treatment to patients and establishes the basis for the statistical analysis.

**Relative risk**
An estimate of the magnitude of an association between exposure and disease which also indicates the likelihood of developing the disease among persons who are exposed relative to those who are not. It is defined as the ratio of
incidence of disease in the exposed group divided by the corresponding incidence in the non-exposed group.

**Retrospective cohort study** A study in which a defined group of persons with an exposure and an appropriate comparison group who are not exposed are identified retrospectively and followed from the time of exposure to the present, and in which the incidence (or mortality) rates for the exposed and unexposed are assessed.

**Sensitivity** In diagnostic testing, this refers to the chance of having a positive test result given that you have the disease or condition. 100% sensitivity means that all those with the disease will test positive, but this is not the same the other way round. A patient could have a positive test result but not have the disease or condition – this is called a false positive. The sensitivity of a test is also related to its negative predictive value (true negatives) – a test with a sensitivity of 100% means that all those who get a negative test result do not have the disease. To fully judge the accuracy of a test, its specificity must also be considered.

**Specificity** In diagnostic testing, this refers to the chance of having a negative test result given that you do not have the disease. 100% specificity means that those without the disease will test negative, but this is not the same the other way round. A patient could have a negative test result but still have the disease or condition – this is called a false negative. The specificity of a test is also related to its positive predictive value (true positives) – a test with a specificity of 100% means that all those who get a positive test result definitely have the disease or condition. To fully judge the accuracy of a test, its sensitivity must also be considered.

**Statistical power** The ability of a study to demonstrate an association or causal relationship between two variables, given that an association exists. For example, 80% power in a clinical trial means that the study has 80% chance of ending up with a p value of less than 5% in statistical test (statistically significant).

**Systematic review** A way of finding, assessing and using evidence from studies (usually RCTs) to obtain a reliable overview.
User: Any one using the guideline.

Validity

The extent to which a variable or intervention measures what it is supposed to measure or accomplish.

*Internal validity:* of a study refers to the integrity of the design

*External validity:* of a study refers to the appropriateness by which its results can be applied to non-study patients or populations.

Wound bed preparation

Management of the wound to promote endogenous healing or to facilitate the effectiveness of therapeutic interventions.

(partially based on *Clinical epidemiology glossary* by the Evidence Based Medicine Working Group, www.ed.ualberta.ca/ebm; *Information for national collaborating centres and guideline development groups, (NICE 2001)* and glossary from the Patient Involvement Unit at NICE.)
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1 EXECUTIVE SUMMARY

The Royal College of Nursing (RCN) and National Institute for Clinical Excellence ('NICE' or 'the Institute') collaborated to develop a clinical guideline on the Management of Pressure Ulcers in Primary and Secondary care. Identification of the topic emerged from a consultation process with RCN members and referral of the topic by the Department of Health and Welsh Assembly Government. This document describes the methods used for developing the guidelines and presents the resulting recommendations. It is the source document for the NICE (abbreviated version for health professionals) and Information for the Public (patient and carers) versions of the guidelines, which will be published by NICE. The Guideline was produced by a multidisciplinary Guideline Development Group and the development process was wholly undertaken by the RCN.

The main areas examined by the Guideline are:

- Holistic assessment for risk of delayed healing or complications of having a pressure ulcer
- The ulcer assessment
- Pressure relieving support surfaces for the treatment of pressure ulcers
- Mobility positioning and re-positioning for the treatment of pressure ulcers
- Dressings and topical agents for the treatment of pressure ulcers
- Debridement for the treatment of pressure ulcers
- Nutritional support
- Surgery for the treatment of pressure ulcers
- Therapeutic ultrasound for the treatment of pressure ulcers
- Electrotherapy and Electromagnetic therapy for the treatment of pressure ulcers
- Topical negative pressure for the treatment of pressure ulcers

Recommendations for good practice based on the best available evidence of clinical and cost effectiveness are presented. Literature searching details including cut-off dates are reported in the methods section for each topic area. Update searches were performed for each area not less than six months prior to submission of the first consultation draft. Recommendations contained in this document are those considered to be central to the management of pressure ulcers. This is a guide to that management not a text book of care.

Healthcare professionals should use their clinical judgement and consult with patients when applying the recommendations which aim at reducing the negative personal, physical, social and financial impact of pressure ulcers.

On completion of the process the versions for health professionals (NICE version) and for patients and carers (Information for the Public) will be published by NICE.
2 PRINCIPLES OF PRACTICE AND SUMMARY OF GUIDELINE RECOMMENDATIONS

2.1 Principles of practice

The principles outlined below, describe the ideal context in which to implement the recommendations contained in this Guideline. They reflect original research and development work previously produced by the RCN, and enable clinicians using evidence based guidance to contextualise and understand the importance of preparation and planning prior to utilising this evidence-based tool.

2.1 Person-centred care

- Patients and carers should be made aware of the Guideline and its recommendations and be referred to the version ‘Information for the Public.’
- Patients and carers should be involved in shared decision-making about the management of pressure ulcers.
- Health professionals are advised to respect and incorporate the knowledge and experience of people who have had, or have a pressure ulcer.
- Patients and carers should be informed about any potential risks and or complications of having a pressure ulcer.

2.2 A collaborative interdisciplinary approach to care

- All members of the inter-disciplinary team should be aware of the Guidelines and all care should be documented in the patient's healthcare records.
- The approach to care should be an interdisciplinary approach involving all necessary in the management of pressure ulcers.

2.3 Organisational issues

- There should be an integrated approach to the management of pressure ulcers with a clear strategy and policy supported by management.
- Care should be delivered in a context of continuous quality improvement where improvements to care following guideline implementation are the subject of regular feedback and audit.
- Commitment to and availability of education and training are needed to ensure that all staff, regardless of profession, are given the opportunity to update their knowledge and are able to implement the guideline recommendations.
The healthcare team should have undergone appropriate training and have demonstrated competence in pressure ulcer management.

- Staffing levels and skill mix should reflect the needs of patients and is paramount to providing high quality services for individuals with pressure ulcers.
- Priority should be given to the provision and allocation of resources in the management of patients with a pressure ulcer/s.

2.4 Summary of Guideline recommendations

**Key recommendations**

Patients with identified grade I pressure ulcers are at a significant risk of developing more severe ulcers and should receive interventions to prevent deterioration. [B]

The most benefit for patients with pressure ulcers is likely to be achieved by adopting a multi-interventional inter-disciplinary approach which includes: [B]

- Local wound management using modern or advanced wound dressings and other technologies
- Pressure relieving support surfaces such as beds, mattresses, overlays or cushions
- Treatment of concurrent conditions which may delay healing
  - And
- Repositioning of the individual [D]

All pressure ulcers should be documented as a clinical incident and the circumstances thoroughly investigated. [GPP]

**Holistic assessment**

Patients with pressure ulcers should receive an initial and on-going holistic assessment. Both intrinsic and extrinsic factors have been identified as important factors for assessment. This assessment should include: [D]

- Health status
  - acute, chronic illness and terminal illness
  - co-morbidity
- Mobility status
- Posture (pelvic obliquity and posterior pelvic tilt)
- Sensory impairment
- Level of consciousness
- Systemic signs of infection
- Nutritional status
- Previous pressure damage
• Pain status
• Psychological factors
• Social factors
• Continence status
• Medication
• Cognition
• Tissue perfusion

Assessment of mobility should include all aspects of independent movement including walking, ability to reposition (e.g. in bed or chair) or transfer (e.g. from bed to chair). [D]

Presence of any sensory impairment in an individual with a pressure ulcer should be recorded. [GPP]

Level and duration of impaired consciousness should be recorded. [GPP]

Presence of acute, chronic or terminal illness and its potential impact on ulcer healing should be recorded [GPP]

Previous pressure damage (site/location, stage or grade of previous ulcer and previous interventions) should be recorded. [D]

Pain assessment should include: whether the individual is experiencing pain; the causes of pain; level of pain (using an appropriate tool); location and management interventions. [D]

In the presence of systemic and clinical signs of infection in the patient with a pressure ulcer, systemic anti-microbial therapy should be considered. [GPP]

Psychological assessment should include concordance and abilities of the individual to self-care (mood, motivation and aptitude) [D]

Assessment of social factors should include suitable home environment, level of supportive provision and the involvement of local support services. [D]

Continence assessment should include whether the individual is continent of urine, faeces and continence interventions which may affect ulcer healing and impair the function of pressure relieving support surfaces. (e.g., pads or bedding). [GPP]
Holistic assessment is the responsibility of the inter-disciplinary team and should be carried out by registered health professionals who have undergone appropriate training and have demonstrated competence. [D]

Ulcer Assessment

Patients with pressure ulcers should receive an initial and on-going pressure ulcer assessment. Ulcer assessment should include: [D]
- Cause of ulcer
- Site/location
- Dimensions of ulcer
- Stage or grade
- Exudate amount and type
- Local signs of Infection
- Pain
- Wound appearance
- Surrounding skin
- Undermining/tracking (sinus or fistula)
- Odour

This should be supported by photography (calibrated with a ruler) and tracings.

Record the pressure ulcer grade using the European Pressure Ulcer Advisory Panel Classification System (page 32). [D]

Measure the dimensions of the pressure ulcer, recording the longest length / longest width as an estimate of surface area (use of tracings); the deepest part of the wound should also measured [D]

Initial and on-going ulcer assessment is the responsibility of the inter-disciplinary team and should be carried out by registered health professionals that have undergone appropriate training and have demonstrated competence. [D]

Reassessment of the ulcer should be performed at least weekly but may be required more frequently, depending on the condition of the wound and the result of holistic assessment of the patient. [D]

Mobility and positioning

Mobilising, positioning and repositioning interventions should be considered for all individuals with pressure ulcers (including those in beds, chairs and wheelchairs). [D]

All patients with pressure ulcers should actively mobilise, change their position or be re-positioned frequently. [D]
Avoid positioning individuals directly on pressure ulcers or bony prominences (commonly the sites of pressure ulcer development). [D]

Mobilising, positioning and re-positioning interventions should be determined by:

- General health status
- Location of ulcer
- General skin assessment
- Acceptability (including comfort) to the patient
- Needs of the carer

Frequency of re-positioning should be determined by the patient’s individual needs and recorded (e.g. a turning chart.) [D]

Passive movements should be considered for patients with pressure ulcers who have compromised mobility [D]

**Pressure relieving support surfaces**

Patients with pressure ulcers should have access to appropriate pressure relieving support surfaces (e.g. mattresses and cushions) 24 hours a day and this applies to all support surfaces. [D]

Decisions about choice of pressure relieving support surfaces for patients with pressure ulcers should be made by registered health professionals that have undergone appropriate training and have demonstrated competence. [D]

Initial choice and subsequent decisions, following re-assessments, related to the provision of pressure relieving support surfaces for patients with pressure ulcers should be based on: [D]

- Ulcer assessment (severity)
- Level of risk: from holistic assessment
- Location and cause of the pressure ulcer
- General skin assessment
- General health status
- Acceptability and comfort for the patient
- Lifestyle of the patient
- Ability of the patient to reposition themselves
- Availability of carer/health professional to reposition the patient

There is no conclusive research evidence that any one pressure relieving support technology is superior to another. However professional consensus recommends that:
1. All individuals assessed as having a Grade 1-2 pressure ulcer should, as a minimum provision, be placed on a high specification foam mattress with pressure-reducing properties combined with very close observation of skin changes and a documented positioning and repositioning regime. [D]

   - Consider AP (replacement or overlay) or sophisticated CLP system (e.g. low air loss, air fluidized, viscous fluid) if there is any perceived or actual deterioration of affected areas or further pressure ulcer development. [D]

2. All individuals assessed as having Grade 3-4 pressure ulcer (including intact eschar where depth - and therefore grade - cannot be assessed) should, as a minimum provision be placed on an alternating pressure mattress (replacement or overlay) or sophisticated continuous low pressure system (e.g. low air loss, air fluidised, viscous fluid). [D]

3. Alternating pressure equipment should, be allocated according to a patient's weight not level of risk or grade of ulcer. Patients within the weight range of alternating pressure overlays should be supplied AP overlays not replacement systems. Replacement systems should be allocated to patients who exceed the weight limit of the overlay used. (N.B. In order to ensure maximum effect the inflated cells of the overlay must support the body weight of the patient in all bed positions (during use of backrest, knee break, etc) and all patient positions (sitting up, side lying, etc)) [D]

GDG Commentary
When selecting pressure relieving devices for young children consider the following factors:
1. Ensure that the mattress does not elevate the child to an unsafe height in relation to cot sides on the bed.
2. Ensure that the child is within the recommended weight range for the mattress
3. Alternating pressure
   a. Minimum weight limit of equipment
   b. Cell size of mattress (small children can sink into gaps created by deflated cells causing discomfort and reducing efficacy)
   c. Position of pressure sensors within the mattress in relation to the child (small children positioned at the top of the mattress may not register as the weight sensor is positioned in the middle of the mattress, thus producing inappropriate cell calibration
d. Many alternating pressure mattresses have a permanently inflated head end which may place the occiput at risk in young children

Dressings and topical agents
Decisions about choice of dressing or topical agent for those with pressure ulcers should be made by registered health professionals that have undergone appropriate training and have demonstrated competence. [D]

Choice of dressings or topical agents for the treatment of pressure ulcers should be based on: [D]
- Ulcer assessment (condition of wound)
- General skin assessment
- Treatment objective
- Dressing characteristics
- Previous positive effect of particular dressing
- Manufacture’s indications for use and contra indications
- Risk of adverse events
- Patient preference (lifestyle, abilities and comfort)

There is no conclusive research evidence to guide clinicians decision making about which dressings are most effective in pressure ulcer management. However professional consensus recommends that:

Create the optimum wound healing environment by using advanced dressings (e.g. hydrocolloids, hydrogels, foams, films, alginates, soft silicones) in preference to basic dressing types (e.g. gauze, paraffin gauze and simple dressing pads). [D]

**Debridement**

Clinicians should recognise the positive potential benefit of debridement in the management of pressure ulcers. Decisions about the method of debridement should be based on: [D]
- Ulcer assessment (condition of wound)
- General skin assessment
- Previous positive effect of debridement techniques
- Manufacture’s indications for use and contra indications
- Risk of adverse events
- Patient preference (lifestyle, abilities and comfort)
- Characteristic of dressing/technique
- Treatment objective

Decisions about debridement methods for patients with pressure ulcers should be made by registered health professionals that have undergone appropriate training and have demonstrated competence. [D]
The link between correcting this deficiency and its causal relationship with pressure ulcer healing has not been clearly established.
3 BACKGROUND TO THE CURRENT GUIDELINES

Background to commissioning of guidelines

The National Institute for Clinical Excellence ('NICE' or 'the Institute') worked collaboratively with the Royal College of Nursing–Quality Improvement Programme to develop this Clinical Guideline on the management of pressure ulcer in primary and secondary care for use in the NHS in England and Wales. This follows referral of the topic by the Department of Health and the Welsh Assembly Government and the identification of pressure ulcer treatment as a priority topic for nurses by RCN members. The Royal College of Nursing Institute through its Quality Improvement Programme has a long-standing and well-respected national guideline development and implementation work. It has established strong links with key organisations in the field of evidence-based information nationally (SIGN) and internationally (GIN and JBI). The guideline will provide recommendations for good practice based on the best available evidence to the Guideline Development Group of clinical and cost effectiveness. This guideline follows on from the recently published NICE guideline ‘Risk Assessment and Prevention of Pressure Ulcers’ (NICE 2001) and a guideline on the use of Pressure Relieving Support surfaces (beds, mattresses and overlays for the prevention of pressure ulcers in primary and secondary care completed in October 2003. It is anticipated that these inter-related topics will provide a compilation of NICE guidance on pressure ulcer care and will form part of the Wound Care Suit of related guidance.

The Institute’s clinical guidelines will support the implementation of National Service Frameworks (NSFs) in those aspects of care where a Framework has been published. The statements in each NSF reflect the evidence that was used at the time the Framework was prepared. The clinical guidelines and technology appraisals published by the Institute after an NSF has been issued will have the effect of updating the Framework.

Clinical guidelines have been defined as ‘systematically’ developed statements that assist clinicians, patients and carers in making decisions about appropriate treatments for specific conditions and aspects of care.

3.1 Clinical need for the guideline

The presence of a pressure ulcer creates a number of significant difficulties; psychologically, physically and clinically to patients, carers and their families. Clinicians, working in a variety of clinical and non-clinical settings including primary care and acute trusts also face challenges when providing holistic, person-centred services for the assessment and treatment of pressure ulcers. These challenges
include clinical decisions regarding methods of assessment and which treatments should be used for individuals with an existing pressure ulcer.

Pressure ulcers are more likely to occur in those who are seriously ill, neurologically compromised, i.e. individuals with spinal cord injuries, have impaired mobility (Allman, 1997; Berlowitz & Wilking, 1990; Berlowitz et al 1997; Bianchetti et al, 1993) or who are immobile (including those wearing a prostheses, body brace or plaster cast), suffer from impaired nutrition (Ek et al, 1990; 1991; Casey, 1997; Banks, 1998; Casey, 1998a; b), obesity (Gallagher, 1997), poor posture or use equipment such as seating or beds which do not provide appropriate pressure relief. Pressure ulcers have been found to affect sub-groups in society including those with spinal cord injury (Krause, 1997; Elliot, 1999; Vesmarovich et al, 1999; Kirsch, 2001;), the elderly (Heffey & Radcliffe, 1990; Waltman et al 1991; Krainski, 1992; Orlando, 1998; Pase & Hoffman, 1998; Spoelhof, 2000; Thomas, 2001; Ronda & Falce, 2002;) and pregnant mothers (Prior, 2002). Pressure ulcers have been associated with increased incidence of infection including osteomyelitis (Darouiche et al, 1994).

Research indicates that pressure ulcers represent a major burden of sickness and reduced quality of life for patients, their carers (Hagelstein & Banks, 1995; Franks et al, 1999; Franks et al, 2002) and their families (Benbow, 1996; Elliott et al, 1999).

Often patients require prolonged and frequent contact with the health care system; suffer much pain, (Emflorgo, 1999; Freeman, 2001; Flock, 2003; Healy, 2003; Manfredi et al, 2003) discomfort and inconvenience (Franks et al, 1999).

The presence of pressure ulcers has been associated with a 2–4-fold increase in risk of death in older people in intensive care units (Thomas et al, 1996; Clough, 1994; Bo, et al, 2003).

Estimates on pressure ulcer incidence and prevalence, from hospital-based studies vary widely according to the definition and grade of ulcer, the patient population and care setting. Based on data that are available, new pressure ulcers are estimated to occur in 4–10% of patients admitted to acute hospitals in the United Kingdom (UK) (Clark and Watts, 1994), the precise rates depending on case mix. In the community, new pressure ulcers affect an unknown proportion of people as reliable data is not available. The financial costs to the NHS are considered to be substantial (Bennett et al, 2004). In 1993, the estimated cost of preventing and treating pressure ulcers in a 600-bed general hospital was between £600,000 and £3 million a year (Touché Ross, 1993). The cost of treating a grade IV pressure ulcer was calculated in 1999 to be £40,000 a year (Collier, 1999). More recent cost data suggest that treating ulcers varies from £ 1,064 for a grade I ulcer to £10,551 for a grade IV with total costs in the UK estimated as being £1.4–£2.1 billion annually equivalent to 4% of the total NHS expenditure (Bennett et al, 2004).
3.2 What are pressure ulcers?

Pressure ulcers (also commonly referred to as bed ulcers, pressure damage, pressure injuries and decubitus ulcers) are areas of localised damage to the skin, which can extend to underlying structures such as muscle and bone (Allman, 1995; 1997). Damage is believed to be caused by a combination of factors including pressure, shear forces, friction and moisture (Allman, 1997). Pressure ulcers can develop in any area of the body (Rycroft-Malone & McInnes, 2000). In adults damage usually occurs over bony prominences, such as the sacrum, whilst presentation in infants and children is more likely to occur on, for example, the occipital area or ears (Willock et al, 1999; Murdock, 2002; Jones et al, 2001).

Definitions and Classifications

Definition and classification of pressure ulcers were agreed with the Guideline Development Group at the 2nd group meeting and will serve to update definitions and classifications used in related published NICE and RCN guidance (Pressure ulcer prevention: Pressure ulcer risk assessment and prevention, including the use of pressure-relieving support surfaces (beds, mattresses and overlays) for the prevention of pressure ulcers in primary and secondary care, NICE, 2003) available at www.nice.nhs.org.uk and www.rcn.org.uk.

A pressure ulcer is defined as:

an area of localised damage to the skin and underlying tissue caused by pressure, shear, friction and or a combination of these.


Classification of pressure ulcer severity

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>non-blanchable erythema of intact skin. Discolouration of the skin, warmth, oedema, induration or hardness may also be used as indicators, particularly on individuals with darker skin.</td>
</tr>
<tr>
<td>2</td>
<td>partial thickness skin loss involving epidermis, dermis, or both. The ulcer is superficial and presents clinically as an abrasion or blister.</td>
</tr>
<tr>
<td>3</td>
<td>full thickness skin loss involving damage to or necrosis of subcutaneous tissue that may extend down to, but not through underlying fascia.</td>
</tr>
<tr>
<td>4</td>
<td>extensive destruction, tissue necrosis, or damage to muscle, bone, or supporting structures with or without full thickness skin loss.</td>
</tr>
</tbody>
</table>


† A range of classification systems are used through the literature the one described above is generally accepted and has been published in previous NICE guidance.
3.3 Groups at risk

- Those who are seriously ill, neurologically compromised, i.e. individuals with spinal cord injuries, have impaired mobility or who are immobile (including those wearing a prostheses, body brace or plaster cast), suffer from impaired nutrition, obesity, poor posture or use equipment such as seating or beds which do not provide appropriate pressure relief.
- Sub-groups in society including those with spinal cord injury, the elderly and those pregnant are also reported to be at risk.

3.4 Interventions under consideration

The guideline will consider interventions such as:

- pressure-relieving support surfaces and supports, including specialised seating and postural support, dressings, removal of devitalised or contaminated tissue (debridement), surgery, nutritional support, electrotherapy, therapeutic ultrasound, low-level laser therapy, suction to drain excess fluid (topical negative pressure) and topical antimicrobials.

4 AIMS OF THE GUIDELINE

- To evaluate and summarize the clinical and cost effectiveness evidence for the management of pressure ulcers in primary and secondary care.
- To highlight gaps in the research evidence;
- To formulate evidence-based and where possible, cost-effective clinical practice recommendations for the management of pressure ulcers based on the best evidence available to the GDG (Guideline Development Group).

4.1 Who the guideline is for

This Guideline is of relevance to health professionals who have direct contact with and make decisions concerning the treatment of patients with pressure ulcers. It will also benefit individuals with pressure ulcers as well those who are carers for people with pressure ulcers.
4.2 Groups covered by the guideline

The guideline recommendations will apply to all patient groups (adults, older people, infants, children and young people) in primary and secondary care.

4.3 Groups not covered

†There are no restrictions.

4.4 Healthcare setting

This guideline will make recommendations for care given by health professionals who have direct contact with and make decisions concerning treatment of patients with pressure ulcers (including those with multiple pathologies and those suffering from chronic and acute disease and terminal illness) in primary and secondary care, including specialist units. Recommendations will apply equally across the primary and secondary care interface. The Guideline will also help to guide, inform and educate patients and carers on pressure ulcer treatments by increasing awareness of strategies to both assess and treat individuals with pressure ulcers and prevent re-occurrence.

This is an NHS guideline. Although it will address the interface with other services, such as those provided by social services, the independent sector, secure settings and the voluntary sector, it will not include services exclusive to these sectors.

4.5 Interventions covered

This Guideline will make clinical and cost-effective recommendations on pressure ulcer treatment, based on the best evidence available to the Guideline Development Group. The recommendations will cover treatments such as:

- pressure-relieving support surfaces and supports, including specialised seating and postural support
- dressings
- removal of devitalised or contaminated tissue (debridement)
- surgery
- nutritional support
- electrotherapy
- therapeutic ultrasound
- low-level laser therapy

†Whilst there are no restriction in terms of inclusion/exclusion criteria it is clear that the research evidence in some areas and for some groups, e.g. infants, children and pregnant women is very limited.
suction to drain excess fluid (topical negative pressure)

- topical antimicrobials.

### 4.6 Interventions not covered

The Guideline will be relevant to, but will not cover, other aspects of pressure ulcer-risk assessment and prevention (such as identifying patients at risk, the use of risk-assessment scales, risk factors, skin inspection and staff education and training). Recommendations relating to these areas are included in other guidance produced by the Institute (see Section 6). This Guideline should be used in conjunction with NICE guidance on related topics.

### Wound healing

The process by which tissue repair takes place is termed wound healing and is comprised of a continuous sequence of inflammation and repair, in which epithelial, endothelial, inflammatory cells, platelets and fibroblasts briefly come together outside their normal domains, interact to restore a semblance of their usual discipline and having done so resume their normal function.

The process of wound repair differs little from one kind of tissue to another and is to some extent independent of the form of injury. Although the different elements of the wound healing process occur in a continuous, integrated manner, the overall process can be divided into three overlapping phases.

### STAGES OF WOUND HEALING

![Fig. 1 Stages of wound healing](image)

Fig. 1 Stages of wound healing. Wound healing can be arbitrarily divided into three phases: inflammation, proliferation and maturation

- Inflammatory
- Proliferate
- Maturation and Remodelling
Some wounds will heal with routine wound care for example wounds with even edges that come together spontaneously (minor cuts) or can be brought together. Wounds with rough edges and tissue deficit (a crater) may take longer to heal. When there is a crater and the edges of a wound are not brought together (left open intentionally), bumpy granulation tissue grows from the exposed tissue. The granulation tissue is eventually covered by skin that grows over the wound from the cut edges to the center. When healing is complete, the granulation tissue develops into tough scar tissue. Wounds heal in three stages.

**Inflammatory Stage**
This stage occurs during the first few days. The wounded area attempts to restore its normal state (homeostasis) by constricting blood vessels to control bleeding. Platelets and thromboplastin make a clot. Inflammation (redness, heat, swelling) also occurs and is a visible indicator of the immune response. White blood cells clean the wound of debris and bacteria.

**Proliferate Stage**
After the inflammatory stage, the proliferate stage lasts about 3 weeks (or longer, depending on the severity of the wound). Granulation occurs, which means that special cells called fibroblasts make collagen to fill in the wound. New blood vessels form. The wound gradually contracts and is covered by a layer of skin.

**Maturation and Remodelling Stage**
This stage may last up to 2 years. New collagen forms, changing the shape of the wound and increasing strength of tissue in the area. Scar tissue, however, is only about 80% as strong as the original tissue. The body’s ability to heal during this stage is impaired in the elderly.

Normal wound healing in acute wounds is a coordinated and rapid process. This process is impaired in chronic wounds. In chronic wounds the cells become unresponsive to chemical messengers such as cytokines and growth factors and such wounds have a prolonged inflammatory response (Van de Berg et al, 1998; Stanley and Osler, 2001).

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† Due to the size of the scope, timelines and resources to complete the guideline it has not been possible to include all interventions indicated in the treatment of pressure ulcers. The topic areas included are those prioritised and agreed through the formal NICE consultation process.
4.7 Guideline Development Group

The Guideline recommendations were developed by a multidisciplinary and lay Guideline Development Group (GDG) convened by the RCN and NICE with membership approved by NICE.

Members include representatives from:
- patient groups
- nursing
- medicine
- surgery
- allied health
- researchers and
- staff from the RCN

The GDG met eleven times between April 2003 and December 2004. Full details of the GDG members can be found on the NICE website www.NICE.nhs.org.uk and on page 4 of this guideline.

All members of the GDG were required to make formal declarations of interest at the outset, which were recorded. GDG members were also asked to declare interest at the beginning of each GDG meeting. This information is recorded in the meeting minutes and kept on file at the RCN.

5 METHODS USED TO DEVELOP THE GUIDELINE

5.1 Summary of development process

The methods used to develop this Guideline are based on those outlined by Eccles and Mason (2001) and those published by NICE (Guideline Development Methods: information for National Collaborating Centres and Guideline Developers. NICE 2004). The structure of the recommendations section (section 6) (ie, recommendations; evidence statements, evidence narrative and guideline development group commentary) came from McIntosh et al. (2001) and has been used in recently published guidelines by the NCC-NSC.

The following sources of evidence were used to inform the guideline:


The stages used to develop this guideline were as follows:

• Develop scope of guideline;
• Convene multidisciplinary guideline development group;
• Review questions set;
• Identify sources of evidence;
• Retrieve potential evidence;
• Evaluate potential evidence relating to cost/economics, quality of life and epidemiology for eligibility quality and relevance;
• Extract relevant data from studies meeting methodological and clinical criteria;
• Interpret each paper taking into account the results, including where reported, the beneficial and adverse effects of the interventions, cost, comfort and acceptability to patients, level of evidence, quality of studies, size and precision of effect and relevance and generalisability of included studies to the scope of the guideline;
• Prepare evidence reviews and tables which summarize and grade the body of evidence;
• Formulate conclusions about the body of available evidence based on the evidence reviews by taking into account factors above;
• Develop and utilise formal consensus methods to generate consensus statement for areas lacking sufficient research evidence;
• Agree final recommendations and apply recommendation gradings;
• Submit first drafts (full version) of guidelines for feedback from NICE registered stakeholders.
• Consideration by GDG of stakeholders’ comments;
• Submit final drafts of all guideline versions (including Information for the Public version, algorithm and audit criteria) to NICE for second stage of consultation;
• Consideration by GDG of stakeholders comments;
• Final copy submitted to NICE.
The main clinical questions addressed were as follows:

<table>
<thead>
<tr>
<th>Question</th>
<th>Method</th>
</tr>
</thead>
<tbody>
<tr>
<td>What assessment process(es) tools should be used to identify modifiable</td>
<td>Epidemiological systematic review of prospective cohort studies.</td>
</tr>
<tr>
<td>risk factors/complications for those with pressure ulcers?</td>
<td></td>
</tr>
<tr>
<td>What are the modifiable risk factors for individuals with existing pressure ulcers?</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>What assessment process(es) tools should be used to assess a pressure ulcer?</td>
<td>Narrative review of studies assessing wound measurement.</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>What is the evidence that pressure relieving support surfaces (beds, mattresses or overlays and seating cushions) are effective and cost-effective in treating pressure ulcers?</td>
<td>Systematic review of effectiveness.</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>What is the most effective positioning (sitting and lying) technique for people with pressure ulcers?</td>
<td>Systematic review of effectiveness.</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>What is the evidence that dressings are effective and cost-effective in treating pressure ulcers?</td>
<td>Systematic review of effectiveness.</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>What is the evidence that debridement is effective and cost-effective in treating pressure ulcers?</td>
<td>Systematic review of effectiveness.</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>What is the evidence that nutritional support is effective and cost-effective in treating pressure ulcers?</td>
<td>Systematic review of effectiveness.</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>What is the evidence that topical antimicrobials are effective and cost-effective in treating pressure ulcers?</td>
<td>Systematic review of effectiveness.</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>What is the evidence that surgical interventions are effective and cost-effective in treating pressure ulcers?</td>
<td>Narrative review of case series.</td>
</tr>
</tbody>
</table>
Additional questions addressed by the evidence reviews included:

<table>
<thead>
<tr>
<th>Question</th>
</tr>
</thead>
<tbody>
<tr>
<td>Are there any differences in comfort and acceptability rating?</td>
</tr>
<tr>
<td>Have there been any adverse events or patient complaints/comments for</td>
</tr>
<tr>
<td>any of the included interventions?</td>
</tr>
<tr>
<td>Is there any information about the ease of use and acceptability of</td>
</tr>
<tr>
<td>interventions for patients, carers or nursing staff?</td>
</tr>
<tr>
<td>What studies have been done looking at the quality of life implications</td>
</tr>
<tr>
<td>of having a pressure ulcer for both patients and carers in a broad sense</td>
</tr>
<tr>
<td>of quality of life?</td>
</tr>
<tr>
<td>What studies have been done that measure quality of life implications of</td>
</tr>
<tr>
<td>pressure ulcers that we can use to compare the implications of having a</td>
</tr>
<tr>
<td>pressure ulcer with other health problems?</td>
</tr>
<tr>
<td>Are there any studies looking at the implications of quality of life of</td>
</tr>
<tr>
<td>different equipment use?</td>
</tr>
</tbody>
</table>

RCN staff worked with an information specialist from the Centre for Reviews and Disseminations at the University of York to develop the search strategies for the topic areas covered in this Guideline. The information scientist ran the searches and all results were saved and stored in bibliographical software. RCN staff sifted all topic areas, conducted systematic reviews either fully in cases where there were no existing review or updated in cases where there were existing reviews. RCN graded the evidence and composed successive drafts of the recommendations and the full guideline documents (which includes full version of guidelines; NICE version and Information for the Public version) based on the evidence reviews and GDG input and deliberations. The GDG formulated and graded the recommendations.

The methods for each review are reported in section 6 for each review. The results are also reported in sections 6.

More details of the individual trials can be found in the evidence tables found in Appendix A.

The resulting recommendations are in section 6 for each review area.

5.2 Clinical effectiveness review methods

The search strategies and databases used are presented in Appendix D. All searches were comprehensive and included a large number of databases (see Appendix D).
All search strategies were adapted for smaller or simpler databases or for web-based sources which did not allow complex strategies or multi-term searching.

A combination of subject heading and free text searches were used for all areas. Free text terms were checked on the major databases to ensure that they captured descriptor terms and their exploded terms.

Extensive hand-searching was not undertaken following NICE advise that exhaustive searching on every guideline review topic is not practical and efficient (Mason et al. 2002).

Reference lists of articles were checked for articles of potential relevance.

**Search strategy**

**Terminology**

The terms for the search strategies were identified through discussion between an Information Officer and the research team, by scanning the background literature, and by browsing the Medline Thesaurus (MeSH). Once drafted, the initial strategy of pressure ulcer terms was circulated round the Guideline Development Group for comment.

**Management of references**

As several databases were searched, some degree of duplication resulted. In order to manage this issue, the titles and abstracts of bibliographic records were downloaded and imported into bibliographic management software to remove duplicate records. Further studies were identified by examining the reference lists of all included articles.

**Preliminary Literature search**

An initial search was undertaken by a Royal College of Nursing Research and Development Fellow to:

- identify any existing guidelines, systematic reviews and Health Technology Assessments (HTAs) covering pressure ulcer management to prevent duplication
- **estimate** the potential size of the literature for this topic area.

All databases were searched from inception date, which varies for each database.

The Following databases and websites were searched using keyword search terms:

- British Nursing Index (OVID) (up to 2002,10)
- Cinahl (OVID) (up to 2002, 10)
Main Literature searches

The following databases were searched:

- Medline (OVID)
- Medline In-Process Citations (OVID)
- Embase (OVID)
- Cinahl (OVID)
- British Nursing Index (OVID)
- Health Management Information Consortium (SilverPlatter)
- Database of Abstracts of Reviews of Effectiveness (DARE) (internal CRD interface)
- AMED (OVID)
- Cochrane Library (internet)
- System for Information of Grey Literature in Europe (SIGLE) (SilverPlatter)

Search dates are reported in the relevant review.

A search of the Cochrane Wounds Group specialist trials register was undertaken for each of the reviews.

Sifting process

Articles were retrieved and stored in an Endnote library and were subjected to the following sifting process.

<table>
<thead>
<tr>
<th>Sift</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st sft</td>
<td>To remove any irrelevant material based on title/abstract</td>
</tr>
<tr>
<td>2nd sft</td>
<td>To identify material that potentially met eligibility criteria based on title/abstract</td>
</tr>
<tr>
<td>3rd sft</td>
<td>Full papers were ordered if they appear relevant and eligible and where relevance/eligibility was not clear from the abstract or the abstract was not available but the title was relevant</td>
</tr>
<tr>
<td>4th sft</td>
<td>Full articles that met eligibility criteria were appraised</td>
</tr>
</tbody>
</table>
Data abstraction

Data from included trials were extracted by 1 or 2 reviewers as indicated in the review into pre-prepared data extraction tables. Discrepancies were discussed and resolved. The following data were extracted from each study:

- patient inclusion/exclusion criteria
- care setting
- key baseline variables by group
- description of the interventions and numbers of patients randomised to each intervention
- description of any co-interventions/standard care
- duration and extent of follow up
- outcomes
- acceptability and reliability if reported

If data were missing from reports then attempts were made to contact the authors to complete the information necessary for the critical appraisal. If studies were published more than once, the most detailed report was used as the basis of the data extraction.

No statistical analysis of inter-rater reliability of dual data extraction was performed. Differences were resolved by discussion.

Masked assessment, whereby data extractors are blind to the details of journal, authors etc, was not undertaken because there is no evidence to support the claim that this minimizes bias (Cullum et al, 2003).

Once individual papers were retrieved, the articles were checked for methodological rigour (using quality checklists appropriate for each study design), applicability to the UK and clinical significance. Assessment of study quality concentrated on dimensions of internal validity and external validity. Information from each study which met the quality criteria was summarized and entered into evidence tables.

All data extraction forms are contained in Appendix A.

Appraisal of methodological quality

The methodological quality of each trial in the effectiveness reviews was assessed by two researchers. The following quality criteria were used:

- description of inclusion and exclusion criteria used to derive the sample from the target population
- description of a priori sample size calculation
- evidence of allocation concealment at randomisation
- description of baseline comparability of treatment groups
- outcome assessment stated to be blinded
Methods of measuring wound healing can be subjective in the studies included in the reviews of this Guideline but had to incorporate at least one objective assessment, such as change in ulcer size, rate of healing, frequency of complete healing or time to complete healing, to meet the inclusion criteria.

Change in ulcer size is presented as a percentage or absolute change over a period of time. Objective methods of measuring changes on wound size include tracing the ulcer outline followed by counting grids on graph paper, weighing uniform-density tracing paper, planimetry or computerised image analysis.

A single standard outcome measure for wound healing does not exist. Both objective and subjective measures are widely used by researchers; however the validity of many of these measurements remain the subject of ongoing investigation and debate.

Objective measures of healing are usually based on wound area. Planimetry, often aided by computer analysis, is the most frequently used method of calculating wound area, though other methods, such as the measurement of wound diameter or weight of a tracing drawn around the area of the wound, are also used. Measurements of wound volume are infrequently reported in the literature; these methods are often cumbersome and their accuracy has not been proven. Computerised image analysis may in the future, as the equipment becomes more affordable and portable, prove to be a useful technique for the assessment of wound volume.

Even though objective measures reduce or eliminate subjective biases and reduce random measurement errors, they have certain inherent biases if the patients being compared have wounds with different baseline size. A change in wound area is often expressed as the percentage change, which unlike the absolute change in area, takes into account the initial size of the wound. For two wounds healing at the same linear rate (as measured by diameter reduction) percentage area calculations will show a larger change for a small wound than for a big wound. The converse is true when the absolute change in area is measured, as for any unit reduction in wound radius, a bigger area reduction will occur for a large wound. This has important consequences for the validity of trial results where there is poor comparability in initial wound size at baseline between the treatment groups. In large trials, randomised allocation should ensure that the mean wound size and variance in each group is similar. In a small trial random allocation is unlikely to result in an even distribution of wound sizes. In a trial where there is poor comparability between groups for wound size at baseline, and the outcome is based on the change in area, the result can only be considered valid if it is obtained either: against the anticipated
direction of the bias for wound size; or where percentage area change and absolute area change are in the same direction. If baseline data are not given then it is not possible to determine the direction of bias and the validity of the result cannot be determined. Despite the potential for objective outcomes to be biased by differences in wound size at baseline, they remain the most reliable assessment of wound healing as, unlike subjective measures, they reduce the biases of the assessor which cannot be estimated.

Data synthesis

For each trial, relative risk (RR) was calculated for outcomes such as complete healing. 95% confidence intervals (95% CI) were included when sufficient detail allowed their calculation. NNT were calculated where possible and appropriate. The results from replicated studies were plotted on to graphs and discussed by narrative review. Unique comparisons were not plotted and the relative risk is stated in the text. Individual study details are presented in the evidence table (Appendix A). Where there was more than one trial comparing similar interventions using the same outcome, and in the absence of obvious methodological or clinical heterogeneity, statistical heterogeneity was tested for by chi-squared test. In the absence of significant statistical heterogeneity, studies with similar comparisons were pooled using a fixed effects model (Clarke 1999). If heterogeneity was observed, both random and fixed effects models were used to pool the data. All calculations were made using Revman 4.2.3 software.

5.3 Cost effectiveness review methods

Aims
The aim of this section is to assess the economic evaluation literature on pressure ulcer management interventions in order to contribute to the pressure ulcer management guidelines for use within the National Health Service for England and Wales. Whilst the clinical effectiveness sections systematically assess the evidence on whether products can and do work, this section also considers the resource use and cost implications associated with interventions. To assess cost-effectiveness, appropriate alternative treatment options are compared in terms of their relevant costs and effects. The technique is used to assess whether an intervention is worth using, compared with other uses to which the same resources could be put.

Background
Pressure ulcers have a substantial impact on the health-related quality of life of patients and in terms of the financial burden on the health service, patients and their families and society as a whole. Recent cost estimates suggest that the cost of treating a pressure ulcer varies from £1,064 for a grade 1 pressure ulcer to £10,551
for a grade 4 pressure ulcer, with higher grade pressure ulcers taking longer to heal and being associated with a higher incidence of complications (Bennett et al, 2004). Bennett et al (2004) estimated that in the UK the annual cost of treating pressure ulcers is between £1.4 and £2.1 billion (price year 2000), that is about 4% of total NHS expenditure.

As seen in the clinical effectiveness review sections, a plethora of interventions are available for the treatment and management of pressure ulcers. However, it is not always clear what works best, given the resource use and costs implications associated with different pressure ulcer treatments.

Previous systematic reviews in which pressure ulcer interventions are assessed found little evidence available on the cost-effectiveness of different treatment options (Bradley et al, 1999ab; Cullum et al, 2001; O’Meara et al, 2000). The importance of obtaining economic evidence in this area has been reiterated with calls for additional research that incorporates economic evaluations in high quality clinical trials (Cullum et al, 2001). As has been suggested before, “measures of clinical effectiveness alone are rarely sufficient to guide healthcare decision-makers, since small incremental improvements in clinical effectiveness may not be worth the costs” (O’Meara et al, 2000). In recognition of this, the Royal College of Nursing, in collaboration with National Institute of Clinical Excellence (NICE) have funded this guideline to include a review of the cost-effectiveness evidence in this field. The benefits of incorporating health economics within NICE guidelines were discussed and formalised within the guideline development methods (Richardson et al, 2004). As stated “Clinicians already take resources and value for money into account in clinical decisions, and the incorporation of good quality health economic evidence into clinical guidelines can help make this more consistent”
Methods

Search questions

Searches for economic evaluations were undertaken in order to assess the cost-effectiveness evidence on ten different questions:

A. What assessment process tools are most cost-effective in identifying modifiable risk factors/complications associated with treating pressure ulcers?
B. What assessment tools are most cost-effective in assessing pressure ulcers?
C. What is the cost-effective evidence on pressure-relieving support surfaces to treat pressure ulcers?
D. What is the cost-effectiveness evidence on pressure ulcer dressings to treat pressure ulcers?
E. What is the cost-effectiveness evidence on pressure ulcer debridement strategies?
F. What is the cost-effectiveness evidence on nutritional support to treat pressure ulcers?
G. What is the cost-effectiveness evidence on adjunct therapies in the treatment of pressure ulcers?
H. What is the cost-effectiveness evidence on topical antimicrobials used to treat pressure ulcers?
I. What is the cost-effectiveness evidence on surgical interventions to treat pressure ulcers?
J. What is the cost-effectiveness evidence on mobility and positioning techniques to treat pressure ulcers?

Databases searched

For each question the following databases were searched from inception date to early 2004 followed by an update search in August-September 2004 (see appendix x for full details):

- Medline (1966–) (OVID interface)
- Medline In-Process Citations (OVID interface)
- Embase (1980–) (OVID interface)
- Cinahl (1982–) (OVID interface)
- British Nursing Index (1985–) (OVID interface)
- Health Management Information Consortium (OVID interface)
- AMED (1985–) (OVID interface)
- PsycInfo (1872–) (SilverPlatter interface)
- System for Information of Grey Literature in Europe (SIGLE) (1980–) (SilverPlatter interface)
Where possible, searches were limited to retrieve literature published in English, to omit animal studies and letters, comments and editorial publication types.

As well as searches undertaken to answer specific questions, three specialist economics databases were searched to retrieve all references to pressure ulcers from inception date to September 2004:

- EconLit (1969–) (SilverPlatter interface)
- HEED (cd-rom)
- NHS Economic Evaluation Database (NHS EED) (1994–) (CRD administration database)

This search is referred to in this document as the 'core' search.

**Search terms**

Given the number of questions and databases searched, all search strategies are presented in appendix x. The Information Officer, in consultation with the Health Economist, identified *economics terms to use* in the strategy. Terms were based on the NHS EED health economics filter strategy (CRD Report 6 (2nd Edition 2001)) with additional quality of life terms. On assessment the quality of life terms were found to introduce high numbers of irrelevant records, so the records once loaded into Endnote bibliographic management software were filtered for assessment by searching on core economic terms:

Cost* or economic* or price* or expenditure* or pharmacoeconomic* or budget* or quality*

The *pressure ulcer terms* for the search strategies were identified through discussion between an Information Officer and the guideline research team, by scanning the background literature, and by browsing the MEDLINE Thesaurus (MeSH). Once drafted, the initial strategy of pressure ulcer terms was circulated round the Guideline Development Group for comment.

For Question A the search results from the clinical effectiveness results were used, as they had not been restricted by study design. The results were loaded into Endnote and searched there using economics terms to identify a subset of references of potential relevance to the Health Economist.

Questions B, C and J were searched separately. Questions D, E, F, G, H & I were combined into a single search strategy to maximise efficient use of searching time.
Selection criteria

For a study to be included in the review the following criteria were applied:

- The study assessed interventions to manage and treat pre-existing pressure ulcers
- The study compared the costs and effects of two or more interventions
- The interventions that were assessed compared A, B, C, D, E, F, G, I or J
- The study had a sample size of two individuals or more

For a study to be excluded from the review the following criteria were applied:

- The study assessed interventions to prevent pressure ulcers
- The study did not report on costs associated with the interventions
- The study did not report on outcomes associated with the interventions
- The study was only available as a conference abstract or conference presentation
- The study was not written in English and no translation of the data into English was available

Data Extraction

Data on the eligible economic evaluations were abstracted (see appendix A) for presentation purposes. Study details were provided including the method of economic evaluation used, the study design, the results and an overview of the conclusions with brief comments.

Quality Assessment

Eligible studies were quality assessed using a quality checklist by Drummond et al (1996) (see appendix B). This checklist asks 35 questions about the study design, data collection and analysis and interpretation aspects of the economic evaluation.

Economic evaluation review

The types of economic evaluations reviewed were full economic evaluations: cost–utility analysis, cost–benefit analysis, cost–effectiveness analysis and cost–minimisation analysis studies and partial economic evaluations including cost–consequence analysis. Full economic evaluations combine costs and health effects whereas, for cost–consequence analysis, costs are reported separately from health effects.

As implied by the names of the different types of economic evaluations, they differ in the way that the health effects are measured. Health effects for use in cost–utility
analyses measure individual or society-based preferences for a set of health states. A utility associated with a particular health state may be adjusted by the length of time spent in that state to calculate a generic outcome such as a Quality-Adjusted Life Year (QALY). Like health effects measured in cost-utility analysis, the effects measured in cost-benefit analysis are also generic, in the sense that they can be used to compare effects across interventions. The difference, compared to cost-utility analysis, is that they are reported in monetary terms. Techniques such as contingent valuation may be used to obtain peoples' willingness to pay for the effects associated with a particular health state. The health effects in cost-effectiveness analysis are measured in the most appropriate natural or physical units such as, in this case, time to complete heal of the pressure ulcer. If the effects are shown to be equivalent then a cost-minimisation analysis may be performed, however, in practice this is very rare. Finally, cost-consequence analysis involves the use of multiple outcome measures and these are not combined with cost (Drummond et al, 1997).

A treatment is deemed cost-effective (a collective term which may be used for all full economic evaluations) based on the following decision criteria:

(i) If a treatment has lower costs and more health effects than its comparator it is cost-effective and cost-saving (area (iv) in figure x).

(ii) If a treatment has higher costs and more health effects than its comparator (area (ii) in figure x) it may be cost-effective, however incremental cost-effectiveness analysis is required. The question then becomes whether the extra costs are worth the extra effects. If so, the treatment is considered to be cost-effective, if not the resources used to provide the treatment may produce higher valued effects elsewhere.

(iii) If a treatment has lower costs and lower health effects than its comparator (area (iii) in figure x) it may be cost-effective, however incremental analysis is required.

(iv) If a treatment has higher costs and lower health effects than its comparator (area (i) in figure x) it is not cost-effective. Incremental cost-effectiveness or incremental net health benefit (if a monetary measurement of health effect is used) is calculated by comparing the difference in cost of treatment 1 to treatment 2 with the difference in outcome of treatment 1 to treatment 2 (see figure 3).
Figure 3: Cost-effectiveness plane

(i) Intervention dominated: treatment 1 less effective and more costly than treatment 2

(ii) Treatment 1 more effective and more costly than treatment 2

(iii) Treatment 1 less effective and less costly than treatment 2

(iv) Treatment 1 dominates: Treatment 1 more effective and less costly than treatment 2
Findings

Search results and management of references

As several databases were searched, some degree of duplication resulted. In order to manage this issue, the titles and abstracts of bibliographic records were downloaded and imported into Endnote bibliographic management software to remove duplicate records. In total, 3,049 abstracts were assessed for eligibility.

The numbers of unique records loaded into Endnote are shown below:

- A. See clinical effectiveness searches + 703
- B. 417
- C. 487
- D, E, F, G, H, I. 989
- J. 304
- Core. 149
- Total. 3049

The selection criteria were applied to the abstracts stored in Endnote and 185 studies were ordered. The selection criteria were then applied to each paper and a total of 26 economic evaluations were included in the review including the following:

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Numbers of studies reviewed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Assessment tools</td>
<td>0</td>
</tr>
<tr>
<td>Pressure-relieving support surfaces (beds, mattresses and overlays) mobility and positioning</td>
<td>3</td>
</tr>
<tr>
<td>Dressings and topical agents including debridement</td>
<td>21</td>
</tr>
<tr>
<td>Adjunct therapies (topical negative pressure, therapeutic ultrasound, electrotherapy and electromagnetic therapy)</td>
<td>2</td>
</tr>
<tr>
<td>Antimicrobials</td>
<td>0</td>
</tr>
<tr>
<td>Nutritional support</td>
<td>0</td>
</tr>
<tr>
<td>Surgical interventions</td>
<td>0</td>
</tr>
</tbody>
</table>
5.4 Submission of evidence process

Stakeholders registered with NICE listed at the beginning of the document, were invited to submit a list of evidence for consideration to ensure that relevant material to inform the evidence base was not missed. The criteria for the evidence included:

- systematic reviews
- randomised controlled trials (RCTs) that examine clinical or cost effectiveness, and/or quality of life and economic analyses based on these findings
- representative epidemiological observational studies
- qualitative studies/surveys that examine patient/carer experiences
- studies of any design which have attempted to formally:
  - assess the cost effectiveness/utility of pressure ulcer treatment
  - assess the cost of having a pressure ulcer
  - assess quality of life or used cost-utilities in relation to pressure ulcer management

Information not considered as evidence included:

- studies with ‘weak’ designs when more robust study designs are available
- commercial in confidence material
- unpublished secondary endpoint trial data, ‘data-on-file’ and economic modelling
- promotional literature
- papers, commentaries or editorials that interpret the results of a published study
- representations or experiences of individuals not collected as part of properly designed research.

Initial submissions were received from:

- British Healthcare Trades Association
- Nutricia Ltd
- Coloplast
- Hill-Rom
- College of Occupational Therapists
- Pegasus UK

Submissions were followed up to request the full references.
5.5 Evidence synthesis and grading

For the update of the clinical effectiveness reviews, data from existing trials of effectiveness were synthesised with new trials. If there were sufficient trials to necessitate the re-analysis of existing meta-analyses this was done. The data from included studies pertaining to costs, economic evaluation, epidemiology and quality of life were also qualitatively synthesised into a narrative format. Information from the reviews on costs, economic evaluations and epidemiology was used in the economic modelling. All included studies are summarized in evidence tables (Appendices E-H) as well as discussed in the appropriate evidence reviews.

Evidence gradings were assigned to each evidence review using the evidence hierarchy shown below (Table 2) which is the only hierarchy recommended by NICE at the time of writing. (It should be noted that the hierarchy strictly applies to questions of effectiveness.)

Table 2: Levels of Evidence

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1++</td>
<td>High-quality meta-analyses, systematic reviews of RCTs, or RCTs with very low risk of bias.</td>
</tr>
<tr>
<td>1+</td>
<td>Well-conducted meta-analyses, systematic reviews of RCTs, or RCTs with low risk of bias.</td>
</tr>
<tr>
<td>1-</td>
<td>Meta-analyses, systematic reviews of RCTs, or RCTs with high risk of bias*</td>
</tr>
<tr>
<td>2++</td>
<td>High-quality systematic reviews of case-control or cohort studies. High-quality case-control or cohort studies with very low risk of confounding bias or chance and high probability that relationship is causal.</td>
</tr>
<tr>
<td>2+</td>
<td>Well-conducted case-control or cohort studies with low risk of confounding bias or chance and a moderate probability that relationship is causal.</td>
</tr>
<tr>
<td>2-</td>
<td>Case-control or cohort studies with a high risk of confounding bias, or chance and a significant risk that the relationship is not causal*</td>
</tr>
<tr>
<td>3</td>
<td>Non-analytic studies (for example case reports, case-series).</td>
</tr>
<tr>
<td>4</td>
<td>Expert opinion, formal consensus.</td>
</tr>
</tbody>
</table>

*Studies with a level of evidence - should not be used as a basis for making a recommendation.

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The evidence tables and reviews were distributed to GDG members for comment on the interpretation of the evidence and grading.
5.6 Results of clinical effectiveness evidence retrieval and appraisal

Study quality

A summary of the methodological quality of each study of the trials is shown in Appendix C.
Characteristics of excluded studies are shown in Appendix B.

Comparisons

The comparisons, relevant to this guideline, able to be made on the basis of the included studies were:

5.7 Formulating and grading recommendations

In order for the GDG to formulate a clinically useful recommendation, it was agreed that the following factors be considered:

- The best available evidence with preference given to empirical evidence over expert judgement, including:
  - a profile of the cost data
  - results of economic modelling
  - effectiveness data taking into account the strength of evidence (the level, quality, precision) as well as the size of effect and relevance of the evidence
  - where reported, data regarding additional outcomes such as comfort, adverse effects and patient acceptability
  - A comparison between the outcomes for alternative interventions where possible.

- The feasibility of interventions, including the cost of the intervention, acceptability to clinicians, patients and carers and appropriateness of the support surface.

- The balancing of benefits against risks – including, where reported, all patient-relevant endpoints (including adverse effects; comfort and acceptability where reported) and the results of the economic modelling.

- The applicability of the evidence to groups defined in the scope of the guideline, having considered the profile of patients recruited to the trials and data obtained from our review of the epidemiological data and quality of life literature.

This information was presented to the group in the form of evidence tables and accompanying summaries which were discussed at GDG meetings. Where the GDG identified issues which impacted on considerations of the evidence and the ability to
formulate ‘implementable’ and pragmatic guideline recommendations, these were summarized in the GDG commentary sections.

Issues with the available data identified by the GDG included:
Issues with the data, interpretation of the evidence and the wording were discussed until there was agreement on the wording and grading.

Where the GDG decided that further ‘higher’ level evidence was essential before any recommendations could be considered, recommendations for future research were made (see section 7). The group then ranked these in order of importance so that the top 5 could be included in the NICE version.

The grading of the recommendations was agreed at GDG meetings using the scheme below.

**Table 8: Recommendation grading**

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>At least one meta-analyses, systematic review, or RCT rated as 1++, and directly applicable to the target population or A systematic review of RCTs or a body of evidence consisting principally of studies rated as 1+, directly applicable to the target population and demonstrating overall consistency of results Evidence drawn from a NICE technology appraisal</td>
</tr>
<tr>
<td>B</td>
<td>A body of evidence including studies rated as 2++, directly applicable to the target population and demonstrating overall consistency of results or Extrapolated evidence from studies rated as 1++ or 1+</td>
</tr>
<tr>
<td>C</td>
<td>A body of evidence including studies rated as 2+, directly applicable to the target population and demonstrating overall consistency of results, or Extrapolated evidence from studies rated as 2++</td>
</tr>
<tr>
<td>D</td>
<td>Evidence level 3 or 4, or Extrapolated evidence from studies rated as 2+, or Formal consensus</td>
</tr>
<tr>
<td>D(GPP)</td>
<td>A good practice point (GPP) is a recommendation for best practice based on the experience of the Guideline Development Group</td>
</tr>
</tbody>
</table>

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The recommendations with accompanying evidence reviews are presented in section
Formal consensus methods

Background
Clinicians often need to make decisions even where there is a variable or undetermined evidence base. Limiting recommendations to where evidence exists may reduce the scope of guidelines and thus limit their value to clinicians (Eccles et al., 1996). Woolf (1992) describes three methods of guideline development but also adds that in reality these are not mutually exclusive and it is possible to draw from each one.

In evidence-based guideline development recommendations are based on a systematic review of the literature and make explicit reference and linkage to the level of supporting evidence, which should enable clinicians to make decisions about adhering to them. Grimshaw et al (1995) argue that in cases where there is a strong level of supporting evidence clinicians should have a very good reason for choosing not to comply with them. However, as Woolf (1992) states, while this approach can be credited with enhancing the scientific rigour of guidelines, in the absence of acceptable evidence one is unable to produce recommendations.

Woolf (1992) suggests that the most common method of guideline development is informal consensus. This method is probably most frequently used at a local level where committees formulate recommendations without drawing on research evidence (Grimshaw and Hutchinson, 1995). By definition, this method tends to be based on poorly defined criteria and lacks the adoption of explicit consensus. Consequently, the resulting guidelines tend to be subjective and ill-defined in nature.

Formal consensus development methods, such as Delphi or Nominal Group Technique, provide a structure to the group decision-making process by, for example, adopting rating methods to represent the extent of agreement about predefined issues or questions. In reality, given situations such as poor or lacking evidence, guideline developers have to adopt strategies based on a framework that utilises facets of more than one guideline development method.

As already described, the evidence base available for this guideline is variable. Despite published and updated systematic reviews which form the main basis of the guideline development there are some areas where systematic searches of the evidence revealed little good quality research evidence. Given this, it was decided to devise and implement a formal consensus process to augment the weaker and more variable evidence base for areas of the guideline. The premise for this decision was that a guideline that contained both evidence-linked and consensus-based
recommendations would be more useful to practitioners than one confined to the limited outcomes of available research-based evidence.

Authors such as Grimshaw and Russell (1993a), Shekelle et al (1999) and Rycroft-Malone (2001), have acknowledged the use of consensus opinion to formulate recommendations in cases where there is an absence of evidence. They stress however, that the process adopted has to be explicit and that the source of recommendations made in the resulting guideline clearly documented. Thus the process devised and used here is based on current best practice of formal consensus in guideline development and also that used in the development of the NICE inherited guideline for the Risk assessment and prevention of pressure ulcers. (NICE, 2002, 2003).

GDG members were asked to rate a number of elements of statement and statements as to the level of importance (see appendix…. for full list) or to indicate don't know if it was outside of their expertise or knowledge base. Ratings were aggregated and mean and interquartile range was calculated. The results were used to develop recommendations statements which would then enter the next phase and formal voting consensus.

Example:

The following refer to statements for risk factors of delayed healing/complications of having a pressure ulcer.

Please indicate how you rate the importance of each statement.

1. A consensus statement about the holistic assessment for those with pressure ulcers may include:

<table>
<thead>
<tr>
<th>Extremes of age</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>Very □</th>
</tr>
</thead>
<tbody>
<tr>
<td>Important</td>
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<td>2</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td>3</td>
<td>2</td>
<td>3</td>
<td>1</td>
<td>2</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Reduced mobility</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>Very □</th>
</tr>
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<tbody>
<tr>
<td>Important</td>
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<td>1</td>
<td>2</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td></td>
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</tbody>
</table>

*Indicates GDG responses.

A modified nominal group technique was used to finalise the recommendations and good practice points. A facilitator was used to chair the meeting. The consensus process was facilitated by computerised voting consoles, which assured anonymity.
and allowed percentages to be quickly calculated. It also allowed the GDG to view the range of responses in the form of a graph immediately voting had occurred. Consensus was set at 80% unless a significant group within the GDG all voted against a recommendation – for example if all the allied health professionals, nurses or physicians voted against a recommendation, even though 80% agreement was achieved, a consensus agreement was not considered to have been reached.

Prior to voting on each recommendation and good practice point, discussion took place and modifications were made as necessary. Recommendations were reworded if necessary and then displayed on a screen so that GDG members could see the recommendation or good practice point they were voting on. If consensus was achieved the GDG moved on to discuss the next recommendation or good practice point. However, if consensus was not achieved, the recommendation or good practice point was discussed a second time, modifications made to reflect the concerns of the GDG and re-voting took place. After debate on some areas, consensus was achieved for all recommendations submitted for first stage consultation.
6. EVIDENCE REVIEWS WITH GUIDELINE RECOMMENDATIONS

The holistic assessment of individuals with pressure ulcers

Background

Pressure ulcer management approaches and management techniques are continuously developing and there remains no overall consensus about them. Over the last thirty years a number of risk assessment tools and scales have been developed with the primary aim of identifying those individuals at risk of developing pressure ulcers. Interventions should then be implemented to help prevent ulceration.

The predictive validity of these assessment tools and scales in predicting which patients go on to develop pressure ulcers has been evaluated (Bergstrom, 1987; Deeks, 1996) clearly identifying variation in sensitivity which means some tools are more effective in identifying and predicting those who are at elevated risk and thus may go on to develop a pressure ulcer.

The importance of using risk assessment tools and scales as an adjunct to but not a replacement for clinical judgement has been stressed (Cullum et al, 1995; Cullum, 2001, Rycroft-Malone & McInnes, 2000) and there still remains little evidence that indicates using a risk tool or scale is better than clinical judgement. The fact that they should be chosen on the basis of their suitability for a particular care setting or patient group as well as the research evidence demonstration of their predictive validity has also been highlighted (Cullum, 2001).

Perhaps more interestingly, for this review their effectiveness and validity for use in those individuals with established pressure ulcers is even more unclear, with indications that some perform poorly in identifying patients with existing ulcers as “at risk” (Williams et al 2000). Yet these same tools and scales appear to be used widely in this patient group in both clinical and non clinical settings in the UK. One explanation may be that the individual is recovering and is therefore no longer at risk, however the validity of this is unclear. Also research indicates that those with existing ulcers are also at elevated risk of developing further ulcers which does not find consistency with indications that some with pressure ulcers are not found to be at risk according to some risk assessment tools.

To what extent these individuals are at further risk, not only of developing additional pressure ulcers, but at risk of developing complications, such as infections and delayed healing, is also unclear.
Reported characteristics of individuals with existing ulcers.

- Activity, mobility, or functional limitation or immobility
- Incontinent
- Altered level of consciousness
- Sensory impairment
- Impaired nutrition
- Acute illness
- Dehydration
- Chronic illness
- Terminal illness

Clinical question.

What assessment process should be used to identify modifiable risk factors for people with existing pressure ulcers?

Objectives.

The objective was to undertake a systematic review of the evidence of assessment of people with pressure ulcers to determine:

- What are the characteristics of people with pressure ulcers
- What are the risk factors for people with pressure ulcers?
- What are the priorities for assessment?
- What is the empirical evidence that this process is effective in the management of pressure ulcers?
Selection Criteria.

Types of studies

Prospective cohort studies of risk factors and characteristics or complications associated with having a pressure ulcer(s) and studies of characteristics and interventions predictive of healing. Prospective cohort studies comparing assessment processes for individuals with pressure ulcers and studies evaluating their effectiveness in individuals with pressure ulcers in the treatment of pressure ulcers.

Types of participants

All: adults and children, including those in primary and secondary care, residential homes, nursing homes, secure settings and the home.

Types of outcome

Risk factors linked to healing/delayed healing, healing, complications and predictors of healing of pressure ulcers and severity.

Search strategy

The databases searched are found in review methods section (3.2). The full search strategies are listed in Appendix D. Databases were searched in July 2003 and update searches performed in August 2004.

Appraisal of methodological quality.

Criteria for inclusion (methodological quality found in Appendix C) and pre-defined principles as outlined in (Appendix E).

Selection

Eligible participant population with well defined demographic information

High percentage of participants equal to or greater than 80% of those approached

Identification of risk factors, characteristics and effectiveness of assessment process

Risk factors and characteristics conceptually relevant to subject of interest

Explicit details of how risk factor and characteristic information is measured
Clear description of assessment process and measurements with comparison clearly defined.

**Confounding**

Statistical adjustment carried out; evidence of sensitivity analysis with method described

**Outcomes**

Clear outcome measurements used

**Follow up**

Participation rates high with explicit details of losses to follow up

**Search results**

<table>
<thead>
<tr>
<th>Results of search strategy</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial search results</td>
<td>2871</td>
</tr>
<tr>
<td>N screened for relevance following sifting</td>
<td>197</td>
</tr>
<tr>
<td>N included</td>
<td>3</td>
</tr>
<tr>
<td>N excluded</td>
<td>11</td>
</tr>
</tbody>
</table>

**Research evidence.**

197 studies were identified from the sifting process and subsequently full papers ordered. This number also included those studies referenced with relevant titles but where the abstract was absent in the citation. After sifting full papers for relevance and duplicates at this stage 183 papers were opinion pieces, editorials, anecdotal reports or fell outside the inclusion criterion for this review. Out of the 5 selected studies, 11 were excluded and 3 included.

**Included Studies**
• The ‘gold standard’ study design to investigate risk factors is the prospective cohort design. Only three studies were found which met the inclusion criteria.
• Generally the studies were medium quality prospective cohort studies.


Allman et al (1995) carried a prospective inception cohort study to identify specific demographic, medical, functional status and nutritional characteristics that predict the development of stage II pressure ulcers or greater. 286 patients met the inclusion criteria: admission within the past three days, age 55 years or more, expected to be confined to bed or chair for at least five days and or hip fracture and without grade 2 or greater pressure ulcers. The main outcome of the study was in-hospital time to develop a grade II or greater ulcer. Results of multivariate analysis shows that grade I pressure ulcer, RR 7.52 CI 1.0-59.12; lymphopenia RR 4.86 CI1.70-13.89; immobility RR 2.36 CI1.14-4.85; dry skin RR 2.31 CI 1.02-5.21 and decrease body weight RR 2.18 CI1.05-4.52 are independent and significant risk factors for development of grade II pressure ulcers in hospital patients. In this study only 24 of the original 286 has a diagnosed grade I pressure ulcer at baseline and it is not clear if this subgroup of patients were analysed separately. The result of this may mean that the results cannot be generalised to patients with existing pressure ulcers.

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Risk Ratio</th>
<th>95% CI</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 1 pressure ulcer</td>
<td>7.52</td>
<td>1.0-59.12</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Lymphopenia</td>
<td>4.86</td>
<td>1.70-13.86</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Immobility</td>
<td>2.36</td>
<td>1.14-4.85</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Dry skin</td>
<td>2.31</td>
<td>1.02-5.21</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Decrease body weight</td>
<td>2.18</td>
<td>1.05-4.52</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Results of multivariate analysis.

Reed et al 2003

Reed et al 2003 conducted a longitudinal prospective cohort study involving 2771 subjects from 47 Veterans Affairs hospitals. The aim was to determine if three risk factors (low serum albumin, faecal incontinence and confusion) were significant risk factors for development of grade II or greater pressure ulcer. Multivariate analysis shows that low albumin OR 1.40 and confusion OR 1.45 to be both statistically significant risk factors of grade II ulcer development while faecal incontinence was
not. Whilst this paper shows that the identification of a stage I pressure ulcer is a risk factor for more severe grade II and above ulcers or an open wound, it does not tell the reader about the extent to which the other identified risk factors contribute to delayed healing or more severe pressure ulcers.

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Odds Ratio</th>
<th>95% CI</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 1 pressure ulcer</td>
<td>3.13</td>
<td>2.41-4.06</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Malnourished</td>
<td>1.69</td>
<td>1.31-2.19</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Urinary catheter on admission</td>
<td>1.55</td>
<td>1.38-1.75</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>DNR order</td>
<td>1.40</td>
<td>1.22-1.90</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Multiple regression analysis for development of grade II or greater risk factors.

Williams et al, 2000

Williams et al, 2000, undertook a prospective study of 267 subjects of which 12.8% had a pressure ulcer present on admission to an acute care environment. The study’s aim was to investigate predictors of pressure ulcer presence and severity using the Braden scale for pressure ulcer risk assessment. Pressure ulcer risk was evaluated and skin inspection was performed. Demographic, physiological and laboratory data were obtained as well as medical history and patient acuity. Inter-rater reliability of data collection was reported as good. Statistical testing was performed using Statistical Package for Social Sciences (SPSS). The study found that the mean Braden score for people without ulcers was 19.7 and 15.9 for those with ulcers ($P, <.05$) indicating that the Braden scale either failed to highlight patients with ulcers “at high risk” or detected recovery in those patients with recovering ulcers. It is not possible to deduce which from the study. The study did however have a cut-off point of 16 to indicate high risk – the lower the score the higher the risk of pressure ulcer development. Analysis of variance showed that subjects with pressure ulcers had significantly lower albumin level, total lymphocyte count, haematocrit level and haemoglobin levels. The paper reports this as indicating poorer nutritional status. Subjects with pressure ulcers were also significantly older and had longer length of stay (LOS). Regression showed that albumin level, oxygen saturation and length of stay were associated with pressure ulcer presence and that albumin level and length of stay ($P <.001$) accounted for 11.2% of the variance in pressure ulcer severity.

Poorer nutritional status and decreased oxygen perfusion were found to be predictors of pressure ulcers on admission while nutritional status and length of stay were predictors of ulcer severity. In this study nutritional status was operationalised by
using biochemical markers such as albumin and haematocrit levels as well as the subscale of the Braden scale and body mass index. This study does not provide information on the role of co-morbidity and the presence of pressure ulcers nor pressure ulcer severity; a high proportion of subjects (n = 141) were on a surgical unit; the effect of this on presence and severity of pressure ulcers, if any, is unclear. The study claims to have calculated odds ratios for significant factors but they are not reported in the paper.

Reviewer's Conclusions

The objective of this review was to determine the following:

- What are the characteristics of people with pressure ulcers
- What are the risk factors for people with pressure ulcers?
- What are the priorities for assessment?
- What is the empirical evidence that the process is effective in the management of pressure ulcer?

It remains unclear what assessment process should be used to identify modifiable risk factors in people with established pressure ulcers. There is not one gold standard assessment available. There is not sufficient evidence to recommend one process or tool over another. What is clear is that the same risk assessment tools and processes are utilised in both populations: those people with established ulcers and those who are at risk of developing pressure ulcers. Some studies report that the predictive validity of assessment tools in those with existing ulcers is poor.

There is limited evidence reporting on the characteristics of those with existing ulcers on admission to a primary or secondary care environment.

What is clear from the available evidence is that the existence of a grade I pressure ulcer is a significant risk factor for the development of a more severe ulcer and therefore an open wound.

There is limited evidence reporting on other the modifiable risk factors and complications for those with established pressure ulcers. Where characteristics are identified they are consequently identified as risk factors. Not all risk factors are modifiable and it is not clear whether it is the individual effects of each risk factor which is significant or the collective effect. The risk factors in individuals with ulcers are not only the risks of developing further pressure ulcers but the risks of delayed healing and the risks of infection and complications. Further research is required to identify the risk factors of having a pressure ulcer. Rigorous intervention studies need to be carried out to determine the significance of risk factors.
The issue of effectiveness in the assessment process has not been found to have been evaluated in the studies.

No economic evaluations assessing tools used to identify modifiable risk factors and/or complications for those with established pressure ulcers were found.

### Research evidence

<table>
<thead>
<tr>
<th>Level of evidence</th>
<th>Evidence statement</th>
</tr>
</thead>
<tbody>
<tr>
<td>2+</td>
<td>The identification of a grade I pressure ulcer is a significant risk factor for the development of a more severe ulcer and therefore an open wound.</td>
</tr>
</tbody>
</table>

### Recommendations:

#### Holistic assessment

Patients with pressure ulcers should receive an initial and on-going holistic assessment. Both intrinsic and extrinsic factors have been identified as important factors for assessment. This assessment should include: [D]

- Health status
  - acute, chronic and terminal illness
  - co-morbidity
- Mobility status
- Posture (pelvic obliquity and posterior pelvic tilt)
- Sensory impairment
- Level of consciousness
- Systemic signs of infection
- Nutritional status
- Previous pressure damage
- Pain status
- Psychological factors
- Social factors
- Continence status
- Medication
- Cognition
- Tissue perfusion

Assessment of mobility should include all aspects of independent movement including walking, ability to reposition (for example in bed or chair) or transfer (for example from bed to chair). [D]

Presence of any sensory impairment in an individual with a pressure ulcer should be recorded. [GPP]
Level and duration of impaired consciousness should be recorded. [GPP]

Presence of acute, chronic or terminal illness and its potential impact on ulcer healing should be recorded [GPP]

Previous pressure damage (site/location, stage or grade of previous ulcer and previous interventions) should be recorded. [D]

Pain assessment should include: whether the individual is experiencing pain; the causes of pain; level of pain (using an appropriate tool); location and management interventions. [D]

In the presence of systemic and clinical signs of infection in the patient with a pressure ulcer, systemic anti-microbial therapy should be considered. [GPP]

Psychological assessment should include concordance and abilities of the individual to self-care (mood, motivation and aptitude) [D]

Assessment of social factors should include suitable home environment, level of supportive provision and the involvement of local support services. [D]

Continence assessment should include whether the individual is continent of urine, faeces and continence interventions which may affect ulcer healing and impair the function of pressure relieving support surfaces. (for example, pads or bedding). [GPP]

Holistic assessment is the responsibility of the inter-disciplinary team and should be carried out by registered health professionals who have undergone appropriate training and have demonstrated competence. [D]

**Guideline Development Group Commentary**

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Commentary.</th>
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<td></td>
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</tbody>
</table>
The EPUAP is the classification tool of choice as it identifies not only the skin colour change of grade 1 pressure ulcers but also other physiological signs resulting from the tissue damage that many other tools ignore – namely the changes in skin temperature and skin texture due to the inflammation process.

Many clinicians identify any redness as a grade 1 pressure ulcer. A level of redness is normal – for example following crossed legs where the lower leg has a red mark when the upper leg is removed. This is not the redness of a grade 1 pressure ulcer – and is not hot to touch etc. The classification system is about what the skin/tissue looks like and is not related to patient group / environment / context etc – these items are part of pressure ulcer risk assessment tools.

Research recommendations.

Well designed prospective cohorts studies including those with pressure ulcers and including relevant identified risk factors to show how the identified risk factors lead to more severe ulcers or delayed healing or complications.

Ulcer assessment

Background

The assessment of the pressure ulcer together with the holistic assessment is the basis for initiating, developing, maintaining and evaluating the plan of care for an individual with a pressure ulcer. The assessment of the pressure ulcer should provide information or data to facilitate the communication of information about the severity of the pressure ulcers and the change of the pressure ulcer over time.


However it is a consistently accurate assessment of pressure ulcers which is key to monitoring changes in pressure ulcer characteristics which will determine treatment interventions. A number of pressure ulcer characteristics are identified in the literature (Bohannon & Pfaller, 1983; Bulstode et al, 1987; Cooper, 1990; Ayello,
1992; Bates-Jensen, 1992; Emparanza et al, 2000; Gardner, 2001) as important indices to include in the pressure ulcer assessment including: location, size, depth, stage, condition of wound edges, tunnelling or undermining, signs of infection, necrotic tissue, exposed bone, granulation tissue presence, epithelialization, exudates, odour etc. The importance and relevance of these indices in the pressure ulcer assessment to ensure the most effective outcomes is the focus of this review together with a clearer understanding of the consistency and accuracy of these measurements in pressure ulcer assessment.

To date there is not one method of assessing pressure ulcer status that is used universally. Yet the importance of a thorough, accurate, consistent and objective assessment of pressure ulcers is strongly advocated (Verhonick, P.J, 1961; Bohannon & Pfaller, 1983; Bulstode et al, 1987; Gosnell, D.J, 1977; Garrigues, 1987; Preston, 1987; Maklebust, 1987; Ayello, 1992; Emparanza et al, 2000; Gardner, 2001). A number of tools have been developed specifically to assess pressure ulcer status. However there remain contentious issues about their validity and reliability. It is now almost ten years since the publication of the Agency for Health Care Research and Quality (AHRQ formerly AHCRQ) guidelines on pressure ulcer prevention and management in which a classification system for pressure ulcers was recommended as well as indices to include in the assessment of a pressure ulcer (www.ahcpr.gov).

Despite these national guidelines there remain problems among healthcare professionals with the communication of pressure ulcer status (Garrigues, 1987; Preston, 1987; Maklebust, 1987; Ayello, 1992; Emparanza et al, 2000; Gardner, 2001). Assessment of the ulcer together with the holistic assessment is viewed as fundamental in ensuring the right interventions or treatment modalities are applied (Bates-Jensen et al 1992). A number of evidence based tools have been developed and are widely used to assess the status of pressure ulcers which include the Pressure Sore Status Tool (Bates-Jensen et al, 1992, 95a, 95b & 97), the Pressure Ulcer Scale for Healing (Thomas et al, 1997), the Sussman Wound Healing Tool (Sussman & Swanson, 1997), the Sessing Scale (Ferrel et al, 1995) and the Wound Healing Scale (Krasner, 1997). To what extent these tools are valid and reliable for implementation and use in general UK populations is not clear. A recent review (Woodbury et al, 1999) suggests that generally the validity and reliability of such tools are variable. However Woodbury et al (1999), suggests that there is sufficient published evidence for the Pressure Sore Status Tool and the Sessing Scale to be considered as valid and reliable.

Many of the techniques advocated in the literature are reported not to be appropriate for routine use in a clinical environment. There are many high and low-tech methods of assessing pressure ulcers status e.g. size, depth and volume of pressure ulcers
using scaling gauges, dental impression material, sodium chloride, ultrasound,
tracings, photographs, planimeter and video image analysis among others. The
effectiveness of these is not clear from the small studies evaluated and it is also not
clear what benefit they have to patients or how they link to wound healing ensuring
that pressure ulcers are assessed accurately to inform the clinical decision-making
process.

Clinical question.

What assessment process should be used to most accurately assess a pressure
ulcer?

OBJECTIVES.

The objective was to undertake a systematic review of the evidence of pressure
ulcers assessment to determine:

• What are the wound characteristics of pressure ulcers?
• What is the significance of these in pressure ulcer assessment?
• What are the priorities for pressure ulcer assessment?
• What are the existing evidence-based tools/instruments for
  assessment/evaluation of pressure ulcers?
• What is the empirical evidence that these processes are effective in the
  management of pressure ulcers?

Selection criteria.

Types of studies

Diagnostic studies reporting the reliability, accuracy and impact on pressure ulcer,
diagnostic tools/processes; studies comparing methods of pressure ulcer assessment
and evaluating their effectiveness in individuals with pressure ulcers in the treatment
of pressure ulcers. Studies comparing methods of measurement.

Types of participants

All: adults and children, including those in primary and secondary care, residential
homes, nursing homes, secure settings and the home.

Types of outcome
Staging performance, sensitivity, specificity, reliability, accuracy and impact linked to healing/delayed healing, healing, complications and pressure ulcers and severity.

**Search strategy**

The databases searched are found in review methods section (3.2). The full search strategies are listed in *Appendix B*. Databases were searched in July 2003 and update searches performed in August 2004.

The full search strategies are listed in *Appendix*.......

**Appraisal of methodological quality.**

Criteria for inclusion (*methodological quality is reported in the evidence tables*) and pre-defined principles as outlined in (*Appendix D*).

**Selection**

Eligible participant population with well defined demographic information

High percentage of participants equal to or greater than 80% of those approached

**Identification of effectiveness of assessment process.**

Clear description of assessment process and measurements with comparison clearly defined

**Confounding**

Statistical adjustment carried out; evidence of sensitivity analysis with method described

**Outcomes**

Clear outcome measurements used

**Search results**

<table>
<thead>
<tr>
<th>Results of search strategy</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial search results</td>
<td>1759</td>
</tr>
<tr>
<td>N screened for relevance following sift</td>
<td>165</td>
</tr>
</tbody>
</table>
Clinical Evidence.

165 studies were identified from the sifting process as potentially relevant to the topic and subsequently full papers ordered. This number also included those studies referenced with relevant titles but where the abstract was absent in the citation. After sifting full papers for relevance and duplicates at this stage 153 papers were opinion pieces, editorials, anecdotal reports or fell outside the inclusion criterion for this review. Out of the 7 selected studies 2 were excluded and 5 included.
Included Studies

- The ‘gold standard’ systematic review for this type of clinical question is a systematic review of diagnostic and screening tests. Whilst it was the reviewer’s intention to conduct this type of review it must be acknowledged that diagnostic reviews are a newly developing methodology.
- The research evidence covering this topic area assessing the diagnostics of pressure ulcer assessment is limited.
- Where studies have addressed and assessed issues such as accuracy, sensitivity and specificity, these tend to be small studies, heterogenic; using varied ulcer measurement parameters and it is not clear how representative these data are. Also raw data is too limited in the appraised papers to allow any further analysis.
- Where a tool or instrument has been evaluated in terms of reliability these have been included in the evidence tables.

Cutler et al, 1993:

A cross-sectional study to evaluate and compare the various methods of measuring the characteristics of pressure ulcers – mainly area. The study included a population of initially 20 patients with 17 remaining on completion. Mix of male and female patients; little other demographic details explicit in the study. Ulcers judged as at stage 3 or 4 with a size range between 2 and 150cm². Patients with signs of infection, exposed bone or cellulitus were excluded from the study. Numbers excluded not included in the reporting. All ulcer assessments were performed by the same research nurse. Initial baseline assessment taken with weekly assessment thereafter. Compared measurements included direct measurement at the bedside of longest length and longest width and depth measurement at the deepest point of the ulcers, tracings and photograph calibrated with ruler. All measurements detected a statistically significant change in wound size and volume at week 4 assessment. Sub group analysis showed that in the <10cm² a statistically significant change in wound size was detected earlier than in the >10cm² group.

Griffin, W et al, 1993:

Aimed to compare test–retest reliability of measurements obtained by the use of photographic methodology and those obtained by use of transparency method, and to compare wound surface are measurements obtained. Twenty patients included in the study, 18 male and 2 female, in a rehabilitation centre in Memphis. Measurements made of 22 ulcers identified all in the pelvic region. Range of wound size 688mm +/- 228mm. Three photographs taken at each wound assessment and three tracings
taken of each wound at each assessment. Both sets of tracing were digitalized. Test–retest reliability obtained measuring five ulcers using both methodologies and repeating assessments after one hour. To compare the two methodologies all 22 ulcers were measured on a single occasion and to compare the two methodologies over time, 16 ulcers were measured at five day intervals for 20 days (four occasions). Test–retest reliability ICC =.99, comparison on a single occasion PCC =.99 and comparison over time r=.996 – .999 p = .001. No evidence of superiority found with the two methodologies.

Houghton, P. E, 2000:

Examined the validity and reliability of using photographs of wounds to accurately assess wound status. Thirteen patients with pressure ulcers and 46 with leg ulcers included in the study. Ulcers that had extensive tunnelling or undermining were too deep and could not be visualized, so were excluded from the study. Measurements performed by trained healthcare professional. Blinded assessment but details not explicit. Six measurement parameters assessed using photographic method: wound edges, necrotic tissue/type and amount, skin colour, granulation tissue type and epithelialisation. Total scores assigned by one trained rater viewing 56 photographs of 13 pressure ulcers on two separate occasions ICC +0.96. Interarater reliability for scores assigned on two occasions for 81 photographs of 34 leg ulcers ICC = 0.86. Wound size estimates from photographs ICC = 0.96. Interrater reliability for pressure ulcers ICC =0.75. Correlation for same observer for individual domain r = 0.75 and with the exception of skin colour r = 0.56. The between raters correlation for six domains r = 0.75 with the exception of wound edges r= 0.68. The concurrent validity was assessed for the Pressure Sore Status Tool and PWAT r+ 0.70 for PSST and r= 0.66 for six domain PWAT. PSST was used as a reference standard in this research and the photographic method had good interrater and interarater reliability with scores ICC = 0.75. Reliability was found to be higher for pressure ulcers than leg ulcers in this study. This could be explained by the fact that the PSST is a pressure ulcer specific assessment tool.


Evaluated pressure ulcer surface area measurement using four different methods. Number of patients not clear set in Division of Geriatric Medicine University Hospital Huddinge, Sweden. Demographic details limited. Planimeter used as reference standard. Four measurements used included: direct measurement with digital planimeter, length and width measurement, number of whole squares, number of whole and partial squares. Planimeter was used as the reference standard. 373 different pressure ulcers were measured in this study. Measurement of length and width gave values significantly higher than the reference value 31% , p = 0.001.
Counting the number of whole squares gave a significantly lower value than the reference standard – 13%, p=0.001. Counting the number of whole and partial squares inside the boundary line gave values that were much closer to the reference value +1%. Counting the number of whole and partial squares within the tracing area gave the best estimate of wound size.


Controlled trial comparing the performance of the MAVIS instrument against three traditional methods of wound measurement for area and volume. Three traditional techniques include: use of ruler, transparency tracing and alginate for volume measurement. Precision established on mock wounds made using plaster cast and each measured 20 times for each technique. Fifty patients, demographic detail limited. Among excluded patients were those with painful ulcers, undermining, and extremely flexible, small and large ulcers. Measurements taken by structured light. Area and volume measurements taken simultaneously. Results reported in graphical form without clear axis. Reported that MAVIS gave overall more precise results for area and volume than the other three methods.

Quality of the studies.

The quality assessment for each study is reported in the evidence table for each study. There are not well established quality criteria for assessing some of the designs included in this narrative review. Generic assessment tools (appendix H) were used to assess each study according to study design. Generally the studies’ aims were clear and although the sample sizes were small (with the exception of Shubert, V (1997) they were justified. Statistical methods were well described in all the studies with clear rationale for their use. Limited reporting in the studies regarding excluded patients and those that did not finish the study.

Reviewer’s Conclusion.

The original objective was to undertake a diagnostic review of the evidence of pressure ulcer assessment to determine:

- What are the wound characteristics of pressure ulcers?
- What is the significance of these in pressure ulcer assessment?
- What are the priorities for pressure ulcer assessment?
- What are the existing evidence-based tools/instruments for assessment/evaluation of pressure ulcers?
- What is the empirical evidence that these processes are effective in the management of pressure ulcers?
The research evidence in this area is limited and it has not been possible to conduct a diagnostic review for several reasons: 1. The research evidence in this area is limited. 2. There is a lack of generally accepted reference standard both for assessment of individual parameters for ulcer assessment or pressure ulcer assessment tool. 3. The reporting of the research evidence lacks raw data for any further analysis to be performed.

Whilst there has been a number of tools developed, these tools have not been evaluated fully. A number of research based pressure ulcer assessment tools such as the PSST has undergone a systematic process of development and their reliability has been assessed. However this review did not find evidence for the use of such tools widely in the UK, nor did it find evidence that these have been tested against an agreed ‘gold standard’. It remains unclear how these tools are linked to outcomes, that is the healing of pressure ulcers, as this is not reported in the literature.

Wound size, that is surface area and volume, appear to be the specific parameters that have been assessed in the literature most frequently and are reported as being useful markers of wound change over time. Various methods of determining these parameters are advocated in the literature; however caution should be taken when interpreting the author’s finding as these finding are generally from small studies. There is also considerable heterogeneity both within and between the studies to be able to combine any of these data.

The inclusion of location, stage, condition of wound edges, tunnelling or undermining, signs of infection, necrotic tissue, exposed bone, granulation tissue presence, epithelialization, exudates, odour etc in the ulcer assessment is advocated in the research. However this evidence base in support of their inclusion is limited. It is also not clear from this evidence whether these parameters are firstly suitable to include in assessment on the basis of their being consistently identifiable by the same assessor, or secondly identifiable at a repeated assessment by the same or different assessor either within the same patient or between patients.

It is also not clear what effect the context has on the wound assessment. Reporting of this information was limited in the research evidence. In terms of who should carry out assessments, one study found significantly better assessments carried out by trained healthcare professionals compared with students with limited training and experience. How often an assessment should take place is also not clear from the evidence.

No economic evaluations assessing tools used to assess a pressure ulcer found.
Recommendations for this area of the guideline were sought via formal consensus methods as outlined in the methods section.

Recommendations:

The aim of the ulcer assessment is to:
- Establish the severity of the pressure ulcers
- To generate a personal ulcer profile to develop a plan of care from which treatment interventions will be initiated
- To evaluate treatment interventions
- To assess for complications
- To communicate information about the pressure ulcer to those involved in pressure ulcer management

Those carrying out ulcer assessments should consider the aims and objectives of the assessment to ensure that maximum benefit to the individual is gained. [GPP]

Ulcer Assessment

Patients with pressure ulcers should receive an initial and on-going pressure ulcer assessment. Ulcer assessment should include: [D]
- Cause of ulcer
- Site/location
- Dimensions of ulcer
- Stage or grade
- Exudate amount and type
- Local signs of Infection
- Pain
- Wound appearance
- Surrounding skin
- Undermining/tracking (sinus or fistula)
- Odour

This should be supported by photography (calibrated with a ruler) and tracings

Record the pressure ulcer grade using the European Pressure Ulcer Advisory Panel Classification System (page 31). [D]

Measure the dimensions of the pressure ulcer, recording the longest length / longest width as an estimate of surface area (use of tracings); the deepest part of the wound should also be measured [D]

Initial and on-going ulcer assessment is the responsibility of the inter-disciplinary team and should be carried out by registered health professionals that have undergone appropriate training and have demonstrated competence. [D]
Reassessment of the ulcer should be performed at least weekly but may be required more frequently, depending on the condition of the wound and the result of holistic assessment of the patient. [D]

<table>
<thead>
<tr>
<th>GDG commentary</th>
</tr>
</thead>
<tbody>
<tr>
<td>Despite the lack of research evidence from which to generate recommendations the GDG felt that it was important to guide clinicians as to the most important parameters to include in an ulcer assessment. Many different variations of tools are used to gather information about pressure ulcers in a variety of NHS setting. A comprehensive and accurate assessment of the pressure ulcer was considered to be paramount to ensuring that the plan of ulcer care reflected ulcer severity.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Research recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Research needs to focus on what methods of measurement and which parameters are of use to clinicians to allow accurate wound evaluation.</td>
</tr>
</tbody>
</table>

**Support Surfaces for Pressure Ulcer Treatment.**

The methods described in this review were those utilised to update the following systematic review:


This review was used as the main source to develop recommendations for this area of the guideline.

**Background**

A range of interventions are currently used in pressure ulcer management. Pressure relieving support surfaces aim to reduce the magnitude and/or duration of pressure between an individual and the support surface which is referred to as the “interface pressure”. Some support surfaces may also minimise friction and shear. Such support surfaces include cushions, mattress overlays, replacement mattresses or whole bed
replacements. The cost of these interventions vary widely; from over £30,000 for some bed replacement systems to less than £100 for some foam overlays. Information on the relative clinical and cost-effectiveness of this equipment is clearly needed to enable clinicians to make evidence-based decisions for their use.

Pressure-relieving surfaces can be divided into two categories: continuous low pressure (CLP) and alternating pressure (AP).

Continuous low pressure surfaces aim to mould around the shape of the individual to redistribute pressure over a greater surface area. Alternating pressure surfaces mechanically vary the pressure beneath the individual, so reducing the duration of the applied pressure.

CLP support surfaces can be grouped according to their construction:

- **Standard Foam**
  The conformability and resilience of foam products may vary considerably between manufacturers. Foam may be shaped, convoluted ("egg crate foam"), of various densities or a combination of densities

- **Visco-elastic Foam**
  Specialised foam available in varying densities that moulds to body shape in response to body temperature

- **Air filled**
  Inflatable mattress with no mechanical parts

- **Air fluidised**
  A constant flow of air is passed into a deep tank containing minute silicone beads retained by a permeable membrane. The agitated beads take on the properties of a fluid. Lying on the surface allows significant immersion and therefore redistribution of pressure

- **Low air loss**
  A constant flow of air inflates a row of permeable fabric cells. Manual or automatic adjustment of airflow allows significant immersion and therefore redistribution of pressure

- **Gel/Fluid**
  Fluid surfaces (e.g. water filled mattress) allow significant immersion and therefore redistribution of pressure. The density/viscosity of the gel/fluid will govern degree of immersion and how stable the support surface in terms of posture.

- **Combination products**
  Many CLP surfaces, particularly cushions, may utilise a variety of materials to provide optimum pressure relief and postural stability.

N.B. The type and construction of cover material may have a significant impact on the conformability of the surface.
Alternating pressure support surfaces provide pressure relief by inflating and deflating alternate air-filled cells. The inflated cells support the body while the deflated cells provide pressure relief. The duration and sequence of alternation varies between manufacturers. Such support surfaces are available as cushions, mattress overlays, and single- or multi-layer mattress replacements.

Pressure ulcer treatment strategies usually comprise a combination of pressure-relief (in the form of support surfaces), positioning and repositioning and wound management strategies including wound dressings, debridement techniques, physical therapies, antibiotics and antiseptics. Pressure ulcer management is therefore considered to be multi-faceted and a multi-faceted approach to care is strongly advocated in the research literature.

Objectives
To undertake a systematic review of pressure-relieving beds, mattresses and cushions in pressure ulcer treatment.

Specific questions to be answered were:
- Do pressure-relieving beds, mattresses and cushions increase the healing rate of existing pressure ulcers compared to standard support surfaces?
- Which types of pressure-relieving surface are most effective in the treatment of pressure ulcers: a) in different patient groups, b) and settings?

Criteria for considering studies for this review

Types of studies
Randomised controlled trials (RCTs) comparing beds, mattresses and cushions which measured pressure ulcer healing as an objective measure of outcome.

Types of participants
Patients with existing pressure ulcers (of any grade), in any setting.

Types of interventions
Studies which evaluated the following interventions for pressure ulcer treatment were included:
- alternating pressure mattresses/overlays
- standard foam mattresses
- specialised foam mattresses/overlays (e.g. convoluted foam, cubed foam)
- gel-filled mattresses/overlays
- fibre-filled mattresses/overlays
- water-filled mattresses/overlays
- air fluidised beds
- low air loss beds
- sheepskins
- turning beds/frames
- bead beds
- wheelchair support surfaces

**Types of outcome measures**
- Healing rates of existing ulcers: Trials were included if they measured healing by some objective method such as time to complete healing, or rate of change in the area/volume of the ulcer.
- Costs of the support surfaces
- Patient comfort
- Durability of the support surfaces
- Reliability of the support surfaces
- Acceptability of the support surfaces

Trials which only measured surrogate outcome measures such as interface pressure were excluded on the basis that interface pressure measurements have not been demonstrated to reliably predict the clinical performance of support surfaces.

**Search strategy for identification of studies**

The search strategy included all trials identified up to August 2004: Databases were searched initially in November 2003 and then updated on 24 June 2004

**Main Literature search**

Searches were not limited by study design but were limited to retrieve literature published in English, omit animal studies and letters, comments and editorial publication types.

**Methods of the review**

Full details can be found in the methods section (page 38)
References identified from searches were reviewed by two reviewers who jointly made a decision to include or exclude a study against the eligibility criteria. References were entered into a bibliographic software package. Details of eligible studies were extracted by the primary reviewer and summarised using a data extraction sheet. Data extraction was checked by a second reviewer.
Description of studies

Fifteen eligible randomised trials were identified. Fourteen trials involved patients with pressure ulcers and assessed the treatment efficacy of pressure-relieving supports [Allman 1987; Caley 1994; Clark 1999; Day 1993; Devine 1995; Evans 2000; Ferrell 1993; Groen 1999; Keogh 2001; Mulder 1994; Munro 1989; Russell 2000; Russell 2003; Strauss 1991]. One further included trial evaluated surface effects for both prevention and treatment of pressure ulcers in the same trial [Ewing 1964].

Two additional trials were identified that also evaluated pressure-relieving support surfaces for both the prevention and treatment of pressure ulcers [Bennett 1998; Lazzara 1991]. However, neither of these trials reported pressure ulcer healing data so were excluded from the review. One further eligible ongoing trial [Nelson 2003] was also identified and these results will be incorporated in future updates of the review.

The studies included a variety of patients and settings, for example those in nursing homes, care of the elderly, medical or surgical wards.

Only one trial evaluated the use of a cushion as a pressure relieving support surface. One trial assessed the use of sheepskins, and the remaining studies evaluated different mattresses, mattress overlays and beds.

Methodological quality of included studies

The methodological quality of the trials was generally poor. Details of the quality of each individual study are included in the Table of Included Studies (Appendix….). Adequate allocation concealment was evident in 9/15 (60%) of the trials: Allman 1987; Clark 1999; Day 1995; Devine 1995; Evans 2000; Ferrell 1993; Keogh 2001; Groen 1999; Russell 2003. In eight of the fifteen included trials the method of randomisation was unclear.

Blinded outcome assessment is rarely used in wound care studies and this was certainly the case in these evaluations of pressure relieving support surfaces. It can be difficult or impossible to disguise the surface that a patient is on for assessment of outcome, and patients are often too ill to be removed from their bed for assessment of their pressure areas. Nevertheless, some studies minimise bias in outcome assessment by having a second assessor and presenting inter-rater reliability data, or by presenting photographic evidence of pressure area status which can then be assessed by an assessor blinded to treatment. Of the 15 randomised trials in this review, we could be confident that some form of blinded outcome assessment had been used in only 4 trials [Allman 1987; Evans 2000; Strauss 1991; Russell 2003].
Importantly in pressure ulcer treatment trials it is essential to ensure baseline comparability for initial area of ulcers. A change in wound area is often expressed as the percentage change, which, unlike the absolute change in area, takes into account the initial size of the wound. For two wounds healing at the same linear rate (as measured by diameter reduction) percentage area calculations will show a larger change for a small wound than a big wound. The converse is true when the absolute change in area is measured, since for any unit reduction in wound radius a bigger area reduction will occur for a large wound. This has important consequences for the validity of trial results where there is poor comparability in initial wound size at baseline between the treatment groups. In large trials, randomised allocation should ensure that the mean wound size and variance in each group is similar. In a small trial random allocation is unlikely to result in an even distribution of wound sizes. In a trial where there is poor comparability between groups for wound size at baseline, and the outcome is based on the change in area, the result can only be considered valid if it is obtained either: against the anticipated direction of the bias for wound size; or where percentage area change and absolute area change are in the same direction. If baseline data are not given then it is not possible to determine the direction of bias and the validity of the result cannot be determined. There were 15 trials of beds, mattresses and cushions for treating pressure ulcers included in this review and of these:

- Eight presented data for baseline ulcer area [Allman 1987; Clark 1999; Day 1993; Devine 1995; Evans 2000; Ferrell 1993; Groen 1999; Munro 1989].
- Six further treatment trial reports did not present baseline ulcer areas [Caley 1994; Keogh 2001; Mulder 1994; Russell 2000; Russell 2003; Strauss 1991].
- One trial by Ewing [Ewing 1964] focused on the effect of sheepskin on resolving red skin and therefore the area of the damaged skin is less important.

The other major deficiency in most of the included trials was the small sample sizes used. Although seven reports described an \textit{a priori} sample size calculation, 12 of the 15 trials involved a total of 100 patients or fewer. The larger trials, involving over 100 patients, were Groen 1999 (120 patients); Russell 2000 (141 patients) and Russell 2003 (158 patients).

Quality was not used to weight the studies in the analysis using any statistical technique, however methodological quality was drawn upon in the narrative interpretation of the results. Methodological flaws are discussed for each study in the Table of Included Studies (Appendix, A).
Results

Results of dichotomous variables are presented as relative risk (RR) with 95% confidence intervals (CI). Relative risk has been used rather than odds ratios as event rates are high in these trials and odds ratios would give an inflated impression of the magnitude of effect (Deeks 1998). Relative risk is the rate of the event of interest, for example pressure ulcers healed, in the experimental group divided by the rate of this event in the control group and indicates the chances of pressure ulcers healing on the experimental treatment compared with the control treatment. As, by definition, the risk of an event occurring in the control group is 1, then the relative risk reduction associated with using an experimental treatment is 1-RR. The relative risk indicates the relative benefit of a therapy but not the actual benefit, that is it does not take into account the number of people whose pressure ulcer would have healed anyway, without treatment. The absolute risk reduction (ARR) can be calculated by subtracting the event rate in the experimental group from the event rate in the control group. The ARR tells us how much the reduction is due to the experimental treatment itself, and its inverse is the number needed to treat, or NNT. Thus a healing rate, for example, of 30% on a control treatment that was reduced to 15% with an experimental treatment, translates into an ARR of 30-15=15% or 0.15, and an NNT of 7. In other words, 7 patients would need to receive the experimental treatment to cure one additional pressure ulcer.

Secondary outcomes such as comfort, durability, reliability and acceptability were not well reported and valid and reliable measures for these concepts are under-developed. Where data was presented it appears in the Table of Included Studies (see section 14.1), however is not incorporated in the meta-analysis.

Air-Fluidised Therapy (AFT)

Three trials compared AFT with a range of conventional therapies for the treatment of pressure ulcers [Allman 1987; Munro 1989; Strauss 1991]. These studies measured outcomes in slightly different ways and none reported the variability around the mean healing rate data. A meta-analysis of two of these studies showed significantly enhanced pressure ulcer healing associated with air-fluidised beds when used in hospital [Allman 1987; Munro 1989] (see Figure 1). A home-based study [Strauss 1991] also showed a benefit from air-fluidised therapy on re-hospitalisation outcomes (see Figures 2 and 3). Munro 1989 showed no significant impact on nursing time associated with the use of air-fluidised beds compared with standard care (see Figure 4).

Figure 1:

<table>
<thead>
<tr>
<th>Study of sub-category</th>
<th>AF n/N</th>
<th>Standard Care n/N</th>
<th>RR (fixed) 95% CI</th>
<th>Weight %</th>
<th>RR (fixed) 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allman 1987</td>
<td>22/31</td>
<td>16/34</td>
<td>1.51 [0.99, 2.27]</td>
<td>57.43</td>
<td>1.51 [0.99, 2.27]</td>
</tr>
<tr>
<td>Strauss 1991</td>
<td>19/22</td>
<td>9/13</td>
<td>1.25 [0.84, 1.73]</td>
<td>42.57</td>
<td>1.25 [0.84, 1.73]</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>53</td>
<td>47</td>
<td>1.40 [1.04, 1.90]</td>
<td>100.00</td>
<td>1.40 [1.04, 1.90]</td>
</tr>
</tbody>
</table>

Total events: 41 (AF), 25 (Standard Care)
Test for heterogeneity: CH² = 0.44, df = 1 (P = 0.51), I² = 0%
Test for overall effect: Z = 2.20 (P = 0.03)
Low Air-Loss Therapy (LAL)

Three trials were identified which compared LAL with a foam mattress overlay [Day 1993; Ferrell 1993; Mulder 1994]. The combined analysis from two trials [Ferrell 1993; Mulder 1994]
showed pressure ulcer healing rates on the LAL bed were not significantly different to healing rates when using a corrugated foam overlay (see Figure 5). Only one trial has compared different types of low air-loss support surfaces [Caley 1994]. This trial showed no significant differences in healing rates between the two interventions but was small and of questionable quality.

Figure 5:

Alternating Pressure (AP)

A variety of alternating pressure (AP) supports are used in hospital and in the community. The depth of the air-cells and mechanical robustness can vary between support surfaces and these factors may be important in determining effectiveness. It is worth emphasising that most of the trials of AP supports did not adequately describe the equipment being evaluated, including the size of the air cells which may limit the utility of the evince to clinical practice.

One small trial of 41 patients [Devine 1995] compared the effectiveness of the Nimbus I DFS (composed of rows of figure-of-8-shaped cells) and the Pegasus Airwave for the treatment of existing pressure ulcers but found no significant difference. A more recent, larger trial [Russell 2000] also failed to demonstrate any significant difference in pressure ulcer healing between two newer AP support surfaces, the Nimbus 3 and the Pegasus Cairwave therapy system (see Figure 6).
In a study by Evans et al [Evans 2000], which was conducted in both hospital and nursing home patients, an alternating pressure mattress replacement system (Huntleigh Nimbus 3) resulted in no significant improvement in any measure of wound surface area when compared with either another alternating pressure mattress replacement system for hospital patients (Pegasus Biwave, Pegasus Airwave, or AlphaXcell) or an alternating mattress overlay for nursing home patients (AlphaXcell or Quattro).

The large (158 patients) Russell 2003 trial also compared the Nimbus 3 alternating pressure mattress with a static fluid overlay mattress, RIK static, and again found no significant difference in rates of pressure ulcer healing (see Figure 7). However, in this trial the co-intervention of re-positioning frequency was not standardised, and patients could request additional turning. As this variable appears to be disproportionate between the groups, the lack of treatment effect may be due to either the non-effect of the experimental support surface and/or the effect of the differential co-intervention distribution.

Figure 7:

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>AP n/N</th>
<th>Fluid overlay n/N</th>
<th>RR (fixed) 95% CI</th>
<th>Weight %</th>
<th>RR (fixed) 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>01 AP vs fluid overlay mattress</td>
<td>Russell 2003</td>
<td>60/83</td>
<td>56/75</td>
<td>100.00</td>
<td>0.97 [0.80, 1.10]</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>95</td>
<td>75</td>
<td>100.00</td>
<td>0.97 [0.80, 1.10]</td>
<td></td>
</tr>
<tr>
<td>Total events: 60 (AP), 56 (Fluid overlay)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for heterogeneity: not applicable</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect: Z = 0.34 (P = 0.74)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

One study involving only 25 patients [Clark 1999] found no significant difference between a dry flotation and an alternating pressure cushion in the number of ulcers completely healed, as measured by either the proportion of ulcers healed (see Figure 8) or the rate of change in pressure ulcer surface area for either superficial (see Figure 9) or deep (see Figure 10) ulcers.

Figure 8:
Continuous Low Pressure supports (CLP)

One small trial which used standard hospital mattresses with and without sheepskin overlays was inconclusive and of poor quality [Ewing 1964].

A trial of 120 nursing home patients with grade 3–4 ulcers [Groen 1999], found no difference in ulcer healing rates between foam replacement mattresses and the Secutex water mattress overlay (see Figure 11).

Figure 11:

Review: Beds, mattresses and cushions for pressure sore treatment
Comparison 01: Comparisons between continuous low pressure supports
Outcome: 01 Pressure sore healing

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>CLP1 n</th>
<th>CLP2 n</th>
<th>RR (fixed) 95% CI</th>
<th>Weight</th>
<th>RR (fixed) 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>01 foam replacement mattress vs water mattress overlay</td>
<td>27/60</td>
<td>29/60</td>
<td>100.00 0.93 [0.63, 1.37]</td>
<td>60/60 0.93 [0.63, 1.37]</td>
<td>0.37 (P = 0.71)</td>
</tr>
</tbody>
</table>
In the Keogh 2001 trial a bed that enabled individual profiling was compared with a standard hospital bed, both also with a pressure reducing foam mattress or cushion. In this small trial (14 patients) the proportion of those with existing grade 1 ulcers were significantly improved using the profiling bed (see Figure 12). However these results should be interpreted with caution as they are only a small subgroup of the 100 patients randomised in the trial for which further data are unavailable.

**Figure 12:**

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>profiling bed n/N</th>
<th>standard bed n/N</th>
<th>RR (fixed)</th>
<th>Weight %</th>
<th>RR (fixed) 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Keogh 2001</td>
<td>4/4</td>
<td>2/10</td>
<td>100.00</td>
<td>5.00</td>
<td>[1.45, 17.2]</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>4</td>
<td>10</td>
<td>100.00</td>
<td>5.00</td>
<td>[1.45, 17.2]</td>
</tr>
<tr>
<td>Test for heterogeneity: not applicable</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect: Z = 2.54 (P = 0.01)</td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

**Discussion**

Despite the frequency of pressure ulcer incidence and the myriad of treatment modalities, this review demonstrates the paucity of good quality evidence that guides current clinical practice for the selection of pressure relieving support surfaces.

The confidence with which we can draw firm conclusions from the studies detailed in this review is greatly tempered by (a) the poor quality of many of the trials and (b) the lack of replication of most comparisons.

There is some evidence to show that air fluidised supports reduce the size of more established pressure ulcers compared to a modified alternating pressure support, standard care (standard bed with CLP supports; sheepskin, gel pads, air-filled supports, water filled mattresses and high density foam pads).

There is no conclusive evidence to support the superiority of either alternating pressure support surfaces or continuous low pressure supports in the treatment of existing pressure ulcers.
comparability and lack of blind outcome assessment further reduce the confidence with which we can regard many of the individual study findings. Future trials should consider the findings of this review and address these deficiencies.

Cost effectiveness of pressure-relieving support surfaces (beds, mattresses and overlays), mobility and positioning

Three economic evaluations of pressure-relieving support surfaces were identified for review (Branom et al, 2001; Ferrell et al, 1995; Strauss et al, 1991). One study was a full economic evaluation (Ferrell et al, 1995), the other two were partial economic evaluations.

Ferrell et al (1995) conducted a cost-effectiveness analysis comparing low air loss therapy beds to conventional foam mattresses used in nursing homes in the United States (see data extraction table 25). Patients with grade 2, 3 or 4 pressure ulcers were followed up until complete heal, death or transfer to another faculty. Effectiveness data to compute this included a statistically significant reduction in surface area of grade 3 and 4 pressure ulcers across the two treatments (9.9 mm² per day vs. 0.7 mm² per day, p<0.02). Pressure ulcers took an average of 75 days to cure for low air loss therapy and 172 days for conventional foam mattresses. Use of the pressure-relieving support surfaces and associated nurse time was costed. While the lease cost per day of the low air loss mattresses evaluated was higher than the cost per day of the conventional foam mattress, on average the low air loss bed was cost-saving due to a much shorter time to heal.

Final results were reported as cost per added day free of a pressure ulcer and were obtained by dividing the additional cost of the low air loss therapy by the additional days without an ulcer. The cost-effectiveness estimate for low air loss therapy was $26 per added day free of a pressure ulcer (1992 prices). No uncertainty associated with this estimate was reported. However, a few one-way sensitivity analyses were conducted and findings were sensitive to the lease cost of the low air loss bed as well as patient and pressure ulcer healing characteristics.

The economic evaluation was based on an analysis of the RCT reported in Ferrell et al (1993) that is included in the clinical effectiveness review of pressure-relieving support surfaces. In the clinical effectiveness review the healing rates of this trial were combined with the Mulder et al (1994) results and this revealed that pressure ulcer healing rates were not statistically significantly different to healing rates using a corrugated foam overlay.

Branom et al (2001) conducted a cost-consequence analysis comparing constant force technology with low air loss therapy beds used in patient care in the United
States (see data extraction table 24). Patients with grade 3 or 4 pressure ulcers were followed up for a maximum of eight weeks and study exit criteria included discharge from inpatient status, flap surgery and death. Effectiveness results included: on average a smaller size pressure ulcer was recorded at discharge from the study for the constant force technology group (6.6cm$^3$ vs. 24.6cm$^3$), the average amount closed at discharge from the study was higher (25.8cm$^3$ vs. 22.2cm$^3$), the average rate of closure per week was faster (3.5cm$^3$ vs. 2.8cm$^3$), the average proportion of pressure ulcers closed (60.0% vs. 39.6%) and a higher average proportion of pressure ulcers closed per week (9.0% (+/-4.8) vs. 5.0% (+/-3.7)) for the constant force technology group compared to the low air loss group. The purchase price of constant force technology was $1,080 (price year not stated) whilst the daily rental cost of the low air loss mattress was $35 per day that totalled to $1,960 over the maximum eight week follow-up period.

In general, although costs and outcomes were not synthesized, results suggest that constant force technology dominated low air loss therapy beds since associated costs were lower and effects better. A number of caveats should be considered when drawing conclusions from this study. This is the only economic evaluation to assess the effectiveness of constant force technology beds. The study is based on a clinical trial but patients were allocated to treatments sequentially which is not truly random and can introduce bias. Only the costs of the mattresses were included and the use of nursing time or other resources used in conjunction with the interventions were omitted. The total cost of the low air loss mattress was dependent on the length of use. Very limited statistical analyses were reported to investigate uncertainty associated with the results.

Strauss et al (1995) conducted a cost-consequence analysis comparing air-fluidized therapy to conventional therapy in the United States (see data extraction table 26). Patients with grade 3 or 4 pressure ulcers were followed up in the RCT over a considerable length of time (36 weeks). However, only 50% of patients receiving air-fluidized therapy completed the study compared to 56% in the conventional therapy group. Two nurses independently assessed outcomes, blind to treatment groups. For each patient who completed the 36 week regimen and for whom interpretable photographs were available, the nurses assessed the photographs and clinical notes. They categorised each patient’s pressure ulcer as (i) improved, (ii) unchanged, (iii) worse or (iv) not assessable. A higher proportion of pressure ulcers in the air-fluidised bed group were classified as improved (82% classified as improved by one nurse versus 91% by the other nurse for the air-fluidized bed group compared to 77% or 62% for the conventional therapy group), however differences were not significant.

---

2 These categories were defined explicitly for the nurses
Additionally, a small proportion of pressure ulcers in this group were classified as unchanged.

The cost of treatments used was computed from the medical charges perspective and the Medicare DRG and doctor payment perspective. Cost per patient for the former was $29,016 versus $34,747 for air-fluidized therapy compared to conventional therapy respectively and this was not statistically significantly different. Cost per patient for the latter was $16,415 compared to $16,800 for air-fluidized therapy compared to conventional therapy respectively and again this was not statistically significantly different.

Costs and outcomes were not synthesized and the cost-effectiveness implications are not straightforward to determine. Overall, costs per patient were similar across groups in spite of significant inpatient cost differences. No significant improvement in pressure ulcers was detected across the two groups either.

The economic evaluation was included alongside the results of RCT on which it was based and these results are reported in the clinical effectiveness review of pressure-relieving support surfaces. There the air-fluidized therapy showed a statistically significant benefit compared to standard care on re-hospitalisation outcomes. Typically such an outcome would not be used in an economic evaluation since the cost of hospital stays are factored into the cost analysis.

**Overview of pressure-relieving support surfaces**

Although the three studies reviewed are based on level one or two effectiveness evidence, the economic evaluation quality assessments (see appendix C) show that there were a number of study limitations. Data collection aspects for the Branom et al (2001) and Ferrell et al (1995) were moderate, but resource use and cost data for the Strauss et al study (1991) was less strong. Analysis and interpretation of results were not strong for any of the studies, particularly in terms of exploration of uncertainty associated with costs and outcomes reported.

**Evidence summaries**
<table>
<thead>
<tr>
<th>Level of evidence</th>
<th>Evidence statement</th>
</tr>
</thead>
<tbody>
<tr>
<td>1++</td>
<td>All pressure relieving support surfaces: No conclusive research evidence to indicate which pressure relieving support surfaces are most effective in the treatment of pressure ulcers.</td>
</tr>
<tr>
<td>1+</td>
<td>Air-Fluidised therapy: some evidence from meta-analysis of two trials indicate that ulcer healing was improved compared to modified AP and a range of other CLP supports in adults with grade 2–4 pressure ulcers (conventional therapy).</td>
</tr>
<tr>
<td>1+</td>
<td>Low-Air loss therapy: evidence of no difference for complete ulcer healing found when compared to foam mattress overlays in individuals with grade 2–4 pressure ulcers.</td>
</tr>
<tr>
<td>1++</td>
<td>Alternating pressure therapy: evidence of no difference in complete ulcer healing found comparing different alternating pressure support surfaces. Evidence of no difference found compared to static fluid overlay mattresses or cushions in the elderly with grade 2 or greater pressure ulcers.</td>
</tr>
<tr>
<td>1+</td>
<td>Continuous Low Pressure therapy: evidence of no difference in ulcer healing rates for water-filled mattresses compared with foam replacement mattresses in adults with grade 3 pressure ulcers. Limited evidence of difference in ulcer healing for profiling beds compared with standard hospital beds in adults with grade 1 or greater pressure ulcers.</td>
</tr>
</tbody>
</table>

**Patients with existing pressure ulcers**

**Recommendations**

Patients with pressure ulcers should have access to appropriate pressure relieving support surfaces such as mattresses and cushions 24 hours a day and this applies to all support surfaces. [D]

Decisions about choice of pressure relieving support surfaces for patients with pressure ulcers should be made by registered health professionals that have undergone appropriate training and have demonstrated competence. [D]
Initial choice and subsequent decisions, following re-assessments, related to the provision of pressure relieving support surfaces for patients with pressure ulcers should be based on: [D]
- Ulcer assessment (severity)
- Level of risk: from holistic assessment
- Location and cause of the pressure ulcer
- General skin assessment
- General health status
- Acceptability and comfort for the patient
- Lifestyle of the patient
- Ability of the patient to reposition themselves
- Availability of carer/health professional to reposition the patient

There is no conclusive research evidence that any one pressure relieving support technology is superior to another. However professional consensus recommends that:

1. All individuals assessed as having a Grade 1-2 pressure ulcer should, as a minimum provision, be placed on a high specification foam mattress with pressure-reducing properties combined with very close observation of skin changes and a documented positioning and repositioning regime. [D]
   - Consider AP (replacement or overlay) or sophisticated CLP system (e.g. low air loss, air fluidized, viscous fluid) if there is any perceived or actual deterioration of affected areas or further pressure ulcer development. [D]

2. All individuals assessed as having Grade 3-4 pressure ulcer (including intact eschar where depth – and therefore grade – cannot be assessed) should, as a minimum provision be placed on an alternating pressure mattress (replacement or overlay) or sophisticated continuous low pressure system (e.g. low air loss, air fluidised, viscous fluid). [D]

3. Alternating pressure equipment should be allocated according to a patient’s weight not level of risk or grade of ulcer. Patients within the weight range of alternating pressure overlays should be supplied AP overlays not replacement systems. Replacement systems should be allocated to patients who exceed the weight limit of the overlay used. (N.B. In order to ensure maximum effect the inflated cells of the overlay must support the body weight of the patient in all bed positions (during use of backrest, knee break, etc) and all patient positions (sitting up, side lying, etc)) [D]

Guideline Development Group Commentary

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Commentary.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Air-Fluidised Therapy</td>
<td>AFT is now rarely used in clinical practice and there is little evidence of difference over AP or many other CLP surfaces and there may be considerations in terms of patient positioning and moving and handling.</td>
</tr>
</tbody>
</table>
### Low-Air Loss therapy

Basic mattress replacement versions often require user calibration (barrel test) which is very subjective. Tends to favour pressure relief at sacrum at expense of the head and heels. Requires constant power / pumped air supply (deflates if power supply removed) placing patient at risk whilst being transported. High end systems have more sophisticated pressure monitoring but are often integrated into bed frames and are therefore expensive for general use.

Mechanical robustness is an artefact of old trials in early days of technology. Small cell systems are rarely used.

AP is widely used in clinical practice however more research is required to understand the ideal depth, inflation pressure, cycle time, etc.

### Alternating Pressure

Mechanical robustness is an artefact of old trials in early days of technology. Small cell systems are rarely used.

AP is widely used in clinical practice however more research is required to understand the ideal depth, inflation pressure, cycle time, etc.

### Research recommendations.

Independent, well-designed, multi-centre, randomised, controlled trials are needed to compare the clinical and cost effectiveness of different types of pressure-relieving support surfaces to treat existing pressure ulcers for patients in a variety of settings. In particular, this research should aim to compare:

- alternating pressure support surfaces with continuous low pressure supports.

Future research must address the methodological deficiencies associated with much of the research described in this review; particular attention should be paid to:

- description of inclusion and exclusion criteria used to derive the sample from the target population
- evidence of an *a priori* sample size calculation
- evidence of allocation concealment at randomisation
- description of baseline comparability of treatment groups
- evidence of blinded outcome assessment
- clear description of main interventions
- adequate description of associated care
The management of pressure ulcers in primary and secondary care
DRAFT full version for 1st round of consultation 5 Jan – 2 Feb 2005

Royal College of Nursing and National Institute for Clinical Excellence

• withdrawals reported by treatment group with reasons

Patients should be:
• truly randomised (with concealed allocation)
• should be of sufficient size to detect clinically important differences have clear criteria for measuring outcomes
• blinded interventions and assessment
• adequate follow-up
• appropriate statistical analysis

Measure patient experiences of pressure-relieving equipment:
• comfort
• pain
• ease of use
• appropriateness for users and settings
• durability of equipment.

The studies should also have evaluations of the cost-benefit trade off of pressure ulcer treatment alternatives undertaken.

Dressings and topical agents in the treatment of pressure ulcers

The methods described in this review are those used to update the following systematic review as they apply to pressure ulcer treatment:


Background

Technological advances have extended the range and complexity of dressing products, making meaningful classification increasingly difficult

For the purposes of this document dressings are divided into five basic categories

1) Contact layers. The key features of a contact layer should be their ability to prevent adherence to the wound bed and allow free drainage of exudate. These materials tend to be used on superficial or lightly exuding wounds, for example Paraffin gauze (Tulle gras), knitted viscose, silicone coated fabric dressings

2) Passive dressings

Dressings that create a local wound environment conducive to healing by controlling the local wound environment (see properties of an ideal dressing) but which do not change their physical state or directly modify or interfere with the physiology of the wound. Such dressings are commonly employed to control exudate but they may also be used for example to prevent contamination or control odour.

Examples include films, foams, hydrogels,

3) Interactive dressings

Dressings that change their physical state in contact with wound exudate. Such products commonly form a gel-like covering on the wound surface that is claimed to promote healing. Examples include hydrocolloids, alginates, and products containing carboxymethylcellulose fibres

4) Active dressings

Products that aim to directly influence the physiology or biochemistry of the wound healing process

A: Contain physiologically active components that act at a biochemical level in the wound bed. Typically influencing cell growth or correcting chemical deficits for example growth factors, collagen, hyaluronic acid

B: Skin grafts

The transplanting of human or animal skin onto a wound bed. May be patients own (auto graft), donated (allograft) or animal – usually pig (Xenograft)

C: Tissue engineered products

Also known as skin substitutes or skin replacements. Products that replicate a layer (or layers) of human skin

5) Antimicrobial dressings

Dressings containing antimicrobials agents.

for example iodine, chorhexidine silver, honey
A number of characteristics of the ‘ideal dressing’ have been described by pharmacists and many manufacturers refer to these characteristics when marketing their products. These are outlined on page 103. However, as this is an ideal list, none of the dressings in current use fulfill all of the criteria.

Gauze

Woven or non-woven fabric produced from cotton, viscose, polyester, or other suitable fibres formed into a swab. Should not be used as a primary dressing as it adheres strongly to wound bed due to capillary looping into the structure.

Contact layers

Includes simple products such as paraffin gauze (tulle gras) (cotton or cotton and viscose woven fabric, which has been impregnated with white soft paraffin) and knitted viscose dressings. More advanced products such as silicone-coated net dressings and hydrocolloid or gel impregnated viscose nets are now generally preferred. Contact layers have no absorbent properties and generally require a secondary absorbent layer.

Wound dressing pads

The basic wound dressing pad consists of an absorbent layer such as cellulose fibre enclosed in a sleeve of a nonwoven fabric. Some pads have a perforated plastic film layer to reduce adherence to the wound surface (e.g. Melolin, Smith & Nephew Healthcare Ltd).

Semi-permeable film dressings

Consist of a transparent polyurethane film coated with a thin layer of adhesive to enable the dressing to adhere to intact skin but not the wound surface. These dressings are permeable to moisture vapour and gases but impermeable to water and microorganisms.

Hydrocolloid Dressings

These dressings comprise an absorbent gel-forming mass, commonly consisting of carboxymethylcellulose, which is contained...
within their structure together with elastomers and adhesives. The dressings are usually presented in the form of a self-adhesive wafer that absorbs wound exudate and traps it in the form of a gel. Hydrocolloid colloid dressings are generally occlusive in their intact state but become semipermeable once in contact with wound fluid.

**Hydrogels**

These consist of hydrophilic polymer commonly made from carboxymethylcellulose or modified starch dissolved or dispersed in water or a mixture of water (80%) and propylene glycol (20%) as a humectant and preservative. They have the ability to absorb exudate or rehydrate slough or necrotic tissue in a wound depending on whether the wound is exuding heavily or dry and necrotic (for example Intrasite®, Smith & Nephew Healthcare Ltd).

**Alginate Dressings**

These are derived from seaweed, usually prepared as the calcium salt of alginic acid. When in contact with serum, wound exudate or solutions containing sodium ions, the insoluble calcium alginate is partially converted to the soluble sodium salt, and a hydrophilic gel is produced.

**Foam dressings**

Most foam dressings are designed to absorb and retain fluid. Modern foams are available in a variety of formats (shaped, adhesive, non-adhesive, bordered, cavity) with varying levels of absorbency and permeability.

**CMC Fibrous dressing**

A primary wound dressing made from sodium carboxymethylcellulose fibres woven into a fleece similar in appearance to the alginates.

**Capillary dressing**

A three-layer, non-woven/woven, low-adherent dressing, which comprises 100% polyester filament outer layers, 65%/35%poly/cotton fibres.
The functions of an “ideal” dressing

- Allow excess exudate to be removed from the wound surface
- Provide a moist micro-environment
- Be sterile/contaminant free
- Do not shed dressing material in the wound
- Reduce wound pain
- Easy to remove and apply
- Do not cause allergic reactions
- Cause no trauma when removed
- Be impermeable to micro-organisms
- Provide thermal insulation

Topical preparations

Topical preparations eligible for inclusion in the present review include growth factors, oxygen-free radical scavengers, zinc oxide paste, tri-peptide copper complex, and silver sulphadiazine cream. Topical antiseptics and antibiotics are not covered here but have been reviewed elsewhere.

Several of these preparations are applied to the wound to compensate for a deficiency in a particular element considered necessary for wound healing. An example of such a topical agent is zinc oxide; zinc deficiency has been associated with poor wound healing. Other preparations are thought to modify the wound environment by killing harmful bacteria (for example silver sulphadiazine).

Debridement

Debridement involves the removal of dead or necrotic tissue or other debris from the wound to reduce the wound’s biological burden. A number of terms are used to describe dead tissue in wounds:

- Necrosis
- Slough
- Eschar

There are six main methods of debridement:

- autolytic
- enzymatic
- sharp (or surgical)
- chemical
- mechanical
Debridement agents

All non-mechanical debridement agents, including the use of dressings and larval therapy were included in this review. These include

- Dextranomer polysaccharide beads or paste
- Cadexomer iodine polysaccharide beads or paste
- Hydrogels
- Enzymatic agents
- Adhesive zinc oxide tape

Mechanical debriding agent wet-to-dry dressings (saline gauze) were also included in this review.

Other types of mechanical debriding agents, such as surgery or sharp debridement were excluded from this review and will be examined separately.

Non-mechanical debridement techniques

Numerous non-mechanical techniques are available for wound debridement and many are easy to apply and may have additional properties that are beneficial for wound healing. Such interventions include hydrogels and hydrocolloids. These materials have largely replaced enzymatic agents and dextranomer beads.

Several different enzyme preparations are available that digest slough and necrotic tissue. In the UK, only the formulation containing streptokinase and streptodornase (Varidase Topical®, Wyeth Laboratories) is licensed for use. This enzyme breaks down the proteins fibrin and pus cells but is ineffective against collagen and elastin, the main structural components of skin and by extension necrotic eschar/slough.

Other enzymatic debriding agents are available and used internationally; these include trypsin and collagenase. Dextranomer polysaccharide is supplied as anhydrous, porous beads with a diameter of 0.1–0.3 mm or as a paste. The beads are highly hydrophilic and rapidly absorb exudate from a necrotic sloughy mass. Prostaglandins, hormones and other relatively small molecules enter the matrix of the beads, while larger particles such as bacteria and wound debris become concentrated at the surface of the dextranomer layer. When the beads are changed by washing with saline, the absorbed and trapped necrotic material is removed. Cadexomer iodine is similar to dextranomer, consisting of small spherical beads that...
are hydrophilic in nature. The beads are made from a modified starch infused with iodine at a concentration of 0.9%. Absorption of fluid from the wound results in a slow controlled displacement of iodine from the matrix, which acts as a bactericidal agent. The slow and consistent release of iodine overcomes the problem of iodine inactivation by protein absorption in the wound. The antibacterial property, biodegradability and high rate of fluid absorption distinguish cadexomer iodine from dextranomer. Bead dressings are difficult to apply and remove and are for this reason now generally used in the form of pastes.

Hydrogels are a group of agents that were primarily developed as debriding agents. These gels are biologically inert and have a significant water content. They complement the body's natural debriding process by providing an advantageous environment for autolysis, while still acting to preserve living healthy tissue. The hydrogel is usually applied directly into the wound bed and held in place by a non-adherent dressing. Once the gel is fully hydrated it is unable to absorb the copious quantities of exudate that are released by some wounds. For this reason hydrogels are often used in conjunction with a highly absorbent dressing. In addition to the amorphous gel, hydrogels are also available in a sheet form. Several types of hydrogel are available manufactured under different trade names (Intrasite® Gel, Smith & Nephew Healthcare Ltd; Sterigel®, Seton Healthcare Group plc; Granugel®, CovaTec UK Ltd).

Larval therapy, also known as maggot therapy or biosurgery, exploits the natural feeding behavior of maggots of Lucilia sericata, the common green bottle, for the benefit of the patient. When placed in a wound maggots have the ability to selectively rapidly remove slough and necrotic tissue leaving healthy tissue intact. They also ingest living bacteria from within the wound which are killed as they pass through the insects gut.

Both sharp and surgical debridement are included in a separate review. In clinical practice there is wide variation in the use of debriding agents and no consensus on which agent is most appropriate for use in pressure ulcers.

**Mechanical debriding agents:**
The use of physical force to remove necrotic tissue and debris from the wound surface. ‘Simple’ methods include the use of wet-to-dry dressings which remove tissue however unselectively, that is healthy and unhealthy tissue. Other methods include wound irrigation – cleansing and pressure irrigation, whirlpool therapy, ultrasonic therapy and laser therapy.
Objectives

To systematically assess the evidence for the effectiveness of dressings and topical agents in the treatment of existing pressure ulcers.

Criteria for considering studies for this review

Types of studies

Only randomised controlled trials (RCTs) were included in this review. Studies that did not employ true random allocation of participants to treatment groups, such as quasi-experimental designs, were excluded. The units of allocation had to be patients or lesions. Studies in which wards, clinics or physicians were the units of allocation were excluded because of the possibility of non-comparability of standard care. Both published and unpublished studies were included.

Types of participants

Studies that recruited people with existing pressure ulcers, of any grade or severity, were eligible for inclusion on the review. The study could be in any setting including hospital, clinic, community facilities, or home.

Types of interventions

Trials in which a dressing or topical agent was compared with another dressing or topical agent(s) or were compared with a placebo, usual care, or no treatment, were eligible for inclusion in the review. All types of dressings or topical agents (as described in the Background section) were eligible for inclusion with the exception of topical antimicrobial agents (in separate review). Non-dressing mechanical debriding agents, sharp and surgical debridement, were excluded.

Types of outcome measures

The primary outcome was wound healing.
Search strategy for identification of studies

Clinical effectiveness searching – debridement

Main Literature search
Searches were undertaken to update the following Health Technology Assessment reviews for the aspects which were relevant to pressure ulcers:


Clinical effectiveness searching – dressings

Main Literature search
Searches were undertaken to update the following Cochrane review:

Searches were limited by study design to retrieve randomised controlled trials. Searches were also limited to retrieve literature published in English, omit animal studies and letter, comments and editorial publication types.

Databases were searched in April 2004 and searches were updated in August 2004.

The strategies are listed in Appendix D

Description of included studies

Sixty eligible randomised trials, involving 3,230 participants, were identified for inclusion in the review.
Most of the trials were conducted in either hospital or an aged care facility, hence most of the enrolled patients were elderly, around 70–80 years old. There was a range of pressure ulcer severity included in the trials with baseline area at enrolment being anywhere from 1–200 cm². This reflects the differing ulcer stages for participants in the trials. On average, ulcers would be at the grade III–IV at commencement of treatment. Thus, many of the ulcers treated within the included trials had persisted for between 3 and 12 months without resolution.

In studies of pressure ulcer treatment it is extremely important for trialists to report on the baseline comparability of the treatment groups for important variables such as baseline ulcer size. A change in wound area is often expressed as the percentage change, which unlike the absolute change in area, takes into account the initial size of the wound. For two wounds healing at the same linear rate (as measured by diameter reduction) percentage area calculations will show a larger change for a small wound than for a big wound. The converse is true when the absolute change in area is measured, as for any unit reduction in wound radius, a bigger area reduction will occur for a large wound. This has important consequences for the validity of trial results where there is poor comparability in initial wound size at baseline between the treatment groups. In large trials, randomised allocation should ensure that the mean wound size and variance in each group is similar. In a small trial random allocation is unlikely to result in an even distribution of wound sizes. This problem will persist in small trials, even when the average wound size appears to be comparable between groups, because the distribution of wound sizes about the mean is likely to differ. In a trial where there is poor comparability between groups for wound size at baseline, and the outcome is based on the change in area, the result can only be considered valid if it is obtained either against the anticipated direction of the bias for wound size, or where percentage area change and absolute area change are in the same direction. If baseline data are not given then it is not possible to determine the direction of bias and the validity of the result cannot be determined. Twenty-eight of the 60 trials included in this review presented data on baseline ulcer size.

In some studies there were concurrent intervention and follow-up periods, ranging from 2 to 25 weeks. Other studies delivered the intervention for less than the full follow-up period. Twenty-two of the 61 included studies used photographic techniques as part of their objective measurement of wound healing. Others used planimetry (n=22), observer opinion of improvement (n=5), and other methods (n=13) such as water displacement techniques and rating scales. Many trials used a combination of these methods, whilst others failed to describe their assessment techniques in any detail.
Topical interventions were assessed in 31 studies. One trial (n=14) compared a topical agent against no treatment, 9 trials (n=405) assessed a topical agent vs a placebo, 7 trials (n=548) compared one topical agent versus another, 7 trials (n=197) examined topical agents compared with traditional dressings, and a further 7 trials (n=444) compared topical agents with modern dressings. Modern dressings were compared with traditional dressings in 12 trials (n=573), with other modern dressings in 16 trials (n=994) and against a placebo in one trial (n=49). The Table of Comparisons which details the individual comparisons examined under these broad groupings (Appendix H).

There were 22 studies that were excluded from the review. The citations and reasons for exclusion are detailed in the Table of Excluded Studies (Appendix I). The most common reasons for exclusion were non-randomised study design or a lack of objective outcome measures reported.

A further 16 studies are still awaiting assessment, mainly due to publication only as abstracts without a subsequent full publication, and thus insufficient information to assess inclusion criteria or to extract results data. The citations and reasons for exclusion are detailed in the Table of Studies Awaiting Assessment.

Methodological quality of included studies

Details of the quality assessment of each study are outlined in the Table of Included Studies (see section 14). The key components of quality that were assessed included \textit{a priori} sample size calculations, allocation concealment, masking of outcome assessment and reporting of withdrawals by treatment group.

Thirty-six of the 60 included studies reported their withdrawal rates and reasons by treatment group. Withdrawals were common, and 34 studies reported withdrawals by treatment group and gave reasons for these withdrawals. There was sufficient data reported in 35 studies to enable results to be extracted and analysed on an 'intention-to-treat' basis.

No attempt was made to weight the studies in the analysis using any statistical technique, however methodological quality was drawn upon in the narrative interpretation of the results.

Results

Many of the comparisons included in this review include only one eligible trial and many of these are of poor methodological quality. Hence, robust conclusions cannot be drawn from such results.

Topical agents versus no treatment

There was only one trial that was included in this comparison category. The incremental benefit of topical insulin (twice a day for five days) in addition to routine supportive nursing care was assessed in a single small trial [van Ort 1976]. The statistical analysis presented suggested that the addition of insulin resulted in a significant improvement in both the healing rate and the number of days that treatment was required. However, this trial was small (n=14) and no primary data or findings were presented, so firm conclusions cannot be drawn from these results.

Topical agents versus placebo


A meta-analysis of available data on complete ulcer healing from four of these seven trials (n=241) showed that overall, compared to placebo, there was no evidence that topical growth factors significantly improved healing rates (relative risk for complete healing with growth factor treatment 1.51; 95% confidence interval 0.96 to 2.38, see below in Figure 1.
However, as there is considerably heterogeneity in these results, both statistical (I² statistic 78.7%) and clinical, an assessment was made of the two trials [Mustoe 1994, Rees 1999] that used the same growth factor (rhBDGF-BB) in the same dosages (100 µg/ml, 300 µg/ml) compared with placebos. Both dosages of this topical agent showed evidence of improvement in ulcer healing (relative risk for ulcer healing with 100 µg/ml rhBDGF-BB 7.17; 95% confidence interval 1.40 to 36.69, see Figure 2; relative risk for ulcer healing with 300 µg/ml rhBDGF-BB 6.23; 95% confidence interval 1.17 to 33.34, see Figure 3). It should be noted that, although these are statistically significant differences, the confidence intervals are wide, suggesting the results should be interpreted with caution.

No other data from this category of studies was suitable for pooling using meta-analysis.

Overall, topical growth factors did appear to reduce mean ulcer size. Robson and colleagues [Robson 1992a, Robson 1992b, Robson 1994, Robson 2000] found increased reduction in wound size or volume with increasing concentrations of various growth factors (see Table of Included Studies for individual results, section 14).
Figure 3:

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Healing</th>
<th>Weight</th>
<th>Healing Rate (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.5S murine nerve growth factor</td>
<td>2.33</td>
<td>50%</td>
<td>0.04 to 0.99</td>
</tr>
<tr>
<td>Placebo</td>
<td>2.5S murine nerve growth factor</td>
<td>2.33</td>
<td>50%</td>
</tr>
</tbody>
</table>

Figure 3: A recent trial that assesses the effect of 2.5S murine nerve growth factor compared with placebo [Landi 2003] found that this treatment reduced ulcer area by 74 cm² in the treatment group, compared to 49 cm² for those receiving placebo. This topical agent also improved the rate of complete ulcer from 1 in 18 in the placebo group to 8 of 18 in the treatment group (see Figure 1).

Topical agents versus topical agents

One trial compared topical collagenase with a topical fibrinolysis agent [Pullen 2002] reported no significant change in wound area, healing or depth, but primary data for these results were not given. The one small trial (n=28) that compared topical collagenase papain-urea ointment [Alvarez 2002] showed that the percentage of non-viable tissue after 4 weeks of treatment was only 1% in the collagenase group compared with 75% in the group that received papain-urea ointment (weighted mean difference -74.00; 95% confidence interval -121.17 to -26.83). Another trial which compared collagenase paste (Santyl) with dextranomer polysaccharide paste (Debrisan) [Parish 1979] showed no difference in ulcer healing rates (relative risk for ulcer healing for dextranomer paste 4.71; 95% confidence interval 0.66 to 33.61).

One larger trial which compared collagenase ointment in two dosing regimes [Burgos 2000a] (24 versus 48 hours) showed no difference in healing rates (relative risk of ulcer healing 1.33; 95% confidence interval 0.63 to 2.830).

Although evidence in the form of RCTs is lacking, many clinicians believe that debridement facilitates wound closure by removing necrotic tissue that acts as a barrier to new tissue growth. This suggests that if debridement really does aid wound closure, then the effectiveness of a debriding agent should be measured by an outcome based on wound healing. Even though the debriding agent is not necessarily used throughout the entire healing process, an outcome measure based on healing remains valid as long as both comparison groups follow a similar schedule of nursing care after the debridement period. In this way, any difference in healing rates between groups can be attributed to the debriding agent used. Some researchers, however, have attempted to estimate the effectiveness of these agents by measuring...
the degree of debridement expressed as the percentage area of wound covered in necrotic material. This measurement may not be a reliable indication of treatment effect as the extent of debridement does not appear to have been scientifically validated as a surrogate or proxy measure of wound healing.

Dextranomer polysaccharide paste (Debrisan) was compared with a hydrogel (Intrasite) in two well designed trials [Colin 1996, Thomas 1993]. The resulting meta-analysis of data from these trials showed no evidence of a significant difference in the rate of complete debridement (relative risk of complete debridement 0.90; 95% confidence interval 0.52 to 1.54, see Figure 4). However, as neither of these trials reported complete ulcer healing, these results should be interpreted in light of the aforementioned comments.

Figure 4:

Topical agents versus traditional dressings

Modern topical agents, such as dextranomer polysaccharide paste (Debrisan), collagenase (Santyl), cadexomer iodine polysaccharide powder (Iodosorb), streptokinase preparation (Varidase), and hydrogel (Clearsite), were compared with traditional dressings such as saline soaked gauze, zinc oxide gauze, eusol and paraffin packs, and sugar and egg white in six trials [Ljungberg 1998, Nasar 1982, Parish 1979, Moberg 1983, Agren 1985, Mulder 1993].

As these agents all had different pharmacology and modes of action, it was inappropriate to combine the results from these trials in a meta-analysis. None of the three trials that reported complete wound healing found a significant improvement in ulcer healing rates with the use of either Debrisan [Parish 1979, Nasar 1982], Santyl [Parish 1979] or Varidase [Agren 1985] compared to traditional dressings (see Figure 5). Again, however, all these trials were small (ranging from 18 to 28 participants) and of only fair methodological quality.

Figure 5:
Topical agents versus modern dressings

Seven trials that met the inclusion criteria compared a topical agent with a modern dressing. Three trials compared a hydrocolloid with a hydrogel [Brown-Etris 1996, Darkovitch 1990, Mulder 1993], two studies compared polysaccharide beads with either a calcium alginate dressing [Sayag 1996] or a collagen sponge dressing [Palmieri 1992], and two compared a hydrocolloid dressing with either collagenase ointment [Burgos 2000b] or a polyhydroxyethyl methacrylate paste [Brod 1990].

One trial [Darkovitch 1990] reported twice the rate of wound ulcer healing with the use of a hydrogel compared to a hydrocolloid dressing (relative risk for ulcer healing with hydrogel 2.23; 95% confidence interval 1.23 to 4.07) However, a smaller, more recent trial, which compared a hydrogel with a modified version of the previous hydrocolloid [Mulder 1993], found no significant difference in mean percent ulcer area reduction (weighted mean difference -4.70; 95% confidence interval -20.12 to 10.72) with the use of a hydrogel. A further comparison of a hydrogel with the same modified hydrocolloid [Brown-Etris 1996], reported insufficient data to estimate a measure of statistical precision and hence meta-analysis of these results was not possible.

In both comparisons between polysaccharide beads and an alternative dressing [Palmieri 1992, Sayag 1996], the results indicated a benefit for the alternative treatment. However, this only reached statistical significance in the comparison with calcium alginate dressings, which showed a mean difference of 2.12 cm²/week in ulcer area reduction in favour of the alginate dressing (weighted mean difference 2.12; 95% confidence interval 0.74 to 3.50). Unfortunately neither of these authors reported ulcer healing rates, hence the significance of these findings should be interpreted with caution.

Modern dressings versus traditional dressings

Six trials (n=296) that met the inclusion criteria compared a hydrocolloid with the traditional treatment of saline soaked gauze [Mulder 1993, Alm 1989, Colwell 1993, Xakellis 1992, Chang 1998, Matzen 1999]. Due to significant clinical and statistical heterogeneity and missing outcome data for some trials, meta-analysis of results was deemed inappropriate.

Four of these trials reported wound healing results [Alm 1989, Xakellis 1992, Colwell...
1993, Matzen 1999] (see Figure 6). The results are varied with some trials finding large improvements in ulcer healing [Alm 1989], others found little difference between the modern hydrocolloid dressing and traditional saline soaked gauze [Xakellis 1992]. As these trials had quite different patterns of ulcer severity at enrolment, such differences might be expected.

Figure 6:

The comparisons of saline soaked gauze and other modern dressings (semi occlusive dressings, polyurethane dressings or hydrogel dressings) were only undertaken in small, single trials and either had insufficient power to detect differences or showed no statistically significant differences between the groups for measures of ulcer healing. A trial of hydrocolloid dressing compared with povidone iodine gauze [Barrois 1992] showed no statistically significant difference between the two groups for ulcer healing (relative risk for ulcer improvement with hydrocolloid 1.11; 95% confidence interval 0.51 to 2.42). Similarly, a semi occlusive dressing was compared in one small trial (n=28) with saline moistened gauze [Kraft 1993] and no evidence of a difference between the two treatments was found (relative risk of ulcer healing with semi occlusive dressing 2.92; 95% confidence interval 0.74 to 11.45). A trial of 48 patients with 77 ulcers [Sebern 1986] compared a polyurethane sterile dressing with saline gauze and found a large improvement in ulcer healing with the modern dressing (relative risk for ulcer healing with polyurethane dressing 16.39; 95% confidence interval 1.06 to 252.82). However the extremely wide confidence intervals for this result would suggest it was not a robust finding. One trial compared a hydrogel dressing with saline soaked gauze [Thomas 1998] and also found no evidence of improved ulcer healing rates (relative risk for ulcer healing with hydrogel 0.97; 95% confidence interval 0.56 to 1.68).

A newer dressing type, noncontact normothermic dressing, was compared with standard wound care in two trials [Kloth 2002, Whitney 2001]. Wound healing results for these two trials showed no evidence of improved healing with the modern dressing (relative risk for ulcer healing with noncontact normothermic dressing 1.28; 95%
Figure 7:

Modern dressings versus modern dressings


Hydrocellular dressings were assessed against hydrocolloid dressings in two trials [Seeley 1999, Bale 1998a]. A meta-analysis of the results from these two trials did not show a significant difference in ulcer healing rates (relative risk for ulcer healing with hydrocolloid 0.61; 95% confidence interval 0.33 to 1.13, see Figure 8). However, again these trials were small and it is likely there was insufficient power to detect real differences in treatment groups.

Figure 8:

Meta-analysis of results from the three trials that examined hydropolymer versus hydrocolloid dressings [Banks 1996, Thomas 1997, Honde 1994] showed no evidence of a significant difference in rates of wound healing (relative risk for ulcer healing with hydrocolloid 0.98; 95% confidence interval 0.71 to 1.35, see Figure 9). As there was a moderate level of statistical heterogeneity ($I^2$ statistic = 63.4%), the meta-analysis was also run using a random effects model, but this made little
difference to the results (relative risk for ulcer healing with hydrocolloid 1.07; 95% confidence interval 0.61 to 1.87, random effects).

Figure 9:

<table>
<thead>
<tr>
<th>Review</th>
<th>Dressings for pressure sore treatment</th>
<th>Outcomes</th>
<th>Hydrocolloid</th>
<th>Polyurethane</th>
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<td>1.00</td>
<td>3.96</td>
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<tr>
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<td>0.67</td>
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Favour hydrocolloid  Favours polyurethane

Three trials assessed hydrocolloid versus polyurethane foam dressings [Banks 1994a, Banks 1994b, Bale 1997]. A meta-analysis showed no evidence of a significant difference in wound healing between these two types of dressings (relative risk for ulcer healing with hydrocolloid 0.82; 95% confidence interval 0.57 to 1.17, see Figure 10).

Figure 10:

<table>
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<tr>
<th>Review</th>
<th>Dressings for pressure sore treatment</th>
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</tbody>
</table>

Favour polyurethane  Favours hydrocolloid

studed in randomised trials. A trial comparing hydrocolloid dressings with collagen dressings [Graumlich 2003] found no evidence of a difference in wound healing (relative risk for ulcer healing with hydrocolloid 0.97; 95% confidence interval 0.60 to 1.57). The use of a calcium alginate dressing (UrgoSorb) for 4 weeks followed by a hydrocolloid dressing (Algoplaque) was compared with a standard hydrocolloid dressing (Duoderm E) for 8 weeks in 100 patients [Belmin 2002]. A significant change in wound surface area at 8 weeks was found for the sequential group with a reduction in mean surface area of 9.7cm² compared with regular hydrocolloid dressing group.
whose mean surface area reduction was 5.2 cm² (weighted mean difference 4.50; 95% confidence interval 1.83 to 7.17). A small (n=35) trial that compared a change indicator dressing (SIG) with a hydrocolloid dressing (Comfeel) [Seaman 2000] saw an increase in wound healing with the change indicator dressings, but this was not statistically significant (relative risk for ulcer healing with hydrocolloid 0.16; 95% confidence interval 0.02 to 1.18). As most of these studies were small and have not been replicated, conclusive findings cannot be drawn from their results.

Similarly, there were a variety of single trial comparisons between several other dressing types. Hydrocellular and polyurethane dressings were compared in a trial of 20 patients [Banks 1997] but although wound healing data was given for all patients, data was not presented for pressure ulcer patients alone. A recent trial of 38 patients compared the effect of hydropolymer and silicone dressings on wound healing [Meaume 2003]. This trial reported no evidence of a significant difference in ulcer healing rates between the two treatments (relative risk for ulcer healing with the hydropolymer dressing 1.13; 95% confidence interval 0.57 to 2.21). Polyurethane foam dressings (Lysofoam A) and low adherence dressings (Tegaderm) were compared in 50 patients [Banks 1994c]. Again, there was no evidence of a significant difference in wound healing between the two treatments (relative risk for ulcer healing with polyurethane 1.17; 95% confidence interval 0.79 to 1.72). When a radiant heat dressing was compared with an alginate dressing [Price 2000], no evidence of a significant difference between the two groups was seen (relative risk for ulcer healing with radiant heat dressing 1.50; 95% confidence interval 0.27 to 8.22). Another study compared two types of hydrogel dressings (Sterigel and Intrasite) [Bale 1998b]. This trial did not report wound healing data, only results for wound debridement. There was no evidence of a significant difference in this outcome between the two types of hydrogel (relative risk for wound debridement with Sterigel 1.44; 95% confidence interval 0.77 to 2.69). None of these fairly small trials showed significant or conclusive results favouring any of the new treatments, suggesting the need for further studies.

Modern dressings versus placebo

One small trial (n=49) compared a wound closure system (Provant) with a placebo (Provant support surface transparently modified so that no treatment was given) [Ritz 2002] and found no evidence of significant difference in wound closure rates for grade II pressure ulcers at six weeks (relative risk for ulcer healing with wound closure system 3.50; 95% confidence interval 0.50 to 24.41).
Discussion

Quality of the studies

Quality assessment suggests that methodological flaws are an issue affecting the validity of studies in chronic wound care. In general, the studies were too small to ensure that wounds of different sizes (and other prognostic variables) were evenly distributed across trial arms, resulting in a bias at baseline in most trials. The majority of studies also had a short follow-up and did not analyse the data by survival analysis, which would account for both whether and when a wound healed and which would be a more efficient method for estimating the rate of healing. If future trials perpetuate many of the methodological flaws highlighted in this review, they are unlikely to provide the necessary evidence to determine an effective wound management strategy. The variability between wounds at baseline for prognostic variables, including size, indicates that recruitment numbers need to be large and that trials should probably be multicentred. If small single-centred trials are to be continued they could be improved by the use of matched or stratified randomisation to ensure a similar distribution of wound sizes between treatment groups at baseline, and the data should be analysed by matched pairs analysis where appropriate. However, even with this improved design a trial still needs to be large enough to ensure comparability for both unknown and known confounding factors.

Dressings and topical agents as treatments for pressure ulcers

Studies that compare treatment with no treatment are very rare in the wound care literature because of concern over ethical issues associated with withholding treatment from a patient. In this review only a single trial was included that assessed the incremental benefit of topical insulin when given in addition to routine supportive care (not including direct management of the wound) for the treatment of pressure ulcers. This trial suggested that application of topical insulin did have a statistically significant benefit on wound healing. However, this requires further exploration and replication.

The alternative to withholding treatment from a patient is to employ a placebo. Eleven trials were included in this review which assessed topical agent versus placebo or dressings versus placebo. In wound care trials such placebo treatments are unlikely to be inert as the application of the placebo or vehicle is likely to change the local environment of the wound, thereby modifying the biological processes associated with healing. A placebo is therefore not a substitute for withholding
treatment in studies to determine the rationale for active treatment. The possible interaction between the vehicle and the healing process together with small sample size, may provide some explanation for why trials do not show a statistically significant difference between an active treatment and a placebo.

Studies directly comparing topical agents for the treatment of pressure ulcers focused primarily on biologically active agents. Most of these trials were too small to provide conclusive results and their heterogeneity prevented pooling. At present the results are highly inconsistent both within and between trials, and further, better-designed studies with larger numbers are required.


Table 1: Overview of economic evaluations to assess dressings and topical agents

<table>
<thead>
<tr>
<th>Full or partial economic evaluation</th>
<th>Author/Country where study was conducted</th>
<th>Interventions compared</th>
</tr>
</thead>
<tbody>
<tr>
<td>Partial</td>
<td>Augilo Sanchez et al, 2001, Spain</td>
<td>Hydrocolloid dressing vs. Saline moistened gauze dressing</td>
</tr>
<tr>
<td>Partial</td>
<td>Bale et al, 1998, UK</td>
<td>Hydrocellular dressing vs. hydrocolloid dressing</td>
</tr>
<tr>
<td>Partial</td>
<td>Bergemann et al, 1999, Germany</td>
<td>Gauze vs. impregnated gauze vs. calcium alginate vs. hydroactive wound dressing in combination with enzymatic wound cleaning collagenase vs. hydroactive wound dressing in combination with enzymatic wound cleaning collagenase during the first 7 days of</td>
</tr>
<tr>
<td>Type</td>
<td>Study</td>
<td>Country</td>
</tr>
<tr>
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</tr>
<tr>
<td>Full</td>
<td>Burgos et al, 2000</td>
<td>Spain</td>
</tr>
<tr>
<td>Full</td>
<td>Capillas Perez et al, 2000</td>
<td>Spain</td>
</tr>
<tr>
<td>Partial</td>
<td>Colwell et al, 1993</td>
<td>US</td>
</tr>
<tr>
<td>Partial</td>
<td>(Gorse et al, 1987)</td>
<td>US</td>
</tr>
<tr>
<td>Partial</td>
<td>Graumlich et al, 2003</td>
<td>US</td>
</tr>
<tr>
<td>Full</td>
<td>Harding et al, 2000/1</td>
<td>UK</td>
</tr>
<tr>
<td>Full</td>
<td>Kerstein et al, 2001</td>
<td>US</td>
</tr>
<tr>
<td>Partial</td>
<td>Kim et al, 1996</td>
<td>Korea</td>
</tr>
<tr>
<td>Partial</td>
<td>Kraft et al, 1993</td>
<td>US</td>
</tr>
<tr>
<td>Partial</td>
<td>Mosher et al, 1999</td>
<td>US</td>
</tr>
<tr>
<td>Study Type</td>
<td>Author(s)</td>
<td>Country</td>
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<td>------------</td>
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</tr>
<tr>
<td>Partial</td>
<td>Motta et al, 1999</td>
<td>US</td>
</tr>
<tr>
<td>Full</td>
<td>Muller et al, 2001</td>
<td>The Netherlands</td>
</tr>
<tr>
<td>Full</td>
<td>Nasar et al, 1982</td>
<td>UK</td>
</tr>
<tr>
<td>Full</td>
<td>Ohura et al, 2004</td>
<td>Japan</td>
</tr>
<tr>
<td>Partial</td>
<td>Robson et al, 1999</td>
<td>US</td>
</tr>
<tr>
<td>Partial</td>
<td>Robson et al, 2000</td>
<td>US</td>
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</table>
Where the studies were conducted and the type of economic evaluation conducted, that is whether the studies were full or partial economic evaluations.

**Dressing and topical agents including debridement.**

The majority (81%) of economic evaluations obtained for review assessed the costs and outcomes associated with dressings and topical agents. Table 1 (above) presents an overview of the treatments that were assessed in this area together with the country where the study was conducted.

<table>
<thead>
<tr>
<th>Treatment comparisons</th>
<th>Number of studies</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydrocolloid dressing versus saline gauze dressing</td>
<td>9</td>
<td>Aguilo Sanchez et al, 2001</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Capillas Perez et al, 2000</td>
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<td></td>
<td></td>
<td>Colwell et al, 1993</td>
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<tr>
<td></td>
<td></td>
<td>Harding et al, 2000/1</td>
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<td></td>
<td></td>
<td>Kerstein et al, 2001</td>
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<tr>
<td>Study Reference</td>
<td>Treatment Comparisons</td>
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<tr>
<td>Kim et al, 1996</td>
<td>Hydrocolloid dressing versus Dakin’s solution (chloramines-T)-soaked wet-to-dry dressings</td>
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<tr>
<td>Ohura et al, 2004</td>
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<tr>
<td>Xakellis et al, 1992</td>
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<tr>
<td>Gorse et al, 1987</td>
<td>2 Hydrocolloid dressing versus hydrocellular dressing</td>
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<tr>
<td>Bale et al, 1982</td>
<td>3 Hydrocolloid dressing versus hydrocellular dressing</td>
<td></td>
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<tr>
<td>Bergemann et al, 1999</td>
<td>4 Gauze versus impregnated gauze versus calcium alginate versus hydroactive wound dressing in combination with enzymatic wound cleaning collagenase versus hydroactive wound dressing in combination with enzymatic wound cleaning collagenase during the first 7 days of treatment</td>
<td></td>
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<tr>
<td>Burgos et al, 2000</td>
<td>5 Collagenase ointment versus hydrocolloid dressing</td>
<td></td>
</tr>
<tr>
<td>Muller et al, 2001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kraft et al, 1993</td>
<td>6 Semi-permeable polyurethane foam dressing vs. moist saline gauze dressing</td>
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Autolysis vs. wet-to-dry saline vs. collagenase vs. fibrinolysin

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<tr>
<th>7</th>
<th>Mosher et al, 1999</th>
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Synthetic polymer vs. hydrocolloid dressing

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<th>8</th>
<th>Motta et al, 1999</th>
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Collagen vs. hydrocolloid dressing

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<tr>
<th>9</th>
<th>Graumlich et al, 2003</th>
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Debrisan vs. Eusol and paraffin dressings

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<tr>
<th>10</th>
<th>Nasar et al, 1982</th>
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Growth factors versus placebo

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<tr>
<th>11</th>
<th>Robson et al, 1999</th>
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<td></td>
<td>Robson et al, 2000</td>
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Transparent moisture vapour permeable dressing versus gauze tape

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<tr>
<th>12</th>
<th>Sebern et al, 1986/9</th>
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Seven (33%) full economic evaluations were reviewed together with 14 (67%) partial economic evaluations. Eleven studies (52%) were conducted in the United States, three in the UK and three in Spain (14% each), and one in Germany, Korea, Japan and the Netherlands (5% each). Twelve different treatment comparisons were made and may be grouped as presented in table 2. Companies who supply pressure ulcer treatments funded most studies. Reviews of the groups of different treatment comparisons follow.

Hydrocolloid dressings versus moist gauze dressings

Eight economic evaluations comparing hydrocolloid dressings to saline gauze dressings were reviewed including three full economic evaluations (Harding et al, 200/1, Kerstein et al, 2001, Ohura et al, 2004) and six partial economic evaluations.
Aguilo Sanchez et al (2001)\(^3\) conducted a cost–consequence analysis based on data obtained from an RCT conducted in a hospital in Spain (see data extraction table 1). It is not clear from the abstract how long patient follow-up was. The effectiveness measure reported was the numbers of patients whose pressure ulcers were completely healed. Twenty (57%) pressure ulcers were completely healed in the hydrocolloid dressing compared to ten (29%) in the saline moistened gauze group. The daily cost of treatment, based on the cost of materials and nursing time, was Pta 180.50 (price year not stated) and Pta 209.36 for the hydrocolloid dressing compared to the saline moistened gauze treatment. It is not clear how the daily cost of treatment was calculated since this could be the cost per day or the cost per day until complete heal of the ulcer. It appears that the hydrocolloid dressing is more effective and associated with lower costs (if indeed the daily cost of treatment takes length of time to heal into account). However, this needs verification before asserting that the hydrocolloid dressing was found to be more cost-effective. No statistical analyses or sensitivity analyses were conducted to assess uncertainty associated with the cost and effect estimates across the two groups.

Capillas Perez et al (2000) also conducted a cost-effectiveness analysis based on an RCT conducted from the perspective of the district health authority in Spain (see data extraction table 5). The two effectiveness measures assessed were time to cicatrise an initial 1 cm\(^2\) wound and proportion of surface healed daily. The median nurse time to cicatrise an initial 1 cm\(^2\) pressure ulcer was 7.12 (first quartile 5.33 to third quartile 11.0) days compared to 12.18 (5.85 to 39.38) days for the hydrocolloid and saline gauze groups respectively. The median proportion of surface area healed daily was 1.42% (0.56% to 2.5%) versus 1.19% (0.59% to 1.55) for the hydrocolloid and saline gauze groups respectively. Neither difference was statistically significant. Costs were calculated based on use of materials and nursing time. The median cost (1st and 3rd percentiles) of the cicatrisation of an initial 1cm\(^2\) pressure ulcer was Pta 4,388 (1,808 to 7,539) (no price data available) compared to Pta 17,983 (6,521 to 87,798) and this difference was found to be statistically significant. Average cost-effectiveness rather than incremental cost-effectiveness was presented. However, it appears that hydrocolloid is cost saving and is associated with better outcomes, dominating the saline gauze intervention.

It is worth noting that patients were allocated to intervention sequentially, which is not a truly random method of allocation. The effectiveness estimates were based on

\(^3\) This review is based on an NHS EED abstract (NHS CRD, 2001). The original paper was written in Spanish.
intermediate outcomes rather than final outcomes (pressure ulcer healed). Median costs were reported whereas, from the economics perspective, mean costs are the most appropriate and informative type of costs to report. The advantage of reporting the mean is the ability of parametric tests to make inferences about the arithmetic mean that is useful for budgetary purposes (Barber and Thompson, 1998).

Colwell et al (1993) conducted a cost–consequence analysis based on an RCT conducted from the hospital perspective in the United States (see data extraction table 6). Patients were followed-up between 6 and 56 days (mean 17) and the outcome assessed was the proportion of pressure ulcers healed. Twenty-two percent (n=11) of pressure ulcers healed in the hydrocolloid group compared to two percent (n=1) in the moist gauze group. The total average cost (including cost of materials and nurse time) per patient was $53.68 (no price date) versus $176.90 for the hydrocolloid versus the gauze group. It appears that the hydrocolloid dressing costs less and is associated with better outcomes, dominating the moist gauze intervention.

A few caveats should be mentioned alongside the study results. The authors randomised by pressure ulcer rather than by patient and some patients had more than one pressure ulcer, both of which were included in the study. This method can introduce bias, for instance if the ulcers are allocated to different treatments then it may be difficult to remember to treat each differently. Also there may be something particular about the patient which impacts on the findings and this undermines the randomisation process. There were statistically significantly more grade 2 pressure ulcers allocated to the hydrocolloid treatment and these types of ulcers tend to have better healing characteristics than grade 3 pressure ulcers, potentially advantaging the hydrocolloid treatment.

Harding et al (2000/1) conducted a cost-effectiveness analysis of saline moistened gauze compared to two hydrocolloid dressings (Comfeel and Granuflex) (see data extraction table 9). The analysis was based on a probability based decision model, utilising data from the published literature and informed by expert opinion. The perspective of the analysis was the UK NHS. The effectiveness estimate was the proportion of pressure ulcers healed in 12 weeks and a meta-analysis was undertaken to pool data from 15 studies for use in the model. The proportion of pressure ulcers healed at 12 weeks in the saline moistened gauze group was 51% compared to 48% in the hydrocolloid Comfeel group and 61% in the hydrocolloid Granuflex group. The average cost per patient healed (with costs including materials, ancillary supplies, nursing and doctor debridement) was £2,663, £642 and £422 (1999 prices) for saline moistened gauze, hydrocolloid Comfeel and hydrocolloid Granuflex respectively. Thus hydrocolloid Granuflex appears to be the most cost-effective option.
Although the unit cost of gauze treatment was lower than the unit cost of either hydrocolloid dressing, the total cost associated with the gauze treatment was highest due to higher nurse input. As the authors state, nurse time is the single most expensive cost for each treatment. The use of cost per wound healed does not take the length of time to healing into consideration. The assumptions and use of expert opinion regarding resource use and effectiveness were not described in a very transparent way. Incremental cost–effectiveness analysis was not undertaken.

Kerstein et al (2001) also conducted a cost-effectiveness analysis using a similar approach to Harding et al (2000/1) comparing saline moistened gauze compared to two hydrocolloid dressings (Comfeel and DuoDERM) and based on a probability based decision model, utilising data from the published literature and informed by expert opinion. However, the perspective of the analysis was different since the Kerstein et al (2001) study was based on a US hypothetical managed care plan setting. The effectiveness results were identical but the cost estimates were estimated using US resource use and costs. In terms of results, the average cost per patient healed (with costs including materials, ancillary supplies, nursing and doctor debridement) was $2,179 (2000 prices), $1,267 and $910 for saline moistened gauze, hydrocolloid Comfeel and hydrocolloid Granuflex respectively. The hydrocolloid DuoDerm dressing appeared to be the most cost-effective option. The same limitations as the Harding et al (2000/1) study apply.

Kim et al (1996) conducted a cost-consequence analysis based on an RCT undertaken in Japan (see data extraction table 11). The length of follow-up was not stated. Effectiveness measures included in the study were proportion of pressure ulcers completely healed, time to complete heal and rate of pressure ulcer heal. 80.8% of pressure ulcers in the hydrocolloid group and 77.8% of pressure ulcers in the gauze group healed completely, and the difference between the two groups was not statistically significant. The time to complete heal was 18.9 days versus 24.3 days for the two comparators and the pressure ulcer healing speed was 9.1 mm² per day and 7.9 mm²/day for the hydrocolloid and the gauze group respectively. The average cost of the interventions was Won 8,204 (+/-2,664) and Won 14,571 (+/-6,700) (no price date) for the two comparators respectively (P<0.05). It appears that the hydrocolloid dressing is more cost-effective than the gauze dressing with lower associated costs and better effects. However, in general, little detail was provided on methods used to conduct the evaluation so it is not clear as the validity and reliability of the results. The costs calculated did not take the cost of staff into account, which seems an important omission, based on results from the evaluations above.

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4 Based on the results it appears the Harding and the Kerstein study may be using the same data, however the perspective of the analysis differs

5 DuoDerm is the US brand name equivalent of the Granuflex UK brand name
Ohura et al (2004) undertook a cost-effectiveness analysis of hydrocolloid DuoDERM dressing with a standardized wound management algorithm, traditional care of ointment & gauze with a standardized wound management algorithm and traditional care of ointment & gauze without a standardized wound management algorithm (see data extraction table 17). The study was based on a multi-centre, non-randomised trial in Japan and considered grade 2 and 3 pressure ulcers over a follow-up period of 12 weeks maximum. Effects were measured in terms of the Pressure Ulcer Status Tool (PSST), with greater reductions in PSST being associated with greater health benefits achieved, and costs were based on use of materials and labour time.

The hydrocolloid dressing was associated with a 11.1 point reduction in PSST compared to a 6.9 point reduction for gauze with standard management and a 9.0 reduction in PSST for the gauze without standard management comparator and the reduction was statistically different when comparing the first two of these interventions. In terms of costs across the three treatments, the average total cost was Yen 87,715, Yen 131,283 and Yen 200,584 (2001 prices). The difference in the cost of the hydrocolloid treatment compared to the gauze without the standardized wound management strategy was statistically significantly different as when materials & total labour costs were analysed separately.

Across all pressure ulcers, the PSST unit difference per Yen was 0.127 for the hydrocolloid dressing compared to 0.045 for gauze without standardized wound management and 0.052 for gauze with standardized wound management. In terms of cost-effectiveness, based on these results the hydrocolloid dressing dominates with lower associated costs and higher associated outcomes.

The Ohura et al study (2004) was based on a multi-centre clinical trial. No tests were undertaken to assess variation across study centres. Patient allocation to groups was non-random. Limited statistical testing was undertaken to explore uncertainty with no sensitivity analysis being conducted to assess the robustness of findings to variables included in the analysis. The generalisability of these results is unclear. Unlike the large majority of other studies, the cost of doctors’ time was included which was a high cost input. Costs were not reported separately from resource use.

Xakellis et al (1992) conducted a cost–consequence analysis of hydrocolloid dressings compared to non-sterile saline gauze dressings, based on an RCT in a long-term care setting in the United States (see data extraction table 21). The study period was 21 months and study endpoints included pressure ulcer heal, progression to stage 4 pressure ulcer, doubling in pressure ulcer area, systemic infection from the
pressure ulcer, no decrease in size of the pressure ulcer at two months and six months of treatment, patient discharge from the long term care facility and death.

Effectiveness was measured in terms of proportions of pressure ulcers completely healed, time to healing and healing rates. Eighty-nine percent (n=16) of pressure ulcers were completely healed in the hydrocolloid group compared to 86% in the comparator group. The median time to healing after randomization was nine days for hydrocolloid group and 11 days for the gauze group and this finding was not statistically significantly different. Seventy-five percent of pressure ulcers healed within 14 days in the hydrocolloid group compared to the 26 days in the gauze group. After adjusting for exudates present at baseline, healing rates were not statistically significantly different across groups although the trend was towards slower healing in the gauze group.

The cost of use of materials and nurse time was assessed and the median total cost per patient was $15.58 (1990 prices) for the hydrocolloid group and $22.65 for the gauze group if local nurse wages used and the difference was not statistically significant. If national nurse wages used, the median total cost was $15.90 and $25.31 respectively (p=0.04). Overall, the hydrocolloid was less costly and associated with greater health effects hence it appears to be the more cost-effective option.

The authors reported median costs and conducted statistical tests based on non-parametric techniques, rather than mean costs and, as mentioned above (see review of Capillas Perez et al 2000), this makes findings difficult to interpret.

**Overview of hydrocolloid dressings versus moist gauze dressings**

Although there were a number of limitations associated with all the economic evaluations comparing hydrocolloid dressing to moist gauze dressings, typically hydrocolloid dressings were found to be the more cost-effective option.

**Hydrocolloid dressing versus Dakin’s solution (chloramines-T)-soaked wet-to-dry dressings**

Gorse et al (1987) (see data extraction table 7) conducted a cost-consequence analysis comparing hydrocolloid dressing with Dakin’s solution (chloramines-T)-soaked wet-to-dry dressings in a hospital in the United States. Patient follow-up was from initiation of conservative treatment until healing, hospital discharge or failure of the initial intervention, however, the time, in days was not stated.

Effectiveness was measured in terms of the rate of healing for each pressure ulcer healed: that is the initial surface area divided by the number of days until complete
healing. If patients died or were discharged prior to complete healing, the surface area at the last examination was subtracted from the initial surface area and the results divided by the number of treatment days. In the hydrocolloid dressing group, 86.8% of pressure ulcers improved compared to 69.2% in the wet-to-dry dressing group. The number of days to complete heal for pressure ulcers that healed was 10.0 (+/-10.5) in the hydrocolloid group compared to 8.7 (+/-6.2) for the wet-to-dry dressing group. The rate of decrease (cm² per day) for pressure ulcers that healed was 0.72 (+/-1.22) compared to 0.55 (+/-0.59) for these groups respectively and this result was not statistically significantly different. Among the incompletely healed pressure ulcer group, the duration of follow-up was significantly longer for the wet-to-dry group but the rate of decrease in surface area was not significantly different. Among the pressure ulcers that worsened, a higher rate of increase in surface area was found in pressure ulcers treated in the hydrocolloid group compared to the wet-to-dry group.

Based on treatment costs alone, a cost of $6.20 per week was estimated for treating each pressure ulcer in the hydrocolloid group compared to $52.50 per week in the wet-to-dry dressing group. Costs associated with the hydrocolloid dressings were lower and more pressure ulcers healed in this group compared to those treated with wet-to-dry dressings, and on this basis the former appears to be the more cost-effective option, dominating wet-to-dry dressings. The cost analysis undertaken as part of this study was particularly weak. As noted above, the cost of nursing time can be substantial but these costs were omitted. Also, the cost was not examined until time to heal or according to any other effectiveness measure. Some patients had more than one pressure ulcer that was entered into the trial and this could bias the results. The allocation of patients to interventions was not random. The uncertainty associated with the estimates was only assessed statistically for the effectiveness dimension of the study.

**Hydrocolloid dressing versus hydrocellular dressing**

Bale et al (1982) conducted a cost–consequence analysis comparing hydrocolloid dressings to hydrocellular dressings (see data extraction table 2). The study was based on an RCT and the perspective of the analysis was the NHS. Patient follow-up was for a maximum of eight weeks. The effectiveness measure reported was the proportion of pressure ulcers healed completely at eight weeks. In this time, 59% of pressure ulcers healed in the hydrocolloid dressing group compared to 27% of the pressure ulcers in the hydrocellular dressing group. Costs were based on materials and nursing time and the total cost of treatment per patient, whether their pressure ulcer had healed or not, was £50 in the hydrocolloid group and £76 in the
hydrocellular group. A number of one-way sensitivity analyses were undertaken, including varying the costs applied if withdrawn prior to 8 weeks, but did not alter the findings. Since more pressure ulcers healed in the hydrocolloid group and the daily cost of treatment was lower, it appears that hydrocolloid dressings may be more the more cost-effective option.

There are a few study limitations that should be considered when interpreting the results. The cost of labour time, typically an important contributor to overall cost, was omitted. Some patients were withdrawn from the study (the authors do not say which wound group they are in) and more patients were withdrawn from the hydrocellular group and this could bias results in favour of this group. Across all wounds, at 7 weeks the numbers of wounds healed was very similar across groups but comparative data was not presented on pressure ulcers at seven weeks.

**Gauze versus impregnated gauze versus calcium alginate versus hydroactive wound dressing in combination with enzymatic wound cleaning collagenese versus hydroactive wound dressing in combination with enzymatic wound cleaning collagenese during the first seven days of treatment**

Bergemann et al (1999) conducted a cost–consequence analysis to compare five different interventions used in four hospitals in Germany (see data extraction table 3). A spreadsheet model was constructed, informed by an expert panel, and data to populate it was obtained using the hospital databases. The treatment of four sizes of pressure ulcers were considered, that is pressure ulcers of (i) 5cm x 8 cm, (ii) 8cm x 12 cm, (iii) 10cm x 15cm and (iv) 12cm x 20cm. It was assumed that the bigger the wound, the longer the treatment duration required. Equal efficacy was assumed or a decrease in the length of hospital stay of 10% for the two hydroactive treatments. Resource use estimates were assumed to vary across wound surface areas, as informed by the expert panel. Costs were based on materials used and nurse time to provide pressure ulcer care. Cost savings of between DM1,138 (DM538 to 1739) for the first hydroactive treatment compared to the impregnated gauze treatment and DM8,234 (DM4610 to DM 11,858) for the first hydroactive treatment compared to gauze only were found. Two-way sensitivity analysis was undertaken on the total costs associated with each intervention as well as the following parameters used to calculate costs; personnel costs per minute, time required to change a dressing, total number of wound dressing changes and results remained fairly robust. Monte Carlo simulation was used to estimated the variation in inputs into the model (95% CI). The main finding was that, despite the higher material costs of the two hydroactive therapies, the reduced labour costs, due to quicker time to heal and reduced duration of treatment or time to inpatient discharge that were assumed, resulted in lower total costs relative to the three comparators.
The model assumed that use of the hydroactive treatments reduced inpatient stays by 10%, but the evidence on this is not strong. Pressure ulcers were followed in the model not only until they had healed but sometimes, instead, until inpatient discharge; hence the pressure ulcer may remain unhealed and does not fully take into account effectiveness. It is unlikely that all treatments are equally efficacious. Length of hospital stay was considered to be a proxy for health effect, however; this was incorporated within the cost estimates.

**Collagenese ointment versus hydrocolloid dressing**

Burgos et al (2000) conducted a cost–effectiveness analysis of collagenese ointment compared to hydrocolloid occlusive dressings (see data extraction table 4). The study was a multi-centre RCT conducted in Spanish hospitals. Patients were followed up for 12 weeks or until complete pressure ulcer heal, whichever occurred first. Reduction in pressure ulcer area was used as the measure of effect. The mean (standard deviation) reduction in pressure ulcer area in the collagenese group was 9.1 (1.2) cm² compared to 6.2 (9.8) cm² in the hydrocolloid group, an area reduction of 44% & 28% respectively. The pressure ulcer area decreased in 83% of cases in the collagenese group compared to 74% in the hydrocolloid group after twelve weeks of follow up and these differences were not statistically significant. Pressure ulcers were completely healed for three patients in each group. Resource use assessed included treatment supply, including ancillary supplies, and nurse time. Collagenese group pressure ulcers cost Pta 41,488 (95%CI: Pta 26,191-Pta 56,784) (price year 1998) compared to Pta 32,963 (95%CI: Pta 23,389-Pta 42,538) for the hydrocolloid dressing group and the difference was not statistically significant. The total cost per 1 cm² reduction in pressure ulcer was Pta 4,559 for the collagenese group and Pta 5,310 for the hydrocolloid group. The cost per reduction in pressure ulcer area was lower for the collagenese group and on this basis it appears to be the more cost-effective option. Material costs very similar but the total cost of collagenese tended to be higher than hydrocolloid dressings due to greater staff input. No allowance for across site differences.

Muller et al (2001) also conducted a cost-effectiveness analysis comparing collagenese with hydrocolloid dressings (see data extraction table 15). The analysis was based on an RCT conducted in a hospital in the Netherlands. Effectiveness measures used included whether or not successfully treated (that is if their pressure ulcer was completely healed), the rate of complete wound healing and the average number of weeks required until pressure ulcer healing was achieved. In the collagenese group, 91.7% (11/12) patients were successfully treated compared to 63.6% (7/11) patients in the hydrocolloid group and this finding was statistically
significant ($p<0.005$). The time to pressure ulcer heal was shorter for the collagenese group at, on average, 10 weeks compared to 14 weeks ($P<0.005$).

Resource use measured use of materials used and labour time, including doctor and nurse time. The average cost per patient of collagenese was NLG1,615.8 compared to NLG1,692.7 for the hydrocolloid dressings (price year 1998). The cost per successfully treated patient was NLG1,762.0 for collagenese compared to NLG2,661.4 for hydrocolloids, therefore the former appears to be more cost-effective with lower associated costs and better effects. A deterministic model and one-way sensitivity analysis and a probabilistic model using Monte Carlo simulation were conducted to explore uncertainty associated with the estimates. In all scenarios, collagenese remained the more cost-effective treatment. The assumption of the independency of model inputs is questionable. Average cost-effectiveness rather than incremental cost-effectiveness reported. Two patients, one in each group, had two pressure ulcers (on the heel) but it was not mentioned which pressure ulcer (the pressure ulcers would be likely to differ) was included in the study.

**Overview of collagenese ointment versus hydrocolloid dressing**

The two studies comparing collagenese ointment with hydrocolloid dressings were full economic evaluations based on RCTs and were of moderate quality. Both economic evaluations suggested that collagenese is more cost-effective than hydrocolloid dressings. Neither study was conducted in the UK and currently, collagenese is not licensed for use in the UK.

**Semi-permeable polyurethane foam dressing versus moist saline gauze dressing**

Kraft et al (1993) conducted a cost–consequence analysis comparing use of semi-permeable polyurethane foam dressings to moist saline gauze dressings in stage 2 and 3 pressure ulcers (see data extraction table 12). The study was conducted in the United States and was based on an RCT conducted in a long-term hospital care spinal cord injury centre. The effectiveness measure chosen was the proportion of patients with completely healed pressure ulcers. At 24 weeks, the follow-up duration, 42% ($n=10$) of PU were healed in the semi-permeable polyurethane foam dressings group compared to 21% ($n=3$) in the gauze group. However this difference was not statistically significant. Treatment supply and nurse time was costed and the average total cost per week was $20.48 for the foam dressing group and $74.97 for the gauze dressing group.

Although costs and outcomes were not synthesised in the study more pressure ulcers were healed in the foam dressing group and the daily cost of treatment was lower, therefore this appears to be the more cost-effective option, dominating the gauze...
option. The methods used to conduct the study were not written up in much detail so critical appraisal is a challenge. Some patients withdrew from treatment (two in the foam dressing group) but no reason for their withdrawal was provided. The cost analysis was not strong because only weekly costs per pressure ulcer treated were provided. The total cost of treatment to, say, time to complete heal, was not calculated. The length of time that the treatment is received can make a difference to the total cost of treatment.

**Autolysis compared to either wet-to-dry saline, collagenese or fibrinolysin**

Mosher et al (1999) conducted a cost–consequence analysis from the third party payer (Medicare) perspective in the United States (see data extraction table 13). A decision analytic model was used and effectiveness data was obtained from the literature and expert opinion. Median values of experts gained were used as probabilities in the decision model. The patient being studied was a hypothetical 78 year old female in a long-term care facility who had not been hospitalised in the prior 12 months who has a new full thickness PU on her trochanter with 50% necrotic tissue (eschar) covering the PU, mild odour, minimal draining, no undermining and intact peri-ulcer skin. A modified Delphi approach was used to reach consensus on critical treatment choices and possible outcomes. The effectiveness measure chosen was the probability of obtaining a clean wound bed for each 28 day treatment of the hypothetical treatment. Resource use measured included drugs, dressing and irrigation supply, doctor visits, ancillary services (for example outpatient laboratory tests), hospitalisation and associated resource use. The probability of a clean wound bed was estimated to be 0.887 (87%) for collagenese, 0.641 for autolysis, 0.376 for wet-to-dry saline and 0.449 for fibrinolysin. The total cost per patient for 28 days was $610.96 (1995 prices) for collagenese, $920.73 for autolysis, $986.38 for fibrinolysin and $1008.72 for wet-to-dry saline. Probabilistic sensitivity analysis was conducted to investigate parameter uncertainty and when all parameter inputs were varied by –10% and +10% the results remained robust. It appears that collagenese was the most cost-effective option for the management of pressure ulcers in long term care, based on the study findings.

The quality of the literature review process and the elicitation of expert opinion was not clear. The authors note that the probability data was non-normally distributed and non-random.

**Synthetic polymer versus hydrocolloid dressing**

Motta et al (1999) conducted a cost–consequence analysis based on pilot, RCT undertaken in the United States and hence the sample size was small (n=10, 5 in each group) (see data extraction table 14). They compared a synthetic polymer
dressing with a hydrocolloid dressing in home health care patients who were followed up for eight weeks.

Effectiveness measures included healing rates, adverse reaction and product performance (based on exudate performance, whether dressing maintains moist environment, promotes autolytic debridement and its overall clinical performance marked out of 1 to 5 with 1 being most favourable and 5 being least favourable). Two pressure ulcers in each group completely healed and all other pressure ulcers demonstrated substantial reductions in size. The overall healing rates were not statistically significantly different. No adverse reactions occurred and the overall performance of the interventions was assessed based on the average score obtained during dressing change for each parameter and no statistically significant differences were found. Dressings and ancillary supplies and nurse time was costed. The total cost of treatment over eight weeks was $57.76 (no price date was given) for the synthetic polymer group and $91.48 for the hydrocolloid dressing group. Since the same number of pressure ulcers healed across groups, if this was taken as the measure of effect, then it appears that the synthetic polymer may be cost saving compared to the hydrocolloid dressing. The sample size was small and it is questionable as to whether the results are generalisable to other settings.

**Collagen versus hydrocolloid dressing**

Graumlich et al (2003) conducted a cost–consequence analysis to compare topical collagen with hydrocolloid dressings (see data extraction table 8). The study was based on a multi-centre RCT of patients with grade 2 or 3 pressure ulcers in nursing homes in the United States and the patients were followed up for eight weeks maximum (median of five weeks). Effects measured included the proportion of pressure ulcers completely healed within eight weeks and secondary outcomes including time to heal, ulcer area healed per day and linear healing of wound edge. Fifty-one percent of pressure ulcers were healed within eight weeks in the collagen group compared to 50% in the hydrocolloid group (95% CI: -26% to 29%). The mean healing time in the topical collagen group was five weeks (95% CI: 4 to 6 weeks), and for the hydrocolloid group it was six weeks (95% CI: 5 to 7 weeks). The mean area healed per day was 6mm² in both groups and the mean linear healing of the wound edge was 3mm for both groups.

Treatment supply including ancillary supplies and nurse time was measured in order to calculate costs. The average cost per patient pressure ulcer over eight week was $627.56 (no price date) for topical collagen and $222.36 for the comparator. Statistical tests to compare findings across groups were undertaken. There were no statistically significant differences in the healing outcome across groups. Topical
collagen was considerably more expensive and offered no major benefits to patients otherwise eligible for hydrocolloid dressings. As the authors state, no analysis was undertaken to adjust for the heterogeneity in healing outcomes identified across nursing homes. The cost analysis was not strong and quantities of resources used was not reported separately from unit costs.

**Debrisan versus Eusol and paraffin dressings**

Nasar et al (1982) conducted a cost–effectiveness analysis based on an RCT in a hospital in the UK (see data extraction table 16). Patients were followed up until the pressure ulcer was clear and granulating and appeared to be less than 25% of its original surface area. For the Debrisan group six out of eight pressure ulcers healed in approximately 39.3 days. One other patient died and one patient withdrew from treatment. For the Eusol group, five out of eight pressure ulcers healed in approximately 62 days. Three patients were switched to Debrisan. Resources measured to calculate costs included use of materials and ancillary supplies and hospital stay. The average cost of a pressure ulcer that healed was £1053.05 (price year not stated) for the Debrisan group and £1667.00 for Eusol group. Overall the, Debrisan cost less and was associated with a higher number of pressure ulcers healed compared to Eusol.

In summary, Debrisan appears to be more cost-effective than Eusol, costing less and being associated with a faster time to heal, for those PU that healed. It is worth noting that some patients had more than one pressure ulcer entered into the trial, the actual length of patient follow-up was not stated and costs only related to those patients whose pressure ulcers had healed.

**Growth factors versus placebo**

Robson et al 1999 conducted a cost–consequence analysis, based on a 16 week long RCT in a hospital in the United States (see data extraction table 18). They compared Recombinant human platelet-derived growth factor-BB. (1) 100 µ g rhPDGF-BB per day with (2) 300 µ g rhPDGF-BB per day, (3) 100 µ g rhPDGF-BB twice daily and (4) placebo.

The effectiveness measure used to compare treatments was wound volume decrease over time. Four surgeons who were blind to patients, assessed changes in the ease of surgical closure of pressure ulcers on a scale from 0 (no need to close, healed) to 13 (not possible to close) based on photographs of pressure ulcers which were taken from a set focal distance and which were obtained weekly. Ninety-four percent of the
possible maximum number of photographs possible were available for rating. At the end of the trial, the pressure ulcers of patients in group one were rated to have improved by six points (mean) on the scale from beginning to end of treatment. For group 2 and 3 patients, the mean pressure score assigned was five points compared to four points assigned to pressure ulcers in the placebo group (4). All outcomes were statistically significantly improved from their respective starting ease of closure scores of 10 (p<0.0001).

In terms of cost, the change in difficulty of wound closure was studied in relation to the composite cost including surgeon’s fee, anaesthesia fee, operating room cost. Costs were arrived at from charges to patients at two university centres. The range of costs was $100 (no price date was stated) for a single buttressed suture placed at the patient’s bedside to $12,000 for a difficult musculocutaneous or free flap. At the beginning of the trial, the mean and median cost of closure was estimated at $8,000 per pressure ulcer as they were rated as requiring a somewhat easy pedicle flap procedure to close the wound. At the end of the trial, according to the raters, group 1 required a difficult direct wound application costing $800 to $1,000 (a cost saving of $7,000 to $7,200), compared to an easy skin graft for pressure ulcers in group 2 and 3 costing $1,200 (a cost saving of $6,800). For the placebo group (4) a slightly more difficult procedure was recommended costing $1,700 (a cost saving of $6,300). The cost savings were statistically significantly different even though 100% wound closure was not routinely achieved.

Based on the results, it appears that the growth factor received by group 1 was more cost-effective than that recommended to patients with pressure ulcers in groups 2 and 3 that, in turn, were more cost-effective than placebo (4). Statistical tests regarding effectiveness and costs were undertaken but the results of the latter were not reported. It is worth noting that the analysis assumes that pressure ulcers would have otherwise been closed via surgical techniques, a very costly intervention. The costs of the surgical interventions were given but no further details were provided. In an attempt to explore uncertainty, the authors tested the correlation between the ease of closure scale and the wound area as photographs are only two-dimensional. Results of the clinical trial are provided in another paper.

Robson et al (2000) also conducted another study using cost–consequence analysis (see data extraction table 19). The study was based on an RCT in a hospital in the United States (see data extraction table 18). The interventions compared were cytokine growth factors; (1) 2.0 µg/cm² GM-CSF therapy topically applied daily for 35 days, (2) 5.0 µg/cm² bFGF therapy applied daily for 35 days, (3) 2.0 µg/cm² GM-CSF applied for 10 days followed sequentially by 25 days of topically applied 5.0 µg/cm²
bFGF and (4) Placebo applied daily for 35 days. Patients with grade 3 or 4 pressure ulcers were followed up for 35 days (five weeks). Effectiveness measured included the wound volume decrease over time. Surgeons rated changes in ease of surgical closure on a scale from (0) (no need to close, healed) to (13) (not possible to close) based on photographs of PU at a set focal distance. An arbitrary response rate of at least 85% wound closure during 35 days of follow-up was chosen as indicative of a responder.

In terms of effectiveness, there were no differences in mean proportion of initial pressure ulcer volume remaining on day 36 across all interventions. However, (2) had a trend toward greater pressure ulcer closure. The proportion of patients responding was statistically significantly higher for all cytokine therapies compared to placebo (4) (p=0.03), with (2) patients doing best. The median ease of closure for all four groups was 11 on day 0. (2) patients PU improved 7 points on the ease of closure scale. (3) patients improved 5 points, (1) patients improved 4 points and (4) patients improved 3 points.

Resource use regarding the amount of topical substance each week of treatment was based on volumetrically determined surface area at baseline and on study days 7, 14, 21, 28. The change in difficulty of pressure ulcer closure in relation to total cost (surgeon’s fee, anaesthesia fee and operating room cost) was calculated. At the beginning of the trial, the median cost of closure was estimated at $10,000 (no price date) per PU. At the end of the trial, patients' pressure ulcers in group (2) were recommended to be healed by a difficult wound approximation costing $800 to $1,000 (a cost saving of $9,000 to $9,200). For patients' pressure ulcers in group (3), the rates recommended patients would require a somewhat easy skin graft costing $1,700 (cost saving of 8,300). For group (1) a somewhat difficult procedure was required costing $2,200 (cost saving of $7,800). For group (4) pressure ulcers could be closed for $3,000 (cost-saving of $7,000). It appears that cytokine (1) was the most cost-effective strategy.

The cost analysis was not strong and the uncertainty around cost estimates for surgical procedures was not explored. A major assumption on which the analysis was based is the assumption that pressure ulcers would have otherwise been closed via surgical techniques. Assessment of inter-rater reliability, using the ease of closure scale, was not undertaken.

**Transparent moisture vapour permeable dressing versus gauze and tape**

Sebern et al (1986/9) conducted a cost–consequence analysis to compare transparent moisture vapour permeable (TMVP) dressing to gauze and tape (see
data extraction table 20). An RCT was conducted using a sample of patients using home-care that was served by a metropolitan visiting nurse association in the United States. Patients were followed-up for eight weeks and effect measures used included their healing status at eight weeks (whether their pressure ulcer had healed, was progressing towards healing, was unchanged, they discontinued treatment or their ulcer deteriorated). Additionally, healing rates and patient comfort was considered. Of the grade 2 pressure ulcers in the TMVP group 64% (n=14) healed compared to none in the gauze and tape group. For grade 3 pressure ulcers there was not significant difference between the two groups and no further details were provided. In terms of healing rates, grade 2 pressure ulcers in the TMVP group had a 52% median decrease in area of the wound compared to 100% median decrease in the gauze group (P<0.01, Wilcoxon). For grade 3 pressure ulcers, in the TMVP group, there was a 67% median decrease in pressure ulcer size compared to a 44% decrease in the gauze group but this findings was not statistically significant. Patients who had intact sensory input from their pressure ulcers reported less pain when the TMVP treatment was used.

Resource use assessed included treatments and nurse time. The mean eight week treatment costs per grade 3 pressure ulcer was $1470 for the TMVP group and $1412 for the gauze group and this difference was not statistically significant. It appears that TMVP was slightly more costly per pressure ulcer for the TMVP strategy; however, effects across the two interventions differed depending on the grade of the pressure ulcer and the effectiveness measure considered. There was no difference in outcome for grade 3 pressure ulcers; however, this may be due to type 2 error. Authors incorrectly re-graded pressure ulcers at the end of the study. The authors randomised by pressure ulcer rather than by patient that can introduce bias. The variance associated with cost estimates was not reported and the statistical tests applied to costs were non-parametric when they should be parametric.

Recommendations

6 The probability of failing to reject the null hypothesis when the latter is false. This probability becomes smaller with increasing sample size. The greater the probability of type 2 error, the weaker the power of the study to detect differences as statistically significant when such differences exist.

Royal College of Nursing and National Institute for Clinical Excellence
Recommendation:

**Dressings and topical agents**

Decisions about choice of dressing or topical agent for those with pressure ulcers should be made by registered health professionals that have undergone appropriate training and have demonstrated competence. [D]

Choice of dressings or topical agents for the treatment of pressure ulcers should be based on: [D]
- Ulcer assessment (condition of wound)
- General skin assessment
- Treatment objective
- Dressing characteristics
- Previous positive effect of particular dressing
- Manufacturer’s indications for use and contra indications
- Risk of adverse events
- Patient preference (lifestyle, abilities and comfort)

There is insufficient research evidence to guide clinicians’ decision making about which dressings are most effective in pressure ulcer management. [A] However professional consensus recommends that:

Create the optimum wound healing environment by using advanced dressings
(eg, hydrocolloids, hydrogels, foams, films, alginates, soft silicones) in preference to basic dressing types (eg, gauze, paraffin gauze and simple dressing pads). [D]

Debridement

Clinicians should recognise the positive potential benefit of debridement in the management of pressure ulcers. Decisions about the method of debridement should be based on: [D]

- Ulcer assessment (condition of wound)
- General skin assessment
- Previous positive effect of debridement techniques
- Manufacturer’s indications for use and contra indications
- Risk of adverse events
- Patient preference (lifestyle, abilities and comfort)
- Characteristic of dressing/technique
- Treatment objective

Decisions about debridement methods for patients with pressure ulcers should be made by registered health professionals that have undergone appropriate training and have demonstrated competence. [D]

<table>
<thead>
<tr>
<th>Research recommendations</th>
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<tbody>
<tr>
<td>The research concerning wound dressings and topical agents is of varied quality. In those trials reviewed, sample sizes were often not sufficient to detect clinically important effects, and poor baseline comparability of the groups introduced bias. Several important messages can be identified for future studies.</td>
</tr>
<tr>
<td>• Recruitment numbers should be based on an a priori sample size calculation. In most trials the sample size is too small to find a statistically significant difference between treatment groups. Multi-centre trials should be considered in order to recruit sufficient patient numbers. These large trials have been undertaken in other areas of health care, and although the field of wound care presents its own difficulties, there is no reason why such trials should not be successful. If these trials are to be commissioned they will require a strong infrastructure to provide support, promote collaboration and establish a common knowledge base.</td>
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<tr>
<td>• A truly objective outcome measure should be used, for example</td>
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time to complete healing of the wound, or wound healing should be expressed as both percentage and absolute change in area.

• For each patient a single reference wound should be selected. Multiple wounds on a patient should not be included in the analysis as they are not independent unless specialised statistical analysis is performed to separate out the effects of the intervention, (that is matched-pairs analysis).

• Experimental groups should be comparable at baseline. In small RCTs, randomisation alone will not achieve comparability; in such situations patients should be paired by prognostically important baseline characteristics and then the individuals of each pair randomised to treatment. Such randomisation is particularly important if ulcers of different aetiologies are to be assessed in the same trial.

• Head-to-head comparisons of modern wound dressings are required and should use agents that are recommended for wounds of a similar nature.

• A complete and thorough description of concurrent treatments including secondary dressings should be given in trial reports.

• Assessment of outcomes should be blind to treatment.

• Survival rate analysis should be adopted for all studies that assess wound healing.

• Studies to determine the biological mechanisms involved in wound healing are needed. A better understanding of the healing process may lead to the development of validated outcome measures.

• All trials should be published where possible. Those involved in primary research should make their data available to those undertaking systematic reviews.

• Future trials should include cost-effectiveness and quality of life assessments, as well as objective measures of dressing performance. These measures would encapsulate those aspects of patient quality of life on which wounds most impact and would be sensitive to meaningful changes in quality of life generated by a change in the wound, including post healing of the wound.

Antimicrobial agents in the treatment of pressure
The role of antimicrobial agents in the treatment of pressure ulcers remains unclear. The lack of clarity is due in part to uncertainty around the issues of whether bacterial presence in an important factor in wound healing. While the results from some studies indicate a positive association between higher bacterial counts and delayed wound healing [Lookingbill 1978, Halbert 1992], others show no such association [Eriksson 1984, Gilchrist 1989]. Clinicians may use systemic antibiotics as a last resort when topical interventions have failed to produce healing [Huovinen 1994].

Moist chronic pressure ulcers are an ideal medium for bacterial growth. Pressure ulcers may have a varied bacterial flora, with aerobic organisms cultured more frequently than anaerobes. Staph. aureus, Streptococcus species, Proteus species, Escherichia coli, Pseudomonas, Klebsiella and Citrobacter species are the most common isolates [Yarkony 1994, Parish 1983, Alvarez 1991]. In serious cases, infected pressure ulcers can lead to osteomyelitis and septicaemia [Yarkony 1994].

### Antimicrobials in current use:

**Systemic agents**

Systemic agents fall into four main groups: penicillins, cephalosporins, aminoglycosides and quinolines. There are also several other drugs in use, including clindamycin, metronidazole and trimethoprim.

The penicillins work by interfering with the development of bacterial cell walls and cross-linkages. Broad spectrum agents such as ampicillin and amoxycillin are active against certain Gram-positive and Gram-negative organisms, but are inactivated by penicillinases produced by Staph. Aureus and E. coli [BMA 1999]. Amoxycillin is sometimes used in combination with clavulanic acid [Chantelau 1996]. This combination produces an increased range of activity and is effective against both Staph. Aureus and E. coli [BMA 1999].

The cephalosporins have a similar action to the penicillins and have a wide range of
activity against both Gram-negative and Gram-positive organisms [BMA 1999].

The aminoglycosides, such as gentamycin, act by interfering with normal protein synthesis. They have a wide range of action, but are potentially nephrotoxic and ototoxic, and serum levels should be monitored. They are active against the more resilient Gram-negative organisms. They are not absorbed from the gut and systemic administration is therefore by injection [BMA 1999].

The quinolones, such as ciprofloxacin, prevent the formation of DNA within the cell nucleus. They are active against both Gram-positive and Gram-negative organisms. Ciprofloxacin is licensed for skin and soft-tissue infections, but there is a high incidence of staphylococcal resistance and it is recommended that its use is avoided in methicillin-resistant *Staph. aureus* (MRSA) infections [BMA 1999].

Clindamycin is active against Gram-positive cocci, including penicillin-resistant staphylococci, and also against many anaerobes. It has an uncommon but serious and potentially fatal side-effect, namely antibiotic-associated colitis. Current prescribing guidelines state that therapy should be withdrawn immediately in any patient developing diarrhea [BMA 1999]. Metronidazole is active against anaerobic organisms [BMA 1999], and has sometimes been used in combination with other agents, such as ampicillin [Lundhus 1989]. Trimethoprim is commonly used to treat urinary and respiratory tract infections [BMA 1999], and has been shown to be active against *E. coli* when used to treat these conditions [Minassian 1998].

Topical agents

Topical agents include antibiotics, antiseptics and disinfectants. Although various definitions exist for these terms, there appears to be a lack of consensus within the literature as to the characteristics of each type of preparation. It has been suggested that both antiseptics and disinfectants destroy micro-organisms or limit their growth in the non-sporing or vegetative state. However, antiseptics are usually applied solely to living tissues, while disinfectants may also be applied to equipment and surfaces [Morgan 1993].

Topical preparations may be divided into two categories, according to their function. One group consists of lotions with antimicrobial properties, used to irrigate or cleanse wounds. These usually have only a brief contact time with the wound surface, unless they are used as a pack or soak. They include the hypochlorites (e.g. Eusol®), hexachlorophene (a constituent of some soaps and other skin cleansers), and substances such as potassium permanganate and gentian violet (both used in solution for skin cleansing).
The second group consists of preparations designed to stay in contact with the wound surface for a longer period of time, ideally until the next dressing change. These include creams, ointments and impregnated dressings. Most topical antibiotics come into this category, and include mupirocin (available as 2% ointment), which has a wide variety of activity, and fusicidic acid (available as an impregnated dressing, or ointment, cream or gel, all 2%) for staphylococcal infections. Neomycin sulphate, available as a cream (0.5%) or ointment (0.25%), is used to treat bacterial skin infections. If large areas of skin are treated, ototoxicity is a possible adverse effect. Silver based products, such as silver sulphadiazine (1% cream and impregnated dressing), have a broad-spectrum action against both Gram-positive and Gram-negative organisms, and also yeasts and fungi [Morison 1997].

Some products that are available in different forms fall into both categories. These include povidone iodine (available as 10% solution, 10% ointment, 5% cream, 2.5% dry powder spray and impregnated dressing), chlorhexidine (available as 0.05% solution, 5% ointment and medicated tulle dressing; it is also a constituent of skin cleansers), benzoyl peroxide (available as lotions, creams and gels in various strengths) and hydrogen peroxide (available as 3% and 6% solutions and 1% cream) [BMA 1999].

Objectives

To systematically assess the evidence for the clinical effectiveness of systemic and topical antimicrobial agents in the treatment of existing pressure ulcers.

Criteria for considering studies for this review

Types of studies

Both randomised controlled trials (RCTs) and prospective controlled clinical trials (CCTs) with concurrent controls were eligible for inclusion in this review. For both RCTs and CCTs, the units of allocation had to be patients or lesions. Studies in which wards or clinics were the units of allocation were excluded because of the possibility of non-comparability of standard care.

Types of participants

Studies that recruited people with existing pressure ulcers, of any grade or severity,
were eligible for inclusion in the review. The study could be in any setting including hospital, clinic, community facilities, or home.

**Types of interventions**

Trials in which an antimicrobial was compared with another antimicrobial agent, or antimicrobial agent(s) were compared with a placebo, usual care, or no treatment were eligible for inclusion in the review. Trials of antibiotics, antifungal and antiviral agents were all considered. Reports of antibiotic cover used with skin grafting of pressure ulcers, and antimicrobials used in conjunction with debriding agents, were excluded.

**Types of outcome measures**

The primary outcome was wound healing. Since some measures of wound healing can be subjective, studies had to incorporate an objective assessment, such as change in ulcer size, rate of healing, frequency of complete healing or time to complete healing, to be included in the review.

Many evaluations of antimicrobial agents focus on microbiological outcomes such as wound cultures, sensitivities of micro-organisms, bacterial counts and bacterial eradication. Studies reporting only these types of results were excluded from this review since these intermediate (surrogate) outcomes have not been shown to be accurate and reliable indicators of healing. Where studies reported both wound healing and microbiological outcomes, only the former were incorporated in the review. Where available, data concerning adverse effects of interventions were to be included.

**Search strategy for identification of studies**

Searches were carried out in April 2004 and an update search performed in June 2004. Full details of the search strategies can be found in (Appendix, D).

**Methods of the review**

Full details are described in the methods section of this guideline (page 38).

**Description of studies**

Five eligible randomised trials were identified. Two of the included trials assessed
antimicrobial agents on patients with other types of chronic wounds [Della Marchina 1997, Worsley 1991], but data relevant to patients with pressure ulcers were able to be extracted separately and were thus included.

Most of the trials were conducted in either a hospital or an aged care facility, resulting in most of the enrolled patients being elderly. There was a range of pressure ulcer severity requiring treatment in the included trials.

The period of either the interventions and/or follow-up assessments ranged from approximately 2–14 weeks. Three of the five included studies used photographic techniques as part of their objective measurement of wound healing.

No eligible trials were identified that assessed the effects of systemic antimicrobial agents in the treatment of pressure ulcers.

A variety of topical interventions were assessed in the included studies. One trial tested the effectiveness of an antiseptic spray [Della Marchina 1997]. Two trials assessed the effects of ointments: Gerding 1992 tested a oxyquinoline based ointment, whilst Toba 1997 compared a gentian violet based ointment with a povidone iodine ointment. Two trials assessed the effects of hydrocolloid dressings [Huchon 1992, Worsley 1991].

**Methodological quality of included studies**

The studies included in this review were small and generally of poor methodological quality. Details of the quality of each individual study are included in the Table of Included Studies.

Sample size ranged from 14 to 137 patients per trial and *a priori* power calculations were not reported in any of the trials. In four of the five eligible trials, the method of random sequence generation was not stated. Only one trial [Toba 1997] reported adequate allocation concealment. Blinding of treatment allocation and/or outcomes assessment was only reported in one trial [Gerding 1992]. Only one study reported withdrawal rates and reasons [Worsley 1991].

In studies of pressure ulcer treatment it is extremely important for trialists to report on the baseline comparability of the treatment groups for important variables such as baseline risk. Risk of pressure ulcer development is usually reported as one of various risk scores such as Norton, Waterlow, Gosnell or Braden. Only one of the studies reviewed here [Huchon 1992] presented such baseline data.
Even more importantly in pressure ulcer treatment trials it is essential to ensure baseline comparability for initial area of ulcers. A change in wound area is often expressed as the percentage change, which unlike the absolute change in area, takes into account the initial size of the wound. For two wounds healing at the same linear rate (as measured by diameter reduction) percentage area calculations will show a larger change for a small wound than a big wound. The converse is true when the absolute change in area is measured, since for any unit reduction in wound radius a bigger area reduction will occur for a large wound. This has important consequences for the validity of trial results where there is poor comparability in initial wound size at baseline between the treatment groups. In large trials, randomised allocation should ensure that the mean wound size and variance in each group is similar. In a small trial random allocation is unlikely to result in an even distribution of wound sizes. In a trial where there is poor comparability between groups for wound size at baseline, and the outcome is based on the change in area, the result can only be considered valid if it is obtained either: against the anticipated direction of the bias for wound size; or where percentage area change and absolute area change are in the same direction. If baseline data are not given then it is not possible to determine the direction of bias and the validity of the result cannot be determined. Three of the five trials included in this review presented data on baseline ulcer size [Gerding 1992, Huchon 1992, Toba 1997].

Quality was not used to weight the studies in the analysis using any statistical technique, however methodological quality was drawn upon in the narrative interpretation of the results. Methodological flaws are discussed for each study in the Table of Included Studies (see Appendix, A).

Results

Five eligible trials were identified that assessed the effectiveness of antimicrobial agents in the treatment of existing pressure ulcers. All used topical antimicrobial agents, no trials were identified that assessed the effects of systemic agents.

Two trials [Huchon 1992, Worsley 1991] compared the use of a hydrocolloid dressing with one impregnated with povidone iodine. Neither trial individually, or when their results were combined in a meta-analysis (see section 14.1), demonstrated a significant difference between the two treatments in terms of the number of pressure ulcers assessed as completely or partially healed at follow up between 8 and 12 weeks (RR 1.19, 95% CI 0.92, 1.54). Worsley et al [Worsley 1991] drew attention to the fact that fewer dressings changes per week were needed in the hydrocolloid group compared with the povidone iodine group (mean ± SD: 3 ± 1.38 versus 4.9 ± 1.69, respectively, p < 0.005).
Two trials evaluated the effects of different ointments on the rate of pressure ulcer healing. A small trial (n=19) by Toba et al [Toba 1997] assessed the effects of GVcAMP ointment (gentian violet 0.1% blended with dibutyryl cAMP) in elderly women with pressure ulcers contaminated with MRSA. There was no statistically significant difference (mean difference –11.1%, 95% CI –27.86, 5.66) between the two groups in change in wound area at 14 weeks (see section 14.2). The authors hypothesised that the lack of difference seen might be due to the fact that the two largest wounds (area greater than 50 cm²) were in the experimental group. However, an absence of power calculations makes assessment of this comment difficult.

The results of the trial by Gerding and colleagues [Gerding 1992] are difficult to assess as although the unit of allocation was said to be patients, the unit of analysis was the number of lesions. From the results presented it is not clear how many of the 74 patients were randomised to each group. It is likely that some patients had more than one lesion. The results were presented divided according to stage of lesion at enrollment. Figure 3 (see section 14.3) demonstrates that although the result for all lesions combined showed a significant increase in the number of ulcers either partially or completely healed with the oxyquinoline ointment (90%) compared to the povidone iodine ointment (63%) (RR 1.41, 95% CI 1.01, 1.91), when assessed by lesion stage sub-group, no significant benefit was observed for either stage I or stage II lesions. Hence, these results should be interpreted with caution.

In a small RCT (n=19) by Della Marchina and colleagues [Della Marchina 1997] no difference was found (RR 2.22, 95% CI 0.24, 20.57) in the rate of complete healing of pressure ulcers between an antiseptic spray containing eosin 2% and chloroxylenol 0.3% and an alternative spray.

No reliable or objective measures of secondary outcomes such as cost-effectiveness, adverse events, comfort, durability, reliability and acceptability of topical antimicrobial interventions were reported in any of the studies.

**Discussion**

Despite the frequency of pressure ulcer incidence, the cost of the condition to the health care budget and the myriad of treatment modalities, this review demonstrates the paucity of good quality evidence that guides current clinical practice in relation to the use of antimicrobial agents in the treatment of existing pressure ulcers.

Oxyquinoline ointment may be more effective than a standard emollient for treating existing pressure ulcer [Gerding 1992, see section 14.3], but no significant differences
were seen when a hydrocolloid dressing was compared with povidone iodine ointment [Huchon 1992, Worsley 1991, see section 14.1], or when a preparation based on gentian violet 0.1% was compared with a povidone iodine and sugar ointment [Toba 1997, see section 14.2]. The trial which compared an antiseptic spray with an alternate spray [Della Marchina 1997, see section 14.4] was small and of poor methodological quality, precluding a reliable assessment of the effectiveness of this intervention.

These few interventions, tested in small trials of generally poor quality, were the only studies identified that assessed the effectiveness of antimicrobials in the treatment of existing pressure ulcers. There were no trials identified that assessed the effects of systemic antimicrobial agents in pressure ulcer management. The confidence with which we can draw firm conclusions from the few studies detailed in this review is greatly tempered by (a) the poor quality of many of the trials and (b) the lack of replication of most comparisons. Hence, much of the research into this subject requires replication on a larger scale. Attention should be paid to detailed baseline data collection and reporting, blinding of outcome assessors, reporting of withdrawals and the use of the intention-to-treat protocol. Rigorous methods of blinding for wound assessors are essential to establish the relationship between different types of products and changes in nurse labour time required. Finally, concurrent interventions should be described in detail, in particular pressure relieving support surfaces, debridement techniques and forms of topical dressing application.

There are very few data on the cost-effectiveness of antimicrobial agents in pressure ulcer healing. Cost–effectiveness studies should be carried out in conjunction with rigorous evaluations of clinical effectiveness in order to determine the relative difference between cost per unit of the clinical effects of two or more treatments. A cost–effectiveness or cost–utility analysis should include both a measure of the clinical benefit from a non-biased study, and a measure of the net resources used [Drummond 1994]. Data should be collected relating to both short- and long-term patterns of wound healing and recurrence.

Information from two of the studies included in this review [Huchon 1992, Worsley 1991] suggests that certain treatments may be associated with reduced nurse labour time, but further research is required to establish this more reliably. Hydrocolloid dressings require significantly fewer changes than do dressings using conventional antiseptics and wound coverings. For the two studies which assessed this intervention [Huchon 1992, Worsley 1991], the effects on nursing time needs to be assessed in relation to the equivalent results seen in terms of clinical effectiveness (wound healing).
Evidence summary

1++ There is insufficient evidence to indicate whether antimicrobials are effective in the treatment of pressure ulcers.

No economic evaluations assessing antimicrobials for the treatment of pressure ulcers were found.

Research Recommendations

The results summarised in this review are based on findings from small trials with methodological problems. Therefore, much of the required research requires replication in larger, well-designed studies using contemporary interventions for antimicrobial activity.

Recommendations:

In the presence of systemic and clinical signs of infection in the patient with a pressure ulcer, systemic anti-microbial therapy should be considered. [GPP]

Mobility and Positioning in the treatment of pressure ulcers

Mobility or more precisely immobility is reported as significant risk factors for both the development of pressure ulcer as well as a contributory factors in delayed healing (Guralnik et al, 1988; Berlowitz & Wilking, 1989; Ek et al, 1991; Allmoan et al, 1995; Bergstromet al, 1996; Schue & Langemo, 1998; Nixon et al, 2000 and Berguist, 2003). Clinicians and carers engage in a range of activities to reduce the effects of immobility on the healing of pressure ulcers. Mobilising, positioning and repositioning patients (turning) to best promote healing by reducing pressure on the wound, maintained muscle mass, and general tissue integrity are all central to the aims of this activity.
The literature suggests that both ‘seated’ and ‘bed bound’ individuals are at risk of delayed healing and many methods have been postulated to reduce this risk. Much of the research around positioning and re-positions reports interface pressures for different sitting and lying positions with and without support surfaces. The effects of these interventions on healing of pressure ulcer is not clear.

Limited sitting and lying times are seen as one aspect of reducing the risks for those with pressure ulcers. Another is posture and combining the sitting and lying regimes with appropriate support surfaces. Re-positioning patients every 2 or 3 hours is generally accepted as an effective method to prevent pressure ulcers in both patients with and without existing pressure ulcers (Defloor, 2000). The research evidence to support these interventions is not clear and is therefore the aim of this review. The literature reports a range of re-positioning times from 2 hourly to 6 hourly (Defloor, 2001) and despite the possible affects on patients and the impact on resources this evidence is limited with suggestion that re-positioning patients has no preventative effect on the development of grade 1 pressure ulcers (Defloor & Grypdonck, 2000).

Clinical question.

What is the evidence that mobility is effective in the treatment of pressure ulcers?

What is the evidence that re-positioning is effective in the treatment of pressure ulcers?

OBJECTIVES.

The objective is to undertake a systematic review of the evidence of mobility and positioning in the treatment of pressure ulcers to determine:

- What are the key mobility interventions/techniques used in pressure ulcer treatment?
- What are the key positioning techniques used in pressure ulcer treatment?
- What is the significance of these in pressure ulcer treatment?
- What are the priorities in pressure ulcer treatment?
- What is the existing evidence based for their use in the treatment of pressure ulcers?
- What is the empirical evidence that these processes are effective in the management of pressure ulcers?

SELECTION CRITERIA.
Types of studies

RCTs evaluating the effectiveness of mobility and or positioning interventions/techniques in the treatment of pressure ulcers. In the absence of any RCT evidence controlled studies evaluating the effectiveness of mobility and positioning interventions in the treatment of pressure ulcers. Studies reporting interface pressure will not be included in this review because it is not clear how such outcomes relate to delayed healing and complications.

Types of participants

All: adults and children, including those in primary and secondary care, residential homes, nursing homes, secure settings and the home.

Types of interventions

Mobilising (exercise interventions) compared to standard care. Different positioning/re-positioning intervention compared and compared to standard care.

Types of outcome

Healing rates, all objective measures of wound change over time.

Clinical evidence.

33 studies were identified from the sifting process and subsequently full papers ordered. This number also included those studies referenced with relevant titles but where the abstract was absent in the citation. After sifting full papers for relevance and duplicates at this stage 26 papers were opinion pieces, editorials, anecdotal reports or fell outside the inclusion criterion for this review. Out of the 6 selected studies 5 were excluded and 1 was included.

Bates-Jensen et al.

Bates-Jensen et al undertook a randomised controlled trial with blinded assessment of outcomes at 3 points. 190 incontinent nursing home residents were randomised to receive standard care or exercise and incontinence care ever 2 hours between 8am and 4.30pm 5 days per week for 32 weeks. Skin health outcomes were the outcome measures of interest which included pressure ulcers. Assessors were blind to treatment group. A priori was performed. Intervention subjects significantly better skin health outcomes than controls however this was limited to the sacral and trochanter regions ($p = .001$)

Because this is a duel intervention trial it is not clear was proportion of the improved outcome is attributed to the exercise (mobilising) intervention. This trial included a
range of skin conditions which included: maceration, papules, macules, blanching erythema, non blanching erythema, non pressure ulcers and pressure ulcers combined. The effects of the interventions on pressure ulcer healing are not clear from this study.

Due to the lack of evidence for mobility and positioning recommendations were sought from formal consensus methods.

Mobilising, positioning and repositioning interventions should be considered for all individuals with pressure ulcers (including those in beds, chairs and wheelchairs). [D]

All patients with pressure ulcers should actively mobilise, change their position or be re-positioned frequently. [D]

Avoid positioning individuals directly on pressure ulcers or bony prominences (commonly the sites of pressure ulcer development). [D]

Mobilising, positioning and re-positioning interventions should be determined by: [D]
- General health status
- Location of ulcer
- General skin assessment
- Acceptability (including comfort) to the patient
- Needs of the carer

Frequency of re-positioning should be determined by the patient’s individual needs and recorded (eg. a turning chart.) [D]

Passive movements should be considered for patients with pressure ulcers who have compromised mobility [D]
Cost-Effectiveness Analysis

Nutrition in the treatment of pressure ulcers

The methods described in this review are those used to update the following systematic review as they apply to pressure ulcer treatment:


The treatment of pressure ulcers involves a number of strategies designed to address both extrinsic factors, e.g. reducing the pressure duration or magnitude at the skin surface by repositioning or using pressure relieving cushions or mattresses; and intrinsic factors which are concerned with providing the optimum tissue environment for wound healing, that is optimum hydration, circulation and nutrition. It has been reported that malnutrition is positively correlated with pressure ulcer incidence and severity (Berlowitz 1989, Bergstrom 1992). Also that decreased calorie intake, dehydration, and a drop in serum albumin may decrease the tolerance of skin and underlying tissue to pressure, friction and shearing force, increasing risk of skin breakdown and reducing wound healing (Mueller 2001). Furthermore serum albumin is commonly used as a measure of the amount of protein in the blood for healing. However the effect of serum albumin level on wound healing is not clear and there is difference of opinion as to the relevance of such levels in pressure ulcer healing and thus the limited value as an inclusion/exclusion criterion in controlled clinical trials (Hill et al, 1994). Low energy and low protein intake feature in reports of nutrition and wound healing. The combination of low energy and low protein intake is often described as protein-calorie or protein-energy malnutrition.

The Prinz (prevalence and incidence) study which collected data from more than 45,000 patients in Austria between 1995 and 1999, reported that malnutrition – defined as a serum albumin less than 3.5 g/dl – has been identified as a risk factor in 25% of patients (van Steelandt 2000). Further studies suggest a correlation between protein-calorie malnutrition and pressure ulcers (Breslow 1991a, Finucane 1995, Strauss 1996).

The effectiveness of special diets in preventing and treating pressure ulcers has not yet been examined sufficiently despite the fact that risk assessment tools (e.g.
Braden 1994; Gosnell 1989) include nutritional status as a part of the assessment process in the prevention of pressure ulcers. Nevertheless, there is a consensus that nutrition is an important factor in both the prevention and treatment of pressure ulcers. This reiterated by the incorporation of nutritional factors in various guidelines, e.g. the EPUAP Pressure Ulcer Prevention Guidelines ("There should be clarification of a full risk assessment in patients to include: [...] nutrition [...] ") or the EPUAP Pressure Ulcer Treatment Guidelines ("Ensure adequate dietary intake to prevent malnutrition [...] ") (EPUAP 1998, EPUAP 2003). A systematic review is therefore required to summarize the best available research evidence and enable evidence-based guidance on the role of nutritional interventions in pressure ulcer prevention and treatment.

Objectives

To evaluate the effect of nutritional support and supplementation on the treatment of pressure ulcers.

Criteria for considering studies for this review

Types of studies
Randomised controlled trials (RCTs) of parallel or crossover design evaluating the effect of enteral and/or parenteral nutrition on the treatment of pressure ulcers by measuring ulcer healing rates or changes in pressure ulcer severity. Controlled clinical trials (CCT) were only considered eligible for inclusion in the absence of RCTs.

Types of participants
People of any age and sex with existing pressure ulcers, in any care setting, irrespective of primary diagnosis. A pressure ulcer was defined as an area of localised damage to the skin and underlying tissue caused by pressure, shear, friction and/or a combination of these for the purpose of this review.

Types of interventions
Clearly described nutritional supplementation (enteral or parenteral nutrition) or special diet. Comparisons between supplementary nutrition plus standard diet versus standard diet alone and between different types of supplementary nutrition (for example enteral vs. parenteral) were eligible.

Types of outcome measures
The primary outcomes were:

- time to complete healing

The following secondary outcomes were summarised:

- acceptability of supplements
- side effects
- costs
- rate of complete healing
- rate in change of size of ulcer (absolute and relative)
- quality of life

Main Literature search

Searches were undertaken to update the following Cochrane Review:

Databases were searched in August 2004:

Full search strategies listed in Appendix B

Appraisal of methodological quality.

Criteria for inclusion (methodological quality is reported in the evidence tables).

No economic evaluations assessing nutritional support in the treatment of pressure ulcers were found.

Clinical Evidence

Ascorbic Acid (Vitamin C) 2 trials:

Taylor 1974 carried out a double-blind, RCT with 20 surgical patients with pressure ulcers. Patients in the treatment group received additional 500 mg ascorbic acid twice daily for four weeks.
ter Riet 1995 conducted a multi-center blinded RCT with 88 patients with pressure ulcers in 11 nursing homes and one hospital. Patients in the intervention group received 500 mg ascorbic acid twice daily with or without ultrasound for a period of 12 weeks. Patients in the control group received 10 mg ascorbic acid twice daily with or without ultrasound. Most patients had nutritional deficiencies on admission.

**Protein 1 trial:**
Chernoff 1990 undertook a RCT with 12 institutionalised tube-fed patients with pressure ulcers. Patients were randomised to a high protein or a very high protein dietary formula and monitored for eight weeks to assess pressure ulcer healing.

**Zinc 2 trials:**
Norris 1971 performed a randomised, double-blind, crossover study with 14 patients with pressure ulcers. Patients received either 3 x 200 mg zinc sulphate per day or placebo for a period of 24 weeks. After 12 weeks the patients switched the groups.

Brewer 1967 conducted a randomised, double-blinded, placebo controlled trial, with 14 spinal cord injury patients. Patients received either zinc sulphate 220 mg, or a placebo capsule, three times a day for 2–3 months.

**Multinutrient supplementation 1 trial:**
Ek 1991 preformed a randomised, controlled trial of 501 patients newly admitted to a long-term medical ward. Patients in the standard care group received the standard hospital diet containing 2200 kcal/day. The intervention group received 200ml liquid supplement, twice daily,
each 10ml of which 4g protein, 4g fat, 11.8h carbohydrates, 419 kJ and minerals and vitamins, for the duration of their hospital stay or for 26 weeks, whichever was the shorter.

Methodological quality of included studies

The included studies were small (average 33 sample size, range 12 to 88 patients) and of poor methodological quality. None of the included studies reported a power calculation.

Ascorbic Acid (Vitamin C) 2 trials:

The RCT by Taylor 1974 with 20 surgical patients was placebo-controlled, and patients were allocated to the treatment groups according to their year of birth, indicating that they were likely to be aware of the allocation. Patients were comparable at baseline, and no dropouts were reported. Outcome assessors were blinded to treatment.

ter Riet 1995 carried out a multi-centre RCT in 88 patients where investigators, nursing staff, physiotherapists and patients were blinded as to treatment allocation but allocation concealment was not described. They performed an intention-to-treat and a per-protocol analysis.

Protein 1 trial:

Chernoff 1990 undertook a RCT with 12 patients. Follow up was for 8 weeks. They published no information about randomisation and allocation method, blinding, baseline characteristics or follow-up.
Zinc 2 trials:

The trial by Norris 1971 was a randomised crossover study which was described as double-blind but the method of allocation was not specified. Only 3 of 14 patients (21%) completed the study after 24 weeks. Pressure ulcer volumes have been measured in four week intervals. No intention-to-treat analysis was given.

The trial by Brewer 1967 was a randomised, double-blinded, placebo-controlled trial, although the methods of random allocation and blinding are not described. Thirteen of the fourteen enrolled patients completed the trial after 2–3 months of treatment. Pressure ulcer healing was described as complete, definite improvement or no change, but the method of outcome assessment was not described.

Multinutrient supplementation 1 trial:

Ek 1991 was a randomised controlled trial but the method of allocation was not specified. The numbers of patients who completed the treatment (to discharge or 26 weeks whichever was shorter) was not stated. Methods of assessing pressure ulcer healing were not reported, but methods of assessing several other outcome measures, such as serum protein analyses, anthropometry, skin testing, malnutrition and the modified Norton Scale score, were reported in detail.

Results

The included trials were heterogeneous with regard to patients (for example some surgical, some critically ill, some residents in nursing homes) and to interventions, including for example type, application form, timing, dose and duration of nutritional supplementation. Furthermore different primary outcomes have been evaluated in the studies; therefore it was considered inappropriate to perform a meta-analysis.
**Ascorbic Acid (Vitamin C)**

Taylor 1974: 20 people in surgical wards were followed up and data reported at one month. In the group treated with ascorbic acid there was a statistically significant mean reduction in pressure ulcer area of 84% (SE 7.60) after one month compared with 42.7% (SE 7.41) in the placebo group. WMD 41.30 (95% CI 34.72 to 47.88 p<0.005). Complete healing of pressure ulcers occurred in six patients in the nutritional intervention group versus three patients in the placebo group. Relative risk for healing with supplement was 2 (95% CI 0.68 to 5.85). Graph: Comparison 2 outcome 2. The mean healing rate was 2.47 cm²/week in the intervention group compared with 1.45 cm²/week in the control group.

Ter Riet 1995: The mean absolute healing rate in the intervention group (n=43) was 0.21 cm²/week and 0.27 cm²/week in the control group (n=45) (difference -0.06 cm²/week; no standard deviations were reported).

The mean volume reduction was 0 ml/week in the intervention group and 0.20 ml/week in the control group (difference -0.20 ml/week).

The mean "clinical change" where improvements (i.e. surface reduction, healing velocity, volume reduction) were scored on a scale from -100 to +100% was 17.89%/week in the intervention group and 26.08%/week in the control group (difference -8.19%/week).

Ter Riet displayed the healing survival curves for both groups and there was no difference in the hazard of healing. From the graphs the proportion healed at 84 days was 17/43 in the treatment group and 22/45 in the control group (RR 0.81 95%CI 0.50 to 1.30 - calculated by reviewers)
Protein

Chernoff 1990: At the start of the study, pressure ulcers ranged in size from 1.6 cm² to 63.8 cm² in the high protein group and from 1.0 cm² to 46.4 cm² in the very high protein group. On both diets, ulcer size decreased, but the improvement was greater in the very high protein group. None of the patients in the high protein group and 4 patients in the very high protein group had complete healing of their ulcer which gives a relative risk of healing of 0.11 (95% CI 0.01 to 1.70) which is not statistically significant. Graph: Comparison 3 outcome 2.

The average decrease in ulcer size was 42% in the high protein group compared with 73% in the very high protein group.
Zinc

Norris 1971: 14 patients treated with zinc sulphate had pressure ulcers with a mean net change in volume of 10 ml (SD 9 ml), 14 patients receiving placebo had pressure ulcers with a mean net change in volume of 6.0 ml (SD 17.5 ml), which is not statistically significant (weighted mean difference (WMD 4.1 ml; CI 95% -8.10 to 16.30; p=0.5).

Brewer 1967: This early and small (n=14) trial reported no significant difference in the rate of pressure ulcer healing in spinal cord injury patients treated with zinc sulphate 220 mg, three times a day for 2-3 months (1 of 6 patients had complete ulcer healing), compared with patients receiving placebo capsules (2 of 7 patients).

Multinutrient supplementation:
Ek 1991: The total number of sores that developed in the experimental group was 67 and in the control group 83. This was from a total of 495 patients on whom data was available (of the 501 patients randomised). However, it is not known how many patients were in each treatment group. Of the 67 sores that developed in the experimental group, 41.8% (28/67) healed completely compared with 30.3% (25) of the 83 pressure sores in the control group that healed completely. These results were reported as not reaching statistical significance.

### Discussion

Studies of nutritional supplementation vary in terms of interventions, outcome measurements and follow up; interpretation of these findings should be made with caution. Studies included too few patients and had a high drop-out rate. Furthermore, the follow-up time was found to be very short. Hence trials are not likely to detect true effects of the intervention. Some trialists reported that laboratory markers of malnutrition improved during treatment, but the clinical effects of protein, calories, and vitamin or zinc supplementation on the healing of existing sores is unclear.

#### Ascorbic Acid

Taylor 1974 trial included a small number of participants (n=20). The method of randomisation (by year of birth) is open to the researchers and there is the potential that people were recruited into the trial according to clinical judgment rather than truly random. They found significant effects on the reduction of pressure sore area with the intervention (500 mg ascorbic acid twice...
daily up to 12 weeks for surgical patients) but the clinical relevance of a reduction in area (rather than complete healing) is not known.

In the trial by ter Riet 1995 most patients were based in nursing homes (n=88) and had nutritional deficiencies on admission. The control group received 10 mg ascorbic acid, the experimental group 500mg. Patients in the control group had better clinical outcomes at 12 weeks. This study used a reasonable control intervention and a larger sample size which would suggest that the effect of ascorbic acid on the treatment of pressure ulcers seems to be at least unclear.

**Protein**

Chernoff 1990 had a small number of institutionalised tube-fed patients (n=12), the lack of information about randomisation and allocation method, blinding, baseline characteristics and follow-up contribute to the poor trial quality. They reported an average decrease in ulcer size which was better in the very high protein group (73% vs. 42%). There is only weak evidence about the effect of very high protein supplementation rather than regular protein supplements for the treatment of pressure ulcers in tube-fed patients.

**Zinc**

The RCT of Norris 1971 is limited by the small number of patients (n=14). Only three patients completed the study after 12 weeks. They found no significant effects of zinc for pressure ulcers, but the trial is far too small to detect clinically important effects as statistically significant.
The trial by Brewer 1967 was also small (n=14) but had a good treatment completion rate (13 of the 14 patients). Again, although not significant differences were not found in the effect of zinc on pressure ulcer healing, the small sample size did not permit the detection of statistically significant or clinically important treatment effects.

**Multinutrient supplementation**

The trial by Ek 1991 was poorly reported with regard to results by treatment group allocation. It is not known how many of the 501 patients randomised were allocated to each group making an assessment of the effects of the treatment on either pressure sore prevention or healing difficult. Many secondary analyses were reported including results according to the patients’ state of malnourishment, functional level of activity, mobility, food intake, albumin levels and other measures, but there was very limited data regarding pressure ulcer healing rates.

Most treatment studies have short trial periods. Therefore, improvement or healing of pressure ulcer wounds is unlikely to be detected.

Most patients in the studies described above seem to have laboratory defined and confirmed nutritional deficiencies which improved throughout treatment with additional nutritional supplements. Whether this has an effect on clinically relevant outcomes such as pressure ulcer healing remains unclear.
### Evidence summaries

<table>
<thead>
<tr>
<th>Level</th>
<th>Summary</th>
</tr>
</thead>
<tbody>
<tr>
<td>1++</td>
<td>There is no evidence to support the routine administration of nutritional supplementation included in this review to promote the healing of pressure ulcers.</td>
</tr>
<tr>
<td>1+</td>
<td>In patients who have detected deficiencies, supplementation to correct the deficiency according to the daily recommended amounts may be indicated following a nutritional evaluation.</td>
</tr>
<tr>
<td>1++</td>
<td>The effect of corrective nutritional supplementation on pressure ulcer healing remains unclear however.</td>
</tr>
</tbody>
</table>

### Recommendations

#### Nutritional support

† Nutritional support should be given to patients with an identified nutritional deficiency. [A]

Nutritional support/supplementation for the treatment of patients with pressure ulcers should be based on: [D]

- Nutritional assessment (using a recognised tool)
- General health status
- Patient preference
- Expert input supporting decision making (Dietician or specialists)

† The link between correcting this deficiency and its causal relationship with pressure ulcer healing has not been clearly established.
Research recommendations

| Further research with larger numbers of patients and sound methodology is required to procure evidence for the impact of nutrition on pressure ulcers. Consideration should be given as to the constituents of the supplement and the method of application as studies have reported low tolerance of nasogastric tube feeding. |
Surgery for the treatment of pressure ulcers

Surgery has been indicated for the treatment of pressure ulcers since the early part of the 20th century. As early as 1950 in a review including 59 ischial pressure ulcers treated surgically was the method of treatment described and an evaluation of complications and short-term outcomes reported (Cannon, B et al, 1950).

Surgery may be indicated when/to:

- Conservative measures have failed to heal the pressure ulcer.
- Accelerate debridement to expedite spontaneous healing.
- Provide a quick by-pass to conservative measures for reasons of comfort, economy or achievement of a superior repair.
- Achieve a more robust repair than could be achieved by conservative treatment.

Identifying candidates for surgical interventions is based on a thorough assessment of the individual including:

- the aetiology of the pressure ulcer
- anatomical site, staging,
- infection status,
- any underlying medical condition,
- nutritional status,
- neurological status
- psychosocial status
- social factors


Surgery is not usually indicated in patients who have grade I or grade II (apart from minor debridement) pressure ulcers and is usually employed as an intervention in those with grade III and IV pressure ulcers (Henderson, 2004)

The current surgical management of pressure ulcers broadly consists of debridement which can be superficial and may or may not include the removal of bone tissue followed by flap coverage. There is a plethora of different techniques, which have been described in the literature. The pressure ulcers can be surgically debrided and left as an open wound to heal conservatively, surgically closed with or without debridement, repaired using a range of myocutaneous flap or the use of skin grafting.
### Types of surgery

Surgery can be sub-divided into:
- Emergency (drainage or abscess).
- Urgent (debridement of necrotic eschar).
- Elective (further debridement followed by closure).

Which techniques are currently considered to be the most effective is not clear. How clinicians reach decisions about which technique to use is also not clear. Indications about choice of technique from the available literature depends on the assessment of the patients and specifically the site of the ulcer; a flap which is specifically indicated for the area involved and the ability of that chosen flap to be re-harvested if the ulcer reoccurs.

### 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.

This review will aim to consider the contribution of surgery in the treatment of pressure ulcers and its effect on wound healing.

### Clinical question.

What is the evidence that surgery is effective in the treatment of pressure ulcers?

### OBJECTIVES.

The objective was to undertake a systematic review of the evidence of surgical interventions for individuals with pressure ulcers to determine:

- What are the surgical techniques / interventions used?
- In which populations are these techniques / interventions used?
- What are the safety implication?
• What is the empirical evidence that surgery is effective in the management of pressure ulcers?

**SELECTION CRITERIA.**

**Types of studies**

RCTs comparing surgery versus conservative treatment, surgical technique versus surgical technique, surgery versus other interventions for the treatment of pressure ulcers (that do not come under the definition of conservative).

**Types of participants**

All: adults and children,

**Types of outcome**

Time to heal, time to wound closure, all objective healing measures. Mortality rates, safety information, quality of life measures.

**SEARCH STRATEGY**

**Main Literature Search.**

This involved searching a range of medical, nursing, psychological and grey literature databases. All databases were search from inception date and searches were not limited by study design. The searches were limited to retrieve literature published in English, omit animal studies and letters, comments and editorial publication types.

Databases were searched in February 2004 and an update search was performed in August 2004. The strategies are listed in *Appendix B.*

**DATA ABSTRACTION**
Papers were screened for relevance and study design. The methodological quality of the papers was assessed using pre-defined principles as outlined in Appendix E. Data were extracted by a single reviewer and the evidence tables compiled.

Appraisal of methodological quality.

No RCTs were identified from the search strategy and so the decision was taken to follow a narrative review with an open study design criteria. The body of evidence for this review was found to be case series.

Case series and case reports consist either of collections of reports on the treatment of individual patients, or of reports on a single patient. Case series and case reports have limited or no use in a review of an effectiveness of an intervention. However they have an important role in alerting to the potential rare harms or the benefits of an effective treatment (Vandenbrouke, 2001).

Case series and case reports have no control group with which to compare outcomes and therefore have no statistical validity.

Cases series studies were assessed against eight ‘quality’ variables to provide a guide to the extent to which the findings or reporting of each study could be relied upon and to highlight any methodological flaws:

- Case series collected in more than one centre (multi-centre study)
- Aims of case series clearly stated
- Case definition clearly reported
- Explicit statement that patients were recruited consecutively
- Prospective data collection
- Reporting of confidence intervals or other estimate of random variability
- Reporting of mortality/recurrences/complications
- Baseline data for ulcers

Quality criteria for case reports and case series are not well established. This is an adaptation of criteria used in other systematic reviews of case series (Vardulaki K A, et al 2000).
Search results

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<tr>
<td>N screened for relevance following sift</td>
<td>53</td>
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Clinical Evidence.

53 studies were identified from the sifting process and subsequently full papers ordered. This number also included those studies referenced with relevant titles but where the abstract was absent in the citation. After sifting full papers for relevance and duplicates at this stage 18 papers were opinion pieces, editorials, anecdotal reports or fell outside the inclusion criterion for this review. Out of the selected studies 11 were excluded, 24 included.

The majority of the included studies were case reports, case series and retrospective chart reviews of variable quality.

Total study population for this review is 1085 cases represented in both individual case reports and case series. Case series number of participants ranged from 2 to 297. Less than 10 participants were included in this review. However a further 16 studies could have been excluded if this criterion was to have been used.

Reported location of ulcers:

- Sacral area
- Trochanteric area
- Ischial area
- Heel
- Malleolar
- Plantar
Age range from reported studies was 5–83 years although not all studies reported full demographic details. The grade or stage of ulcer was only described in five (Aggarwal et al, 1996; Gusenoff, 2002; Higins et al, 2002; Margara, et al, 2002; Tizian et al, 1986;) of the studies and a range of grading systems was used. Grades ranged from grade III to VII indicating that despite the grade or staging system it was the higher grades that were indicated for surgical interventions. However surgical intervention in lower grades cannot be ruled out due to the grading and staging systems not adequately being described. Baseline data for ulcer size was only given in seven studies (Aggarwal et al, 1996; Akan, et al, 2001; Aydan, et al, 2003; Benito; Forster, et al, 1997; Gusenoff, 2002; Higins et al, 2002; Hiroyuki et al, 1995; Little, et al, 1982; Margara, et al, 2002; Tizian et al, 1986;) either as a range or largest and smallest ulcer.

Follow up period varied greatly from less than 1 month to 60 months.

Complications as a result of surgery was reported in 21 studies with rates of up to 60% reported on one study (Klien, 1988).

**Reported complications**

- Wound dehiscence
- Flap necrosis
- Wound infection
- Osteomyelitis
- Sepsis
- Seroma
- Muscle atrophy
- Blisters
- Suture sinuses
- Hematoma
- Abscess
- Recurrent ulcer
- Death
- Aspiration pneumonia
- Intraop. Myocardial infaction
- Deep venous thrombosis

Generally co-interventions were poorly described in the included studies. Studies that did report on co-interventions were Bocchi et al, (200); Margara et al, (200); Rubayi, (1999); Waiter et al, (1999); and Tizian et al, (1986).
Reported co-interventions.

- 2 hourly position changes
- Water mattresses
- Air mattress
- Vacume assisted closure
- Oral fluids 30ml/Kg 24hours
- Vitamins/minerals
- No smoking
- Nutrition 30–35cal/Kg / Body Weight
- Protein of 1–2 g/Kg 24 hours
- Physiotherapy
- Compliance interventions
- Sitting programme

Conclusions

The lack of any randomized studies means that reporting on the effectiveness of surgical interventions is not possible given the available evidence.

There is no evidence to indicate whether surgery is effective in the treatment of pressure ulcers and consequently no evidence to indicate which technique is the most effective in the treatment of pressure ulcers. However surgery is clearly indicated as a treatment option and its use mainly indicated in those with spinal cord injury, the elderly and, although less frequently reported, in children. Recurrence rates are variable in the limited evidence but reports indicate that they can be as high as 50%.

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No economic evaluations assessing surgical interventions for the treatment of pressure ulcers were found

Recommendations for this area of the guideline have been made using formal consensus methods.

**Recommendations:**

**Surgery**
Referral for surgical interventions for patients with pressure ulcers should be based on: [D]
- Level of risk (anaesthetic and surgical intervention; recurrence)
- Patient preference (lifestyle, abilities and comfort)
- Ulcer assessment
- General skin assessment
- General health status
- Competing care needs
- Assessment of psycho-social factors regarding the risk of recurrence
- Practitioner's experience
- Previous positive effect of surgical techniques
- Failure of previous conservative management interventions

Topical negative pressure, Electrotherapy and Electromagnetic therapy and therapeutic Ultra Sound in the treatment of pressure ulcers.
The methods described in this review are those used to update the following systematic review:


The treatment of pressure ulcers can be broken down into four main areas:

- Local treatment of the wound using wound dressings and other topical applications.
- Pressure relief using beds, mattresses or cushions, and repositioning of the patient.
- Treatment of concurrent conditions which may be delaying healing, for example poor nutrition, infection.
- Use of adjunct therapies such as electrical stimulation, ultrasound, laser therapy and negative pressure.

Adjunct therapies are being increasingly used to assist the healing of pressure ulcers (Lyder 2003, Hess 2003), usually when conventional therapy has failed to make significant improvements in wound healing. The clinical and cost effectiveness of many of these treatments has not been rigorously assessed.

Description of adjunct therapies to be included in the review

Topical negative pressure

One way of manipulating the wound environment in order to promote healing is to apply a topical negative pressure (TNP) (measured in mm Hg) across the wound surface, via a dressing (Davydov 1992, Davydov 1994, Fleischmann 1993, Fleischmann 1995, Argenta 1997). The concept of negative pressure to create a suction force enabling the drainage of surgical wounds to promote wound healing is well documented (Fox 1976, Fay 1987). It has been suggested that if excess fluid is not adequately removed from a wound following surgery, its components may serve as both physical and chemical deterrents to wound healing (Fay 1987). The basic
concept that mechanical forces influence the shape and growth of tissues is also well
documented (Ovington 1999). TNP is reported to do both, that is remove excess
interstitial fluid and transmit mechanical forces to surrounding tissues with resultant
deformation of the extracellular matrix and cells (Morykwas 1998). Both factors are
thought to result in increased wound healing through a variety of mechanisms
(Banwell 1999). The transparent adhesive dressing employed to secure the dressing
may also help maintain a moist wound environment (Mendez-Eastman 1998, Banwell
1999).

There are a number of names to describe the treatment of a wound with TNP
including sub-atmospheric pressure therapy or dressing, vacuum sealing technique,
vacuum assisted wound closure, vacuum assisted closure, negative pressure therapy
or dressing, foam suction dressing, vacuum compression, vacuum pack, sealed
surface wound suction (Banwell 1999, Banwell 2003), or sealing aspirative therapy.
For the purposes of this review this intervention will be referred to as TNP.

TNP requires an open cell dressing (e.g. foam, felt, surgical towel, gauze) to pack the
wound, tubing to connect the dressing to a suction pump via a cannister which
collects any exudate, and an air tight seal around the dressing (Baxandall 1997). All
non-viable tissue is removed beforehand (Argenta 1997). TNP is generally viewed as
contra-indicated if the wound or surrounding tissues are cancerous, there are fistulas
to organs or body cavities, there is necrotic tissue, or there is untreated osteomyelitis
(Mendez-Eastman 1998).

Laboratory evidence of the effectiveness of TNP on the wound environment has been
obtained from several animal studies (Morykwas 1993, Morykwas 1997, Fabian
2000).
The use of TNP in chronic human wounds has been described by a number of
treatment of chronic wounds has been reviewed (Weinberg Group 1999) by referring
to trials using non concurrent/historical control groups. This review examines the
impact of TNP on chronic human wounds by referring to trials where the patients
have been randomised to concurrent control groups. In 2001, a group of Canadian
wound care opinion leaders was convened (with the financial assistance of a TNP
support surface manufacturer) to assess the potential role of TPN in the treatment of
chronic wounds (Sibbald 2003). They noted that there was a gap between the
evidence-base and current practices with regard to this form of adjunct therapy.

**Therapeutic ultrasound**

The mechanisms by which ultrasound may affect wound healing have been reviewed by Dyson 1982. The cellular effects of ultrasound can be divided in thermal and non-thermal (Dyson 1982); the lower intensities used therapeutically mean that any beneficial effects are likely to be due to non-thermal mechanisms (Dyson 1987). Non-thermal effects include the production of standing waves, acoustic streaming, microstreaming and cavitation. Some of these effects may be beneficial whilst others are potentially harmful; standing waves may cause the arrest of blood flow, whilst cavitation may cause bubble formation within the blood stream (Dyson 1987). Careful choice of exposure time, intensity, and continuous movement of the ultrasound applicator should minimize these effects. Therapeutic ultrasound has been evaluated in a number of different regimens: varying pulse duration, power output, and frequency.

**Electrotherapy and electromagnetic therapy**

Electrical stimulation has been used for decades as a treatment for chronic wounds (Hewitt 1956) and is often applied by physical therapists; however, its role in promoting pressure ulcer healing as an adjunct to or in the absence of other proven therapies is unclear.

Research into the role of electricity in wound healing has been undertaken since at least the 1940s (Burr 1940). Experimental animal studies have shown that electrical potentials over the wound during healing are initially positive, becoming negative after the fourth day of healing (Weiss 1990). It has been concluded that the proliferative phase of healing is related to a negative electrical potential over the wound; however, some studies have experimented with positive wound electrodes, and others by reversing the electrode during healing. It is hypothesised that electrical stimulation influences the migratory, proliferative and synthetic functions of fibroblasts, and also results in increased expression of growth factors (Weiss 1990). It seems likely that a moist wound environment is essential to maintain endogenous or applied current flow.

There are several types of electric treatment modalities including low-voltage direct current (LVDC), high-voltage pulsed direct current (PDC), low-voltage alternating current (LVAC) and pulsed electromagnetic field (PEMF) (Sheffet 2000, Unger 2000). All have different administration regimes 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 or a form of radiation. The terminology Pulsed Electromagnetic Field (PEMF) is used to distinguish it from short wave diathermy, which uses either capacitance or induction to produce indirect heating of tissues and can be thought of as a field effect (Stiller 1992).

Objective
To systematically assess the evidence for the effectiveness of adjunct therapies in the treatment of existing pressure ulcers.

Criteria for considering studies for this review

Types of studies
Only randomised controlled trials (RCTs) were included in this review. Studies that did not employ true random allocation of participants to treatment groups, such as quasi-experimental designs, were excluded. The units of allocation had to be patients or lesions. Studies in which wards, clinics or physicians were the units of allocation were excluded because of the possibility of non-comparability of standard care. Both published and unpublished studies were included, with no restriction on date or language.

Types of participants
Studies that recruited people with existing pressure ulcers, of any grade or severity, were eligible for inclusion on the review. The study could be in any setting including hospital, clinic, community facilities, or home.

Types of interventions
Trials in which an adjunct therapy or therapies (as described in section 2) were compared with a placebo, usual care, or no treatment were eligible for inclusion in the review. All modes of delivery/administration/dose for the named adjunct therapies were considered for the review. It was anticipated that, where appropriate, similar regimens would be grouped and subjected to sub-group analyses.

Types of outcome measures
The primary outcome was wound healing. Since some measures of wound healing
can be subjective, studies had to incorporate at least one objective assessment, such as change in ulcer size, rate of healing, frequency of complete healing or time to complete healing, to be included in the review. Change in ulcer size may have been presented as a percentage or absolute change over a period of time. Objective methods of measuring changes on wound size included tracing the ulcer outline followed by counting grids on graph paper, weighing uniform-density tracing paper, planimetry or computerised image analysis.

A single standard outcome measure for wound healing does not exist. Both objective and subjective measures are widely used by researchers, but little effort has been made to determine the validity of many of these measurements. Comfort, ease of application, ease of removal, exudate, handling are frequently used measures of dressing performance, but they are not validated outcomes on which to base decisions of effectiveness. In this review the most commonly validated outcome measures encountered were based on wound healing. The non-ambiguity of complete healing and its importance to clinicians and patients alike (because of its potential impact on quality of life and burden of care), make it the preferred outcome measure with which to compare studies of clinical effectiveness.

Objective measures of healing are usually based on wound area. Planimetry, often aided by computer analysis, is the most frequently used method of calculating wound area, though other methods, such as the measurement of wound diameter or weight of a tracing drawn around the area of the wound, are also used. Measurements of wound volume are infrequently reported in the literature; these methods are often cumbersome and their accuracy has not been proven. Computerised image analysis may in the future, as the equipment becomes more affordable and portable, prove to be a useful technique for the assessment of wound volume.

Even though objective measures reduce or eliminate subjective biases and reduce random measurement errors, they have certain inherent biases if the patients being compared have wounds with different baseline size. A change in wound area is often expressed as the percentage change, which, unlike the absolute change in area, takes into account the initial size of the wound. For two wounds healing at the same linear rate (as measured by diameter reduction) percentage area calculations will show a larger change for a small wound than for a big wound. The converse is true when the absolute change in area is measured, as for any unit reduction in wound radius, a bigger area reduction will occur for a large wound. This has important consequences for the validity of trial results where there is poor comparability in initial
wound size at baseline between the treatment groups. In large trials, randomised allocation should ensure that the mean wound size and variance in each group is similar. In a small trial random allocation is unlikely to result in an even distribution of wound sizes. In a trial where there is poor comparability between groups for wound size at baseline, and the outcome is based on the change in area, the result can only be considered valid if it is obtained either: against the anticipated direction of the bias for wound size; or where percentage area change and absolute area change are in the same direction. If baseline data are not given then it is not possible to determine the direction of bias and the validity of the result cannot be determined. Despite the potential for objective outcomes to be biased by differences in wound size at baseline, they remain the most reliable assessment of wound healing as, unlike subjective measures, they reduce the biases of the assessor which cannot be estimated.

Secondary outcomes such as costs, quality of life, pain and acceptability of the adjunct therapy were assessed where possible.

**Search strategy for identification of studies**

**Clinical effectiveness searching**

**Main literature search**

Searches were undertaken to update the following Cochrane review:


Searches were limited by study design to retrieve randomised controlled trials.

Searches were also limited to retrieve literature published in English, omit animal studies and letters, comments and editorial publication types.

Databases were searched in February 2004 and update searches were carried out in June 2004:

The strategies are listed in *Appendix B.*
Description of included studies

Ten eligible randomised trials were identified for inclusion in the review. One trial (Joseph 2000) assessed the effect of topical negative pressure on a variety of chronic wounds including pressure ulcers. Three RCTs examined the effect of therapeutic ultrasound in the treatment of pressure ulcers (McDiarmid 1985, ter Riet 1995, Nussbaum 1994). Four trials compared electrotherapy to sham therapy for the treatment of pressure ulcers (Gentzkow 1991, Griffin 1991, Wood 1993, Ritz 2002) and a further two trials assessed the effect of electromagnetic therapy for the treatment of pressure ulcers (Comorosan 1993, Salzburg 1995). See Table of Included Studies (Appendix J) for a detailed description of the included studies.

Included studies for topical negative pressure

Joseph and colleagues (Joseph 2000) assessed 24 patients with 36 chronic wounds (resulting from pressure, wound dehiscence, trauma, venous stasis or radiation), defined as present for greater than one month, in a randomised parallel group study. Eighteen wounds received TNP (open cell foam dressing with continuous suction (125 mm Hg)) changed every 48 hours. Eighteen wounds received normal saline wet to moist gauze dressings (with an occlusive dressing used to secure the gauze) changed three times a day. It appears that if patients had multiple wounds, the individual wounds were treated during randomisation and data analysis as if they were independent from each other. At three and six weeks the percent change in wound volume was measured by volume displacement of alginate impression molds. Additional outcome measures were given by Joseph, such as histology and culture, but they did not fulfill the selection criteria of this review. The trial employed a commercially available support surface (VAC Pump, KCI) to apply the negative pressure.

A total of twenty-one studies reporting the effects of TNP on pressure ulcer healing were excluded from the review (see Table of Excluded Studies, section 14). The main reason for exclusion was that they were not RCTs. Patients were either not randomly allocated to the two concurrent treatment groups, or the control group was non concurrent / historical, or, as in the majority of studies, there was no control or comparison group at all. Some of the studies were prospective RCTs but on animals not humans, and some assessed the effect of topical negative pressure on other types of chronic wounds other than pressure ulcers. Those prospective RCTs on humans were reporting the effects of TNP on acute wounds.
A further seven studies are still awaiting assessment, mainly due to publication as abstracts only without a subsequent full publication, and thus insufficient information to assess inclusion criteria or to extract results data, or the primary paper is yet to be sourced and assessed for inclusion. The citations and reasons for not yet being assessed are detailed in the Table of Studies Awaiting Assessment (see section 15).

**Included studies for therapeutic ultrasound**

Three RCTs were identified that examined the effectiveness of ultrasound treatment in the healing of pressure ulcers. The studies all contained small numbers of patients with group sizes varying from 20 patients in three arms to 88 patients in two arms.

Two trials (McDiarmid 1985, ter Riet 1995) compared ultrasound therapy delivered at approximately 3MHz to sham therapy, whilst a third (Nussbaum 1994) compared a combination of ultrasound and ultraviolet with laser treatment (820nm laser diode) with standard wound care. McDiarmid 1985 and Nussbaum 1994 studied patients with superficial pressure ulcers. ter Riet 1995 studied patients with stage II pressure ulcers (partial skin thickness or worse).

The first of these studies (McDiarmid 1985) compared 3MHz of ultrasound with sham treatment for patients with pressure ulcers. Treatment was for a minimum of five minutes (timing dependent on wound size), three times per week. The duration of follow up for the study was unclear.

ter Riet 1995 randomised 88 nursing home patients with pressure ulcers to receive either ultrasound or sham treatment five times a week over a 12 week period. The ultrasound was at a frequency of 3.28MHz with a pulse duration of 2ms.

Nussbaum 1994 compared a combination of ultrasound and ultraviolet treatment (given alternately for 5 days a week), with laser treatment (820nm laser diode), with standard wound care twice daily (cleansing with 0.05% chlorine solution, paraffin tulle dressing and pressure relief). Treatment continued until healing occurred.

Two trials were excluded from the review as they were not randomised controlled trials (see Table of Excluded Studies, section 14).
Included studies for electrotherapy and electromagnetic therapy

Four trials comparing electrotherapy to sham therapy for the treatment of pressure ulcers were suitable for inclusion in this review (Gentzkow 1991, Griffin 1991, Wood 1993, Ritz 2002). These four studies contained a total of 137 patients.

The first of these RCTs (Gentzkow 1991) recruited both hospital and community patients with stage two, three, or four pressure ulcers who were randomised to receive either electrical stimulation twice daily for four weeks or sham stimulation. Patients with more than one pressure ulcer could have all ulcers randomised into the study. Both groups received standard treatment of cleansing with normal saline, a wound dressing (type not stated), and turning to relieve pressure on the effected area in addition to the electrotherapy or sham electrotherapy. The grading of ulcers was described by the authors as stage 2: full thickness skin defect to subcutaneous tissue; stage 3 to muscle; stage 4 to bone/joint.

The second study (Griffin 1991) examined 17 male patients with spinal cord injury and a pressure ulcer graded between 2 and 4 on the Delisa system. Participants were randomised to receive electrotherapy and standard treatment or sham therapy plus standard treatment. The standard treatment consisted of wound cleansing and dressing – pressure ulcers were cleansed using Cara-Klenz application of Carrington gel (dermal wound cleanser) and dressed using a dry dressing. Mechanically debrided as necessary. There was no change of mattress for any patient during the study.

The third study (Wood 1993) compared electrotherapy with sham for the treatment of chronic stage two or three pressure ulcers which had shown no improvement with standard nursing care over the proceeding five weeks. Both groups received standard treatment of wound cleansing, simple moist dressing and whirlpool baths. No hydrocolloids, films or foam dressings were used. There was no description of the system for grading pressure ulcers in the study.

The final study (Ritz 2002) compared the Provant wound closure system (which uses radiofrequency stimuli to induce fibroblast and epithelial cell proliferation) twice daily with sham treatment in high risk patients with grade II to IV pressure ulcers. This treatment was in addition to standard care. Patients treated with concurrent adjunct therapy support surfaces (e.g. hyperbaric oxygenation, electrical stimulation) were excluded.
Two studies of electromagnetic therapy for the treatment of pressure ulcers were included in the review (Comorosan 1993, Salzburg 1995). These two studies contained a total of 60 patients. The first study (Comorosan 1993) was a three arm study comparing electromagnetic therapy, a combination of sham electromagnetic therapy and standard therapy, and standard therapy alone, over a two week treatment and follow up period. Treatment was given for 30 minutes, twice a day. The participants were all patients in an elderly care unit with grade two or grade three pressure ulcers. The grading system for the ulcers was not described.

The second study (Salzburg 1995) compared electromagnetic therapy with sham electromagnetic therapy over a 12 week period. The patients included in the study were all male hospital inpatients with a spinal cord injury. This study also gave treatment for 30 minutes twice a day, although the electromagnetic therapy regimen differed from the Cormorosan study. The pressure ulcers were graded as two or three with an even distribution of each between the groups. A clear definition of the grading of the ulcers was provided by the authors – with grade two ulcers defined as a partial thickness skin loss involving epidermis or dermis, superficial and clinically presenting as a deep crater, abrasion, blister or shallow crater. Stage three was defined as full thickness skin loss involving damage or necrosis of subcutaneous tissue extending down to, but not through, underlying fascia; clinically presented as a deep crater with or without undermining of adjacent tissue.

Two trials that assessed either electrotherapy or electromagnetic therapy were excluded from the review as they were not randomised controlled trials (see Table of Excluded Studies, section 14) and a further five studies are awaiting assessment (see Table of Studies Awaiting Assessment, section 15, for reasons and citations).

**Methodological quality of included studies**

Details of the quality assessment of each study are outlined in the Table of Included Studies (see section 13). The key components of quality that were assessed included *a priori* sample size calculations, allocation concealment, masking of outcome assessment and reporting of withdrawals by treatment group. Quality was not used to weight the studies in the analysis using any statistical technique; however methodological quality was drawn upon in the narrative interpretation of the results.

**Methodological quality of included topical negative pressure studies**

In Joseph 2000, of the 24 patients recruited to the study 12 patients had multiple wounds resulting in a total of 36 wounds. It is not clear how many patients in each
arm of the study had multiple wounds and if these patients were evenly distributed across groups. This could potentially impact on baseline comparability of groups. Baseline comparability was reported for age, sex, initial wound volume, ethnicity, smoking status and wound duration. Each wound was randomised to either TNP or saline gauze dressings. Of the 12 patients with multiple wounds 3 patients were randomised to both therapies. It is inappropriate to randomise and analyse multiple wounds as if they were independent from each other unless using a within subjects design. The preferable way of dealing with multiple wounds using a between patients design is to have a single reference wound. Random assignment of wounds to treatments was achieved using files, marked with silver or black labels on the inside panel that were randomly organised in a locked cabinet. It is not clear if these files were sealed so the adequacy of allocation concealment is unclear. Neither the patient nor the providers were blind to the treatment used. The outcome assessors were blinded as they were not involved in the daily care of the study patients and they only assessed the wounds once the dressings, etc., had been removed. Appropriate outcome measures were used for example percent change in wound volume over time but also extraneous ones which would be reflected in the change in volume. The authors stated that follow up beyond the six week study period continued until complete wound closure was demonstrated for each patient but unfortunately this time to complete healing data was not reported. It was not reported if there were any withdrawals. It is unclear whether intention to treat analysis was performed.

**Methodological quality of included therapeutic ultrasound studies**

None of the three included trials that assessed therapeutic ultrasound (McDiarmid 1985, Nussbaum 1994, ter Riet 1995) included information on the method of randomisation although ter Riet 1995 stated that the method of allocation was concealed (that is the person randomising the patient to the trial was unaware of which group they would enter before randomisation). The two trials that evaluated only ultrasound (McDiarmid 1985, ter Riet 1995) attempted to mask the patients to which group they were in by using a sham therapy group. All three trials used blinded outcome assessment. None of the trials used intention to treat analysis. Concurrent interventions such as support surfaces used were described in two of the three studies (ter Riet 1995, Nussbaum 1994).
Methodological quality of included electrotherapy and electromagnetic therapy studies

It was difficult to extract some of the details on methodological quality due to poor reporting in the five studies that assessed either electrotherapy or electromagnetic therapy (Comoroson 1993, Salzberg 1995). Attempts to contact the authors for clarification were unsuccessful.

None of the studies that assessed electrotherapy (Gentzkow 1991, Griffin 1991, Wood 1993, Ritz 2002) provided information about the method of randomisation used for their trials, and none incorporated an intention to treat analysis. However all four studies did provide information about the baseline features of the pressure ulcer area which enables more accurate interpretation of the results. Whilst all three studies reported the type of wound dressing used during the trials, none reported specific other concurrent interventions such as support surfaces (beds, mattresses and cushions) used.

Neither study that assessed electromagnetic therapy (Comoroson 1993, Salzberg 1995) stated the method of randomisation, nor conducted an intention to treat analysis. Both studies however used blinded outcome assessment. Whilst both studies reported the types of wound dressings used during the study, neither reported other concurrent interventions such as support surfaces (bed, mattresses and cushions) used. The study by Comorosan 1993 did not provide information on the strategies used for randomisation and so there is no rationale as to why the three arms in the study contain an uneven distribution of patients.

Results
Results for topical negative pressure studies

Synthesis of results using statistical pooling methods was not appropriate, as only one trial fulfilled the selection criteria.

Joseph 2000 reported a significantly greater reduction in wound volume (expressed as a percentage of the initial volume at 6 weeks) in favour of topical negative pressure dressings (TNP) when compared with standard wet-to-moist saline gauze dressings. (78% vs 30% p=0.038). It was not clear whether mean or median values were provided. No standard deviations, ranges or confidence intervals were provided. The trialists stated that follow up beyond the 6 week study period continued until
complete wound closure and that all patients were offered operative wound closure for any remaining open wounds. Unfortunately this time to healing data was not reported. Adverse outcomes: 3/18 wounds with TNP had osteomyelitis and/or calcaneal fractures. Two of the patients suffered calcaneal fractures whilst ambulating on the TNP dressing (which Joseph 2000 states is against the manufacturer's recommendations and medical advice). Both patients eventually required amputation. 8/18 wounds with control dressing had osteomyelitis, other wound infections or fistulas (p=0.0028).

There were no RCTs evaluating the effectiveness of TNP on cost, quality of life, pain or comfort and there were no RCTs evaluating the effectiveness of different TNP regimens.

Results for therapeutic ultrasound studies

Two trials compared therapeutic ultrasound with sham ultrasound (McDiarmid 1985, ter Riet 1995). The third trial compared a combination of ultrasound and ultraviolet light with laser therapy, and standard treatment (Nussbaum 1999)

Ultrasound therapy versus sham therapy

McDiarmid 1985: 10/21 (48%) pressure ulcers healed in the ultrasound group compared with 8/19 (42%) in the sham group (RR 1.13, 95% CI 0.57, 2.26). Treatment was delivered three times a week for an unspecified period of time.

Ter Riet 1995: 18/45 (40%) of pressure ulcers healed in the intervention group compared with 19/43 (44%) in the control group (RR 0.91, 95% CI 0.55, 1.48). Treatment was given five times a week for 12 weeks or until healing had occurred.

The trials by McDiarmid 1985 and ter Riet 1995 were considered sufficiently similar to pool (chi-squared = 0.26, I²=0%) giving a pooled relative risk of 0.97 (95% CI 0.65, 1.45; p=0.89). Thus two studies involving only 128 patients in total found no evidence of a benefit of ultrasound on the healing rates of pressure ulcers (see Figure 1).

Figure 1:
Ultrasound and ultraviolet therapy versus laser therapy versus standard treatment

Ultrasound combined with UV therapy was compared with laser alone and standard therapy in 20 patients with spinal cord injury and pressure ulcers up to 1cm in depth (Nussbaum 1994). Groups were broadly similar in terms of area and depth of ulcers. Four patients dropped out leaving 16 patients with 18 wounds. After 12 weeks all ulcers (6/6) had healed in the combined ultrasound/ultraviolet treatment group. In the laser treatment group 4/6 (66%) ulcers healed, and in the standard wound care group 5/6 (83%) ulcers healed. There was no statistically significant difference between the groups due to the extremely small sample size, and the consequent lack of power as shown below:

- ultrasound/UV therapy versus laser therapy: RR 1.5, 95% CI 0.85, 2.64
- ultrasound/UV therapy versus standard treatment: RR 1.2, 95% CI 0.84, 1.72
- laser therapy versus standard therapy: RR 0.8, 95% CI 0.41, 1.56

No secondary outcome measures, including costs, quality of life, pain and acceptability, were measured in any of the RCTs included.

Results for electrotherapy and electromagnetic therapy studies

Electrotherapy versus sham electrotherapy

Four trials compared electrotherapy with sham electrotherapy.

Gentzkow 1991: After four weeks there was a mean percentage ulcer healing of 49.8% (SD 30.9) in the electrotherapy group and a 23.4% (SD 47.4) mean percentage ulcer healing in the sham group (p=0.042). The baseline ulcer areas given demonstrated larger ulcers in the intervention group. Thus the result is against the direction of bias, as the outcome of percentage healing favoured the control group.

Griffin 1991: 3/8 (37.5%) ulcers healed in the electrotherapy group compared with 2/9 (22%) in the control group (RR 1.69, 95% CI 0.37-7.67).

Wood 1993: 25/ 43 (58%) electrotherapy group ulcers healed, compared to only 1/31
(3%) in the sham therapy group (RR 18.02, 95% CI 2.58-126.01). As the ulcers were larger at baseline in the intervention group this result is against the direction of bias.

Ritz 2002: 4/8 (50%) ulcers in the electrotherapy group healed completely, compared with only 1/7 (14%) in the sham therapy group (RR 3.50, 95% CI 0.50, 24.41). This was a very small, industry-sponsored study.

Three studies had outcomes regarding the numbers of ulcers healed and were considered sufficiently similar to pool (Griffin 1991, Wood 1993, Ritz 2002) (Chi-square 4.69, I²=57%); resulting in a pooled relative risk of 4.41 (95% CI 0.9-21.35; p=0.07), see Figure 2. This shows no evidence of improved healing of pressure ulcers treated with electrotherapy compared with sham therapy. Again however, as this result is drawn from three small studies with a total of 106 patients, the results should be interpreted with caution.

**Figure 2:**

Electromagnetic therapy versus sham therapy

Two trials compared electromagnetic therapy with sham therapy, although the trial by Comorosan included a third arm in which only standard therapy was applied.

Comorosan 1993: 17/20 (85%) ulcers healed in the electromagnetic therapy group within 2 weeks compared with no ulcers healing in either of the other two groups (0/5 and 0/5) (RR 10, 95% CI 0.7-143.7).

Salzburg 1995: Grade 3 pressure ulcers – 3/5 (60%) healed in the electromagnetic therapy group compared with no ulcers healing in the sham electrotherapy group (0/5) at 12 weeks (RR 7, 95% CI 0.45-108.26). Grade 2 pressure ulcers – median of 84% healing in the electromagnetic therapy group at one week compared with 40% in
the sham therapy group (p=0.01). Groups could not be combined due to the different timings and outcome measures between the grade 2 and grade 3 pressure ulcers.

Secondary outcome measures such as financial costs, quality of life, pain and acceptability were not measured in either of the RCTs included.

**Discussion**

**Quality of the included studies**

Quality assessment suggests that methodological flaws are an issue affecting the validity of most studies in chronic wound care. In general, the studies were too small to ensure that wounds of different sizes (and other prognostic variables) were evenly distributed across trial arms, resulting in a bias at baseline in most trials. The majority of studies also had a short follow-up and did not analyse the data by survival analysis, which would account for whether and when a wound healed and which would be a more efficient method for estimating the rate of healing. If future trials perpetuate many of the methodological flaws highlighted in this review, they are unlikely to provide the necessary evidence to determine an effective wound management strategy. The variability between wounds at baseline for prognostic variables, including size, indicates that recruitment numbers need to be large and that trials should probably be multi-centered. If small single-centered trials are to be continued they could be improved by the use of matched or stratified randomisation to ensure a similar distribution of wound sizes between treatment groups at baseline, and the data should be analysed by matched pairs analysis where appropriate. However, even with this improved design a trial still needs to be large enough to ensure comparability for both unknown and known confounding factors.

It is important to ensure, when conducting an RCT, that systematic differences in: comparison groups (selection bias); care provided apart from the intervention being evaluated (performance bias); outcome assessment (detection bias); and withdrawals from the trial (attrition bias) are avoided (or made explicit) (Clarke 2003). The logical basis for this being that any differences in group outcomes could be due to these systematic differences. Differences in group outcomes could then be wrongly attributed to the intervention being evaluated. Selection bias can be eliminated by assembling comparison groups in such a way that the process is impervious to any subconscious influence by the individuals making the allocation. This is most securely achieved if an assignment schedule generated using true randomisation is concealed. Allocation concealment can always be implemented (Clarke 2003). Performance and
detection biases can occur if there are unintended differences in the way the treatment and placebo groups are treated, either whilst receiving the intervention or being assessed at follow-up. The best way to avoid these potential biases is for those providing and receiving care, and those undertaking the outcome assessments to be blinded so that they do not know the group to which the recipients of care have been allocated (Clarke 2003). There is limited empirical evidence of a relationship between parameters thought to measure validity and actual trial outcomes. More research is needed to establish which criteria for assessing validity are important determinants of study results and when (Clarke 2003).

When critically appraising the validity of the studies, the reviewers had to rely on adequate reporting of the trials. Assuming that if something was not reported it was not done is not necessarily correct. The reviewers relied on the good will of experts in the field to provide information on completed or ongoing, published or unpublished studies.

The reviewers did attempt to obtain additional clarifying data from investigators; however no response was received.

The alternative to withholding treatment from a patient is to employ a placebo. In wound care trials such placebo treatments are unlikely to be inert as the application of the placebo or vehicle is likely to change the local environment of the wound, thereby modifying the biological processes associated with healing. A placebo is therefore not a substitute for withholding treatment in studies to determine the rationale for active treatment. The possible interaction between the vehicle and the healing process, together with small sample size, may provide some explanation for why so few of the trials included in this review showed a statistically significant difference between an active treatment and a placebo.

Generally, the methodological quality and sample size of the trials included in this review was only fair. Very few trials reported their methods of randomisation or allocation concealment, and few calculated a priori sample size estimates. However, several studies used sham therapy in order to maintain blinding of treatment allocation to the patients, clinicians and outcomes assessors.

**Topical negative pressure as an adjunct treatment for pressure ulcers**

In the study by Joseph (Joseph 2000) the assignment schedule appeared to be generated using true randomisation but the adequacy of allocation concealment was
unclear, hence risking selection bias. The study was also at risk of performance bias as the experimental group received TNP delivered via a foam dressing whereas the control groups had saline gauze dressings so it was impossible to "blind" those providing and receiving care. However, outcome assessors were blind regarding treatment allocation thereby reducing the risk of detection bias. It is uncertain whether the Joseph 2000 study was at risk of attrition bias. In this study it was not clear whether intention-to-treat analysis was used, if exclusions were made, and, if they were, the reasons for these (protocol deviations, withdrawals, dropouts, and losses to follow up).

Due to the poor reporting of this study, precise effects measures cannot be calculated. This coupled with the small sample size and methodological flaws means that this trial does not provide any evidence of benefit regarding the use of topical negative pressure as an adjunct therapy for pressure ulcer treatment. Further controlled trials are needed to address this question.

Therapeutic ultrasound as an adjunct treatment for pressure ulcers

The results of the two included trials in this review (McDiarmid 1985, ter Riet 1995) do not suggest a benefit associated with therapeutic ultrasound in the healing of pressure ulcers. Again however, as the numbers of randomised patients are small and methodological quality relatively poor, the results should be viewed with caution. Further randomised trials are warranted.

Electrotherapy or electromagnetic therapy as an adjunct treatment for pressure ulcers

The four trials identified that assessed these interventions (Getzkow 1991, Griffin 1991, Wood 1993, Ritz 2002) all suggested a trend toward benefit associated with using electrotherapy to treat pressure ulcers. However this suggestion is drawn from a total of only 186 patients. The three studies whose results were pooled (Griffin 1991, Wood 1993, Ritz 2002) all had unmatched groups for ulcer size at baseline. Griffin 1991 had larger ulcers in the control group. The result (RR 1.69, 95% CI 0.37-7.67) whilst not statistically significant, favours electrotherapy, is therefore with the direction of bias. There were only small numbers of patients in each group in this study. Wood 1993 included patients whose ulcers were larger in the intervention group. The result of this study (RR 18.02, 95% CI 2.58-126.01) is statistically significant whilst being against the direction of bias. Overall, there was no evidence of a statistically significant benefit in pressure ulcer healing with the use of
electrotherapy. The extent to which electrotherapy contributes to healing in patients who are otherwise receiving pressure relief and moist wound healing strategies needs be explored further using rigorous methodology.

Whilst the two trials (Comorosan 1993, Salzburg 1995) that assessed the effect of electromagnetic therapy are both suggestive of a benefit for the healing of pressure ulcers, neither reaches statistical significance and the evidence is rather unreliable. Both trials contained small numbers of patients, had differing regimens of treatment over varying time scales. The extent to which electromagnetic therapy contributes to healing in patients who are otherwise receiving pressure relief and moist wound healing strategies should be explored further. The trials do not adequately report severity of pressure ulcers and baseline comparisons. As such the results should be viewed as unreliable and further research is needed involving larger numbers of patients.

**Cost effectiveness of Adjunct therapies (topical negative pressure, therapeutic ultrasound, electrotherapy and electromagnetic therapy)**

One full economic evaluation and one partial economic evaluation of adjunct therapies were identified for review (Macario et al, 2002; Philbeck et al, 1999 respectively).

Macario et al (2002) conducted a cost–utility analysis comparing noncontact normothermic wound therapy to current standard care (see data extraction table 22). The study was conducted in a long-term care institution in the United States. The authors reported that the perspective of the analysis was societal. The analysis included societal-based utilities, however the costing was undertaken from the perspective of the health care payer (see data extraction table 22). The study was based on a decision-analytic model. The base case analysis involved a hypothetical, 72 year old patient with a two month old, ischial grade 3 pressure ulcer who was living in a nursing home. The secondary analysis involved a grade 4 pressure ulcer. Monte Carlo simulation was undertaken to resample from the data to estimate results for 10,000 hypothetical patients.
Data to populate the model was obtained from national statistics, the literature and author opinion. A Markov model was used which comprised of six mutually exclusive health states including: (i) grade 3 pressure ulcer, (ii) grade 4 pressure ulcer, (iii) healing wound, (iv) closed wound healed back to normal, (v) complications requiring hospitalisation and (vi) death. Patient progression through the model was divided into eight week cycles over 40 months.

Utility estimates were based on author assumption, informed by the literature. The quality of life a patient with a pressure ulcer was determined by assigning levels of disability and distress to each health state. The authors used the Rosser-Kind index, which includes disability and distress dimensions to attach utilities to each of the six health states (above). The change in utility attached to patients’ health status as they progressed through the model was combined with life expectancy to calculate QALY estimates. The resources measured and costed included nurse and doctor time, use of supplies and equipment and the cost of complications.

Over the 40 month timeframe, for grade 3 pressure ulcers it was estimated that 0.10 (SE = 0.0005) QALYs were gained per patient using noncontact normothermic wound therapy over current standard care, and for grade 4 pressure ulcers the gain in QALYs was 0.14 (SE = 0.0010) per patient. In terms of costs, for grade 3 pressure ulcers it was estimated that noncontact normothermic wound therapy cost $6,3340 (SE = $98) (price year 2000) less than current standard care and for grade 4 pressure ulcers the cost was estimated to be $15,216 (SE = $186) less. Thus noncontact normothermic wound therapy was identified as the dominant strategy in treating grade 3 and 4 pressure ulcers. Probabilistic sensitivity analysis was undertaken to test the robustness of the results by simultaneously considering uncertainty associated with all probabilities, utilities and costs included in the model. Results were most sensitive to the following model inputs; daily treatment costs and the probability of healing to a normal closed wound with standard care, the cost of the complication state and the acquisition cost of noncontact normothermic wound therapy. If the cost of the latter increased to $421 its use increased overall costs. The Monte Carlo simulations showed that noncontact normothermic wound therapy is likely to reduce costs and increase quality of life for at least 75% (SE=0.4%) of patients with stage 3 pressure ulcers and to reduce costs by around 81% (SE=0.4%) for patients with stage 4 pressure ulcers.

 SE = Standard Error. This statistic indicates the degree of uncertainty in calculating an estimate from a sample
These results should be considered in the light of a number of assumptions that underpin the Macario et al (2002) model. As the authors mention, their assumption that transition probabilities remain constant over time may be questioned. For instance in practice the probability of healing after the first eight week cycle may not be equal to the probability of healing after the fourth eight week cycle. Utilities were attached to health states indirectly, that is the patients themselves did not value health states as this data was not available. The model assumed that reduction in wound size directly improved the probability of wound healing. Data to populate the model was obtained from numerous sources, based on controlled and randomised trials, and there was much variability due to differences in delivery of care across settings (standard care varies in particular), confounding comorbidities, variability in types, sizes and locations of pressure ulcers.

Philbeck et al (1999) conducted a cost–consequence analysis comparing negative pressure wound therapy to saline soaked gauze dressing applied to patients placed on either a low-air loss mattress or a foam mattress bed for grade 3 or 4 pressure ulcers (see data extraction table 23). The analysis was conducted from the perspective of the health care payer although this was not stated.

For the negative pressure wound therapy group a Medicare observational dataset was used which covered a 180 day follow-up period. For the comparator, data from the Ferrell et al study (1993) were used (see table 25 which presents an economic evaluation by Ferrell et al (1995) which was also based on this trial). The study was excluded from the clinical-effectiveness review because it was based on retrospective, observational data for the negative pressure wound therapy and a historical control (Ferrell et al 1993) for the comparator.

Effectiveness measures from both studies included healing rates as a reduction in wound area and volume over 30 days and time to heal. The reduction in cm$^2$ per day of the wound was faster for negative pressure wound therapy at 0.230 cm$^2$ per day compared to 0.090 cm$^2$ for the comparator. Time to heal, based on wound healing rates, was expected to be 97 days for negative pressure wound therapy compared to 247 days for the comparator. The total cost of negative pressure wound therapy per day, including the cost of materials and nursing visits was $149.96 versus $95.00 (the price year was not stated). However, due to a faster expected healing rate, the expected total cost to complete heal was lower, on average for each patient in the negative pressure wound therapy group ($14,546 versus $23,465).
It appears that negative pressure wound therapy dominates saline soaked gauze dressing applied to patients placed on either a low-air loss mattress or a foam mattress bed for grade 3 or 4 pressure ulcers. However, there are a number of substantial limitations associated with the study that cast doubts on the validity and reliability of the results. Whilst the authors aimed to closely match patients from either study, the potential variability and uncertainty introduced into the study as a result of the study design was not explored. The authors' state that the Medicare dataset did not contain data on duration of previous interventions, medical history and laboratory values relevant to wound healing and the homogeneity of the patients across the two groups, apart from the treatment received, is questionable. The initial surface area of the wounds was very different (22.2 cm\(^2\) versus 4.3 cm\(^2\) for the negative pressure and comparator treatments respectively), however this may be expected to favour the latter.

### 1.1.1 Overview of adjunct therapies

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drawn from three studies with a total of only 137 patients, therefore the results should be viewed with caution as it is difficult to determine clinically important effects from such small samples. Further research is required into this potentially beneficial treatment before definitive recommendations for practice can be made.

There is no reliable evidence of benefit of using electromagnetic therapy in the treatment of pressure ulcers. The possibility of benefit or harm cannot be ruled out due to the small number of trials with methodological limitations and small numbers of participants.

Overall, whilst adjunct therapies are increasingly being used in clinical practice, there is currently little good quality evidence to support their use.

**Cost effectiveness**

The effectiveness evidence on which the two economic evaluations were based was moderate to low, primarily due to lack of data. The two studies compare different treatments (?) so it would not be appropriate to synthesize the data. The economic evaluation presented by Macario et al is the stronger of the two studies and it appears that noncontact normothermic wound therapy may be more cost-effective than current standard care. Although the Philbeck et al (1999) study suggests that negative pressure wound therapy might be a more cost-effective option than saline soaked gauze dressing applied to patients placed on either a low-air loss mattress or a foam mattress bed for grade 3 or 4 pressure ulcers, the internal validity and generalisability of the findings is questionable.

**Recommendations:**
Adjunct therapies

The use of adjunct therapies (electro-therapy technologies and topical negative pressure therapy) for the treatment of pressure ulcers should be based on:

- Ulcer assessment
- Level of risk from holistic assessment
- General skin assessment
- General health status
- Previous positive effects of the technology/therapy
- Patient preference (lifestyle, abilities and comfort)
- Practitioner’s competence

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<tr>
<td>There is a need for well designed, adequately powered, multi-centre RCTs to evaluate the contribution of adjunct therapies to the healing of pressure ulcers.</td>
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<tr>
<td>Evidence for the relative effectiveness of adjunct therapies compared to other treatment modalities in pressure ulcer management is likely to be provided by trials in which the comparison is an adjunct therapy against a background of standard care (preferably treatments based on the best available evidence), or adjunct therapies compared with sham therapies.</td>
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<tr>
<td>Well designed, multi-centre RCTs evaluating the effectiveness of adjunct therapies on healing rates, healing times, cost, quality of life, pain and comfort, and whether there are optimal regimes, for patients with existing pressure ulcer, of varying degrees of severity, are thus required.</td>
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Education and information giving

Recommendations

All health care professionals should be educated about:

- Pressure ulcer management;
- ; and
- patient education and information giving (Level IV) [D].

Individuals with pressure ulcers and their carers should be informed verbally and in writing about:

- 
- 
- where they can seek further advice and assistance (Level IV) [D].

6.2.7 Guideline Development Group comment

These are consensus-based statements.

7 RECOMMENDATIONS FOR RESEARCH

The following research gaps were identified by the GDG (following NICE requirements, the first 5 are those that were prioritized by the GDG using a group consensus process in which every research recommendation was ranked by each group member -latter process may only be necessary if the GDG generates too many)
8. ALGORITHM: Pressure Ulcer Management Algorithm

Patient presents with Pressure Ulcer

**Holistic Assessment**
(Conducted by a competent healthcare professional and recorded)

Risk of delayed healing/complications

Ulcer Assessment
(Supported by photography/tracings)

- Health status
  - (Acute/chronic/terminal)
  - Previous ulcer history
  - Co-morbidity
  - Cognition
  - Sensory Impairment
  - Conscious level
  - Nutritional status
  - Psycho-social factors
  - Continence status
  - Tissue perfusion

- Pain
- Medication
- Mobility

- Cause
  - Exudate (type/amount)
  - Site/location
  - Dimensions of ulcer
  - Stage/grade recorded
  - Infection
  - Surrounding skin
  - Undermining/tracking
  - (sinus or fistula)
  - Odour

Treatment plan should address all aspects of assessment

Relieve the pressure

For all grades of ulcer select an appropriate pressure relieving device

Select further treatment options

- Debridement
- Surgical Antimicrobial referral
- Antimicrobial therapy
- Dressing selection
- Nutritional support
- Pain relief therapies

Evaluate impact of treatment interventions by regular re-assessment

Remember that all patients with pressure ulcers should actively mobilise, change their position or be re-positioned frequently.

Remember, patients should have access to appropriate pressure relieving support surfaces (eg. mattresses and cushions) 24 hours a day and this applies to all support surfaces.

Identification of a Grade 1 ulcer is a significant risk factor for the development of a more severe ulcer (eg. Grade 2+).

Patient management should be multi interventional and an inter-disciplinary team approach.
9. AUDIT CRITERIA

The audit criteria below are to assist with implementation of the guideline recommendations. The criteria presented here are considered to be the key criteria associated with the guideline recommendations. They are suitable for use in primary and secondary care, for all patients______________________________.

Caveats for guideline user

a. Objectives for an audit

b. Individuals to be included in an audit

c. Data sources and documentation of audit

Systems for recording the necessary information (which will provide data sources for audit) should be agreed by Trusts.

Whatever method is used for documentation, the documentation should be accessible to all members of the multidisciplinary team.

Documentation of the factors taken into consideration when deciding the most appropriate intervention should occur.

The fact that carers and patients have been informed about pressure ulcers should be documented. Patients and carers should be directly questioned about their satisfaction with, and the adequacy of, the information provided and this should be documented in either the patient notes or in another source as agreed by the Trust.

Trusts should establish a system of recording when staff have been educated in the management of pressure ulcers and should implement a process for reviewing pertinent education needs.

Audit criteria should be read alongside the PUM algorithm

The GDG have listed essential questions that form the basis of broad audit criteria in relation to the PUM algorithm. These are colour coded and relate to the algorithm.
Patient presents with Pressure Ulcer
- Family, medical, personal and domestic activities of daily living, social history?
- Cognitive ability?
- Features of the care environment that they have come from (including current resources)?
- Level of family and social support?
- Carer involvement and ability of unpaid carer/s

Holistic Assessment
- Who conducted the assessment?
- When was it conducted?
- Did it incorporate all aspects of risk and ulcer assessment?
- Is the treatment plan triggered by the findings of the holistic assessment?
- Is the period of re-assessment clearly stated and evidence that it has taken place?

For all grades of ulcer, use a pressure support surface
- What pressure support device was requested (Time and date recorded)?
- Type of device supplied (Time and date recorded)?
- Recorded first use by patient (Time and date recorded)?
- Is there an equivalent pressure support from bed to chair?
- Has an assessment of patient mobility, ability to reposition or be repositioned been undertaken?

Consider treatment options
- What treatments or interventions used in the management plan?
- Have identified treatment options been addressed?

Evaluate impact of treatment interventions by regular re-assessment
- Effect of treatments or interventions used in the management plan?
- Is there evidence of re-assessment?
- Has this influenced the ongoing management plan?
10. **DISSEMINATION OF GUIDELINES**

The Guideline will be produced in a full and summary format and a version for the public (Information for the Public)

Full copies of the Guideline will be available through the NICE website (http://www.nice.org.uk) in PDF format and summary through the National Electronic Library for Health NeLH (http://www.nelh.nhs.uk/) and National Guideline Clearinghouse (http://www.guidelines.gov).

11. **VALIDATION**

The guideline will be validated through two stakeholder consultation processes. The first and second drafts will be submitted to NICE in December 2004 and March 2005, who will obtain and collate stakeholders comments for consideration by the GDG.

12. **SCHEDULED REVIEW OF GUIDELINE**

The process of reviewing the evidence is expected to begin 4 years after the date of issue of this guideline. Reviewing may begin earlier than 4 years if significant evidence that affects the guideline recommendations is identified sooner. The updated guideline will be available within 2 years of the start of the review process.
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