Health Technology Assessment 2001; Vol. 5: No. 9

Review

Systematic reviews of wound care management: (5) beds; (6) compression; (7) laser therapy, therapeutic ultrasound, electrotherapy and electromagnetic therapy

N Cullum
EA Nelson
K Flemming
T Sheldon

Health Technology Assessment
NHS R&D HTA Programme

How to obtain copies of this and other HTA Programme reports.
An electronic version of this publication, in Adobe Acrobat format, is available for downloading free of charge for personal use from the HTA website (http://www.hta.ac.uk). A fully searchable CD-ROM is also available (see below).

Printed copies of HTA monographs cost £20 each (post and packing free in the UK) to both public **and** private sector purchasers from our Despatch Agents.

Non-UK purchasers will have to pay a small fee for post and packing. For European countries the cost is £2 per monograph and for the rest of the world £3 per monograph.

You can order HTA monographs from our Despatch Agents:

– fax (with **credit card** or **official purchase order**)
– post (with **credit card** or **official purchase order** or **cheque**)
– phone during office hours (**credit card** only).

Additionally the HTA website allows you **either** to pay securely by credit card **or** to print out your order and then post or fax it.

Contact details are as follows:

HTA Despatch
c/o Direct Mail Works Ltd
4 Oakwood Business Centre
Downley, HAVANT PO9 2NP, UK

Email: orders@hta.ac.uk
Tel: 02392 492 000
Fax: 02392 478 555
Fax from outside the UK: +44 2392 478 555

NHS libraries can subscribe free of charge. Public libraries can subscribe at a very reduced cost of £100 for each volume (normally comprising 30–40 titles). The commercial subscription rate is £300 per volume. Please see our website for details. Subscriptions can only be purchased for the current or forthcoming volume.

Payment methods

Paying by cheque
If you pay by cheque, the cheque must be in **pounds sterling**, made payable to *Direct Mail Works Ltd* and drawn on a bank with a UK address.

Paying by credit card
The following cards are accepted by phone, fax, post or via the website ordering pages: Delta, Eurocard, Mastercard, Solo, Switch and Visa. We advise against sending credit card details in a plain email.

Paying by official purchase order
You can post or fax these, but they must be from public bodies (i.e. NHS or universities) within the UK. We cannot at present accept purchase orders from commercial companies or from outside the UK.

How do I get a copy of *HTA on CD*?

Please use the form on the HTA website (www.hta.ac.uk/htacd.htm). Or contact Direct Mail Works (see contact details above) by email, post, fax or phone. *HTA on CD* is currently free of charge worldwide.

The website also provides information about the HTA Programme and lists the membership of the various committees.

Systematic reviews of wound care management: (5) beds; (6) compression; (7) laser therapy, therapeutic ultrasound, electrotherapy and electromagnetic therapy

N Cullum*
EA Nelson
K Flemming
T Sheldon

Department of Health Studies, University of York, UK

* Corresponding author

Competing interests: N Cullum has: received funds from the NHS R&D Programme to undertake primary research in wound care; received sponsorship of trial-related educational meetings from Huntleigh Healthcare and Beiersdorf Ltd. EA Nelson has: conducted one of the trials reviewed; been reimbursed for attending symposia by Smith and Nephew Ltd, ConvaTec and Huntleigh Healthcare

Published May 2001

This report should be referenced as follows:

Cullum N, Nelson EA, Flemming K, Sheldon T. Systematic reviews of wound care management: (5) beds; (6) compression; (7) laser therapy, therapeutic ultrasound, electrotherapy and electromagnetic therapy. *Health Technol Assess* 2001;**5**(9).

Health Technology Assessment is indexed in *Index Medicus*/MEDLINE and *Excerpta Medica*/EMBASE. Copies of the Executive Summaries are available from the NCCHTA website (see opposite).

NHS R&D HTA Programme

The NHS R&D Health Technology Assessment (HTA) Programme was set up in 1993 to ensure that high-quality research information on the costs, effectiveness and broader impact of health technologies is produced in the most efficient way for those who use, manage and provide care in the NHS.

Initially, six HTA panels (pharmaceuticals, acute sector, primary and community care, diagnostics and imaging, population screening, methodology) helped to set the research priorities for the HTA Programme. However, during the past few years there have been a number of changes in and around NHS R&D, such as the establishment of the National Institute for Clinical Excellence (NICE) and the creation of three new research programmes: Service Delivery and Organisation (SDO); New and Emerging Applications of Technology (NEAT); and the Methodology Programme.

This has meant that the HTA panels can now focus more explicitly on health technologies ('health technologies' are broadly defined to include all interventions used to promote health, prevent and treat disease, and improve rehabilitation and long-term care) rather than settings of care. Therefore the panel structure has been redefined and replaced by three new panels: Pharmaceuticals; Therapeutic Procedures (including devices and operations); and Diagnostic Technologies and Screening.

The HTA Programme will continue to commission both primary and secondary research. The HTA Commissioning Board, supported by the National Coordinating Centre for Health Technology Assessment (NCCHTA), will consider and advise the Programme Director on the best research projects to pursue in order to address the research priorities identified by the three HTA panels.

The research reported in this monograph was funded as project number 93/29/01.

The views expressed in this publication are those of the authors and not necessarily those of the HTA Programme or the Department of Health. The editors wish to emphasise that funding and publication of this research by the NHS should not be taken as implicit support for any recommendations made by the authors.

Criteria for inclusion in the HTA monograph series
Reports are published in the HTA monograph series if (1) they have resulted from work commissioned for the HTA Programme, and (2) they are of a sufficiently high scientific quality as assessed by the referees and editors.

Reviews in *Health Technology Assessment* are termed 'systematic' when the account of the search, appraisal and synthesis methods (to minimise biases and random errors) would, in theory, permit the replication of the review by others.

The editors and publisher have tried to ensure the accuracy of this report but do not accept liability for damages or losses arising from material published in this report. They would like to thank the referees for their constructive comments on the draft document.

ISSN 1366-5278

Published by Core Research, Alton, on behalf of the NCCHTA.
Printed on acid-free paper in the UK by The Basingstoke Press, Basingstoke.

G

Contents

Overview of Parts 1 to 7

This publication marks the completion of a series of seven systematic reviews on various aspects of chronic wound management. Chronic wounds are typically defined as those that take more than 6 weeks to heal, and the majority are leg and foot ulcers, pressure sores and surgical wounds that break down and/or become infected. Management of chronic wounds usually involves treating the underlying cause where possible, for example by reducing pressure and managing the local wound environment, typically with dressings.

We selected the topics for the seven reviews with reference to the research available, the views of an expert panel, variation in practice and costs.

We searched 19 electronic databases, several wound care journals, conference proceedings and bibliographies of trials retrieved by hand. Experts, manufacturers and content experts were asked for additional trials.

Studies were included if they were randomised controlled trials (RCTs), published or unpublished, that provided objective outcomes of healing (treatment studies) or incidence (prevention studies).

Results

- *Thirty-five RCTs of debriding agents were found. There is insufficient evidence to conclude whether debridement increases healing or to recommend one debriding agent over another.*
- *Ninety-three RCTs of dressings or topical agents were included. There is weak evidence that hydrocolloids increase healing of pressure sores compared to moistened gauze. There is insufficient evidence to recommend any particular agent or dressing for leg ulcers or chronic surgical wounds.*
- *From 30 trials we concluded that there is no robust evidence for the use of antimicrobial agents in chronic wounds.*
- *From 39 RCTs in diabetic foot ulcers we concluded that there is some evidence that a foot health programme reduces amputation rates and that growth factors and off-loading increase healing rates.*
- *Forty-five RCTs of beds, mattresses or cushions for pressure sore prevention or treatment were found. Foam alternatives to standard hospital mattresses reduce the incidence of pressure sores, as can pressure-relieving overlays on the operating table. One study suggests that air-fluidised therapy may increase pressure sore healing rates.*
- *From 24 RCTs we concluded that compression is more effective in healing venous leg ulcers than no compression, and multilayered high compression is more effective than single-layer compression. High-compression hosiery was more effective than moderate compression in preventing ulcer recurrence.*
- *From 31 RCTs we concluded that there is insufficient reliable evidence on the contribution of laser therapy, therapeutic ultrasound, electrotherapy and electromagnetic therapy to chronic wound healing.*

Discussion

This series of reviews has drawn on the available evidence. There are a number of important areas where no trials have been identified (e.g. the impact of debridement on wound healing, the use of antibiotics for diabetic foot ulcers).

Studies were generally small and of poor methodological quality. Evaluations of the cost-effectiveness of interventions were rare. In addition, few studies assessed the impact of the intervention on patients' quality of life or recorded adverse effects of interventions.

Further high-quality trials are required in order to assess the impact of both new and established wound care interventions.

Executive summary to Parts 5 to 7

Background

Chronic wounds such as leg ulcers, diabetic foot ulcers and pressure sores are common in both acute and community healthcare settings. The prevention and treatment of these wounds involves many strategies: pressure-relieving beds, mattresses and cushions are universally used as measures for the prevention and treatment of pressure sores; compression therapy in a variety of forms is widely used for venous leg ulcer prevention and treatment; and a whole range of therapies involving laser, ultrasound and electricity is also applied to chronic wounds. This report covers the final three reviews from a series of seven.

Aims

To assess the clinical effectiveness and cost-effectiveness of:

1. pressure-relieving beds, mattresses and cushions for pressure sore prevention and treatment
2. compression therapy for the prevention and treatment of leg ulcers
3. low-level laser therapy, therapeutic ultrasound, electrotherapy and electromagnetic therapy for the treatment of chronic wounds.

Methods

Data sources

Nineteen electronic databases, including MEDLINE, CINAHL, EMBASE and the Cochrane Controlled Trials Register (CENTRAL), were searched. Relevant journals, conference proceedings and bibliographies of retrieved papers were handsearched. An expert panel was also consulted.

Study selection

Randomised controlled trials (RCTs) which evaluated these interventions were eligible for inclusion in this review if they used objective measures of outcome such as wound incidence or healing rates.

Results

Beds, mattresses and cushions for pressure sore prevention and treatment

A total of 45 RCTs were identified, of which 40 compared different mattresses, mattress overlays and beds. Only two trials evaluated cushions, one evaluated the use of sheepskins, and two looked at turning beds/kinetic therapy.

Compression for leg ulcers

A total of 24 trials reporting 26 comparisons were were included (two of prevention and 24 of treatment strategies).

Low-level laser therapy, therapeutic ultrasound, electrotherapy and electromagnetic therapy

Four RCTs of laser (for venous leg ulcers), 10 of therapeutic ultrasound (for pressure sores and venous leg ulcers), 12 of electrotherapy (for ischaemic and diabetic ulcers, and chronic wounds generally) and five of electromagnetic therapy (for venous leg ulcers and pressure sores) were included. Studies were generally small, and of poor methodological quality.

Conclusions

- Foam alternatives to the standard hospital foam mattress can reduce the incidence of pressure sores in people at risk, as can pressure-relieving overlays on the operating table. One study suggests that air-fluidised therapy may increase pressure sore healing rates.
- Compression is more effective in healing venous leg ulcers than is no compression, and multi-layered high compression is more effective than single-layer compression. High-compression hosiery was more effective than moderate compression in preventing ulcer recurrence.
- There is generally insufficient reliable evidence to draw conclusions about the contribution of laser therapy, therapeutic ultrasound, electrotherapy and electromagnetic therapy to chronic wound healing.

Systematic reviews of wound care management (5): pressure-relieving beds, mattresses and cushions for the prevention and treatment of pressure sores

N Cullum*
EA Nelson
T Sheldon

Department of Health Studies, University of York, UK

* Corresponding author

Competing interests: N Cullum has: received funds from the NHS R&D Programme to undertake primary research in wound care; received sponsorship of trial-related educational meetings from Huntleigh Healthcare and Beiersdorf Ltd. EA Nelson has: conducted one of the trials reviewed; been reimbursed for attending symposia by Smith and Nephew Ltd, ConvaTec and Huntleigh Healthcare

Contents to Part 5

List of abbreviations

AP	alternating pressure
CI	confidence interval
CLP	constant low pressure
DARE	Database of Abstracts of Reviews of Effectiveness
df	degrees of freedom
RCT	randomised controlled trial
RR	relative risk

Executive summary to Part 5

Background

Pressure sores (also known as bedsores, pressure ulcers, decubitus ulcers) are areas of localised damage to the skin and underlying tissue due to pressure, shear or friction. They are common in the elderly and immobile, and costly in financial and human terms. Pressure-relieving beds, mattresses and seat cushions are widely used as aids to the prevention and treatment of pressure sores in both institutional and non-institutional settings.

Objectives

This systematic review seeks to answer the following questions:

- Do pressure-relieving cushions, beds, mattress overlays and mattress replacements reduce the incidence of pressure sores compared with standard support surfaces?
- Do pressure-relieving cushions, beds, mattress overlays and mattress replacements increase the healing rate of pressure sores compared with standard support surfaces?
- Which types of pressure-relieving surface are the most effective for prevention and treatment?

Methods

Data sources

The specialised trials register of the Cochrane Wounds Group (compiled from regular searches of many electronic databases, including MEDLINE, CINAHL and EMBASE, plus handsearching of specialist journals and conference proceedings) was searched for the period up to April 2000. The reference sections of the obtained studies were also searched for further trials.

Study selection

Randomised controlled trials (RCTs), published or unpublished, which assessed the effectiveness of beds, mattresses, mattress overlays and seating cushions for the prevention and/or treatment of pressure sores, in any patient group in any setting. RCTs were eligible for inclusion if they reported an objective, clinical outcome measure, such as the incidence and severity of new pressure sores (in prevention studies) and the healing rates of existing pressure sores in treatment studies. Studies which only reported proxy outcome measures, such as interface pressure, were excluded.

Data extraction and synthesis

Trial data were extracted by one researcher and checked by a second. The results from each study are presented as relative risk (for dichotomous variables) or effect sizes (for continuous variables). Where deemed appropriate, similar studies were pooled in a meta-analysis.

Results

A total of 45 RCTs were identified.

- Foam alternatives to the standard hospital foam mattress can reduce the incidence of pressure sores in people at risk of developing pressure sores.
- The relative merits of alternating and constant low-pressure devices and of the different alternating pressure devices for pressure sore prevention are unclear.
- Pressure-relieving overlays on the operating table have been shown to reduce postoperative pressure sore incidence.
- There is insufficient evidence to draw conclusions about the value of seat cushions, limb protectors, various constant low-pressure devices and sheepskins as pressure sore prevention strategies.
- One high-quality trial suggests that air-fluidised therapy may improve pressure sore healing rates. There is insufficient evidence to draw conclusions about the value of other beds, mattresses and seat cushions as pressure sore treatments.

Conclusions

Implications for practice

- In people at high risk of developing pressure sores, consideration should be given to the use of higher specification foam mattresses rather than standard hospital foam mattresses.
- The relative merits of more sophisticated constant low-pressure and alternating pressure devices for the prevention and treatment of pressure sores are unclear.
- Organisations might consider the use of pressure relief for high-risk patients in the operating theatre, as this is associated with a reduction in the postoperative incidence of pressure sores.
- Good evidence from RCTs suggests that air-fluidised supports may improve pressure sore healing rates.
- Seat cushions have not been adequately evaluated.

Recommendations for research

Independent, well-designed, multicentre RCTs are needed to compare the clinical effectiveness and cost-effectiveness of different types of pressure-relieving devices for patients at different levels of risk in a variety of settings. In particular, this research should aim to compare:

- alternating pressure devices with other 'high-tech' equipment (e.g. low-air-loss and air-fluidised beds) in very high-risk groups
- alternating pressure mattresses with less costly alternating pressure overlays
- alternating pressure devices with 'lower tech' alternatives (e.g. different types of high-specification foam mattresses, other constant low-pressure devices).

Evaluation of alternating pressure is given high priority here on the basis of its wide-spread use in prevention and treatment, and its cost.

Research is needed into valid and reliable methods of measuring wound healing, of detecting early skin damage that is prognostic of pressure sore development, and of the impact of pressure sores on quality of life.

Future research must address the methodological deficiencies associated with much of the research described in this review. Patients should be truly randomised (with concealed allocation), trials should be of sufficient size to detect clinically important differences, and there should be clear criteria for measuring outcomes which, ideally, should be assessed without knowledge of the intervention received (blinded) or, as a minimum, independently verified. Interventions under evaluation should be thoroughly and clearly described. Researchers should be encouraged to develop measures to assess patients' experiences of pressure-relieving equipment (e.g. comfort). The studies should also have adequate follow-up and appropriate statistical analysis.

Given the high costs associated with the prevention and treatment of pressure sores generally, and of pressure-relieving surfaces specifically, greater emphasis should be given in the future to robust economic evaluations.

Chapter 1
Introduction

Pressure sores (also known as pressure ulcers, decubitus ulcers and bed sores) are areas of localised damage to the skin and underlying tissue, believed to be caused by pressure, shear or friction.[1] They usually occur over bony prominences such as the base of the spine, hips and heels. Pressure sores occur in both hospital and community settings, most often in the elderly and immobile (e.g. orthopaedic patients), those with severe acute illness (e.g. patients in intensive care units) and in people with neurological deficits (e.g. with spinal cord injuries).

The development of pressure sores is quite common. For example, new pressure sores occurred in 4–10% of patients admitted to a UK district general hospital, depending on the case mix.[2] They represent a major burden of sickness and reduced quality of life for patients and their carers, and are costly to the NHS. The cost of preventing and treating pressure sores in a 600-bed large general hospital has been estimated to be between £600,000 and £3 million per year.[2]

It is commonly thought that most pressure sores are avoidable, and a number of initiatives have been established to prioritise their prevention.[3,4] The 1994–95 NHS Priorities and Planning Guidance[5] encouraged health authorities to set annual targets for an overall reduction in prevalence of at least 5%. However, target setting in this area may not be sensible, and the achievement of targets is not straightforward. For example, pressure sore prevalence surveys conducted on the same 29 wards in a district health authority in 1986 and 1989 demonstrated an increase in prevalence from 6.8% to 14.2%, despite a large investment in pressure sore prevention equipment during the intervening period.[6]

A pressure sore can be defined as "a new or established area of skin and/or tissue discoloration or damage which persists after the removal of pressure and which is likely to be due to the effects of pressure on the tissues".[3] Healthcare professionals attempt to reduce the incidence of severe pressure sores by the identification of people at high risk and the use of prevention strategies such as pressure-relieving equipment. It is essential that initiatives are based on the best available evidence of clinical effectiveness and cost-effectiveness, and we have therefore undertaken a systematic review of the evidence for the effectiveness of pressure-relieving support surfaces such as beds, mattresses, cushions and repositioning interventions. A systematic review of the epidemiology of pressure sores is outside the scope of this review.

Identifying people at risk

Interventions to prevent pressure sores can be very expensive, and it is important to ensure that resources are targeted at patients who are at high risk of developing sores. Various scales have been developed to identify these high-risk patients. Most scales have been developed in an *ad hoc* fashion; it is unclear which is the most accurate. There is little evidence that using a pressure sore risk scale is better than clinical judgement or that the use of such a scale improves outcomes. The predictive validity of pressure sore risk calculators has been summarised in a previous systematic review and little research has been published since its completion.[7]

Types of pressure-relieving intervention

The aim of pressure sore prevention strategies is to reduce the magnitude and/or duration of pressure between a patient and their support surface (the **interface pressure**). This may be achieved by regular manual repositioning (e.g. 2-hourly turning), or by using pressure-relieving support surfaces such as cushions, mattress overlays, replacement mattresses or whole bed replacements. The cost of these interventions varies widely; from over £30,000 for some bed replacements to less than £100 for some foam overlays (*Table 1*). Information on the relative cost-effectiveness of this equipment is clearly needed to aid rational use.

Pressure-relieving cushions, beds and mattresses either mould around the shape of the patient to distribute the patient's weight over a larger area (constant low-pressure (CLP) devices), or mechanically vary the pressure beneath the patient, so

TABLE 1 *Examples of purchase prices (December 2000) of various pressure-relieving beds, mattresses and cushions*

Type of device	Trade name	Example purchase price*
Air-filled cushion	Repose	£49
Air-filled mattress	Repose system	£79
Air-fluidised bed	Clinitron	£2995
Alternative foam	Therarest	From £995
Alternative foam	Softform	£193
Alternative foam	Transfoam	£151–163 (depending on thickness)
AP	Pegasus Viaclin	£897
AP	Pegasus Aircare	£745
AP cushion	Proactive	£733
AP mattress	Transair	£3185
AP mattress	Nimbus III	£3499
AP mattress	Pegasus Cairwave	£4177
AP mattress	Pegasus Biwave	£2455
AP overlay	Transair	£849
AP overlay	Alpha-X-Cell	£845
Cushion	Transflo	From £83.32
Dry flotation mattress	Sofflex	US $1980
Dry flotation mattress	Roho	£1499
Foam overlay	Propad	£106
Gel and foam cushion	Jay	US $350
Low air loss	Clinirest Overlay	£1995
Low air loss	Clinirest Mattress	£3195
Silicore fibre-filled overlay	Spenco	US $230

AP, alternating pressure
**Many of these devices are available for rental or purchase. The cost of either rental or purchase is likely to vary depending on the particular contract, and therefore the prices given are merely indicative*

reducing the duration of the applied pressure (alternating pressure (AP) devices).[8] CLP devices (either overlays, mattresses or replacement beds) can be grouped according to their construction (foam, foam and air, foam and gel, profiled foam, hammocks, air suspension, water suspension, air–particulate suspension/air-fluidised). These devices fit or mould around the body so that the pressure is dispersed over a large area. AP devices generate alternating high and low interface pressures between the patient's body and their support, usually by alternate inflation and deflation of air-filled cells. Such devices are available as cushions, mattress overlays and single- or multilayer mattress replacements.

Turning beds, such as turning frames, net beds, and turning and tilting beds move those patients, either manually or automatically, who are unable to turn themselves. Pressure sore prevention is often not the reason for using turning and tilting beds; they are used in intensive and critical care units for other reasons (e.g. to promote chest drainage).

Pressure sore treatment strategies usually comprise a combination of pressure relief (as above) and wound care. Wound management strategies such as wound dressings, debridement techniques, physical therapies, antibiotics and antiseptics are the focus of other Health Technology Assessment reports.

Aims

The aim of this systematic review was to answer the following questions:

- Do pressure-relieving cushions, beds, mattress overlays and mattress replacements reduce the incidence of pressure sores compared with standard support surfaces?
- Do pressure-relieving cushions, beds, mattress overlays and mattress replacements increase the healing rate of pressure sores compared with standard support surfaces?
- Which types of pressure-relieving surface are the most effective?

Chapter 2
Methods

A systematic review of primary research was undertaken using the NHS Centre for Reviews and Dissemination structured guidelines.[9]

Search strategy

Nineteen electronic research databases were searched for the period 1966 and June 1998 using a sensitive search strategy designed in collaboration with an information specialist at the NHS Centre for Reviews and Dissemination (appendix 1). Subsequently the Specialist Trials Register of the Cochrane Wounds Group (compiled and regularly updated from searches of the Cochrane Controlled Trials Register (CENTRAL), MEDLINE, CINAHL, EMBASE, etc.) was searched for the period up to April 2000. The electronic search was supplemented by a handsearch of five specialist wound care journals, 12 conference proceedings and a search of systematic reviews held on the NHS Centre for Reviews and Dissemination Database of Abstracts of Reviews of Effectiveness (DARE). The bibliographies of all retrieved and relevant publications were searched for further studies. Companies with an interest in wound care products were approached for unreported trials. An advisory panel of experts in wound management, established to comment on the review as it progressed, was also asked to identify any additional trials (appendix 2). Relevant economic evaluations were searched for by adding economic-related search terms to those used in the search for clinical trials. Authors of trials published between 1985 and 1998 were contacted and asked to provide details of any associated economic evaluations.

Inclusion and exclusion criteria

Types of studies

Randomised controlled trials (RCTs) comparing beds, mattresses and cushions, which measured the incidence of new pressure sores (in prevention studies) or pressure sore healing (in treatment studies) as objective measures of outcome.

There was no restriction on the basis of the language in which the study reports were written or on the basis of publication status.

Studies which used only subjective measures of outcome were excluded, as were studies which reported only proxy measures such as interface pressure.

Types of participants

Prevention studies

Patients receiving healthcare who were deemed to be at risk of pressure sore development, in any setting.

Treatment studies

Patients with existing pressure sores, in any setting.

Types of intervention

Studies which evaluated the following interventions for pressure sore prevention or treatment were included:

1. Standard foam mattresses.
2. Alternative foam mattresses/overlays (e.g. convoluted foam, cubed foam): these are conformable and aim to redistribute pressure over a larger contact area.
3. Gel-filled mattresses/overlays: mode of action as above.
4. Fibre-filled mattresses/overlays: mode of action as above.
5. Air-filled mattresses/overlays: mode of action as above.
6. Water-filled mattresses/overlays: mode of action as above.
7. Bead-filled mattresses/overlays: mode of action as above.
8. AP mattresses/overlays: the patient lies on air-filled sacs, which sequentially inflate and deflate and relieve pressure at different anatomical sites for short periods; these devices may incorporate a pressure sensor.
9. Air-fluidised beds: warmed air is circulated through fine ceramic beads covered by a permeable sheet; allows support over a larger contact area.
10. Low-air-loss beds: patients are supported on a series of air sacs through which warmed air passes.
11. Sheepskins: proposed mode of action unclear.
12. Turning beds/frames: beds that either aid manual repositioning of the patient or

reposition the patient by motor-driven turning and tilting.

13. Wheelchair cushions: conforming or mechanical (e.g. alternating pressure) cushions reduce contact pressure by increasing the surface area in contact with the patient's body.
14. Operating-table overlays: as above.
15. Limb protectors: pads and cushions of different forms to protect bony prominences.

We classified items 1–7 as 'low-tech' surfaces and items 8–10 as 'high-tech' surfaces.

Types of outcome measure

Prevention studies

Incidence of new pressure sores

Many evaluations have simply measured the pressure on different parts of the body in contact with the support surface (interface pressure). However, interface pressure is an intermediate or surrogate outcome measure which has serious limitations as a proxy for clinical outcome, since the process that leads to the development of a pressure sore almost certainly involves the complex interplay of several factors. Unfortunately, because it is relatively simple, quick and inexpensive to measure, most evaluations only compare interface pressure. This is also true of Department of Health comparative evaluations of mattresses.[10] In this review we considered only trials which reported clinical outcome measures.

Some studies, when reporting outcomes of interventions for prevention, did not differentiate between people developing grade 1 sores (in which the skin is unbroken) and those developing more severe sores. Studies which compared the incidence of pressure sores of grade 2 or greater are more likely to be reliable (see below for details of the grading system). However, we included all studies, irrespective of whether grade 1 sores were described separately.

Grades of new pressure sores

A range of pressure sore grading systems is used in pressure sore trials. An example of a commonly used grading system is presented below.

- Grade 1: persistent discoloration of the skin, including non-blanchable erythema; blue/purple/black discoloration.
- Grade 2: partial-thickness skin loss involving epidermis and dermis.
- Grade 3: full-thickness skin loss involving damage to or necrosis of subcutaneous tissues, but not through the underlying fascia and not extending to the underlying bone, tendon or joint capsule.
- Grade 4: full-thickness skin loss with extensive destruction and tissue necrosis extending to the underlying bone, tendon or joint capsule.

Treatment studies

Where pressure-relieving interventions are evaluated as aids to the healing of pressure sores we looked at reported wound healing rates. However, there is no single standard outcome measure for wound healing. Both objective and subjective measures are widely used by researchers, but little effort has been made to determine the validity of these measurements.

Most subjective measures, such as visual estimates of oedema, erythema, granulation, pus and debris, are unlikely to be applied consistently between wounds or by different assessors. Unless assessment is blinded to treatment allocation this method is likely to result in significant biases. Blinding may be difficult to achieve in wound care trials as many of the products are easily identified visually and it is usually not feasible to move a patient in order to assess the condition of their pressure-affected areas. This review excluded studies which reported only subjective measures.

Objective measures of healing are usually based on wound area and/or volume. Planimetry, often aided by computer, is the most frequently used method of calculating wound area, although 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.[11] Computerised image analysis may prove to be a useful technique for the assessment of wound volume in the future, as the equipment becomes more affordable and portable.

Even though objective measures reduce or eliminate subjective biases and reduce random measurement errors, they cannot address inherent biases if the patients being compared have wounds of 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 large wound. The converse is true when the absolute change in area is measured, since for any unit reduction in wound radius a larger 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 against the anticipated direction of the bias for wound size, or when the percentage area change and absolute area change are in the same direction. If baseline data are not given it is not possible to determine the direction of bias, and the validity of the results 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 since they reduce the biases of the assessor, which cannot be estimated.

All studies

For all studies, we looked at the following aspects:

- the costs of devices
- patient comfort
- the durability of devices
- the reliability of devices
- the acceptability of devices.

Retrieved studies were assessed for relevance by a single reviewer, and decisions on the final inclusion of a study was checked by a second reviewer. Disagreements were resolved by discussion with a third reviewer. Rejected studies were checked by a second reviewer (one of FS, AF, AN, KF, TS).

Where study details were lacking, the authors were invited to provide further information.

Data extraction

Data from included trials were extracted by a single reviewer into pre-prepared data-extraction tables and checked by a second reviewer. The following data were extracted from each study:

- patient inclusion and exclusion criteria
- care setting
- key baseline variables by group (e.g. age, sex, baseline risk, baseline area of existing sores)
- a description of the interventions and the number of patients randomised to each intervention
- a description of any co-interventions or standard care
- duration and extent of follow-up
- outcomes (e.g. incidence and severity of new pressure sores; healing rates)
- acceptability and reliability of equipment if reported.

If data were missing from reports 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 for the data extraction.

Methodological quality

The methodological quality of each trial was assessed by two researchers independently. The following quality criteria were used:

- description of inclusion and exclusion criteria used to derive the sample from the target population
- description of the *a priori* sample-size calculation
- evidence of allocation concealment at randomisation
- a description of baseline comparability of treatment groups
- whether the outcome assessment was stated to be blinded
- whether incident sores were described by severity grading as well as frequency (grade 1 sores are not breaks in the skin and are subject to more interrater variation)
- a clear description of the main interventions.

Data synthesis

For each trial the relative risk (RR) was calculated for categorical outcomes, such as the number of patients developing sores and the number of pressure sores healed. The 95% confidence intervals (95% CI) were included when sufficient detail to allow their calculation was provided. The results from replicated studies were plotted on 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 structured tables. Where there was more than one trial comparing similar devices using the same outcome, and in the absence of obvious methodological or clinical heterogeneity, statistical heterogeneity was tested for by using the χ^2 test. In the absence of significant statistical heterogeneity, studies with similar comparisons were pooled using a fixed-effects model.[12] If heterogeneity was observed, both random- and fixed-effects models were used to pool the data. All statistical analysis was performed using Revman (v3.1.1). Continuous outcome variables such as change in wound volume were reported where appropriate and summarised as the weighted mean difference across studies. Where outcomes for continuous variables were presented as medians without confidence intervals, standard deviations or some other measure of the precision of the result, the median was entered in the analysis table and the data were not used in the data synthesis.

Chapter 3
Results

Studies included in the review

Forty-five relevant RCTs were identified (see appendix 3). Thirty trials involved patients without pre-existing pressure sores (intact skin) in assessments of the effectiveness of pressure-relieving interventions in the prevention of pressure sores. Twelve trials involved patients with pressure sores in assessments of the treatment efficacy of pressure-relieving supports, and three trials involved a mixture of patients with and without pre-existing sores.

Three studies evaluated different operating-table surfaces;[13–15] six evaluated different surfaces in intensive care units;[16–21] and seven studies confined the evaluation to orthopaedic patients.[22–28] The remaining studies looked at a variety of patients (e.g. those in nursing homes, those on care of the elderly, those on medical and surgical wards).

Only two trials evaluated cushions: one evaluated the use of sheepskins and two looked at turning beds/kinetic therapy. The remaining studies evaluated different mattresses, mattress overlays and beds.

A summary of the methodological quality of each of the trials is given in appendix 4. Methodological rigour in RCTs is essential in order to minimise bias. Although the majority (87%) of trials discussed the criteria for including patients, only 38% of the reports gave information which made us confident that patients were truly randomly allocated,[29] and only 9/45 (20%) trials adopted blinded assessment of outcomes. Small sample size was a major limitation of many of the studies; the median sample size was 80 (range 25–505) and only 14/45 studies described an *a priori* sample size.

Three studies assessed the effectiveness of pressure-relieving interventions for both the prevention and treatment of pressure sores. The results are summarised according to the type of devices tested.

TABLE 2 *Summary of studies excluded from the review*

Study	Reason for exclusion
Bliss and co-workers[30]	Not an RCT. Patients were allocated in a rota fashion, and the possibility that knowledge of the next mattress to be allocated might have influenced allocation was acknowledged. Rotas were changed on the basis of availability of mattresses, etc.
Bliss[31]	While eight surfaces were evaluated in this prospective trial, not all surfaces were in use in the trial at any time, and therefore the surfaces were not truly compared with one another contemporaneously. Furthermore, it was possible for patients to be re-randomised back into the study, and this occurred frequently (a total of 457 mattress trials were reported in only 238 patients). The data were not presented by patient; only by mattress trial
Branom and Knox[32]	No healing data presented
Collins[33]	Study on two wards; wards, not patients, were randomised
Hawkins[34]	Not an RCT
Jesurum and co-workers[35]	Not an RCT
Koo and co-workers[36]	Not an RCT; a study of interface pressures in healthy volunteers
Marchand and Lidowski[37]	Not an RCT
Regan and co-workers[38]	This study reports an audit of pressure sore incidence after implementation of a comprehensive pressure sore policy. Not a prospective RCT
Rosenthal and co-workers[39]	Not an RCT
Stoneberg and co-workers[40]	Historical control group
Zernike[41]	Incidence of pressure sores not reported

The implications for prevention and treatment are considered separately in chapter 5.

Studies excluded from the review

The studies excluded from the review and the reasons for their exclusion are summarised in *Table 2*.

Prevention of pressure sores

‘Low-tech’ constant pressure supports

Trials of the standard hospital mattress

This section considers comparisons of the standard foam hospital mattress with other low-tech, constant-pressure supports.

Seven RCTs comparing ‘standard’ mattresses or surfaces with low-tech supports for the prevention of pressure sores were identified.[24,25,27,42–45] When compared with standard hospital mattresses, the incidence and severity of pressure sores in ‘high-risk’ patients were reduced when patients were placed on either the Comfortex DeCube mattress,[25] (RR = 0.34; 95% CI, 0.14 to 0.85) the Beaufort bead bed[24] (RR = 0.32; 95% CI, 0.14 to 0.76), the Softform mattress[44] (RR = 0.2; 95% CI, 0.09 to 0.45) or the water-filled mattress[42] (RR = 0.35; 95% CI, 0.15 to 0.79) (*Figures 1* and *2*). In an unpublished British study of older people with hip fractures admitted to orthopaedic trauma wards, patients allocated to receive a NHS standard foam mattress (manufactured by Relyon) experienced over three times the rate of pressure sores as those using one of a number of foam alternatives (Clinifloat, Therarest, Transfoam, Vaperm – see appendix 3).[27]

The four trials comparing foam alternatives with the standard hospital foam mattress[25,27,44,45] were pooled in the absence of significant statistical heterogeneity (χ^2 = 1.64; degrees of freedom (df) = 2) (see *Figure 1*). These trials were of mixed quality; three of the four provided evidence of allocation concealment, but none used blinded outcome assessment. To avoid double counting the control patients in the trials with more than two comparisons, and in the absence of major differences between the effects of different foams, the foam alternatives were pooled. This approach maintains the randomisation, but results in comparison groups of unequal size. This analysis yielded a pooled relative risk of 0.29 (95% CI, 0.19 to 0.43), or a relative reduction in pressure sore incidence of 71% (95% CI, 57 to 81). Therefore, foam alternatives to the standard hospital mattress can reduce the incidence of pressure sores in at-risk patients, including patients with fractured neck of femur.

One small trial of the standard hospital mattress with and without sheepskin overlays was inconclusive and of poor quality.[43]

Comparisons between foam alternatives

This section covers the results of studies that involved head-to-head comparisons of high-specification foam products (i.e. contoured foam, supports comprising foam of different densities).

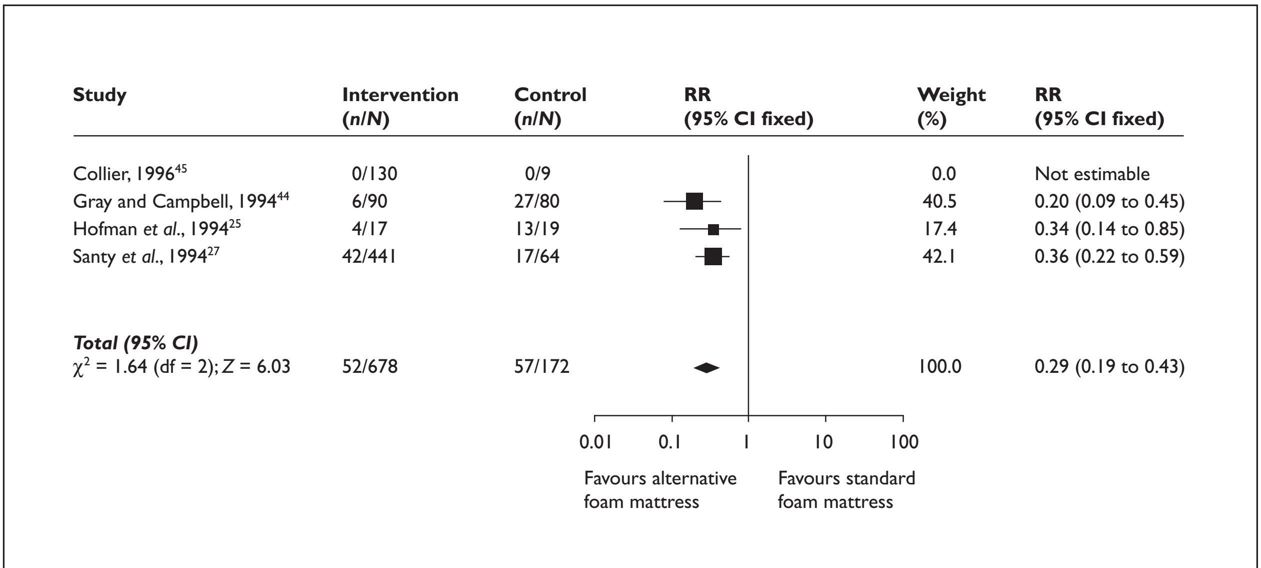

FIGURE 1 *A comparison of the effect of various alternative foam mattresses (pooled data) and standard foam mattresses on the incidence of pressure sores*

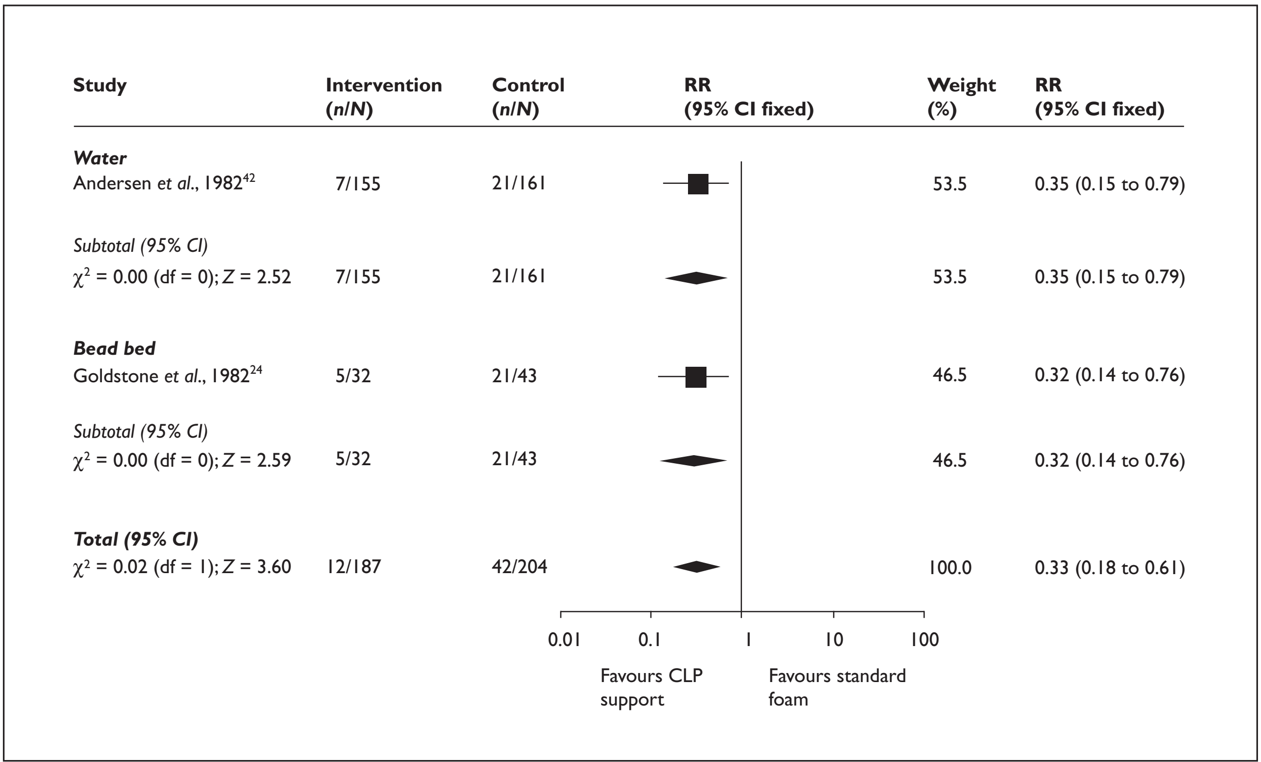

***FIGURE 2** A comparison of the effect of CLP devices and standard foam mattresses on the incidence of pressure sores*

Five RCTs[27,45–48] compared different foam alternatives. Santy and co-workers[27] compared five alternative foam mattresses (Clinifloat, Vaperm, Therarest, Transfoam, NHS standard foam) and found significant reductions in pressure sore incidence associated with Clinifloat, Therarest, Vaperm and Transfoam compared with the standard mattress, and a significant reduction with Vaperm compared with Clinifloat. Vyhlidal and co-workers[48] compared a 4-inch thick foam overlay (Iris 3000) with a foam and fibre mattress replacement (Maxifloat), and reported a significant reduction in pressure sore incidence (RR = 0.42; 95% CI, 0.18 to 0.96) with the mattress replacement. However, this trial appeared to have used neither allocation concealment nor blinded outcome assessment. The relative risk translates to a relative reduction in the incidence of pressure sores of 58% associated with use of the five-section foam and fibre mattress replacement (an absolute risk reduction of 0.35 (35%) and a number needed to treat of 3, or one additional pressure sore prevented for every three patients receiving a Maxifloat mattress replacement).

No patient developed a pressure sore in the trial reported by Collier.[45] Kemp and co-workers[47] compared a convoluted foam overlay with a solid foam overlay in 84 patients. They found no significant difference in pressure sore incidence rates. However, this may be a type 2 error (i.e. the small sample size may have precluded detection of a significant difference). Gray and Smith[46] compared the Transfoam and Transfoamwave foam mattresses. However, only one patient in each group developed a sore.

Comparisons between constant low-pressure supports

This section covers head-to-head comparisons of the following types of support: foams, static air-filled supports (including dry flotation), water-filled supports, gel-filled supports, Silicore-filled supports and heel elevators. Seven RCTs compared different low-tech CLP devices for prevention.[19,21,22,28,42,49,50] Most of these trials were seriously underpowered and/or had other methodological flaws.

A trial from Finland[21] comparing the Optima (Carital) CLP mattress (which comprises 21 double air bags on a base) with the standard hospital mattress found that 37% of patients on the standard mattress developed sores compared with none on the Optima (RR = 0.06; 95% CI, 0 to 0.99). The report of this study did not describe either allocation concealment or blinded outcome assessment.

One trial compared a proprietary heel elevation device (Foot Waffle), comprising a vinyl boot with a built-in foot cradle, with elevation of the heels using a hospital pillow.[50] More heel sores developed in the group using the Foot Waffle (6 versus 2), although this difference was not statistically significant (the trial involved only 52 patients).

The remaining trials were all unique comparisons of low power, and none found statistically significant differences between the surfaces tested.

'High-tech' pressure relief

Alternating pressure supports

A variety of AP supports are used in hospital and the community. The depth of the air cells and the mechanical robustness vary between devices, and these factors may be important in determining effectiveness. It is worth emphasising that most of the RCTs of AP supports did not adequately describe the equipment being evaluated, including the size of the air cells.

Eleven RCTs of AP supports for pressure sore prevention were identified: between AP and standard hospital mattresses in one study;[42] between AP and various CLP devices in eight studies (water,[19,42] static air,[19,26] Silicore,[19,51,52] foam,[19,53] various[54]); and with other AP supports in two studies.[23,55]

Alternating pressure compared with the standard hospital mattress

One RCT reported that the use of AP surfaces reduces the incidence of pressure sores as compared with standard hospital mattresses (RR = 0.32; 95% CI, 0.14 to 0.74).[42] The report of this large trial (482 patients) gave no indication that either allocation concealment or blinded outcome assessment had been used.

Alternating pressure compared with constant low pressure

Eight trials compared AP devices with various CLP devices, but they obtained conflicting evidence as to the relative effectiveness of these devices. One study compared a range of AP supports with a range of CLP supports in a range of specialities in acute-care settings[54] and reported significantly more pressure sores in patients in the CLP group (34% compared with 13% in the AP group) (RR = 0.38; 95% CI, 0.22 to 0.66). This trial is difficult to interpret given the wide variety of surfaces used in the study. There is currently insufficient evidence to support a class effect for all AP devices and all CLP devices.

In contrast, eight small RCTs comparing different types of AP supports and a variety of CLP devices, such as the Silicore overlay,[28,51,52] a water mattress,[19,42] a foam pad[28,53] and static air mattresses[19,26] reported no difference in effectiveness. The studies which compared AP with Silicore or foam overlays were pooled.[28,51–53] To avoid double counting of the patients in the AP arm of the Stapleton three-arm trial, and in the absence of obvious heterogeneity in the outcomes for Silicore and foam, the Silicore and foam arms were pooled against the AP arm (maintaining the randomisation, avoiding double counting, but resulting in unequal comparison groups). Overall, the pooled relative risk for AP versus Silicore or foam overlays (using a fixed-effects model; $\chi^2 = 0.03$; df = 3) was

Study	Intervention (*n/N*)	Control (*n/N*)	Weight (%)	RR (95% CI fixed)
Conine *et al.*, 1990[51]	39/72	45/76	62.3	0.91 (0.69 to 1.21)
Daechsel and Conine, 1985[52]	4/16	4/16	5.7	1.00 (0.30 to 3.32)
Stapleton, 1986[28]	11/32	26/68	23.7	0.90 (0.51 to 1.58)
Whitney *et al.*, 1984[53]	5/25	6/26	8.4	0.87 (0.30 to 2.48)
Total (95% CI) $\chi^2 = 0.03$ (df = 3); $Z = 0.73$	59/145	81/186	100.0	0.91 (0.71 to 1.17)

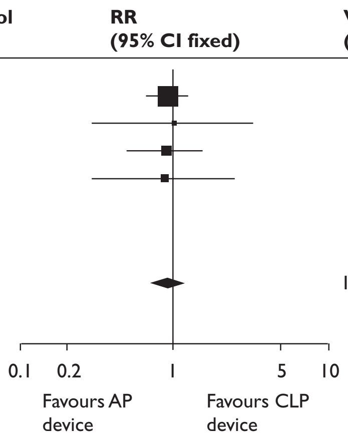

FIGURE 3 *A comparison of the effect of AP devices and CLP devices (Silicore or foam overlay) on the incidence of pressure sores*

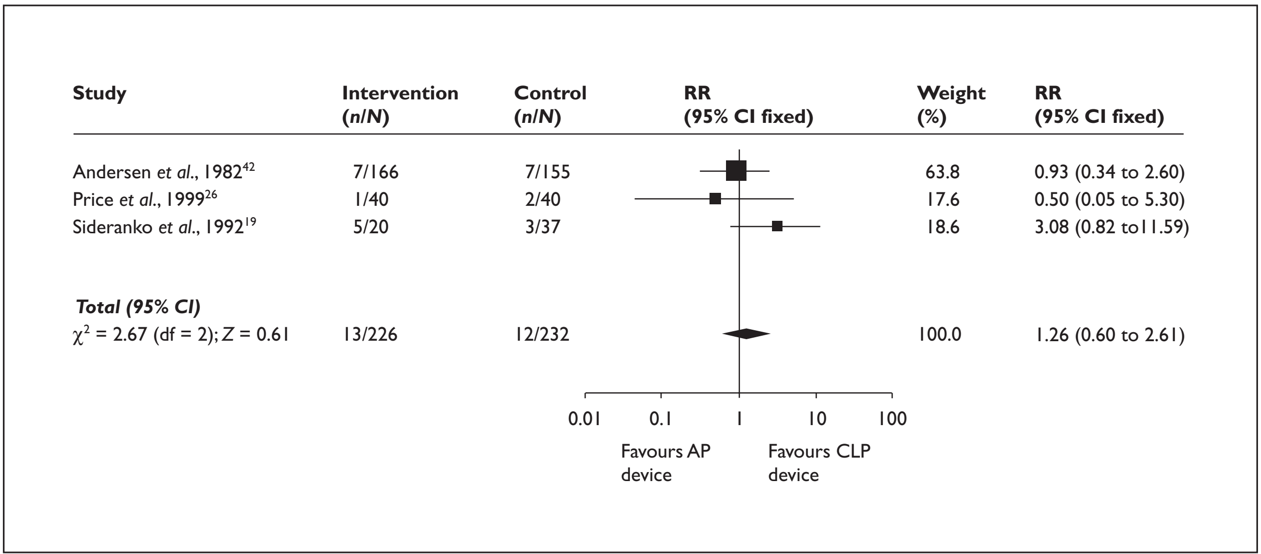

FIGURE 4 *A comparison of the effect of AP devices and CLP devices (water or static-air mattress) on the incidence of pressure sores*

0.91 (95% CI, 0.71 to 1.17), indicating no statistically significant difference between Silicore or foam overlays and AP (*Figure 3*).

The studies which compared AP with static water or static air mattresses were similarly considered together.[19,26,42] The Sideranko trial also contained three comparison groups, and for the purposes of the meta-analysis the water and static air arms of this study were considered sufficiently similar to pool together against AP in order to avoid double counting of the AP patients. Pooling these three trials to answer the question of whether AP is more effective than air- or water-filled mattresses using a random-effects model ($\chi^2 = 2.67$; df = 2) yielded a pooled relative risk of 1.26 (95% CI, 0.6 to 2.61), indicating no statistically significant difference (*Figure 4*).

It is worth emphasising, however, that all these studies were small, and even when pooled were too underpowered to detect clinically important differences in effectiveness as statistically significant.

All eight RCTs comparing the various CLP devices and AP devices were pooled in order to try to answer the question of whether AP is more effective than CLP in pressure sore prevention. Double counting was avoided in the trials by Sideranko and coworkers[19] and Stapleton,[28] as before. In view of the different devices evaluated in the studies, and the χ^2 value of 12.81 (df = 7), a random-effects model was applied. This yielded an overall relative risk of 0.82 (95% CI, 0.57 to 1.19), suggesting no statistically significant difference between the rates of pressure sore incidence on AP versus CLP (*Figure 5*).

Finally, one trial used a complex factorial design to compare various combinations of standard, CLP and AP supports in surgical patients during and after their stay in the intensive care unit. This trial (which involved only 75–80 patients in each group) did not identify any significant effect of using AP in the intensive care unit.[18]

Comparisons between alternating pressure devices

AP devices differ somewhat in structure, including the size of the inflatable air cells. One early study of pressure sore prevention[23] compared two large-cell AP devices (Pegasus Airwave and Large Cell Ripple, which are similar except that the Airwave has two layers of cells). It was found that the Airwave System was significantly more effective than the Large Cell Ripple in preventing and reducing the severity of pressure sores in a high-risk group of elderly patients. However, the allocation was not truly random, and an intention-to-treat analysis would not have shown a statistically significant difference in the rate of pressure sores (16% versus 34%; $p > 0.05$).

More recently, Hampton[55] compared the Pegasus Airwave mattress with a new Cairwave Therapy system (by the same manufacturer) in 75 patients. No patients developed a sore in either arm of this study.

Low-air-loss beds

One trial showed that low-air-loss beds were more cost-effective at decreasing the incidence of pressure sores in critically ill patients than were standard (but poorly described) intensive care unit beds (RR = 0.24; 95% CI, 0.11 to 0.53).[17] A second trial compared low-air-loss hydrotherapy with standard care (some patients received AP in this group); more patients developed sores of grade 2 or greater in the low-air-loss hydrotherapy group (19%) than in the standard care group (7%), although this did not reach significance (the trial involved only 98 patients).[56]

Air-fluidised beds versus dry flotation

One small trial in patients after plastic surgical repair of pressure sores showed no difference between an air-fluidised bed and the Roho dry flotation mattress in postoperative tissue breakdown rates.[57]

Kinetic turning tables

Turning beds contain motors which constantly turn and tilt the patient, and are used in critical care settings primarily to prevent pneumonia and atelectasis. Four RCTs were identified in a meta-analysis of kinetic therapy.[58] However, only two of the reports could be obtained.[16,20] Sample sizes in all the trials was small, and no beneficial effect of kinetic therapy on pressure sore incidence was detected.

Operating-table overlays

Three RCTs have evaluated different methods of pressure relief on the operating table. The first compared a viscoelastic polymer pad with a standard table and found a relative reduction in the incidence of postoperative pressure sores of 47% associated with using the polymer pad for patients undergoing elective major general, gynaecological or vascular surgery (supine or lithotomy) (RR = 0.53; 95% CI, 0.33 to 0.85).[14]

Study	Intervention (*n/N*)	Control (*n/N*)	Weight (%)	RR (95% CI fixed)
AP (various) vs CLP (various)				
Gebhardt, 1994[54]	15/115	39/115	19.5	0.38 (0.22 to 0.66)
Subtotal (95% CI)				
χ^2 = 0.00 (df = 0); *Z* = 3.49	15/115	39/115	19.5	0.38 (0.22 to 0.66)
AP vs Silicore or foam overlay				
Conine *et al.*, 1990[51]	39/72	45/76	27.8	0.91 (0.69 to 1.21)
Daechsel and Conine, 1985[52]	4/16	4/16	7.3	1.00 (0.30 to 3.32)
Stapleton, 1986[28]	11/32	26/68	18.6	0.90 (0.51 to 1.58)
Whitney *et al.*, 1984[53]	5/25	6/26	8.9	0.87 (0.30 to 2.48)
Subtotal (95% CI)				
χ^2 = 0.03 (df = 3); *Z* = 0.74	59/145	81/186	62.7	0.91 (0.72 to 1.16)
AP vs water or static-air mattress				
Andersen *et al.*, 1982[42]	7/166	7/155	9.3	0.93 (0.34 to 2.60)
Price *et al.*, 1999[26]	1/40	2/40	2.3	0.50 (0.05 to 5.30)
Sideranko *et al.*, 1992[19]	5/20	3/37	6.3	3.08 (0.82 to 11.59)
Subtotal (95% CI)				
χ^2 = 2.67 (df = 2); *Z* = 0.57	13/226	12/232	17.8	1.31 (0.51 to 3.35)
Total (95% CI)				
χ^2 = 12.81 (df = 7); *Z* = 1.04	87/486	132/533	100.0	0.82 (0.57 to 1.19)

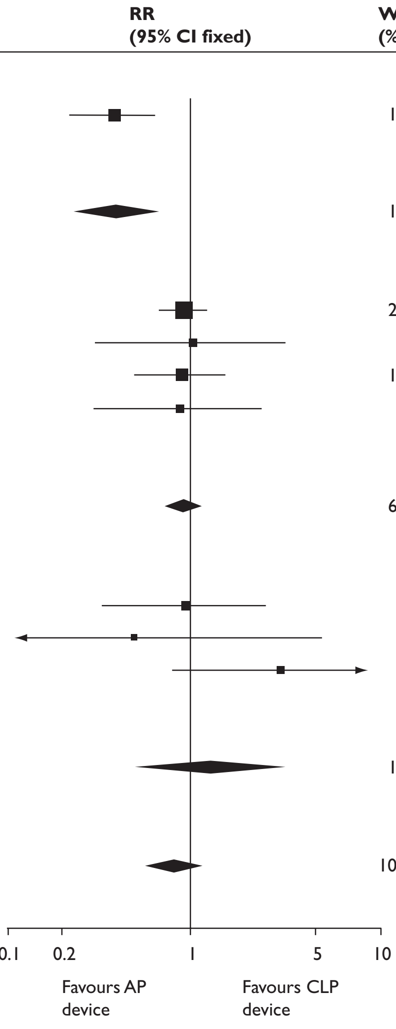

FIGURE 5 *A comparison of the effect of AP devices and CLP devices on the incidence of pressure sores*

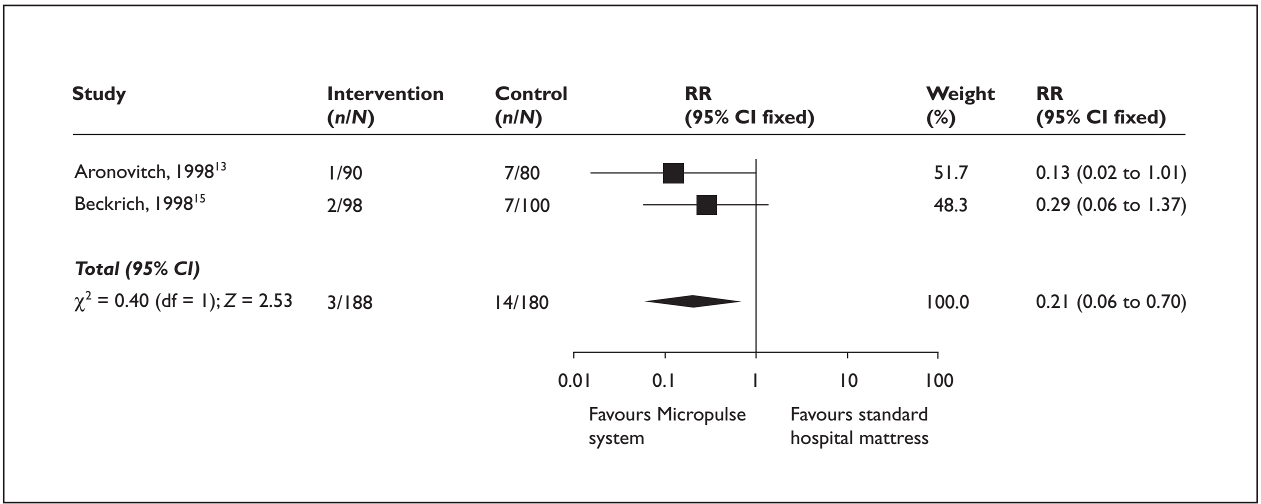

FIGURE 6 *A comparison of the effect of the Micropulse system and the standard hospital mattress on the incidence of pressure sores*

Two further RCTs compared the Micropulse alternating system (applied both during surgery and postoperatively) with the use of a gel pad during surgery and a standard mattress postoperatively, and reported a pooled relative risk (fixed effects) of 0.21 (95% CI, 0.06 to 0.7) in favour of the Micropulse system[13,15] (*Figure 6*). It is not clear from these two trials whether the effect is due to the intraoperative or the postoperative pressure relief, or both.

Seat cushions

Two RCTs have compared different types of seat cushion for preventing pressure sores. One study compared slab foam with bespoke contoured foam and found no difference (RR = 1.06; 95% CI, 0.75 to 1.49).[59] The second study[60] compared the Jay gel and foam wheelchair cushion with a foam cushion in 141 patients, and found fewer sores in the Jay cushion group, although this did not reach statistical significance (RR = 0.61; 95% CI, 0.37 to 1.00).

Treatment of pressure sores

Comparisons between constant low-pressure supports

One trial compared the TheraRest foam replacement mattress with a water-filled overlay (Secutex) on top of a hospital foam mattress in elderly nursing home patients with grade 3 or 4 pressure sores.[61] Of sores in the TheraRest group, 45% were healed at 4 weeks compared with 48% in the Secutex group. Ulcers were reported as having ‘improved’ at the same rate in the two groups. The authors concluded that there was no difference in the abilities of TheraRest and Secutex to heal pressure sores. However, as wound size was measured neither at baseline nor at follow-up, and the trial involved only 120 patients, the results of this study cannot be regarded as demonstrating equivalence.

Air-fluidised therapy

Three RCTs compared air-fluidised therapy with a range of conventional therapies for the treatment of pressure sores.[62–64] These studies measured outcomes in slightly different ways, and none reported the variability around the mean healing rate. Two studies showed enhanced healing associated with air-fluidised beds used in hospital; however, while the study by Allman and co-workers[62] was methodologically robust, the other study[63] was extremely weak (see appendix 3) and small in size. A small home-based study found no statistically significant difference.[64]

Low-air-loss therapy

Two trials have compared low-air-loss with a low-tech foam alternative. One reported that the low-air-loss bed was more effective in treating sores than was a corrugated foam overlay when the outcome was measured as healing rate, although not when the outcome was the number of sores completely healed;[65] the second found no difference.[66] These trials were pooled for the number of sores completely healed, and there was no statistically significant difference. However, the numbers of patients in the studies were too small to safely conclude that there is no difference (pooled RR = 1.25; 95% CI, 0.84 to 1.86) (*Figure 7*). Only one trial compared different types of low-air-loss support surface,[67] and no statistically significant difference was found.

Study	Intervention (n/N)	Control (n/N)	RR (95% CI fixed)	Weight (%)	RR (95% CI fixed)
Ferrell *et al.*, 1993[65]	26/43	19/41		83.7	1.30 (0.87 to 1.96)
Mulder *et al.*, 1994[66]	5/31	3/18		16.3	0.97 (0.26 to 3.58)
Total (95% CI)					
$\chi^2 = 0.19$ (df = 1); $Z = 1.10$	31/74	22/59		100.0	1.25 (0.84 to 1.86)

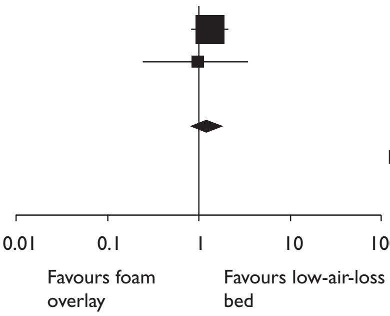

FIGURE 7 *A comparison of low-air-loss beds and a foam overlay on the number of pressure sores completely healed*

Alternating-pressure devices

A small RCT (41 patients) compared the effectiveness of the Nimbus I (composed of rows of figure-of-eight-shaped cells) and the Pegasus Airwave for the treatment of existing pressure sores, but no statistically significant difference was found.[68] A second small study (32 patients) compared the Nimbus III with various standard-care options for the treatment of pressure sores in older people in both hospital and nursing-home settings.[69] No statistically significant difference was found; however, the small sample size of this study cannot be overemphasised. A third study compared Nimbus III with a Cairwave (both AP devices) in elderly patients with pressure sores.[70] There was a trend towards greater ulcer healing in the Cairwave group for sacral sores (51% versus 45%), and this difference was statistically significant for heels at 12 weeks (57% versus 33%; $p = 0.025$).

Seat cushions

One treatment study involving only 25 patients found no statistically significant difference between a dry-flotation and an AP cushion in the number of sores completely healed.[71]

Summary

- Foam alternatives to the standard hospital foam mattress can reduce the incidence of pressure sores in people at risk.
- The relative merits of AP and CLP devices, and of the different AP devices, for pressure sore prevention are unclear.
- Pressure-relieving overlays used on the operating table and in the postoperative period have been shown to reduce postoperative pressure sore incidence.
- There is insufficient evidence to draw conclusions about the value of seat cushions, various CLP devices and sheepskins as pressure sore prevention strategies.
- There is evidence from one high-quality trial that air-fluidised therapy may improve pressure sore healing rates. There is insufficient evidence to draw conclusions about the value of other beds, mattresses and seat cushions as pressure sore treatments.

Chapter 4
Discussion

The confidence with which we can draw firm conclusions from the studies detailed in this review is greatly tempered by the poor quality of many of the trials and the lack of replication of most comparisons. The clearest conclusion one can draw is that standard hospital mattresses have been consistently out-performed by a range of foam-based, low-pressure mattresses and overlays, and also by higher-tech pressure-relieving beds and mattresses, both in the prevention and the treatment of pressure sores. The application of this conclusion to current clinical practice is, however, hampered by the fact that the 'standard' was poorly described in many of these studies, and what is standard varies by hospital, country and over time. Nevertheless, the effects of using alternative foam mattresses are noteworthy in their consistency.

None of the trials reviewed provided convincing reassurance that manual repositioning was provided equally to each group of participants. This is a possible confounder, as care providers were not blinded to treatment allocation in any of the trials and may have moved patients in one group more frequently if they perceived a particular mattress to be less effective.

The results of three trials evaluating the use of pressure-relieving overlays on the operating table suggest that these are beneficial in reducing subsequent pressure sore incidence in high-risk surgical patients. These three trials were of reasonable or good quality; in particular, the trial by Nixon and co-workers[14] was adequately powered, with allocation concealment and blinded outcome assessment, lending further weight to the result. At present the most effective means of pressure relief on the operating table is unclear; Nixon and co-workers[14] found a gel-filled overlay to be significantly better than a standard operating table, while in the other two trials a gel-filled overlay on the operating table was less effective than an AP overlay (the Micropulse system), both intra- and postoperatively. The Micropulse trials are confounded by their provision of a standard mattress postoperatively in the gel overlay arm, and an AP overlay postoperatively in the Micropulse arm. Thus, while there is clearly a reduction in pressure sore incidence associated with the AP system, it is not clear whether this is merely a result of better postoperative pressure relief.

It appears that low-air-loss beds are effective in preventing pressure sores compared with foam mattresses, although the evidence for a treatment effect is weak. There are no studies comparing low-air-loss therapy with AP surfaces and other high-tech low-pressure supports.

Water-filled and bead-filled mattresses were both associated with reductions in the incidence of pressure sores in trials published in the early 1980s. However, the particular products evaluated are no longer available.

There are tentative indications that two interventions may be harmful. First, foot waffle heel elevators were associated with a trebling of the incidence of pressure sores, but this result was not statistically significant due to the small sample size of the study. Secondly, low-air-loss hydrotherapy was evaluated in a trial in which 19% of low-air-loss hydrotherapy patients developed sores compared with 7% of standard care patients. Again the difference is not statistically significant, possibly as a result of the small sample size of the trial (98 patients in total).[56]

The comparisons that have been undertaken are summarised in appendix 5. Few comparisons have been replicated and, as most of the trials that have been undertaken were underpowered, there is little information from which to draw conclusions. For example, air-fluidised therapy as a prevention strategy has only been compared with dry flotation, and low-air-loss therapy only with standard care, in one trial, as a treatment. There are clearly many gaps in the knowledge base, and a rational research agenda could be developed.

Common methodological flaws, such as open randomisation, lack of baseline comparability, high attrition rates, lack of an intention-to-treat analysis and lack of a blind outcome assessment, further reduce the confidence with which we can regard many of the individual study findings. Future trials should address these deficiencies and collect data on aspects of equipment performance, such as reliability.

Chapter 5
Conclusions

Implications for practice

- In people at high risk of pressure sore development, consideration should be given to the use of higher specification foam mattresses rather than standard hospital foam mattresses.

- The relative merits of higher-tech CLP and AP for prevention and treatment are unclear. Organisations should consider the use of pressure relief for high-risk patients in the operating theatre, as this is associated with a reduction in the postoperative incidence of pressure sores.

- Air-fluidised supports may improve pressure sore healing rates.

- Seat cushions have not been adequately evaluated.

Implications for research

Independent, well-designed, multicentre RCTs are needed to compare the clinical effectiveness and cost-effectiveness of different types of pressure-relieving devices for patients at different levels of risk in a variety of settings. Particular gaps in the available information, which are evident from appendix 5, include comparisons of:

- AP devices with other high-tech equipment (such as low-air-loss and air-fluidised beds) for pressure sore prevention in very high-risk groups
- AP mattresses with less costly AP overlays
- AP devices with lower-tech alternatives (such as different types of high-specification foam mattresses and other CLP devices).

The evaluation of AP devices is given particular emphasis as they are viewed as standard preventive interventions in some areas and not others, and vary widely in cost (from less than £1000 to more than £4000).

Research is needed into valid and reliable methods of measuring wound healing, of detecting early skin damage, which is prognostic of pressure sore development, and of the impact of pressure sores on quality of life.

Future research must address the methodological deficiencies associated with much of the research described in this review. Patients should be truly randomised (with concealed allocation), trials should be of sufficient size to detect clinically important differences, and there should be clear criteria for measuring outcomes, which ideally should be assessed without knowledge of the intervention received (blinded). Interventions under evaluation should be thoroughly and clearly described. Researchers should be encouraged to develop measures to assess patients' experiences of pressure-relieving equipment (e.g. comfort). The studies should also have adequate follow-up and appropriate statistical analysis.

Given the high costs associated with the prevention and treatment of pressure sores generally, and of pressure-relieving surfaces specifically, greater emphasis should be given in the future to robust economic evaluations.

Acknowledgements

This study was commissioned by the NHS R&D HTA programme. The authors are indebted to the HTA referees for their perseverance in reading this report and the quality of their comments. The views expressed in this report are those of the authors, who are responsible for any errors.

The authors are extremely grateful to: Julie Glanville and Alison Fletcher for early assistance with the search, location and collection of the literature; to Fujian Song and Jon Deeks, who participated in early versions of this review; and to Sally Bell-Syer, Roz Thompson (Trial Search Coordinator and Secretary, respectively, of the Cochrane Wounds Group) and Kate Flemming for help in the ongoing search and retrieval of RCTs, contact with authors, maintenance of the Wounds Group trials register and data checking. We are also grateful to our expert panel (appendix 2) for their helpful comments on the review protocol and early drafts.

Early versions of this review have appeared as an *Effective Healthcare* bulletin[7] and as a Cochrane Review[72] (this review will be maintained in the Cochrane Library).

References

1. Allman RM. Pressure ulcers among the elderly. *N Engl J Med* 1989;**320**:850–3.

2. Clark M, Watts S. The incidence of pressure sores during a National Health Service Trust Hospital during 1991. *J Adv Nurs* 1994;**20**:33–6.

3. Department of Health. Pressure sores: a key quality indicator. London: Department of Health; 1993.

4. NHS Executive. Pressure sores: a preventable problem. London: NHS Executive; 1994. VFM Update No. 12.

5. NHS Management Executive. Priorities and planning guidance 1994–5. Leeds: NHS ME. Report No. EL (93)54.

6. Clark M, Cullum N. Matching patient need for pressure sore prevention with the supply of pressure redistributing mattresses. *J Adv Nurs* 1992;**17**:310–16.

7. Effective Health Care. The prevention and treatment of pressure sores. *Effective Health Care* 1995;**2**(Pt 1):1–16.

8. Bliss MR, Thomas JM. Clinical trials with budgetary implications: establishing randomised trials of pressure-relieving aids. *Professional Nurse* 1993; **8**(Pt 5):292–6.

9. NHS Centre for Reviews and Dissemination. Undertaking systematic reviews of effectiveness. York: University of York; 1996. Report No. 4.

10. Medical Devices Directorate. Foam mattresses. London: Medical Devices Directorate; 1993. Evaluation PS1. p. 1–24.

11. Brown-Etris M, Pribble J, LaBreque J. Evaluation of two wound measurement methods in a multicentre controlled study. *Ostomy Wound Management* 1994; **40**(Pt 7):44–8.

12. Clarke M, Oxman AD, editors. Summarising effects across studies. Cochrane Reviewers' Handbook 4.0 [updated July 1999]; Section 8.3. Oxford: Update Software; 2000. Cochrane Library [database on CD ROM], issue 1.

13. Aronovitch SA. A comparative, randomized, controlled study to determine safety and efficacy of preventive pressure ulcer systems: preliminary analysis. *Adv Wound Care* 1998;**11**(Pt 3 Suppl): 15–16.

14. Nixon J, McElvenny D, Mason S, Brown J, Bond S. A sequential randomised controlled trial comparing a dry visco-elastic polymer pad and standard operating table mattress in the prevention of postoperative pressure sores. *Int J Nurs Stud* 1998;**35**:193–203.

15. Beckrich K. Personal communication: Micropulse. A 7-day comparative, parallel randomised single centre study to determine the safety and efficacy of the Micropulse system for the prevention of pressure ulcers in patients undergoing cardio-thoracic procedures. 1998.

16. Gentilello L, Thompson DA, Tonnesen AS, Hernandez D, Kapadia AS, Allen SJ, *et al*. Effect of a rotating bed on the incidence of pulmonary complications in critically ill patients. *Crit Care Med* 1998;**16**(Pt 8):783–6.

17. Inman KJ, Sibbald WJ, Rutledge FS, Clark BJ. Clinical utility and cost-effectiveness of an air suspension bed in the prevention of pressure ulcers. *JAMA* 1993;**269**:1139–43.

18. Laurent S. Effectiveness of pressure decreasing mattresses in cardiovascular surgery patients: a controlled clinical trial. Proceedings of the 3rd European Conference for Nurse Managers; 1997; Brussels.

19. Sideranko S, Quinn A, Burns K, Froman RD. Effects of position and mattress overlay on sacral and heel pressures in a clinical population. *Res Nurs Health* 1992;**15**(Pt 4):245–51.

20. Summer WR, Curry P, Haponik EF, Nelson S, Elston R. Continuous mechanical turning of intensive care unit patients shortens length of stay in some diagnostic groups. *J Crit Care* 1989;**4**(Pt 2): 45–53.

21. Takala J, Varmavuo S, Soppi E. Prevention of pressure sores in acute respiratory failure: a randomised controlled trial. *Clin Intensive Care* 1996;**7**:228–35.

22. Cooper PJ, Gray DG, Mollison J. A randomised controlled trial of two pressure reducing surfaces. *J Wound Care* 1998;**7**(Pt 8):374–6.

23. Exton-Smith AN, Overstall PW, Wedgwood J, Wallace G. Use of the 'air wave system' to prevent pressure sores in hospital. *Lancet* 1982;**i**(Pt 8284): 1288–90.

24. Goldstone LA, Norris M, O'Reilly M, White J. A clinical trial of a bead bed system for the prevention of pressure sores in elderly orthopaedic patients. *J Adv Nurs* 1982;**7**(Pt 6):545–8.

25. Hofman A, Geelkerken RH, Wille J, Hamming JJ, Hermans J, Breslau PJ. Pressure sores and pressure-decreasing mattresses: controlled clinical trial. *Lancet* 1994;**343**(Pt 8897):568–71.

26. Price P, Bale S, Newcombe R, Harding K. Challenging the pressure sore paradigm. *J Wound Care* 1999;**8**(Pt 4):187–90.

27. Santy JE, Bulter MK, Whyman JD. A comparison study of 6 types of hospital mattress to determine which most effectively reduces the incidence of pressure sores in elderly patients with hip fractures in a District General Hospital. Northern and Yorkshire Regional Health Authority; 1994. Unpublished report.

28. Stapleton M. Preventing pressure sores – an evaluation of three products. *Geriatr Nurs (London)* 1986;**6**(Pt 2):23–5.

29. Schulz KF, Chalmers I, Hayes RJ, Altman DG. Empirical evidence of bias: dimensions of methodological quality associated with estimates of treatment effects in controlled trials. *JAMA* 1995;**273**:408–12.

30. Bliss MR, McLaren R, Exton-Smith AN. Mattresses for preventing pressure sores in geriatric patients. *Med Bull Ministry Health* 1966;**25**:238–67.

31. Bliss MR. Preventing pressure sores in elderly patients: a comparison of seven mattress overlays [published erratum appears in *Age Ageing* 1995;**24**:543]. *Age Ageing* 1995;**24**:297–302.

32. Branom R, Knox L. Proceedings of the 31st Wound, Ostomy and Continence Conference; 1999 June; Minneapolis.

33. Collins F. The contribution made by an armchair with integral pressure-reducing cushion in the prevention of pressure sore incidence in the elderly, acutely ill patient. *J Tissue Viability* 1999; **9**(Pt 4):133–7.

34. Hawkins JE. The effectiveness of pressure-reducing table pads as an intervention to reduce the risk of interoperatively acquired pressure sores. *Military Med* 1997;**162**:759–61.

35. Jesurum J, Joseph K, Davis JM. Balloons, beds, and breakdown. Effects of low-air loss therapy on the development of pressure ulcers in cardiovascular surgical patients with intra-aortic balloon pump support. *Crit Care Nurs Clin North Am* 1996;**8**(Pt 4): 423–40.

36. Koo TKK, Mak AFT, Lee YL. Evaluation of an active seating system for pressure relief. *Assist* 1995;**7**: 119–28.

37. Marchand AC, Lidowski H. Reassessment of the use of genuine sheepskin for pressure ulcer prevention and treatment. *Decubitus* 1993;**6**(Pt 1):44–7.

38. Regan MB, Byers BH, Mayrovitz HN. Efficacy of a comprehensive pressure ulcer prevention program in an extended care facility. *Adv Wound Care* 1995; **8**(Pt 3):51–5.

39. Rosenthal MJ, Felton RM, Hileman DL, Lee M, Friedman M, Navach JH. A wheelchair cushion designed to redistribute sites of sitting pressure. *Arch Phys Med Rehab* 1996;**77**:278–82.

40. Stoneberg C, Pitcock N, Myton C. Pressure sores in the homebound: one solution. *Am J Nurs* 1986; **86**(Pt 4):426–8.

41. Zernike W. Heel pressure relieving devices: how effective are they? *Aust J Adv Nurs* 1997;**14**(Pt 4): 12–19.

42. Andersen KE, Jensen O, Kvorning SA, Bach E. Decubitus prophylaxis: a prospective trial on the efficiency of alternating-pressure air-mattresses and water-mattresses. *Acta Dermatol Venereol* 1982; **63**(Pt 3):227–30.

43. Ewing MR, Garrow C, Presley TA, Ashley C, Kisella NM. Further experiences in the use of sheep skins as an aid in nursing. *Austr Nurse J* 1964;**Sept**:215–19.

44. Gray DG, Campbell M. A randomised clinical trial of two types of foam mattresses. *J Tissue Viability* 1994;**4**:128–32.

45. Collier ME. Pressure-reducing mattresses. *J Wound Care* 1996;**5**(Pt 5):207–11.

46. Gray DG, Smith M. Comparison of a new foam mattress with the standard hospital mattress. *J Wound Care* 2000;**9**(Pt 1):29–31.

47. Kemp MG, Kopanke D, Tordecilla L, Fogg L, Shott S, Matthiesen V, *et al.* The role of support surfaces and patient attributes in preventing pressure ulcers in elderly patients. *Res Nurs Health* 1993;**16**(Pt 2): 89–96.

48. Vyhlidal SK, Moxness D, Bosak KS, Van-Meter FG, Bergstrom N. Mattress replacement or foam overlay? A prospective study on the incidence of pressure ulcers. *Appl Nurs Res* 1997;**10**(Pt 3):111–20.

49. Lazzara DJ, Buschmann MT. Prevention of pressure ulcers in elderly nursing home residents: are special support surfaces the answer? *Decubitus* 1991;**4**(Pt 4): 42–6.

50. Tymec AC, Pieper B, Vollman K. A comparison of two pressure-relieving devices on the prevention of heel pressure ulcers. *Adv Wound Care* 1997;**10**(Pt 1): 39–44.

51. Conine TA, Daechsel D, Lau MS. The role of alternating air and Silicore overlays in preventing decubitus ulcers. *Int J Rehab Res* 1990;**13**(Pt 1): 57–65.

52. Daechsel D, Conine TA. Special mattresses: effectiveness in preventing decubitus ulcers in

chronic neurologic patients. *Arch Phys Med Rehab* 1985;**66**(Pt 4):246–8.

53. Whitney JD, Fellows BJ, Larson E. Do mattresses make a difference? *J Gerontol Nurs* 1984;**10**(Pt 9): 20–5.

54. Gebhardt K. A randomized trial of alternating pressure (AP) and constant low pressure (CLP) supports for the prevention of pressure sores. *J Tissue Viability* 1994;**4**(Pt 3):93.

55. Hampton S. Evaluation of the new Cairwave therapy system in one hospital trust. *Br J Nurs* 1997;**6**(Pt 3):167–70.

56. Bennett RG, Baran PJ, DeVone L, Bacetti H, Kristo E, Tayback M, *et al*. Low air loss hydrotherapy versus standard care for incontinent hospitalised patients. *JAGS* 1998;**46**:569–76.

57. Economides NG, Skoutakis VA, Carter CA, Smith VH. Evaluation of the effectiveness of two support surfaces following myocutaneous flap surgery. *Adv Wound Care: J Prev Healing* 1995;**8**(Pt 1):49–53.

58. Choi SC, Nelson LD. Kinetic therapy in critically ill patients: combined results based on meta-analysis. *J Crit Care* 1992;**7**:57–62.

59. Lim R, Sirett R, Conine TA, Daechsel D. Clinical trial of foam cushions in the prevention of decubitus ulcers in elderly patients. *J Rehab Res* 1988;**25**:19–26.

60. Conine TA, Hershler C, Daechsel D, Peel C, Pearson A. Pressure ulcer prophylaxis in elderly patients using polyurethane foam or Jay wheelchair cushions. *Int J Rehab Res* 1994;**17**(Pt 2):123–37

61. Groen HW, Groenier KH, Schuling J. Comparative study of a foam mattress and a water mattress. *J Wound Care* 1999;**8**(Pt 7):333–5.

62. Allman RM, Keruly JC, Smith CR. Cost effectiveness of air-fluidized beds versus conventional therapy for pressure sores. *Clin Res* 1987;**35**(Pt 3):A728.

63. Munro BH, Brown L, Heitman BB. Pressure ulcers: one bed or another? *Geriatr Nurs NY* 1989;**10**(Pt 4): 190–2.

64. Strauss MJ, Gong J, Gary BD, Kalsbeek WD, Spear S. The cost of home air-fluidized therapy for pressure sores. A randomized controlled trial. *J Fam Pract* 1991;**33**(Pt 1):52–9.

65. Ferrell BA, Osterweil D, Christenson P. A randomized trial of low-air-loss beds for treatment of pressure ulcers [published erratum appears in *JAMA* 1993;**269**(Pt 21):2739] [see comments]. *JAMA* 1993;**269**(Pt 4):494–7.

66. Mulder GD, Taro N, Seeley JE, Andrews K. A study of pressure ulcer response to low air loss beds vs conventional treatment. *J Geriatr Dermatol* 1994; **2**(Pt 3):87–91.

67. Caley L, Jones S, Freer J, Muller JS. Randomized prospective trial of two types of low-air-loss therapy. 1994. Unpublished conference paper.

68. Devine B. Alternating pressure air mattresses in the management of established pressure sores. *J Tissue Viability* 1995;**5**(Pt 3):94–8.

69. Evans D, Land L, Geary A. A clinical evaluation of the Nimbus 3 alternating pressure mattress replacement system. *J Wound Care* 2000;**9**(Pt 4): 181–6.

70. Russell L, Reynolds TM, Carr J, Evans A, Holmes M. Randomised controlled trial of two pressure-relieving systems. *J Wound Care* 2000;**9**(Pt 2):52–5.

71. Clark M, Donald IP. A randomised controlled trial comparing the healing of pressure sores upon two pressure-redistributing seat cushions. In: Proceedings of the 7th European Conference on Advances in Wound Management. London: EMAP Healthcare Ltd; 1999; p. 122–5.

72. Cullum N, Deeks, Sheldon T, Song, Fletcher A. Beds, mattresses and cushions for preventing and treating pressure sores. Oxford: Update Software; 2000. Cochrane Review, Cochrane Library, issue 1.

Appendix 1

Databases searched and search strategies

The review was compiled using RCTs from the Cochrane Wounds Group Specialist Trials Register. The Wounds Group Trials Register was searched for the period up to April 2000 and has been assembled and maintained as described below.

Electronic searches

MEDLINE

MEDLINE (SilverPlatter version 4.0) has been searched for RCTs and controlled clinical trials from 1966 to December 1997 using a mixture of free text terms and MeSH headings: Since January 1998 it has been unnecessary to search MEDLINE as this is searched centrally by the UK Cochrane Centre for all trials and the results are transferred to CENTRAL/CCTR. Since January 1998, CENTRAL/CDSR has been searched instead of MEDLINE for all issues of the Cochrane Library. The search strategy used was as follows:

1. decubitus ulcer/ or foot ulcer/
2. leg ulcer/ or varicose ulcer/
3. pilonidal cyst/
4. skin ulcer/
5. diabetic foot/
6. ((plantar or diabetic or heel or venous or stasis or arterial) adj ulcer$).tw.
7. ((decubitus or foot or diabetic or ischaemic or pressure) adj ulcer$).tw.
8. ((pressure or bed) adj sore$).tw.
9. ((pilonidal adj cyst) or (pilonidal adj sinus) or bedsore$).tw.
10. ((diabetic adj foot) or (cavity adj wound)).tw.
11. ((varicose or leg or skin) adj ulcer$).tw.
12. (decubitus or (chronic adj wound$)).tw.
13. ((sinus adj wound$) or (cavity adj wound$)).tw.
14. or/1–13
15. debridement/ or biological dressings/ or bandages/
16. occlusive dressings/ or clothing/ or wound healing/
17. antibiotics/ or growth substances/ or platelet-derived growth factor/
18. fibroblast growth factor/ or electrical stimulation therapy.ti,ab,sh.
19. lasers/ or nutrition/ or surgery/ or surgery, plastic/
20. surgical flaps/ or skin transplantations/ or homeopathy/ or homeopathic/
21. acupuncture therapy/ or acupuncture/ or alternative medicine/
22. alternative medicine/ or massage/ or iloprost/ or alginates/
23. zinc/ or zinc oxide/ or ointments/ or anti-infective agents/
24. dermatologic agents/ or colloids/ or cushions/ or wheelchairs/
25. beds/ or wound dressings/
26. (debridement or dressing$ or compress$ or cream$ or (growth adj factor$)).tw.
27. (pressure-relie$ or (recombinant adj protein$) or bandag$ or stocking$).tw.
28. (antibiotic$ or (electric adj therapy) or laser$ or nutrition$ or surg$).tw.
29. (homeopath$ or acupuncture or massage or reflexology or ultrasound).tw.
30. (iloprost or alginate$ or zinc or paste$ or ointment$ or hydrocolloid$).tw.
31. ((compression adj therapy) or (compression adj bandag$) or wrap$).tw.
32. (bed$ or mattress$ or wheelchair$ or (wheel adj chair) or cushion$).tw.
33. ((wound adj dressing$) or vitamin$ or bind$ or gauze$ or heals or healing).tw.
34. (diet or lotion$ or infect$ or reduc$ or (wound adj healing)).tw.
35. (treat$ or prevent$ or epidemiol$ or aetiol$ or etiol$ or therap$ or prevalence or incidence).tw.
36. or/15–35
37. 14 and 36
38. random allocation/ or randomized controlled trials/
39. controlled clinical trials/ or clinical trials phase I/ or clinical trials phase II/
40. clinical trials phase III/ or clinical trials phase IV/ or clinical trials overviews/
41. single-blind method/ or double-blind method/
42. publication bias/ or review/ or review, academic/
43. review tutorial/ or meta-analysis/ or systematic review/
44. ((random$ adj controlled adj trial$) or (prospective adj random$)).tw.
45. ((random adj allocation) or random$ or (clinical adj trial$) or control$).tw.
46. ((standard adj treatment) or compar$ or single-blind$ or double-blind$).tw.
47. (blind$ or placebo$ or systematic$ or (systematic adj review)).tw.

48. (randomized controlled trial or clinical trial).pt. or comparative study.sh.
49. or/38–48
50. 37 and 49
51. limit 50 to human
52. burns/ or wounds, gunshot/ or corneal ulcer/ or exp dentistry/
53. peptic ulcer/ or duodenal ulcer/ or stomach ulcer/
54. ((peptic adj ulcer) or (duodenal adj ulcer) or traum$).tw.
55. ((aortocaval adj fistula) or (arteriovenous adj fistula)).tw.
56. (bite adj wound$).tw.
57. or/52–56
58. 51 not 57

CENTRAL/CDSR

The CENTRAL/CDSR was searched on the Cochrane Library CD-ROM. The search strategy used was as follows:

1. ((DECUBITUS and ULCER*) or (VARICOSE and ULCER*))
2. ((LEG or LEGS) and ULCER*)
3. ((FOOT or FEET) and ULCER*)
4. ((LEG or LEGS) and VARICOSE)
5. (SKIN and ULCER*)
6. SKIN-ULCER*:ME
7. ((FOOT or FEET) and DIABETIC)
8. (((((PLANTAR or DIABETIC) or HEEL) or VENOUS) or STASIS) or ARTERIAL) and ULCER*)
9. ((ISCHEMIC or PRESSURE) and ULCER*)
10. ((BED or BEDS) near (SORE or SORES))
11. (PRESSURE near (SORE or SORES))
12. (PILONIDAL and CYST*)
13. (PILONIDAL and SINUS*)
14. (PILONIDAL and ABSCES*)
15. ((WOUND or WOUNDS) and CAVITY)
16. ((WOUND or WOUNDS) and SINUS*)
17. ((WOUND or WOUNDS) and CHRONIC)
18. ((WOUND or WOUNDS) and DECUBITUS)
19. WOUND-INFECTION*:ME
20. ((WOUND or WOUNDS) and MALIGNANT)
21. WOUND-HEALING*:ME
22. WOUNDS-GUNSHOT*:ME
23. ((GUN or GUNS) or GUNSHOT)
24. WOUNDS-STAB*:ME
25. LACERATION*
26. SURGICAL-WOUND-DEHISCENCE*:ME
27. BITES-AND-STINGS*2:ME
28. ((BITE or BITES) or BITING)
29. TRAUMATOLOGY*:ME
30. BURNS*:ME
31. (WOUND* and BURN*)
32. (BURN* or SCALD*)
33. ((SITE or SITES) near DONOR)
34. SELF-MUTILATION*:ME
35. ((STAB or STABS) or STABBING)
36. SOFT-TISSUE-INJURIES*:ME
37. (((((((((((#1 or #2) or #3) or #4) or #5) or #6) or #7) or #8) or #9) or #10) or #11) or #12)
38. (((((((((((#13 or #14) or #15) or #16) or #17) or #18) or #19) or #20) or #21) or #22) or #23) or #24)
39. (((((((((((#25 or #26) or #27) or #28) or #29) or #30) or #31) or #32) or #33) or #34) or #35) or #36)
40. (#37 or #38 OR #39)
41. DENTAL
42. (#40 not #41)
43. CORNEAL
44. (#42 not 43)
45. DUODENAL-ULCER*1:ME
46. (#44 not #45)
47. CORNEAL-ULCER*1:ME
48. (#46 not #47)
49. CORNEAL-DISEASES*:ME
50. (#48 not #49)
51. ACNE
52. (#50 not #51)
53. BEDNET
54. (#52 not #53)

CINAHL

CINAHL (SilverPlatter version 4.0) was searched for the period from its inception to July 1999. The search strategy used was as follows:

1. (pressure-ulcer* or foot-ulcer* or leg-ulcer* or skin-ulcer*) in de
2. (diabetic-foot* or diabetic-neuropathies*) in de
3. ((diabetic-angiopathies*) in de) or diabetes-mellitus/complications/ all age subheadings
4. (pilonidal-cyst* or surgical-wound-infection*) in de
5. (plantar or diabetic or heel or venous or stasis or (arterial near ulcer*)) in ti,ab
6. (decubitus or foot or diabetic or ischaemic or (pressure near ulcer*)) in ti,ab
7. (pressure or (bed near sore*))in ti,ab
8. ((pilonidal near cyst) or (pilonidal near sinus) or bedsore) in ti,ab
9. (diabetic near foot) or ((cavity near wound)in ti,ab)
10. (varicose or leg or (skin near ulcer*)) in ti,ab
11. ((decubitus or chronic) near wound*) in ti,ab
12. (sinus near wound*) or ((cavity near wound*) in ti,ab)
13. ((burn near wound*) or (gunshot near wound*) or (bite near wound*) or trauma) in ti,ab
14. #1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13

15. (clinical-trials or single-blind-studies or double-blind-studies) in de
16. (control-group or placebos or meta-analysis) in de
17. (random* near clinical near trial*) or ((prospective near random*) in ti,ab)
18. ((random near allocation) or random* or controlled-clinical-trial* or control) in ti,ab
19. (comparison group* or (standard near treatment) or compar*)in ti,ab
20. (single-blind* or (single near blind) or double-blind or (double near blind)) in ti,ab
21. (blind* or placebo* or systematic or (systematic near review)) in ti,ab
22. ((meta analysis or meta-analysis) or (trial* or prospective)) in ti,ab
23. ((clinical-trials) or (comparative-studies)) in de
24. #15 or #16 or #17 or #18 or #19 or #20 or #21 or #22 or #23
25. #14 and #24
26. explode dentistry/ all topical subheadings/ all age subheadings
27. (peptic-ulcer*) or (duodenal-ulcer*) or ((corneal-ulcer*)in de)
28. (peptic near ulcer) or (duodenal near ulcer) or ((corneal near ulcer) in ti,ab)
29. dentist* in de
30. #26 or #27 or #28 or #29
31. #25 not #30

Other databases

Other databases that were searched, from the earliest date available until 1997, were:

- EMBASE (SilverPlatter version 4.0)
- ISI Science Citation Index (on BIDS)
- BIOSIS (on EDINA)
- British Diabetic Association Database
- CISCOM (Complementary Medicine Database of the RCCM)
- Conference Proceedings (on BIDS)
- Dissertation Abstracts
- Royal College of Nursing Database (CD-ROM)
- British Nursing Index (on ARC) to December 1998.

Handsearching

Journals

The following wound care specialist journals were being prospectively handsearched for all RCTs:

- *CARE – Science and Practice*, 1979–90 (later, *Journal of Tissue Viability*, searched until present)
- *Decubitus*, 1987–93
- *Journal of Tissue Viability*, 1991–present
- *Journal of Wound Care*, 1991–present
- *Phlebology*, 1986–present.

Conference proceedings

Wound care conference proceedings that were handsearched for RCTs were as follows:

- Proceedings of the 1st European Conference on Advances in Wound Management, September 1991, Cardiff, UK
- Proceedings of the 2nd European Conference on Advances in Wound Management, October 1992, Harrogate, UK
- Proceedings of the 3rd European Conference on Advances in Wound Management, October 1993, Harrogate, UK
- Proceedings of the 4th European Conference on Advances in Wound Management, September 1994, Copenhagen, Denmark
- Proceedings of the 5th European Conference on Advances in Wound Management, November 1995, Harrogate, UK
- Proceedings of the 6th European Conference on Advances in Wound Management, October 1996, Amsterdam, The Netherlands
- Proceedings of the 7th European Conference on Advances in Wound Management, November 1997, Harrogate, UK
- Proceedings of the 8th European Conference on Advances in Wound Management, April 1998, Madrid, Spain
- 3rd Annual Symposium on Advanced Wound Care, March 1990, Orlando, FL, USA
- 4th Annual Symposium on Advanced Wound Care, April 1991, San Francisco, CA, USA
- 5th Annual Symposium on Advanced Wound Care, April 1992, New Orleans, USA
- 8th Annual Symposium on Advanced Wound Care & Medical Research Forum on Wound Repair, April 1995, San Diego, CA, USA
- 9th Annual Symposium on Advanced Wound Care, April 1996, Atlanta, GA, USA
- Proceedings of: Going into the '90s: The Pharmacist and Wound Care, September 1992, London, UK
- Proceedings of the Second Joint British/Swedish Angiology Meeting, 1991, London, UK
- Symposium on Venous Leg Ulcers, 1985, London, UK
- Venous Forum of the Royal Society of Medicine, 16 April 1999, Leeds, UK.

Other strategies

Identification of unpublished studies

Several databases were searched (up to December 1997) in an attempt to identify unpublished studies. The databases included the following:

- CRIB (Current Research in Britain)
- DHS Database
- SIGLE
- UK National Research Register.

Experts in the field of wound care were contacted to enquire about ongoing and recently published trials in the field of wound care. In addition, manufacturers of wound care materials were contacted for details of the trials they were conducting.

Citations within the reviews and papers obtained were scrutinised to identify additional studies.

Appendix 2
Advisory panel

Dr Mary Bliss	Homerton Hospital, London
Carol Dealey	Southern Birmingham Community Health NHS Trust
Krzys Gebhardt	St George's Hospital, London
Peter Lowthian	Watford
Jane Nixon	St James's University Hospital, Leeds
Dr John Young	St Luke's Hospital, Bradford

Appendix 3

Summary of included studies

***TABLE 3** RCTs of pressure-relieving interventions for the prevention of pressure sores*

Study	Patients	Devices (sample size)	Follow-up period	Incidence of pressure sores in patients without sores at entry	Healing of established sores	Notes
Goldstone *et al.*, 1982[24]	Patients (>60 years) with femur fracture (mean Norton score 13) Groups comparable at baseline	1. Beaufort bead bed (32): bead-filled mattresses on A&E trolleys, theatre table, boots, etc. 2. Standard supports (43)	?	Grading of sores was not given Beaufort bed: 16% Standard surface: 49% Maximum width of broken skin (mean): 6.4 mm on Beaufort beds; 29.5 mm on standard supports	–	Alternate allocation rather than random-ised. Patients were removed from Beaufort bed standard surfaces due to unknown reasons Number of with-drawals unclear; no intention-to-treat analysis
Hofman *et al.*, 1994[25]	Patients with a femoral-neck fracture and risk score ≥18 (Dutch consensus scale) Excluded patients: pressure sores of grade 2 or greater on admission Groups similar at baseline	1. Cubed foam mattress (Comfortex DeCube) (21): allows removal of small cubes of foam beneath bony prominences. 2. Standard hospital foam mattress (23) Both groups treated as per Dutch pressure sore guidelines	2 weeks	Grade 2 or greater sores: Comfortex DeCube, 24% (4/17) Standard, 68% (13/19) Maximum pressure sore gradings were significantly higher for the standard mattress than the DeCube mattress at 1 and 2 weeks	–	78% follow-up. No intention-to-treat analysis DeCube mattress was not always used correctly and its size was not optimum for all patients

Continued

TABLE 3 contd RCTs of pressure-relieving interventions for the prevention of pressure sores

Study	Patients	Devices (sample size)	Follow-up period	Incidence of pressure sores in patients without sores at entry	Healing of established sores	Notes
Santy *et al.*, 1994[27]	Patients (>55 years) with hip fracture with or without pressure sores Excluded patients: a pressure sore of grade 3 or 4 at entry Patients well matched at baseline	1. Clinifloat (87): deep cut foam cubes 2. NHS contract (150 mm) (64): single block foam 3. Vaperm (116): four layers of foam of varying density with holes and profiled head and heel cushions 4. Therarest (136): three layers of foam; extra soft top layer 5. Transfoam (102): 150 mm thick layered foam with stretchable vapour-permeable cover (all foam)	14 days	Rate of removal from study due to skin deterioration: Clinifloat, 9% NHS contract, 27% Transfoam, 10% Therarest, 11% Vaperm, 8%	–	9% attrition At interim analysis, Clinifloat and NHS contract mattresses were removed from the study; Clinifloat due to superior performance and the NHS mattress due to high rates of pressure sore development. This explains why fewer patients were on these surfaces Omnifoam mattresses showed foam collapse after 6 weeks and were withdrawn from use and replaced with Vaperm mattresses. Problems with the mattress cover were found on two Therarest mattresses, three Transfoam mattresses and three Clinifloat mattresses

Continued

TABLE 3 contd *RCTs of pressure-relieving interventions for the prevention of pressure sores*

Study	Patients	Devices (sample size)	Follow-up period	Incidence of pressure sores in patients without sores at entry	Healing of established sores	Notes
Andersen *et al.*, 1982[42]	Acute patients with high risk of pressure sores (own sore scale) without existing pressure sores	1. Alternating air mattress (166) 2. Water-filled mattress (155) 3. Standard mattress (161)	10 days	Grade 2 or greater sores: Alternating air mattress, 4.2% (7/166) Water-filled mattress, 4.5% (7/155) Standard mattress, 13.0% (21/161)	–	118/600 selected patients withdrew in the first 24 hours, before skin inspection The alternating air mattress is easily punctured and in this study was not always set at the optimum pressure The water-filled bed is heavy and time-consuming to fill Patients were more satisfied with the ordinary bed; they complained about the noise and pressure changes of alternating air mattress

Continued

TABLE 3 contd RCTs of pressure-relieving interventions for the prevention of pressure sores

Study	Patients	Devices (sample size)	Follow-up period	Incidence of pressure sores in patients without sores at entry	Healing of established sores	Notes
Ewing *et al.*, 1964[43]	Elderly patients (mean age 73 years) in the geriatric unit of a convalescent hospital, confined to bed with reduced mobility in legs No baseline data given and baseline comparability not described	1. Sheepskins: adjusted so that both legs were supported on the woolly fleece (18) 2. Control: without sheepskins (18) All patients received the same 4-hourly routine of skin care, involving washing, drying, powdering, light massage of pressure areas, bed cradle	6 months	–	The study was too small and poorly designed to detect a difference No reports of withdrawals	
Gray and Campbell, 1994[44]	Patients from orthopaedic trauma, vascular and medical oncology units without breaks in the skin (Waterlow score ≥15) Groups well matched at baseline	1. Softform mattress (90) 2. Standard NHS mattress (80)	10 days	Grade 2 or greater sore: Softform, 7% Standard, 34% Rate of transfer to dynamic support surface: standard group, 19%; Softform group, 2%	–	Impossible to calculate the attrition rate as the incidence was reported as percentages only and it was unclear what the denominator was Nurses were more positive and patients gave higher comfort scores to the Softform mattress

Continued

***TABLE 3 contd** RCTs of pressure-relieving interventions for the prevention of pressure sores*

Study	Patients	Devices (sample size)	Follow-up period	Incidence of pressure sores in patients without sores at entry	Healing of established sores	Notes
Collier, 1996[45]	Patients on a general medical ward; no further detail given	Comparison of eight foam mattresses: 1. New Standard Hospital Mattress (Relyon) (130 mm) (9) 2. Clinifloat (11) 3. Omnifoam (11) 4. Softform (12) 5. STM5 (10) 6. Therarest (13) 7. Transfoam (10) 8. Vapourlux (14)	Not clear	No sores of any grade reported in any of the patients	–	Nine patients were allocated the Cyclone mattress; however, this group was withdrawn from the study at the manufacturer's request and no data were presented All mattresses assessed for 'grounding', deterioration of cover, contamination of inner foam core and interface pressures There was no 'grounding' of any mattresses during the evaluation period There was softening of the centre of the foam base in the Standard and Omnifoam mattresses at completion of the study (detected using a 'fist test' of unknown reliability) All mattress covers remained intact and the inner foam protected

Continued

TABLE 3 contd *RCTs of pressure-relieving interventions for the prevention of pressure sores*

Study	Patients	Devices (sample size)	Follow-up period	Incidence of pressure sores in patients without sores at entry	Healing of established sores	Notes
Gray and Smith, 2000[46]	Patients admitted to a district general hospital for bed rest or surgery, with intact skin, no other skin abnormalities, no terminal illness, weight <160 kg Mean Waterlow score on admission: group 1, 14 (3.6); group 2, 13 (2.5)	Two foam mattresses: 1. Transfoam mattress (50) 2. Transfoamwave (50)	10 days	1. One grade IV sore 2. One grade II sore	–	95% follow-up; intention-to-treat analysis
Kemp *et al.*, 1993[47]	Hospitalised elderly patients (65–98 years) without pressure ulcers (Braden score ≤16) Groups similar at baseline	1. Convoluted foam overlay, 3 inches thick (45) 2. Solid sculptured foam overlay, 4 inches thick (39)	1 month	Included grade 1 sores: Convoluted foam overlay, 47% Solid foam overlay, 31%	–	All patients appear to have completed the study

Continued

TABLE 3 contd *RCTs of pressure-relieving interventions for the prevention of pressure sores*

Study	Patients	Devices (sample size)	Follow-up period	Incidence of pressure sores in patients without sores at entry	Healing of established sores	Notes
Vyhlidal *et al.*, 1997[48]	Patients newly admitted to a skilled nursing facility; estimated stay at least 10 days; free of pressure sores, but at risk (Braden score <18, subscale score of <3 in sensory perception, mobility or activity levels) Diagnoses: Musculoskeletal, 45% Cardiovascular, 27% Neurological, 12% Other, 15% Patients in the MAXIFLOAT group were younger, but not significantly. Braden scores similar at baseline	1. IRIS 3000 (20): 4-inch thick foam overlay with dimpled surface 2. MAXIFLOAT (20): mattress replacement in five sections – water/bacteria-repellent top cover; 1.5-inch thick antimicrobial foam; centre core of cut foam; non-removable polyester fibre heel pillow; water/bacteria-proof bottom cover	10–21 days	All grades of sore: 1. IRIS 3000, 60% (12/20): grade 1, 25% (4/20) grade 2, 40% (8/20) 2. MAXIFLOAT, 25% (5/20): grade 1, 10% (2/20) grade 2, 15% (3/20) $p = 0.025$ Time to sore: 1. IRIS 3000, 6.5 days 2. MAXIFLOAT, 9.2 days (NS)	–	No record of any withdrawals The IRIS 3000 is an overlay which goes on an existing mattress, resulting (in the trial) in a bed height of 29 inches. One subject refused the IRIS because of the height of the bed IRIS is lighter (6.9 lb) than the MAXIFLOAT (25 lb) and easier to manipulate; however, the latter is still lighter than the standard hospital mattress (48 lb) IRIS can be sent home with the patient IRIS costs $38, compared with $260 for the MAXIFLOAT

Continued

TABLE 3 contd RCTs of pressure-relieving interventions for the prevention of pressure sores

Study	Patients	Devices (sample size)	Follow-up period	Incidence of pressure sores in patients without sores at entry	Healing of established sores	Notes
Sideranko *et al.*, 1992[19]	Adult, surgical intensive care unit patients: stay in unit >48 h; no existing skin breakdown on admission Groups similar at baseline, although the water mattress group were heavier and stayed for a shorter time in the unit	1. Alternating air mattress (20): 1.5-inch thick Lapidus Airfloat system 2. Static air mattress (20): 4-inch thick GayMar SofCare 3. Water mattress (17): 4-inch thick Lotus	9.4 days	Grade of sores not reported 1. Alternating air mattress: 25% (5/20) 2. Static air mattress: 5% (1/20) 3. Water mattress: 12% (2/17)	–	No withdrawals reported
Takala *et al.*, 1994[21]	Non-trauma patients admitted to the intensive care unit who were expected to stay >5 days Treatment groups well matched at baseline; however, the pressure sore risk status was not reported	1. Carital Optima (21): constant-low-pressure mattress comprising 21 double air bags on a base 2. Standard hospital foam mattress (19): 10 cm thick foam, density 35 kg/m^3	14 days	1. No sores 2. 7/19 patients (37%) developed a total of 13 sores $p < 0.005$ Nine sores were grade 1A (erythema), four were grade 1B (superficial and limited to the dermis)	–	40% withdrawals; intention-to-treat analysis undertaken

Continued

***TABLE 3 contd** RCTs of pressure-relieving interventions for the prevention of pressure sores*

Study	Patients	Devices (sample size)	Follow-up period	Incidence of pressure sores in patients without sores at entry	Healing of established sores	Notes
Cooper *et al.*, 1998[22]	Emergency orthopaedic trauma wards; patients aged >65 years (mean age 83 years); Waterlow score >15 Well matched at baseline	1. Dry flotation mattress (Roho) (49) [data supplied for only 43] 2. Dry flotation mattress (Sofflex) (51) [data supplied for only 41]	7 days	Grade 2 and above sores: 1. Roho, 0 2. Sofflex, 1/51 (2%) Grade 1 sores: 1. Roho, 5/43 (12%) 2. Sofflex, 2/41 (5%)	–	Roho: 79% patients found it comfortable or very comfortable; five patients found it uncomfortable Sofflex: 90% patients found it comfortable or very comfortable Staff had difficulty setting the level of inflation correctly; this can now be done automatically 16% attrition; no intention-to-treat analysis
Stapleton, 1986[28]	Female elderly patients with fractured neck of femur, without existing pressure sores, Norton score ≤14 Groups appeared well matched at baseline	1. Large Cell Ripple (32) 2. Polyether foam pad (34) 3. Spenco pad (34)	?	Sores of grade 2 or greater: 1. Large Cell Ripple, 34% (11/32) 2. Polyether foam pad, 41% (14/34) 3. Spenco pad, 35% (12/34) Sores of grade 3 and greater: 1. Large Cell Ripple, 0% 2. Foam pad, 24% 3. Spenco pad, 6%	–	45 Large Cell Ripple mattresses required 50 motor repairs and 90 material repairs during the 12-month study Patients did not like the feel of the ripples No mention of withdrawals

Continued

TABLE 3 contd *RCTs of pressure-relieving interventions for the prevention of pressure sores*

Study	Patients	Devices (sample size)	Follow-up period	Incidence of pressure sores in patients without sores at entry	Healing of established sores	Notes
Lazzara and Buschmann, 1991[49]	Elderly private nursing home residents (modified Norton scale ≥15); 9/66 participants had pressure sores on entry	1. Air overlay (33): SofCare 2. Gel mattress (33)	6 months	Grade 2 or greater sores: 1. Air overlay, 16% (5/31) 2. Gel mattress, 15% (4/26)	–	Interventions not well described. Of the 74 who entered the study, only those who participated for 4–6 months were included in the analysis (total 66); 19 patients died and were excluded from the analysis, but these might have been the patients at highest risk It was difficult to maintain inflation of the air overlay; it also punctured easily. During the trial, 110 air overlays were used for 76 patients. The gel mattress was heavy

Continued

TABLE 3 contd *RCTs of pressure-relieving interventions for the prevention of pressure sores*

Study	Patients	Devices (sample size)	Follow-up period	Incidence of pressure sores in patients without sores at entry	Healing of established sores	Notes
Tymec *et al.*, 1997[50]	52 patients (23 women, 29 men) admitted to selected nursing units of a large hospital, with a Braden score of ≤16 (risk) and intact skin on heels. Age 27–90 years (mean 66.6 ± 16.5 years); mean Braden score on admission 11.8; 21 patients with respiratory conditions, 6 with cancer, 5 with cerebrovascular accident	Factorial design evaluating the effect of a heel-elevation device plus positioning and order of positioning 1. Foot Waffle: FDA-approved, non-abrasive vinyl boot with built-in foot cradle and inflated air chamber 2. Hospital pillow: placed under both legs from below the knee to the Achilles tendon Number of patients in each group unclear	14 days	Pressure sores developed: 1. Foot Waffle, 6 2. Hospital pillow, 2 Denominators unclear	–	Do not appear to have been any losses
Price *et al.*, 1999[26]	Patients with fractured neck of femur and Medley score >25 (very high risk), aged >60 years	1. Repose system (40): low-pressure inflatable mattress and cushion in polyurethane material 2. Nimbus III and TransCell cushion(40): dynamic flotation All other care was standard best practice, including regular repositioning	14 days postoperatively	Blister + grade II: 1. At admission, 1 + 1/40; preoperatively, 1 + 0/36; at 7 days 2 + 1/32; at 14 days 0 + 3/24 2.At admission, 0 + 2/40; preoperatively, 1 + 3/37; at 7 days, 1 + 0/31; at 14 days 1 + 1/26	–	80 patients were randomised; 50 in the final analysis (i.e. 38% attrition)

Continued

TABLE 3 contd RCTs of pressure-relieving interventions for the prevention of pressure sores

Study	Patients	Devices (sample size)	Follow-up period	Incidence of pressure sores in patients without sores at entry	Healing of established sores	Notes
Conine *et al.*, 1990[51]	Non-geriatric adult patients (aged 18–55 years) in an extended care facility for chronic neurological conditions; Norton score ≤14	1. Alternating air overlay (72): 10 cm air cells; manufacturer not given 2. Silicore (Spenco) overlay (76): siliconised hollow fibres in waterproofed cotton, placed over standard hospital mattress	3 months	Included grade 1 sores: 1. Alternating air overlay, 54% (39/72) 2. Spenco overlay, 59% (45/76)	The alternating air overlay group had a slightly lower Exton-Smith severity score (1.59 vs 1.69) and a shorter healing duration (25 days vs 29 days); these differences were not statistically significant	The alternating air overlay needed frequent monitoring and expensive prolonged repairs. It was reported that the patients sank into the Spenco overlay and found it difficult to move. Patients complained of bad odour build-up, instability (especially of the Spenco), and the noise of the alternating pressure motor. High dropout rate due to discomfort
Daechsel and Conine, 1985[52]	Patients , aged 19–60 years, in a long-term care hospital for chronic neurological conditions at high risk of developing pressure sores, but with no pressure sores at entry	1. Alternating pressure overlay (16): Gaymar 2. Silicore (JW Westman Inc.) overlay (16)	3 months	Included grade 1 scores: 1. Alternating pressure overlay, 25% (4/16) 2. Spenco overlay, 25% (4/16) No statistically significant differences were found between the two groups with regard to location and severity of pressure sores	–	100% follow-up Patients' satisfaction was similar for both devices

Continued

TABLE 3 contd *RCTs of pressure-relieving interventions for the prevention of pressure sores*

Study	Patients	Devices (sample size)	Follow-up period	Incidence of pressure sores in patients without sores at entry	Healing of established sores	Notes
Whitney *et al.*, 1984[53]	Patients on medical–surgical units who were in bed for ≥20 h/day. Most patients had relatively little skin breakdown	1. Alternating pressure mattress (25) 2. Convoluted foam pad (26): Eggcrate In both groups patients were turned every 2 h	8 days	Changes in skin condition did not differ significantly between patients using the alternating pressure air mattress and the foam mattress (better, 20% vs 19%; same, 60% vs 58%; worse, 20% vs 23%)	–	Four patients died. Analysis was by intention to treat Alternating pressure mattress: pump maintenance was costly; patients objected to the movement. The alternating pressure mattress was more easily cleaned and retained its original properties over several weeks compared to the foam, which compressed and flattened.
Gebhardt, 1994[54]	Newly admitted patients aged >18 years in intensive care unit, oncology, general medicine, care of the elderly, orthopaedic). Norton scores <14 and no existing pressure sores Groups well matched at baseline for age, sex and Norton score	1. Alternating pressure air mattresses (115): various 2. Constant low-pressure supports (115): foam, fibrefill, air, water, gel (various) Patients with deteriorated sores were transferred to a more sophisticated medium-cost support in the same group (e.g. Pegasus, Nimbus, Orthoderm, Convertible, Roho)	Mean 16 days	Grade 2 or greater sore: 1. Alternating pressure, 16% (18/115) 2. Constant low-pressure, 55% (63/115)	–	Analysis by intention to treat Mechanical unreliability and poor management of alternating pressure supports was a problem

Continued

TABLE 3 contd RCTs of pressure-relieving interventions for the prevention of pressure sores

Study	Patients	Devices (sample size)	Follow-up period	Incidence of pressure sores in patients without sores at entry	Healing of established sores	Notes
Exton-Smith *et al.*, 1982[23]	Newly admitted geriatric patients, with fractured neck of femur, and long-stay patients; with no grade 2 or greater pressure sores. Norton score ≤14 Patients were matched in pairs for sex and Norton score. Where no match was possible, the Airwave patient was matched with a Large Cell Ripple patient with a higher risk score Groups appear well matched at baseline	1. Pegasus Airwave system (31): two layers of air cells; pressure alternated by deflating every third cell in a 7.5-minute cycle 2. Large Cell Ripple Mattress (31): not described	2 weeks	Grade 2 sore or greater: 1. Airwave, 16% (5/31) 2. Large Cell Ripple, 39% (12/31)	–	During the trial period there were no break-downs with the Airwave and 10 break-downs with the Large Cell Ripple mattresses Four patients withdrawn; 94% follow-up

Continued

***TABLE 3 contd** RCTs of pressure-relieving interventions for the prevention of pressure sores*

Study	Patients	Devices (sample size)	Follow-up period	Incidence of pressure sores in patients without sores at entry	Healing of established sores	Notes
Hampton, 1997[55]	Very little detail given. Average age 77 years No data regarding baseline status of patients were presented in the published paper and therefore it was impossible to judge the baseline comparability of the groups Limited information was obtained from the authors on request: Number of patients at high to very high risk: Airwave group, 31; Cairwave group, 27. Mean age: Airwave group, 79; Cairwave group, 75	1. Alternating pressure (Cairwave System) (36): three cell, 7.5-minute cycle; manufacturer claims that zero pressure is achieved for more than 20% of the cycle 2. Alternating pressure (Airwave System) (39): cells arranged in sets of three and inflated in waves; 7.5-minute cycle; manufacturer claims that zero pressure is applied for 15% of the time	20 days	No patient developed a pressure sore	–	Attrition unclear

Continued

TABLE 3 contd *RCTs of pressure-relieving interventions for the prevention of pressure sores*

Study	Patients	Devices (sample size)	Follow-up period	Incidence of pressure sores in patients without sores at entry	Healing of established sores	Notes
Laurent, 1997[18]	Patients aged ≥15 years (mean 64 years) undergoing cardio-vascular surgery; expected hospital stay of at least 5 days, and expected time in the intensive care unit (ICU) Few data given on baseline comparability of groups	2 × 2 factorial design 1. Standard mattress ICU; standard mattress postoperatively (80) 2. Nimbus (alternating pressure) ICU; standard mattress postoperatively (80) 3. Standard mattress ICU; Tempur (contin-uous low-pressure) postoperatively (75) 4. Nimbus ICU; Tempur postopera-tively (77)	Not stated	Incidence of sores of grade 2 or above (partial or full-thickness skin loss and worse): 1. 18% (14/80) 2. 13% (10/80) 3. 15% (11/75) 4. 13% (10/77) Differences not significant	–	No reports of withdrawals
Inman *et al.*, 1993[17]	Patients (aged >17 years) with an Acute Physiology and Chronic Health Evaluation (APACHE II) score >15 who had an expected intensive care unit stay of ≥3 days	1. Low-air-loss bed (49) 2. Standard ICU bed (49): patients turned every 2 h	17 days (mean)	Grade 2 or greater sores: 1. Low-air-loss beds, 12% 2. Standard ICU bed, 51% Patients with multiple pressure sores: 1. 2% 2. 24%	–	98% follow-up. No intention-to-treat analysis

Continued

***TABLE 3 contd** RCTs of pressure-relieving interventions for the prevention of pressure sores*

Study	Patients	Devices (sample size)	Follow-up period	Incidence of pressure sores in patients without sores at entry	Healing of established sores	Notes
Bennett *et al.*, 1998[56]	Acute and long-term care patients who were incontinent of urine and/or faeces, in bed >16 h/day, with pressure sores of grade 2 or below (or none). If urinary catheter present, this was removed in the low-air-loss hydrotherapy group (but not in the control group). Most common diagnoses: sepsis, malignancy, fractured neck of femur, hypovolaemia, dementia	1. Low-air-loss hydrotherapy Clensicair (SSI/Hill Rom) (42): permeable, fast-drying filter sheet over low-air-loss cushions (circulating air); urine collection device integral to bed 2. Standard care (56): standard bed or foam, air or alternating pressure mattresses; skin care not standardised	60 days Median length of follow-up: 1. 4 days (1–60 days) 2. 6 days (1–62 days) $p < 0.017$	Number of patients who developed any kind of skin lesion more than 1 day after enrolment: 1. 27/42 (64%) 2. 10/56 (18%) Number of patients who developed pressure sores of grade 2–4: 1. 8/42 (19%) 2. 4/56 (7%) $p = 0.11$ (not significant) Number of patients with non-blanchable erythema (grade 1): 1. 6/42 (14%) 2. 0/56 $p = 0.008$	Only 26 sores present on enrolment, and only three of these were grade 3 or 4, so no healing data were presented	The first 68 patients were discounted and a further 26 patients of 116 withdrew. No intention-to-treat analysis Nurses received special extra training for the low-air-loss bed. Patients with low-air-loss beds were interviewed about satisfaction, control patients were not There were many nurse complaints about the low-air-loss bed; there was a firmly held belief that it was associated with more ulceration Two subjects in the low-air-loss bed group developed hypothermia

Continued

TABLE 3 contd *RCTs of pressure-relieving interventions for the prevention of pressure sores*

Study	Patients	Devices (sample size)	Follow-up period	Incidence of pressure sores in patients without sores at entry	Healing of established sores	Notes
Economides *et al.*, 1995[57]	12 patients who had stage 4 pressure sores needing myocutaneous flap closure. 10/12 patients were paraplegic or quadriplegic	1. Dry floatation mattress (Roho) (6): bed overlay of 720 air cells that conform to the body and increase the support area 2. Air-fluidised bed (Clinitron) (6): ceramic beads, through which warm air is blown, covered with a polyester sheet	2 weeks	–	Wound breakdown: 2/6 on Roho; 2/5 on Clinitron. No significant difference between the two support surfaces in the prevention of flap breakdown in the immediate post-operative period	Do not appear to have been any withdrawals
Gentilello *et al.*, 1988[16]	Critically ill patients immobilised because of head injury, spinal injury or traction Groups well matched at baseline, except for cigarette smoking (more in conventional bed group)	1. Kinetic treatment table (27): rotates through an arc of 124° every 7 minutes 2. Conventional bed (38): patients turned in a conventional fashion every 2 h	?	Kinetic treatment table: 30% Conventional: 26%	–	One patient withdrew and was not included in the analysis
Summer *et al.*, 1989[20]	Patients admitted to the intensive care unit. Diagnostic groups: sepsis, pneumonia, respiratory failure, drug overdose	1. Kinetic treatment table (43): 7 feet × 3 feet; padded, vinyl covered platform which turns through an arc every 1.7 s 2. Routine turning on conventional beds (43)	?	One kinetic treatment table patient developed a small facial ulcer; no conventional bed patients developed ulcers	–	3/86 (3%) patients lost to follow-up

Continued

***TABLE 3 contd** RCTs of pressure-relieving interventions for the prevention of pressure sores*

Study	Patients	Devices (sample size)	Follow-up period	Incidence of pressure sores in patients without sores at entry	Healing of established sores	Notes
Nixon *et al.*, 1998[14]	Patients aged ≥55 years admitted for elective major general, gynaecological or vascular surgery in supine or lithotomy position and free of preoperative pressure damage greater than grade 1	1. Dry viscoelastic polymer pad on operating table (222) 2. Standard operating theatre table mattress plus gamgee heel support (224)	8 days	Incidence of pressure sores: Overall, 16% (65/416) 1. Dry viscoelastic polymer pad on operating table, 11% (22/205) 2. Standard mattress, 20% (43/211) $p = 0.01$; OR = 0.46; 95% CI, 0.26 to 0.82 Episodes of skin damage: Conversion from grade 0 to grade 1 sores, 56/65 Conversion from grade 0 to grade 2a, 4/65 Conversions from grade 0 to grade 2b, 5/65 The data were not broken down by group	–	Main end-point data reported for 416 patients; incomplete data for 30 patients (lost forms, 3; incomplete postoperative skin assessment, 27). Patients for whom data were incomplete were not reported by group Interrater reliability of skin assessments was measured; there was disagreement in only 2% of cases

Continued

TABLE 3 contd RCTs of pressure-relieving interventions for the prevention of pressure sores

Study	Patients	Devices (sample size)	Follow-up period	Incidence of pressure sores in patients without sores at entry	Healing of established sores	Notes
Aronovitch, 1998[13]	Patients aged ≥18 years, free of pressure sores, undergoing elective surgery under general anaesthesia, of at least 3 h operative time No significant differences between groups for age, sex, race, weight, height or smoking status at baseline, but patients in the conventional management group were at greater risk of pressure sore development, as defined by the Knoll score	1. Alternating pressure system intra- and postoperatively (Micropulse) (112): a thin pad with over 2500 small air cells in rows; 50% of the cells are inflated at any time 2. Conventional management (105): use of a gel pad in the operating room and a replacement mattress postoperatively	7 days	1. MicroPulse system: 1% (1/90); however, the sore was due to a foreign body and was thus considered 'not related to the bed' 2. Conventional management: 9% (7/80) (7 patients developed 11 ulcers) Grade 1: 1 Grade 2: 4 Unstageable: 6 $p < 0.005$	–	1. MicroPulse system: device was inadvertently turned off during treatments of four patients; four patients asked to withdraw for various unreported reasons; three patients withdrew due to back pain; 12 patients assigned to this group were placed on another surface post-operatively for reasons unrelated to the surface 2. Conventional management: six patients were placed on the MicroPulse postoperatively Analysis was on an intention-to-treat basis

Continued

TABLE 3 contd *RCTs of pressure-relieving interventions for the prevention of pressure sores*

Study	Patients	Devices (sample size)	Follow-up period	Incidence of pressure sores in patients without sores at entry	Healing of established sores	Notes
Beckrich, 1998[15]	Patients admitted for cardiothoracic surgery (operative period of at least 4 h), aged ≥18 years, free of pressure sores at baseline	1. Alternating pressure system intra- and post-operatively (Micropulse) (98) 2. Conventional management (100): gel pad during surgery and standard hospital mattress postoperatively	7 days	1. MicroPulse System: 2% (2/98) (1/2 discounted by original authors from their analysis as thought to occur for reasons 'not related to the use of the MicroPulse system') 2. Conventional management 7% (7/100 patients developed 10 ulcers) Grade of ulcers: 1. MicroPulse – grade 2, 2 2. Conventional – grade 1, 2; grade 2, 5; grade 3, 3	–	No equipment-related adverse events were reported

Continued

TABLE 3 contd RCTs of pressure-relieving interventions for the prevention of pressure sores

Study	Patients	Devices (sample size)	Follow-up period	Incidence of pressure sores in patients without sores at entry	Healing of established sores	Notes
Lim *et al.*, 1988[59]	Residents of an extended-care facility (>60 years), using a wheelchair for 3 h/day or more, at high risk of developing pressure sores (Norton score ≤14)	1. Polyurethane foam wheelchair cushions in slab form (33): 2.5 cm medium-density foam glued to 5 cm firm chipped foam 2. Customised contoured foam wheelchair cushions (29): same foam as above, cut to a customised shape to relieve pressure Both cushions were fitted with identical snug-fitting polyester covers	5 months	Included grade 1 sores: 1. Slab foam, 73% (19/26) 2. Contoured foam, 69% (18/26)	Mean severity score: slab foam, 1.9; contoured foam, 1.7 ($p > 0.05$) Mean healing time: slab foam, 6.2 weeks; contoured foam, 5.4 weeks ($p > 0.05$)	84% follow-up

Continued

TABLE 3 contd *RCTs of pressure-relieving interventions for the prevention of pressure sores*

Study	Patients	Devices (sample size)	Follow-up period	Incidence of pressure sores in patients without sores at entry	Healing of established sores	Notes
Conine *et al*., 1994[60]	Elderly patients (mean age 82 years) in an extended-care hospital who were deemed at high risk of pressure sores (Norton score ≤14); sitting in a wheelchair daily for a minimum of 4 consecutive hours; free of progressive disease likely to confine them to bed. Patients were excluded if they were diabetic, had peripheral vascular disease, or were confined to bed for more than 120 consecutive hours (except if to heal a pressure sore) No significant differences in baseline variables	1. Jay cushion (68): contoured urethane foam base over a gel pad 2. Foam cushion (73): 32 kg/m^3 density foam bevelled at the bottom to prevent a sling effect Both cushions were fitted with identical Jay air-exchange covers of knitted polyester. Patients were assigned to their specific wheelchairs by a seating specialist as per a local policy that was unaffected by the trial	3 months	1. Jay cushion: 17/68 (25%) 2. Foam cushion: 30/73 (41%) Pressure sore incidence data were presented as the number of sores and the number of affected patients for all grades of sore, but only as the number of sores by grade (and there were cases of multiple sores on the same patient). Therefore, it is impossible to present the incidence data as the number of patients affected by sores of grade 2 or above	–	13% attrition; not analysed by intention to treat

TABLE 4 RCTs of pressure-relieving interventions for the treatment of pressure sores

Study	Patients	Devices (sample size)	Follow-up period	Incidence of pressure sores in patients without sores at entry	Healing of established sores	Notes
Groen *et al.*, 1999[61]	Patients in a nursing home, aged ≥60 years, with a pressure ulcer on the trunk of grade III (superficial cutaneous or sub-cutaneous necrotic) or grade IV (deep subcutaneous necrotic)	1. TheraRest foam replacement mattress: 14-inch thick, three layers of foam of varying density 2. Secutex water mattress on top of a hospital foam mattress (60): three PVC sections, each containing 26 l of warmed water, held by a foam frame	4 weeks	–	Outcome (healing of pressure sores) measured by using a scoring system rather than by measurement of area or volume; measurement not blinded % ulcers completely healed at 4 weeks: 1. 45% 2. 48% Ulcers reported to have improved at the same rate in each group	19/120 patients withdrew; 11 from TheraRest and 8 from Secutex group, most commonly due to severe illness or discharge No intention-to-treat analysis
Allman *et al.*, 1987[62]	Surgical patients (>18 years) from surgical units with pressure sores, and with activity expected to be limited to bed/chair in the hospital for at least 1 week Groups appear well matched at baseline, including for ulcer area	1. Air-fluidised bed (Clinitron) (31) 2. Conventional treatment (34): included alternating air mattress, 2-hourly turning, heel and elbow protectors, plus 19 mm foam	Mean: 13 days Range: 4–77 days	–	Median change in total sore surface area (cm^2): 1. Air-fluidised bed, –1.2 2. Conventional therapy, +0.5 (p = 0.01) The difference between air-fluidised beds and alternating air mattresses were more marked for larger sores (median –5.3 vs +4.0; p = 0.01)	90% follow-up. Four patients withdrew because of difficulty in transferring in/out of the air-fluidised bed

Continued

TABLE 4 contd *RCTs of pressure-relieving interventions for the treatment of pressure sores*

Study	Patients	Devices (sample size)	Follow-up period	Incidence of pressure sores in patients without sores at entry	Healing of established sores	Notes
Munro *et al.*, 1989[63]	Patients with pressure sores of grade 2–3 who were expected to remain in the hospital for at least 15 days Excluded patients with grade 4 ulcers and those weighing >250 lb or who were malnourished	1. Air-fluidised bed (Clinitron) (20) 2. Standard bed plus usual nursing measures such as sheepskin or gel pads placed beneath pressure areas (20)	15 days	–	Mean size of ulcers was reduced in the Clinitron group, and increased in the standard bed group ($p = 0.05$) Pressure sore healing was enhanced on the Clinitron bed; fewer medications were used to treat the sores in the Clinitron group than in the standard hospital bed group	Extent of follow-up unclear The air-fluidised bed group rated their satisfaction higher than did the control group ($p = 0.067$)
Strauss *et al.*, 1991[64]	Patients (>16 years) at home with grade 3–4 pressure sores, who would probably require future hospitalisation for the sore, who had severely limited mobility, and for whom air-fluidised therapy was a practical option	1. Air-fluidised bed (Clinitron) (47) 2. Conventional care, including alternating pressure pads (50)	36 weeks	–	A higher proportion of air-fluidised bed patients was classified as improved ($p > 0.05$; this value is unreliable as a considerable amount of data were missing). Air-fluidised bed patients had significantly fewer pressure-sore-related hospitalisations per patient (0.23 vs 0.58; $p < 0.05$)	Withdrawal rate: 13% Six air-fluidised beds had minor bead leaks and seven overheated. Several patients noted dry skin and one experienced mild dehydration

Continued

TABLE 4 contd *RCTs of pressure-relieving interventions for the treatment of pressure sores*

Study	Patients	Devices (sample size)	Follow-up period	Incidence of pressure sores in patients without sores at entry	Healing of established sores	Notes
Ferrell *et al.*, 1993[65]	Elderly nursing home residents with multiple medical problems, and with trunk or trochanter pressure ulcers (Shea stage 2 or greater). If a patient had multiple ulcers, the larger ulcer was chosen as the index ulcer Groups appear well matched at baseline, except that patients in the low-air-loss bed group had significantly lower serum albumin	1. Low-air-loss bed (Kinair) (43) 2. Convoluted foam mattress (41): 10 cm convoluted foam overlay on top of a standard mattress Both groups received similar co-interventions	33–40 days	–	Decrease in size of ulcers was 9.0 mm^2/day for low-air-loss beds compared with 2.5 mm^2/day for foam mattresses (p = 0.0002); 26 (60%) completely healed on low-air-loss beds vs 19 (46%) on foam mattresses (p = 0.19) Number of patients that died: 11 (26%) on low-air-loss beds vs 7 (17%) on foam mattresses	It is not clear how many patients were randomised and, therefore, while the numbers of and reasons for with-drawals are listed, it is impossible to calculate attrition rates
Mulder *et al.*, 1994[66]	Patients at 25 nursing homes with full-thickness ulcers of grade III and IV, ranging in dimension between 1.5 cm × 1.5 cm and 20 cm × 10 cm Excluded patients with cancer, osteomyelitis, infection of the ulcer, immunodeficiency disorders, poor nutrition	1. Low-air-loss bed (Therapulse) (31): a pulsating air-suspen-sion therapy (cushions alternately inflate and deflate, but classed as a low-air-loss rather than alternating-pressure device) 2. Convoluted foam overlay (Geomatt) (18)	12 weeks	–	Ulcers completely healed: 1. 5/31 (16%) 2. 3/18 (17%) Ulcers classed as 'healed or improved': 1. 15/31 (48%) 2. 8/18 (44%)	Impossible to calculate attrition as it was not stated how many patients were random-ised to each group

Continued

TABLE 4 contd *RCTs of pressure-relieving interventions for the treatment of pressure sores*

Study	Patients	Devices (sample size)	Follow-up period	Incidence of pressure sores in patients without sores at entry	Healing of established sores	Notes
Caley *et al.*, 1994[67]	Acute-care patients with existing pressure ulcers for whom low-air-loss therapy had been recommended by their physician or nurse	1. Low-air-loss bed (Monarch, Mediscus) (23) 2. Low-air-loss overlay (SPR, Gaymar) (32)	24 days (mean)	–	Reported as no significant difference in the change in ulcer size between subjects in the two groups; however, very few data were presented (median change in area and range)	Staff satisfaction was reported to be similar for both products. No description of co-interventions, except that both groups received a routine skin care protocol. 41% of the patients randomised were not included in analysis
Devine, 1995[68]	Patients in a geriatric unit with pressure sores (grade 2 or above). Mean age 83 years (range 69–98 years)	1. Alternating pressure mattress (Nimbus 1) (22): modular, with rows of figure-of-eight-shaped cells 2. Alternating pressure mattress (Pegasus Airwave) (19): double-layer mattress	4 weeks	–	11 patients (24%) died or were moved to other hospitals The rate of complete healing was higher for the Nimbus mattress, but the difference was not statistically significant (10/16 vs 5/14) The reduction in size of pressure sores was similar in the two groups	Neither the Pegasus Airwave nor the Nimbus I mattresses showed any significant breakdown. There were no significant differences in patient/staff acceptability

Continued

TABLE 4 contd RCTs of pressure-relieving interventions for the treatment of pressure sores

Study	Patients	Devices (sample size)	Follow-up period	Incidence of pressure sores in patients without sores at entry	Healing of established sores	Notes
Evans *et al.*, 2000[69]	Patients aged ≥65 years admitted to acute medical and surgical units in two hospitals and two nursing homes with either grade III or IV pressure sores or a grade II pressure sore plus one or more of other risk factors (difficulty repositioning, weight >17 stone, bed-bound, surgery lasting ≥2 h)	1. Alternating pressure mattress (Nimbus III) (17; 7 hospital, 10 nursing home) 2. Standard care (15; 5 hospital, 10 nursing home): various surfaces, mainly of alternating-pressure type, such as Pegasus Airwave, Pegasus Egerton	2 weeks	–	Median (range) reduction in wound surface area: 1. Nimbus III (hospital patients), 0.12 cm^2/day (0–0.21 cm^2/day) 2. Standard care (hospital patients), 0.08 cm^2/day (0.04–0.33 cm^2/day) 3. Nimbus III (nursing home patients), 0.11 cm^2/day (0.04–0.41 cm^2/day) 4. Standard care (nursing home patients), 0.05 cm^2/day (0–0.48 cm^2/day) Differences not significant Median (range) relative reduction in wound surface area: 1. Nimbus III (hospital patients), 2.44% (0–7.14%) 2. Standard care (hospital patients), 1.34% (1.11–2.88%)	Median comfort scores (hospital patients): 1. Nimbus III, 5 (very comfortable) 2. Standard care, 4 (comfortable) $p = 0.006$ Median comfort scores (nursing home patients): 1. Nimbus III, 5 (very comfortable) 2. Standard care, 4 (comfortable) $p = 0.002$ A large proportion of patients did not complete follow-up (11/20 in nursing home group; 75% in hospital group). However, analysis was by intention to treat

Continued

TABLE 4 contd *RCTs of pressure-relieving interventions for the treatment of pressure sores*

Study	Patients	Devices (sample size)	Follow-up period	Incidence of pressure sores in patients without sores at entry	Healing of established sores	Notes
					3. Nimbus III (nursing home patients), 1.57% (0.45–5.0%) 4. Standard care (nursing home patients), 0.99% (0–2.54) Differences not significant	
Russell *et al.*, 2000[70]	Patients admitted to an elderly care hospital unit with pressure sores of grade II or greater Patients were excluded if the randomised equipment was unavailable (not stated how often this occurred)	1. Alternating pressure (Nimbus III) + Aura cushion + 4-hourly change of position (70) 2. Alternating pressure (Cairwave) + Proactive cushion + 8-hourly change of position (71)	18 weeks	–	No measurement of ulcer area reported. Healing reported as the number of ulcers healed and the change in severity (Torrance) score 1. Sacral ulcers, 45%; heels, 33% 2. Sacral ulcers, 51%; heels, 55% $p < 0.019$	61% follow-up. No intention-to-treat analysis

Continued

TABLE 4 contd RCTs of pressure-relieving interventions for the treatment of pressure sores

Study	Patients	Devices (sample size)	Follow-up period	Incidence of pressure sores in patients without sores at entry	Healing of established sores	Notes
Clark and Donald, 1999[71]	Elderly patients in acute care hospitals and nursing homes, with existing pressure sores, who were predicted to remain in the trial for a minimum of 7 days. No surgical or chemical debridement of sores; patients able to sit on the allocated cushion Groups appear well matched at baseline for pressure sore risk status, mobility, nutritional status, continence	1. Alternating-pressure (ProActive 2) cushion (14): alternating-pressure cushions for day chairs and wheelchairs; seating adjusts automatically to patient weight 2. Dry flotation cushion (Roho) (11) All patients had an alternating-pressure system (Pegasus Airwave) on their bed	Unclear 1. Mean 58.6 days 2. Mean 43.7 days	No new sores developed in either group	On admission, all subjects had a single sore (23 sacral, 2 ischial): 1. 50% superficial (grades 1 and 2) 2. 63.6% superficial Sores healing completely: 1. 3/14 (21%) 2. 5/11 (46%) Healing rate: 1. 0.16 cm^2/day 2. 0.34 cm^2/day Difference not significant Healing rate: 1. 0.72 cm^3/day 2. 0.62 cm^3/day Difference not significant	24% attrition. No intention-to-treat analysis

Appendix 4

Quality assessment of included studies

TABLE 5 *Quality of RCTs of pressure-sore prevention and treatment*

Trial	Clear inclusion and exclusion criteria	Sample-size total number (arms)	*A priori* sample-size calculation stated	True randomisation with allocation concealment described	Baseline comparability of treatment groups described	Blinded outcome assessment	Grade 1 sores excluded or presented separately	Main interventions well described
Goldstone *et al.*, 1982[24]	✓	75 (2)	✗	✗	✓	✗	✗	✓
Hofman *et al.*, 1994[25]	✓	44 (2)	✓	✗	✓	✗	✓	✓
Santy *et al.*, 1994[27]	✓	505 (5)	✓	✓	✓	✗	✗	✓
Andersen *et al.*, 1982[42]	✓	482 (3)	✓	✗	✓	✗	✓	✗
Ewing *et al.*, 1964[43]	✗	30 (2)	✗	✗	✗	✗	✗	✓
Gray and Campbell, 1994[44]	✓	170 (2)	✗	✓	✓	✗	✓	✓
Collier, 1996[45]	✗	99 (9)	✗	✓	✗	✗	NA	✓
Gray and Smith, 2000[46]	✓	100 (2)	✗	✓	✓	✓	✓	✗
Kemp *et al.*, 1993[47]	✓	84 (2)	✗	✓	✓	✓	✗	✗
Vyhlidal *et al.*, 1997[48]	✓	40 (2)	✗	✗	✓	✗	✓	✓
Sideranko *et al.*, 1992[19]	✓	57 (3)	✗	✗	✓	✗	✗	✗
Takala *et al.*, 1996[21]	✓	40 (2)	✓	✗	✓	✗	✓	✓
Cooper *et al.*, 1998[22]	✓	100 (2)	✗	✓	✓	✗	✓	✓
Stapleton, 1986[28]	✓	100 (3)	✗	✗	✗	✗	✓	✗
Lazzara and Buschmann, 1991[49]	✓	74 (2)	✗	✓	✗	✗	✓	✗
Tymec *et al.* , 1997[50]	✓	52 (2)	✓	✗	✗	✗	✓	✓
Price *et al.*, 1999[26]	✓	80 (2)	✓	✓	✓	✗	✓	✗
Conine *et al.*, 1990[51]	✓	187 (2)	✗	✗	✓	✓	✓	✗
Daechsel and Conine, 1985[52]	✓	32 (2)	✗	✗	✓	✗	✗	✓
Whitney *et al.*, 1984[53]	✗	51 (2)	✗	✗	✗	✗	✗	✗

Continued

TABLE 5 contd *Quality of RCTs of pressure-sore prevention and treatment*

Trial	Clear inclusion and exclusion criteria	Sample-size total number (arms)	*A priori* sample-size calculation stated	True randomisation with allocation concealment described	Baseline comparability of treatment groups described	Blinded outcome assessment	Grade 1 sores excluded or presented separately	Main interventions well described
Gebhardt, 1994[54]	✓	230 (2)	✗	✗	✓	✗	✓	✓
Exton-Smith *et al.*, 1982[23]	✓	66 (2)	✗	✗	✓	✗	✓	✓
Hampton, 1997[55]	✗	75 (2)	✗	✗	✗	✗	✗	✓
Laurent, 1997[18]	✓	312 (4)	✓	✗	✓	✗	✓	✓
Inman *et al.*, 1993[17]	✓	100 (2)	✓	✗	✓	✗	✓	✗
Bennett *et al.*, 1998[56]	✓	98 (2)	✗	✗	✓	✗	✓	✗
Economides *et al.*, 1995[57]	✓	12 (2)	✗	✓	✓	✗	✓	✓
Gentilello *et al.*, 1998[16]	✓	65 (2)	✗	✓	✓	✗	✗	✓
Summer *et al.*, 1989[20]	✓	83 (2)	✗	✗	✓	✗	✗	✓
Nixon *et al.*, 1998[14]	✓	446 (2)	✓	✓	✓	✓	✓	✓
Aronovitch, 1998[13]	✓	217 (2)	✗	✗	✓	✓	✓	✓
Beckrich, 1998[15]	✓	198 (2)	✗	✗	✓	✗	✓	✓
Lim *et al.*, 1988[59]	✓	62 (2)	✗	✗	✓	✓	✓	✓
Conine *et al.*, 1994[60]	✓	163 (2)	Sequential trial	✗	✓	✓	✓	✓
Groen *et al.*, 1999[61]	✓	120 (2)	✓	✓	✓	✗	NA	✓
Allman *et al.*, 1987[62]	✓	65 (2)	✓	✓	✓	✓	✓	✓
Munro *et al.*, 1989[63]	✓	40 (2)	✗	✗	✗	✗	✓	✓
Strauss *et al.*, 1991[64]	✓	112 (2)	✗	✗	✓	✓	✓	✗
Ferrell *et al.*, 1993[65]	✓	84 (2)	✓	✓	✓	✗	✓	✓
Mulder *et al.*, 1994[66]	✓	49 (2)	✗	✗	✗	✗	NA	✓
Caley *et al.*, 1994[67]	✗	55 (2)	✗	✗	✗	✗	✗	✓
Devine, 1995[68]	✓	41 (2)	✗	✓	✓	✗	✓	✓

Continued

TABLE 5 contd *Quality of RCTs of pressure-sore prevention and treatment*

Trial	Clear inclusion and exclusion criteria	Sample-size total number (arms)	*A priori* sample-size calculation stated	True randomisation with allocation concealment described	Baseline comparability of treatment groups described	Blinded outcome assessment	Grade 1 sores excluded or presented separately	Main interventions well described
Evans *et al.*, 2000[69]	✓	32 (2)	✓ (not achieved)	✓	✓	✗	NA	✓
Russell *et al.*, 2000[70]	✓	112 (2)	✓	✓	✓	✗	✓	✓
Clark and Donald, 1999[71]	✗	25 (2)	✗	✗	✓	✗	NA	✓

✓, yes; ✗, no or not reported; NA, not applicable

Appendix 5

Comparisons undertaken in the included studies

***TABLE 6** Comparisons undertaken in pressure-sore prevention studies*

	AFL	AFI	AF	AP	B	DF	FC	GFS	KTT	LAL HT	LP	P	SS	SHM	SR	SC	TTO	Var. AP	Var. CLP	WF
AFL						45														
AFI				19, 26		22		37								21				
AF			34, 35, 36	28, 41										25, 27, 32, 33	28					49
AP				23, 43										30	28, 39, 40	13, 15				30, 19
B																24				
DF																				
FC							47, 48													
GFS																				
KTT																16, 20				
LAL HT																44				
LP												38								
P																				
SS																31				
SHM																				
SR																				
SC																	14			
TTO																				
Var. AP																			18, 42	
Var. CLP																				
WF																				

AF, alternative foam; AFI, air filled; AFL, air fluidised; AP, alternating pressure; B, beads; CLP, constant low pressure; DF, dry flotation; FC, foam cushion; GFS, gel-filled surface; KTT, kinetic turning table; LAL HT, low-air-loss hydrotherapy; LP, limb protector; P, pillow; SC, standard care; SHM, standard hospital mattress; SR, Silicore; SS, sheepskin; TTO, theatre table overlay; Var., various; WF, water filled

** Numbers in boxes refer to the reference number in the references section for each trial*

***TABLE 7** Comparisons undertaken in pressure-sore treatment studies*

	Air filled	Air fluidised	Alternative foam	AP	AP cushion	Dry flotation cushion	Low-air-loss bed	Low-air-loss overlay	Standard care	SHM
Air filled			54							
Air fluidised									50, 51, 52	
Alternative foam							53			
AP				56, 58					57	
AP cushion						59				
Dry flotation cushion										
Low-air-loss bed							17		55	
Low-air-loss overlay										
Standard care										
SHM										

AP, alternating pressure; CLP, constant low pressure; SHM, standard hospital mattress
** Numbers in boxes refer to the reference number in the references section for each trial*

Systematic reviews of wound care management (6): compression for the prevention and treatment of venous leg ulcers

N Cullum*
EA Nelson

Centre for Evidence Based Nursing, Department of Health Studies, University of York, UK

* Corresponding author

Competing interests: N Cullum has: received funds from the NHS R&D Programme to undertake primary research in wound care; received sponsorship of trial-related educational meetings from Huntleigh Healthcare and Beiersdorf Ltd. EA Nelson has: conducted one of the trials reviewed; been reimbursed for attending symposia by Smith and Nephew Ltd, ConvaTec and Huntleigh Healthcare

Contents to Part 6

List of abbreviations

ABPI	ankle/brachial pressure index
CCT	controlled clinical trial
CI	confidence interval
df	degrees of freedom
RCT	randomised controlled trial
RR	relative risk

Executive summary to Part 6

Background

Leg ulceration is a common, recurring condition which affects around three in every 2000 adults in the UK. Most people with leg ulcers are elderly women. There is a considerable cost to the patient in terms of pain, social isolation and quality of life. The health service provides nursing and medical care, as well as dressings, bandages and drug treatments. Most leg ulcers are associated with venous disease and this is treated by preventing venous hypertension through the application of external graduated compression.

There are many methods of applying external graduated compression, such as elasticated bandages, Unna's boots (non-compliant, plaster-type bandages), multilayer elastic compression bandages, short stretch bandages and elastomeric hosiery (stockings).

Objectives

To assess the clinical effectiveness and cost-effectiveness of compression bandaging and stockings in the prevention and treatment of venous leg ulcers. The research questions were:

- Does the application of compression bandages or stockings to legs at risk of venous ulceration prevent skin breakdown?
- If compression prevents recurrence, what is the optimal level of compression?
- Does the application of compression bandages or stockings aid the healing of venous ulcers?
- What is the optimum level of compression?
- Which compression bandage or stocking system is the most clinically effective for healing venous ulcers?
- Which system is the most cost-effective in healing venous ulcers?

Methods

Data sources

Searches were made of 19 databases (including MEDLINE, CINAHL, EMBASE and CENTRAL), and journals, conference proceedings and bibliographies were handsearched. Manufacturers of compression bandages and stockings and an advisory panel were contacted for unpublished studies. Searches were completed in December 1999.

Study selection

Randomised trials that evaluated compression bandaging or stockings, either for the prevention of or as a treatment for venous leg ulcers, were included in the review. There was no restriction on date or language. Ulcer incidence and healing were the primary endpoints. Prevention trials were only included if they provided data on ulcer incidence. Healing trials were only included if they provided objective data on the rate of ulcer healing or the number of ulcers healing in the trial period.

Data extraction and synthesis

Details of eligible studies were extracted and summarised using a data extraction sheet. Data extraction was verified independently by two reviewers.

Results

Twenty four trials reporting 26 comparisons were included in the review (two in ulcer prevention, 24 in ulcer treatment). High compression was more effective than moderate compression in preventing ulceration (one trial), and one trial found no difference in healing rates between two means of applying moderate compression.

Compression was more effective in healing ulcers than was no compression (4/6 trials). When multilayered systems were compared, elastic compression was more effective at healing ulcers than was non-elastic compression (five trials). There was no difference in healing rates between four-layer bandaging and other high-compression multilayered systems (three trials). There was no difference in healing rates between different elastomeric multilayered systems (four trials). Multilayered high-compression was more effective in healing ulcers than was single-layer compression (four trials). Compression stockings for healing were evaluated in two trials. One found a high-compression stocking plus a thrombostocking to be more effective than a short stretch bandage. A second small trial reported no difference in outcome between a compression stocking and Unna's boot.

There were insufficient data to draw conclusions about the relative cost-effectiveness of different regimens.

Conclusions

Prevention of recurrence of leg ulceration

There is evidence from one large trial that high-compression stockings are more effective at preventing recurrence of leg ulcers than are moderate-compression stockings.

Healing of ulcers

Compression increases ulcer healing rates compared with no compression. Multilayered systems are more effective than single-layered systems. High compression is more effective than low compression, but there are no clear differences in the effectiveness of different types of high compression (e.g. Unna's boot, compression hosiery, multilayer high-compression elastomeric regimens, short-stretch bandages).

Implications for research

Priority questions that have not been answered by the research published to date are:

- At what level of the ankle/brachial pressure index is it safe to apply compression?
- What is the most reliable method of identifying those venous leg ulcer patients with concurrent diabetes or rheumatoid arthritis who would benefit from compression?
- Which are the most effective multilayered high-compression regimens in terms of cost and quality of life?
- Which are the most effective non-elastomeric compression regimens in terms of cost and quality of life?
- What contribution can self-care and lay care make towards improving quality of life in patients with venous leg ulcers?
- What are the most effective ways of delivering compression to prevent recurrence of venous ulcers once healed (e.g. one high compression sock or stocking compared to two socks or stockings, each applying moderate compression)?
- What is an acceptable rate of adverse events for the widely used compression regimens?

Methodological issues that need to be addressed in future trials are:

- Trial numbers should be based on an *a priori* sample-size calculation so that clinically important differences can be detected as statistically significant.
- Patients receiving different interventions should be comparable at the start of the trial. This may require paired randomisation or stratified randomisation in order to ensure that factors which may influence healing are equally distributed between treatment groups.
- Assessment of outcomes should be blind to treatment.
- To ensure the inclusion of all clinical trials in systematic reviews, prospective registration of research studies should become mandatory.
- Contemporaneous economic evaluations should be conducted in future trials.
- A complete and thorough description of the method of application of compression and any concurrent treatments, including dressings, should be given in trial reports.
- Ulcer healing should be expressed as both a relative and an absolute change in area.
- For each patient, a single reference ulcer should be selected. Multiple ulcers on a patient should not be included in the analysis as individual ulcers are not independent unless specialised statistical analysis is performed to separate out the effects of the intervention (i.e. matched pairs analysis). Survival-rate analysis should be adopted for all studies that assess ulcer incidence or healing.

Chapter 1
Introduction

The prevalence of active leg ulceration in the UK has been estimated at 1.5/1000,[1,2] and a similar rate has been reported in Australia.[3] Prevalence increases with age, and is higher in women. Leg ulceration is typically a chronic recurring condition, with 45% of patients in a Scottish study reporting episodes of ulceration for more than 10 years.[1] There is a considerable cost both to the patient[4] and to the health service.[5] Most leg ulcers are associated with venous disease, and a history of a deep vein thrombosis is widely regarded as a predisposing factor to venous insufficiency and hence venous ulceration. However, the aetiology of leg ulceration remains poorly understood. Venous insufficiency has been shown to be associated with increased hydrostatic pressure in the veins of the leg, and it is in an attempt to reverse this and aid venous return that external compression, in various forms, is applied as a therapy for venous leg ulcers.

Various forms of bandaging have been applied over the years. In the seventeenth century, compression was applied as rigid lace-up stockings, while elasticated bandages were first produced in the middle of the nineteenth century.[6] At present there is wide variation in the management of venous leg ulcers. In the USA, Unna's boot (a non-compliant, plaster-type bandage) is favoured; in the UK, multilayer elastic compression is widely used; while in mainland Europe and Australia the inelastic, short stretch bandaging is common. This review summarises the evidence for the effectiveness of the different forms of compression bandaging and compression stockings for venous leg ulcers. Devices that apply intermittent or pulsed compression to the limb were specifically excluded from this review.

There are many ways of applying compression (e.g. a single layer of bandage, multiple layers of bandages, compression stockings, combinations of bandages and/or stockings). The interpretation of comparisons between compression systems is complicated by the lack of internationally agreed performance standards; for example, the classification systems for compression stockings are different in the UK and in mainland Europe. In the UK, performance indicators for bandages and compression stockings have been developed.[7]

Stockings are classified according to the amount of force required to extend them and hence the level of compression they can apply to a limb (*Table 1*).

Bandages are categorised as retention, support or compression, depending on their performance in standardised laboratory tests. Compression bandages are further subdivided according to the amount of force required to extend them, and therefore the level of compression which they can apply to a limb (*Table 2*). It is important to note that the laboratory performance or classification of a bandage may not reflect its performance in clinical use, as this is dependent on the technique of application and operator training.

Compression systems consisting of **combinations of compression layers** (stockings and/or bandages), sometimes incorporating an initial layer of paste bandage or orthopaedic wool, are commonly used. A number of these are listed in *Box 1*.

The use of compression to enhance venous return and aid the healing of venous ulcers is not without risk. The external application of very high pressures will reduce the blood supply to the skin and

***TABLE 1** Classification of compression hosiery in the UK*

Class	Support level	Compression exerted	Uses
1	Light	14–17 mmHg at the ankle	Treatment of varicose veins
2	Medium	18–24 mmHg at the ankle	Treatment of more severe varicosities; prevention of venous leg ulcers
3	Strong	25–35 mmHg at the ankle	Treatment of severe chronic hypertension and severe varicose veins; prevention of venous leg ulcers

***TABLE 2** Classification of bandages in the UK[6,7]*

Class	Descriptor	Function and level of compression
1	Retention	Used to retain dressings
2	Support	Used to support strains and sprains (e.g. crepe). Other bandages in this category can apply mild to moderate compression (e.g. Elastocrepe (Smith and Nephew), Comprilan (Beiersdorf)) when particular application techniques are used and the bandages are reapplied frequently
3a	Light compression	These bandages exert 14–17 mmHg compression at the ankle when applied in a simple spiral (e.g. Elset (SSL))
3b	Moderate compression	These bandages exert 18–24 mmHg compression at the ankle when applied as a simple spiral (e.g. Granuflex Adhesive Compression Bandage (ConvaTec))
3c	High compression	These bandages exert 25–35 mmHg compression at the ankle when applied as a simple spiral (e.g. Setopress (SSL), Tensopress (Smith and Nephew))
3d	Extra-high compression	These bandages exert up to 60 mmHg compression at the ankle when applied as a simple spiral (e.g. blue line webbing)

may lead to pressure damage. Similarly, the application of moderate pressures to patients with impaired blood supply to the legs may also result in pressure damage.

Patients' arterial blood supply must be assessed prior to the application of compression by palpating the pulses in the feet or, more accurately, by measuring the ankle/brachial pressure index (ABPI).

BOX 1 Combination compression systems

- **Short stretch/inelastic**: orthopaedic wool plus 1–3 rolls of short stretch bandage (e.g. Comprilan (Beiersdorf))
- **Inelastic paste system**: paste bandage plus support bandage (e.g. Elastocrepe (Smith and Nephew))
- **Unna's boot**: non-compliant paste bandage covered with a cohesive compression bandage
- **Three-layer elastic multilayer**: orthopaedic wool plus class 3c bandage (e.g. Tensopress (Smith and Nephew)) plus a shaped tubular bandage (e.g. Shaped Tubigrip (SSL))
- **Four-layer elastic multilayer**: orthopaedic wool plus support bandage (crepe) plus a class 3a bandage (e.g. Elset (SSL)) and a cohesive bandage (e.g. Coban (3M))

Aims

The aim was to undertake a systematic review of all reliable evaluations of the clinical effectiveness and cost-effectiveness of compression regimens in the prevention and treatment of venous leg ulceration.

Specific questions addressed by the review were:

- Does the application of compression bandages or stockings to legs at risk of venous ulceration prevent ulcer recurrence?
- If compression prevents the recurrence of venous ulcers, what is the optimum level of compression?
- Does the application of compression bandages or stockings aid the healing of venous ulcers?
- If compression aids the healing of venous ulcers, what is the optimum level of compression?
- Which compression bandage or stocking system is the most clinically effective for healing venous ulcers?
- Which compression bandage or stocking system is the most cost-effective in healing venous ulcers?

Chapter 2
Methods

Search strategy

The search strategy of the Cochrane Wounds Group was used to identify randomised controlled trials (RCTs) and controlled clinical trials (CCTs) of bandages or stockings in the treatment of venous leg ulcer trials (see appendix 1). This search strategy includes electronic searches of MEDLINE, CINAHL, EMBASE and CENTRAL (formerly the Cochrane Controlled Trials Register), as well as handsearches of conference proceedings and wound care journals.

Experts in wound care and pharmaceutical companies were contacted to enquire about unpublished, ongoing and recently published trials. Citations within obtained reviews and papers were scrutinised to identify additional studies. An advisory panel was established at the outset of this series of reviews (appendix 2). The panel assisted by helping to prioritise the questions to be answered, checking the lists of trials for any omissions, and informing us of unpublished, ongoing or recently completed trials.

Inclusion and exclusion criteria

Types of studies

Prospective RCTs and CCTs which employed quasi-random methods of allocation (e.g. day of the week, surname) and which evaluated compression bandaging or stockings in the treatment of venous ulceration were eligible for inclusion. Cohort studies reporting ulcer incidence, healing or adverse effects were not included.

Prevention trials were included if they reported ulcer incidence. Healing trials were included if they reported an objective measure of ulcer healing (e.g. healing, time to complete healing). Trials which only reported surrogate outcome measures or subjective assessments of improvement or deterioration were excluded. There was no restriction on articles on the basis of language or publication status.

Types of participants

People of any age with existing venous leg ulceration (which may also be described as ‘stasis’ or ‘varicose ulceration’) in any care setting, and patients identified as being at risk of developing venous ulceration. As the method of diagnosis of venous ulceration may vary between studies, no standardised definition was applied, but each study must refer to the use of compression for venous rather than other types of leg ulcers (e.g. arterial, mixed, vasculitic). People who have had a venous ulcer are at increased risk of developing a second ulcer, and therefore ‘history of ulceration’ was used as the indicator of being at risk.

Types of intervention

Trials which evaluated any form of bandage or compression stockings in patients at risk of or with existing venous leg ulcers were included. The types of bandage and compression stockings evaluated were:

- elastic bandages
- inelastic bandages
- short stretch bandages
- multilayer systems
- compression hosiery (i.e. stockings)
- single-layer bandage systems.

These groupings are not mutually exclusive, and comparisons are complicated by the lack of standard use of terminology and performance indicators.

Trials reporting the use of intermittent pneumatic compression were excluded from this review.

Types of outcome measure

Primary outcomes:

- ulcer incidence
- objective measures of healing (e.g. rate of change in ulcer area)
- time to complete healing
- proportion of ulcers healed within the trial period.

Secondary outcomes:

- costs
- compliance
- quality of life

- pain
- reliability
- acceptability.

Decisions on the inclusion of studies

References identified from searches were entered into a bibliographic software package (ProCite), and decisions regarding the inclusion or exclusion of studies were jointly made by two reviewers.

Data extraction

Details of eligible studies were extracted and summarised using a data extraction sheet. The following data were extracted:

- patient inclusion and exclusion criteria
- care setting
- key baseline variables by group (e.g. age, sex, baseline area of ulcers, duration of ulceration)
- description of the interventions and the numbers of patients randomised to each intervention
- descriptions of any co-interventions and standard care
- follow-up period
- outcomes (e.g. number of ulcers recurring, number of ulcers healed, reduction in ulcer area)
- acceptability of treatment.

Attempts were made to obtain data missing from reports by contacting the authors. Studies published in duplicate were included only once. Data extraction was verified by two reviewers independently. Any disagreement was resolved by discussion.

Methodological quality

Each study was individually critically appraised using a checklist to assess methodological quality using the following quality criteria:

- description of an *a priori* sample-size calculation
- evidence of allocation concealment at randomisation
- description of the baseline comparability of groups
- intention-to-treat analysis
- clear description of the method of application and the frequency of renewal of interventions
- description of blinded outcome assessment.

Data synthesis

For each trial, relative risks with 95% confidence intervals (CIs) were calculated for all important dichotomous outcomes. Relative risk (RR) is presented in preference to odds ratios as the latter give an inflated impression of the size of effect where event rates are high, as is the case in the trials included in this review.

Where two or more studies undertook similar comparisons using similar outcome measures, heterogeneity was assessed using the χ^2 test. Where clinical, methodological and statistical heterogeneity were not apparent, similar studies were pooled using a fixed-effects model. A random-effects model was applied where there was statistical heterogeneity in the absence of apparent clinical or methodological heterogeneity. Where pooling was not possible or appropriate, trials are discussed in a narrative fashion.

Chapter 3

Results

Studies included in the review

In total 24 trials (23 RCTs and one CCT) were included in this review, of which two were published only in conference proceedings.[8,9]

The number of patients in the included trials ranged from 10 to 300. All patients were described as having recently healed or open venous ulcers, but only four trials reported the criteria by which this diagnosis was made. Exclusion of arterial insufficiency by calculation of the ABPI using Doppler ultrasound was reported in 12 studies. The cut-off point for the application of compression was 0.8 in 10 of these studies, 0.7 and 0.9 in another two, and a toe systolic pressure below 60 mmHg in one.

The amount of pressure applied to a leg depends not only on the selection of an appropriate bandage or stocking, but also on the technique of bandage application or stocking fitting applied. Many trials did not describe the method of stocking fitting or bandage application sufficiently well to allow replication.

Two trials evaluated different strengths and brands of compression hosiery for the prevention of venous ulcer recurrence.[10,11]

Three trials compared the use of compression with the use of dressings alone.[12–14] Three other studies compared different forms of compression bandage (four-layer, short stretch and two-layer bandages, respectively) with treatments involving the use of non-compressive bandages.[15–17]

Three studies compared elastic high-compression three-layer bandaging with low compression.[18–20]

Two trials compared four-layer bandaging with single-layer compression bandaging.[8,21] Similar, but much smaller, studies compared four-layer or three-layer and self-adhesive single-layer bandages.[9,22]

Five small studies compared multilayer high-compression with inelastic compression. The comparisons were:

- orthopaedic wool plus a short stretch bandage versus a four-layer bandage[23]
- Unna's boot versus a four-layer bandage[24]
- a short stretch bandage versus gauze plus a long stretch bandage[25]
- orthopaedic wool plus a short stretch bandage plus a cohesive bandage versus a four-layer bandage.[26]

The original 'Charing Cross' four-layer bandage has been compared both with a kit (Profore (Smith and Nephew)) that provides all the constituents to make up a four-layer bandage[27] and with a regimen adapted to achieve similar levels of compression using materials available on prescription to community-based patients in the UK.[28] Another small study compared a four-layer bandage with a combination of three bandages plus class 2 compression stockings.[8]

A trial of only 30 patients compared Unna's boot with moderate compression provided by a single bandage (Coban).[29]

A combination of two compression stockings (thrombo plus Sigvaris 503) has been compared with a short stretch bandage.[30] Another study compared compression stockings with Unna's boot.[31]

Further details of the studies included in this review are given in appendix 3.

Studies excluded from the review

The studies excluded from the review and the reasons for their exclusion are summarised in *Table 3*. Trials that potentially fulfil the inclusion criteria and ongoing trials are given in *Table 4*.

Methodological quality of included studies

The quality of research in this area is generally poor. Trials were often too small, the follow-up period was short, ulcer recurrence was rarely considered and sometimes multiple ulcers were

TABLE 3 Summary of studies excluded from the review

Study	Reason for exclusion
Cameron and co-workers[32]	Historical control; non-randomised trial
Cherry[33]	Healing not measured as an outcome
Eriksson[34]	Essentially a comparison between dressings (paste or hydrocolloid)
Sabolinski and co-workers[35]	Both groups received compression; comparison was of dressings
Sironi and co-workers[36]	Insufficient details given
Walker and Faria[37]	Have abstract only; author did not reply to request for more information

incorrectly regarded as independent. Several papers did not report the method of bandage application, the experience of staff and other aspects of bandage use and patient mobility. The same system applied by different staff under different circumstances may result in the attainment of widely different pressures, thus making interpretation of results difficult.

The quality indicators of the included trials are summarised in appendix 4.

Presentation of results

Results of dichotomous variables are presented as relative risks with 95% CIs. The relative risk has been used rather than the odds ratio as event rates are high in the included trials and odds ratios would give an inflated impression of the magnitude of effect.[40] Relative risk is the ulcer healing rate in the experimental group divided by the ulcer healing rate in the control group, and indicates the likelihood of ulcer healing with an experimental bandage compared with a comparison bandage. As, by definition, the risk of an ulcer healing in the control group is 1, then the relative-risk reduction associated with using the experimental bandage is 1 – RR. The relative risk indicates the relative benefit of a therapy, but not the actual benefit (i.e. it does not take into account the number of people in whom the ulcer would have healed anyway). The absolute risk reduction can be calculated by subtracting the healing rate in the experimental group from the healing rate in the control group. The absolute risk reduction tells us how much the increase in healing is due to the bandage itself. The relative benefit increase is the proportional increase in the rate of a good event, such as healing, between experimental and control participants, expressed as a percentage. Thus a healing rate of 30% with a control bandage, increased to 50% with an experimental bandage, translates into an absolute risk reduction of 30–50 (= –20%; or a relative benefit increase of 20%).

The results are presented with reference to the original questions posed in the review.

Application of compression bandages or stockings to prevent breakdown of legs at risk of venous ulceration

No studies were identified that compared ulcer incidence in people with and without compression. The trial by Harper and co-workers,[10] however, suggests that there may be a dose response to compression, and this may be indirect evidence that compression reduces ulcer recurrence (*Figure 1* (for convienience, figures are grouped together at the end of the chapter)). However, 5-year follow-up data from this trial have still to be reported.

Optimum level of compression

One trial[10] (300 patients followed up for 3–5 years) compared ulcer recurrence rates in patients allocated to class 2 (18–25 mmHg pressure at ankle) or class 3 (25–35 mmHg pressure at the ankle). A lower recurrence rate was found in the high-compression group compared with the moderate compression group (32% versus 23%). Compliance was higher in the moderate-compression group, and there may be a trade-off between compression and compliance. The 5-year follow-up data from this trial are not yet available. Franks and co-workers[11] compared two brands of moderate strength stockings (class 2) and found no statistically significant difference in the ulcer recurrence rate (see *Figure 1*).

Application of compression bandages or stockings to aid venous ulcer healing

In total, six RCTs investigated this aspect (*Figure 2*). Three trials compared the use of compression

TABLE 4 *Trials that potentially fulfil the inclusion criteria and ongoing trials*

Study	Description
Trials that potentially fulfil the inclusion criteria	
Olofsson and co-workers[41]	A comparison of two regimens for treating venous leg ulcers: 1. in a specialist clinic with one bandage 2. in the usual setting with the usual bandage Awaiting further information from the authors to determine what 'usual care' was
Moody[42]	A comparison of short stretch and elastomeric bandages in the treatment of venous leg ulcers. There were insufficient data in the journal article to include the study in this review. The author has been contacted several times for additional information, but this has not been forthcoming
Freak and McCollum (unpublished, Manchester)	An RCT of four-layer versus short stretch bandages which was abandoned after approximately 48 patients had been enrolled. Further information about this trial is being sought from the investigators
Ongoing trials	
Burnand, St Thomas' Hospital, London	Comparison of four-layer and multilayered elastomeric bandaging using Setopress in treating venous leg ulcers. Recruitment has been completed, but no results have been reported to date
Cullum, University of York	VenUS bandaging trial (an HTA commissioned trial, coordinated from the University of York). Comparison of four-layer and short stretch bandaging in the treatment of venous leg ulcers in the community (400 patients, 12 months follow-up). Recruitment was started in 1999; results will be reported in early 2002

(provided by Unna's boot) with the use of dressings alone. Two of these found a statistically significantly higher proportion of healed ulcers when compression was used.[12,13] A third small study showed a non-statistically significant increase in healing with Unna's boot.[14]

Three other studies, which compared different forms of compression (four-layer, short stretch and two-layer bandages) with treatments using non-compressive bandages, showed that healing improved with compression.[15–17]

The results of these six trials were not pooled, as very different comparisons were presented. However, all the trials found greater healing with compression, although this difference was significant in only four of the six trials. Overall, there is reasonable evidence that venous ulcers heal more rapidly with compression than without.

What is the optimum level of compression?

As none of the studies measured the amount of pressure applied by the bandages or stockings in use, the dose–response relationship between compression and ulcer healing is unknown and there is no basis for recommending a particular level of pressure.

Clinical effectiveness of compression bandage and stocking systems

Elastic compression versus inelastic compression

Three RCTs compared elastic high-compression three-layer bandaging with multilayered low compression (*Figure 3*).[18–20] The results of these studies were pooled (χ^2 (test for heterogeneity) = 2.11; degrees of freedom (df) = 2) showing an overall statistically significant relative benefit increase for healing for the high-compression bandaging of 54% (95% CI, 19 to 99).

Multilayer high compression versus single-layer compression

Four RCTs were identified (*Figure 4*). Two RCTs showed four-layer bandaging to increase the percentage of ulcers healed at 24 and 12 weeks, compared with single-layer compression bandaging (Granuflex Adhesive Compression Bandage[21] and

Setopress[8]). Similar, but much smaller, studies found no difference in healing between four-layer or three-layer and self-adhesive single-layer bandages.[9,22] Pooling the studies using a random-effects model (χ^2 (test for heterogeneity) = 2.08; df = 2; $p < 0.1$) showed that the use of multilayer high-compression bandages instead of single-layer bandages results in an increase in healing of 41% (95% CI, 12 to 76).

Multilayer high compression versus inelastic compression

Four small RCTs found no difference in healing between multilayer high-compression (four-layer bandage or gauze plus long stretch bandage) and two forms of inelastic compression (Unna's boot[24] and short stretch bandage[25,26,41]). The relative benefit increase for healing in multilayer bandages was 10% (95% CI, –12 to 55; not statistically significant) (*Figure 5*).

Both four-layer and short stretch bandages resulted in higher healing rates than a paste bandage plus an outer support bandage (cotton crepe): 44%, 40% and 23% healed at 3 months, respectively[41] (*Figure 6*).

Original four-layer versus other multilayer high-compression systems

Three RCTs were identified[8,27,28] (*Figure 7*). The original 'Charing Cross' four-layer bandage has been compared both with a kit that provides all the constituents to make up a four-layer bandage[27] and a regimen adapted to achieve similar levels of compression.[28] No statistically significant difference in outcome was found in either study, although the latter trial was very small. Another small study found no difference in the numbers healed at 12 weeks between a four-layer bandage and those receiving a combination of three bandages plus class 2 compression stockings.[8] Pooling these studies using a fixed-effects model (χ^2 = 1.81; df = 2; $p > 0.1$) showed that there was no benefit of using the four-layer system rather than the alternatives (RR = 1.02; 95% CI, 0.87 to 1.18).

Inelastic compression versus single-layer compression

An RCT of only 30 patients, comparing Unna's boot with moderate compression provided by a single bandage (Coban), found no difference in healing at 12 weeks[29] (*Figure 8*).

Compression stockings versus compression bandaging

An RCT of 50 patients found that 84% of those receiving a combination of two compression stockings (thrombo plus Sigvaris 503) healed completely at 3 months compared with 52% in those receiving a short stretch bandage.[30] A small, poor-quality CCT found no difference between compression stockings and Unna's boot.[31] Pooling the results of these two trials using a fixed-effects model (χ^2 (test for heterogeneity) = 1.84; df = 1; $p = 0.17$) showed a relative increase in healing with stockings of 39% (95% CI, 0 to 92) (*Figure 9*). This just misses statistical significance as the 95% CI includes 0.

Cost-effectiveness of compression bandage and stocking systems

Only two trials included comparisons of costs.[8,42] These strongly suggest that compression systems, if applied in a consistent way, can improve the effectiveness of care (and may even reduce overall costs). However, these economic evaluations only consider four-layer bandages. The key question is not whether it is cost-effective to apply high compression, but rather what the cost-effectiveness is of different forms of high compression. To date, no trials or economic models have been reported that have examined the issue of relative cost-effectiveness between high-compression regimens. Therefore, the only evidence we have is the acquisition costs of high-compression regimens, and until better evidence is produced the most cost-effective is the least expensive.

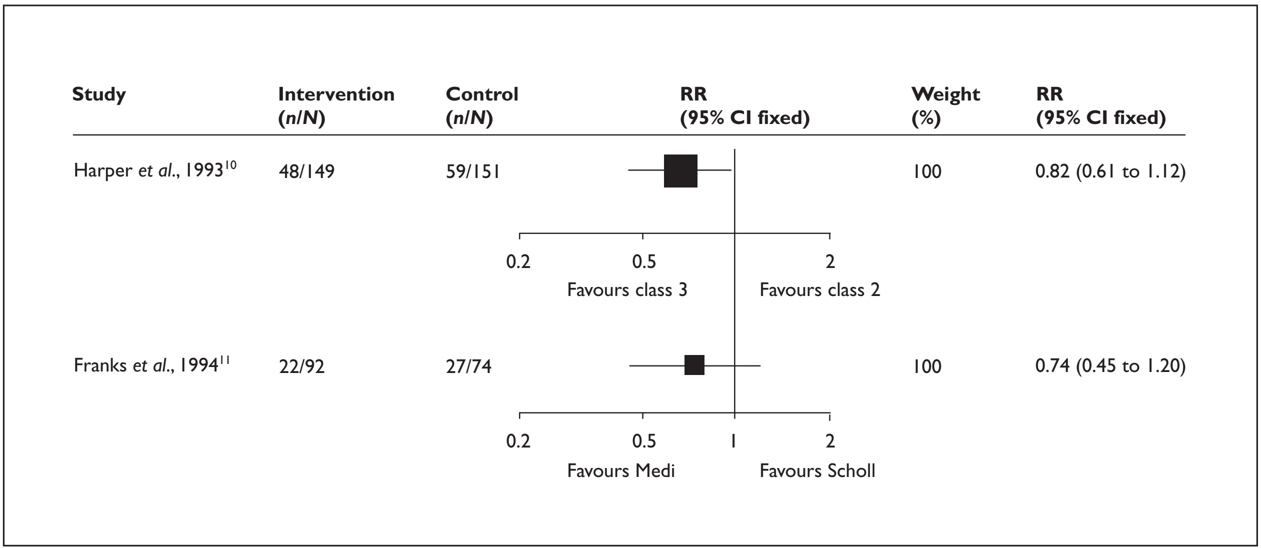

FIGURE 1 *A comparison of the effect of different types of compression hosiery on the recurrence of venous ulcers*

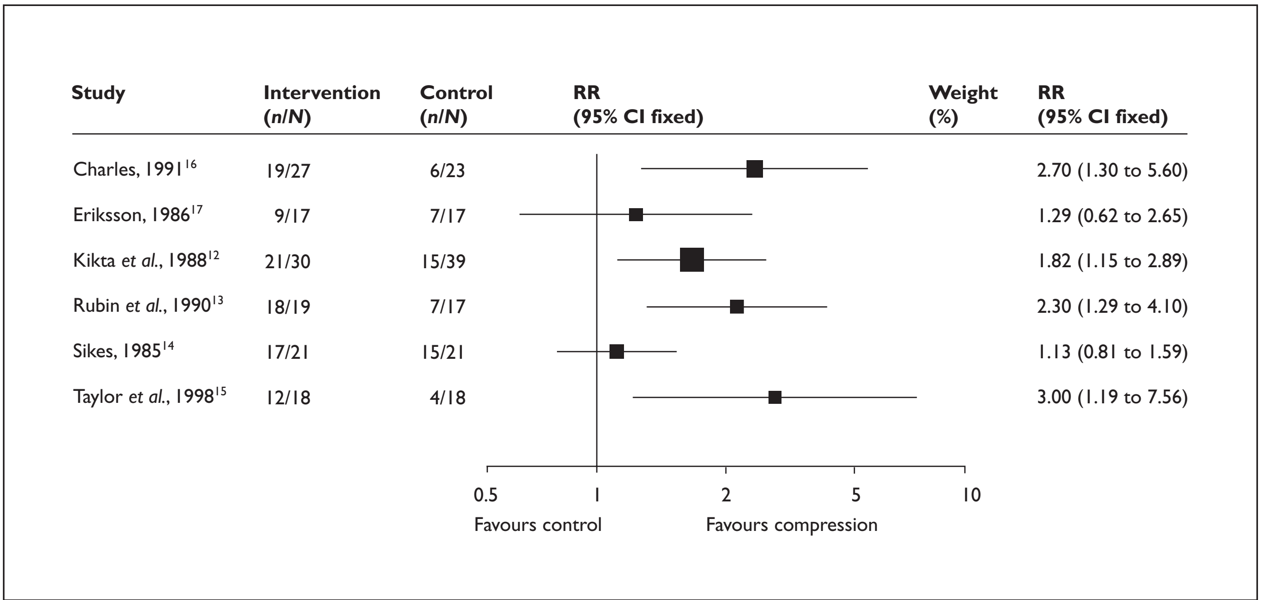

FIGURE 2 *A comparison of the effect of compression and no compression on the healing of venous ulcers*

Study	Intervention (*n*/*N*)	Control (*n*/*N*)	RR (95% CI fixed)	Weight (%)	RR (95% CI fixed)
Callam *et al.*, 1992[19]	35/65	19/67		36.7	1.90 (1.22 to 2.95)
Gould *et al.*, 1993[18]	11/20	7/20		13.7	1.57 (0.77 to 3.22)
Northeast *et al.*, 1990[20]	31/49	26/52		49.5	1.27 (0.90 to 1.79)
Total (95% CI) $\chi^2 = 2.11$ (df = 2, $p = 0.35$); $Z = 3.28$ ($p = 0.0010$)	77/134	52/139		100.0	1.54 (1.19 to 1.99)

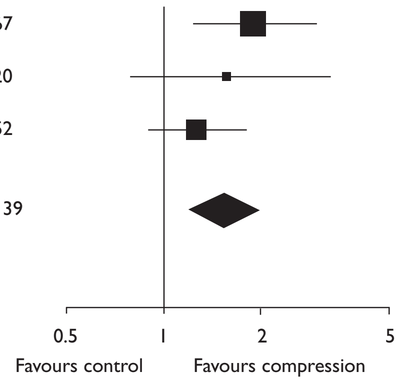

FIGURE 3 *A comparison of the effect of elastic high compression and multilayer inelastic compression on the healing of venous ulcers*

Study	Intervention (*n*/*N*)	Control (*n*/*N*)	RR (95% CI fixed)	Weight (%)	RR (95% CI fixed)
Colgan *et al.*, 1996[8]	6/10	2/10		3.4	3.00 (0.79 to 11.44)
Kralj *et al.*, 1996[9]	7/16	8/18		12.9	0.98 (0.46 to 2.10)
Nelson *et al.*, 1995[21]	69/100	49/100		83.7	1.41 (1.11 to 1.79)
Travers *et al.*, 1992[22]	0/13	0/13		0.0	Not estimable
Total (95% CI) $\chi^2 = 2.08$ (df = 2, $p = 0.35$); $Z = 2.96$ ($p = 0.003$)	82/139	59/141		100.0	1.41 (1.12 to 1.77)

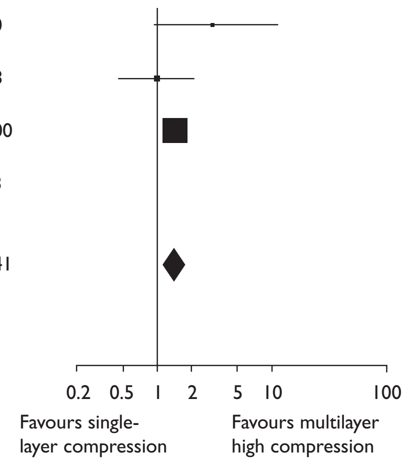

FIGURE 4 *A comparison of the effect of multilayer high compression and single-layer compression on the number of venous ulcers healed*

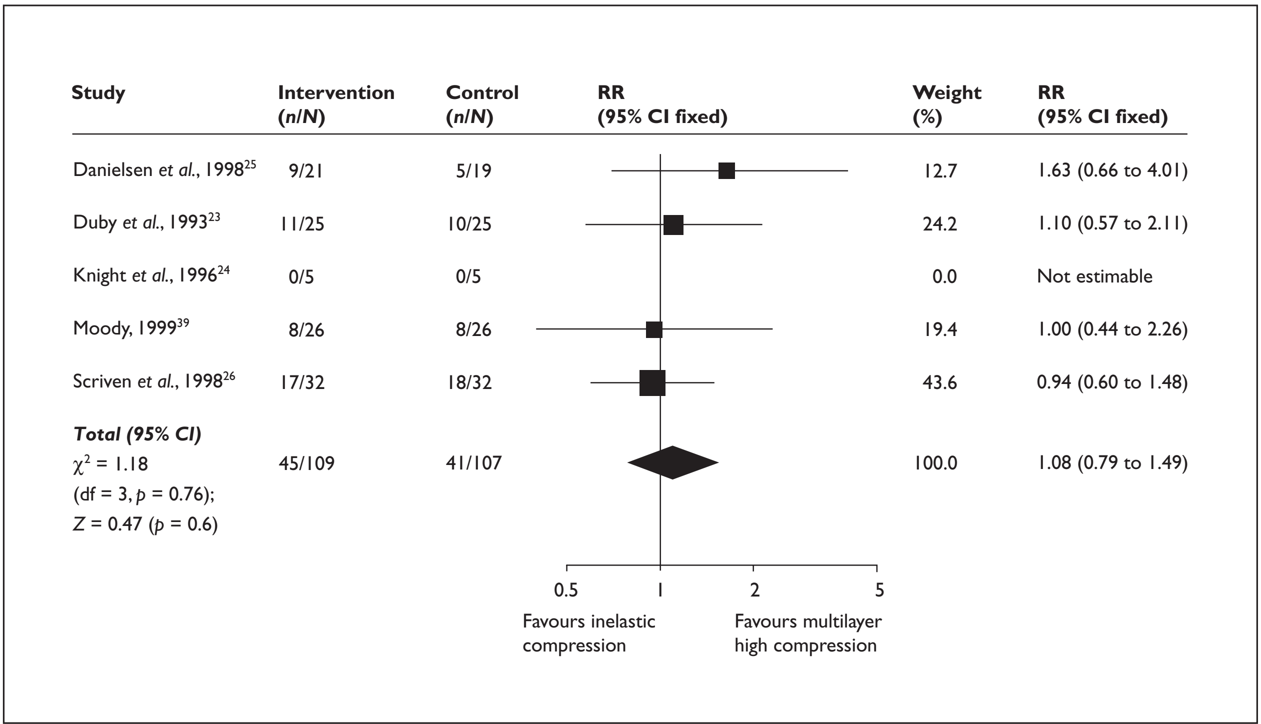

FIGURE 5 *A comparison of the effect of multilayer high compression and inelastic compression on the number of venous ulcers healed*

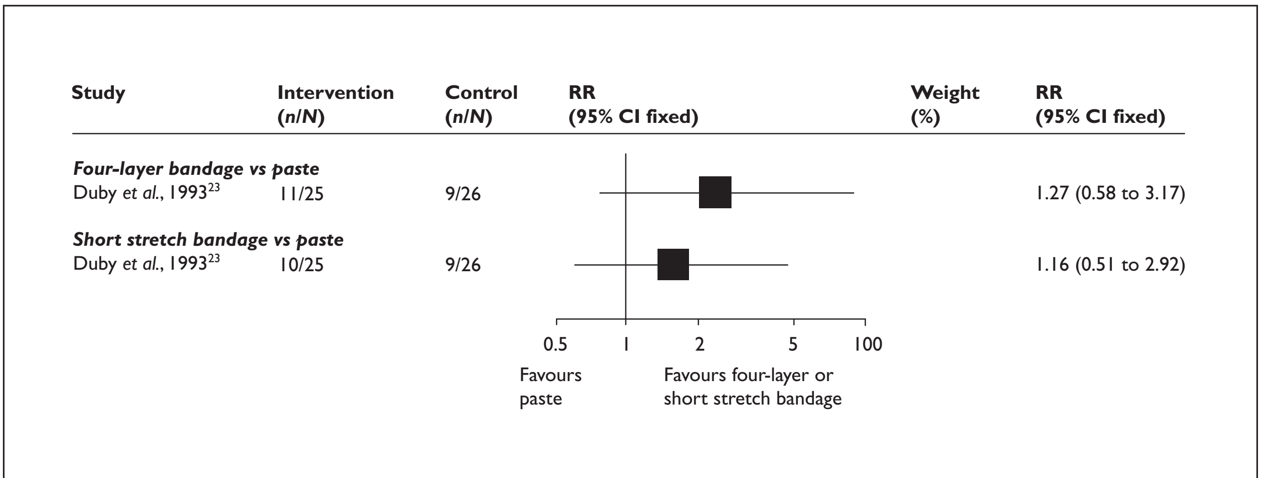

FIGURE 6 *A comparison of the effect of four-layer or short stretch bandage and paste on the number of venous ulcers healed*

Study	Intervention (n/N)	Control (n/N)	RR (95% CI fixed)	Weight (%)	RR (95% CI fixed)
Colgan *et al.*, 1996[8]	7/10	6/10		6.1	1.17 (0.61 to 2.23)
McCollum *et al.*, 1997[27]	82/115	85/115		86.9	0.96 (0.82 to 1.13)
Wilkinson *et al.*, 1997[28]	10/17	7/18		7.0	1.51 (0.75 to 3.05)
Total (95% CI) $\chi^2 = 1.81$ (df = 2, $p = 0.4$); $Z = 0.19$ ($p = 0.8$)	138/215	144/214		100.0	1.02 (0.87 to 1.18)

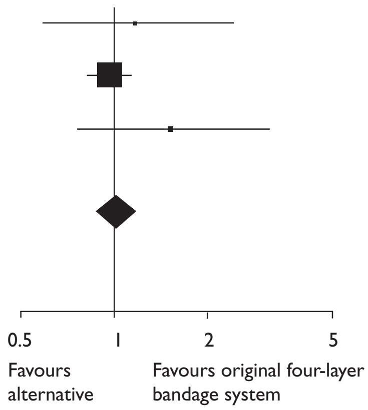

***FIGURE 7** A comparison of the effect of four-layer and other multilayer high compression bandages on the number of venous ulcers healed*

Study	Intervention (n/N)	Control (n/N)	RR (95% CI fixed)	Weight (%)	RR (95% CI fixed)
Cordts *et al.*, 1992[29]	8/16	6/14		100	1.17 (0.54 to 2.54)

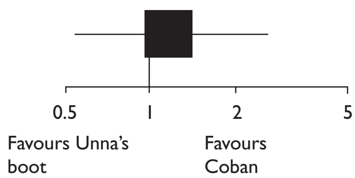

***FIGURE 8** A comparison of the effect of the Coban bandage and Unna's boot on the number of venous ulcers healed*

Study	Intervention (*n*/*N*)	Control (*n*/*N*)	Weight (%)	RR (95% CI fixed)
Hendricks and Swallow, 1985[31]	10/14	7/10	0.0	1.02 (0.60 to 1.72)
Partsch and Horakova, 1994[30]	21/25	13/25	0.0	1.62 (1.07 to 2.44)
Total (95% CI) χ^2 = 1.84 (df = 1, p = 0.17); Z = 1.97			100.0	1.39 (1.00 to 1.92)

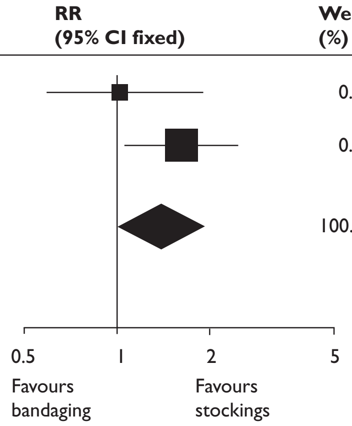

FIGURE 9 *A comparison of the effect of compression stockings and compression bandaging on the number of venous ulcers healed*

Chapter 4

Discussion

There is currently considerable variation in the proportion of patients with venous ulceration who receive compression therapy in the form of bandaging or stockings and the type of compression they receive.

In the UK and the USA, compression is normally applied by nurses. There is some evidence that nurses do not know which bandage to choose for a particular clinical application,[43] and that inexperienced nurses or those without additional training in compression bandaging apply bandages at inappropriate and widely varying pressures.[44,45] There is poor reporting of adverse effects of compression. Callam and co-workers[46] have reported the results of a survey of Scottish doctors, indicating that inappropriate or inexpert application of compression regimens can lead to pressure damage, which in extreme cases resulted in amputation.

The results of the review suggest that venous ulcer healing is increased when compression is applied as bandages or stockings. High compression delivered in layers (usually three or four) performs better than systems giving low compression and single-layer compression. The few small studies that have compared different high-compression systems (e.g. multilayer and short stretch bandages and Unna's boot) have shown no difference in effectiveness. Compression stockings were more effective than short stretch compression bandaging in one trial and this may be related to the skill required to apply bandages properly, and the need for all short stretch bandages to be reapplied frequently.

A number of key comparisons have not yet been addressed in trials. The comparisons that have been reported are given in *Table 5*. Important omissions include:

- comparisons between different forms of non-elastomeric compression (e.g. Unna's boot versus short-stretch bandages)
- comparisons between different forms of multi-layered, elastomeric, high-compression regimens (e.g. four-layer high compression versus three-layer high compression)
- comparisons between high compression (class 3), moderate compression (class 2) and layered compression hosiery (class 1 and class 2, or two class 2 stockings worn at the same time) on patient compliance with hosiery use and on the incidence of venous ulcer recurrence.

Furthermore, the majority of trials did not undertake prospective cost-effectiveness evaluations or assess the impact of the compression on patients' quality of life.

No trials have examined the contribution of professional application of bandages compared with lay or self-application. In some countries and healthcare systems, lay care forms a significant contribution to leg ulcer care, and this may influence patients' healing (e.g. if compression is not applied sufficiently firmly to aid healing or if it is applied too tightly). Furthermore, it may affect the experience of having an ulcer if the patient or a carer is able to apply or reapply the compression bandage or hosiery as required, to fit in with the patient's lifestyle.

TABLE 5 *Summary of RCTs of compression regimens for treating venous leg ulcers*[*]

	Multilayer elastic compression (high pressure)[†]	Non-elastomeric compression[‡]	Single layer, elastic	Low compression, layered
No compression	15, 17	12, 13, 14, 16	No trials	No trials
Multilayer elastic compression (high pressure)	8, 27, 28	24–26, 41	8, 9, 21, 22	18, 19, 20, 41
Non-elastomeric compression	24–26, 41	No trials	29, 30, 31	41

[*] *Numbers refer to the reference which relates to that trial*
[†] *For example, elastic bandage and hosiery, four-layer bandages, paste and high-compression bandage*
[‡] *For example, Unna's boot, short stretch bandages*

The majority of trials have used a hand-held Doppler to measure the ABPI and only included patients with an ABPI of at least 0.7. In addition, studies usually excluded patients with concurrent diseases that may compromise peripheral arterial circulation, such as diabetes and rheumatoid arthritis. The application of compression to a venous leg ulcer in a patient with minimally compromised arterial circulation, represented by an ABPI reading of around 0.8, appears to be beneficial (this is a tentative conclusion because of the poor reporting of adverse events in trials and cohort studies). The balance between harm and benefit, depending on the degree of arterial impairment, needs to be determined as it may be different for the various types of compression regimen.

Chapter 5

Conclusions

Implications for practice

High compression is more effective than moderate compression in the prevention of ulcer recurrence. Compliance is lower with high-compression stockings, and patients should be prescribed the firmest class stocking that they will wear.

Compression treatment increases the healing of ulcers compared with no compression. High compression is more effective than low compression, but should only be used in the absence of significant arterial disease. It is not clear which of the high-compression systems (three-layer, four-layer, short stretch, high-compression hosiery, Unna's boot) is the most cost-effective.

Implications for research

Much of the research concerning ulcer treatment is of poor quality. In the trials reviewed, sample sizes were rarely sufficient to detect clinically important effects, and poor baseline comparability of the groups introduced bias. In addition, our poor understanding of the biological processes involved in healing may influence the ability of a study to detect significant differences in healing rates. Several important messages can be identified for future studies.

Recruitment numbers should be based on an *a priori* sample-size calculation. In most trials the sample size was too small to find a statistically significant difference between treatment groups. In order to recruit sufficient patient numbers, multicentre trials should be considered. These large trials have been undertaken in other areas of healthcare, and although the field of wound care presents its own difficulties, there is no reason why such trials should not be performed. If these trials are to be commissioned they will require a strong infrastructure for providing support and promoting collaboration.

Methodological recommendations

- A truly objective outcome measure should be used, or wound healing should be expressed as both percentage and absolute change in area.
- Unwanted effects of compression (e.g. pressure damage, sensitivity to the components of the fabrics used, the impact of compression on the patient's ability to wear their usual footwear) should be fully reported.
- For each patient a single reference ulcer should be selected. Multiple ulcers on a patient should not be included in the analysis, since individual ulcers are not independent unless specialised statistical analysis is performed to separate out the effects of the intervention (i.e. 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 baseline characteristics, and then the individuals of each pair should be randomised to treatment. Such randomisation is particularly important if ulcers of mixed aetiology are to be assessed in the same trial.
- Head-to-head comparisons are required and should use interventions that are recommended for similar patients and ulcers (e.g. ambulant patients, moderately exuding ulcers).
- A complete and thorough description of concurrent treatments, including primary and secondary dressings, should be given in trial reports.
- Assessment of outcomes should, where possible, be blind to treatment.
- Survival-rate analysis should be adopted for all studies that assess ulcer healing.
- Studies to determine the biological mechanism involved in ulcer healing are needed. A better understanding of the healing process will lead to the development of validated outcome measures.
- To prevent publication bias and ensure the inclusion of unpublished trials in systematic reviews, prospective registration of research

studies should become mandatory. Those involved in primary research should also make their data available to those undertaking systematic reviews, particularly in those trials where participants have given their written consent on the understanding that their involvement will add to medical knowledge.

- Contemporaneous economic evaluations should be conducted in future trials.

Priority research questions

- At what level of ABPI is it safe to apply compression?
- What is the most reliable method of identifying venous leg ulcer patients with concurrent diabetes or rheumatoid arthritis who would benefit from compression?
- What are the most effective multilayer high-compression regimens with respect to cost-effectiveness and quality of life?
- What are the most effective non-elastomeric compression regimens with respect to cost-effectiveness and quality of life?
- What contribution can self-care or lay care make towards improving the quality of life in patients with venous leg ulcers?
- What are the most effective ways of delivering compression to prevent recurrence of venous ulcers once healed (e.g. one high-compression sock or stocking compared with two socks or stockings, each applying moderate compression)?
- What is an acceptable rate of adverse events for the widely used compression regimens?

Acknowledgements

This study was commissioned by the NHS R&D HTA programme. The authors are indebted to the HTA referees for their perseverance in reading this report and the quality of their comments. The views expressed in this report are those of the authors, who are responsible for any errors.

We are extremely grateful to Professor Trevor Sheldon of the University of York for his guidance and good humour throughout this review. Dr Alison Fletcher contributed to this review by searching, data extraction and checking, and project management. Sally Bell-Syer contributed to this review by searching, data extraction and checking and database management. Roz Thompson contributed to the review by managing the citation database, expeditious document acquisition and administrative support.

The assistance of the Information Staff, notably Julie Glanville, of the NHS Centre for Reviews and Dissemination, University of York, is gratefully acknowledged.

We are extremely grateful to the members of the advisory panel (appendix 2) who gave generously of their time and expertise. Andrew Herxheimer, Gillian Leng, Stephen Blair and Charles McCollum also provided useful feedback. We would also like to thank Georg Waernhjelm, who kindly translated a Swedish paper for us.

A less detailed version of this review has previously appeared in print.[47] It was also published as an Effective Health Care Bulletin and a Cochrane Review.[48] The latter two publications included reviews of assessment, intermittent pneumatic compression, organisation of care and prevention of ulcer recurrence. This review will be maintained (updated in the light of users' comments and new trial data) in the Cochrane Library.

References

1. Callam MJ, Ruckley CV, Harper DR, Dale JJ. Chronic ulceration of the leg: extent of the problem and provision of care. *Br Med J* 1985; **290**:1855–6.

2. Lees TA, Lambert D. Prevalence of lower limb ulceration in an urban health district. *Br J Surg* 1992;**79**(Pt 10):1032–4.

3. Baker SR, Stacey MC, Jopp-McKay AG, Hoskin SE, Thompson PJ. Epidemiology of chronic venous ulcers. *Br J Surg* 1991;**78**:864–7.

4. Charles H. The impact of leg ulcers on patients' quality of life. *Professional Nurse* 1995;**10**:571–4.

5. Bosanquet N. Costs of venous ulcers: from maintenance therapy to investment programmes. *Phlebology* 1992;(Suppl 1):44–6.

6. Thomas S. Compression bandages. In: Cullum N, Roe BH, editors. Leg ulcers: nursing management. Harrow: Scutari; 1995.

7. British Standards Institution. British Standard 7505: elastic properties of extensible bandages. Milton Keynes: BSI, 1995.

8. Colgan MP, Teevan M, McBride C, O'Sullivan L, Moore D, Shanik G. Cost comparisons in the management of venous ulceration. In: Proceedings of the 5th European Conference on Advances in Wound Management. London: Macmillan Magazines; 1996. p. 103.

9. Kralj B, Kosicek M. A randomised comparative trial of single-layer and multi-layer bandages in the treatment of venous leg ulcers. In: Leaper DJ, Cherry GW, Dealey C, Lawrence JC, Turner TD, editors. Proceedings of the 6th European Conference on Advances in Wound Management. London: Macmillan Magazines; 1996. p. 158–60.

10. Harper DR, Nelson EA, Gibson B, Brown D, Ruckley CV. A prospective, controlled, randomized trial of class 2 and class 3 elastic compression in the prevention of venous ulceration. In: Cherry GW, Gottrup F, Lawrence JC, Moffatt CJ, Turner TD, editors. Proceedings of the 5th European Conference on Advances in Wound Management. London: Macmillan Magazines; 1996. p. 55.

11. Franks PJ, Oldroyd MI, Dickson D, Sharp EJ, Moffatt CJ. Risk factors for leg ulcer recurrence: a randomized trial of two types of compression stocking. *Age Ageing* 1995;**24**(Pt 6):490–4.

12. Kikta MJ, Schuler JJ, Meyer JP, *et al.* A prospective, randomized trial of Unna's boots versus hydroactive dressing in the treatment of venous stasis ulcers. *J Vasc Surg* 1988;**7**:478–83.

13. Rubin JR, Alexander J, Plecha EJ, Marman C. Unna's boot vs polyurethane foam dressings for the treatment of venous ulceration. A randomized prospective study. *Arch Surg* 1990;**125**(Pt 4):489–90.

14. Sikes E. Evaluation of a transparent dressing in the treatment of stasis ulcers of the lower limb. *J Enterostomal Ther* 1985;**12**(Pt 4):116–20.

15. Taylor AD, Taylor RJ, Marcuson RW. Prospective comparison of healing rates and therapy costs for conventional and four layer high compression bandaging treatments of venous leg ulcers. *Phlebology* 1998;**13**:20–4.

16. Charles H. Compression healing of ulcers. *J District Nurs* 1991;**4**:6–7.

17. Eriksson G. Comparison of two occlusive bandages in the treatment of venous leg ulcers. *Br J Dermatol* 1986;**114**:227–30.

18. Gould DJ, Campbell S, Harding EF. Short stretch vs. long stretch bandages in the management of chronic venous leg ulcers. *Phlebology* 1993;**8**:43.

19. Callam MJ, Harper DR, Dale JJ, *et al.* Lothian and Forth Valley leg ulcer healing trial. Part 1: elastic versus non-elastic bandaging in the treatment of chronic leg ulceration. *Phlebology* 1992;**7**(Pt 4): 136–41.

20. Northeast ADR, Layer GT, Wilson NM, Browse NL, Burnand KG. Increased compression expedites venous ulcer healing. *R Soc Med Venous Forum* 1990.

21. Nelson EA, Harper DR, Ruckley CV, Prescott RJ, Gibson B, Dale JJ. A randomised trial of single layer and multi-layer bandages in the treatment of chronic venous ulceration. *Phlebology* 1995;(Suppl 1): 915–16.

22. Travers JP, Dalziel KL, Makin GS. Assessment of a new one-layer adhesive bandaging method in maintaining prolonged limb compression and effects on venous ulcer healing. *Phlebology* 1992; **7**(Pt 2):59–63.

23. Duby T, Cherry G, Hoffman D, Cameron J, Dobloff-Brown D, Ryan T. A randomized trial in the treatment of venous leg ulcers comparing short stretch bandages, four layer bandage system, and a

long stretch-paste bandage system. *Wounds Compendium Clin Res Pract* 1993;**5**(Pt 6):276–9.

24. Knight CA, McCulloch J. A comparative study between two compression systems in the treatment of venous insufficiency in leg ulcers. In: Proceedings of the Symposium on Advanced Wound Care and Medical Research Forum on Wound Repair; 1996; Wayne, PN. p. 117.

25. Danielsen L, Madsen SM, Henriksen L. Venous leg ulcer healing: a randomized prospective study of long-stretch versus short-stretch compression bandages. *Phlebology* 1998;**13**:59–63.

26. Scriven JM, Taylor LE, Wood AJ, Bell PR, Naylor AR, London NJ. A prospective randomised trial of four-layer versus short stretch compression bandages for the treatment of venous leg ulcers. *Ann R Coll Surg Engl* 1998;**80**(Pt 3):215–20.

27. McCollum CN, Ellison DA, Groarke L, *et al.* Randomised trial comparing Profore and the original four layer bandage. In: Proceedings of the Conference of the European Wound Management Association. London: Macmillan; 1997. p. 8.

28. Wilkinson E, Buttfield S, Cooper S, Young E. Trial of two bandaging systems for chronic venous leg ulcers. *J Wound Care* 1997;**6**(Pt 7):339–40.

29. Cordts PR, Hanrahan LM, Rodriguez AA, Woodson J, LaMorte WW, Menzoian JO. A prospective, randomized trial of Unna's boot versus Duoderm CGF hydroactive dressing plus compression in the management of venous leg ulcers. *J Vasc Surg* 1992;**15**(Pt 3):480–6.

30. Partsch H, Horakova MA. Compression stockings for the treatment of venous leg ulcers. *Wien Med Wochenschr* 1994;**144**(Pt 10–11):242–9.

31. Hendricks WM, Swallow RT. Management of stasis leg ulcers with Unna's boots versus elastic support stockings. *J Am Acad Dermatol* 1985;**12**(Pt 1):90–8.

32. Cameron J, Hofman D, Poore S, Duby T, Cherry G, Ryan T. A comparative study of two bandage systems. In: Proceedings of the 3rd European Conference on Advances in Wound Management. London: Macmillan; 1994. p. 168.

33. Cherry G. Clinical comparison of a new compression bandage. *Nursing Stand* 1990;**8**(Suppl):8–11.

34. Eriksson G. Comparison of two occlusive bandages in the treatment of venous leg ulcers. *Br J Dermatol* 1986;**114**:227–30.

35. Sabolinski M, Borchard G, Mulder G. Cost benefit analysis of living skin equivalent versus graduated, multi-layered compression therapy for the treatment of venous skin ulcers. *Diabetes* 1995; **44**(Suppl 1):107.

36. Sironi G, Losa S, DiLuca G, Pezzoni F. Treatment of venous leg ulcers with Intrasite gel, Opsite Flexigrid, Allevyn hydrocellular dressing and Flexobande (elastic compression bandage) in vascular surgery. A protocol for clinical evaluations. In: Proceedings of the 3rd European Conference on Advances in Wound Management. London: Macmillan Magazines; 1994. p. 164.

37. Walker P, Faria DT. Evaluation of a three layer bandage system versus a four layer bandage system in venous leg ulcers. In: Symposium on Advanced Wound Care and Medical Research Forum on Wound Repair. Wayne: Health Management Publications; 1996. p. 121.

38. Olofsson B, Ljunghall K, Nordin-Bjorklund K, Sorensen S, Leppert J. [Two therapeutic models in venous leg ulcers are compared: better results with optimized compression.] *Lakartidningen* 1996;**93**(Pt 51–52):4752–4.

39. Moody M. Comparison of Rosidal K and Surepress in the treatment of venous leg ulcers. *Br J Nurs* 1999;**6**:345–55.

40. Deeks J. Odds ratios should be used only in case control studies and logistic regression analyses. *BrMed J* 1998;**317**:1155–6.

41. Duby T, Hofman D, Cameron J, Dobloff Brown D, Cherry G, Ryan T. A randomized trial in the treatment of venous leg ulcers comparing short stretch bandages, four layer bandage system, and a long stretch-paste bandage system. *Wounds Compendium Clin Res Pract* 1993;**5**(Pt 6):276–9.

42. Taylor A. A prospective study to compare healing rates and associated treatment costs for current management of venous leg ulcers in the community and a four-layer compression bandage regime. In: Proceedings of the 4th European Conference on Advances in Wound Management. London: Macmillan Magazines; 1995. p. 199–200.

43. Magazinovic N, Phillips-Turner J, Wilson GV. Assessing nurses' knowledge of bandages and bandaging. *J Wound Care* 1993;**2**(Pt 2):97–101.

44. Logan RA, Thomas S, Harding EF. A comparison of sub-bandage pressures produced by experienced and inexperienced bandagers. *J Wound Care* 1992; **1**(Pt 2):23–6.

45. Stockport JC, Groarke L, Ellison DA, McCollum C. Single-layer and multilayer bandaging in the treatment of venous leg ulcers. *J Wound Care* 1997; **6**(Pt 10):485–8.

46. Callam MJ, Harper DR, Dale JJ, Ruckley CV. Arterial disease in chronic leg ulceration: an underestimated hazard? Lothian and Forth Valley leg ulcer study. *Br Med J* 1987;**294**:929–31.

47. Fletcher A, Cullum N, Sheldon TA. A systematic review of compression treatment for venous leg ulcers. *Br Med J* 1997;**315**:576–80.

48. Cullum N, Nelson EA, Fletcher A, Sheldon TA. Compression therapy for venous leg ulcers. Oxford. Update Software. Cochrane Library. 2000(1).

Appendix 1

Databases searched and search strategies

MEDLINE

MEDLINE was searched for RCTs for the period 1966 to December 1999 using a mixture of free text terms and the following MeSH headings:

WOUND INFECTION
PILONIDAL CYST
WOUNDS AND INJURIES
WOUND HEALING
LEG ULCER
VARICOSE ULCER
SKIN ULCER
DECUBITUS

The MEDLINE search strategy used was as follows:

1. decubitus ulcer/ or foot ulcer/
2. leg ulcer/ or varicose ulcer/
3. pilonidal cyst/
4. skin ulcer/
5. diabetic foot/
6. ((plantar or diabetic or heel or venous or stasis or arterial) adj ulcer$).tw.
7. ((decubitus or foot or diabetic or ischaemic or pressure) adj ulcer$).tw.
8. ((pressure or bed) adj sore$).tw.
9. ((pilonidal adj cyst) or (pilonidal adj sinus) or bedsore$).tw.
10. ((diabetic adj foot) or (cavity adj wound)).tw.
11. ((varicose or leg or skin) adj ulcer$).tw.
12. (decubitus or (chronic adj wound$)).tw.
13. ((sinus adj wound$) or (cavity adj wound$)).tw.
14. or/1–13
15. debridement/ or biological dressings/ or bandages/
16. occlusive dressings/ or clothing/ or wound healing/
17. antibiotics/ or growth substances/ or platelet-derived growth factor/
18. fibroblast growth factor/ or electrical stimulation therapy.ti,ab,sh.
19. lasers/ or nutrition/ or surgery/ or surgery, plastic/
20. surgical flaps/ or skin transplantations/ or homeopathy/ or homeopathic/
21. acupuncture therapy/ or acupuncture/ or alternative medicine/
22. alternative medicine/ or massage/ or iloprost/ or alginates/
23. zinc/ or zinc oxide/ or ointments/ or anti-infective agents/
24. dermatologic agents/ or colloids/ or cushions/ or wheelchairs/
25. beds/ or wound dressings/
26. (debridement or dressing$ or compress$ or cream$ or (growth adj factor$)).tw.
27. (pressure-relie$ or (recombinant adj protein$) or bandag$ or stocking$).tw.
28. (antibiotic$ or (electric adj therapy) or laser$ or nutrition$ or surg$).tw.
29. (homeopath$ or acupuncture or massage or reflexology or ultrasound).tw.
30. (iloprost or alginate$ or zinc or paste$ or ointment$ or hydrocolloid$).tw.
31. ((compression adj therapy) or (compression adj bandag$) or wrap$).tw.
32. (bed$ or mattress$ or wheelchair$ or (wheel adj chair) or cushion$).tw.
33. ((wound adj dressing$) or vitamin$ or bind$ or gauze$ or heals or healing).tw.
34. (diet or lotion$ or infect$ or reduc$ or (wound adj healing)).tw.
35. (treat$ or prevent$ or epidemiol$ or aetiol$ or etiol$ or therap$ or prevalence or incidence).tw.
36. or/15–35
37. 14 and 36
38. random allocation/ or randomized controlled trials/
39. controlled clinical trials/ or clinical trials phase I/ or clinical trials phase II/
40. clinical trials phase III/ or clinical trials phase IV/ or clinical trials overviews/
41. single-blind method/ or double-blind method/
42. publication bias/ or review/ or review, academic/
43. review tutorial/ or meta-analysis/ or systematic review/
44. ((random$ adj controlled adj trial$) or (prospective adj random$)).tw.
45. ((random adj allocation) or random$ or (clinical adj trial$) or control$).tw.
46. ((standard adj treatment) or compar$ or single-blind$ or double-blind$).tw.
47. (blind$ or placebo$ or systematic$ or (systematic adj review)).tw.

48. (randomized controlled trial or clinical trial).pt. or comparative study.sh.
49. or/38–48
50. 37 and 49
51. limit 50 to human
52. burns/ or wounds, gunshot/ or corneal ulcer/ or exp dentistry/
53. peptic ulcer/ or duodenal ulcer/ or stomach ulcer/
54. ((peptic adj ulcer) or (duodenal adj ulcer) or traum$).tw.
55. ((aortocaval adj fistula) or (arteriovenous adj fistula)).tw.
56. (bite adj wound$).tw.
57. or/52–56
58. 51 not 57

CINAHL

The CINAHL search strategy used was as follows:

1. pressure ulcer/ or foot ulcer/ or leg ulcer/ or skin ulcer/
2. diabetic foot/ or diabetic neuropathies/
3. diabetic angiopathies/ or diabetes mellitus/co
4. pilonidal cyst/ or surgical wound infection/
5. ((plantar or diabetic or heel or venous or stasis or arterial) adj ulcer$).tw.
6. ((decubitus or foot or diabetic or ischaemic or pressure) adj ulcer$).tw.
7. ((pressure or bed) adj sore$).tw.
8. ((pilonidal adj cyst) or (pilonidal adj sinus) or bedsore).tw.
9. ((diabetic adj foot) or (cavity adj wound)).tw.
10. ((varicose or leg or skin) adj ulcer$).tw.
11. (decubitus or (chronic adj wound$)).tw.
12. ((sinus adj wound$) or (cavity adj wound$)).tw.
13. or/1–12
14. debridement/ or biological dressings/ or occlusive dressings/
15. (bandages.ti,sh,ab,it. and 'Bandages and Dressings'/) or
16. compression garments/ or antibiotics/
17. electric stimulation/ or Laser Surgery/ or lasers/th lasers/ or Nutrition Care (Saba HHCC)/ or diet therapy/ or Nutrition Therapy (Iowa NIC)/
18. surgery, reconstructive/ or surgery, plastic/ or surgical flaps/
19. surgical stapling/ or skin transplantation/ or alternative therapies/
20. acupuncture/ or massage/ or zinc/ or ointments/
21. antiinfective agents, local/ or antibiotics/ or dermatologic agents/
22. dermatology nursing/ or colloids/ or beds and mattresses/
23. flotation beds/ or wheelchairs/ or positioning:wheelchair/ or positioning:therapy/
24. patient positioning/ or positioning/ or wound care/ or wound healing/
25. (debridement or dressing$ or compress$ or cream$).tw.
26. ((growth adj factor$) or pressure relie$ or (recombinant adj protein$) or bandag$).tw.
27. (stocking$ or antibiotic$ or (electric adj therapy) or laser$ or nutrition$ or surg$).tw.
28. (iloprost or alginate$ or zinc or paste$ or ointment$ or hydrocolloid$).tw.
29. ((compression adj therapy) or (compression adj bandag$) or wrap$).tw.
30. (bed$ or mattress$ or wheelchair$ or (wheel adj chair) or cushion$).tw.
31. ((wound adj dressing$) or vitamin$ or bind$ or gauze$ or heals or healing).tw.
32. (diet or lotion$ or infect$ or reduc$ or etiol$ or (wound adj healing)).tw.
33. (treat$ or prevent$ or epidemiol$ or aetiol$ or therap$ or prevalence or incidence).tw.
34. 'Bandages and Dressings'/ or skin transplantation/ or homeopathy/ or ointments/ or 'beds and mattresses'/
35. or/14–34
36. 13 and 35
37. clinical trials/ or single-blind studies/ or double-blind studies/
38. control group/ or placebos/ or meta analysis/
39. ((random$ adj clinical adj trial$) or (prospective adj random$)).tw.
40. ((random adj allocation) or random$ or controlled clinical trial$ or control).tw.
41. (comparison group$ or (standard adj treatment) or compar$).tw.
42. (single-blind$ or (single adj blind) or double-blind or (double adj blind)).tw.
43. (blind$ or placebo$ or systematic or (systematic adj review)).tw.
44. (meta analysis or meta-analysis).tw. or (trials or trial or prospective).tw.
45. (clinical trials).sh. or (comparative studies).sh.
46. or/37–45
47. 36 and 46
48. burns/ or wounds, gunshot/ or corneal ulcer/ or exp dentistry/
49. peptic ulcer/ or duodenal ulcer/
50. ((peptic adj ulcer) or (duodenal adj ulcer) or trauma).tw.
51. (burn$ or (gunshot adj wound$) or (corneal adj ulcer) or dentist$ or (bite adj wound)).tw.
52. or/48–51
53. 47 not 52

Other databases

- ISI Science Citation Index (on BIDS)
- BIOSIS (on SilverPlatter)
- British Diabetic Association Database
- CISCOM (database of the Research Council for Complementary Medicine)
- Cochrane Controlled Trials Register (Central)
- Cochrane Database of Systematic Reviews (CDSR)
- Cochrane Wounds Group register of trials
- Current Research in Britain (CRIB)
- Database of Abstract of Reviews of Effectiveness (DARE)
- Dissertation Abstracts
- DHSS Data (on Knight-Ridder Datastar)
- EconLit
- EMBASE (on Knight-Ridder Datastar)
- Index to Scientific and Technical Proceedings (searched on BIDS)
- National Research Register (to locate ongoing research in NHS)
- NHS Economic Evaluation Database (NHS Centre for Reviews and Dissemination)
- Royal College of Nursing Database (CD-ROM)
- System for Information on Grey Literature in Europe (SIGLE) (on Blaise Line)

Appendix 2
Advisory panel

Dr Mary Bliss	Department of Medicine for the Elderly, Homerton Hospital, London
Professor Nick Bosanquet	Department of General Medicine, Imperial College School of Medicine, London
Professor Andrew Boulton	Department of Medicine, Manchester Royal Infirmary, Manchester
Dr Richard Bull	Department of Dermatology, Homerton Hospital, London
Mr Michael Callam	Department of Vascular Surgery, Bedford Hospital, Bedford
Mrs Carol Dealey	Moseley Hall Hospital, Birmingham
Professor Peter Friedman	Department of Dermatology, Royal Liverpool University Hospital, Liverpool
Mr Brian Gilchrist	Department of Nursing Studies, King's College, London
Dr Keith Harding	Wound Healing Research Unit, University of Wales College of Medicine, University Department of Surgery, Cardiff
Mrs Deborah Hofman	Department of Dermatology, Churchill Hospital, Oxford
Mrs Vanessa Jones	Wound Healing Research Unit, University of Wales College of Medicine, University Department of Surgery, Cardiff
Dr Christina Lindholm	Department of Nursing Research, Uppsala University Hospital, Uppsala
Dr Raj Mani	Department of Medical Physics, Southampton University Hospital, Southampton
Ms Andrea Nelson	Department of Nursing, University of Liverpool, Liverpool
Dr Steve Thomas	Surgical Materials Testing Laboratory, Bridgend General Hospital, Mid Glamorgan
Dr Ewan Wilkinson	Buckinghamshire Health Authority, Aylesbury

Appendix 3

Summary of included studies

TABLE 6 *Trials of the use of compression in the prevention and treatment of venous leg ulcers*

Study	Methods	Participants	Interventions*	Outcomes	Notes
Callam *et al.*,[19] 1992, UK	Multicentre, factorial design, RCT Patients also randomised to a knitted viscose dressing or a hydrocellular poly-urethane foam	132 patients in two arms, attending leg ulcer clinics Inclusion criteria: all patients referred to leg ulcer clinics at Edinburgh and Falkirk Royal Infirmaries (Scotland) with evidence of chronic venous disease Exclusion criteria: ABPI < 0.8; diabetes; seropositive rheumatoid arthritis; lived too far away; refused consent	1. Elastic compression (orthopaedic wool (Soffban) + Tensopress + Tensoshape) (65) 2. Non-elastic compression (orthopaedic wool (Soffban) + Elastocrepe + Tensoplus Forte) (67)	% completely healed at 12 weeks: 1. 54% 2. 28%	No interaction between dressings and bandages (interaction test, $p = 0.87$). Bandages applied by experienced leg ulcer nurses No difference in quality of life between two groups
Charles,[16] 1991, UK	RCT	53 community-based patients from inner London, aged 37–99 years Inclusion criteria: ABPI > 0.8	1. Short stretch bandage (Rosidal K) applied by project nurse (27) 2. 'Usual treatment' given by district nurse (26)	Complete healing in 3 months: 1. 71% 2. 25% Ulcers increased in size: 1. 0% 2. 21%	Withdrawals: 3 in each group No clear inclusion and exclusion criteria; randomisation not stated; baseline comparability of groups not clear (bigger ulcers in control group but not analysed)

continued

TABLE 6 contd Trials of the use of compression in the prevention and treatment of venous leg ulcers

Study	Methods	Participants	Interventions*	Outcomes	Notes
Colgan *et al.*,[8] 1996, Eire	RCT	30 patients at routine venous ulcer outpatient clinic in Ireland Inclusion criteria: diagnosis of venous aetiology; ulcer size greater than 1 cm × 1 cm Exclusion criteria: arterial disease Mean age: 1, 65.5 years; 2, 67.5 years; 3, 56 years Median (mean) ulcer size: 1, 9 cm^2 (48.5 cm^2); 2, 7 cm^2 (27.5 cm^2); 3, 20 cm^2 (42.8 cm^2) Median (mean) ulcer duration: 1, 24 months (66.5 months); 2, 10 months (9.3 months); 3, 12 months (53.5 months)	1. Modified Unna's boot (paste bandage + Elastocrepe + Elastoplast + class 2 compression sock) (10) 2. Four-layer bandage (Profore) (10) 3. Lyofoam dressing + Setopress bandage (10)	% completely healed at 12 weeks: 1. 60% 2. 70% 3. 20% Withdrawals due to poor application: 1. 1/10 2. 0/10 3. 3/10	Treatment given by a clinic nurse Costs of bandages were calculated, but costs of nursing time were not, due to wide variation in services Average cost (range) per patient per 12 weeks: 1. Ir£66.24 (Ir£18.14–108.84) 2. Ir£82.54 (Ir£27.94–177.20) 3. Ir£58.33 (Ir£19.11–83.24) Lyofoam and Setopress (option 3) was the least expensive, but the least effective. This may be due to poor patient compliance and/or inadequate application

continued

TABLE 6 contd *Trials of the use of compression in the prevention and treatment of venous leg ulcers*

Study	Methods	Participants	Interventions*	Outcomes	Notes
Cordts *et al.*,[29] 1992, USA	RCT	43 patients from an out-patient clinic with grade III chronic venous insufficiency Inclusion criteria: age >18 years; venous leg ulcer confirmed by duplex scanning Exclusion criteria: signs and symptoms of clinical infection; arterial ulcers; ulcer area >50 cm^2; uncontrolled diabetes mellitus; venous surgery within 1 month on affected leg; ulcer with exposed muscle, tendon or bone; pregnancy; patients on antibiotics, steroids or chemotherapy; known HIV infection Ulcer size varied greatly between patients: 1, 9.1 cm^2 (SE = 1.7); 2, 6.0 cm^2 (SE = 2.4)	1. Hydrocolloid dressing (Duoderm) + Coban (16) 2. Unna's boot (14)	Complete healing at 12 weeks: 1. 50% 2. 43% Ulcer healing rate correlated with ulcer area and perimeter Withdrawals: Duoderm group, 7; Unna's boot, 6	Costs not reported. Patient acceptance of bandage was higher with Duoderm than Unna's boot

continued

TABLE 6 contd *Trials of the use of compression in the prevention and treatment of venous leg ulcers*

Study	Methods	Participants	Interventions*	Outcomes	Notes
Danielsen *et al.*,[25] 1998, Sweden	RCT	43 patients were initially recruited, but only 40 patients with 40 ulcerated legs were included in the analysis as three patients had been inappropriately randomised Inclusion criteria: lipodermatosclerosis; leg ulcers and incompetent veins demonstrated by Doppler and/or clinical examination; informed consent given Exclusion criteria: significant arterial insufficiency (systolic blood pressure in first toe <60 mmHg or ABPI < 0.9); suspected immunological aetiology; diabetes; uncompensated heart disease; walking impairment	1. Leg padded with gauze, long stretch, non-adhesive elastomeric bandage (Setopress); applied in a spiral, with 50% overlap and approximately 86% extension; changed as little as possible (tried to leave bandage on for 7 days); all bandages applied by study nurse 2. Leg padded with gauze, short stretch, non-adhesive bandage (Comprilan); applied in a spiral, with 50% overlap, using 'similar tension to that in long stretch bandage'; changed daily or every other day; most bandages applied by community nurse Concurrent treatment: hydrocolloid dressing, if possible; large ulcers or maceration of surrounding skin treated with an ointment or gel; for suspected local infection, mupirocin, silver sulphadiazine cream or Iodosorb; observed cellulitis, systemic antibiotics Patients had to keep wearing the bandages after healing	Relative ulcer area at 1, 6 and 12 months: 1. Long stretch bandage: 0.45, 0.81, 0.25 2. Short stretch bandage: 0.72, 0.6, 0.95 Number of ulcer-free limbs (number of limbs assessed) at 1, 6 and 12 months: 1. Long stretch bandage: 4 (15), 9 (18), 12 (17) 2. Short-stretch bandage: 1 (19), 5 (14), 3 (10) Withdrawals: 1. Long stretch bandage: 5 (2 preferred stockings after healing, 2 preferred alternative treatments, 1 because bandage caused swelling of knee) 2. Short-stretch bandage: 9 (1 preferred stockings after healing, 3 preferred alternative treatments, 3 were withdrawn due to poor compliance, 1 changed address, 1 died) Development of cellulitis: 1. Long stretch bandage: 7 2. Short stretch bandage: 8	The outcome measure 'ulcer-free limb at assessment' means that the healing rate is potentially underestimated compared with other trials (where the incidence of ulcer healing is generally used), as an ulcer may have healed and recurred before the assessment point. In this trial a recurrence occurred after the 6 month assessment (1 patient in the short stretch bandage group), and therefore the number of ulcer-free limbs at 6 months is equivalent to the number of limbs healed at 6 months

continued

TABLE 6 contd *Trials of the use of compression in the prevention and treatment of venous leg ulcers*

Study	Methods	Participants	Interventions*	Outcomes	Notes
Duby *et al.*,[23] 1993, UK	RCT	67 patients (76 legs), mean age 70–73 years, 45 women, 22 men. Setting not stated, but was in the UK Mean duration of ulcer: 1. 26.7 months; 2. 20.5 months; 3. 34.5 months Inclusion and exclusion criteria: none stated	1. Short stretch system (orthopaedic wool + short stretch bandage (Comprilan) + Tricofix) (25 legs) 2. Four-layer (wool + crepe + Elset + Coban) (25 legs) 3. Paste layer system (Icthopaste + Elastocrepe + Tubigrip) (26 legs) All irrigated with saline and a non-adherent dressing applied	% completely healed at 12 weeks: 1. 40% 2. 44% 3. 34.5% Healing rate (reduction in ulcer area): 1. –60% 2. –76% 3. –43%	Higher proportion on males in group 3 (11/24) compared with the other two groups combined (11/43) All bandages changed on average twice a week
Eriksson,[17] 1986, Sweden	RCT	44 patients in a multicentre trial; setting unclear, but the study was undertaken in Sweden. Mean age approx. 70 years Inclusion criteria: not stated Exclusion criteria: overt diabetes mellitus; manifest arterial insufficiency; erysipelas; cellulitis	1. Skintec porcine skin dressing (no compression) (11) 2. Metallina aluminium foil dressing (no compression) (20) 3. Double-layer bandage (ACO paste bandage + Tensoplast) (13)	Decrease in ulcer area and volume at 8 weeks: 1. 60%, 67% 2. 10%, 0% 3. 80%, 90% Not possible to separate out the effects of the porcine skin and the double-layer bandage, due to crossover	No statistical analysis reported Initial ulcer size and duration not stated In the 'middle' of the trial, patients in the porcine skin group were crossed over to the double-layer bandage as the former treatment was no longer available
Franks *et al.*,[11] 1995, UK	RCT	188 patients with newly healed venous leg ulcers; 166 could apply a compression sock	1. Below knee (Medi) class 2 2. Below knee (Scholl) class 2	Recurrence rate at 18 months: 1. 21% 2. 34%	

continued

TABLE 6 contd *Trials of the use of compression in the prevention and treatment of venous leg ulcers*

Study	Methods	Participants	Interventions*	Outcomes	Notes
Gould *et al.*,[18] 1993, UK	RCT, single blind	39 patients from GPs attending outpatient clinics in the UK. Age range 44–87 years (mean 71.5 years) Inclusion criteria: venous ulcers; ABPI > 0.8; ambulatory Exclusion criteria: arterial or mixed ulcers; diabetes mellitus; peripheral neuropathy; congestive heart failure; chronic renal or liver disease; infected wounds; ankle circumference <18 cm or >25 cm; known sensitivity to paste bandages; ulcer duration <2 months	1. Elastic compression: medicated paste + Setopress + elasticated viscose stockinette (20) 2. Non-elastic compression medicated paste + Elastocrepe + elasticated viscose stockinette (20) All patients received potassium permanganate soaks for 5 minutes, followed by a medicated paste bandage as a primary dressing, and a layer of stockinette	% completely healed in 15 weeks: 1. 58% (11/19) 2. 35% (7/20) Improved: 1. 6/19 2. 4/20 Deteriorated: 1. 2/19 2. 9/20	Costs not considered. Setopress rated as easier to use
Harper *et al.*,[10] 1996, UK	RCT	300 patients with newly healed venous leg ulcers	1. Class 3 hosiery 2. Class 2 hosiery Both groups were assessed every 4 months at a specialist leg ulcer clinic and had access to a 'hot-line' in case they had any problems with their leg ulcer	% recurrence at 36–60 months: 1. 21% 2. 34%	

continued

***TABLE 6 contd** Trials of the use of compression in the prevention and treatment of venous leg ulcers*

Study	Methods	Participants	Interventions*	Outcomes	Notes
Hendricks and Swallow,[31] 1985, USA	RCT	21 patients attending an outpatient clinic; age range 35–86 years Inclusion criteria: 'stasis ulcers' (not defined) Exclusion criteria: not stated	1. Unna's boot + Kerlix roll + elastic bandage; seen at clinic every 3–9 days (10) 2. Open-toe, below-knee, graduated compression sock (24 mmHg at ankle); self-care between clinic visits (weekly or fort-nightly) (11) Other treatments: Surgical debridement at clinic, polysporin ointment, ulcers cleansed with hydrogen peroxide 3%	% complete healing (78 weeks): 1. 70% 2. 71% (but 3 of these had been transferred from group 1)	Crossover between arms, depending on progress
Kikta *et al.*,[12] 1988, USA	RCT	84 patients (with 87 ulcers) from vascular surgery clinics Inclusion criteria: leg ulcer caused by chronic venous insufficiency Exclusion criteria: arterial insufficiency (ABPI < 0.7); uncontrolled diabetes mellitus; use of cancer therapeutic agents or systemic steroids; recent venous surgery; infected ulcers; inability to comply with treatment or follow-up	1. Unna's boot (42) 2. Duoderm hydrocolloid dressing (45) Ulcers washed with chlorhexidine solution and 3% hydrogen peroxide, then rinsed with saline and left to air dry	Completely healed at 6 months: 1. 70% 2. 38% Ulcers healed at 15 weeks (life-table analysis): 1. 64% 2. 35%	Complication rate: 1. 0% 2. 26% Attrition: 1. 12 2. 16 Acceptability of hydrocolloid better, but healing rate lower Cost of therapy was comparable for the two dressings for all ulcers and for healed ulcers. Among those not healing, the hydrocolloid dressing was significantly more expensive

continued

TABLE 6 contd Trials of the use of compression in the prevention and treatment of venous leg ulcers

Study	Methods	Participants	Interventions*	Outcomes	Notes
Knight and McCulloch,[24] 1996, USA	RCT	10 patients randomly chosen from patients at a wound care centre in the USA Inclusion criteria: venous insufficiency (not defined) Exclusion criteria: refused consent	1. Four-layer (Profore) (5) 2. Unna's boot (5)	Average rate of ulcer healing: 1. 1.14 cm^2/week 2. 0.34 cm^2/week Maximum rate of ulcer healing: 1. 2.24 cm^2/week 2. 1.00 cm^2/week Minimum rate of healing: 1. 0.365 cm^2/week 2. 0.005 cm^2/week	Costs not considered

continued

TABLE 6 contd *Trials of the use of compression in the prevention and treatment of venous leg ulcers*

Study	Methods	Participants	Interventions*	Outcomes	Notes
Kralj and Kosicek,[9] 1996, Slovenia	RCT	40 inpatients and outpatients, aged 36–86 years (mean 61–65 years) Inclusion criteria: stasis leg ulcer; age <86 years; complete mobility; written, informed consent Exclusion criteria: ABPI < 0.8; systemic connective tissue disease; serologically positive rheumatoid arthritis; severe concurrent diseases Mean (range) ulcer area at baseline: 1. 18.6 cm^2 (1–57 cm^2) 2. 17.2 cm^2 (1–47 cm^2) Mean (range) duration of ulcers: 1. 7.9 months (1–24 months) 2. 6.9 months (1–36 months)	1. Four-layer (Profore) (wool, + crepe + Litepress + Co-Plus) (20) 2. Hydrocolloid dressing (Tegasorb) + single-layer bandage (Porelast) (20)	Complete healing: 1. 44% 2. 44% Mean time to healing: 1. 57.6 days (7–106 days) 2. 84.9 days (28–180 days) Ulcers healed by 15 August 1996: 1. 7/20 2. 8/20	Costs not considered

continued

TABLE 6 contd Trials of the use of compression in the prevention and treatment of venous leg ulcers

Study	Methods	Participants	Interventions*	Outcomes	Notes
McCollum *et al.*,[27] 1997, UK	RCT	232 patients from community leg ulcer services in the UK; mean age 67–68 years Inclusion criteria: age ≥18 years; not pregnant; venous ulceration; informed consent Exclusion criteria: ABPI < 0.8; non-venous ulceration; patients who had entered the trial previously Median (range) ulcer duration: 1, 8 weeks (0–2080 weeks); 2, 7 weeks (0–728 weeks) Patients with ulcers <10 cm^2: 1, 82%; 2, 84% Patients walking freely: 1, 74%; 2, 79%	1. Charing Cross four-layer – original (wool + crepe + Elset + Coban), or as indicated by ankle circumference (115) 2. Profore four-layer (wool + crepe + Litepress + Co-Plus), or as indicated by ankle circumference (117) Dressing standardised – knitted viscose dressing (Tricotex)	Complete healing at 24 weeks: 1. 71% 2. 74% Healing rates at 24 weeks (withdrawals excluded): 1. 82% 2. 84% Withdrawn at 24 weeks: 1. 16% 2. 15%	Costs not considered

continued

TABLE 6 contd *Trials of the use of compression in the prevention and treatment of venous leg ulcers*

Study	Methods	Participants	Interventions*	Outcomes	Notes
Nelson *et al.*,[21] 1995, UK	RCT, 2 × 3 factorial design	200 patients in leg ulcer clinics in Falkirk and Edinburgh, who had ulcers for >2 months Inclusion criteria: age >17 years; informed, written consent; sign of venous disease by hand-held Doppler Exclusion criteria: severe concurrent disease; ABPI < 0.8; diabetes; serologically positive rheumatoid arthritis; participation in concurrent drug trial; taking vasoactive drugs, warfarin or steroids	1. Single-layer compression bandage (Granuflex Adhesive) (100) 2. Four-layer bandage (wool + crepe + Elset + Coban) (100) Also, comparison of dressing (knitted viscose or hydrocolloid dressing) and drug treatment (oxpentifylline versus placebo)	Complete healing in 6 months: 1. 49% 2. 69%	Treatment given by experienced leg ulcer nurses
Northeast *et al.*,[20] 1990, UK	RCT	106 patients from an outpatient clinic Inclusion criteria: evidence of venous pump abnormality Exclusion criteria: arterial disease; diabetic disease; other obvious cause of ulceration	1. Three layers (Calaband paste bandage + Elastocrepe + Tensogrip) (54) 2. Three layers (Calaband paste bandage + Tensopress + Tensogrip) (52) Bandages changed 1 or 2 times weekly	% completely healed at 3 months: 1. 51% 2. 54%	Only one group received anabolic steroids. It is unclear whether the design was factorial, or whether one compression group had treatment supplemented by steroids

continued

TABLE 6 contd *Trials of the use of compression in the prevention and treatment of venous leg ulcers*

Study	Methods	Participants	Interventions*	Outcomes	Notes
Partsch and Horakova,[30] 1994, Austria	CCT	59 patients attending a dermatology clinic; age 34–93 years Inclusion criteria: venous ulcers (not defined) Exclusion criteria: ABPI < 0.8; ulcers of non-venous origin Groups not comparable for ulcer duration or area (larger and 'older' ulcers in bandage group)	1. Thin layer of padding + short stretch bandage (Rosidal K) (25) 2. Thrombo stocking + compression stocking (outer layer removed at night) (25)	Complete healing at 3 months: 1. 52% 2. 84%	Randomisation by surname (A–M or N–Z) Costs not considered
Rubin *et al.*,[13] 1990, USA	RCT	36 consecutive ambulatory hospital patients Inclusion criteria: chronic venous ulceration (not defined) Exclusion criteria: history of non-compliance; ABPI < 0.8; history of risk factors such as collagen, vascular disease, uncontrolled diabetes, other dermatological disorders, chronic corticosteroid therapy Ulcer size larger in group 1 (76 cm^2 vs 32.2 cm^2)	1. Unna's boot (19) 2. Polyurethane foam dressing (Synthaderm) (17) Bandages changed once or twice weekly	Complete healing: 1. 94.7% 2. 41.2% Withdrawals: 1. 0 2. 9	Costs not considered. Length of follow-up unclear

continued

***TABLE 6 contd** Trials of the use of compression in the prevention and treatment of venous leg ulcers*

Study	Methods	Participants	Interventions*	Outcomes	Notes
Scriven *et al.*,[26] 1998, UK	RCT Randomisation stratified by ulcer area (<10 cm^2 or >10 cm^2)	53 ambulant patients with 64 ulcerated limbs recruited from a dedicated venous ulcer assessment clinic Median (range) ulcer area: 1, 13.3 cm^2 (2–378 cm^2); 2, 8.3 cm^2 (2–104 cm^2) (p = 0.05) Number of limbs with ulcers >10 cm^2: 1, 21; 2, 14 Median (range) age: 1, 70 years (45–91 years); 2, 73 years (36–93 years) Median ulcer duration: 1, 13 months; 2, 21 months 42/53 patients had unilateral ulcers; 11 patients had bilateral ulcers, which were randomised independently	1. Four-layer (orthopaedic wool + crepe + Elset + Coban) (32 limbs) 2. Short stretch system (orthopaedic wool + short stretch bandage + Coban (unstretched)) (32 limbs) All ulcers were dressed with a knitted viscose dressing covered by gauze Bandages were changed once a week, unless there was strike through of exudate	Complete healing at 1 year: 1. 17/32 (53%) 2. 18/32 (56%) Complete healing at 3 months: 1. 11/32 (34%) 2. 13/32 (41%) Adverse events: 1. None 2. ischaemic damage, 2; maceration, 2 Loss to follow-up: 1 death (group unclear), 2 did not attend (1 from each group)	The Coban bandage was applied as a simple spiral on top of the short stretch system in order to prevent slippage. Limbs are not independent with respect to healing, and this may have influenced the results
Sikes,[14] 1985, USA	CCT	13 male patients with 42 ulcers (convenience sample) from an outpatient vascular surgery clinic; age 34–71 years Ulcers were of longer duration in the Opsite group (6.9 versus 3.5 years), but the significance of this is questionable	1. Unna's boot (7) 2. Polyurethane, moisture vapour permeable, transparent film dressing (Opsite) (6) Irrigation with povidone iodine, rinsed with saline, patted dry and dressed Patients educated about pathophysiology, the rationale for treatment and how to behave during treatment	Completely healed at 1 year: 1. 81% 2. 71%	Costs not considered. Very small numbers. Pain reportedly decreased or was eliminated by Opsite, but this group required more frequent dressing changes due to maceration

continued

TABLE 6 contd *Trials of the use of compression in the prevention and treatment of venous leg ulcers*

Study	Methods	Participants	Interventions*	Outcomes	Notes
Taylor *et al.*,[15] 1998, UK	RCT	36 consecutive patients referred to a leg ulcer clinic from both primary and secondary care; age 28–85 years Six patients were lost to follow-up Inclusion criteria: venous ulceration (not defined) Exclusion criteria: ABPI < 0.8 Mean (range) baseline age: 1, 73 years (28–85 years); 2, 77 years (60–84 years) Median (range) baseline ulcer area: 1, 5.4 cm^2 (0.4–74.8 cm^2); 2, 4.2 cm^2 (0.6–76.0 cm^2)	1. Four-layer bandage (orthopaedic wool + crepe + Elset + Coban) (18) 2. Conventional treatment (range of preparations) (18) Group 1 treated by an experienced community nurse or a trial nurse; group 2 treated by usual nurse with no specialist training. The proportion of patients receiving compression in group 2 is unclear	Complete healing of all ulcers on limb at 12 weeks: 1. 12/18 (66.7%) (including withdrawals 12/16 (75%)) 2. 4/18 (22.2%) (including withdrawals 3/14 (21%)) Median healing time: 1. 55 days 2. 84 days Median (range) weekly cost: 1. £17.26 (£13.45–20.16) 2. £21.07 (£8.71–42.47) Authors state $p = 0.042$	Control group received a range of primary dressings and bandages, some of which can apply compression Four-layer compression was less expensive (difference in weekly costs £6.46; 95% CI, 1.22 to 11.68) The trial compared two packages of care: usual care versus four-layer bandage and care by specialist nurse or experienced grade G nurse Randomisation was performed by minimisation of prognostic factors (age, sex, body mass index, range of ankle movement, ulcer area, ulcer duration, living alone)
Travers *et al.*,[22] 1992, UK	RCT	27 patients attending a leg ulcer clinic; mean age 54–59 years Inclusion criteria: venous ulcers (not defined) Exclusion criteria; not stated	1. Self-adhesive bandage (Panelast Acryl) (15) 2. Three-layer system (paste bandage (Calaband) + Tensopress + Tensogrip) (12)	Reduction in ulcer area in 7 weeks: 1. 86% 2. 83%	States that costs were equivalent, but no data given

continued

***TABLE 6 contd** Trials of the use of compression in the prevention and treatment of venous leg ulcers*

Study	Methods	Participants	Interventions*	Outcomes	Notes
Wilkinson *et al.*,[28] 1997, UK	RCT	29 patients with 35 ulcerated legs, referred from GPs; age 72–77 years Inclusion criteria: uncomplicated venous leg ulcer being treated by district (community) or practice nurse Exclusion criteria: peripheral vascular disease; cellulitis; ABPI < 0.8; allergy to latex; ulcer on foot or toes; rheumatoid arthritis; collagen vascular disease; ankle circumference <18 cm or >25 cm Stratified by size of ulcer (>10 cm^2 or <10 cm^2). Ulcers in the four-layer group were larger Mean duration of ulcer: 1. <10 cm^2, 14.2 months; >10 cm^2, 36.8 months 2. <10 cm^2, 18.3 months; >10 cm^2, 28.2 months	1. Four-layer (wool + crepe + Elset + Coban) (17 legs) 2. Lint, Tubifast, Setopress, Tubifast (18 legs) Knitted viscose dressings (Tricotex) were used in both groups	Complete healing at 12 weeks: 1. <10 cm^2, 75%; >10 cm^2, 59% 2. <10 cm^2, 42%; >10 cm^2, 33% Overall, 59% of the ulcers in the four-layer group and 39% in the control group healed in 12 weeks	Costs not considered

ABPI, ankle/brachial pressure index; CCT, controlled clinical trial; CI, confidence interval; RCT, randomised controlled trial
** Numbers in parentheses are the numbers of study subjects*

Appendix 4

Quality assessment of included studies

***TABLE 7** Quality of trials of compression in the prevention and treatment of venous leg ulcers*

Study	Number of patients and arms in trial	Inclusion and exclusion criteria	*A priori* sample-size calculation	Method of randomisation	Groups comparable at baseline	Blinded outcome assessment	Analysis by intention to treat
Callam *et al.*,[19] 1992, UK	132 patients; 2 arms	Listed	Not stated	Not stated	Yes	Not stated	Not stated
Charles,[16] 1991, UK	53 patients; 2 arms	Not listed	Not stated	Not stated	Not clear	No	No
Colgan *et al.*,[8] 1996, Eire	30 patients; 3 arms	Listed	No	Sealed envelopes	Ulcer size larger in bandage group; ulcer duration higher in boot group	No	Yes
Cordts *et al.*,[29] 1992, USA	43 patients; 2 arms	Listed	No	Not stated	Yes	Not stated	No
Danielsen *et al.*,[25] 1998, Sweden	43 patients; 2 arms (40 patients after randomisation)	Listed	No	Stated 'blind, using stratification according to ulcer size (less than or more than 20 cm^2)'	Ulcer area in short stretch group was smaller	Not stated	No
Duby *et al.*,[23] 1993, UK	63 patients (76 legs); 3 arms	Not listed	Not stated	Not stated	Yes (except longer mean ulcer duration in paste group)	Not stated	No
Eriksson,[17] 1986, Sweden	44 patients; 3 arms	Not listed	Not stated	Not stated	Yes	Not stated	Not stated
Franks *et al.*,[11] 1995, UK	188 patients; 2 arms (166 entered trial)	Not listed	Stated	Not stated	Yes	Not stated	Unclear
Gould *et al.*,[18] 1993, UK	38 patients (48 legs); 2 arms	Listed	Not stated	Not stated	Yes	Yes	No
Harper *et al.*,[10] 1996, UK	300 patients; 2 arms	Not listed	Not stated	Remote telephone	Yes	No	Yes
Hendricks and Swallow,[31] 1985, USA	21 patients; 2 arms	Not listed	Not stated	Not stated	Not stated	Unclear	No

Continued

TABLE 7 contd *Quality of trials of compression in the prevention and treatment of venous leg ulcers*

Study	Number of patients and arms in trial	Inclusion and exclusion criteria	*A priori* sample-size calculation	Method of randomisation	Groups comparable at baseline	Blinded outcome assessment	Analysis by intention to treat
Kikta *et al.*,[12] 1988, USA	45 patients; 2 arms	Listed	Not stated	Coin toss	Yes	Not stated	No
Knight and McCulloch,[24] 1996, USA	10 patients; 2 arms	Not listed	Not stated	Not stated	Not stated	Not stated	Not stated
Kralj and Kosicek,[9] 1996, Slovenia	40 patients; 2 arms	Listed	Not stated	Sealed envelopes	Yes	Not stated	No
McCollum *et al.*,[27] 1997, UK	232 patients; 2 arms	Listed	Yes	Not stated	Yes	No	Yes
Nelson *et al.*,[21] 1995, UK	200 patients; 2 arms	Not listed	Yes	Sealed envelopes	Not comparable	No	Yes
Northeast *et al.*,[20] 1990, UK	106 patients; 2 arms	Listed	No	By computer	Yes	Yes	Not stated
Partsch and Horakova,[30] 1994, Austria	59 patients; 2 arms	Not listed	Not stated	Surname	Stocking group contained larger ulcers of longer duration	Not stated	No
Rubin *et al.*,[13] 1990, USA	22 patients; 2 arms	Not listed	Not stated	Medical record number	Yes	Not stated	No
Scriven *et al.*,[26] 1998, UK	53 patients (64 ulcerated limbs); 2 arms (stratified by ulcer size)	Listed	No	Sealed envelopes	Yes	No	Yes
Sikes,[14] 1985, USA	13 patients; 2 arms	Not listed	Not stated	Alternate allocation	Mean longer duration in Opsite group	Not stated	Not appropriate
Taylor *et al.*,[15] 1998, UK	36 patients; 2 arms	Not listed	Not stated	Minimisation	Yes	Not stated	Yes
Travers *et al.*,[22] 1992, UK	27 patients; 2 arms	Not listed	Not stated	Not stated	No	Not stated	Not appropriate
Wilkinson *et al.*,[28] 1997, UK	29 patients (35 legs); 2 arms	Listed	Not stated	Not stated	Yes	No	Yes

Systematic reviews of wound care management (7): low-level laser therapy, therapeutic ultrasound, electrotherapy and electromagnetic therapy for the treatment of chronic wounds

K Flemming*
N Cullum

Centre for Evidence Based Nursing, Department of Health Studies, University of York, UK

* Corresponding author

Competing interests: N Cullum has: received funds from the NHS R&D Programme to undertake primary research in wound care; received sponsorship of trial-related educational meetings from Huntleigh Healthcare and Beiersdorf Ltd

Contents to Part 7

List of abbreviations

CI	confidence interval
df	degrees of freedom*
GaAs	gallium arsenide
HeNe	helium–neon
PEMF	pulsed electromagnetic field
RCT	randomised controlled trial
RR	relative risk
SD	standard deviation

* Used only in tables and figures

Executive summary to Part 7

Objectives

To evaluate the evidence of the effectiveness of low-level laser therapy, therapeutic ultrasound, electrotherapy and electromagnetic therapy in the treatment of chronic wounds.

Methods

Data sources

Nineteen electronic databases, including MEDLINE, EMBASE, CINAHL and the Cochrane Wounds Group's specialised trials register, and wound care journals were searched for the period up to December 1999. Organisations, manufacturers, researchers and healthcare professionals concerned with wound care were contacted for additional trials. The reference sections of the obtained studies were also searched for further trials.

Study selection

Randomised controlled trials (RCTs), published or unpublished, which assessed the effectiveness of low-level laser therapy, therapeutic ultrasound, electrotherapy or electromagnetic therapy in the treatment of chronic wounds were included in the review. Studies in any language were eligible for inclusion. Studies were only included if they reported either the proportion of wounds healed within a certain time period or the percentage or absolute change in wound area. Decisions on the relevance of primary studies were made independently by two reviewers.

Data extraction and synthesis

Details of the studies were extracted and summarised using a data-extraction sheet. If data were missing from a report, an attempt was made to contact the authors to obtain missing information. Studies published in duplicate were included only once. Data extraction was undertaken by one reviewer and checked for accuracy by a second.

Data were assessed on the following aspects of quality: use of clear inclusion and exclusion criteria; adequacy of allocation concealment; baseline comparability of treatment groups for important variables (e.g. wound size); use of intention-to-treat analysis; extent of loss to follow-up; and use of blinded outcome assessment

The studies included in the review were combined by narrative overview, with a quantitative summary of the results of similar trials where appropriate. This involved meta-analysis of outcome data using the Cochrane Revman software. For each trial with important dichotomous outcomes (e.g. number of ulcers healed), the relative risk and the 95% confidence intervals were calculated.

Results

Low-level laser therapy for the treatment of venous leg ulcers

Only four studies met the inclusion criteria. The only suggestion of therapeutic benefit was shown in one small RCT where a combination of laser and infrared light led to a significant improvement in the healing rates of venous ulcers. However, the results of this trial and the others included in this section were drawn from small studies without clear inclusion criteria for venous leg ulcers and of poor baseline comparability. As such, the results should be viewed with caution.

Therapeutic ultrasound for the treatment of venous leg ulcers

There was no clear evidence of a benefit of treating venous leg ulcers with therapeutic ultrasound, as the seven small trials eligible for inclusion in the review were inconclusive.

Therapeutic ultrasound for the treatment of pressure sores

Three studies were eligible for inclusion. The results of these studies do not suggest a benefit associated with therapeutic ultrasound in the healing of pressure sores. The trials included in this section involved small numbers of patients, different regimens of therapeutic ultrasound and different follow-up periods. The trials also had inadequate staging of pressure sores and baseline comparisons. The results should therefore be viewed with caution.

Electrotherapy for the treatment of chronic wounds

The results suggest that there may be some benefit associated with electrotherapy in the healing of chronic wounds. This suggestion is made with caution, as there are only three small trials with a total of 63 patients involved, making it impossible to determine clinically important effects.

Electrotherapy for the treatment of ischaemic ulcers

The results were difficult to interpret as the five trials eligible for inclusion in this section were small and mostly of poor quality. Those trials that had better methodological quality were biased for baseline ulcer area. As such, no recommendations can be made for practice.

Electrotherapy for diabetic ulcers

The one small trial identified demonstrated no significant benefit of the use of electrotherapy to treat diabetic ulcers.

Electrotherapy for pressure sores

The three trials identified suggest a benefit associated with using electrotherapy to treat pressure sores. However, this suggestion is drawn from three small studies with a total of 140 patients, and therefore the results should be viewed with caution as it is difficult to determine clinically important effects from such small samples.

Electromagnetic therapy for the treatment of venous leg ulcers

The three small, poor-quality trials identified provide no evidence of a benefit of electromagnetic therapy for the treatment of venous leg ulcers.

Electromagnetic therapy for the treatment of pressure sores

Two small, poor-quality studies were identified. These provided no clear evidence of a benefit of electromagnetic therapy in the treatment of pressure sores.

Conclusions

Implications for clinical practice

There is generally insufficient evidence to state whether the use of any of the therapies identified for this review are beneficial or not in the treatment of any of the chronic wounds studied.

Recommendations for research

This review found that for two of the interventions there is a suggestion of benefit. These therapies should have research priority:

- therapeutic ultrasound for venous leg ulcers
- electrotherapy for chronic wounds including pressure sores.

Within all studies examining the effectiveness of the therapies outlined in this review, research methodology could be significantly improved, and commissioning groups may wish to consider the following aspects for future research:

- The number of patients in a trial should be based on an *a priori* sample-size calculation.
- A truly objective outcome measure should be used, or wound healing should be expressed as both percentage and absolute change in area.
- For each patient a single reference wound should be selected.
- Experimental groups should be comparable at baseline.
- Wherever possible, each therapy should be compared with sham therapy.
- A complete and thorough description of concurrent treatments, including secondary dressings, should be given in trial reports.
- Assessment of outcomes should ideally be blind to treatment or be completely objective.
- Survival-rate analysis should be adopted in all studies that assess wound healing.
- Future trials should include cost-effectiveness and quality-of-life assessments, as well as objective measures of the effectiveness of physical therapies.
- Economic evaluations should be incorporated in trials that are sufficiently large in order to detect appropriate economic and clinical outcomes.
- In order to prevent publication bias and ensure the inclusion of unpublished trials in systematic reviews, those involved in primary research should make their data available to those undertaking systematic reviews.

Chapter 1
Introduction

This report is one of a series of systematic reviews aimed at identifying effective interventions for the prevention and treatment of chronic wounds. This report focuses specifically on the effectiveness of the following therapies for the treatment of chronic wounds:

- low-level laser therapy
- therapeutic ultrasound
- electrotherapy
- electromagnetic therapy.

The following were selected for this review as they are the most common chronic wounds encountered in clinical practice:

- venous leg ulcers
- pressure sores
- diabetic ulcers
- ischaemic ulcers.

The interventions for the review were selected through consultation with the advisory panel (see appendix 2), the National Coordinating Centre for Health Technology Assessment, and on the basis of current practice, clinical variation and uncertainty.

Types of wound

Venous leg ulcers

The prevalence of active leg ulceration in the UK has been estimated at 1.5 in 1000,[1,2] and a similar rate has been reported in Australia.[3] Prevalence increases with age, and is higher among women. Leg ulceration is typically a chronic recurring condition, with 45% of patients in a Scottish study reporting episodes of ulceration for more than 10 years.[4] There is a considerable cost both to the patient[5] and to the health service.[6] Most leg ulcers are associated with venous disease, and a history of a deep vein thrombosis is widely regarded as a predisposing factor to venous insufficiency and hence to venous ulceration. However, the aetiology of leg ulceration remains poorly understood. Venous insufficiency has been shown to be associated with increased hydrostatic pressure in the veins of the leg, and it is in an attempt to reverse this and aid venous return that external compression in various forms is applied as a therapy for venous leg ulcers.[7] However, while compression therapy is the mainstay of venous ulcer therapy, various other interventions, including dressings, are used as an adjunct to compression or in the absence of compression where compression is contraindicated (e.g. in the presence of arterial disease).

Pressure sores

Pressure sores (also known as bed sores, decubitus ulcers and pressure ulcers) are areas of localised damage to the skin and underlying tissue caused by pressure, shear or friction. They usually occur over bony prominences such as the sacrum, heels, hips and elbows, and most often in immobile elderly people (e.g. elderly orthopaedic patients), patients with severe acute illnesses (e.g. patients in intensive care units) and in people with neurological problems (e.g. people with spinal cord injuries).

Pressure sores have been recorded as occurring in 4–10% of patients admitted to a UK district general hospital (the precise rate depends on the case mix) and in an unknown proportion of patients in the community. These sores represent a major burden of sickness and reduced quality of life for patients and their carers, and are costly to health service providers.

Pressure sores present as a continuum of tissue damage, from unbroken skin with sustained redness after the release of pressure (non-blanching erythema) to the destruction of muscle and bone.

The treatment of pressure sores covers four main strategies:

- local treatment of the wound using dressings and other topical applications
- pressure relief, using beds, mattresses or cushions, or by repositioning the patient
- treating concurrent conditions that may delay healing (e.g. poor nutrition, infection)
- the use of physical therapies, such as electrical stimulation, ultrasound and laser therapy.

In a Dutch Consensus Report (1985),[64] ultrasound was described as “potentially useful in individual cases of Grade IIIa pressure sore”, although a survey in The Netherlands found that only approximately 25% of nursing-home doctors and nurses regarded ultrasound as "effective or very effective" for treating pressure sores.[8]

Diabetic ulcers

Foot ulceration in diabetes (type 1, formerly called insulin-dependent diabetes mellitus; and type 2, formerly called non-insulin-dependent diabetes mellitus) is a major contribution to the morbidity and mortality of the disease, and is thought to affect 15% of all people with diabetes at some time during their life.[9] There is some uncertainty as to the true incidence and prevalence, as much of the treatment is delivered in the community and outpatient departments, where data collection is patchy and surveillance limited. The cost to the NHS is thought to be about £12.9 million per year.[10] In the USA, diabetic foot ulceration accounts for $350 million of hospital costs and 50% of non-traumatic lower-limb amputations.

Population-based studies have identified trends in hospital admissions, the incidence of foot ulceration and the risk factors for diabetic foot ulceration. Other studies have identified that there is a positive correlation between diabetic foot ulceration and the rate of non-traumatic amputation.[11]

Aetiology of foot ulceration in diabetes

The pathway to foot ulceration in diabetes involves a complex combination of peripheral vascular disease (reduced blood supply) and peripheral neuropathy (reduced sensation and/or change in lower-limb movement). Decreased pain sensation and muscular spatial awareness (proprioception) due to neuropathy lead to abnormal loading of the foot, and this in turn leads to areas of increased pressure on the plantar (base) aspects of the foot (e.g. metatarsal heads, base of the toes). These increased foot pressures lead to the formation of thick, hard skin (callus) that can then lead to further increased foot pressure in the affected areas. If left untreated, this can lead to tissue damage.

Ischaemic ulcers

Leg ulceration affects around 1% of the population in industrialised countries. The major causes of ulceration include venous insufficiency, diabetes and arterial disease. Although the majority of leg ulcers are due to venous disease, a significant number (around 25%) of patients have arterial insufficiency.[12,13]

Arterial (ischaemic) leg ulcers are due to inadequate blood supply to the skin. This may be caused by an embolism blocking the artery or to a narrowing of the arteries to the legs (atherosclerosis).

It is essential to differentiate between arterial and venous ulcers, as the compression therapy recommended for venous ulcers[14] may lead to skin necrosis, and potentially to amputation, if applied to an arterial leg ulcer.[15]

The key to treatment is improvement in the blood supply, and therefore surgery is often required in order to bypass or clear the blockage or narrowing in the arteries. In a number of patients surgery may not be possible due to:

- patient preference
- patient age and general health
- diffuse, distal arterial disease where the vessels to be reconstructed are very small.

In this instance the role of other therapies (e.g. laser therapy, therapeutic ultrasound, electrotherapy, electromagnetic therapy) which are used in place of surgery needs to be evaluated.

For all the chronic wound types discussed herein there is general professional uncertainty as to effective forms of treatment, thus warranting a systematic review.

The role of physical therapies in wound healing

Low-level laser therapy

Research into the role of low-level laser therapy began in the late 1960s, in Eastern Europe.[16] The research into low-level laser therapy has concentrated on three areas: cellular function, animal studies and human trials.[17] Much of the research undertaken in humans has concentrated on soft-tissue wound healing. Lasers work at a local cellular and humoral level on various biological systems. Increased numbers of fibroblasts, mast cells and degranulation have been observed, together with increased activity of succinic acid dehydrogenase in the tissues surrounding the wound rim. Local prostaglandin changes and increased epithelial activity have also been noted.[18] It is hypothesised that by exposing impaired cells to the photon energy produced by low-level laser therapy, repair may be enhanced via proliferation or cellular migration.[19]

There are a number of different types of laser used for medical purposes, including crystalline laser medium, semiconductor lasers, liquid lasers and gas lasers. For wound healing, gas lasers such as helium–neon (HeNe) and gallium arsenide (GaAs) are used for biostimulation and are the main types of laser on the market. The HeNe laser was the first laser available and is reported to have beneficial effects in both wound healing and dentistry. The HeNe laser has the advantage that it emits red light, which is visible and therefore the blink reflex protects the eyes from it. The GaAs laser has most commonly been used for the treatment of pain and inflammation, and is less suited to wound healing, as it has the deepest tissue penetration of the common therapeutic lasers. Lower doses are used than with the HeNe laser. The GaAs laser has the disadvantage that its light is invisible, and therefore eye protection is required.[20]

Laser therapy is widely used as a treatment for chronic wounds[21] and is often applied by healthcare professionals. However, its role in promoting ulcer healing as an adjunct to, or in the absence of, other proven therapies such as compression remains unclear.

Therapeutic ultrasound

The mechanisms by which ultrasound is thought to affect wound healing have been reviewed.[22,23] Briefly, the cellular effects of ultrasound can be divided into thermal and non-thermal.[22] The lower intensities of ultrasound used therapeutically mean that any beneficial effects are likely to be due to non-thermal mechanisms.[23] Non-thermal effects include the production of standing waves, acoustic streaming, microstreaming and cavitation. Some of these effects may be beneficial, while others are harmful; standing waves may cause the arrest of blood flow, while cavitation may cause bubble formation within the bloodstream.[22] Careful choice of exposure time and intensity and continuous movement of the ultrasound applicator aims to minimise these effects.

In a number of trials, therapeutic ultrasound has been delivered using different pulse widths, power output from the probe and frequencies.

Electrotherapy

Electrical stimulation has been used for decades as a treatment for chronic wounds[24] and is often applied by healthcare professionals. However, its role in promoting ulcer healing as an adjunct to, or in the absence of, other proven therapies such as compression remains unclear.

Research into the role of electricity in wound healing has been undertaken since at least the 1940s.[25] Experimental animal studies have shown that electrical potentials over the wound during healing are initially positive, becoming negative after the fourth day of healing.[26] 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 with alternating or reversing the polarity of 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.[26] It seems likely that a moist wound environment is essential to maintain endogenous or applied current flow.

Electromagnetic therapy

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. It is often termed pulsed electromagnetic field (PEMF) 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.[27]

Aims and objectives

Aim

The aim was to undertake a systematic review of the evidence of the effectiveness of low-level laser therapy; therapeutic ultrasound, electrotherapy and electromagnetic therapy in the treatment of chronic wounds. This series of reviews has regarded leg and foot ulcers, pressure sores, cavity wounds and surgical wounds healing by secondary intention as chronic wounds.

Objectives

This review sought to answer the following general questions:

- Do low-level laser therapy, therapeutic ultrasound, electrotherapy and electromagnetic therapy increase the healing of chronic wounds?
- If yes, what is the optimum treatment regimen with each therapy?

More specifically, for each therapy this review sought to answer the following questions:

Laser therapy

- Does low-level laser therapy stimulate chronic wound healing?

- If yes, what is the optimum treatment regimen, in terms of source, energy and power?

Therapeutic ultrasound

- Does therapeutic ultrasound stimulate chronic wound healing?

- If yes, what is the optimum treatment regimen, in terms of duration, pulses, power output from the probe, ultrasound frequency, and the length and frequency of treatment?

Electrotherapy

- Does electrotherapy stimulate chronic wound healing?

- If yes, what is the optimum treatment regimen, in terms of polarity, waveform, current density, and the duration and frequency of treatments?

Electromagnetic therapy

- Does electromagnetic therapy stimulate chronic wound healing?

- If yes, what is the optimum treatment regimen, in terms of polarity, waveform, current density, and the duration and frequency of treatments?

Chapter 2
Methods

Search strategy

The search strategy is presented in detail in appendix 1. Briefly, 19 electronic databases, including MEDLINE, EMBASE, CINAHL and the specialised trials register of the Cochrane Wounds Group, and wound care journals were searched for the period up to December 1999. Organisations, manufacturers, researchers and healthcare professionals concerned with wound care were contacted for additional trials. The reference sections of the obtained studies were also searched for further trials.

Inclusion criteria

Types of studies

Prospective randomised controlled trials (RCTs) comparing the therapies outlined below were eligible for inclusion. The size (and hence power) of a study was not an inclusion criterion because sample size itself is not a measure of quality or validity. Leaving the review open to small studies leaves the possibility of pooling similar small studies to increase precision.

Low-level laser therapy

- Low-level laser therapy versus sham or no laser therapy
- head-to-head comparisons of different regimens of laser therapy (e.g. variations in source, energy power, frequency).

Therapeutic ultrasound

- Therapeutic ultrasound versus sham ultrasound or no ultrasound
- different regimens of ultrasound stimulation (e.g. variations in duration of pulses, power output, frequency).

Electrotherapy

- Electrical stimulation versus sham or no stimulation
- different regimens of electrical stimulation (e.g. variations in current, waveform, frequency).

Electromagnetic therapy

- Electromagnetic stimulation versus sham or no electromagnetic therapy
- different regimens of electromagnetic stimulation (e.g. variations in current, waveform, frequency).

Types of participants

Patients of any age and in any care setting and described as having a chronic wound were included. As the means of diagnosis of venous ulceration can differ between trials and is usually not described, it was not possible to apply a standard definition.

Types of outcome measure

The primary outcome was regarded as wound healing. Some measures of wound healing are subjective (e.g. whether a wound is 'improved'); we only included studies which incorporated objective measures of healing, such as the rate of change in ulcer area, time to complete healing and/or the proportion of ulcers healed within the trial period.

Financial costs, quality of life, adverse effects and pain were regarded as secondary outcome measures, and these data were extracted if presented.

All studies

Titles and abstracts of studies identified from each search were assessed against the criteria by one reviewer (KAF) for their relevance and design. Full versions of articles were obtained if from this initial assessment it was deemed possible that the inclusion criteria were satisfied. Rejected articles were checked by another reviewer (NC).

The full text of papers was checked for eligibility (by KAF). This was repeated independently by another reviewer (NC) in order to provide verification. Any disagreement was resolved by discussion.

Data extraction

Details of the studies were extracted and summarised using a data extraction sheet. If data were missing from reports, attempts were made to

TABLE 1 *Summary of studies excluded from the review*

Study	Comparison	Reason for exclusion
Goldin *et al.*, 1981[29]	Electrotherapy versus sham electrotherapy	Not chronic wounds
Jivegard *et al.*, 1995[30]	Electrotherapy versus standard care	Not a wound healing study
Katelaris *et al.*, 1987[31]	Electrotherapy	Not an RCT
Muirhead *et al.*, 1991[32]	Electromagnetic therapy versus standard care	Not chronic wounds
Santoianni *et al.*, 1984[33]	HeNe laser versus standard care	Patients acted as their own internal control

contact the authors to obtain missing information. Studies published in duplicate were included only once. Data extraction was undertaken by one reviewer (KAF) and checked for accuracy by a second (NC). Data were extracted from each study on the following criteria (appendix 3):

- inclusion and exclusion criteria
- method of randomisation
- setting
- treatment and control group interventions
- baseline characteristics of patients (by treatment group)
- extent and duration of follow-up
- results.

Methodological quality

Each study was appraised using a standard checklist to assess the validity of the methods used. Data were extracted on the following aspects of quality:

- use of clear inclusion and exclusion criteria
- adequacy of allocation concealment
- baseline comparability of treatment groups for important variables (e.g. wound size)
- use of intention-to-treat analysis
- extent of loss to follow-up
- use of blinded outcome assessment.

Retrieved trials that did not meet the inclusion criteria are given in *Table 1*.

Data synthesis

The method used to synthesise the studies depended on the quality, design and heterogeneity of the studies identified. Clinical heterogeneity was explored by examining influential factors, such as the parameters of the physical therapy used, the care setting and co-interventions (e.g. compression therapy). Statistical heterogeneity was tested by means of a χ^2 test. For each trial, the relative risk and the 95% confidence intervals (CI) were calculated for all important, dichotomous outcomes (e.g. the number of patients developing new pressure sores). Relative risk (RR) is presented in preference to odds ratios as the latter give an inflated impression of the size of effect where event rates are high, as was the case in these trials.[28] Where synthesis was inappropriate, a narrative overview was undertaken.

Chapter 3
Results

Quality of included studies

All the trials incorporated in this review were considered together for quality assessment (see appendix 4) as they were small in number and suffered from similar methodological flaws.

Thirty studies were identified for inclusion in this review. Generally the quality of the studies was poor, all studies having small sample sizes (6–140 patients). Only 23% of the studies reported an *a priori* estimate of the number of participants required for the study to have sufficient power to detect a clinical effect as statistically significant. The method of treatment allocation was reported as truly concealed in 50% of the studies, while there was blinded outcome assessment in 66% of studies. Baseline ulcer area was not reported in 27% of studies, making the interpretation of results in these studies impossible. Withdrawals occurred in most studies and were recorded by group and cause in 50% of trials, but only one study analysed the results on an intention-to-treat basis.

No economic evaluations were identified.

The results are presented below with reference to the original questions posed by the review for each type of physical therapy.

Studies excluded from the review

The studies excluded from the review and the reasons for their exclusion are given in *Table 1*.

Low-level laser therapy

Four RCTs of laser treatment were eligible for inclusion in this review.[34–37] All examined the use of laser therapy to treat venous leg ulcers. The trials used different laser sources: two used a HeNe laser,[35,37] one used a GaAs laser[31] and the fourth evaluated a combination of laser and ultraviolet light and did not specify the type of laser source.[34]

Healing of venous leg ulcers

Two RCTs compared treatment with laser therapy with sham laser treatment,[36,37] and one study compared laser therapy with 'placebo' (non-coherent unpolarised red light).[35] All three trials were small (sample size 42–46 patients) and none described how the diagnosis of leg ulcer was reached. The HeNe trials both used lasers working at 4 J/cm^2, while the GaAs trial applied 1.9 J/cm^2.

The two trials comparing laser therapy with sham laser therapy found no evidence of a difference between healing rates in ulcers treated with the laser or the sham. However, both trials were small and lacked the power to detect a clinically important difference even if it existed. In the first trial (HeNe),[37] 4/23 (17%) ulcers healed in the laser group compared with 3/23 (13%) in the sham group over 12 weeks (RR = 1.33; 95% CI, 0.34 to 5.3). In the second study (GaAs),[36] a higher rate of healing was achieved, with 13/21 (62%) ulcers healing in the laser group compared with 11/21 (52%) in the sham group (RR = 1.18; 95% CI, 0.7 to 2.0) over the same time period. While these two studies used different laser sources, the decision was taken to pool the results in order to seek evidence for a benefit of laser therapy *per se* (on the grounds that the mechanism of action of the two lasers is presumed to be the same). There was no evidence of heterogeneity by χ^2 test, and pooling the trials did not demonstrate a significant benefit of laser therapy on the healing of leg ulcers (RR = 1.21; 95% CI, 0.73 to 2.03) (*Figure 1*).

The three-arm trial that compared laser alone with non-coherent unpolarised light and laser plus infrared light[35] did demonstrate a significant benefit on ulcer healing associated with laser combined with infrared light, compared with non-coherent light. In the laser plus infrared group 80% of ulcers healed during the 4-week study (RR = 2.4; 95% CI, 1.12 to 5.13). More ulcers healed in the laser-only group (67%) than the non-coherent light group (33%), but this difference was not significant (RR = 2.0; 95% CI, 0.9 to 4.45). The combination of infrared light with laser did not confer a statistically significant benefit on ulcer healing compared with laser alone. Importantly, this trial did not report the baseline ulcer area, which makes it impossible to determine the validity of the results.

In summary, we cannot confidently answer the question of whether low-level laser stimulates ulcer

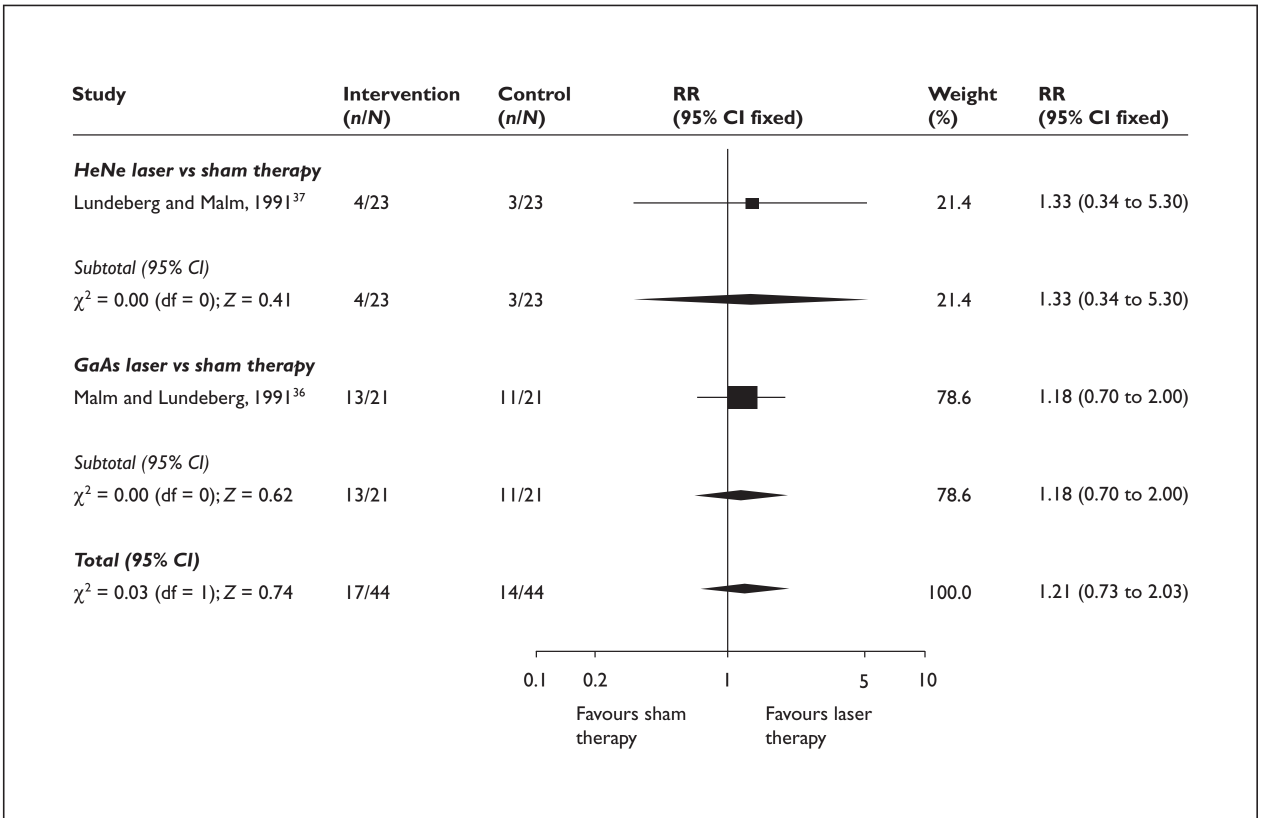

***FIGURE 1** Meta-analysis of the effect of laser therapy versus sham laser therapy on the number of ulcers completely healed at the end of the trial*

healing as the trials were small and one was fatally flawed in that we could not judge the baseline comparability of ulcer area. There is, however, little to suggest that treatment with low-level laser therapy improves the healing of venous leg ulcers.

The trial comparing ulcers treated with laser and ulcers treated with ultraviolet light[34] found no significant difference in healing using an outcome measure of rate of change in ulcer area. However, there were only three patients in each group and the baseline ulcer areas were not given, and therefore the study provides no useful information.

Secondary outcome measures such as costs, quality of life, pain and reliability and acceptability were not measured in any of the RCTs included in this review.

Therapeutic ultrasound

Treatment of venous leg ulcers

Seven RCTs of therapeutic ultrasound were eligible for inclusion in this review.[38–44] Most of these studies involved small sample sizes (12–44 patients); the largest study recruited 108 patients.[40] Patients in all trials were stated to have venous leg ulceration, although only one trial reported the criteria by which this diagnosis was made.[40]

There was no consistency in treatment regimens between the trials: the ultrasound frequency varied between 0.03 and 3 MHz; the intensity was either 0.5 W/cm^2 or 1 W/cm^2; the treatment time varied between 1 and 10 minutes and often depended on ulcer size; the treatment frequency varied between 1 and 3 times a week; and the treatment period ranged between 4 and 12 weeks. Standard treatment varied between trials, and included the application of paste bandage and support bandage, topical fibrinolytic therapy and compression therapy.

Six of the seven RCTs provided either the mean or the median ulcer area at baseline.[39–44] However, in three of the studies the control and intervention groups had dissimilar baseline areas.[39,43,44]

Four trials compared ultrasound therapy with sham,[38,39,41,42] and three trials compared ultrasound therapy with standard treatment.[40,43,44]

Healing of venous leg ulcers

The first study[42] compared active and sham ultrasound over an 8-week period. There was no difference in baseline ulcer size between the treatment and control groups. Six of 19 ulcers (32%) healed in the intervention group, compared with 4/19 (21%) ulcers in the control group (RR = 1.5; 95% CI, 0.5 to 4.48); this difference is not statistically significant.

In a study of slightly longer duration[41] it was reported that 10/22 (45%) ulcers healed over 12 weeks in the ultrasound group compared with 8/22 (36%) ulcers in the sham group (RR = 1.25; 95% CI, 0.61 to 2.56).

A further study[39] compared ultrasound with sham over an 8-week period using the percentage change in ulcer area as the outcome measure. However, the ulcers were larger at baseline in the ultrasound group, which for this outcome favours small ulcers (the sham group). Ulcers in the ultrasound group showed a mean decrease in ulcer area of 35.3% (standard deviation (SD) = 30.06) compared with 7.0% (SD = 36.7) in the sham group. The outcome measure used is against the direction of bias, and therefore the results are more convincing.

The fourth trial[38] compared ultrasound with sham over 4 weeks. However, it failed to report baseline ulcer area and involved only 25 patients. Therefore, imbalance between groups at baseline is highly likely. Outcomes were reported as the mean percentage of initial ulcer area: 66.4 ± 8.8% for ulcers treated with ultrasound compared with 91.6 ± 8.9% for ulcers treated with sham. While this difference is reported as statistically significant ($p < 0.05$), the result cannot be interpreted due to the lack of information about baseline ulcer area.

Three trials compared ultrasound therapy with standard treatment.[40,43,44] The largest trial[40] reported good comparability between groups for baseline ulcer area, but only 76% follow-up was achieved. In this trial 25/41 (61%) ulcers healed in the ultrasound group at 12 weeks compared with 17/41 (41%) in the standard treatment group (RR = 1.47; 95% CI, 0.95 to 2.28).

Ultrasound was compared with standard therapy in a trial of only 12 patients.[43] Ulcers were larger at baseline in the control group, which for an outcome of percentage decrease in ulcer area biases the study in favour of the small ulcers (i.e. the ultrasound group). The mean percentage decrease in ulcer area was 55% at 12 weeks in the ultrasound group compared with 16% in the standard therapy group ($p < 0.007$). While the difference is significant it cannot be interpreted due to the biased distribution of baseline ulcer area.

The final study[44] compared ultrasound with standard therapy in 37 patients. The mean percentage change in initial ulcer area at the end of the study was 41.5% in the ultrasound group and 9.5% in the standard therapy group. However, the baseline ulcer area was larger in the standard therapy group, and therefore the outcome measure favours the ultrasound group, which had smaller ulcers. One ulcer completely healed in the ultrasound group compared to none in the control group.

The four studies[40–42,44] which measured similar outcomes (i.e. the number of ulcers healed at the end of the trial) were tested for heterogeneity, and this was non-significant ($\chi^2 = 0.34$). The notable difference between these trials lies in the dissimilar comparison groups: sham ultrasound[41,42] and standard therapy.[40,44] Despite this, we pooled the results of these four trials (fixed-effects model) while acknowledging that the trials without a sham group may exaggerate any perceived treatment effect. This resulted in a borderline statistically significant result in favour of ultrasound (RR = 1.44; 95% CI, 1.01 to 2.05) (*Figure 2*). The difference in the pooled result remained significant when a random-effects model was applied (the random-effects model includes both within- and between-studies variation in the assessment of the uncertainty of the meta-analysis and is therefore more conservative). If one study[44] (which was biased in favour of ultrasound, and in which only one patient healed) is removed from the analysis the difference is no longer significant (RR = 1.41; 95% CI, 0.99 to 2.02) (fixed-effects model).

The remaining three studies used continuous outcome measures and could not be included in the meta-analysis. The direction of effect was consistently in favour of ultrasound in these trials. However, none reached statistical significance.

Secondary outcome measures such as costs, quality of life, pain, and reliability and acceptability were not measured in any of the RCTs included in this review.

There is insufficient evidence about the effect of therapeutic ultrasound on venous leg ulcers since, despite the existence of seven RCTs (274 patients in total), the results of each of which tended to favour ultrasound, none of these results reached statistical significance, and the methodological quality of the studies tended to be poor.

Treatment of pressure sores

Three RCTs were included that examined the effectiveness of ultrasound treatment in the healing of pressure sores.[45–47] All three studies contained only small numbers of patients, with group sizes varying from 20 patients in three arms to 88 patients in two arms.

Two trials[45,47] compared ultrasound therapy, delivered at approximately 3 MHz, to sham therapy, and the third study[46] compared ultrasound plus ultraviolet light plus laser treatment (820 nm laser diode) with standard wound care.

Healing of pressure sores

There was no consistency between the treatment regimens in the three the trials. Two trials compared therapeutic ultrasound (3 MHz) with sham ultrasound[45,47] and one[46] compared a combination of ultrasound plus ultraviolet light plus laser therapy (820 nm laser diode) with standard treatment. Treatment periods varied from three times a day to five times a week, for up to 12 weeks or until healing had occurred.

Therapeutic ultrasound versus sham therapy

The first trial[45] compared ultrasound three times per week with sham in 40 patients with superficial pressure sores. No data on the baseline comparability of the groups (including data for ulcer area) were reported. In this study 10/21 (48%) pressure sores completely healed in the ultrasound group compared with 8/19 (42%) in the sham group (RR = 1.13; 95% CI, 0.57 to 2.26).

Ultrasound therapy was compared with sham in 88 nursing-home patients with superficial pressure sores.[47] Eighteen of 45 (40%) pressure sores healed in the ultrasound group compared with 19/43 (44%) in the sham group (RR = 0.91; 95% CI, 0.55 to 1.48), and the ulcers in the different treatment groups were comparable for baseline ulcer area and volume. Treatment was given five times a week for 12 weeks or until healing had occurred, and the duration of each treatment was calculated on the basis of the size of the ulcer.

Two trials were considered sufficiently similar to pool[45,47] ($\chi^2 = 0.26$); giving a pooled relative risk of 0.97 (95% CI, 0.65 to 1.45). Thus two studies involving only 128 patients in total found no evidence of a benefit of ultrasound on the healing rates of superficial pressure sores (*Figure 3*).

Therapeutic ultrasound plus ultraviolet light versus laser therapy versus standard treatment

Ultrasound combined with ultraviolet light was compared with laser alone and standard therapy in 20 patients with spinal cord injury and pressure sores up to 1 cm in depth.[46] Groups were broadly similar in terms of the area and depth of sores. The combined ultrasound and ultraviolet therapy healed more pressure sores at 6 weeks (6/6) than did standard therapy (3/6 ulcers). However, this difference was not quite significant (RR = 2.0; 95%

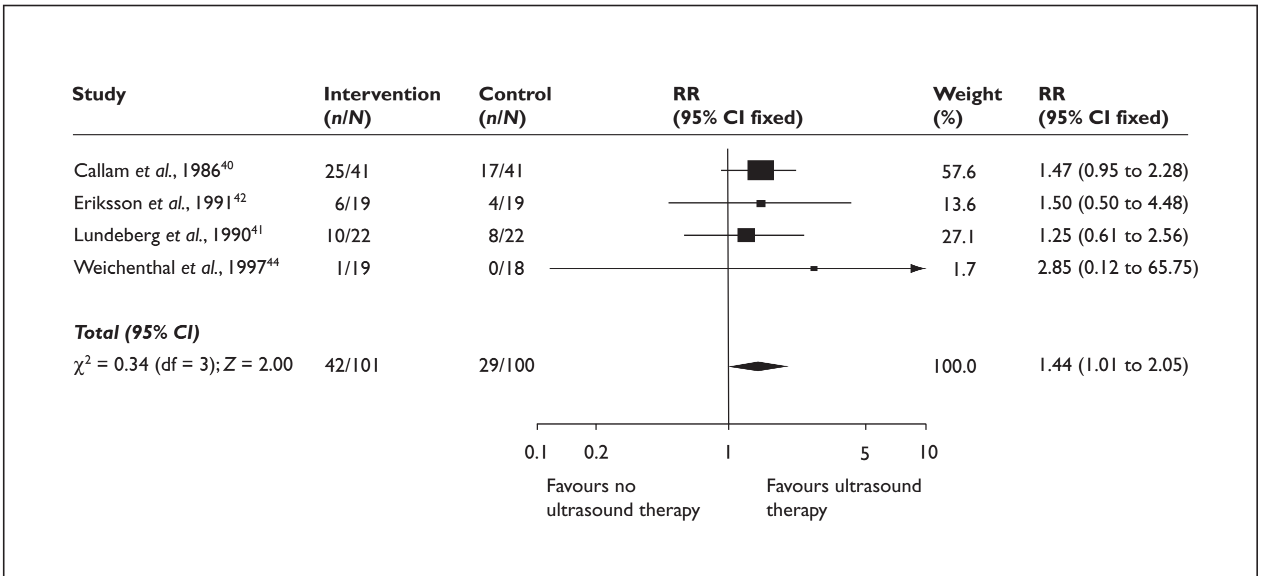

***FIGURE 2** Meta-analysis (fixed-effects model) of the effect of ultrasound therapy versus no ultrasound therapy on the number of ulcers healed*

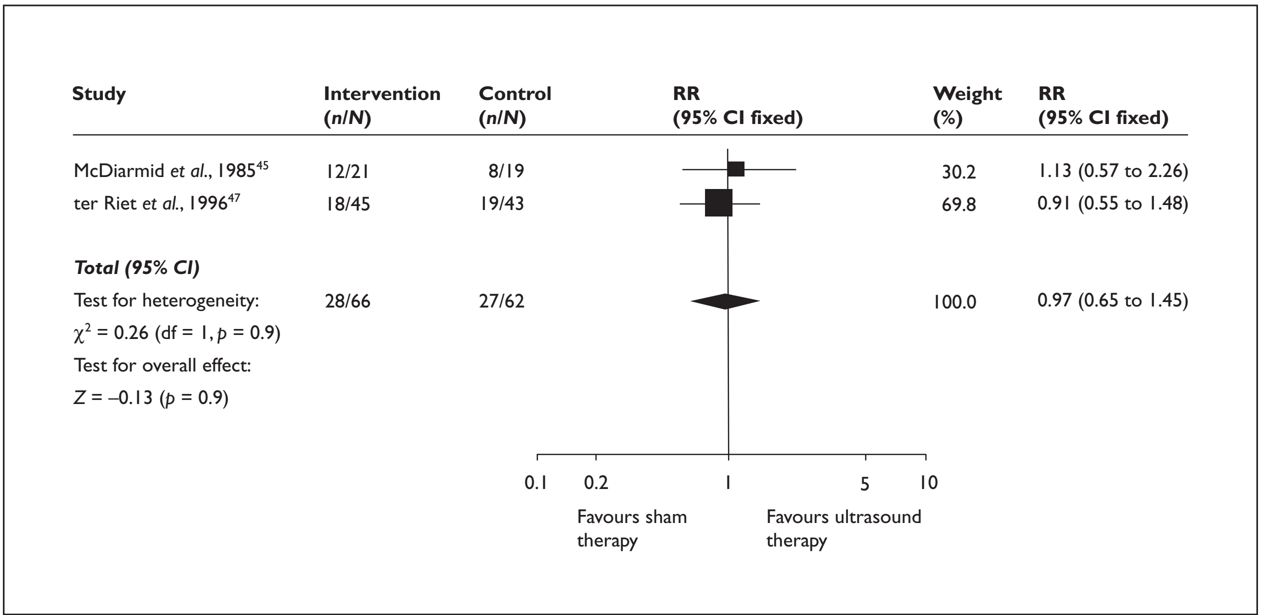

***FIGURE 3** Meta-analysis of the effect of ultrasound therapy versus sham ultrasound therapy on the number of pressure sores healed*

CI, 0.9 to 4.45). The difference in healing was reduced at 12 weeks, by which time 5/6 pressure sores in the standard therapy group had healed. In comparison, ultrasound plus ultraviolet therapy healed more pressure sores at 6 weeks (6/6) than did laser therapy (2/6 ulcers) (RR = 3.0; 95% CI, 0.97 to 9.3). This difference just misses significance due to the extremely small sample size. In the same study, 4/6 laser-treated pressure sores had healed by 12 weeks (RR = 1.5; 95% CI, 0.85 to 2.64). When the results for laser therapy versus standard therapy are compared, there is more healing with standard therapy at both 6 weeks (3/6 versus 2/6) and 12 weeks (5/6 versus 4/6), although neither result is significant.

The secondary outcome measures highlighted (i.e. costs, quality of life, pain, reliability and acceptability) were not measured in any of the RCTs included in this review.

Therapeutic ultrasound versus sham therapy and standard treatment

There are important differences between comparing an intervention to a sham intervention or to the use of standard therapy alone. There may be a placebo effect associated with the sham therapy (i.e. patients think they are receiving ultrasound) and the patients receiving the sham therapy must have the same period of rest and leg elevation as the active ultrasound group. Thus an RCT using sham therapy as the control may report a smaller treatment difference. This is clearly demonstrated in *Figure 4* where trials of equal quality (i.e. used both allocation concealment and blinded outcome assessment) in ultrasound are plotted. It can be seen that there is a greater effect size when ultrasound is compared with ultrasound therapy than when it is compared with sham therapy.

Electrotherapy

Sixteen RCTs[48–63] were included that examined the effectiveness of various electrical therapies on a variety of chronic wounds. The trials were separated into those which evaluated electrotherapy[48–58] and those which evaluated electromagnetic therapy.[59–63] Two trials evaluated electrotherapy in patients with a range of chronic wounds[48,49] and have been grouped under the heading of 'chronic wounds' for the purpose of this report. Five trials[50–54] were identified that evaluated the use of electrotherapy to treat ischaemic ulcers; one which evaluated its use in diabetic ulcers;[55] and three trials of electromagnetic therapy were identified for the treatment of venous ulcers.[59–61]

Chronic wounds

Two RCTs[48,49] were eligible for inclusion in this review. The trials examined the effectiveness of electrotherapy on the healing of pressure, vascular and arterial ulcers. Both trials included patients with ulcers of various aetiologies. The first[48] included patients with stage 4 pressure sores and venous ulcers, while the second[49] included pressure sores, vascular lesions and surgical wounds. The number of patients in each trial was small, varying from 16 to 47. In both trials the baseline ulcer area

Study	Intervention (*n/N*)	Control (*n/N*)	RR (95% CI fixed)	Weight (%)	RR (95% CI fixed)
Ultrasound vs sham therapy					
McDiarmid *et al.*, 1985[45]	10/21	8/19		15.9	1.13 (0.57 to 2.26)
ter Riet *et al.*, 1996[47]	18/45	19/43		36.8	0.91 (0.55 to 1.48)
Subtotal (95% CI)					
Test for heterogeneity:	28/66	27/62		52.7	0.97 (0.65 to 1.45)
χ^2 = 0.26 (df = 1, *p* = 0.61)					
Test for overall effect:					
Z = –0.13 (*p* = 0.9)					
Ultrasound vs standard therapy					
Callam, 1986[40]	25/41	17/41		32.2	1.47 (0.95 to 2.28)
Lundeberg, 1990[41]	10/22	8/22		15.1	1.25 (0.61 to 2.56)
Subtotal (95% CI)				47.3	1.40 (0.96 to 2.04)
Test for heterogeneity:	35/63	25/63			
χ^2 = 0.14 (df = 1, *p* = 0.7)					
Test for overall effect:					
Z = 1.76 (*p* = 0.08)					
Total (95% CI)				100.0	1.18 (0.89 to 1.54)
Test for heterogeneity:	63/129	52/125			
χ^2 = 2.13 (df = 3, *p* = 0.55)					
Test for overall effect:					
Z = 1.16 (*p* = 0.2)					

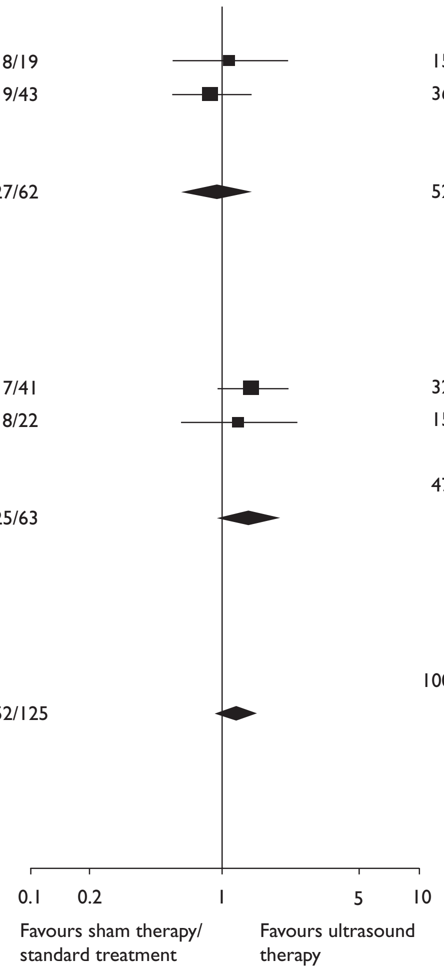

FIGURE 4 *Comparison of the effect of ultrasound therapy with sham therapy and standard treatment on the number of ulcers healed at the end of the trial*

was greater in the control group, which for the outcome used (the percentage change in ulcer area) biases the results in favour of the experimental group. The electrotherapy regimen administered varied substantially between the trials. The length of treatment in the two studies was 4 and 16 weeks.

Healing of chronic wounds

The two trials comparing electrotherapy with sham electrotherapy suggested some benefit associated with treating wounds with electrotherapy. In the first trial[48] all nine ulcers (both pressure and venous ulcers) healed in the electrotherapy group, compared with none in the sham group (RR = 15.2; 95% CI, 1.03 to 223.39). Both groups received standard wound care in addition to the trial treatment. The second trial[49] found a 56% mean reduction in ulcer area in the electrotherapy group after 4 weeks compared with 33% in the sham group. This result was reported as significant ($p < 0.05$). However, no standard deviation or standard error data were presented, and therefore we were unable to check the veracity of this significance (we were unable to contact the author). The study originally recruited 59 patients with 67 wounds. Furthermore, 12 (17%) patients with a total of 17 (25%) of wounds were lost to follow-up; these drop-outs were not reported by treatment group.

While these two trials suggest a benefit of electrotherapy compared with sham electrotherapy or no electrotherapy in healing chronic ulcers, the trials were small, were biased for baseline area and lacked the power to detect clinically important differences. Importantly, one study[49] incorporated patients with multiple wounds, but regarded the wound as the unit of analysis. This approach is flawed because separate wounds on the same patient cannot be regarded as independent.

It is not possible to identify an optimum protocol for the use of electrotherapy as there was no consistency in the electrotherapy treatment regimens used in the three trials.

Venous leg ulcers

No RCTs of the use of electrotherapy in treating venous leg ulcers were identified.

Ischaemic ulcers

Five studies examined electrotherapy as a treatment for ischaemic ulcers.[50–54] These studies were published between 1969 and 1997, and the treatment regimens used varied. Two studies[50,51] included patients with two ulcers, randomising one ulcer to the intervention group and one ulcer to the control group. The other studies randomised individuals, not wounds, to the treatment or control groups. Only one study[53] reported the baseline ulcer area. It is also a feature of each of these studies that they had small sample sizes, varying from 12 to 66 patients.

Healing of ischaemic ulcers

Three trials have compared the use of electrotherapy with various standard therapies[50–52] and one has compared electrotherapy with sham treatment.[53] The fifth study[54] studied patients with non-reconstructable Fontaine stage 4 ulcers or gangrene.

In the first study comparing electrotherapy with standard therapies,[50] 6/8 (75%) ulcers healed in the electrotherapy group compared with none in the standard therapy group (RR = 13.0; 95% CI, 0.85 to 198.15). In this study both groups received standard therapy of debridement where required, and cleansing with an antibacterial detergent. Details of the baseline ulcer area were not provided by the authors. Each patient had two ulcers and therefore acted as their own control. It is noteworthy also that the average age of patients in this study was 25.8 years (10–41 years). Most studies examining chronic ulceration involve populations over the age of 60 years.

Patients were also used as their own controls in a study comparing electrotherapy combined with standard therapy against standard therapy alone.[51] The objective outcome for the study was the percentage ulcer area healed at 12 weeks in the six patients recruited to the study. The electrotherapy group had a mean healing of 74%, compared with 27% in the standard therapy group. No variance or baseline ulcer area data were reported, which makes interpretation of the results impossible.

In the most recent study comparing electrotherapy and standard treatment[52] no ulcers healed in either group. The results of this study are confounded by the fact that the 15 patients receiving electrotherapy were also treated with a variety of topical measures. These differed from the those given to the patients in the standard treatment group, although little detail about the standard regimen was reported. At end of treatment (5 weeks), ulcers in the electrotherapy group had a mean reduction in volume of 4.24 cm^3 (SD = 1.32) versus a mean reduction of 1.76 cm^3 (SD = 1.14) in the control group ($p < 0.01$). This difference is in the same direction as the bias in baseline volume (where experimental ulcers were larger), and therefore the results are impossible to interpret.

The fourth study[53] compared electrotherapy with sham electrotherapy in 59 patients with 67 wounds. The primary outcome measure was the percentage of initial wound size at the end of the 4-week study period. The electrotherapy group had 44% of initial wound size at the end of the trial, compared with 67% of initial wound size in the control group ($p < 0.02$). However, the smaller mean baseline area in the intervention group favours the outcome measure used (i.e. the percentage reduction in wound size), thus biasing the results. It is also worth noting that 20% of the patients recruited into the study and 25% of the wounds were lost to follow-up, although these losses were not reported by group.

A fifth study[54] compared electrotherapy in combination with intravenous prostaglandin therapy to prostaglandin therapy alone in non-reconstructable ulcers classed as Fontaine stage 4. The presence of gangrene for more than 4 weeks was also an inclusion criterion. This study found that 31/45 (69%) ulcers healed in the combined electrotherapy and prostaglandin group compared with 7/41 (17%) of ulcers in the prostaglandin group (RR = 4.03; 95% CI, 2.00 to 8.15). However, no details of baseline area were reported.

Overall, the results of these trials are difficult to interpret as those trials of reasonable quality (i.e.

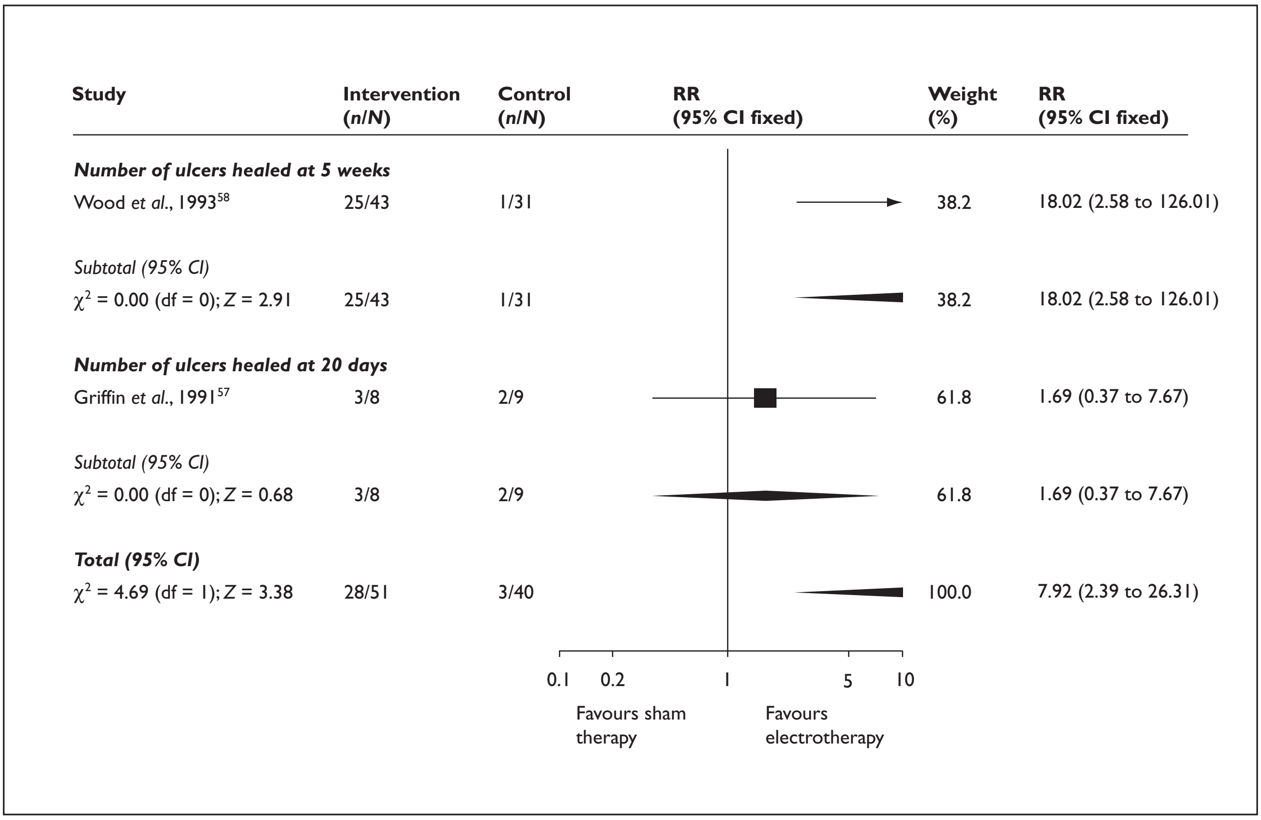

***FIGURE 5** Meta-analysis of the effect of electrotherapy versus sham electrotherapy on the healing of pressure sores*

having both allocation concealment and blinded outcome assessment) were biased in favour of effect for baseline area. None of the studies comparing electrotherapy with sham therapy[50–52] provided baseline ulcer data. One study[53] demonstrated a significant percentage reduction in ulcer size, but did not report the baseline ulcer area and studied only 50 patients. Each study used entirely different treatment parameters, and it is therefore impossible to recommend an electrotherapy treatment regimen.

Diabetic ulcers

One study examined the effectiveness of the use of electrotherapy for the treatment of diabetic ulcers.[55] Patients were recruited and randomised to receive electrical nerve stimulation at 80 Hz, pulse width 1 ms, for 20 minutes twice daily, 7 days a week for 12 weeks, plus standard treatment. The control group received sham electrical nerve stimulation plus standard treatment of cleansing, paste and support bandage and exercise.

Healing of diabetic ulcers

It was reported that 10/32 (31%) ulcers in the electrotherapy group healed compared with 4/32 (12%) ulcers in the sham electrotherapy group (RR = 2.5; 95% CI, 0.87 to 7.15). In this trial 8/32 patients in the electrotherapy group and 5/32 in the sham group were lost to follow-up. In our analysis we regarded these losses as treatment failures. While there is a trend towards greater healing in the electrotherapy group, the result is not statistically significant.

Treatment of pressure sores

Three RCTs comparing electrotherapy with sham therapy for the treatment of pressure sores were suitable for inclusion in this review.[56–58]

The first of these RCTs[56] recruited patients with stage 2, 3 or 4 pressure ulcers, who were randomised to receive either electrical stimulation twice daily for 4 weeks or sham stimulation. Both groups received standard treatment of cleansing with normal saline, a wound dressing (type not stated), and turning to relieve pressure on the affected area. After 4 weeks there was a mean percentage area of ulcer healed of 49.8% (SD = 30.9) in the electro-therapy 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 ulcer healing favoured the control group.

The second study[57] examined only 17 male patients with spinal cord injury and a pressure sore. Participants were randomised to receive electrotherapy plus standard treatment or sham therapy plus standard treatment. The standard treatment consisted of wound cleansing and dressing. In this trial 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 to 7.67).

The final study of this type[58] compared electrotherapy with sham therapy for the treatment of chronic pressure ulcers. Both groups received standard treatment of wound cleansing, moist dressing and whirlpool baths. After 8 weeks 25/43 (58%) ulcers in the electrotherapy group had healed, compared with 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.

Two studies[50,51] were considered sufficiently similar to pool ($\chi^2 = 2.16$) and gave a pooled relative risk of 7.91 (95% CI, 3.32 to 18.85) (*Figure 5*). This demonstrates a statistically significant increase in the healing of pressure sores treated with electrotherapy compared with sham therapy. However, as this result is drawn from two small studies with a total of 91 patients, the results should be interpreted with caution.

Electromagnetic therapy

Electromagnetic therapy is distinct from other forms of electrotherapy in that it provides a field effect rather than a direct electrical effect or a form of radiation.

Treatment of venous leg ulcers

Three RCTs of electromagnetic therapy for the treatment of venous leg ulcers were included in this review.[59–61] Each trial contained a small number of patients, varying from 19 patients in three arms to 44 patients in two arms. Different treatment parameters and standard concomitant therapies were used in each trial, and treatment was given over 50–90 days. Each trial provided detailed baseline data of the ulcers.

Healing of venous leg ulcers

Two trials compared electromagnetic therapy with sham therapy[59,60] and one trial[61] compared electromagnetic therapy with standard topical treatments.

The first study[59] compared electromagnetic therapy with sham therapy given over a period of 90 days. Twelve of 18 (66%) ulcers healed in the electromagnetic therapy group compared with 6/19 (32%) in the sham therapy group (RR = 2.11; 95% CI, 1.01 to 4.42). If the four (18%) patients from the electromagnetic therapy group and three (14%) patients from the sham therapy group who were lost to follow-up are regarded as treatment failures, the difference is not significant (RR = 2.0; 95% CI, 0.92 to 4.37). In the second study,[60] 2/10 (20%) venous ulcers healed in the electromagnetic therapy group, compared with 2/9 (22%) in the sham therapy group (RR = 0.9; 95% CI, 0.16 to 5.13) after a 50-day period All patients received compression therapy, and had ulcer dressings applied by community staff. No drop-outs were reported in this study.

The results of these two studies were pooled using a fixed-effects model. Overall, more ulcers treated with electrotherapy healed than did those treated with sham therapy, but this difference was not significant (RR = 1.79; 95% CI, 0.91 to 3.51).

In a third study,[61] pulsed electromagnetic therapy was compared with standard care. All patients received compression therapy. On average, ulcers in the electrotherapy group had decreased in size by 47% at 8 weeks, while in the control group ulcers increased in size by 49% over the same time period ($p < 0.0002$, analysis of variance). The ulcers were matched at baseline for size.

Overall, these three small, poor-quality trials provide no good evidence of a positive benefit of electromagnetic therapy for the healing of venous leg ulcers. Each of the RCTs included in this review delivered electromagnetic therapy using a variety of electrical and magnetic parameters, over different time periods and with differing treatment regimens. It is therefore impossible to identify an optimum regimen from these trials.

Treatment of pressure sores

Two studies of the use of electromagnetic therapy for the treatment of pressure sores were included in the review.[62,63]

The first of these studies[62] was a three-arm study, comparing electromagnetic therapy with electromagnetic therapy in combination with standard therapy and with standard therapy alone. At the end of the 2-week treatment period 17/20 (85%) ulcers had healed in the electrotherapy group compared with no ulcers in either of the other two groups (n = 5 and 5) (RR = 10; 95% CI, 0.7 to 143.7). However, this trial was extremely small, and the process of randomisation was not described, despite the unequal distribution between groups.

The second study[63] was a straight comparison between electromagnetic therapy and sham therapy in 30 male patients with a spinal cord injury and a grade 2 or 3 pressure sore. Different outcomes were presented for the two grades of pressure sore. After 1 week in the stage 2 pressure sores the median area of ulcer healed was 84% in the electromagnetic therapy group and 40% in the sham therapy group (p = 0.01). As the stage 2 pressure sores were significantly smaller at baseline in the electrotherapy group than in the sham group, this result goes with the direction of bias, as the outcome (percentage healing) favours smaller ulcers. For stage 3 pressure sores, 3/5 (60%) sores healed in the electromagnetic therapy group compared with none in the sham therapy group (RR = 7; 95% CI, 0.45 to 108.26).

These two studies were small and of questionable validity, and therefore they provide no clear evidence of a benefit of electromagnetic therapy on pressure sore healing. Secondary outcome measures such as financial costs, quality of life, pain and acceptability were not measured in any of the RCTs included in this review.

Chapter 4
Discussion

Low-level laser therapy

Treatment of venous leg ulcers

There is insufficient evidence to suggest a benefit of treating venous ulcers with low-level laser therapy. The only suggestion of a therapeutic benefit was given in one small RCT where the combination of laser and infrared light led to a significant improvement in the healing rates of venous ulcers.[42] However, the results of this trial and the others included in this review were drawn from small studies and no clear inclusion criteria for venous leg ulcers were given and there was poor baseline comparability between study arms. Thus the results of the trials included in this review should be viewed with caution.

Therapeutic ultrasound

Treatment of venous leg ulcers

There is no clear, reliable evidence of a benefit of treating venous leg ulcers with therapeutic ultrasound. Only seven small trials were included in this review, with a total of 269 patients. Thus it is impossible to determine clinically important effects of this treatment modality.

Treatment of pressure sores

The results of the studies included in this review do not suggest a benefit associated with therapeutic ultrasound in the healing of pressure sores. All the trials included involved small numbers of patients, different regimens of therapeutic ultrasound and differing follow-up periods. The trials also had inadequate staging of pressure sores and baseline comparisons. Thus the results should be viewed with caution.

Electrotherapy

Treatment of chronic wounds

The two small trials identified suggest a benefit associated with electrotherapy compared with sham electrotherapy or no electrotherapy to heal chronic ulcers. However, the trials were biased for baseline area and lacked the power to detect clinically important differences. Importantly, one study[49] incorporated patients with multiple wounds, but regarded the wound as the unit of analysis. This approach is flawed, because separate wounds on the same patient cannot be regarded as independent. As such, it is impossible to draw conclusions about the effectiveness of electrotherapy to treat chronic wounds.

Treatment of ischaemic ulcers

The results of the five studies eligible for inclusion in this section of the review are difficult to interpret as the trials were small and mostly of poor quality. Those trials that had superior methodological quality were biased for baseline ulcer area. As such, no recommendations for practice can be made.

Treatment of diabetic ulcers

The one trial identified demonstrated no significant difference in ulcer healing between the intervention and control groups. The number of ulcers healing in both groups was very small. Therefore, no significant benefit was demonstrated for the use of electrotherapy to treat diabetic ulcers.

Treatment of pressure sores

The three trials identified suggest a benefit associated with using electrotherapy to treat pressure sores. However, this suggestion is drawn from three small studies with a total of only 140 patients, and therefore the results should be viewed with caution.

Electromagnetic therapy

Treatment of venous leg ulcers

Only three small trials with a total of 92 patients were identified. These trials provided no evidence of a benefit of electromagnetic therapy for venous leg ulcers.

Treatment of pressure sores

Two small trials, with a total of 55 patients, were identified. These provide no clear evidence of a benefit of electromagnetic therapy for the treatment of pressure sores.

Secondary outcome measures

None of the secondary outcome measures highlighted at the start of the review (i.e. financial costs, quality of life, adverse effects, pain) were addressed in any of the trials included in the review. It is therefore impossible to provide any conclusions on these issues.

Chapter 5

Conclusions

Implications for clinical practice

There is insufficient evidence to state whether the use of any of the physical therapies identified for this review are beneficial or not in the treatment of any of the chronic wounds studied.

Implications for future research

Further research is required to clarify the relationship between the various physical therapies and chronic wound healing. The most promising physical therapies for further investigation are ultrasound for the treatment of venous leg ulcers and electrotherapy for the treatment of pressure sores. Future research should include detailed reporting of co-interventions (e.g. wound dressings, and compression for venous leg ulcers, pressure relief for pressure sores), as these may affect healing and details of their use are essential for the interpretation of results.

In all the studies included in this review the research methodology could be significantly improved, and commissioning groups may wish to consider the following aspects for future research.

- The number of patients in a trial should be based on an *a priori* sample-size calculation.
- A truly objective outcome measure should be used, or wound healing should be expressed as both a percentage and an absolute change in wound area.
- A single reference wound should be selected for each patient.
- Experimental groups should be comparable at baseline.
- Wherever possible, each therapy should be compared with sham therapy.
- A complete and thorough description of concurrent treatments, including secondary dressings, should be given in trial reports.
- Assessment of outcomes should ideally be blind to treatment or be completely objective.
- Survival-rate analysis should be done in all studies that assess wound healing.
- Cost-effectiveness and quality-of-life assessments should be included in addition to objective measures of effectiveness of physical therapies.
- Economic evaluations should be incorporated in trials that are sufficiently large to detect appropriate economic and clinical outcomes.

To prevent publication bias and ensure the inclusion of unpublished trials in systematic reviews, those involved in primary research should make their data available to those undertaking systematic reviews.

Acknowledgements

This study was commissioned by the NHS R&D HTA programme. The authors are indebted to the HTA referees for their perseverance in reading this report and the quality of their comments. The views expressed in this report are those of the authors, who are responsible for any errors.

The authors are extremely grateful to Roz Thompson and Sally Bell-Syer (Secretary and Trial Search Coordinator, respectively, of the Cochrane Wounds Group) for help with searching and careful maintenance of the Trials Register.

References

1. Callam MJ, Ruckley CV, Harper DR, Dale JJ. Chronic ulceration of the leg: extent of the problem and provision of care. *Br Med J* 1985; **290**:1855–6.

2. Lees TA, Lambert D. Prevalence of lower limb ulceration in an urban health district *B J Surg* 1992;**79**:1032–4.

3. Baker SR, Stacey MC, Singh G, Hoskin SE, Thompson PJ. Aetiology of chronic leg ulcers. *Eur J Vasc Surg* 1991;**6**:245–51.

4. Callam M. Chronic leg ulceration: the Lothian and Forth Valley Leg Ulcer Study [ChM thesis]. Dundee: University of Dundee; 1989.

5. Charles H. The impact of leg ulcers on patients' quality of life. *Prof Nurse* 1995;**10**:571–4.

6. Bosanquet N. Costs of venous ulcers – from maintenance therapy to investment programs. *Phlebology* 1992;**7**:44–6.

7. Cullum N, Fletcher AW, Nelson EA, Sheldon TA. Compression bandages and stockings in the treatment of venous leg ulcers. Oxford: Update Software; 1998. Cochrane review, Cochrane Library, Issue 3.

8. Riet ter G. Vitamin C and ultrasound in the treatment of pressure ulcers (dissertation). Maastricht: University of Limburg; 1994.

9. Reiber GE. The epidemiology of diabetic foot problems. *Diabetic Med* 1996;**13**(Suppl 1):S6–11.

10. Kings Fund. Counting the cost. The real impact of non-insulin dependent diabetes. London: Kings Fund Policy Unit; 1996.

11. Moss SE, Klein R, Klein BE. The prevalence and incidence of lower extremity amputation in a diabetic population. *Arch Int Med* 1992;**152**:610–16.

12. Callam MJ, Ruckley CV, Harper DV, Dale JJ. Chronic ulceration of the leg: extent of the problem and provision of care. *Br Med J* 1985; **290**:1855–6.

13. Andersson E, Hansson C, Swanbeck G. Leg and foot ulcer prevalence and investigation of peripheral arterial and venous circulation in a randomized elderly population – an epidemiologic survey and clinical investigation. *Acta Dermatol Venerol* 1993;**73**:57–61.

14. Cullum NA, Fletcher AW, Nelson EA, Sheldon TA. Compression bandages and stockings in the treatment of venous leg ulcers. Oxford: Update Software. Cochrane Library, Issue 4.

15. Callam MJ, Ruckley CV, Dale JJ, Harper DR. Hazards of compression treatment of the leg: an estimate from Scottish surgeons. *Br Med J* 1987; **295**:1382.

16. Mester E. Mester AF, Mester A. The biomedical effects of laser application. *Lasers Surg Med* 1988; **5**:607–14.

17. Basford JR. Low-energy laser therapy: controversies and new research findings. *Lasers Surg Med* 1989;**9**: 1–5.

18. James J. Laser therapy on trial *Primary Health Care* 1994;**4**(Pt 10):18–20.

19. James J. Low-power laser therapy. In: Proceedings of the 5th European Conference on Advances in Wound Management. London: Macmillan; 1996. p. 119–21.

20. Swedish Laser-Medical Society. http://www.laser.nu/lllt/faq1.htm; 1998.

21. Basford JR. Low intensity laser therapy: still not an established clinical tool. *Lasers Surg Med* 1995;**16**: 331–42.

22. Dyson M. Non-thermal cellular effects of ultrasound. *Br J Cancer* 1982;**45**(Pt 5 Suppl):165–71.

23. Dyson M. Mechanisms involved in therapeutic ultrasound. *Physiotherapy* 1987;**73**:116–20.

24. Hewitt GK. Chronic leg ulcers *Physiotherapy* 1956;**42**:43–5.

25. Burr HS, Taffel M, Harvey SC. An electrometric study of the healing wound in man. *Yale J Biol Med* 1940;**12**:483–5.

26. Weiss DS, Kirsner R, Eaglstein WH. Electrical stimulation and wound healing. *Arch Dermatol* 1990;**126**(Pt 2):222–5.

27. Stiller MJ, Pak GH, Shupack JL, Thaler S, Kenny C, Jondreau L. A portable pulsed electromagnetic field (PEMF) device to enhance healing of recalcitrant venous ulcers: a double-blind, placebo-controlled clinical trial. *Br J Dermatol* 1992;**127**: 147–54.

28. Deeks J. Odds ratios should be used only in case control studies and logistic regression analyses. *Br Med J* 1998;**317**:1155–6.

29. Goldin JH, Broadbent NRG, Nancarrow JD, Marshall T. The effects of Diapulse on the healing of wounds: a double blind randomised controlled trial in man. *Br J Plastic Surg* 1981:**34**;267–70.

30. Jivegard LEH, Augustinsson LE, Holm J, Risberg B, Ortenwall P. Effects of spinal cord stimulation in patients with inoperable severe lower limb ischaemia: a prospective randomised controlled trial. *Eur J Endovasc Surg* 1995;**9**:421–5.

31. Katelaris PM, Fletcher JP, Little M, McEntyre RJ, Jeffcoate KW. Electrical stimulation in the treatment of chronic venous ulceration. *Austr NZ J Surg* 1987;**57**:605–7.

32. Muirhead RJ, Place D, Buswell WA, Heselting J. Pulsed electromagnetic energy and pre-tibial lacerations: a randomised clinical trial. *Arch Emerg Med* 1991;**8**:152–60.

33. Santoianni P, Monfrecola G, Martellotta D, Ayala F. Inadequate effect of helium–neon laser on venous leg ulcers. *Photodermatology* 1984;**1**:245–9.

34. Crous L, Malherbe C. Laser and ultraviolet light irradiation in the treatment of chronic ulcers. *Physiotherapy* 1988;**44**:73–7.

35. Bilhari I, Mester AR. The biostimulative effect of low level laser therapy of long-standing crural ulcers using helium neon laser, helium neon plus infrared lasers, and noncoherent light: preliminary report of a randomized double-blind comparative study. *Laser Ther* 1989;**1**(Pt 2):97–8.

36. Malm M, Lundeberg T. Effect of low power gallium arsenide laser on healing of venous ulcers. *Scand J Plastic Reconstruct Surg Hand Surg* 1991;**25**(Pt 3): 249–51.

37. Lundeberg T, Malm M. Low-power HeNe laser treatment of venous leg ulcers. *Ann Plastic Surg* 1991;**27**(Pt 6):537–9.

38. Dyson M, Franks C, Suckling J. Stimulation of healing of varicose ulcers by ultrasound. *Ultrasonics* 1976;**14**:232–6.

39. Roche C, West J. A controlled trial investigating the effect of ultrasound on venous ulcers referred from general practitioners. *Physiotherapy* 1984;**70**:475–7.

40. Callam MJ, Dale JJ, Ruckley CV, Harper DR. Trial of ultrasound in the treatment of chronic leg ulceration. In: Negus D, Jantet G, editors. Phlebology '85. London: Libbey; 1986. p. 625–6.

41. Lundeberg T, Nordstrom F, Brodda-Jansen G, Eriksson SV, Kjartansson J, Samuelson UE. Pulsed ultrasound does not improve healing of venous ulcers. *Scand J Rehab Med* 1990;**22**:195–7.

42. Eriksson SV, Lundeberg T, Malm M. A placebo controlled trial of ultrasound therapy in chronic leg ulceration. *Scand J Rehab Med* 1991;**23**:211–13.

43. Peschen M, Vanscheidt W. Low frequency ultrasound of chronic venous leg ulcers as part of an out-patient treatment. In: Proceedings of the 5th European Conference on Advances in Wound Management. London: Macmillan; 1996. p. 271.

44. Weichenthal M, Mohr P, Stegmann W, Brietbart EW. Low-frequency ultrasound treatment of chronic venous ulcers. *Wound Repair Regeneration* 1997;**5**(Pt 1):18–22.

45. McDiarmid T, Burns PN, Lewith GT, Machin D. Ultrasound in the treatment of pressure sores. *Physiotherapy* 1985;**71**:66–70.

46. Nussbaum EL, Biemann I, Mustard B. Comparison of ultrasound/ultraviolet-C and laser for treatment of pressure ulcers in patients with spinal cord injury. *Phys Ther* 1994;**74**(Pt 9):812–25.

47. ter Riet G, Kessels AGH, Knipschild P. A randomized clinical trial of ultrasound in the treatment of pressure ulcers. *Phys Ther* 1996; **76**(Pt 12):1301–11.

48. Kloth LC, Feedar JA. Acceleration of wound healing with high voltage, monophasic, pulsed current [published erratum appears in *Phys Ther* 1989;**69**(Pt 8):702]. *Phys Ther* 1988;**68**:503–8.

49. Mulder GD. Treatment of open-skin wounds with electric stimulation. *Arch Phys Med Rehab* 1991;**72**: 375–7.

50. Wolcott LE, Wheeler PC, Hardwicke HM, Rowley BA. Accelerated healing of skin ulcer by electrotherapy: preliminary clinical results. *South Med J* 1969;**62**:795–801.

51. Gault WR, Gatens Jr PF. Use of low intensity direct current in management of ischaemic skin ulcers. *Phys Ther* 1976;**56**:265–9.

52. Carley P, Wainapel SF. Electrotherapy for acceleration of wound healing: low intensity direct current. *Arch Phys Med Rehab* 1985;**66**(Pt 7):443–6.

53. Feedar JA, Kloth LC, Gentzkow GD. Chronic dermal ulcer healing enhanced with monophasic pulsed electrical stimulation. *Phys Ther* 1991;**71**:639–49.

54. Claeys LGV, Horsch S. Effects of spinal cord stimulation on ischaemic inflammatory pain and wound healing in patients with peripheral arterial occlusive disease. *Pain Digest* 1997;**7**:200–3.

55. Lundeberg TCM, Eriksson SV, Malm M. Electrical nerve stimulation improves healing of diabetic ulcers. *Ann Plastic Surg* 1992;**29**(Pt 4):328–31.

56. Gentzkow GD, Pollack SV, Kloth LC, Stubbs HA. Improved healing of pressure ulcers using Dermapulse, a new electrical stimulation device. *Wounds: Compend Clin Res Pract* 1991;**3**(Pt 5):158–70.

57. Griffin JW, Tooms RE, Mendius RA, Clifft JK, Vander Zwaag R, el-Zeky F. Efficacy of high voltage

pulsed current for healing of pressure ulcers in patients with spinal cord injury. *Phys Ther* 1991;**71**: 433–42, discussion 442–4.

58. Wood JM, Evans PE III, Schallreuter KU, Wyman MD, Jacobson E, Sufit R, *et al*. A multicentre study on the use of pulsed low-intensity direct current for healing chronic stage II and stage III decubitus ulcers [see comments]. *Arch Dermatol* 1993;**129**: 999–1009.

59. Ieran M, Zaffuto S, Bagnacani M, Annovi M, Moratti A, Cadossi R. Effect of low frequency pulsing electromagnetic fields on skin ulcers of venous origin in humans: a double-blind study. *J Orthopaed Res* 1990;**8**:276–82.

60. Kenkre JE, Hobbs FD, Carter YH, Holder RL, Holmes EP. A randomized controlled trial of electromagnetic therapy in the primary care management of venous leg ulceration. *Family Pract* 1996;**13**(Pt 3):236–41.

61. Stiller MJ, Pak GH, Shupack JL, Thaler S, Kenny C, Jondreau L. A portable pulsed electromagnetic field (PEMF) device to enhance healing of recalcitrant venous ulcers: a double-blind, placebo-controlled clinical trial. *Br J Dermatol* 1992;**127**: 147–54.

62. Comorosan S, Vascilco R, Arghiropol M, Paslaru L, Jieanu V, Stelea S. The effect of Diapulse therapy on the healing of decubitus ulcer. *Romanian J Physiol* 1993;**30**:1–2, 41–5.

63. Salzberg CA, Cooper-Vastola SA, Perez F, Viehbeck MG, Byrne DW. The effects of non-thermal pulsed electromagnetic energy on wound healing of pressure ulcers in spinal cord-injured patients: a randomized, double-blind study. *Ostomy Wound Management* 1995;**41**:42–4, 46, 48.

64. Central Begeleidingsorgaan voor de Intercollegiale Toetsing. Consensus bijeenkomst: behandeling Decubitus. Utrecht: CBO; 1985.

Appendix 1

Databases searched and search strategies

The review was compiled using RCTs from the Cochrane Wounds Group Specialist Trials Register. Multiple and repeated searches have been carried out since 1995, and our searching has, to some extent, been validated by searches carried out by BMJ Publishing Ltd for the publication *Clinical Evidence*. It is not possible at this stage to present a flowchart describing search yields and exclusions, as the search has been ongoing for so many years and initially was part of a larger search covering eight related wound management topics.

The Wounds Group Trials Register was searched up to April 2000 and has been assembled and maintained as described in the following sections.

Electronic searches

MEDLINE

MEDLINE (SilverPlatter version 4.0) was been searched for RCTs and controlled clinical trials from 1966 to December 1997, using a mixture of free text terms and MeSH headings: From January 1998 it was unnecessary to search MEDLINE as this is searched centrally by the UK Cochrane Centre for all trials and the results are transferred to CENTRAL/CCTR. Since January 1998, CENTRAL/CDSR was searched instead of MEDLINE for all issues of the Cochrane Library.

The search strategy used was as follows:

1. decubitus ulcer/ or foot ulcer/
2. leg ulcer/ or varicose ulcer/
3. pilonidal cyst/
4. skin ulcer/
5. diabetic foot/
6. ((plantar or diabetic or heel or venous or stasis or arterial) adj ulcer$).tw.
7. ((decubitus or foot or diabetic or ischaemic or pressure) adj ulcer$).tw.
8. ((pressure or bed) adj sore$).tw.
9. ((pilonidal adj cyst) or (pilonidal adj sinus) or bedsore$).tw.
10. ((diabetic adj foot) or (cavity adj wound)).tw.
11. ((varicose or leg or skin) adj ulcer$).tw.
12. (decubitus or (chronic adj wound$)).tw.
13. ((sinus adj wound$) or (cavity adj wound$)).tw.
14. or/1–13
15. debridement/ or biological dressings/ or bandages/
16. occlusive dressings/ or clothing/ or wound healing/
17. antibiotics/ or growth substances/ or platelet-derived growth factor/
18. fibroblast growth factor/ or electrical stimulation therapy.ti,ab,sh.
19. lasers/ or nutrition/ or surgery/ or surgery, plastic/
20. surgical flaps/ or skin transplantations/ or homeopathy/ or homeopathic/
21. acupuncture therapy/ or acupuncture/ or alternative medicine/
22. alternative medicine/ or massage/ or iloprost/ or alginates/
23. zinc/ or zinc oxide/ or ointments/ or anti-infective agents/
24. dermatologic agents/ or colloids/ or cushions/ or wheelchairs/
25. beds/ or wound dressings/
26. (debridement or dressing$ or compress$ or cream$ or (growth adj factor$)).tw.
27. (pressure-relie$ or (recombinant adj protein$) or bandag$ or stocking$).tw.
28. (antibiotic$ or (electric adj therapy) or laser$ or nutrition$ or surg$).tw.
29. (homeopath$ or acupuncture or massage or reflexology or ultrasound).tw.
30. (iloprost or alginate$ or zinc or paste$ or ointment$ or hydrocolloid$).tw.
31. ((compression adj therapy) or (compression adj bandag$) or wrap$).tw.
32. (bed$ or mattress$ or wheelchair$ or (wheel adj chair) or cushion$).tw.
33. ((wound adj dressing$) or vitamin$ or bind$ or gauze$ or heals or healing).tw.
34. (diet or lotion$ or infect$ or reduc$ or (wound adj healing)).tw.
35. (treat$ or prevent$ or epidemiol$ or aetiol$ or etiol$ or therap$ or prevalence or incidence).tw.
36. or/15–35
37. 14 and 36
38. random allocation/ or randomized controlled trials/
39. controlled clinical trials/ or clinical trials phase I/ or clinical trials phase II/
40. clinical trials phase III/ or clinical trials phase IV/ or clinical trials overviews/

41. single-blind method/ or double-blind method/
42. publication bias/ or review/ or review, academic/
43. review tutorial/ or meta-analysis/ or systematic review/
44. ((random$ adj controlled adj trial$) or (prospective adj random$)).tw.
45. ((random adj allocation) or random$ or (clinical adj trial$) or control$).tw.
46. ((standard adj treatment) or compar$ or single-blind$ or double-blind$).tw.
47. (blind$ or placebo$ or systematic$ or (systematic adj review)).tw.
48. (randomized controlled trial or clinical trial).pt. or comparative study.sh.
49. or/38–48
50. 37 and 49
51. limit 50 to human
52. burns/ or wounds, gunshot/ or corneal ulcer/ or exp dentistry/
53. peptic ulcer/ or duodenal ulcer/ or stomach ulcer/
54. ((peptic adj ulcer) or (duodenal adj ulcer) or traum$).tw.
55. ((aortocaval adj fistula) or (arteriovenous adj fistula)).tw.
56. (bite adj wound$).tw.
57. or/52–56
58. 51 not 57

CENTRAL/CDSR

The CENTRAL/CSDR was searched on the Cochrane Library CD-ROM. The search strategy used was as follows:

1. ((DECUBITUS and ULCER*) or (VARICOSE and ULCER*))
2. ((LEG or LEGS) and ULCER*)
3. ((FOOT or FEET) and ULCER*)
4. ((LEG or LEGS) and VARICOSE)
5. (SKIN and ULCER*)
6. SKIN-ULCER*:ME
7. ((FOOT or FEET) and DIABETIC)
8. (((((PLANTAR or DIABETIC) or HEEL) or VENOUS) or STASIS) or ARTERIAL) and ULCER*)
9. ((ISCHEMIC or PRESSURE) and ULCER*)
10. ((BED or BEDS) near (SORE or SORES))
11. (PRESSURE near (SORE or SORES))
12. (PILONIDAL and CYST*)
13. (PILONIDAL and SINUS*)
14. (PILONIDAL and ABSCES*)
15. ((WOUND or WOUNDS) and CAVITY)
16. ((WOUND or WOUNDS) and SINUS*)
17. ((WOUND or WOUNDS) and CHRONIC)
18. ((WOUND or WOUNDS) and DECUBITUS)
19. WOUND-INFECTION*:ME
20. ((WOUND or WOUNDS) and MALIGNANT)
21. WOUND-HEALING*:ME
22. WOUNDS-GUNSHOT*:ME
23. ((GUN or GUNS) or GUNSHOT)
24. WOUNDS-STAB*:ME
25. LACERATION*
26. SURGICAL-WOUND-DEHISCENCE*:ME
27. BITES-AND-STINGS*2:ME
28. ((BITE or BITES) or BITING)
29. TRAUMATOLOGY*:ME
30. BURNS*:ME
31. (WOUND* and BURN*)
32. (BURN* or SCALD*)
33. ((SITE or SITES) near DONOR)
34. SELF-MUTILATION*:ME
35. ((STAB or STABS) or STABBING)
36. SOFT-TISSUE-INJURIES*:ME
37. ((((((((((#1 or #2) or #3) or #4) or #5) or #6) or #7) or #8) or #9) or #10) or #11) or #12)
38. ((((((((((#13 or #14) or #15) or #16) or #17) or #18) or #19) or #20) or #21) or #22) or #23) or #24)
39. (((((((((((#25 or #26) or #27) or #28) or #29) or #30) or #31) or #32) or #33) or #34) or #35) or #36)
40. (#37 or #38 OR #39)
41. DENTAL
42. (#40 not #41)
43. CORNEAL
44. (#42 not 43)
45. DUODENAL-ULCER*1:ME
46. (#44 not #45)
47. CORNEAL-ULCER*1:ME
48. (#46 not #47)
49. CORNEAL-DISEASES*:ME
50. (#48 not #49)
51. ACNE
52. (#50 not #51)
53. BEDNET
54. (#52 not #53)

CINAHL

The Cumulative Index of Nursing and Allied Health Literature (CINAHL) (SilverPlatter version 4.0) was been searched for the period from its inception to July 1999. The search strategy used was as follows:

1. (pressure-ulcer* or foot-ulcer* or leg-ulcer* or skin-ulcer*) in de
2. (diabetic-foot* or diabetic-neuropathies*) in de
3. ((diabetic-angiopathies*) in de) or diabetes-mellitus/complications/ all age subheadings

4. (pilonidal-cyst* or surgical-wound-infection*) in de
5. (plantar or diabetic or heel or venous or stasis or (arterial near ulcer*)) in ti,ab
6. (decubitus or foot or diabetic or ischaemic or (pressure near ulcer*)) in ti,ab
7. (pressure or (bed near sore*))in ti,ab
8. ((pilonidal near cyst) or (pilonidal near sinus) or bedsore) in ti,ab
9. (diabetic near foot) or ((cavity near wound)in ti,ab)
10. (varicose or leg or (skin near ulcer*)) in ti,ab
11. ((decubitus or chronic) near wound*) in ti,ab
12. (sinus near wound*) or ((cavity near wound*) in ti,ab)
13. ((burn near wound*) or (gunshot near wound*) or (bite near wound*) or trauma) in ti,ab
14. #1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13
15. (clinical-trials or single-blind-studies or double-blind-studies) in de
16. (control-group or placebos or meta-analysis) in de
17. (random* near clinical near trial*) or ((prospective near random*) in ti,ab)
18. ((random near allocation) or random* or controlled-clinical-trial* or control) in ti,ab
19. (comparison group* or (standard near treatment) or compar*)in ti,ab
20. (single-blind* or (single near blind) or double-blind or (double near blind)) in ti,ab
21. (blind* or placebo* or systematic or (systematic near review)) in ti,ab
22. ((meta analysis or meta-analysis) or (trial* or prospective)) in ti,ab
23. ((clinical-trials) or (comparative-studies)) in de
24. #15 or #16 or #17 or #18 or #19 or #20 or #21 or #22 or #23
25. #14 and #24
26. explode dentistry/ all topical subheadings/ all age subheadings
27. (peptic-ulcer*) or (duodenal-ulcer*) or ((corneal-ulcer*)in de)
28. (peptic near ulcer) or (duodenal near ulcer) or ((corneal near ulcer) in ti,ab)
29. dentist* in de
30. #26 or #27 or #28 or #29
31. #25 not #30

Other databases

Other databases that were searched from the earliest date available until 1997 are:

- EMBASE (SilverPlatter version 4.0)
- ISI Science Citation Index (on BIDS)
- BIOSIS (on EDINA)
- British Diabetic Association Database
- CISCOM (Complementary Medicine Database of the RCCM)
- Conference Proceedings (on BIDS)
- Dissertation Abstracts
- Royal College of Nursing Database (CD-ROM)
- British Nursing Index (on ARC), to December 1998

Handsearching

Journals

The following wound care specialist journals are being prospectively handsearched for all RCTs as follows:

- *CARE – Science and Practice*, 1979–1990 (later *Journal of Tissue Viability*, searched until present)
- *Decubitus*, 1987–1993
- *Journal of Tissue Viability*, 1991–present
- *Journal of Wound Care*, 1991–present
- *Phlebology*, 1986–present.

Conference proceedings

Wound care conference proceedings that have been handsearched for RCTs are:

- Proceedings of the 1st European Conference on Advances in Wound Management, September 1991, Cardiff, UK
- Proceedings of the 2nd European Conference on Advances in Wound Management, October 1992, Harrogate, UK
- Proceedings of the 3rd European Conference on Advances in Wound Management, October 1993, Harrogate, UK
- Proceedings of the 4th European Conference on Advances in Wound Management, September 1994, Copenhagen, Denmark
- Proceedings of the 5th European Conference on Advances in Wound Management, November 1995, Harrogate, UK
- Proceedings of the 6th European Conference on Advances in Wound Management, October 1996, Amsterdam, The Netherlands
- Proceedings of the 7th European Conference on Advances in Wound Management, November 1997, Harrogate, UK
- Proceedings of the 8th European Conference on Advances in Wound Management, April 1998, Madrid, Spain

- 3rd Annual Symposium on Advanced Wound Care, March 1990, Orlando, FL, USA
- 4th Annual Symposium on Advanced Wound Care, April 1991, San Francisco, CA, USA
- 5th Annual Symposium on Advanced Wound Care, April 1992, New Orleans, LA, USA
- 8th Annual Symposium on Advanced Wound Care & Medical Research Forum on Wound Repair, April 1995, San Diego, CA, USA
- 9th Annual Symposium on Advanced Wound Care, April 1996, Atlanta, GA, USA
- Proceedings of Going into the '90s: The Pharmacist and Wound Care, September 1992, London, UK
- Proceedings of the Second Joint British/Swedish Angiology Meeting, 1991, London, UK
- Symposium on Venous Leg Ulcers, 1985, London, UK
- Venous Forum of the Royal Society of Medicine, April 1999, Leeds, UK

Other strategies

Identification of unpublished studies

Several databases were searched (up to December 1997) in an attempt to identify unpublished studies. These include:

- Current Research in Britain (CRIB)
- DHS Database
- SIGLE
- UK National Research Register.

Experts in the field of wound care were contacted to enquire about ongoing and recently published trials in the field of wound care. In addition, manufacturers of wound care materials were contacted for details of the trials they are conducting. Citations within obtained reviews and papers were scrutinised to identify additional studies.

Appendix 2
Advisory panel

Dr Mary Bliss	Department of Medicine for the Elderly, Homerton Hospital, London (now retired)
Professor Andrew Boulton	Department of Medicine, Manchester Royal Infirmary, Manchester
Professor Nick Bosanquet	Department of General Medicine, Imperial College School of Medicine, London
Dr Richard Bull	Department of Dermatology, Homerton Hospital, London
Mr Michael Callam	Department of Vascular Surgery, Bedford Hospital, Bedford
Carol Dealey	Moseley Hall Hospital, Birmingham
Professor Peter Friedman	Department of Dermatology, Royal Liverpool University Hospital, Liverpool (now Southampton)
Mr Brian Gilchrist	Department of Nursing Studies, King's College, London
Dr Keith Harding	Wound Healing Research Unit, University of Wales College of Medicine, University Department of Surgery, Cardiff
Deborah Hofman	Dermatology Department, Churchill Hospital, Oxford
Vanessa Jones	Wound Healing Research Unit, University Department of Surgery, Cardiff
Christina Lindholm	Department of Nursing Research, Uppsala University Hospital, Uppsala
Dr Raj Mani	Southampton University Hospital, Medical Physics Department, Southampton
Andrea Nelson	Department of Nursing, University of Liverpool (now Department of Health Studies, University of York)
Dr Steve Thomas	Surgical Materials Testing Laboratory, Bridgend, Mid Glamorgan
Dr Ewan Wilkinson	Bucks Health Authority, Aylesbury

Appendix 3

Summary of included studies

***TABLE 2** Details of included studies*

Study and design	Inclusion and exclusion criteria	Interventions	Baseline characteristics	Results	Withdrawals	Comments
Crous and Malherbe, 1988,[29] South Africa Study design: RCT (method of randomisation not stated) Objective outcome: percentage of original surface area (observation from photographs regarding wound healing parameters) Setting and length of study: inpatients (5), outpatients (1); 4 weeks	Inclusion criteria: presence of a chronic venous ulcer Exclusion criteria: none stated	1. Laser therapy (3): M3-UP scanning laser, intensity 1.4 mW, 10 minutes, three times weekly for 4 weeks 2. Ultraviolet therapy (3): necrotic tissue, dose ≥E4; granulation tissue, dose E1, three times weekly for 4 weeks Other treatment: saline dressing (group 1, 1; group 2, 1); Granuflex (group 1, 1; group 2, 2); Betadine ointment (group 1, 0; group 2, 1); no mention of compression therapy	Mean age: 1. 75 years 2. 69 years Gender (male/female): 1. 1/2 2. 2/1 No baseline ulcer areas given	% decrease in ulcer size: 1. 49.6% 2. 33.6%	None	Is this really an RCT or just a case series?
Bihari and Mester, 1989,[35] Hungary Method of randomisation: unclear Objective outcome: complete healing (blind) Subjective outcomes: 'improved', 'no change', 'got worse' Setting and length of treatment: setting unclear; 9 months of treatment, one session a week	Inclusion criteria: 'crural' ulcers resistant to conventional therapy Exclusion criteria: unclear	1. Hand-held HeNe laser, 4 J/cm^2 (15) 2. Scanned HeNe laser and infrared, 4 J/cm^2 (15) 3. Non-coherent unpolarised red light, 4 J/cm^2 (15) All patients received standard treatment, including compression bandaging and antibiotics (no detail given regarding compression)	Mean ulcer area: no baseline data given	1. 10/15 (66%) healed, 4 improved, 1 no change 2. 12/15 (80%) healed, 2 improved, 1 no change 3. 5/15 (33%) healed, 3 improved, 3 no change, 2 worse	3. Two (no reason given)	

Continued

TABLE 2 contd *Details of included studies*

Study and design	Inclusion and exclusion criteria	Interventions	Baseline characteristics	Results	Withdrawals	Comments
Malm and Lundeberg, 1991,[36] Sweden Method of randomisation: permuted blocks Objective outcome: time to healing (weeks); analysis by life table; blinded Setting and length of treatment: setting unclear; 12 weeks, twice weekly	Inclusion criteria: venous leg ulcers; patients from medicine, surgery, primary care Exclusion criteria: skin allergy to standard treatment, evidence of peripheral vascular disease, rheumatoid arthritis or diabetes mellitus; traumatic cause; ankle pressure <75 mmHg	1. GaAs laser: wavelength 904 nm; power 4 mW (average), 10 mW (peak), 3.8 kHz; energy 1.96 J/cm^2 2. Sham laser (21) Both groups received standard treatment: saline cleansing, paste bandage, elastic diachylon bandage at 15–25 mmHg; exercise programme	Mean (range) ulcer area: 1. 12 cm^2 (4–52 cm^2): 3 deep (>1 cm), 18 superficial (<1 cm) 2. 14 cm^2 (3–44 cm^2): 1 deep (>1 cm), 20 superficial (<1 cm) Other characteristics: 1. 21 patients (11 women, 10 men); mean age 60 years (range 43–77 years) 2. 21 patients (12 women, 9 men), mean age 61 years (range 46–76 years)	No. of ulcers healed at 12 weeks: 1. 13/21 (62%) 2. 11/21 (52%)	1. Allergy (1), unable to attend for treatment (3) 2. Allergy (1), unable to attend for treatment (4), pain (1)	*A priori* sample-size calculation. 80% power $p < 0.05$ to detect a 440% difference in healing
Lundeberg and Malm, 1991,[37] Sweden Method of randomisation: permuted blocks Objective outcome: healed ulcers; percentage change in area (blind) Setting and length of treatment: setting unclear; 12 weeks, twice weekly	Inclusion criteria: venous ulcers; referral from medicine, surgery or primary care; consent Exclusion criteria: allergy to standard treatment; evidence of peripheral vascular disease, rheumatoid arthritis or diabetes mellitus; traumatic ulcer	1. HeNe laser (23): wavelength 632.8 nm; power 6 mW; energy 4 J/cm² 2. Placebo laser (23) Both groups received standard treatment: saline cleansing, paste bandage, support bandage, exercise sheet	Mean ulcer area: 1. 9 cm^2 (3–32 cm^2): 5 deep (≥1 cm), 18 superficial (<1 cm) 2. 11 cm^2 (4–36 cm^2): 2 deep, 21 superficial Other characteristics: 1. 23 patients (15 women, 8 women), mean age 62 years (range 49–73 years) 2. 23 patients (14 women, 9 men), mean age 54 years (range 41–69 years)	No. of ulcers healed at 12 weeks: 1. 4/23 (17%) 2. 3/23 (13%) Difference not significant % ulcer area healed at 12 weeks: 1. 48 ± 9% 2. 49 ± 12%	1. 8/23 (35%): allergy to paste (3), pain (1), unable to attend (4) 2. 4/23 (17%): allergy (1), pain (1), unable to attend (2) Difference not significant	80% power; $p < 0.05$ to detect 40% difference in healing

Continued

TABLE 2 contd *Details of included studies*

Study and design	Inclusion and exclusion criteria	Interventions	Baseline characteristics	Results	Withdrawals	Comments
Dyson *et al.*, 1976,[38] UK Study design: controlled (allocation by alternation); if bilateral ulcers present, one included in intervention and one in control group (allocation not stated) Objective outcome: decrease in the surface area of the ulcer as measured from photographic transparencies or tracings Setting and length of treatment: measurement (as above) at baseline and at weekly intervals; 4 weeks minimum, three times weekly	Inclusion criteria: venous ulceration Exclusion criteria: dermatitis artefacta; arterial insufficiency	1. Skin immediately adjacent to the ulcer treated with insonation (13): intensity 1.0 W/cm^2, frequency 3 MHz, pulsing regimen 2:10 ms, treatment time 5 minutes for ulcers ≤2.5 cm^2, plus 1 minute for each extra 0.5 cm^2 of ulcer area, to a maximum of 10 minutes 2. Mock insonation (12): calculated and given in the same manner as the insonation Other characteristics: ulcers dressed throughout the trial as per pre-trial, described as bathing with normal saline or Eusol, covered with a non-absorbent dressing and a crepe bandage or elastic stockings	No baseline data (e.g. ulcer area) presented	% of initial ulcer area at 28 days: 1. 66.4 ± 8.8% 2. 91.6 ± 8.9% $p < 0.05$ No significant difference between age, sex or initial size of ulcer, but no baseline areas provided	1. None 2. Two: cellulitis (1), self-inflicted skin damage (1)	Tracings and photographs were coded to avoid assessor bias

Continued

TABLE 2 contd *Details of included studies*

Study and design	Inclusion and exclusion criteria	Interventions	Baseline characteristics	Results	Withdrawals	Comments
Roche and West, 1984,[39] UK Study design: RCT; level of concealment unclear Objective outcome: average area of ulcer Setting and length of treatment: physiotherapy department; three times weekly for 4 weeks and again at 8 weeks; tracings taken at baseline, weekly up to 4 weeks and at 8 weeks	Inclusion criteria: diagnosis of a venous ulcer, minimum area 2 cm^2; ambulatory Exclusion criteria: ulcer depth 5 mm; ulcer in a non-continually weight-bearing area; ultra-sound treatment given prior to inclusion in the trial	1. Ultrasound to the periphery of the ulcer (13): frequency 3 MHz, intensity 1 W/cm^2, pulse ratio 1:4 (2 ms active, 8 ms rest); duration of treatment varied with ulcer size (ulcers <5 cm^2, 5 minutes, plus 1 minute for every extra 1 cm^2, to a maximum of 10 minutes) 2. Mock ultrasound (13): intensity 0 W/cm^2 Other conditions: any treatment being given prior to study inclusion continued throughout the trial; neither patients nor those measuring the ulcers were aware of the treatment being received (the instrumentation panel was shielded from all patients at the time of treatment)	Two males in each group Mean age: 1. 70.1 years 2. 75.9 years Mean ulcer area: 1. 32.5 cm^2 2. 23.6 cm^2 Duration of ulcer: 1. 5.37 years (range 0.16–36 years) 2. 12.35 years (range 0.33–40 years)	Greater reduction in ulcer size in the active treatment group No complete healing data given An increase in ulcer size occurred after 4 weeks of treatment in both groups No detail given regarding compression		Other treatments used (group 1/group 2): Dry dressing 5/6 Jelonet 1/3 Bactigras 3/2 Viscopaste 1/1 Germolene 1/1 Fucidin 1/0 Betodine 1/0

Continued

***TABLE 2 contd** Details of included studies*

Study and design	Inclusion and exclusion criteria	Interventions	Baseline characteristics	Results	Withdrawals	Comments
Callam *et al*., 1986,[40] Scotland Study design: RCT, remote randomisation Objective outcome: decrease in ulcer area Setting and length of study: physiotherapy departments; 12-week follow-up	Inclusion criteria: attending one of five physiotherapy departments for treatment of a chronic leg ulcer (whatever source) Exclusion criteria: failure to obtain consent from patient or doctor; allergy to standard treatment; impalpable ankle pulses	1. Standard treatment (56): cleansing with standard regimen of cemtrimide 1%/normal saline, application of arachis oil without massage to surrounding skin, application of Calabrand paste bandage, and Lestreflex support bandage; advice on exercise from a standard instruction sheet 2. Standard treatment + weekly ultrasound (52): 0.5 W/cm^2 pulsed ultrasound at 1 MHz (Therasonic), 1 minute per probe head, with aquasonic gel as couplant Both groups: treatment undertaken once weekly for 12 weeks or until healing occurred	Gender (male/female): 1. 22/34 2. 20/32 Mean (range) age: 1. 65 years (14.3 years) 2. 69.5 years (12.2 years) Mean (SD) ulcer area: 1. 14.2 cm^2 (34.9 cm^2) 2. 14.5 cm^2 (31.6 cm^2) Number of deep/superficial ulcers: 1. 3/53 2. 7/45 Ulcer aetiology: 1. Venous, 49; venous/arterial, 3; venous/rheumatoid, 2; venous/diabetic, 2; rheumatoid, 0; post-traumatic, 0 2. Venous, 45; venous/arterial, 2; venous/rheumatoid, 2; venous/diabetic, 1; rheumatoid, 1; post-traumatic, 1	Number of ulcers completely healed at 12 weeks: 1. 25/41 (61%) 2. 17/41 (41%) Log rank test: $\chi^2 = 4.8$, $p = 0.03$ If withdrawals are included as failures, the percentage healing is 30% (group 1) and 49% (group 2) There was a 20% difference in the decrease in ulcer area at 4 weeks in groups 1 and 2 for those completing ($p < 0.05$); this difference was maintained Mean residual ulcer area at 12 weeks: 1. 27% 2. 9% $p < 0.02$ Mean residual ulcer area (healed ulcers excluded): 1. 28% 2. 22%	1. 11 (20%): allergy (4), pain (4), refused/DNA (2), death (1) 2. 15 (29%): allergy (6), pain (3), refused/DNA (3), deterioration (2), arterial disease (1) Difference between groups not statistically significant	All tracings were analysed by code numbers only in order to exclude treatment bias; ulcer areas were calculated using a computer graphics program

Continued

TABLE 2 contd *Details of included studies*

Study and design	Inclusion and exclusion criteria	Interventions	Baseline characteristics	Results	Withdrawals	Comments
Lundeberg *et al.*, 1990,[41] Sweden Study design: RCT, randomised permuted Objective outcomes: percentage healed ulcer area; percentage healed ulcers at 4, 8, 12 weeks Duration of follow-up: 12 weeks	Inclusion criteria: venous leg ulcer Exclusion criteria: skin allergy to standard treatment; evidence of peripheral arterial disease, rheumatoid arthritis or diabetes; venous ulcer due to trauma	1. Standard treatment + placebo ultrasound (22) 2. Standard treatment + pulsed ultrasound (22): 0.5 W/cm^2 at 1 MHz for 10 minutes Standard treatment: ulcer cleansed with saline, application of paste bandage, support bandage and advice on exercise from a standard instruction sheet Treatment: three times weekly for 4 weeks, twice weekly for 4 weeks, and once weekly for 4 weeks, unless healing occurred	Mean age: 1. 66.9 years 2. 63.8 years Difference not significant Mean ulcer area: 1. 19.1 ± 26.3 cm^2 2. 18.3 ± 34.9 cm^2 Difference not significant Number of deep/superficial ulcers: 1. 3:19 2. 2:20 Difference not significant	Ulcers healing at 12 weeks: 1. 10/22 (45%) 2. 8/22 (36%) No significant difference in the cumulative percentage of cases healed in relation to time (life-table methods) No significant difference on an intention-to-treat analysis No significant difference between groups in reduction of ulcer area (Wilcoxon rank sum test)	1. 5: allergy (2), pain (1), DNA (2) 2. 7: allergy (3), pain (1), DNA (3)	All tracings identified by use of code numbers to exclude observer bias *A priori* power calculation undertaken to detect a 30% increase in ulcer healing frequency with 80% power

Continued

TABLE 2 contd *Details of included studies*

Study and design	Inclusion and exclusion criteria	Interventions	Baseline characteristics	Results	Withdrawals	Comments
Eriksson *et al*., 1991,[42] Sweden Study design: RCT Objective outcome: percentage change in ulcer area over time Setting and length of study: setting unclear; ulcer area tracings done at baseline; ulcers classified as deep (>1 cm) or superficial (<1 cm); treatment twice weekly for 8 weeks, unless healing occurred; follow-up 8 weeks	Inclusion criteria: presence of venous leg ulcer Exclusion criteria: skin allergy to standard treatment; evidence of peripheral arterial disease or rheumatoid arthritis; diabetic ulcer or venous ulcer due to trauma	1. Standard treatment + ultrasound (19): 1 W/cm^2 at 1 MHz (enraf-nonius), aquasonic gel for contact; diameter of the ultrasound head was 2.8 cm when treating superficial ulcers and 1.2 cm for deep ulcers (to enable treatment of the complete area); ultrasound applied to ulcer surface area and surrounding tissue for 10 minutes 2. Standard treatment + placebo ultrasound (19): using same unit as above, but with no output Standard treatment: cleaning with saline, application of paste bandage, support bandage, advice on exercise from a standard sheet	Gender (male/female): 1. 8/11 2. 7/12 Mean ± SD age: 1. 63.2 ± 13.4 years 2. 59.2 ± 16.3 years Number of deep/superficial ulcers: 1. 4/15 2. 3/16 Median area of deep ulcers: 1. 2 cm^2 (2–4 cm^2) 2. 2 cm^2 (2–6 cm^2) Median area of superficial ulcers: 1. 11 cm^2 (4–97 cm^2) 2. 10 cm^2 (3–89 cm^2)	Number of ulcers healed at 8 weeks: 1. 6 2. 4 Difference not significant (Wilcoxon rank sum test) % original area: Week 0: 1, 100%; 2, 100% Week 2: 1, 79%; 2, 86% Week 4: 1, 65%; 2, 73% Week 6: 1, 54%; 2, 61% Week 8: 1, 42%; 2, 48% Ulcers completely healed at 8 weeks: 1. 6/19 (32%) 2. 4/19 (22%) Difference not significant	1. 7 (37%): allergy (3); pain (2); DNA (2) 2. 6 (32%): allergy (2); pain (1); DNA (3)	Tracings were identified by code numbers to exclude observer bias. A computer graphics program was used to calculate ulcer area Patient numbers were chosen to be sufficient to detect a 40% increase in ulcer healing frequency with 80% power ($\alpha < 0.05$)

Continued

TABLE 2 contd *Details of included studies*

Study and design	Inclusion and exclusion criteria	Interventions	Baseline characteristics	Results	Withdrawals	Comments
Peschen and Vanscheidt, 1996,[43] Germany Study design: RCT; method of randomisation not stated Objective outcome: percentage change in ulcer area; planimetry and colour photos of the ulcers taken at 0, 2, 4, 6, 8, 10, 12 weeks	Inclusion criteria: chronic ulceration of the leg due to venous insufficiency Exclusion criteria: not stated	1. Topical application of fibrinolytic agents + compression therapy (no detail) (6) 2. Conventional therapy (as above) + ultrasound treatment (6): 10 minutes of foot-bathing, 30 kHz (100 mW/cm^2), three times weekly Both groups: after each treatment local findings and side-effects were recorded	No baseline characteristics given	Mean % decrease in ulcer area: 1. 9% 2. 65% $p \leq 0.05$	None	Minor side-effects of mild erythema and occasional small pin-head size bleeding reported in ultra-sound group
						Continued

TABLE 2 contd *Details of included studies*

Study and design	Inclusion and exclusion criteria	Interventions	Baseline characteristics	Results	Withdrawals	Comments
Weichenthal *et al.*, 1997,[44] Germany Study design: RCT; randomisation by sequential treatment cards Objective outcome: reduction in ulcer area Setting and length of study: outpatient clinic for chronic leg ulcers; length of study not stated, but last outcome measure was at 8 weeks; colour photos of ulcers taken once a week; ulcer area measured under planimetry at 3 and 8 weeks of treatment	Inclusion criteria: venous leg ulceration for >3 months diagnosed by Doppler sonographic or phlebographic findings Exclusion criteria: diabetes mellitus; arterial vascular disease	1. Conventional therapy + ultrasound (19): 30 kHz, intensity 100 mW/cm^2, 10 minutes, applicator mounted in a footbath 2. Conventional therapy (18): fibrinolytic agents, antibiotics or other anti-septic agents; occlusive dressings and 'generally compression therapy performed with elastic bandages'; wound dressings changed at least three times weekly	Median (range) age: 1. 62 years (39–80 years) 2. 68 years (44–88 years) Gender (male/female): 1. 7/12 2. 9/9 Median (range) duration of ulcer: 1. 14 months (3–168 months) 2. 13 months (3–180 months) Mean (SD) ulcer area: 1. 10.6 ± 7.8 cm^2 2. 14.8 ± 10.2 cm^2	Mean (SD) ulcer area at 3 weeks: 1. 8.3 ± 6.4 cm^2 2. 14.7 ± 10.4 cm^2 ($p < 0.005$ for group 1 compared to pretreatment measurement; difference not significant for group 2) Mean (SD) ulcer area at 8 weeks: 1. 6.2 ± 5.9 cm^2 2. 13.4 ± 12.1 cm^2 ($p < 0.01$ for group 1 compared to pretreatment measurement; difference not significant for group 2) Change in ulcer area at 8 weeks: 1. 57% 2. 87% $p < 025$ Number of ulcers healed completely at 8 weeks: 1. 1 2. 0	None reported	

Continued

TABLE 2 contd *Details of included studies*

Study and design	Inclusion and exclusion criteria	Interventions	Baseline characteristics	Results	Withdrawals	Comments
McDiarmid *et al.*, 1985,[45] UK Study design: RCT; randomisation by randomly allocated numbers Objective outcome: sore survival time Study length: duration of follow-up unclear	Inclusion criteria: sores considered to be a result of pressure and limited to the superficial tissues, not extending beyond the dermis; age ≥18 years; possible to remove pressure on sore Exclusion criteria: malignancy in the area to be treated; radiotherapy to the area in the preceding 6 months; evidence of deep vein thrombosis in the area to be treated	1. Ultrasound (21): 3 MHz, three times weekly; minimum of 5 minutes for all pressure sores up to 3 cm^2; one additional minute for each additional 0.5 cm^2, up to a maximum of 10 minutes 2. Placebo ultrasound (19): same machine, but no pulse; same treatment regimen	Mean age 80 years; 10 men Baseline measures taken before randomisation: Norton score; classification of clean or infected sore from clinical examination; details of pressure sore (site, date of onset) Dressings or medications used were not reported	Number of ulcers healed: 1. 10 2. 8 Median number of days to healing: 1. 32 (not significant; $\chi^2 = 0.1$, df = 1, $p = 0.08$) 2. 36 (not significant) Other mediating variables: (a) ultrasound on clean sores (not significant) (b) ultrasound on cleaning infected sores (significant; unpaired *t*-test: week 3, ≤0.02; week 4, ≤0.02) Survival analysis of the effect of age, gender, nutrition, Norton score, mattress type, baseline size of sore did not indicate how these factors affected healing	Total: 13 1. 8 (discharge, 6; death, 2) 2. 5 (discharge, 1; death, 4)	

Continued

TABLE 2 contd *Details of included studies*

Study and design	Inclusion and exclusion criteria	Interventions	Baseline characteristics	Results	Withdrawals	Comments
Nussbaum *et al*., 1994,[46] Canada Study design: RCT; method of randomisation not stated Objective outcome: tracings on to trans-parency, area calculated by planimetry, depth measured using disposable measuring tape; percentage change in ulcer size and mean healing rate (wound closure defined as no scab remaining) Setting and length of treatment: hospitalised patients at a spinal cord centre; treatment continued until healing occurred; measurements of tracing of ulcer perimeter and depth (deepest point) taken at baseline and every 14 days until healing	Inclusion criteria: diagnosis of spinal cord injury and skin wounds; gave informed consent Exclusion criteria: none stated	1. Laser (6): 800 cluster probe, 820 nm laser diode 2. Ultrasound/ultraviolet treatment (6): alternated for 5 days a week 3. Standard wound care (6): cleansing with Hygeol (1:20), Jelonet dressing and avoidance of pressure on the area	Mean age: 1. 42 years 2. 42 years 3. 36 years Gender (male/female): 1. 5/1 2. 6/0 3. 5/1 Ulcer area (range): 1. 2.8 cm^2 (0.9–5.4 cm^2) 2. 1.9 cm^2 (0.9–3.1 cm^2) 3. 2.1 cm^2 (0.9–3.3 cm^2) Number of ulcers 1–5 mm deep: 1. 4 2. 6 3. 6 Number of ulcers 6–10 mm deep: 1. 2 2. 0 3. 0	All tracings taken and analysed by an individual blind to the allocation of patients Number of ulcers healed at 6 weeks: 1. 2/6 (33%) 2. 6/6 (100%) 3. 3/6 (50%) Number of ulcers healed at 12 weeks: 1. 4/6 (66%) 2. 6/6 (100%) 3. 5/6 (83%) Analysis of variance of significance: for group 1 versus group 2, $p = 0.032$; group 2 versus group 3, not significant Ulcers were larger at baseline in group 1, i.e. there was a treatment effect against the bias	Total: 4 1. transfer (1) 2. 0 3. transfer (1), surgical repair (2) Results analysed for the remaining 16 subjects (18 wounds)	No detail of support surfaces used

Continued

TABLE 2 contd *Details of included studies*

Study and design	Inclusion and exclusion criteria	Interventions	Baseline characteristics	Results	Withdrawals	Comments
ter Riet *et al*., 1996,[42] The Netherlands Study design: RCT; randomised in blocks of 4 after stratification by nursing home, whether muscle was affected, whether ascorbic acid supplements taken; allocated a treatment code which then matched with codes allocated to the ultrasound devices Objective outcome: colour slides taken at baseline, 1, 2, 4, 6, 8, 10 and 12 weeks from which changes in surface area were measured	Inclusion criteria: stage 2 pressure ulcer Exclusion criteria: systemic glucocorticoids	1. Ultrasound (45): frequency 3.28 MHz, pulse duration 2 ms, pulse repetition frequency 100 Hz, spatial average temporal average intensity 0.10 W/cm^2, beam non-uniformity ratio <4, effective radiating area 4 cm^2; 5 times weekly for 12 weeks or until healing occurred 2. Sham ultrasound (43): detuned ultrasound, 5 times weekly for 12 weeks	All nursing home patients 60 co-variables measured at baseline No data given on baseline areas of pressure sores	Mean change in surface area: 1. 0.18 cm^2 (23%) 2. 0.31 cm^2 (14%) Group 1 minus group 2: –0.13 cm^2 (9%) Adjusted difference (taking into account 60 co-variables): –0.12 (8.27%) Ulcers healed at 12 weeks: 1. 18/45 (40%) 2. 19/43 (44%) p = 0.61 (log–rank test, one-tailed) Blinded outcome assessment	11 patients lost to follow-up. Estimated in a sensitivity analysis: trend of each drop-out, extra-polated using the sham group trend, the patient treatment group trend and deletion. Results of all analyses were almost identical	Co-intervention: nursing care consisted of identical water beds, 3 hourly repositioning, and once daily gentle cleansing of the wound with saline; enzymatic or surgical debridement performed when indicated; ulcers were covered with paraffin and hydrophilic gauze Subgroup of infected ulcers (75): no treatment difference found Healing at 12 weeks: 1. 15/38 (39%) 2. 15/37 (41%) p = 0.45 (log–rank test, one-tailed)
Kloth and Feedar, 1988,[48] USA Study design: RCT; by coin toss (by person not involved in the study) Objective outcome: time to healing Setting and length of study: setting not stated; length of treatment not stated for any group	Inclusion criteria: stage 4 ulcers (pressure sores and venous) Exclusion criteria: not stated	1. Electrical stimulation for tissue repair (ESTR) (9): frequency 105 Hz, interphase interval 50 µs, voltage 100–175 V; 45 minutes, once daily, 5 days a week 2. Sham ESTR (7) Both groups: necrotic tissue was debrided, where required, using enzymatic and manual debridement; wounds were dressed with saline soaks; all patients used pressure relieving devices and were on high-protein diets	Mean (range) age: 1. 70.13 ± 21 years (20–89 years) 2. 65.61 ± 21 years (20–85 years) Gender (male/female): not stated Baseline wound area (range): 1. 4.08 cm^2 (0.24–15.55 cm^2) 2. 5.2 cm^2 (0.63–16.51 cm^2)	Ulcers healed at 16 weeks: 1. 9/9 2. 0/7 Mean (range) post-treatment wound area: 1. 0 cm^2 2. 6.1 cm^2 (0.32–16.68 cm^2) Healing or erosion rate (range) (minus indicates erosion): 1. 44.8 %/week (21.43 to 92.39 %/week) 2. –11.59 %/week (–53.46 to 3.70 %/week)		

Continued

***TABLE 2 contd** Details of included studies*

Study and design	Inclusion and exclusion criteria	Interventions	Baseline characteristics	Results	Withdrawals	Comments
Mulder, 1991,[49] USA Study design: RCT, double blind Objective outcome: percentage decrease in wound size Setting and length of treatment: multicentre study, 9 sites; 4 weeks; patients treated at home, or as inpatients; measurements taken of ulcer length, depth and width at 0, 1, 2, 3 and 4 weeks; ulcers photographed at baseline	Inclusion criteria: presence of a pressure ulcer, vascular lesions or surgical wound Exclusion criteria: wounds which were malignant or were located near the eyes, larynx or other area where electrical stimulation may not be safe; completely occluded by eschar; haemorrhaging from major blood vessels involved; peripheral vascular problems; osteomyelitis; severe systemic disease; pregnancy; cardiac pacemaker; obese; long-term steroid therapy; chemotherapy; radiotherapy	Total: 59 patients, 67 wounds 1. Electrical stimulation (26 wounds): Dermapulse 30, 35 and 40 mA, pulse width 140 μs, charge/pulse 4.2, 4.9 and 5.6 μC, frequency 64 and 128 pps; 30-minute sessions twice daily, 4–8 hours between sessions (a) Infected wounds: 128 pps, intensity 35 mA negative polarity, until wound free of necrotic tissue, clean and serosanguinous drainage appeared (b) Uninfected stage 2 wounds: as (a) but positive polarity applied after 3 days, then alternated as indicated by healing 2. Sham stimulation (24 wounds)	Median duration of wounds: 1. 3.4 months (2 days to 2.1 years) 2. 6.0 months (4 days to 6.6 years) Initial wound size: 1. 15 cm^2 2. 17 cm^2 Wound stage 2/3/4: 1. 0/22/4 2. 2/17/5 Difference between groups not significant (Student *t*-test)	Total: 47 patients, 50 wounds Decrease in initial wound size at 4 weeks: 1. 56% 2. 33% $p < 0.05$	Total: 12 patients, 17 wounds (numbers not given by group) – wound measurements inconsistent (5), not complete at 4 weeks (4), wounds did not meet pretreatment range (3), DNA (2), protocol violations (2)	A variety of aetiologies, but randomisation not stratified. No details of wound measurement techniques given

Continued

TABLE 2 contd Details of included studies

Study and design	Inclusion and exclusion criteria	Interventions	Baseline characteristics	Results	Withdrawals	Comments
Wolcott *et al*., 1969,[50] USA Study design: controlled trial Objective outcome: percentage of ulcer healed Setting and length of study: medical rehabilitation unit; 18 month study	Inclusion criteria: patients with two ischaemic ulcers Exclusion criteria: patients requiring extensive skin grafts; haemoglobin <12 g/100 ml; cardiac pacemaker	1. Electrotherapy + standard treatment (8): 400–600 mA depending on ulcer status, negative polarity, 2 hours treatment, 4 hours rest, three times daily; when no new granulation occurred, polarity was reversed 2. Standard treatment (8): debrided if necessary, cleansed with pHisoHex or other antibacterial agent	Gender (male/female): 3:5 Mean (range) age: 25.8 years (10–41 years) No ulcer size data presented	Number of ulcers healed: 1. 6/8 2. 0/8 70% ulcer healing: 1. 2/8 2. 2/8 20–50% ulcer healing: 1. 0/8 2. 3/8 No healing: 1. 0/8 2. 3/8 Mean (range) treatment time: 7.9 weeks (0.8–15.4 weeks) Mean (range) healing rate: 1. 27 %/week (7.6–125 %/week) 2. 5 %/week (6–14.7 %/week)		Main open study involved 75 patients

Continued

***TABLE 2 contd** Details of included studies*

Study and design	Inclusion and exclusion criteria	Interventions	Baseline characteristics	Results	Withdrawals	Comments
Gault and Gatens, 1976,[51] USA Study design: controlled trial (patients contralateral ulcer was control) Objective outcome: percentage ulcer healed Setting and length of study: multicentre study, nine health centres; mean treatment duration 4 weeks (range 8 days to 8 weeks)	Inclusion criteria: bilateral, symmetrical skin ulcers closely matched in size; patients classified as spinal cord injury, cerebral vascular accident, brain tumour, cardiac diseases, peripheral vascular disease, burns, diabetes, tuberculosis, fracture, amputation Exclusion criteria: not stated	1. (a) Non-Infected ulcers (6): negative polarity for 3 days, then positive polarity; dosage dependent on status of ulcer; 2 hours treatment, 4 hours rest, three times daily, 7 days per week (b) Infected ulcers: negative polarity until 3 days after infection cleared, then positive polarity + standard guidelines for care 2. Standard guidelines (6): (a) eliminate pressure/shearing from affected areas (b) maintain hygiene of the ulcer (c) emphasise high-protein diet (d) maintain circulation and control oedema (e) treat systemic conditions	Not reported	Mean of healing: 1. 74.0% 2. 27.3% Mean healing ratio: 1. 30.0 %/week 2. 14.7 %/week Mean treatment time: 1. 4 weeks 2. 4 weeks	None	Six patients in a larger open study had symmetrical bilateral ulcers – one ulcer received intervention 1 and other acted as control, on each patient

Continued

TABLE 2 contd *Details of included studies*

Study and design	Inclusion and exclusion criteria	Interventions	Baseline characteristics	Results	Withdrawals	Comments
Carley and Wainapel, 1985,[52] USA Study design: RCT; pairs matched for age, diagnosis, wound aetiology Objective outcome: time to healing Setting and length of study: hospital inpatients; follow-up for 5 weeks or until the ulcer was healed; length, width, depth of ulcer recorded at 0, 1, 2, 3, 4 and 5 weeks	Inclusion criteria: indolent ulcer below knee or in sacral area Exclusion criteria: not stated	All wounds debrided before treatment 1. Low intensity direct current (LIDC) (15): 2 hours daily, 5 days per week; stimulation for normal innervated tissues 300–500 µA; stimulation for denervated tissues 500–700 µA; current density 30–110 µA/cm^2; wounds irrigated with saline solution and packed with saline gauze or 'various absorption gels', covered by waterproof tape or adhesive trans-parent dressing; negative polarity at the wound site for the first 3 days, then positive polarity, until the wound healed; if a plateau in healing occurred, treatment swapped to negative polarity 2. Conventional wound therapy (15): little detail given; mainly wet to dry gauze dressings, solution-soaked dressings (Dakins solution/Betadine); four patients received whirlpool therapy 4 or 5 times weekly	Mean ± SD age: 1. 70.3 ± 18.4 years 2. 73.6 ± 13.9 years Gender (male/female): 1. 8/7 2. 7/8 Mean ± SD wound duration: 1. 8.6 ± 3.7 months 2. 5.2 ± 2.9 months Mean ± SD baseline volume: 1. 4.74 ± 1.39 cm^3 2. 3.92 ± 1.24 months	Mean ± SD wound measurement, week 1: 1. 3.34 ± 1.19 cm^3 2. 3.52 ± 1.16 cm^3 Mean ± SD wound measurement, week 2: 1. 2.09 ± 0.72 cm^3 2. 2.76 ± 0.94 cm^3 Mean ± SD wound measurement, week 2: 1. 1.11 ± 0.42 cm^3 ($p < 0.05$) 2. 2.62 ± 0.98 cm^3 Mean ± SD wound measurement, week 4: 1. 0.69 ± 0.26 cm^3 ($p < 0.05$) 2. 2.48 ± 0.85 cm^3 Mean ± SD wound measurement, week 5: 1. 0.50 ± 0.20) cm^3 ($p < 0.01$) 2. 2.16 ± 0.88 cm^3 (Wilcoxon rank sum test)	None stated	Weekly measurements of length, width and depth carried out by nursing staff without knowledge of previous measurements

Continued

***TABLE 2 contd** Details of included studies*

Study and design	Inclusion and exclusion criteria	Interventions	Baseline characteristics	Results	Withdrawals	Comments
Feedar *et al.*, 1991,[53] USA Study design: RCT; random numbers, allocation concealed; double blind Objective outcome: percentage decrease in wound size Setting and length of study: mixture of inpatients and outpatients, treated by family or self-treatment; 4 weeks follow-up	Inclusion criteria: stage 2, 3 or 4 chronic dermal ulcer Exclusion criteria: cardiac pacemaker; peripheral vascular disease; pregnancy, long-term radiotherapy; steroid therapy; chemotherapy	1. Pulsed cathodal electrical stimulation (26): (a) if wound was necrotic or draining non-serosanguinous fluid, 128 pps, peak amplitude 29.2 mA, two 30-minute treatments a day, 7 days a week; (b) treatment continued for 3 days after wound was debrided and drained of serosanguinous fluid; (c) polarity of treatment electrode then changed every 3 days until wound progressed to stage 2; (d) pulse frequency reduced to 64 pps and polarity changed daily until healing. If the wound was initially stage 2 and clean, treatment started at (b) 2. As above, but with sham electrode (24)	Mean ± SD age: 1. 66.6 ± 15.6 years 2. 60.7 ± 19.2 years Gender (male/female): 1. 53.8/46.2% 2. 50/50% Ulcer stage: 1. stage 2, 0; stage 3, 22; stage 4, 4 2. stage 2, 2; stage 3, 17; stage 4, 5 Aetiology: 1. pressure sore, 17; surgical, 6; vascular, 0; traumatic, 3 2. pressure sore, 18; surgical, 3; vascular, 1; traumatic, 2 Location: 1. hip/ischium, 8; sacrum/coccyx, 4; leg, 5; foot, 5; other, 4 2. hip/ischium, 6; sacrum/coccyx, 9; leg, 1; foot, 6; other, 2 Baseline area (SD): 1. 14.65 cm^2 (11.37 cm^2) 2. 16.93 cm^2 (19.79 cm^2)	Percentage of initial wound size: 1. 44% 2. 67% ($p < 0.02$) Average healing rate: 1. 14%/week 2. 8.25%/week Tunnels or undermining found by multiple-regression analysis to adversely affect wound healing ($p = 0.001$). Greater numbers of these wounds were in group 1	Total 59 patients randomised (67 wounds): dropped out, 12; not complete, 4; wound size did not meet entry criteria, 4; uninterpretable measurements, 3; omitted or incorrect treatments, 6 No group allocation given for withdrawals 47 patients remained (50 wounds)	No intention-to-treat analysis Wound size ascertained by measuring the largest diameter and width as largest diameter perpendicular to the length Baseline areas skewed to favour group 1

Continued

TABLE 2 contd Details of included studies

Study and design	Inclusion and exclusion criteria	Interventions	Baseline characteristics	Results	Withdrawals	Comments
			Duration: 1. <1 month, 23%; 1–6 months, 35%; 6–12 months, 23%; >12 months, 19% 2. <1 month, 21%; 1–6 months, 34%; 6–12 months, 25%; >12 months, 21%			

Continued

TABLE 2 contd *Details of included studies*

Study and design	Inclusion and exclusion criteria	Interventions	Baseline characteristics	Results	Withdrawals	Comments
Claeys and Horsch, 1997,[54] Germany Study design: RCT; method of randomisation not stated Objective outcome: ulcer healing, Fontaine stage, level of amputation, changes in foot $TcPO_2$ Setting and length of study: setting not stated, but presumably inpatients; length of treatment not stated	Inclusion criteria: non-reconstructable Fontaine stage 4 ulcer or gangrene present for ≥3 weeks, ankle pressure ≤50 mmHg Exclusion criteria: patients suitable for reconstructive procedures, short life expectancy, patients with heart failure, renal failure, liver disease, uncontrolled hypertension, Buergers disease, unstable angina, neuropsychiatric distress	1. Pulse generator + prostaglandin E1 therapy (45): initially internally, but after 1 week changed to externally implanted pulse generator, stimulation amplitude 1–2.5 V, frequency 70 Hz, pulse width 180–210 µs, stimulation intermittent or continuous; intravenous prostaglandin E1 therapy (80 µg/day for 21 days) 2. Prostaglandin therapy (21): as above	Mean ± SD age: 1. 67.7 ± 11.9 years 2. 69.9 ± 10.2 years Gender (male/female): 1. 26/19 2. 23/18 Peripheral arterial occlusive disease: 1. 39 2. 34 Peripheral arterial occlusive disease and diabetes mellitus: 1. 6 2. 7 One ischaemic lesion: 1. 37 2. 29 Two ischaemic lesions: 1. 4 2. 9 Three ischaemic lesions: 1. 4 2. 3 No significant differences between the groups on any parameter	Total ulcer healing (non-diabetic patients): 1. 28/39 (72%) 2. 6/34 (18%) $p < 0.0001$ ≥50% ulcer healing (non-diabetic patients): 1. 32/39 (82%) 2. 11/34 (41%) $p < 0.0005$ Total ulcer healing (diabetic patients): 1. 3/6 (50%) 2. 1/7 (14%) Difference not significant 50% ulcer healing (diabetic patients): 1. 5/6 (83%) 2. 1/7 (14%) $p < 0.029$	None	

Continued

TABLE 2 contd *Details of included studies*

Study and design	Inclusion and exclusion criteria	Interventions	Baseline characteristics	Results	Withdrawals	Comments
Lundeberg *et al.*, 1992[55] Sweden Study design: RCT; randomised permuted blocks Objective outcome: percentage healing and number of healed ulcers Setting and length of study: at home after the first week of study; 12 weeks; coded tracings of ulcer area made at 0, 2, 4, 8 and 12 weeks	Inclusion criteria: chronic diabetic ulcer Exclusion criteria: skin allergy to standard treatment, rheumatoid arthritis, traumatic venous ulcer, osteomyelitis, abscess or gangrene, ankle pressure <75 mmHg	1. Electrical nerve stimulation (32): alternating constant current square wave pulses, 80 Hz, pulse width 1 ms, polarity changed after each treatment, two 20-minute treatments daily for 12 weeks 2. Placebo electrical nerve stimulation + standard treatment (32): no output from electrodes; cleansing with saline, paste bandage plus support bandage, exercise from standard instruction sheet	Mean ± SD age: 1. 67.5 ± 8.6 years 2. 66 ± 7.9 years Gender (male/female): 1. 13/18 2. 13/18 Mean ± SD ulcer area: 1. 24.2 ± 12.6 cm^2 2. 22 ± 9.6 cm^2 Number of deep/superficial ulcers: 1. 4/28 2. 6/26 Difference between groups not significant	Number of ulcers completely healed at 12 weeks: 1. 10/32 (31.25%) 2. 4/32 (12.5%) Number of ulcers completely healed at 12 weeks – after drop-out: 1. 10/24 (41.6%) 2. 4/27 (14.8%) Mean ± SD percentage ulcer area at 12 weeks (in patients completing the study): 1. 39 ± 14% 2. 59 ± 11% $p < 0.05$	Allergy: 1. 2 2. 1 Pain: 1. 3 2. 2 Refusal/DNA: 1. 3 2. 2 Difference between groups not significant	*A priori* sample size calculation; 30% increase in ulcer healing frequency with 80% power ($\alpha < 0.05$). Ulcers measured by tracing and computer planimetry

Continued

***TABLE 2 contd** Details of included studies*

Study and design	Inclusion and exclusion criteria	Interventions	Baseline characteristics	Results	Withdrawals	Comments
Gentzkow *et al*., 1991,[56] USA Study design: RCT; method of randomisation not stated; double-blind Objective outcome: percentage change in length and width of ulcer size Setting and length of study: nine-site multicentre trial in hospital and community; 4 weeks; ulcer length and width measured at 0, 1, 2, 3 and 4 weeks	Inclusion criteria: stage 2, 3 or 4 pressure ulcer Exclusion criteria: ulcer totally excluded by eschar, had bleeding or involved major blood vessels; located in pre-sternal, peri-orbital, laryngeal/pharyngeal regions; pregnant; cardiac pacemaker; osteomyelitis; peripheral vascular disease; malignancy; long-term steroids; chemotherapy; radio-therapy; very obese	1. Stimulation (25): negative polarity unit, wound debrided and serosanguinous drainage appeared, then polarity alternated every 3 days; 128 pps, 35 mA, 0.89 C per 30-minute treatment, twice daily for 4 weeks; when ulcer healed to stage 2, treatment at 64 pps and polarity changed daily 2. Sham stimulation (24) Both groups: 100% received wound cleansing with normal saline and dressing; 10% received surgical or whirlpool debridement; 100% received turning to relieve pressure; 55% received bed rest and elevation of an extremity	Mean ± SD (range) age: 1. 63.3 ± 17.8 years (29–91 years) 2. 62.2 ± 18.4 years (31–90 years) Gender (male/female): 1. 61.9/38.1% 2. 47.4/52.6% Mean ± SD ulcer depth at week 0: 1. 1.1 ± 2.1 cm 2. 1.4 ± 2.3 cm Mean ± SD ulcer area at week 0: 1. 19.2 ± 23.2 cm^2 2. 12.5 ± 11.9 cm^2 Number of stage 2 ulcers: 1. 0 2. 1 Number of stage 3 ulcers: 1. 16 2. 14 Number of stage 4 ulcers: 1. 5 2. 4	Mean ± SD percentage of ulcer healed at 4 weeks: 1. 49.8 ± 30.9% 2. 23.4 ± 47.4% $p = 0.042$ (Student *t*-test) Rate of healing: 1. 12.5%/week 2. 5.8%/week Mean ± SD healing at 1 week: 1. 18 ± 19.6% 2. 3.7 ± 25.7% $p = 0.053$ Mean ± SD healing at 2 weeks: 1. 33.2 ± 29% 2. 10.2 ± 38.1% $p = 0.037$ Mean ± SD healing at 3 weeks: 1. 35.1 ± 36.1% 2. 23.1 ± 40.3% $p = 0.325$	Patient had <4 weeks of treatment: 1. 2 2. 4 Protocol violation: 1. 2 2. 1	Stage 2: full-thickness skin defect to subcutaneous tissue; stage 3 defect to muscle; stage 4 defect to bone/joint Patients with more than one ulcer could have both randomised into the study *A priori* sample-size calcula-tion required 23 patients to detect a 15% difference in healing at 4 weeks, error of 0.05 and 80% power and an estimated variance of 18% Size measured by longest diameter and widest width Ulcers in group 1 were larger, and therefore measures of percentage healing favours group 2

Continued

TABLE 2 contd *Details of included studies*

Study and design	Inclusion and exclusion criteria	Interventions	Baseline characteristics	Results	Withdrawals	Comments
			Duration of ulcer ≤12 months: 1. 85% 2. 66.7% Duration of ulcer >12 months: 1. 15% 2. 33.3%			

Continued

TABLE 2 contd *Details of included studies*

Study and design	Inclusion and exclusion criteria	Interventions	Baseline characteristics	Results	Withdrawals	Comments
Griffin *et al*., 1991,[52] USA Study design: RCT; randomisation stratified by grade of ulcer and smoking status Objective outcome: percentage change in ulcer size Setting and length of study: inpatients, specialist spinal injuries unit; 20 days; wound surface area measured at 0, 5, 10 15 and 20 days, by computerised planimetry from projected transparencies	Inclusion criteria: male; spinal cord injury; pressure sore grade 2–4, Delisa system, on sacral/coccygeal or gluteal/ischial region Exclusion criteria: severe cardiac disease; cardiac arrhythmia; uncontrolled autonomic dysreflexia; cardiac pacemaker	1. Stimulation + routine dressings (8): frequency 100 pps, 200 V, negative polarity, 1 h/day for 20 consecutive days; pressure sore cleansed using Cara-Klenz, application of Carrington gel and a dry dressing; wound mechanically debrided as necessary 2. Sham stimulation + routine dressing (9) All patients: 2 hourly turning; no change of mattress during the study	Median (range) age: 1. 32.5 years (17–54 years) 2. 26 years (10–74 years) Median (range) ulcer duration: 1. 4.5 weeks (2–116 weeks) 2. 3.0 weeks (1–30 weeks) Mean (range) ulcer size at day 0: 1. 234.1 mm^2 (126–1027 mm^2) 2. 271.8 mm^2 (41–4067 mm^2) Ulcer grade 2: 1. 2 2. 2 Ulcer grade 3: 1. 5 2. 6 Ulcer grade 4: 1. 1 2. 1	Median (range) change in wound surface area: Day 5: 1. –32% (–12% to –100%) 2. –14% (+17% to –74%) $p = 0.03$ Day 10: 1. –47% (–23% to –100%) 2. –42% (+42% to –41%) $p = 0.14$ Day 15: 1. –66% (–42% to –100%) 2. –44% (+22% to –100%) $p = 0.05$ Day 20: 1. –80% (–52% to –100%) 2. –52% (–14% to –100%) $p = 0.05$ Number of grade 2 ulcers completely healed at 20 days: 1. 2/2 2. 2/2 Number of grade 3 ulcers completely healed at 20 days: 1. 1/5 2. 0/6 Number of grade 4 ulcers completely healed at 20 days: 1. 0/1 2. 0/1	Medical complications, 2; surgical repair of ulcer, 1 Withdrawals not reported by group	

Continued

TABLE 2 contd *Details of included studies*

Study and design	Inclusion and exclusion criteria	Interventions	Baseline characteristics	Results	Withdrawals	Comments
Wood *et al.*, 1993,[53] USA Study design: RCT; method of randomisation not stated; double blind Objective outcome: percentage decrease in surface area of ulcer Setting and length of study: multicentre; 8 weeks; diameter, perimeter and photograph of ulcer taken weekly over weeks 0–8	Inclusion criteria: stage 2 or 3 chronic pressure sores showing no improvement with standard nursing care over preceding 5 weeks Exclusion criteria: patients receiving steroids or other drugs that influence wound healing	1. Pulsed low-intensity direct current + standard treatment (41 patients, 43 ulcers): 600 µA, pulse frequency 0.8 Hz, three applications around each ulcer, alternate days, three times weekly; for larger ulcers, one or more additional electrode placements 2. Sham pulsed low-intensity direct current + standard treatment (30 patients, 31 ulcers) Standard treatment: wound cleansing, simple moist dressing, whirlpool baths; no hydrocolloids, films or foam dressings were used	Mean age: 1. 75.6 years 2. 74.9 years Gender (male/female): 1. 26/15 2. 15/15 Mean duration of ulcer: 1. 5.5 months 2. 4.9 Mean ulcer area: 1. 2.61 cm^2 2. 1.91 cm^2 $p < 0.05$ Mean ulcer depth: 1. 2.81 cm 2. 2.84 cm	Number of ulcers completely healed at 8 weeks: 1. 25/43 (58%) 2. 1/31 (3%) Decrease in ulcer area >80% at 8 weeks: 1. 31/43 (72.9%) 2. 4/31 (12.9%) $p < 0.0001$ (Fisher *t*-test) Mean ± SD ulcer area at 8 weeks (number of ulcers): 1. 0.41 ± 0.99 cm^2 (41) 2. 1.66 ± 2.14 cm^2 (25) Mean ± SD ulcer depth at 8 weeks: 1. 1.0 ± 1.1 cm 2. 2.6 ± 1.0 cm	Died: 1. 2 2. 4 Lost to follow-up: 1. 0 2. 2	

TABLE 3 *Electromagnetic therapy*

Study and design	Inclusion and exclusion criteria	Interventions	Baseline characteristics	Results	Withdrawals	Comments
Ieran *et al.*, 1990,[59] Italy Study design: RCT; computer-generated schedule in blocks of four; double-blind Objective outcome: time to healing Setting and length of study: home or hospital clinic; 90 days; patients seen every 2 weeks; at each visit, picture of ulcer obtained and assessed blind, presence of granulation tissue determined, presence of bacteria in ulcer determined	Inclusion criteria: patients with venous ulcers of ≥3 months duration Exclusion criteria: steroids, systemic disease, concomitant arterial occlusive disease	1. Stimulation of ulcer (22): single pulse electric current generating a magnetic field of 2.8 mT, frequency 75 Hz, pulse width 1.3 ms, 3–4 h/day for a maximum of 90 days, or until ulcer healed 2. Sham electric current (22): same frequency and duration of treatment as group 1 All patients: no compression therapy during the study	Mean (range) age: 1. 65 years (24–85 years) 2. 66 years (25–82 years) Gender (male/female): 1. 8/10 2. 6/13 Obesity: 1. 10 2. 9 Diabetes: 1. 5 2. 2 Mean (range) duration of ulcer: 1. 30 months(3–360 months) 2. 23 months (3–240 months) Number (mean ± SD) of ulcers >15 cm^2: 1. 4 (34.2 ± 15.5) 2. 7 (39.9 ± 23.9) Number (mean ± SD) of ulcers <15 cm^2: 1. 14 (4.8 ± 2.9) 2. 12 (5.0 ± 3.3)	Healing at 90 days: 1. 12/18 (66.6%) 2. 6/19 (31.5%) $p < 0.02$ Healing at 90 days (including withdrawals): 1. 12/22 (55%) 2. 6/22 (27%) Mean time to healing: 1. 71 days 2. 76 days Healing at 1 year after start of study: 1. 16/18 (88.8%) 2. 8/19 (42.1%) $p < 0.005$ Healing by size (<15 cm^2) at 90 days: 1. 12/14 (85%) 2. 6/12 (50%) $p < 0.05$ Mean ± SD area of ulcers >15 cm^2 at 90 days: 1. 18.1 ± 18.8 2. 27.8 ± 18.4 Difference not significant Mean size decrease >15 cm^2 at 90 days: 1. 47% 2. 30% Difference not significant	Stopped use of simulator by 3 weeks: 1. 1 2. 2 Patient used stimulation discontinuously: 1. 1 2. 1 Allergic reaction to drugs: 1. 1 2. 0 Developed rheumatoid arthritis: 1. 1 2. 0	

Continued

TABLE 3 contd *Electromagnetic therapy*

Study and design	Inclusion and exclusion criteria	Interventions	Baseline characteristics	Results	Withdrawals	Comments
Kenkre *et al.*, 1996,[60] UK Study design: RCT; allocation by pre-determined codes; pilot study Objective outcome: time to healing Setting and length of study: clinic developed for the study; 6 weeks treatment (30 days), follow-up visit 4 weeks (50 days) after treatment end; measurement (by weight of acetate sheet that covered ulcer) and photograph of ulcer at days 0, 5, 20, 30 and 50	Inclusion criteria: venous leg ulcer, with unsatisfactory healing in preceding 4 weeks Exclusion criteria: none reported	1. Electric field (600 Hz), magnetic field (25 μT) (5): Elmedistraal 2. Electric field (600 Hz, days 1–5; 800 Hz, days 6–30), magnetic field (25 μT) (5): Elmedistraal, 30 minutes, 5 days a week for 30 days, followed by 4 weeks observation 3. Sham therapy (9) All patients: ulcer dressings changed by community staff; no standardisation of dressings; all patients reported to be receiving compression therapy (authors reported that only two patients received 'adequate' compression)	Mean age: 1. 59 years ($p < 0.05$) 2. 78 3. 73 Gender (male/female): 1. 1/4 2. 2/3 3. 2/7 Mean (range) duration of ulcer: 1. 230.4 weeks (36–728 weeks) 2. 418 weeks (36–1368 weeks) 3. 962.6 weeks (160–2548 weeks) Mean (range) length of ulcer: 1. 26.6 mm (11–75 mm) 2. 49 mm (35–74 mm) 3. 49.1 mm (26–115 mm) Mean (range) ulcer area: 1. 63 mm^2 (6–269 mm^2) 2. 81 mm^2 (46–197 mm^2) 3. 119 mm^2 (35–526 mm^2) Patients with repeated ulceration: 1. 4 2. 3 3. 8	Number of ulcers healed at day 30: 1. 0 2. 0 3. 1 Number of ulcers healed at day 50: 1. 1 2. 1 3. 2 Mean (range) area of ulcer at day 50: 1. 103 mm^2 (0–394 mm^2) ($p < 0.05$) 2. 30 mm^2 (0–100 mm^2) 3. 78 mm^2 (0–373 mm^2) ($p < 0.05$) Change in ulcer area from baseline at day 50: 1. 63.5% 2. 63% 3. 34.5%	Not reported	

Continued

TABLE 3 contd *Electromagnetic therapy*

Study and design	Inclusion and exclusion criteria	Interventions	Baseline characteristics	Results	Withdrawals	Comments
Stiller *et al.*, 1992,[61] USA Study design: RCT; computer-generated randomisation based on order of admission to study Objective outcomes: percentage change in wound area; mean decrease in wound depth; percentage change in granulation tissue Setting and length of study: multicentre study; 8 weeks; measurements at 0, 4 and 8 weeks of wound surface area, wound depth, granulation tissue; blinded measures	Inclusion criteria: venous leg ulcer ≤7.0 cm diameter; no response to non-surgical treatment in 4 weeks prior to study; ulcer stability (≤15% change in diameter, ≤15% change in percentage of granulation tissue in 2 weeks prior to study) Exclusion criteria: claudication; ischaemic heart disease; cerebrovascular disease; decubitus ulcers; ulcer due to diabetes, vasculitis, neuropathy, infection, acute ischaemia; thrombophlebitis; pacemaker; DVT; alcoholism; nutritional deficiency; anaemia; congestive cardiac failure; hepatic or renal failure; malignancy; uncontrolled diabetes; immunosuppression	1. Pulsed electromagnetic limb ulcer therapy + topical treatment (18): three-part pulse 3.5 ms, 0.06 mV/cm, polarity – +, –, +; 3 h/day; ancillary topical treatment (see below) 2. Ancillary topical treatment (13): ace compression bandage (20 mmHg at ankle level) + leg elevation + dressing Duoderm: 1. 0 2. 1 Gentamicin ointment + Duoderm: 1. 3 2. 2 Mupirocin ointment + Vigilon: 1. 2 2. 1 Mupirocin ointment + non-absorbent gauze: 1. 8 2. 6 Elase ointment and gauze: 1. 3 2. 2 Unna's boot: 1. 2 2. 1	Mean (range) age: 1. 63.3 years (41–87 years) 2. 63.8 years (39–76 years) Gender (male/female): 1. 9/9 2. 8/5 Mean ± SD ulcer duration: 1. 38.9 ± 5.2 weeks 2. 46.8 ± 11.3 weeks Mean ± SD ulcer area: 1. 7.25 ± 1.02 cm^2 2. 7.66 ± 1.62 cm^2 Mean ± SD ulcer depth: 1. 0.24 ± 0.04 cm 2. 0.26 ± 0.01 cm Each subject had one designated study ulcer	Change in ulcer size at 8 weeks: 1. –47.1% 2. +48.7% $p < 0.0002$ (ANOVA) Change in ulcer size (intention-to-treat analysis, discontinuing study before 42 weeks): 1. –47.7% 2. +42.3% $p < 0.0002$ Mean ± SD wound depth at 8 weeks: 1. 0.13 ± 0.02 cm 2. 0.25 ± 0.03 cm $p < 0.04$ Mean ± SD granulation at 8 weeks: 1. 83.2 ± 4.4% 2. 67.5 ± 7.7% $p < 0.04$	1. 1 2. 3 Reasons not given by group	Wound surface area calculated by tracing and computer planimetry

Continued

TABLE 3 contd *Electromagnetic therapy*

Study and design	Inclusion and exclusion criteria	Interventions	Baseline characteristics	Results	Withdrawals	Comments
Comorosan *et al.*, 1993,[57] Romania Study design: RCT; no method of randomisation stated; double blind Objective outcome: percentage of ulcer healed at 2 weeks Setting and length of study: care of the elderly unit; 2 weeks; daily assessment of photography and ulcer scaling	Inclusion criteria: pressure ulcer Exclusion criteria: none stated	1. Stimulation (20): Diapluse, local application, frequency 600 pps, peak power 6 (117 V, 27.12 MHz), 30 minutes, twice daily; hepatic application – 400 pps, peak power 4 (117 V, 27.12 MHz), 20 minutes, once daily, following initial treatment 2. Placebo stimulation ± conventional therapy (5): Diapulse; H_2O_2 cleansing, application of talcum powder, methylene blue in solution, tetracycline ointment 3. Conventional therapy (5): see above	Mean (range) age: 60.56 years (60–84 years) Gender (male/female): 17/13 Number of ulcers: stage 2, 16; stage 3, 14 Mean (range) ulcer area: 1. 4.46 cm^2 (1.5–12 cm^2) 2. 8.52 cm^2 (1–25 cm^2) 3. 5.41 cm^2 (1.5–14 cm^2)	Stage 2 ulcers healed at 2 weeks: 1. 8/10 2. 0/3 3. 0/3 Stage 3 ulcers healed at 2 weeks: 1. 9/10 2. 0/2 3. 0/2 Stage 2 ulcers 75–95% healed at 2 weeks: 1. 2/10 2. 0/3 3. 0/3 Stage 2 ulcers <25% healed at 2 weeks: 1. 0/10 2. 1/3 3. 1/3 Stage 3 ulcers <25% healed at 2 weeks: 1. 0/10 2. 0/2 3. 1/2 Stage 2 ulcers unhealed at 2 weeks: 1. 0/10 2. 2/3 3. 2/3 Stage 3 ulcers unhealed at 2 weeks: 1. 0/10 2. 2/2 3. 1/2	Not reported	

Continued

TABLE 3 contd *Electromagnetic therapy*

Study and design	Inclusion and exclusion criteria	Interventions	Baseline characteristics	Results	Withdrawals	Comments
Salzberg *et al.*, 1995,[63] USA Study design: RCT; stratified by ulcer stage; method of randomisation unclear Objective outcome: percentage ulcer healed at 1 week; time to 100% healing; percentage of patients healed completely Setting and length of study: hospital inpatients; 12 weeks treatment; pressure ulcers measured (width and length) and photographed weekly	Inclusion criteria: male patients with a spinal cord injury and a stage 2 or 3 pressure ulcer Exclusion criteria: more than one ulcer; recent ulcer surgery; cardiac pacemaker; intercurrent disease; active cellulitis; sepsis; terminal illness; total joint replacement; stage 1 or 4 pressure sore	1. Electromagnetic therapy (15): 27.12 MHz, pulse repetition 80–600 pps, pulse width 65 µs, pulse power range 293–975 W, delivered through the wound dressing, 30 minutes treatment twice daily for 12 weeks 2. Sham treatment (15): as above All patients: ulcers dressed with moist saline gauze	Stage 2 patients Median (range) age: 1. 58 years (24–69 years) 2. 50 years (29–67 years) Median (range) area of pressure ulcer: 1. 15 cm^2 (4–200 cm^2) 2. 33 cm^2 (9–140 cm^2) $p = 0.089$ Median (range) granulation: 1. 23% (0–100%) 2. 45% (0–100%) Median (range) epithelialisation: 1. 8% (0–50%) 2. 10% (0–30%)	Number of stage 2 patients: 1. 10 2. 10 Percentage healing at 1 week: 1. 84% 2. 40% $p = 0.01$ Median size of ulcer at 1 week: 1. 2.7 cm^2 2. 16.5 cm^2 $p = 0.015$ Median time to complete healing: 1. 13 days 2. 31.5 days Number of stage 3 patients: 1. 5 2. 5 Number of ulcers completely healed in 12 weeks: 1. 3/5 2. 0/5 Mean ulcer area decrease: 1. 70.6% 2. 20.7%	One stage 2 patient in group 1 died due to unrelated causes	Stage 2 group had a greater number of the five larger ulcers (>60 cm^2) in the control group (4/5) (group 2) than in the intervention group (1/5) (group 1) The results for stage 2 and stage 3 patients cannot be pooled due to different outcome measures

Appendix 4

Quality assessment of included studies

TABLE 4 *RCTs of low-level laser therapy on wounds*

Study	**Clear inclusion and exclusion criteria**	**Overall sample size (number of arms)**	***A priori* sample-size calculation**	**Allocation concealment**	**Baseline comparability of treatment groups**	**Blinded outcome assessment**	**Appropriate outcome measures**	**Withdrawals***	**Intention-to-treat analysis**
Crous and Malherbe, 1988[34]	✗	6 (2)	✗	✗	Age and sex only	✗	✓	None	✗
Bihari and Mester, 1989[35]	✗	45 (3)	✗	✗	✗	✓	✓	✓b	✗
Malm and Lundeberg, 1991[36]	✓	42 (2)	✓	✗	✓	✓	✓	✓a	✗
Lundeberg and Malm, 1991[37]	✓	46 (2)	✓	✗	✓	✓	✓	✓a	✗

✓, Yes; ✗, no

* *Withdrawals: ✓a, reported by group and with reason; ✓b, not reported by group or reason not given*

TABLE 5 *RCTs of ultrasound therapy on wounds*

Study	**Clear inclusion and exclusion criteria**	**Overall sample size (number of arms)**	***A priori* sample-size calculation**	**Allocation concealment**	**Baseline comparability of treatment groups**	**Blinded outcome assessment**	**Appropriate outcome measures**	**Withdrawals***	**Intention-to-treat analysis**
Dyson *et al.*, 1976[38]	✓	25 (2)	✗	✗	Not reported	✓	✗	✓a	✗
Roche and West, 1984[39]	✓	26 (2)	✗	✓	✓	✓	✓	✗	✗
Callam *et al.*, 1987[40]	✓	108 (2)	✗	✓	✓	✓	✓	✓a	✗
Lundeberg *et al.*, 1990[41]	✓	22 (2)	✓	✓	✓	✓	✓	✓a	✓
Eriksson *et al.*, 1991[42]	✓	38 (2)	✓	✗	✓	✓	✓	✓a	✗
Peschen and Vanscheidt, 1996[43]	✓	24 (2)	✗	Not stated	✓	✗	✓	✓b	None
Weichenthal *et al.*, 1997[44]	✓	37 (2)	✗	✓	✓	Not reported	✓	Not reported	✗
McDiarmid *et al.*, 1985[45]	✓	40 (2)	✗	✓	Data not presented	✓	✓	✓a	✗
Nussbaum *et al.*, 1994[46]	✗	20 (3)	✗	Not stated	✓	✓	✓	✓a	✗
ter Riet *et al.*, 1996[47]	✗	88 (2)	✗	✓	✓	✓	✓	✓a	✗

✓, Yes; ✗, no

* *Withdrawals: ✓a, reported by group and with reason; ✓b, not reported by group or reason not given; ✗, withdrawals not reported*

***TABLE 6** RCTs of electricity on wounds*

Study	Clear inclusion and exclusion criteria	Overall sample size (number of arms)	*A priori* sample-size calculation	Allocation concealment	Baseline comparability of treatment groups	Blinded outcome assessment	Appropriate outcome measures	Withdrawals*	Intention-to-treat analysis
Kloth and Feedar, 1988[48]	✗	16 (2)	✗	✓ (coin toss by someone not involved in study)	Part	✗	✗	✓a	✗
Mulder, 1991[49]	✗	50 (2)	✗	✓ (double blind)	✓	✓ (double blind)	✗	✓a	✗
Wolcott *et al.*, 1969[50]	✗	16 (2)	✗	Controlled trial	✗	✗	✓	✗	✗
Gault and Gatens, 1976[51]	✗	12 (2)	✗	✗	✗	✗	✗	None	✗
Carley and Wainapel, 1985[52]	✗	30 (2)	✗	✓	Control group small	✓	Reliability and precision of measurements doubtful	✗	✗
Feedar *et al.*, 1991[53]	✓	50 (2)	✗	✓	✓	✓	✗	✗	✗
Claeys and Horsch, 1997[54]	✓	66 (2)	✗	✗	✓	✗	✓	✓b	✗
Lundeberg *et al.*, 1992[55]	✓	64 (2)	✓	✓	✓	✓	✓	✓a	✗
Gentzkow *et al.*, 1991[56]	✓	49 (2)	✓	Not stated	✓	✓	✗	✓a	✗
Griffin *et al.*, 1991[57]	✓	17 (2)	✓	Unclear	✓	✗	✗	✓b	✗
Wood *et al.*, 1993[58]	✓	76 (2)	✗	✓ (double blind)	Ulcers larger in intervention group	✓	✓	✓a	✗

Continued

TABLE 6 contd ***RCTs of electricity on wounds***

Study	Clear inclusion and exclusion criteria	Overall sample size (number of arms)	*A priori* sample-size calculation	Allocation concealment	Baseline comparability of treatment groups	Blinded outcome assessment	Appropriate outcome measures	Withdrawals*	Intention-to-treat analysis
Ieran *et al.*, 1990[59]	✓	44 (2)	✗	✓	More ulcers >15 cm^2 in control group	✓	✓	✓a	✗
Kenkre *et al.*, 1996[60]	✗	19 (3)	✗	✓	Intervention 1 group significantly younger Control ulcers larger and of longer duration	✗	Insufficient follow-up to see complete healing – important as not well matched for size at baseline	✗	✗
Stiller *et al.*, 1992[61]	✓	31 (2)	✗	✓	✓	✓	✓	✗	✗
Cormorosan *et al.*, 1993[62]	✗	30 (3)	✗	Not stated	Ulcers larger in intervention 2 group	✓	✗	✗	✗
Salzerg *et al.*, 1995[63]	✓	30 (2)	✗	✗	✓	✗	✗	✓a	✗

✓, Yes; ✗, no

* *Withdrawals: ✓a, reported by group and with reason; ✓b, not reported by group or reason not given; ✗, withdrawals not reported*

Health Technology Assessment Programme

Prioritisation Strategy Group

Members

Chair
Professor Kent Woods
Director,
NHS HTA Programme, &
Professor of Therapeutics
Leicester Royal Infirmary

Professor Bruce Campbell
Consultant General Surgeon
Royal Devon & Exeter Hospital

Professor Shah Ebrahim
Professor of Epidemiology of Ageing
University of Bristol

Dr John Reynolds
Clinical Director
Acute General Medicine SDU
Oxford Radcliffe Hospital

Dr Ron Zimmern
Director, Public Health Genetics Unit
Strangeways Research Laboratories, Cambridge

HTA Commissioning Board

Members

Programme Director
Professor Kent Woods
Director, NHS HTA Programme, &
Professor of Therapeutics
Leicester Royal Infirmary

Chair
Professor Shah Ebrahim
Professor of Epidemiology of Ageing
University of Bristol

Deputy Chair
Professor Jon Nicholl
Director, Medical Care Research Unit
University of Sheffield

Professor Douglas Altman
Director, ICRF Medical Statistics Group
University of Oxford

Professor John Bond
Director, Centre for Health Services Research
University of Newcastle-upon-Tyne

Ms Christine Clark
Freelance Medical Writer
Bury, Lancs

Professor Martin Eccles
Professor of Clinical Effectiveness
University of Newcastle-upon-Tyne

Dr Andrew Farmer
General Practitioner & NHS R&D Clinical Scientist
Institute of Health Sciences
University of Oxford

Professor Adrian Grant
Director, Health Services Research Unit
University of Aberdeen

Dr Alastair Gray
Director, Health Economics Research Centre
Institute of Health Sciences
University of Oxford

Professor Mark Haggard
Director, MRC Institute of Hearing Research
University of Nottingham

Professor Jenny Hewison
Senior Lecturer
School of Psychology
University of Leeds

Professor Alison Kitson
Director, Royal College of Nursing Institute, London

Dr Donna Lamping
Head, Health Services Research Unit
London School of Hygiene & Tropical Medicine

Professor David Neal
Professor of Surgery
University of Newcastle-upon-Tyne

Professor Gillian Parker
Nuffield Professor of Community Care
University of Leicester

Dr Tim Peters
Reader in Medical Statistics
University of Bristol

Professor Martin Severs
Professor in Elderly Health Care
University of Portsmouth

Dr Sarah Stewart-Brown
Director, Health Services Research Unit
University of Oxford

Professor Ala Szczepura
Director, Centre for Health Services Studies
University of Warwick

Dr Gillian Vivian
Consultant in Nuclear Medicine & Radiology
Royal Cornwall Hospitals Trust
Truro

Professor Graham Watt
Department of General Practice
University of Glasgow

Dr Jeremy Wyatt
Senior Fellow
Health Knowledge Management Centre
University College London

Current and past membership details of all HTA 'committees' are available from the HTA website (see inside front cover for details)

continued

continued

Current and past membership details of all HTA 'committees' are available from the HTA website (see inside front cover for details)

Feedback

The HTA programme and the authors would like to know your views about this report.

The Correspondence Page on the HTA website (http://www.ncchta.org) is a convenient way to publish your comments. If you prefer, you can send your comments to the address below, telling us whether you would like us to transfer them to the website.

We look forward to hearing from you.

Copies of this report can be obtained from:

The National Coordinating Centre for Health Technology Assessment,
Mailpoint 728, Boldrewood,
University of Southampton,
Southampton, SO16 7PX, UK.
Fax: +44 (0) 23 8059 5639 Email: hta@soton.ac.uk
http://www.ncchta.org

ISSN 1366-5278