Electroanalgesia: Historical and Contemporary Developments

PhD Thesis (Volume II)

1998

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Electroanalgesia: Historical and Contemporary Developments

A Thesis in Partial Fulfilment of the Degree of Doctor of Philosophy

Volume II

Sections 7-8
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   3.3 The Rev. John Wesley MA (1703-1791) Pioneer Electrotherapist: A History of Medicine Study
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1. Title:

**Acupuncture - like Transcutaneous Electrical Nerve Stimulation (ALTENS) as an adjuvant therapy within Palliative Medicine.**

2. Personnel identification:

Dr Ian Johnson: Consultant in Palliative Medicine/Independent Assessor; The Leicestershire Hospice: Tel: (0533) 313771.

Mr Gordon Gadsby: Nurse Practitioner/Post Graduate Researcher. 47 Milton Crescent, Leicester: Tel: (0533) 352204.

Dr Frank Dewhurst: Principal Lecturer/Director of Studies; Dept of Applied Biology and Biotechnology. De Montfort University. Leicester: Tel: (0533) 577730:

Dr Alison Franks: Senior Registrar in Palliative Medicine. The Leicestershire Hospice: Tel (0533) 313771

Mr Philip Jarvis: Senior Lecturer in Statistics: Dept of Mathematical Sciences. De Montfort University. Tel: (0533) 551551 x8481

3. Aims and Objectives:

**Aim**

- To determine if there is a role for acupuncture-like transcutaneous electrical nerve stimulation (ALTENS) in improving the quality of care within palliative medicine.

**Objectives**

- To assess the effectiveness of this non-invasive therapy as an antiemetic and analgesic as an adjunct to conventional care,

- To record biophysical measurements of electrical resistance in cancer patients and to compare with measurements in non-cancer controls.

- To assess the usefulness of these measurements of electrical resistance as a diagnostic and therapeutic indicator in palliative medicine.
4. Rationale:

a. acupuncture and electrostimulation in palliative medicine:

The study originated following informal discussions between IJ and GG and their mutual interest in acupuncture and related therapies in relation to antiemesis and analgesia. A considerable amount of work on anti-emesis using acupuncture and electrical stimulation has recently been conducted by, amongst others, the late Prof. John Dundee and his team (1984-1992), which demonstrated a significant antiemesis benefit within post-operative sickness, morning sickness of pregnancy and cancer chemotherapy sickness. There are also numerous studies on pain relief within musculo-skeletal and neurological systems (see Richardson & Vincent's 1986 review), using acupuncture and electrostimulation techniques but there is little documentation available to support its application within palliative medicine. There would appear to be few ethical objections to this treatment since it is known to be very safe with few contraindications and because of its intended use as an adjuvant therapy to conventional antiemetic and analgesic medications. It is anticipated that the application of this treatment will enhance the effectiveness of both conventional antiemetics and analgesics, with an expected reduction in their usage.

b. biophysical measurements:

On the basis of a large sample of biophysical electrical measurements recorded by members of The Society of Biophysical Medicine, it has been found that patients in good health show hand to hand and foot to foot resistance measurements of 20-30 kilohm and 40-50 kilohm respectively (ISBM 1984). These measurements are the cornerstone investigations of medical and paramedical practitioners of Biophysical Medicine (ISBM) and members of the Society of Electrotherapists (SET). Lower than average values are typically found in inflammatory conditions and higher values in degenerative conditions. It is characteristic of this measurement scale that people who are ill show readings which are a long way from the normal range. It is proposed that these non-invasive biophysical measurements of electrical resistance are taken during this trial, pre and post treatment, using a standard multimeter to record hand to hand and foot to foot electrical resistance in kilohms, in order to make a comparison between advanced stage cancer patients and the average normal readings described above. It is predicted that the electrical resistance measurements of terminal patients will be significantly higher than normal and their usefulness as a diagnostic and therapeutic indicator may then be assessed. This has not previously been carried out by other researchers.
5. Design:

The double-blind condition cannot easily be maintained in trials of physical treatments, and trials of acupuncture are often single blind design. (Vincent 1989, Dundee et al 1992). However, the present study is designed to fulfil double-blind criteria as far as possible and employs a control condition which should be seen as a credible, bona fide treatment by patients.

The treatment under study will be acupuncture-like transcutaneous nerve stimulation (ALTENS) given as an adjuvant to the recognised standard techniques for pain and antiemesis. Patients will be randomly allocated to receive standard treatment only, standard + ALTENS or standard + placebo.

The placebo therapy will be a fully functional transcutaneous nerve stimulation (TENS) unit with flashing frequency LED’s using the same apparatus type as the real therapy under investigation, but with non-functioning output leads. The full range of biophysical measurements of electrical resistance will also be recorded pre and post treatment to enhance the credibility of the placebo.

Randomisation is by the sealed envelope technique in conjunction with random number tables both for the pilot study and the main trial.

Patient numbers:

A pilot study of 15 patients will be conducted to test the research tools i.e. assessment sheets, questionnaires, statistical software and to estimate the standardised difference in order to determine the number of patients to be entered in the main study.

Main study: On the basis of previous evaluations of acupuncture pain relief trials (Richardson and Vincent 1986) with response rates of 35%, 50% and 80% for placebo, sham and real treatment respectively; acupuncture/ALTENS antiemesis relief trials (Dundee & McMillan 1991) with response rates from 50% -95% relief depending on the mode of application; TENS pain relief trials (Long 1991) with response rates from 50%-80% in acute and chronic pain conditions; TENS in intractable cancer pain from 35%-65% (Avellanosa 1982), it is anticipated that around 30 patients will be required for each arm of the main study = a total of 90. This should give the study a power rating of 85-90% at the 0.05 level. (Lewith 1983)

Investigators: There will be two independent assessors (IJ & AF) and one therapist (GG).

The duration of treatment will be for 25-30 minutes each day for 5 days/treatments between the times of 5.45 pm and 6.45pm.

The duration of the study will depend on the number of patients required for the full trial but is expected to last for up to one year.
6. Patient selection:

Criteria for inclusion: to be determined by the independent clinical assessor (IJ)

- Ambulant patients with pain and/or emesis problems, admitted to the Leicestershire Hospice.
- Age range 35-75
- Caucasian.

Criteria for exclusion: to be determined by the independent clinical assessor (IJ)

- all patients unwilling to provide informed consent
- patients too ill to cope with 25-30 minutes of restrictive treatment because of severe physical or mental problems including confusion, restlessness and history of fits
- patients with an on-demand pacemaker
- pre-menopausal women.
- patients with vomiting due to intestinal obstruction
- patients with vomiting due to raised intracranial pressure
- patients with iatrogenic vomiting e.g. GI irritation by NSAID

Informed consent to be obtained by the Independent assessor (IJ) following explanation of trial objectives (see appendix script 1).

7. Methodology:

Day 0
1. entry into the trial (pilot or main) following independent assessment by IJ or AF and completion of consent form, assessment of WHO score and completion of EORTC quality of life questionnaire.

2. randomisation - patients allocated to receive standard treatment only, standard treatment + active ALTENS or standard treatment + placebo.

Days 1 - 5
1. daily biophysical measurements of body electrical resistance pre and post treatment with a standard multimeter.

2. daily new or placebo treatment of 30 minutes duration using the VTENS Stimulator, supplied by Body Clock Health Care, a 2 Hz frequency pulse rate, a pulse width setting of 200 msecs, and an amplitude setting at mark 1.5 for the real and placebo treatments under investigation. One pair of lightly gelled electrodes, for the real and placebo treatments, to be attached one to the acupuncture point P6 and one to CO4 of the dominant hand by GG and secured with tape.

Conventional treatments will continue as usual throughout the study period.
Day 6
1. Completion of EORTC quality of life questionnaire
2. Retrospective assessment of analgesic and antiemetic use over study period.
3. second assessment at death or discharge

Concurrent with study.
Standardised measurements of average normal basic readings of electrical resistance will also be made from volunteers from the general and/or University populations, matched for age and sex with the study population, together with a sensitivity to treatment assessment in a small group of volunteers.

Quality control
The output leads will be coloured tagged, real and placebo, and the code changed at bi-weekly intervals during the study in order to help maintain the double-blind element. This will be undertaken by an independent observer (Eileen Millington) who will keep a record of the codes throughout the trial.

Using a standard multimeter, a daily quality control check on battery charge will be made by GG before commencement of each treatment.

There will be minimal interpersonal interaction between GG and the patient to reduce operator bias (see appendix script 2).

Using the EORTC questionnaire, patients are asked about many different symptoms in addition to the two (pain and nausea/vomiting) under investigation.

Patients will be monitored by medical and nursing staff at the hospice throughout the study period and any problems dealt with as appropriate.

Records and Data:
Consent form - completed by patient after explanation by IJ or AF. Patient recruited into study 1-2 days after admission to the hospice.

EORTC questionnaire - form completed by patient.

Daily record of any adverse events on the appropriate section of the data sheets

Data ownership:

- All patient data will be confidential and individuals will not be identified except with their consent.
- Information obtained from the study will be owned jointly by GG and IJ as representative of LOROS and will not be used for publication or public presentation without mutual agreement. GG may use data for PhD thesis but LOROS reserves the right to withhold its identity.
8. Responsibilities:

Dr Ian Johnson:

• submission for ethical committee approval
• patient selection,
• initial baseline and completion assessments,
• publications together with GG..

Mr Gordon Gadsby:

• preparation and funding of research study,
• daily treatments and records, collection and collation of data,
• statistical analysis in association with De Montfort University,
• presentation and publication of and completion of study.
• arranging lead tag changing and colour code records with Eileen Millington RGN.

9. Statistical considerations:

a. Study size: to be determined as outlined above.

b. Sample population: to be selected from The Leicestershire Hospice by the assessors.

c. Randomisation: by the sealed envelope method and random number tables.

d. Analysis of data via computerised statistical packages

1. Descriptive and inferential statistics for unrelated samples,
2. Differences between series to be tested by the Chi-squared test for independence and Kruskal-Wallis one way analysis of variance by ranks.

e. Interpretation and drawing conclusions in line with the aims of the study.

f. Presentation of data in Ph.D. thesis and submission for publication in mainstream medical journals and specialist journals by mutual agreement between the principal authors.
11. References & Bibliography.


APPENDIX 1.

Script 1: The Independent Assessor

We are trying out a new treatment over the next few weeks, in addition to our normal treatments, to see if we can improve on the quality of care we give you.

This new treatment involves a daily 30 minutes treatment session which lasts for 5 days and is given in the late afternoon.

The treatment consists of attaching a small electrode to your wrist and thumb of your right hand and then attaching you to a small stimulator. You may feel the gentle treatment stimulation as a tingling sensation or as a pressure depending on the prescribed dose of the treatment ordered for you.

This treatment will be carried out each day between 4.45 and 5.45 by Gordon Gadsby, a nurse practitioner.

If you would like to take part in this new treatment then it will also involve asking you some extra questions before the course begins, during and also after the course of treatment ends.

Would you be interested in taking part in this trial within the next day or so?
APPENDIX 2.

Script 2: The Therapist.

I'm here to set up the new treatment for you... the one you have agreed to take part in with Dr Johnson... in addition to your normal treatment.

First of all ..I will not be doing anything to hurt you in any way...

Do you wish to use the toilet or have a drink before we start the treatment ...

Before we begin the treatment though I am going to take some readings with this machine...

First I am going to take some readings from the hands...

Then some readings from the feet...I will be doing these again after the treatment.

Now I am going to set up the treatment by attaching these two electrodes, one to your wrist and the other to your thumb and then secure them in place with tape like this...

Now I am switching the unit on...

You may feel the treatment sensation either as a tingling sensation or as pressure depending on the dose prescribed for you... during the next 25-30 minutes..

Everything is working now...and I will be back in around 25 minutes or so....

But if you are worried in any way please press your call bell and I will come to you...OK.

If asked for further information ... this treatment uses a low frequency electrical current to stimulate your body to release various substances, working alongside your other treatments, to help stabilise your general condition.
Sequential Studies:
Sequential designs are often seen as desirable since they combine the advantages of a randomised study with the attractive feature of taking into account the results so far in determining how long the trial continues. The main advantage over an ordinary two-group study is that the required sample size will be smaller if the treatment effect is large, so the bigger the difference between the treatments the fewer the number of patients who receive the less successful treatment. The major difficulty is that we need the results for each patient to be available quickly, since we will not know whether to recruit more patients until the outcome for the current patient is known. In sequential designs it is difficult to allow for more than one response variable, or for more than two treatments, and will be administratively complex if the trial is multicentre. A comprehensive (but mathematical) discussion of sequential designs is provided by Whitehead, J. (1983). The Design and Analysis of sequential Clinical Trials. Chichester: Ellis Horwood, and a briefer less mathematical account is provided by Gore, S.M. (1981). Assessing Clinical Trials - design II. BMJ.; 282: pp. 1861-1863. Sequential designs are likely to be of limited use for complementary therapies since the treatment results will generally be known too late to limit patient entry; however, if this is not the case a sequential design may provide very efficient use of resources, from Crichton, N. (1990). The Importance of Statistics in research Design. Complementary Medical Research. 4(2). pp. 42-50.

This study would therefore appear to be suitable for this type of design in view of the proposed methodology meeting most of the above indications especially in respect of the short treatment periods involved.

Zelen's Model: One problem with clinical trials is that of obtaining 'informed consent' where the patient is asked to agree to enter a trial without knowing which of the treatments they will receive; this is often difficult to explain to the patients particularly if they are very sick. Zelen, M. (1979). A new design for randomised clinical trials. New England Journal of Medicine. 300. pp. 1242-1245. proposed the following design which avoids this problem. He proposed that of the subjects entering a trial, we randomly assign half to group 1 and the rest to group 2. The patients in group 1 all receive the standard treatment, so they are treated as if they were not in a trial, apart from the need for standardized assessment and record keeping. There is no need to obtain special consent or explain about the trial for those in group 1. The patients in group 2 are given a choice, they are offered the new treatment B, which is under investigation, but may have the standard treatment A if they wish. It is proposed that within this study that one third of all suitable patients be randomly assigned to group 1 as outlined above and the remaining two thirds to group 2. The Group 2 members will then be randomly assigned to either the new or the placebo group in equal proportions, from Crichton, N. (1990). The Importance of Statistics in research Design. Complementary Medical Research. 4(2). pp. 42-50.
APPENDIX 4.

The term ‘Opiate Equivalent’ is used in this study to indicate equivalent potency with respect to oral morphine.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Route</th>
<th>Equivalent oral morphine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morphine</td>
<td>10 mg</td>
<td>po</td>
<td>10 mg</td>
</tr>
<tr>
<td>Morphine</td>
<td>10 mg</td>
<td>sc,im,iv</td>
<td>20 mg</td>
</tr>
<tr>
<td>Diamorphine</td>
<td>10 mg</td>
<td>sc,im,iv</td>
<td>30 mg</td>
</tr>
<tr>
<td>Dextromoramide</td>
<td>10 mg</td>
<td>po, sl</td>
<td>20 mg</td>
</tr>
<tr>
<td>Methadone</td>
<td>10 mg</td>
<td>po</td>
<td>10 mg</td>
</tr>
<tr>
<td>Methadone</td>
<td>10 mg</td>
<td>sc</td>
<td>20 mg</td>
</tr>
<tr>
<td>Phenazocine</td>
<td>10 mg</td>
<td>po</td>
<td>50 mg</td>
</tr>
<tr>
<td>Codeine</td>
<td>30 mg</td>
<td>po</td>
<td>2.5 mg</td>
</tr>
<tr>
<td>Dihydrocodeine</td>
<td>30 mg</td>
<td>po</td>
<td>3 mg</td>
</tr>
<tr>
<td>Buprenorphine</td>
<td>0.2 mg</td>
<td>sl</td>
<td>10 mg</td>
</tr>
<tr>
<td>Fentanyl</td>
<td>100 mcg</td>
<td>iv</td>
<td>5 mg</td>
</tr>
<tr>
<td>Co proxamol</td>
<td>2 tabs</td>
<td>po</td>
<td>7 mg</td>
</tr>
</tbody>
</table>

(Adapted from A Guide to Symptom Relief in Advanced Cancer, 3rd Edn. 1992, Regnard & Tempest)

Standard antiemetic doses

The following is a list of the antiemetics in common use at the Leicestershire Hospice. For the purposes of this study the doses which are most commonly used in this setting are referred to as ‘standard doses’. The number of standard doses (both prophylactic and breakthrough ‘prn’) which are given each day, will be used as an objective outcome measure.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Route</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cyclizine</td>
<td>oral</td>
<td>50 mg</td>
</tr>
<tr>
<td></td>
<td>parenteral</td>
<td>50 mg</td>
</tr>
<tr>
<td>Haloperidol</td>
<td>oral</td>
<td>1.5 mg</td>
</tr>
<tr>
<td></td>
<td>parenteral</td>
<td>2 mg</td>
</tr>
<tr>
<td>Metoclopramide</td>
<td>oral</td>
<td>10 mg</td>
</tr>
<tr>
<td></td>
<td>parenteral</td>
<td>10 mg</td>
</tr>
<tr>
<td>Domperidone</td>
<td>oral</td>
<td>10 mg</td>
</tr>
<tr>
<td></td>
<td>rectal</td>
<td>30 mg</td>
</tr>
</tbody>
</table>
ALTENS as an adjuvant therapy in palliative medicine

Information leaflet

Your doctor has asked if you would mind taking part in a trial of a treatment called ALTENS. This leaflet give more information about the trial and if, after reading it, you have any questions, then just ask any of the doctors.

ALTENS stands for 'acupuncture-like transcutaneous nerve stimulation. It is a simple very safe type of treatment that has been used for many years to help people with all sorts of problems, including backache, travel sickness, asthma, hayfever and many other common ailments. The doctors at the hospice are working with an experienced nurse practitioner, Mr Gordon Gadsby to see if ALTENS can help improve the way we help our patients with their symptoms.

The treatment consists of having two small rubber pads, each about an inch square, attached by sticky tape to the back of one hand. These are then connected to a small machine, about the size of a pack of cards, which generates a very weak electric current from a battery. This may cause a tingling sensation in your hand or arm but as we are testing different strengths of electric current, the sensation may be too small to feel and you will feel nothing apart from the sticky tape. It will not hurt and it definitely is not dangerous. The doctors will only ask you to take part in this test if they are certain that it will have no side effects on you.

The treatment is given for half an hour each day for five days and you will be asked to answer some questions about your health and symptoms before the first treatment and after the last treatment.

If you do agree to take part in this trial you are under no obligation to continue with it if you change your mind later - just tell one of the doctors or a nurse that you don't want to carry on with it. Whether or not you take part, you will still have all the other treatments that you would normally have at the hospice. In other words, taking part in this trial does not in any way change your other treatments.

If you have any questions at all then please feel free to ask one of the doctors at any time.
ALTENS as an adjuvant therapy in palliative medicine

Consent form

Name of patient ....................................................................................

I have had the purpose and nature of this study explained to me by

........................................... and I have been given and read the information leaflet and I
agree to participate. I understand that I will continue to receive all my usual
treatments and that I am free to withdraw from the study at any time.

Signed ......................................................... Date .........................

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The Leicestershire Hospice & The Society of Electrotherapists
Electrotherapy Research Project

**Assessors Data Sheet**

**DAY: 0.**
Name of Patient................................................. Trial number ..................

Age:................. Sex:.................. Diagnosis..................

WHO performance score .............. EORTC:........................................

Informed consent obtained on: ........

<table>
<thead>
<tr>
<th>Retrospective Drug Evaluation</th>
<th>Day 1</th>
<th>Day 2</th>
<th>Day 3</th>
<th>Day 4</th>
<th>Day 5</th>
<th>Sub Total 1</th>
<th>At death/discharge</th>
<th>Sub Total 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Daily Opiate Equivalent given as regular medication</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total daily opioid equivalent dose given for breakthrough pain</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of breakthrough pain doses</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No of antiemetic standard doses given as regular medication</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of antiemetic standard doses given for breakthrough</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Day: 6.**
EORTC:..................... RDE calculations:..................
At Death/Discharge RDE calculations:..................
Comments:
The Leicestershire Hospice & The Society of Electrotherapists
Electrotherapy Research Project

Therapists Data Sheet:

Name........................................

Trial No.............

<table>
<thead>
<tr>
<th>Date</th>
<th>Treatment</th>
<th>Basic readings pre-treatment</th>
<th>Basic readings post treatment</th>
<th>Treatment Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Comments and untoward occurrences:

Signed by principal investigators:

Ian Johnson

Gordon Gadsby
APPENDIX

A(ii)

(ii) Application for Research Ethics Committee Approval for 3.6
Leicestershire Health Authority

Project Id: 
Date Received: 
Decision Code: 

COMMITTEE ON THE ETHICS OF CLINICAL RESEARCH INVESTIGATION
APPLICATION FOR RESEARCH ETHICS APPROVAL

The following application form is for submission to the Ethics Committee for approval of proposed medical research involving human subjects*. Please complete the form in typescript and return to the address given at the bottom of this page for approval.

The following must also be submitted with the protocol:

Detailed Protocol
Questionnaires Used
Proposed Consent Form
Patient Information Leaflet

N.B. The Ethics Committee in considering an application for ethical approval, bears in mind the Royal College of Physicians guideline that "badly planned, poorly designed research that causes inconvenience to subjects and may carry risk without producing useful or valid results, is unethical."

Notes for completing application

Please complete every section of the form as fully as possible. The shaded areas are only for office use, so please do not fill these in. Respond to all Yes/No questions by circling the appropriate answer.

Address: Director of Public Health
Leicestershire Health
Gwendolen Road
Leicester
LE5 4QF

(* This application form is available on computer floppy disc (3.5in) as a template in WORD for Windows 2.0 format.)
1. Title Of Project.

Acupuncture-like transcutaneous nerve stimulation (ALTENS) as an adjuvant therapy within palliative medicine

2. Miscellaneous Details

2.1 Where will the research be done? (tick one as appropriate) Hospital [ ] GP [ ] Other [✔]
   If other please state where: The Leicestershire Hospice

2.2 Starting Date (DD-MON-YY): 01 09 1994
2.3 Duration (in months): 03

3. Responsible Investigator (Supervisor of Project) Dr Ian Johnson

N.B. This is the individual with overall responsibility of the proposed study, not necessarily the individual who will be carrying out the study.

3.1 Name: Ian Johnson Title (Dr, Prof etc.): Dr
   Address: The Leicestershire Hospice
   Groby Road Leicester.
   Position/post held (Consultant, Senior Nurse etc.): Honorary Consultant
   Qualification: MB ChB MRCGP MFCM

3.2 List the individual(s) who will be carrying out the study.

<table>
<thead>
<tr>
<th>Name</th>
<th>Position/Post Held</th>
<th>Qualification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ian Johnson</td>
<td>Hon consultant</td>
<td>MB ChB MRCGP MFCM</td>
</tr>
<tr>
<td>Gordon Gadsby</td>
<td>Nurse practitioner</td>
<td>BA(Hons) RMN RGN DN</td>
</tr>
<tr>
<td>Alison Franks</td>
<td>Senior registrar</td>
<td>MB ChB MRCGP</td>
</tr>
</tbody>
</table>
4. Purpose of Research

4.1 Please state the objectives of the research and briefly and simply describe the scientific background.

The objectives of this study are to assess the effectiveness of acupuncture-like transcutaneous electrical nerve stimulation therapy as an antiemetic and analgesic as an adjunct to conventional care within palliative medicine. Secondly, to record biophysical measurements of electrical skin resistance in cancer patients and then compare with measurements in non-cancer controls. Thirdly, to then assess the usefulness of these measurements of electrical skin resistance as a diagnostic and therapeutic indicator in palliative medicine.

A considerable amount of work on anti-emesis using acupuncture and electrical stimulation has recently been conducted by, amongst others, the late Prof. John Dundee and his team (1984-1992), which demonstrated a significant antiemesis benefit within post-operative sickness, morning sickness of pregnancy and cancer chemotherapy sickness. There are also numerous studies on pain relief within musculo-skeletal and neurological systems (see Richardson & Vincent's 1986 review), using acupuncture and electrostimulation techniques but there are no research studies available to support its application within palliative medicine at this time.

5. Design of Study

5.1 Please describe what will be done, what results you expect and how you will analyse the results. Remember to attach a full copy of the protocol. Please identify potential dangers, discomfort or inconvenience to subjects of any of the techniques involved.

Patients will be randomly allocated to the trial to receive standard treatment only, standard + ALTENS or standard + placebo. The initial pilot study of 15 patients will test the research tools i.e. assessment sheets, questionnaires, statistical software and then calculate the standard difference in order to determine the final number of patients to be entered in the main study.

On the basis of previous evaluations of acupuncture pain relief trials (Richardson and Vincent 1986) with response rates of 35%, 50% and 80% for placebo, sham and real treatment respectively; acupuncture/ALTENS antiemesis relief trials (Dundee & McMillan 1991) with response rates from 50%-95% relief depending on the mode of application; TENS pain relief trials (Long 1991) with response rates from 50%-80% in acute and chronic pain conditions; TENS in intractable cancer pain from 35%-65% (Avellanosa 1982), it is anticipated that the pilot study will reflect these significant responses together with an expected improvement in the participants quality of life. The results will be analysed in conjunction with the Department of Mathematical Sciences - Medical Statistics Section, De Montfort University.

There are few potential dangers if any inherent in this non-invasive procedure.
6. Specific Details on Purpose and Design of Study

6.1 Has this work been carried out before? No

Work has been done to verify the effectiveness of this technique in controlling nausea and pain in other settings (e.g. post-operative) but there are no studies which specifically investigate symptom control in a palliative care setting.

6.2 Is this a multi-centre study? No

6.3 What type of a study is this (tick one as appropriate):
- Pilot
- Definitive
- Follow on of a previous study
- Modification of a previous study

If a follow on or modification of a previous study, please give reference number of previous application and approval date:
Previous study reference number:
Approval date:

N.B. For the next two sections indicate one as appropriate.

6.4 Is this research of direct benefit to the subject: Yes/No - Yes

6.5 Is this research related to: Diagnosis/Therapy/Neither - Therapy

If yes to therapy then what type (tick any as appropriate):
- Drugs
- Surgery
- Other

7. New Chemical Entity/Therapeutic Agent or Established Agent

7.1 Is this an investigation of an established agent? Yes

If yes, is the established agent being used for a new/unlicensed indication? No

7.2 Is this a study of a new chemical entity/therapeutic agent? No

If yes, What stage is this in its evaluation? (tick one as appropriate)
- Phase II
- Phase III
- Phase IV

7.3 If this drug is being supplied by a pharmaceutical company as part of sponsored research, has a clinical trial certificate/exemption certificate been provided? Yes/No - N/A
<table>
<thead>
<tr>
<th>Route</th>
<th>Amount/ Frequency</th>
<th>Risks</th>
<th>Precautions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drugs* NONE</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Isotopes NONE</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fluids &amp; Diets NONE</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Others: Transcutaneous Electrical Nerve Stimulation</td>
<td>Topical 30 mins daily for 5 days</td>
<td>None known or anticipated. Theoretical risk with patients with pacemakers</td>
<td>Defined exclusion criteria. Regular surveillance by nursing and medical staff</td>
</tr>
</tbody>
</table>

* On completion of a clinical trial the investigator should notify the pharmacist who will destroy any chemical trial material still being held.
9. Financial Arrangements

9.1 Will you be receiving any financial contributions towards your research?
No: - 4 TENS machines donated by a manufacturer (Body Clock).
If yes, from whom and how much?
N.B. Tick main source only.
Whom:  
- Pharmaceutical Company 
- Research Grant 
- (MRC, BHF, RHA e.t.c) 
- Other

How much? (Please state approx total amount): £ N/A

9.2 How will these funds be spent?
(tick any as appropriate)
- Staff costs
- Running Costs
- Other

If 'other' briefly describe:

10. Recruitment of Subjects

Please say how you will recruit subjects, with rules of inclusion and exclusion and any proposals to deny and delay treatment and any other relevant details e.g. age, sex, type of patient.

N.B. Investigators are reminded of the need to notify General Practitioners when patients under their immediate care are to be included in a study. Investigators should ensure that any patients or healthy volunteers involved in a particular project are not included in another study which also involves drugs or isotopes.

10.1 Subjects? Inclusion - all patients admitted to the Leicestershire hospice who:
1. are ambulant
2. have pain or emesis problems
3. are aged between 35 and 75
4. are Caucasian

Exclusion -
1. unwilling or unable to provide informed consent
2. too ill to cope with treatment lasting 30 mins and which restricts movement whilst electrodes attached
3. pacemaker
4. women who are still having menstrual periods
5. intestinal obstruction
6. raised intracranial pressure
7. iatrogenic vomiting

**Inclusion in this trial will not prevent or delay treatment which would otherwise be given.
10.2 Controls: Same inclusion/exclusion criteria - patients willing to participate will be randomly allocated to receive active ALTENS, placebo or no additional treatment other than that offered routinely.

10.3 Number of subjects to be recruited: 15 (pilot)

10.4 Type of subjects to be recruited? Patients

(tick any as appropriate)

Volunteers

If volunteers, then please tick any of the options from the list below to specify the type:

Staff

Student

Other

10.5 Any financial inducements offered to subjects or relatives? No

10.6 Informed Consent

N.B. Written informed consent is preferred, a copy of the consent form and information leaflet to be used should be supplied.

Please note that special consideration must be given to children, mentally ill and handicapped.

Will informed consent be obtained? Yes

If yes, then tick any of the options from the list below to specify the method used:

Written: 

Oral

10.7 Compensation

What kind of arrangements for compensation/indemnity for subjects are in place for the study, please tick any of the options from the list below:

ABPI Guidelines on compensation for medicine induced injury

Crown Indemnity

Other

If yes to 'Other', please give details: Medical investigators all carry medical insurance necessary for full time hospital practice. Nurse practitioner also carries professional insurance indemnity appropriate for full-time acupuncture practice.
Investigations of Subjects/Controls:
Venous samples  No
Arterial samples  No

N.B. If yes to any of the following questions, please give details below.
X-rays  No
Radiation  No
Ultrasoundics  No
Biopsies  No
Anaesthesia  No
Other invasions NONE

Any non-invasive tests?  Measurement of electrical resistance skin using multimeter
Psychological tests?  No
Questionnaires?  Yes - EORTC quality of life questionnaire.
If yes, please include copy.
Other Activities  No

Additional Details:

11. Likely Benefits Of Study

Improved control of symptoms commonly found in patients with advanced terminal illness with reduction in requirements for drugs such as analgesic and antiemetics. Patients in the trial will have particular attention paid to formal assessment of quality of life using a well validated instrument which is expected to show a general overall improvement.
12. Documents Enclosed

Please remember to enclose the following documents where appropriate:

- Detailed Protocol  Yes
- Questionnaire  Yes
- Proposed Consent Form  Yes
- Patient Information Leaflet  Yes

13. Applicant(s) Signature

Signature(s) of Applicant(s)  Date:

14. Countersignature of Consultant

Countersignature of Consultant (in the case of junior medical and dental staff), Head of Department, Nurse Tutor, Director of Nursing Services etc.

I have discussed the research proposal with the investigator, who is in my department, and I support his/her application to the Ethical Committee.

Signature(s)  Date:
APPENDIX

A(iii)

ACUPUNCTURE-LIKE TRANSCUTANEOUS ELECTRICAL NERVE STIMULATION (ALTENS) WITHIN PALLIATIVE MEDICINE. A PILOT STUDY.

A Franks, I Johnson, The Leicestershire Hospice. LE3 9QE
J G Gadsby, P Jarvis & F Dewhurst. De Montfort University Leicester LE7 9SU

Summary
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Methods
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white

Results 1
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white

Results 2
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white

Bodyclock: Colour illustration of a VTENS Unit

Introduction
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Quality control
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white

Discussion
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white

404
SUMMARY

Objective:
To assess the role of acupuncture-like transcutaneous electrical nerve stimulation (ALTENS) in improving the quality of care within palliative medicine with particular reference to control of pain, nausea and vomiting.

Design:
Double-blind randomized placebo controlled trial.

Setting:
The Leicestershire Hospice.

Patients:
15 patients admitted for symptom control.

Interventions:
Patients randomly allocated to receive standard treatment, standard plus ALTENS or standard plus placebo.

Outcome Measures:
1 EORTC QLQ-C30 Quality of Life Questionnaire.
2 Retrospective analysis of drug use including breakthrough medication for pain, nausea and vomiting.

Results:
The indicators of control of pain and nausea and vomiting did not show a benefit over standard treatment. However there was an improvement in the overall quality of life as measured by the EORTC instrument with a particularly beneficial change reflected in the item relating to fatigue.

Conclusions:
The results of this pilot study did not show any evidence of a beneficial effect of ALTENS in the treatment of emesis or pain in a hospice palliative care setting. However, the possibility of effecting an improvement in fatigue may merit further investigation, from the results of this study it is estimated that a sample size of 48 patients per group respectively would be needed.
INTRODUCTION

Many studies have shown likely benefit from the use of transcutaneous electric nerve stimulation (TENS) in the alleviation of pain, nausea and other symptoms. However there have been few published reports of the effectiveness of this treatment within the palliative care setting. The present study was designed to assess the effectiveness of ‘acupuncture-like transcutaneous nerve stimulation’ (ALTENS), a specific type of TENS, in the management of pain, nausea and vomiting in hospice patients.

ALTENS differs from conventional TENS in that it consists of treatment with an electrical current of much lower frequency but higher intensity. ALTENS treatment at 2 pps for 30 minutes has been shown to produce a marked increase in beta-endorphins and met-enkephalins whereas TENS treatment at 80-100 pps does not produce this increase and is thought to work by a different mechanism.

Subjects

15 ambulant, Caucasian patients between ages 35 - 75 with pain and/or emesis problems admitted for symptom control to The Leicestershire Hospice. Excluded from the study were patients unwilling or unable to provide informed consent, patients too ill to cope with 30 minutes of restrictive treatment, patients with an on-demand pacemaker, pre-menopausal women, patients with vomiting due to intestinal obstruction or raised intracranial pressure or iatrogenic causes and patients who had previously received (and were thus familiar with) TENS or ALTENS treatment.
METHOD

Patients were entered into the trial following an independent assessment by a clinician (AF, IJ) and completion of a consent form and the EORTC QLQ-C30. They were then randomly assigned to receive either:

1. Standard therapy consisting of all necessary drugs and supportive care for the treatment of pain, nausea, vomiting and other symptoms as routinely used in the hospice.

2. Active ALTENS consisting of functional TENS unit and functional electrical leads and Standard therapy

3. Inactive (placebo) ALTENS consisting of functional TENS unit with leads rendered non functional by the manufacturer but which were indistinguishable from the functional leads and Standard therapy.

Entry into the trial was followed by five consecutive daily treatments given by the nurse practitioner to the active and placebo groups using a colour coded system of leads. Lightly gelled carbon vinyl electrodes 4 cm² were attached to the patient, one to the acupuncture point Pe6 (Neiguan) and one to the point Li4 (Hegu) of the dominant hand and secured with tape.

Electrical stimulation was given using a 'Body Clock VTENS unit' with the pulse rate set at 2 pulses per second with a symmetrical biphasic pulsewave in continuous mode, the pulse width at 200 microseconds and the amplitude setting at 2.5 on the unit output scale. The timer was set at 30 minutes for the duration of each treatment.

On day 6 a second EORTC QLQ-C30 was completed by the independent clinical assessor together with a retrospective assessment of analgesic and antiemetic use over the study period and recorded on the data collection sheets.
QUALITY CONTROL:

The colour code for the functional and non-functional leads were changed at bi-weekly intervals by an independent observer in order to prevent the operator becoming familiar with their relative performance.

Using a standard multimeter, a daily quality control check on battery charge was made before the commencement of each treatment.

There was minimal interpersonal interaction between the nurse practitioner and patient as far as possible, this was restricted to a script which was followed for all patients.

Using the EORTC questionnaire, patients were asked about many different symptoms thus preventing the patient identifying the two symptoms (pain and nausea/vomiting) as being the main focus of the investigation.

The credibility of the placebo was enhanced by incorporating measurement of electrical resistance of the skin of all subjects with the implication that this was part of the procedure. Interestingly this showed that the mean skin resistance of the cancer patients in this study was approximately 50 times greater than that of normal controls. This is likely to explain the (expected) observation that cancer patients receiving active ALTENS were barely sensible of the electrical stimulation whilst normal controls find stimulation of this magnitude quite uncomfortable. In this way, the present study goes some way towards overcoming one of the main obstacles to providing a credible placebo control to a physical treatment such as ALTENS in that cancer patients find great difficulty distinguishing between active and dummy treatment.
# RESULTS 1

## Pain scores

<table>
<thead>
<tr>
<th></th>
<th>Active</th>
<th>Placebo*</th>
<th>Standard</th>
</tr>
</thead>
<tbody>
<tr>
<td>Improved</td>
<td>1</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Not improved</td>
<td>4</td>
<td>2</td>
<td>2</td>
</tr>
</tbody>
</table>

Odds ratio: Active : Placebo = 0.5  
Active : Standard = 0.16

## Nausea & Vomiting scores

<table>
<thead>
<tr>
<th></th>
<th>Active</th>
<th>Placebo*</th>
<th>Standard</th>
</tr>
</thead>
<tbody>
<tr>
<td>Improved</td>
<td>3</td>
<td>0**</td>
<td>3</td>
</tr>
<tr>
<td>Not improved</td>
<td>2</td>
<td>3</td>
<td>2</td>
</tr>
</tbody>
</table>

Odds ratio: Active : Placebo = Infinite  
** NB: no patients on placebo improved so Odds Ratio for active vs. placebo is infinite  
Active : Standard = 1

## Fatigue level scores

<table>
<thead>
<tr>
<th></th>
<th>Active</th>
<th>Placebo*</th>
<th>Standard</th>
</tr>
</thead>
<tbody>
<tr>
<td>Improved</td>
<td>4</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Not improved</td>
<td>1</td>
<td>2</td>
<td>4</td>
</tr>
</tbody>
</table>

Odds ratio: Active : Placebo = 8  
Active : Standard = 16
RESULTS 2

Total EORTC QLQ-30 scores

<table>
<thead>
<tr>
<th></th>
<th>Standard</th>
<th>Active</th>
<th>Placebo*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Improved</td>
<td>4</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Not improved</td>
<td>1</td>
<td>1</td>
<td>2</td>
</tr>
</tbody>
</table>

Odds ratio  
Active : Placebo = 2  
Active : Standard = 2.7

Average daily morphine

<table>
<thead>
<tr>
<th></th>
<th>Standard</th>
<th>Active</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1166 mg</td>
<td>230 mg</td>
<td>538 mg</td>
</tr>
</tbody>
</table>

Average number of ‘equivalent’ breakthrough doses in 5 days

<table>
<thead>
<tr>
<th></th>
<th>Standard</th>
<th>Active</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>analgesic</td>
<td>6.5</td>
<td>5</td>
<td>3.5</td>
</tr>
<tr>
<td>antiemetic</td>
<td>8.8</td>
<td>7.6</td>
<td>10</td>
</tr>
</tbody>
</table>

* Footnote
Although 5 patients were recruited to each arm of the study, complete data are available for only 13 of them, two patients in the placebo group being unable to complete the second EORTC QLQ-C30 due to a rapid deterioration in their condition.
DISCUSSION

Whilst the pilot study shows several interesting observations in respect of the global quality of life and the symptoms of fatigue, the main objectives of using acupuncture-like transcutaneous electrical nerve stimulation to alleviate pain and nausea and vomiting were not supported.

Although a larger study would be necessary to allow statistically valid conclusions, the numbers required were deemed too great for our resources.

The choice of acupuncture point P6 was informed by previous work by Dundee et al which provided convincing evidence for the efficacy of this point in the treatment of nausea and vomiting in other clinical settings. The choice of LI4 however was based upon it's widespread use as a non-specific point for the treatment of a large range of conditions, including pain, fatigue and to improve general wellbeing.

In the present study, no attempt was made to tailor the treatment to the patient's individual pain problems and this must be seen as a major shortcoming when interpreting the results. It is worth noting that the average daily opiate requirement was much higher amongst patients in the active treatment arm suggesting that they may have had more severe pain at the outset than other patients.

The strength of current used in the active treatment was relatively small in an attempt to maintain as far as possible double blind conditions. However, whilst a person in normal health would have no difficulty feeling the stimulation, the patients in this study were rarely aware of the current. This interesting finding is likely to be due to the fact that patients with degenerative diseases tend to have much lower skin conductivity and indeed this was confirmed in the present study, an observation which may have hitherto unrecognised diagnostic application.
ACUPUNCTURE -LIKE TRANSCUTANEOUS ELECTRICAL NERVE STIMULATION (ALTENS) WITHIN PALLIATIVE MEDICINE: A PILOT STUDY.

A. Franks, I Johnson, The Leicestershire Hospice. LE3 9QE
J. G. Gadsby, P. Jarvis & F. Dewhurst. De Montfort University Leicester LE7 9SU

Aim of Investigation: the aim was to determine the role of ALTENS in improving the quality of life within palliative medicine and to record measurements of electrical skin resistance in cancer patients.

Method: Fifteen consenting patients with pain and/or emesis problems admitted for symptom control were entered in a three treatment randomised double-blind controlled trial to compare ALTENS, placebo ALTENS or no ALTENS in addition to recognised standard therapies for pain and antiemesis. Outcomes were measured using the EORTC QLQ-C30 questionnaire.

Results: Although no statistically significant differences were detected in this small study, calculations indicating that a sample size in excess of 30 for each of the three groups would be required, there is a clear clinical indication of the beneficial effect of ALTENS in improving the overall quality of life (2.67 times (95% CI: 0.15, 45.14) that of the control) and in improving fatigue symptoms (16 times (95% CI: 0.72, 35.48) that of the control) but no evidence to support the use of ALTENS for antiemesis and analgesia. Electrical skin resistance recordings in cancer patients showed highly significant differences at 28 - 34 times normal, the significance of which is not known.

Conclusions: The use of ALTENS was not supported in the alleviation of pain and nausea and vomiting in this group of patients although the study showed several interesting observations in respect of improvements in the global quality of life and symptoms of fatigue which may deserve further investigation both within palliative medicine and in chronic fatigue states.
APPENDIX

A(iv)

(iv) Interim report for Transfer of Registration between MPhil and PhD
11.2 In support of the application, the student shall prepare for the Research Degrees Committee a full progress report on the work undertaken. The progress report should typically be 3000 to 6000 words in length and include:

(a) a brief review and discussion of the work already undertaken;
(b) a statement of the intended further work, including details of the original contribution to knowledge which is likely to emerge.

The Chair of the Research Degrees Committee shall select an assessor for the transfer report and advise the Research Degrees Committee of the outcome.

INTERIM REPORT

Title: Electroanalgesia: Historical and contemporary developments.

Prepared by:
J Gordon Gadsby BA(Hons) RGN RMN DipN(Lond) MISBM DHP DHS
M.Phil./Ph.D. student - November 1995

Director of Studies:
Dr F Dewhurst BSc LLB PhD DCC CBiol FIBiol CChem FRSC
Principal Lecturer, Department of Biological Sciences

Second Supervisors:
Professor M Saks BA MA PhD
Head of School, School of Health and Community Studies
Mr P Jarvis BSc MSc FSS
Senior Lecturer, Department of Medical Statistics
PROPOSED Ph.D. THESIS STRUCTURE (at 1995)

**Electroanalgesia: Historical and Contemporary Development.**

**Part I: Historical Development:**
Chapter 1. Early developments in electroanalgesia.

**Part II: Mechanisms of Pain and Electrical pain relief:**
Chapter 3. Mechanisms of pain
Chapter 4. Mechanisms of electrical pain relief.

**Part III: Contemporary developments:**
Chapter 5. Contemporary applications of electroanalgesia *
Chapter 6. Research:
   a. electroanalgesia/electroantiemesis in palliative medicine *
   b. a randomised controlled trial: a pilot study *
   c. a new electroanalgesia training package
   d. a new society - The Society of Electrotherapists
   e. a study in electroanalgesia and colonoscopy

**Part IV: Systematic reviews of the effects of health care interventions:**
Chapter 7. Systematic reviews, meta-analysis and the Cochrane Collaboration. *
Chapter 8. Research: A systematic review of electroanalgesia for chronic low back pain. *

**Part V: Conclusions, recommendations and the contribution to knowledge.**

**Part VI: Reference Section:**

**Part VII: Appendices:** *
1. The training package
2. Research protocol for RCT of electroanalgesia in palliative medicine
3. Research protocol for the systematic review
4. Ethics committee application document
5. Society of Electrotherapists: documentation and sample Newsletter
6. Specification and development of a new electroanalgesia unit
7. Interim Report
8. Statistical information

**N.B.** 1. sections underlined are now complete.
2. * source materials collected and ready for write up.
Title: Electroanalgesia: Historical and contemporary developments.

Introduction:

The initial aims of this investigation were to examine if the therapeutic claims for electroanalgesia could be upheld, to what extent it is safe and effective, to establish guidelines for future comparative studies and to ultimately enhance clinical training and practice at the micro-level. The literature was to be comprehensively reviewed and critically analysed to identify the range and variation of techniques used, types of observations recorded, results obtained and conclusions reached. The development and increasing professional recognition of electroanalgesia within conventional and unorthodox medicine was to be examined. The range and usage of the techniques and the development and provision of education and training will also be evaluated. The evolving theoretical foundations will also be reviewed critically in the light of published studies on mechanisms of action and biochemical/physiological effects.

The initial results form a basis for analysis of published studies, establishing criteria for comparative evaluation and carrying out a systematic review and meta-analysis of appropriate published work. Amongst factors to be considered will be patient selection, initial diagnosis, background and previous history, study size, use and nature of controls, comparison treatments, data collection and observations made, criteria for evaluating outcomes and efficacy, statistical methodology, type of trial, consideration and role of placebo effects and conclusions drawn. Methodological variation considered will include such electrical parameters as waveform, phase duration, pulse rate, polarity and amplitude and current modulation modes as well as treatment schedules, type of practitioner etc. Meta-analysis involves
the identification of good study design features and their weighting before evaluation of therapeutic effectiveness and safety, and the comparative value of differing approaches to electroanalgesia.

The aim of the proposed doctoral programme extends beyond evaluation of published work to the formulation of guidelines for the conduct of future comparative studies in electroanalgesia and a range of orthodox and unorthodox studies on pain relief. It is also intended to identify effective treatment strategies and procedures and provide guidelines for the selection of suitable patients who would benefit from the treatments. It is a further aim to produce guidelines and educational material targeted at the practitioner and training level in the areas of both orthodox and unorthodox medicine.

I. A brief review of the work already undertaken:

Part I: Historical Development:

1. Early developments in electroanalgesia.

The first chapter is now complete and examines the early history of electrical treatments from the use of animated minerals such as amber, magnetite or lodestone, which were all known to ancient man,1 through to the use of the electric torpedo fish, which was first recorded in AD 64, when Scribonus Largus introduced the electrical powers of the fish into clinical medicine as a cure for headache and gout.2 It appears that the use of the torpedo fish continued within general medicine from that time and by the sixteenth century its application had been broadened to include those suffering from mi-

---

graine, melancholy, and epilepsy.\textsuperscript{3} Instances of Europeans using electric fish as medical shocking machines are to be found in the literature up to about 1850. This is followed by an account of the early developments of electrical machines from Cardano in 1551 and Gilbert, one-halff century later, who laid the groundwork for the production and leashing of man made electricity to replace the piscean variety. This development of Gilbert's crude electrostatic induction machines was archetypal of apparatus of that kind in use for the next three hundred years. In the seventeenth century, von Guericke 1672, was the first to construct an early prototype of an electrostatic generator and he produced electricity by rotating sulfur against the friction of his hand. This effort being the first controlled artificial production of electricity. Hauksbee elaborated the crude implement of Von Guerick further into an electrostatic generator early in the eighteenth century.\textsuperscript{4} In 1745, von Kleist constructed the first electrical condenser, an achievement independently duplicated the following year in Leyden by Van Musschenbroek, and the Abbé Nollet called this the 'Leyden jar'.\textsuperscript{5} The invention of the Leyden jar permitted the use of far stronger shocks than the older static machines had been able to deliver, and called attention in a most dramatic manner to the effect of electricity on the human body. Armed with a better understanding of electrophysiology and new devices such as the battery and the induction coil, electrical practitioners set off in pursuit of cures for diseases. This chapter then goes on the examine in detail the application of electricity as a pain relieving modality in Europe and the New world throughout the eighteenth, nineteenth and twentieth centuries.


2. Research:
The Rev. John Wesley MA Electrotherapist:
A case study in eighteenth century alternative medicine.

Compared with his position as one of the founders of Methodism, John Wesley's interest in electricity and his work as an electrotherapist are virtually unknown. In Britain, Richard Lovett (a lay clerk at Worcester Cathedral) claimed in 1757 to be successfully treating many conditions including mental disease by electric sparks and current. John Wesley was so impressed by Lovett's electrical treatment that he too took up the application of electrotherapy. He published his *The Desideratum* in 1759, which extolled the virtues of electricity in many diseases, its popularity can in some way be measured by the fact that the book went into its fifth edition by 1781. He believed so strongly in the therapeutic properties of electricity that he bought four machines to treat the people of London. Wesley saw the 'subtle fluid' as the soul of the universe. He advocated electrical therapy for the following conditions: angina pectoris, bruising, cold feet, gout, gravel in the kidneys, headaches, hysterics and memory loss, pain in the toe, sciatica, pleuritic pain, stomach pain, palpitations and so on. His chief motivation for this promiscuous use of electrotherapeutics was his beliefs that this was an extremely effective cure that was, above all, cheap and therefore accessible to everyone. The cataloguing of cases by Wesley in the above book, is evidence of the strictly empirical approach that dominated electroanalgesia in the eighteenth century. The wonder of sudden pain relief by discharging the marvellous electrical 'fire' through the afflicted body.

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parts seemed to obviate any speculations regarding the physiology of the procedures.\textsuperscript{10}

Stillings (1974a) goes on to suggest that most of Wesley's applications would seem to many to be farfetched today. However, this observation is not strictly correct, and the proposed case study will examine not only Wesley's role as an alternative medicine practitioner,\textsuperscript{11} an issue not yet considered by nineteenth or twentieth century writers, but also the eighteenth century applications of electro-analgesia in relation to the current applications and research of the late twentieth century. The source materials for this study, including copies of Wesley (1747) and (1760), have now been collected and collated and are ready for writing up as Chapter Two.

\textbf{Part II: Mechanisms of Pain and Electrical pain relief:}


The third chapter examines pain as one of the commonest symptoms in medicine and which is said to be the prime cause of one third of all first consultations. While cure of the causative condition usually relieves the pain, it may on the other hand continue beyond its diagnostic usefulness, either because the disease is itself incurable, or because irreversible anatomical changes lead to continuing noxious stimulation. Acute and chronic pain control is now a major concern especially with population ageing and associated pain of the chronic degenerative conditions of the elderly such as osteoarthritis, post-herpetic neuralgia, trigeminal neuralgia, reflex sympathetic dystrophy, 'thalamic pain syndrome' and malignant diseases. Thus in an ageing population the medical, social, and economic consequences of chronic pain may be expected to increase.\textsuperscript{12} This chapter examines the mechanisms of pain in relation to electroanalgesia and includes a


review of pain thresholds, types of pain, pain receptors and their afferent nerve fibres, the dorsal horn and segmental mechanisms, the gate-control theory, central pain pathways, opioid peptides, opioid peptide mediated descending inhibitory system, non-opioid peptide mediated descending systems and neurogenic pain, and ends with a discussion of the gate-control theory again in relation to electrical stimulation. The gate-control theory has been extensively criticised in the past, not least by Professor Nathan who concluded that the gate-control theory was worked out to explain certain facts that had been found from investigating the physiology of the region where afferent fibres deliver impulses into the posterior horns. The theory itself has been productive of further work in this territory. It was one way of explaining some of the facts that had been observed. But, as fortunately always happens, further physiological and histological investigations have shown that what happens here is more complicated than was first thought. However recent studies appear to be consistent with the concept of the ‘gate control theory of pain’ in that less noxious information would be involved in the pain perception process for dorsal horn neurons which can potentially transmit noxious information to supraspinal levels, can have their cell activity decreased during TENS application to somatic receptive fields. Garrison and Forman’s (1994) study now represents the most important development in confirming the ‘gate control theory of pain’ since its first publication back in 1965.


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14 ibid.
18 op.cit. 12.
19 op.cit. 12.
20 op.cit. 12.
21 op.cit. 13.
22 op.cit. 12.
The fourth chapter examines in detail the principles and practice of contemporary analgesia, pain control by medication and their side effects, pain control by electrical methods, therapeutic currents as conventional TENS and Acupuncture-like TENS, electrical equipment and physiological responses, methods of administration of electrical treatments and a discussion on treatment parameters. An examination of the most important differences between ALTENS and conventional TENS is also conducted. ALTENS differs in the main from conventional TENS in that it consists of treatment with an electrical current of much lower frequency but much higher intensity. ALTENS treatment at 2 pps for 30 minutes has been shown to produce a marked increase in beta-endorphins and met-enkephalins whereas TENS treatment at 80-100 pps does not produce this increase and is thought to work by a different mechanism which is presumed to be the 5-hydroxytryptamine response.

Part III: Contemporary developments:
1. Contemporary applications of electroanalgesia:

The source materials for this chapter have been collected and collated and are ready for writing up. The collected papers are mainly organised in systems and will be presented as a literature review in the following format:
(a) an introduction
(b) the musculoskeletal system
(c) the neurological system
(d) the reproductive system as obstetrics and gynaecology

26 ibid.
30 op.cit 29
31 ibid
(e) other conditions with a pain component e.g. dental applications, cancer and palliative medicine, post-operative analgesia etc.

(f) anti-emesis, whilst not a pain problem in itself is often linked with many of the above applications especially within post-operative care, hyperemesis of pregnancy, cancer and in palliative medicine which is the subject of the randomised clinical trial described later in this report.

2. Research:

In order to gain both theoretical and practical experience with research methodology and the randomised controlled clinical trial the following programme of research was devised in association with the medical staff of The Leicestershire Hospice (LOROS) and the Department of Medical Statistics De Montfort University. Initially, instruction on the preparation of and statistical methods of clinical trials was sought, the literature searches were organised, the preparation of the research protocol and submission to the ethics committee of the Leicestershire Health Authority organised, and this was followed by conducting and completing the double-blind randomised clinical trial together with the statistical analysis. This procedure took nearly one year to complete. The source materials on electroanalgesia and electroantiemesis in palliative medicine, which had been collected and collated, are now ready for writing up together with an account of the trial itself.
The aim of this Investigation was to determine the role of ALTENS in improving the quality of life within palliative medicine and to record measurements of electrical skin resistance in cancer patients. Many studies have shown likely benefit from the use of transcutaneous electric nerve stimulation (TENS) in the alleviation of pain, nausea and other symptoms. However there have been few published reports of the effectiveness of this treatment within the palliative care setting. The present study was designed to assess the effectiveness of ‘acupuncture-like transcutaneous nerve stimulation’ (ALTENS) in the management of pain, nausea and vomiting in hospice patients. The use of acupuncture points Pe6 for electro-antiemesis is well accepted in the literature and the use of LI4 for electroanalgesia is a standard procedure both within Traditional and Western acupuncture.

Fifteen ambulant Caucasian patients between the ages 35-75 with pain and/or emesis problems admitted for symptom control to The Leicestershire Hospice were entered in a randomised double-blind controlled trial to active ALTENS, placebo ALTENS or no ALTENS groups in addition to recognised standard therapies for pain and antiemesis. Outcomes were measured using the EORTC QLQ-C30 questionnaire and retrospective drug estimations. Excluded from the study were patients unwilling or unable to provide informed consent, patients too ill to cope with 30 minutes of restrictive treatment, pa-

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32This study was registered with The European Commission COST action B4 on ‘Unconventional Medicine’
33The study was also registered with the European Organisation for Research and Treatment of Cancer (EORTC) Quality of Life Group which has “granted permission to J Gordon Gadsby to employ the EORTC QLQ-C30 in an academic quality of life study entitled Randomised Controlled Trial of Acupuncture-Like TENS”.

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tients with an on-demand pacemaker, pre-menopausal women, patients with vomiting due to intestinal obstruction or raised intracranial pressure or iatrogenic causes and patients who had previously received (and were thus familiar with) TENS or ALTENS treatment. Patients were entered into the trial following an independent assessment by a clinician (AF, IJ) and completion of a consent form and the EORTC QLQ-C30. They were then randomly assigned to receive either:

1. Standard therapy consisting of all necessary drugs and supportive care for the treatment of pain, nausea, vomiting and other symptoms as routinely used in the hospice.

2. Active ALTENS consisting of functional TENS unit and functional electrical leads and Standard therapy

3. Inactive (placebo) ALTENS consisting of functional TENS unit with leads rendered non-functional by the manufacturer but which were indistinguishable from the functional leads and Standard therapy.

Entry into the trial was followed by five consecutive daily treatments given by the nurse practitioner (JGG) to the active and placebo groups using a colour coded system of leads. Lightly gelled carbon vinyl electrodes 4 cm² were attached to the patient, one to the acupuncture point Pe6 (Neiguan) and one to the point Li4 (Hegu) of the dominant hand and secured with tape. Electrical stimulation was given using a 'Body Clock VTENS unit' with the pulse rate set at 2 pulses per second with a symmetrical biphasic pulsewave in continuous mode, the pulse width at 200 microseconds and the amplitude setting at 2.5 on the unit output scale. The timer was set at 30 minutes for the duration of each treatment. On day 6 a second EORTC QLQ-C30 was completed by the independent clinical assessor together with a retrospective assessment of analgesic and antiemetic use over the study period and recorded on the data collection sheets.

Although no statistically significant differences were detected in this small study there is a clear clinical indication of the beneficial ef-
fect of ALTENS in improving the overall quality of life, 2.67 times (95% CI: 0.15, 45.14) that of the control and in improving fatigue symptoms 16 times (95% CI: 0.72, 35.48) that of the control but no evidence to support the use of ALTENS for antiemesis and analgesia. Electrical skin resistance recordings in cancer patients showed highly significant differences at 28 - 34 time's normal the significance of which is not known at this time.

The use of ALTENS was not supported in the alleviation of pain and nausea and vomiting in these patients. However, the pilot study shows several interesting observations in respect of the global quality of life and the symptoms of fatigue, which may deserve further investigation as may the significance of the findings of elevated electrical skin resistance.

Comments:

The negative outcomes of this pilot trial in respect of analgesia and antiemesis in these patients necessitated an abandonment of further studies. However, statistical methods of power calculations were used to determine the required number of patients to meet the trials positive outcome, i.e. in respect of the Fatigue and Malaise (FM) symptoms - and for an 80% chance of deeming a difference in the 'fatigue difference' of 0.54 and to be statistically significant at the 2-sided 5% level, a sample size of 48 patients/group would be required.

This latter trial size would lend itself to further study and may be considered at a later date if circumstances at the Leicestershire Hospice permit.
An abstract based on the above information was submitted for consideration to The Palliative Care Research Forum on the 27th May for presentation, either as an oral or as a poster presentation on the 9-11th November 1995 at the Research Forum in Harrogate U.K. This was subsequently accepted and delivered as a poster presentation on these dates. The abstract will subsequently be published in the November/December (1995) edition of the Journal of Palliative Medicine.

3. A new evidence-based electroanalgesia training package:

This part of the study was completed in September 1994 and a pilot study of students has completed the course and/or is in progress. This training package will be further developed by the Society of Electrotherapists within the framework of the European Federation of Modern Acupuncture, to which it is affiliated, on completion of this programme of study. A copy of both parts of the training package will be available as an appendix to the completed thesis which it is planned will include an evaluation of the pilot study and its success.

4. A new practitioner society:

The Society of Electrotherapists was formed in 1993, by the writer, from the defunct International Society of Biophysical Medicine and is now in the third year of its existence as a professional support group to practising electrotherapists. A Society newsletter is produced three times a year and edited by the writer. Previous attempts to 'professionalise' electrotherapists, including The International Society of Biophysical Medicine, had failed for various reasons. The progress of the current Society will be evaluated as part of this project and the problems of placing ‘alternative medical practice’ on a firm professional footing reviewed. The well documented development of chemistry in Britain leading to the establishment and current position of the Royal Society of Chemistry will be used as a comparison.
5. Advising a study in electroanalgesia and colonoscopy

The postgraduate student (JGG) has been invited to collaborate in a research project based at the Leicester General Hospital-Gastroenterology Unit investigating the effects of TENS analgesia during colonoscopy. The study is being conducted by Dr John Mayberry's team and is directed by Dr Richard Robinson, Senior Registrar and Research Fellow, Leicester University Medical School. The research protocol, based on the model described above for ALTENS in palliative medicine, has been submitted to the ethics committee of the Health Authority and the trial is scheduled to commence in late November 1995. JGG has also been invited to organise the randomisation and blinding methodology and to collaborate in providing the research team with methodological and technical support during the trial and this offer has been accepted.

Part IV: Research: Systematic reviews of the effects of health care interventions:

1. Systematic reviews and meta-analysis;

Over two million health research papers are published each year, making it impossible for health care workers to keep up to date on current knowledge. Reviews are needed to provide manageable information on which decisions on health policy, and individual treatment can be based. The state of the art review at this time is the Systematic Review or Meta-Analysis. The term 'systematic review' implies that a review has been prepared using some kind of systematic approach to minimising biases and random errors, and that the components of the approach will be documented in a materials and methods section. Meta-analysis implies that a systematic approach to a review entails quantitative synthesis of primary data to yield an overall summary statistic. However, in addition to those circumstances in which
statistical synthesis of results of primary research is not advisable, there will be others in which it is quite impossible and it is just as important to control biases in reviews in these circumstances as it is to do so in circumstances in which meta-analysis is both indicated and possible.\textsuperscript{34} Most meta-analyses to date have attempted to ensure that they dealt with primary studies of sufficient quality by means of exclusion criteria intended to eliminate the less reliable results. A preferable approach is to perform sensitivity analyses of the results of meta-analysis to explore the effects of study quality on the conclusions. In the following study, randomized and non-randomised studies, blind and unblind studies and studies of varying power are included in the database of studies to be analysed by meta-analysis, but subsidiary analyses will restrict attention to randomised or blind or powerful studies to investigate the impact of these measures of study quality.\textsuperscript{35} One major area for exploration within the meta-analysis will be the source of the heterogeneity (statistical, clinical and methodological) of the study's findings, that is, disagreement in the results of the different studies included in this meta-analysis will be rigorously searched out\textsuperscript{36} within the framework of the Cochrane Collaboration Tool Kit\textsuperscript{37}.

The Cochrane Collaboration evolved in response to the challenge of Archie Cochrane, twenty years ago, who drew attention to the collective ignorance about the effects of health care. Contributor's in many countries and specialities are now preparing and maintaining systematic reviews of RCTS and reviews of other evidence where appropriate. The source materials necessary to examine the Cochrane Collaboration in detail have been collected, collated and filed ready for

use and writing up\textsuperscript{38} as an introduction to the research study. The process of joining a suitable Cochrane Collaboration Group to support this study within the Musculo-Skeletal Field, has not been without problems of its own. It has taken over ten months to overcome the bureaucracy and join a 'suitable group' but this is now well advanced in association with the University of Limburg Maastricht, The Ludwig-Maximilian University of Munchen, Germany, The Universities of Ottawa and Toronto, and Prof. Nachemson, Sahlgrenska Hospital, Gothenburg, Sweden. This review when complete will then be entered into REVMAN\textsuperscript{39} and disseminated through the Cochrane Collaboration as electronic media through The Cochrane Database of Systematic Reviews on CD ROM and the Internet.

2. A systematic review of electroanalgesia for chronic low back pain:

The practitioner specialising in musculo-skeletal diseases is fully aware that the most common complaint worldwide is chronic low-back pain. The frequency of this complaint stands in contrast to the significant lack of understanding of its effective treatment and prognosis\textsuperscript{40} and attempts to decrease its impact by different educational, ergonomic, or treatment methods have generally failed.\textsuperscript{41} There has been many trials of TENS and ALTENS since 1965 with over 600 publications recorded to 1991\textsuperscript{42} including those supporting its efficacy in low back pain, with up to 80% in acute back pain problems and at least 50% in chronic back pain\textsuperscript{43}. However, there have been other

\textsuperscript{38}ninety papers in all
studies\textsuperscript{44}, which have refuted this effectiveness. In view of these claims and counterclaims it would now seem appropriate to prepare and maintain a systematic review within the framework of the Cochrane Collaboration methodology in order to evaluate the claims more rigorously. If TENS and ALTENS, are proved to be therapeutically effective and cost-effective using the Cochrane Collaboration systematic review techniques, then the potential scale of their use world-wide would be enormous. To this end a team of reviewers to meet the requirements of the Cochrane Collaboration organisation has been selected and is now functional and consists of:-

1. J Gordon Gadsby, Electroacupuncturist and postgraduate student De Montfort University.
2. Prof. Alan Bennett, Kings College Hospital School of Medicine and Dentistry \textsuperscript{45}
3. Dr Michael Flowerdew, The Society of Electrotherapists.\textsuperscript{46}

The source materials, 53 research papers in the English language, have already been collected and collated, a research protocol prepared and variously revised and a pilot study to test the research tools has been completed. The systematic review of 53 papers in English has just commenced at the time of writing this report (Oct. 1995). The University of Limburg has suggested recruiting reviewers in non-English speaking countries through the Cochrane Collaboration to review relevant trials for us and we are waiting for more details on this.

\textsuperscript{45}Prof. Bennett is sponsored by Body Clock Health Care London
\textsuperscript{46}Dr Flowerdew is sponsored by The Society of Electrotherapists Leicester
Part V: Conclusions, recommendations and the contribution to knowledge.

This section of the study will be prepared on the completion of the research projects and writing up as the thesis.

Part VI: Reference Section:

A substantial reference listing has been completed over the last three years or so and extends to over 45 pages. This reference listing will almost certainly represent one of the most comprehensive databases on electroanalgesia at this time.

Part VII: Appendices:

1. The training package is complete for both the basic and post-basic course and several students have completed the course and are now in practice (including a consultant ENT surgeon now working in Tallinn Estonia).

2. Research protocol for RCT of electroanalgesia in palliative medicine is complete.

3. Research protocol for the systematic review has been completed.

4. Ethics committee application document is complete.

5. Society of Electrotherapists: documentation and sample newsletter is complete.

6. Producing the specification and aiding in the development of a new electroanalgesia unit in association with Dr Riccardo Cuminetti. This project is now in progress and should represent the state of the art for electrostimulation on its completion.
Discussion:

Considerable progress has been made with this study over the last three years, one year of pre-registration literature searching and reading followed by two years of postgraduate registration work, with thesis development under academic supervision, has generated a considerable amount of material as outlined in the previous pages of this report. The initial process of literature searching, collection and collation of papers has resulted in the production of a considerable database of over 800 items of source material at the last count, and this work has laid down a solid foundation for progression and transfer to the Ph.D. degree as discussed in this document. The initial aims of this investigation, as outlined on page 3, have been modified somewhat during the course of the last two years as more information became available and is now represented on page 2 of this document as the M.Phil./Ph.D. Thesis Structure document.

In order to understand the present day practice of electrotherapy an historical review was commenced early on in the programme of study. The recently proposed history of medicine case study of John Wesley, as an alternative medicine practitioner of both electrotherapy and other unorthodox techniques, developed from the discovery of this little known aspect of his life through the content of the literature review as laid down in chapter one. So this case study was not an original part of the programme but one which developed from the research process and which may now be seen as increasing in importance and originality. A secondary literature search revealed over 30 relevant papers and books and also involved the Wellcome Institute for the History of Medicine and Related Sciences. This search and subsequent collection and collation of references is now complete and ready for review.

The initial aims of the study were to examine the therapeutic claims made for the practice of electroanalgesia together with consid-
eration of its safety and efficacy, the evolving theoretical foundations and the range and variation of techniques used today.

In order to understand the research methodologies and outcomes of these trials it was considered advisable to conduct our own randomised controlled clinical trial as described earlier. This proved to be invaluable in understanding the research methodologies and statistical techniques of clinical trials, albeit time consuming as the practical research project turned out to be, which, although the findings were negative for the efficacy of electroanalgesia in these patients and which was probably due to the massive amounts of opiates these subjects consumed, there were some most interesting and positive outcomes the significance of which has not yet been fully considered. This study led directly to an invitation from the Leicester General Hospital to assist them in their trial on TENS and colonoscopy.

In a similar way, it became clear that a scientific systematic review of one aspect of electroanalgesia was indicated because of the complexities of the different treatments, methodologies, conditions, and patients rather than an overall review of all applications. A macroview based on the systems level will still be performed but not as a systematic review with meta-analysis. It was eventually decided to examine by systematic review and within the framework of the Cochrane Collaboration one of the most frequent application of electroanalgesia i.e. the treatment of chronic low-back pain.

The main aims of the revised doctoral programme of study are to consolidate the basic structure of the thesis by further research and by completing the two proposed major projects as original contributions to knowledge. On completion of this programme of research it is proposed that guidelines for the conduct of future comparative studies in orthodox and alternative techniques of electroanalgesia will be constructed, effective treatment strategies identified and guidelines suggested for selection of suitable patients who would benefit from the treatments. It is also intended that the educational material already
prepared will be extended and promoted more fully on completion of the programme of study. It is also expected that the completed parts of the thesis will be strengthened over the next two years and the sum of its parts will become apparent in its totality as a definitive and important resource document for both conventional and alternative practitioners of this century but more importantly as a resource for practitioners of the fast approaching twenty-first century. The next two years of research should prove to be most exciting and fulfilling as the completion of the programme draws rapidly nearer.

2. Statement of the intended further work:

Part I: Historical Development:
1. Medical history research: A case study in eighteenth century alternative medicine of The Rev. John Wesley MA as an electrotherapist will be completed.

Part III: Contemporary developments:
1. The contemporary applications of electroanalgesia to be written up within a systems format as described earlier.
2. Research:
   a). electroanalgesia/electroantiemesis in palliative medicine and a randomised controlled trial: the pilot study write up to be completed.
   b) to present the above as a poster at the meeting of palliative medical practitioners in November 1995.
   c) input to the Leicester General Hospital trial to be recorded and evaluated.

Part IV: Research: Systematic reviews of the effects of health care interventions:
(a) to examine the scientific bases of systematic reviews and meta-analysis within the framework of the Cochrane Collaboration.
(b) to conduct a systematic review and meta-analysis of the effects of health care as electroanalgesia for chronic low back pain within the framework of the Cochrane Collaboration.

**Part V: Conclusions, recommendations and the contribution to knowledge.**

To be completed at the end of the research programme.

**Part VI: Reference Section:** ongoing updating of the reference listing.

3. The original contribution to knowledge, which is likely to emerge from this study, may be summarised as follows:-

1. An original research (pilot) study - as a randomised clinical trial on electro-analgesia, electro-antiemesis and electro-anti-fatigue within palliative medicine. This study represents one of the few treatments shown to be effective in alleviating the symptoms of fatigue and malaise in palliative medicine. Although the results are based on a few subjects the potentially enormous benefits to cancer patients and chronic fatigue syndromes such as M.E. has yet to be considered and the procedure subjected to further research. If these results are repeatable then they may represent a most important step forward in anti-fatigue treatment.

2. An original research study - The Rev. John Wesley MA as an Electrotherapist: A case study in eighteenth century alternative holistic medicine. This is an issue which has not yet been considered by nineteenth or twentieth century writers but is especially relevant at the present time with the current interest and growth of alternative and complementary holistic practice, which may be subject to the same forces that were active in the past and still at work now but expressing themselves in modern form. The eighteenth century represents, perhaps, the adolescence of present-day medicine both ortho-
dox and unorthodox, for history is not so remote and we will understand our mature present day medical structures only if we can appreciate its history.47

3. An original research study - conducting a systematic review and meta-analysis of the effects of health care in the form of electrostimulation for chronic low back pain within the framework of the Cochrane Collaboration.48 This contribution to the Cochrane Collaboration Database and electronic network represents the first review of electrotherapy either within orthodox or alternative medicine practice.

4. To maintain and promote an evidence-based electroanalgesia training package, which is already in operation, in order to place electroanalgesia on a sound scientific basis and remove it from any possible claims of Electroquackery?49

5. To produce by 1996 a state of the art electrostimulation unit, with electrical parameters based on the findings of this thesis, for practitioner use, in association with Dr Riccardo Cuminetti a bio-electrical engineer based in Welwyn.

6. Finally, the sum of the parts of this study make up a substantial whole contribution to knowledge as an original research and definitive reference document on electroanalgesia not only for twentieth century practitioners but for students, academics and researchers of the present and of the future.

48 see the Cochrane Collaboration Handbook (1994) Section VI. The Cochrane Collaboration Toolkit
APPENDIX

B

(Tertiary Research)
APPENDIX B(i)

The Cochrane Collaboration

(ia) Cochrane Collaboration Mission Statement

(ib) Cochrane Musculoskeletal Group (CMMSG)

(ic) Cochrane Back Subgroup
The Cochrane Collaboration/Steering Group
(Extracted from The Cochrane Library Issue 4 1997)

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Mission Statement
The Cochrane Collaboration is an international organisation that aims to help people make well-informed decisions about healthcare by preparing, maintaining and promoting the accessibility of systematic reviews of the effects of healthcare interventions.

Principles
The Cochrane Collaboration's work is based on eight key principles:
1. Collaboration...by internally and externally fostering good communications, open decision-making and teamwork.
2. Building on the enthusiasm of individuals...by involving and supporting people of different skills and backgrounds.
3. Avoiding duplication...by good management and co-ordination to maximise economy of effort.
4. Minimising bias...through a variety of approaches such as scientific rigour, ensuring broad participation, and avoiding conflicts of interest.
5. Keeping up to date...by a commitment to ensure that Cochrane Reviews are maintained through identification and incorporation of new evidence.
6. Striving for relevance...by promoting the assessment of healthcare interventions using outcomes that matter to people making choices in health care.
7. Promoting access...by wide dissemination of the outputs of the Collaboration, taking advantage of strategic alliances, and by promoting appropriate prices, content and media to meet the needs of users worldwide.

8. Ensuring quality...by being open and responsive to criticism, applying advances in methodology, and developing systems for quality improvement.

**Memorandum and Articles of Association**

The Cochrane Collaboration is a not-for-profit organisation, established as a company, limited by guarantee, and registered as a charity in the UK under the Charities Act 1993. A copy of the Memorandum and Articles of Association of The Cochrane Collaboration can be obtained from the /pub' sub-directory of the UK Cochrane Centre's FTP site (username anonymous', password guest', filename articles').

**The Cochrane Collaboration Steering Group (CCSG)**

All registered entities are eligible to vote in the election of members to the CCSG, and to vote at the Annual General Meeting of the Cochrane Collaboration. The CCSG has twelve members, who are elected by the overall membership of the Collaboration for three years, with annual rotation of one-third of its members. The current Chair of the Steering Group is Professor Chris Silagy. The CCSG meets once during the annual Cochrane Colloquium and on one other occasion in the year: the minutes of its meetings can be obtained from the /pub' sub-directory of the UK Cochrane Centre's FTP site (username anonymous', password guest', filename [meeting date]. In between these meetings, its various working groups have regular meetings by teleconference.
These working groups, which report directly to the CCSG, are as follows:

The Executive Group (chaired by Chris Silagy) is responsible for making interim recommendations on policy issues to the whole CCSG between its bi-annual meetings.

The Software Development Group (chaired by Monica Fischer) is responsible for the development of the Collaboration's software (RevMan, ModMan, Criticism Manager, and the Parent Database).

The Trials Registers Development Group (co-convened by Kay Dickersin and Jean-Pierre Boissel) is responsible for co-ordinating the development of trials registers within the Collaboration.

The Colloquium Organising Group (chaired in 1997 by Jos Kleijnen) consists of the Cochrane Centre Director(s) hosting the forthcoming Annual Cochrane Colloquium, together with co-opted members to assist her/him.

The Handbook Editorial Group (co-convened by Andy Oxman and Cindy Mulrow) is responsible for editorial input to the Handbook on preparing and maintaining systematic reviews.

The Editorial Group (chaired by Jos Kleijnen) is responsible for ensuring a high standard of core written material about the Collaboration.

The Registration Group (chaired by Jean Jones) is responsible for considering and making recommendations to the whole CCSG regarding registration of potential applicants to become official entities' within the Collaboration.
The Publishing Policy Group (chaired by Chris Silagy) is responsible for controlling the pricing, distribution and marketing arrangements for Cochrane products.

**Current CCSG Membership**

Collaborative Review Group representatives (4): - Reviewer and editor representatives: Zarko Alfirevic (UK) Cindy Farquhar (New Zealand) Cecilia Hammarquist (Sweden)
Co-ordinator representative: Beverley Shea (Canada)
Centre representatives (4): - Director representatives: Lisa Bero (USA) Jos Kleijnen (The Netherlands) [Treasurer] Chris Silagy (Australia) [Chair] - Non-Director representative: Monica Fischer (Denmark)

The work of the CCSG and its sub-groups is supported by a small secretariat based in Oxford, UK. Present staff members are:
Administrator: Jini Hetherington Secretary: Barbara Roberts Company Secretary (Honorary): Muir Gray

**Strategic Plan**

The Cochrane Collaboration has developed a set of goals and objectives which are outlined in its Strategic Plan. This is available via the /pub' sub-directory of the UK Cochrane Centre's FTP site (username anonymous', password guest', filename stratpln').
Cochrane Musculoskeletal Review Group
(Extracted from The Cochrane Library Issue 4 1997)

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Exploratory meeting held on 8 July 1993
Registered with the Collaboration on 1 November 1993
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The CMSG editorial team conforms to the following peer review process:
Submission of Titles and Protocols to the Coordinating facilitator(s) of the various subgroups Feedback from the facilitator(s)
Submission to the CMSG Editorial Team (External Reviewer)* Feedback from the CMSG Editorial Team Submission of revised protocol to facilitator(s) and CMSG Editorial Team Protocol entered into the CDSR through the CMSG module
Completion of the review and entry into Review Manager 3.0 (RevMan 3.0)
Submission of review to the Coordinating Facilitator (s) of the various subgroups
Feedback from the facilitator (s)
Submission of the review to the CMSG Editorial Team
Feedback from the CMSG Editorial Team
Submission of revised review to the Coordinating Facilitator (s) and the CMSG Editorial Team
Entry into the CMSG module for dissemination through CDSR
Future Updates and submission of reviews to the facilitator (s) of the various subgroups and the CMSG Editorial Team
* There is at least one editor external to the review

Sources of support
Department of Medicine, University of Ottawa, Ottawa, Ontario, Canada Canada
Clinical Epidemiology Unit, Ottawa Civic Hospital, Ottawa, Ontario, Canada Canada
Medical Research Council of Canada and The Canadian Arthritis Society CANADA
National Health Research Development Programme (NHRDP) Canada

Scope
Randomized controlled trials (RCTs) and Controlled Clinical Trials (CCT) of interventions in the prevention and treatment of musculoskeletal disorders. The CMSG exists to facilitate development of subgroups tackling each of the separate areas of musculoskeletal disease. The only subgroups so far established with their own administrative support is the Musculoskeletal Injuries Review Group and the Back Review Group. For further details, see separate entries
in the Cochrane Database of Systematic Reviews. Progress towards
development of individual subgroups in the areas so far not covered is
summarized in the contents of our most recent newsletter April 1997.

In topics where no RCTs or CCTs have been identified, systematic
reviews may be produced using observational data. The topic list
below is based on topics which have been suggested by reviewers and
on some of the trials which have been identified to date. This is not a
complete list and further development of topics is underway. If there
are topics in which you are particularly interested in carrying out or
feel should be added to the list, please contact the Cochrane
Musculoskeletal Group.

TOPICS

(R) = Review (P)= Protocol (T) = Title

[Facilitators responsible]

BACK (see separate entry for complete scope)

Pharmacological Physiotherapy: Active Physical Therapy, Passive
Physical Therapy Behavioral Therapy Surgical Interventions
Multidisplinary Approaches Educational Alternative Medicine
Prognosis Causality Diagnosis [Claire Bombardier & Alf Nachemson]

Review Group Coordinator: Rosmin Esmail

The Effectiveness of Transcutaneous Electrical Nerve Stimulation
(TENS) and Acupuncture-like Transcutaneous Electrical Nerve
Stimulation (Altens) in the Treatment of Patients with Chronic
Low Back Pain (R) Gordon Gadsby

Spinal Manipulation for Low Back Pain Pim Assendelft

Conservative Management of Mechanical Neck Disorders: Part One:
Manual therapy Peter Aker

Conservative Management of Mechanical Neck Disorder: Part two:
Physical Medicine Modalities Anita Gross

Conservative Management of Mechanical Neck Disorder: Part three:
Drug Therapies Paul Peloso

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Conservative Management of Mechanical Neck Disorder: Part four: Patient Education Anita Gross
The effect of low-level laser therapy in musculoskeletal pain: A meta-analysis Arne Gam
Exercise Therapy for Low Back Pain Maurits van Tulder
Injection Therapy for Patients with Chronic Benign Low Back Pain Rob de Bie
Epidural Steroid Injections in the Management of Low Back Pain: A systematic review and meta-analysis Jodie Hasselkorn
Bed rest for Acute Low Back and Sciatica Kare Birger Hagen
The Surgical Management of Degenerative Lumbar Spondylosis JNA Gibson
Multidisciplinary Teams in Chronic Low Back Pain Jaime Guzman
Back Schools for Low Back Pain Maurits van Tulder
Primary Care Advice on Staying Active for Acute or Sub-acute Low Back Pain Kare Birger Hagen
The Surgical Management of Lumbar Disc Prolapse JNA Gibson
NSAIDs for Low Back Pain Maurits van Tulder
GOUT: Pharmacological Interventions:
The Treatment of Hyperurcemia on Chronic and Intercritical Gout.
Dan Baker [Ralph Schumacher & Dan Baker]
LUPUS ERYTHEMATOSUS:
Treatment of Lupus Nephritis Steven Edworthy
1. Chronic Widespread Pain
a) Fibromyalgia
b) Regional pain syndromes and myofacial pain
2. Upper Extremity (may come under the Back subgroup)
Therapies Pharmacologic NSAIDs Analgesics Centrally Active Anti-depressants Hypnotics Other eg. hormonal Physical Therapies Exercise TENS Laser Pschological Therapy EMG Biofeedback Cognitive Therapy Education [Vibeke Strand & Steven Edworthy]
MUSCULOSKELETAL INJURIES (see separate entry for complete scope):
Gamma Nails Versus Sliding Hip Screw for Hip Fracture
Musculoskeletal Injuries (R) Martyn Parker
Vitamin D analogues in the prevention of fractures Musculoskeletal Injuries (R) William Gillespie
Ankle ligament injuries—Prevention Musculoskeletal injuries (R) Katheryn Quinn
Extracapsular Fractures: Arthroplasty Musculoskeletal Injuries (R) Martyn Parker
After Care Following Hip Fracture Musculoskeletal Injuries (R) Ian Cameron
Traction: Pre-op for Hip Fractures Musculoskeletal Injuries (R) Martyn Parker
Lateral ligament ankle Injuries—Treatment Paul Parker
Heel Pain Treatment Fay Crawford
Fall Prevention in the Elderly Lesley Gillespie
DVT Prevention Post Hip Fracture Osteoporosis William Gillespie
Proximal Humeral Fracture Treatment Panos Thomas
Distal Radial Fracture Management Noelle Murphy
Intracapsular Hip Fracture Management Ian Mclean
Extracapsular Fractures: Nail Plates Martyn Parker
Soft Tissue Injuries of the Knee (Prevention) Ian McLean
Antibiotic Prophylaxis: Hip Fracture Bill Gillespie
Anterior Dislocation of the Shoulder Paul Parker
Achilles Tendon Rupture Sean Kelly
Stress Fractures of Lower Limb William Gillespie
Knee Ligament and Meniscal Injuries—Treatment Ian Mclean
Bioabsorbable Implant: Ankle Fractures James Hutchison
Achilles Tendinitis George McLauchlan
Open Tibial Fractures—Management John Keating
Anterior Knee Pain Colin Walker
Extracapsular Fractures: Conservative v Operative Martyn Parker

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Extracapsular Fractures: Ender Nails Martyn Parker
Randomized controlled trials of interventions used in prevention, management and rehabilitation of fractures, dislocations and soft tissue injuries of the musculoskeletal system. [Bill Gillespie]
Review Group Coordinator: Helen Handoll
OSTEOARTHRITIS (OA):
Pharmacological Interventions:
NSAIDs for the Treatment of OA of the Knee
Osteoarthritis (R) Margaret Watson
NSAIDs Treatment of OA of the Hip Tanveer Toheed
Intra-articular Injections Therapy for OA Nick Bellamy
Rehabilitation Interventions: Exercise in OA Mary Bell [John Kirwan]
Secretary and hand searching co-ordinator: Sara Browning
OSTEOPOROSIS:
Pharmacological Interventions:
Calcitonin for Osteoporosis Ann Cranney
Hormone Replacement Therapy (HRT) for Osteoporosis Peter Tugwell/ David Henry
Steroid Induced Osteoporosis Joanne Homik
Calcium for the Prevention of Osteoporosis Beverley Shea
Vitamin D Mannny Papadimitropoulos
Bisphosphonates for Osteoporosis Ann Cranney
Rehabilitation Interventions: Exercise in Osteoporosis Donatella Bonaiuti [Rick Adachi, David Henry & Peter Tugwell]
PEDIATRIC RHEUMATOLOGY:
Pharmacological Interventions
Review of Second Line Agents in Patients with Juvenile Chronic Arthritis [Editorial Team]
RHEUMATOID ARTHRITIS
Pharmacological Interventions:
1) Disease Controlling Anti Rheumatic Therapy (DCARTs only)
2) Disease Modifying Anti Rheumatic Drugs (Phamacol) (DMARDS)
-Also called Slowly Acting Anti Rheumatic Drugs; Remission
Inducing Drugs; Second Line Agents Methotrexate Gold (Aurarofin, Myochrisine, Solgonal Hydroxychloroquine Chloroguine Azathioprine Cyclophosphamide Cyclosporine Nitrogen Mustard Mycophenolic Acid Sulfasalazine (SAARDs)
3) Symptom Modifying Anti Rheumatic Drugs (SMARDs) NSAIDs Cox 2 Inhibitors Corticosteroids
4) Radiation Synnectomy (Yttrium90)
5) Physical Therapy Active and Passive
6) Occupational Therapy
7) Alternative Therapy Herbal, Copper Bracelets, Acupuncture
8) Biologics
9) Analgesics for Chronic not Acute
10) Bone Marrow transplant
11) Stem Cell transplant

Registered Titles and Protocols and Reviews:
Short-term corticosteroid in rheumatoid arthritis
Rheumatoid Arthritis (R) Peter Gotzsche
Second Line Agents for RA (DMARDs) Maria Suarez-Almazor
Folic Acid and Folinic Acid for Rheumatoid Arthritis. Zulma Ortiz
Short term Corticosteroid for Rheumatoid Arthritis Peter Gotzsche
Long Term Corticosteroid for Rheumatoid Arthritis Kenneth Saag
Yttrium90 for RA Nick Bellamy
Antimicrobial Therapy for Rheumatoid Arthritis Laura Gonzalez-Lopez
Use of Eythropoietin for the Anemia Treatment of Rheumatoid Arthritis Jorge I. Gamez-Nava
Biologics Vibeke Strand
Rehabilitation Interventions: Exercise in RA Els van de End
Balneotherapy for RA Arianne Verhagen [Dan Furst, Maria Suarez-Almazor, Peter Gotzsche, Nick Bellamy & Piet van Riel]

SOFT TISSUE RHEUMATISM
Pharmacological Interventions:
Treatments of Shoulder Pain Sally Green, Rachelle Buchbinder
Pharmacological and Non-Pharmacological Treatment for Fibromyalgia
Paul Peloso

Ultrasound Therapy for Musculoskeletal Disorders Danielle van der Windt & Geert van der Heijden

Efficacy of 904 mm laser therapy in musculoskeletal disorders Rob de Bie

Pharmacological and behavioural interventions for generalized and regional syndromes Types of Pain:
TMJ
Generalized pain - fibromyalgia
Regional pain syndromes

Pharmacological Interventions:
Analgesics NSAIDs Trigger point injections Rehabilitation Physiotherapy [Paul Peloso & Fred Wolfe]

SPONDYLO-ARTHROPATHY:
The Effectiveness of Pharmaceutical Treatment in Psoriatic Arthritis
Spondylo-Arthropathy (R) Graeme Jones
Physiotherapy in AS Maria Crotty
Clinical presentations i.e. ankylosing spondylitis, psoriasis, backs
Treatments NSAIDs Antibiotics Rehab Sulfazine Local Therapy [Marcos Bosi-Ferraz & Sjef van de Linden]

SYSTEMATIC SCLEROSIS
Pharmacological Interventions:
Treatments of Raynaud Phenomenon Janet Pope [Alan Silman]

VASCULITIS:
Pharmacological Alternative Therapies [David G. Scott & Stephen Hall]

Search strategy for specialised register
The Cochrane Musculoskeletal Group's Specialized Register of Controlled Clinical Trials

1. INTRODUCTION
The editorial team of the Cochrane Musculoskeletal Group (CMSG) have prepared a register to assemble, maintain and administer
centrally a specialized register of controlled trials as a service to the reviewers of the CMSG. This specialized register was created to assist members of the CMSG and consists of records referring to completed and ongoing trials.

2. ELIGIBILITY CRITERIA
Topic Scope: Controlled trials of interventions for the following areas of musculoskeletal disorders: back, gout, lupus erythematosus, musculoskeletal injuries, osteoarthritis, osteoporosis, pediatric rheumatology, rheumatoid arthritis, soft tissue rheumatism, spondylo-arthropathy, systematic sclerosis, vasculitis.

3. SEARCH FOR ELIGIBLE CONTROLLED TRIALS
(1) Electronic search of bibliographic databases
The National Library of Medicine MEDLINE database will be searched back to 1966. The current search strategy, using SilverPlatter MEDLINE, is as follows: (Not all subgroups are incorporated to date)
1 RANDOMIZED-CONTROLLED TRIAL in PT
2 RANDOMIZED-CONTROLLED-TRIALS
3 RANDOM-ALLOCATION
4 DOUBLE-BLIND-METHOD
5 SINGLE-BLIND-METHOD
6 CLINICAL-TRIAL in PT
7 explode CLINICAL-TRIALS
8 (clin* near trial*) in TI
9 (clin* near trial*) in AB
10 (singl* or doubl* or trebl* or tripl*) near (blind* or mask*)
11 (#10 in TI) or (#10 in AB)
12 PLACEBOS
13 placebo * in TI
14 placebo in AB
15 random * in TI
16 random * in AB
17 RESEARCH DESIGN
18 #1 #2 #3 #4 #5 #6 #7 #8 #9 #10 #11 #12 #13 #14 #15 #16 #17
19 EXPLODE (* see note)
20 EXPLODE (* see note)
21 EXPLODE (see* note)
22 TEXT WORDS for all SYNONYMS or /
23 #19 or #20 or # 21 or #22
24 #18 AND # 23
25 TG=ANIMAL not ( TG=HUMAN and TG=ANIMAL)
26 #24 not 25
*Note: Please explode your specific topic area.

(2) Handsearch of journals
A systematic journal handsearch for all trials of the journals listed below is being carried out by the members of the Cochrane Musculoskeletal Review Group.
Prospective Searching:
The Journal of Rheumatology-1966 to 1996
British Journal of Rheumatology-1966 to 1996
Arthritis and Rheumatism 1966 to 1996
Arthritis Care and Rheumatism 1988 to 1996
Acta Orthopedica Scandinavica 1995
American Journal of Sports Medicine
Annals of the Rheumatic Disease-1995 -prospectively
Arthrosopy-1995-ongoing
Nederlands Tijdschiff voor Geneeskunde 1995-ongoing
Netherlands Journal of Medicine 1995-prospectively
Osteoarthritis and Cartilage-1995 -prospectively
Revue de Rheumatism-prospectively 1995-ongoing
International Orthopaedics 1977-ongoing
Bone and Joint Surgery (Amer) 1948-1995
Journal of Chiropractics 1995
Dutch Journals in Rehabilitation (Retrospective and Prospective)
Clinical Journal of Rheumatology (1995-ongoing)
Ryumachi (Toyko) 1980-1995
(3) Handsearch of Conference proceedings
American College of Rheumatology PANLAR ILAR APLAR EULAR
(4) Registers for unpublished and ongoing trials
(5) Bibliography lists
(6) Content experts
(7) Current Contents

Conflict of interest
The Cochrane Musculoskeletal Group (CMSG) follows the conflict of interest statement set out by the Cochrane Collaboration.
Cochrane Back Review Group
(Extracted from The Cochrane Library Issue 4 1997)

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Editorial information
COCHRANE BACK REVIEW GROUP - A subgroup of the Cochrane Musculoskeletal Review Group Exploratory meeting of Cochrane Musculoskeletal Group held on 8 July 1993
Cochrane Musculoskeletal Group registered with the Collaboration on 1 November 1993
Proposal to start collaborating with the Cochrane Collaboration in low back pain on 25 October 1993
Exploratory meeting of Musculoskeletal Working Subgroup-Backs on 12 April 1994
Preliminary meeting of Cochrane Musculoskeletal Back Sub-group in Hamilton on 1 October 1994
Editorial board acceptance from Rob de Bie (January 1996), Rick Deyo (January 1996), Lex Bouter (January 1996), Dr. Waddell (July 1996), Dr. Paul Shekelle (July 1996), Dr. Roland (September 1996), and Dr. Francis Guillemin (December 1996)
Hiring of a coordinator for the Back Review Group April 1996

EDITORIAL TEAM
Editors:
Dr Claire Bombardier (Canada) (Co-ordinating Editor)
Dr Alf Nachemson (Sweden) (Co-ordinating Editor)
Dr Richard Deyo (USA)
Mr Rob de Bie (the Netherlands)
Prof Lex Bouter (the Netherlands)
Dr Paul Shekelle (USA)
Dr Gordon Waddell (UK)
Dr. Martin Roland (UK)
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Librarian:
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Director, Research Operations and Diffusion:
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Trial Identification:
Handsearcher: Tina Teow

FUNDING SOURCES
Intramural: Institute for Work and Health, Toronto, Canada
Extramural: Swedish Council on Technology Assessment in Health Care, Sweden
CITATION


Sources of support

Swedish Council on Technology Assessment in Health Care Sweden Institute for Work & Health Canada

Scope: To conduct reviews of randomised controlled trials and controlled clinical trials of primary and secondary prevention of neck, back pain, and other spinal disorders, excluding inflammatory diseases and fractures.

TOPICS (Reviewer) (status):

(R) = Review (completed review accepted, may be updated)

(P) = Protocol (protocol accepted, review in preparation or being revised)

(T) = Title (title accepted, protocol in preparation or being revised)

Topics submitted to the Cochrane Database of Systematic Reviews up to September 1997 are indicated by *. Suggestions of other relevant areas or titles are welcome.

1. PHARMACOLOGICAL

Epidural steroid injections and the management of low back pain (JK Haselkorn, USA) (T)

*Conservative management of mechanical neck disorders: Part three: drug therapies (PD Peloso, Canada) (P)

*Injection therapy for patients with chronic benign low back pain (R deBie, the Netherlands) (P)

*The effectiveness of non-steroidal anti-inflammatory drugs (NSAIDS) in the treatment of low back pain (MW van Tulder, the Netherlands) (P)

Muscle Relaxants for low back pain

Antidepressants for low back pain

Analgesics for low back pain

2. ACTIVE PHYSICAL THERAPY
*The effectiveness of exercise therapy for low back pain (MW van Tulder, the Netherlands) (P)
*Conservative management of mechanical neck disorders. Part two: physical medicine modalities (AR Gross, Canada) (P)

3. PASSIVE PHYSICAL THERAPY

*The effectiveness of transcutaneous electrical nerve stimulation (TENS) and acupuncture-like transcutaneous electrical nerve stimulation (ALTENS) in the treatment of patients with chronic low back pain (JG Gadsby, UK) (R)

*Spinal Manipulation for low back pain (WJ Assendelft, the Netherlands) (P)
Bed rest for acute low back pain or sciatica (KB Hagen, Norway) (T)
The effect of low-level laser therapy in musculoskeletal pain (AN Gam, Denmark) (T)

*Conservative management of mechanical neck disorders. Part one: manual therapy (PD Aker, Canada) (P)

Traction for low back pain
Orthoses for low back pain

4. BEHAVIOURAL THERAPY
Primary care advice on staying active for acute or sub-acute low back pain (KB Hagen, Norway) (T)
The effectiveness of behavioural therapy in the treatment for chronic low back pain (MW Tulder, the Netherlands) (T)

5. SURGICAL INTERVENTIONS
*The surgical management of lumbar disc prolapse (JNA Gibson, UK) (P)
*The surgical management of degenerative lumbar spondylosis (JNA Gibson, UK) (P)

6. MULTIDISCIPLINARY APPROACHES
Multidisciplinary approaches to the management of chronic low back pain (J Guzman, Canada) (T)

7. EDUCATIONAL
*Conservative management of mechanical neck disorders. Part four: patient education (AR Gross, Canada) (P)

*The effectiveness of back schools in the treatment of low back pain (MW Tulder, the Netherlands) (P)

8. ALTERNATIVE MEDICINE
The effectiveness of acupuncture in the treatment of low back pain (MW Tulder, the Netherlands) (T)

EMG Biofeedback for low back pain

9. PROGNOSIS

10. CAUSALITY

11. DIAGNOSIS

Search strategy for specialised register

A. Current Searching Activities

1. Electronic Database Searching

Refer to the Cochrane Musculoskeletal Review Group search strategy.

2. Journal Handsearches of randomised controlled trials, controlled clinical trials, meta-analysis and literature review articles Spine 1976 to March 1997 - completed

Please contact the review group coordinator before undertaking a handsearch to avoid errors and duplication of effort.

Conflict of interest: The Cochrane Back Review Group follows the conflict of interest statement set out by the Cochrane Collaboration.
APPENDIX

B(ii)

Data Collection

(iia) Reviewers Check List and data collection sheets

(iib) Data Sheets: summary sheets of all trials
Reviewers Check List

1. Reviewer initials: ........................................... Date....................................................

2. Trial identification surname: .......................................................... Year......................

3. Types of participants - key characteristics:
Do the participants of this trial meet the inclusion criteria for patients with chronic low- back pain? = Y/N. Is there at least 8 weeks duration of illness? = Y/N.

4. Types of intervention - key characteristics:
Do the interventions in this trial meet the inclusion criteria for TENS? = Y/N or ALTENS? = Y/N; Is there a credible control? = Y/N;
State the treatment frequency used = Hz/pps;
The waveform described as = continuous/burst/modulated;
The no. of treatments given = ; The length of treatment = minutes.

5. Types of outcome measures - key characteristics:

<table>
<thead>
<tr>
<th>Outcome: Pain Relief</th>
<th>TENS/ALTENS Treatment</th>
<th>Control Treatment</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients improved</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. with no improvement</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Outcome: Activity Level</th>
<th>TENS/ALTENS Treatment</th>
<th>Control Treatment</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients improved</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. with no improvement</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td></td>
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</tbody>
</table>

6. Methodological quality of study - for weighting the meta-analysis:

1. Was the allocation concealment adequate: A/B/C
   (A = yes; B = partial C = no;)
a. Was the study described as double-blind? Y/N
b. Were the physical characteristics of the control/placebo credible.? Y/N/None
c. Were the pain and/or activity assessments assessment techniques valid? Y/N
   1. pain assessment: a valid method as.................................................. none........
   2. activity assessment as: subjective by patient/objective by examiner/none
Trials Contributing Data to the Review - to include the following information:

<table>
<thead>
<tr>
<th>Trial (1)</th>
<th>Methodology (2)</th>
<th>Participants (3)</th>
<th>Comparison Groups (4)</th>
<th>Outcomes (5)</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>e.g.</td>
<td>e.g.</td>
<td>e.g.</td>
<td>e.g.</td>
<td>e.g.</td>
<td>e.g.</td>
</tr>
<tr>
<td>author and date</td>
<td>intervention as TENS/ALTENS?</td>
<td>number, country setting, sex of participants</td>
<td>TENS or ALTENS group</td>
<td>Outcome measurement:- appropriateness of measures used?</td>
<td>further information required</td>
</tr>
<tr>
<td>e.g. (Smith 1992)</td>
<td>standardisation of intervention?</td>
<td>other characteristics of participants:-</td>
<td>Control Groups:- appropriateness of control group?</td>
<td>validity of measures?</td>
<td>any patient follow up indicated</td>
</tr>
<tr>
<td>(*)</td>
<td>randomisation method?</td>
<td>length of time of chronic low back pain?</td>
<td>randomisation details?</td>
<td>blinding of subjects and observers?</td>
<td>a pilot or a full trial etc</td>
</tr>
<tr>
<td>* p = published data</td>
<td>blinding technique?</td>
<td>adequacy and comparability of source population?</td>
<td>adequacy of baseline matching?</td>
<td>side-effects of treatments?</td>
<td>trials excluded with details</td>
</tr>
<tr>
<td>m = mixture</td>
<td>pain intensity assessment method and activity level assessment method?</td>
<td>eligibility and exclusion criteria?</td>
<td>group comparability?</td>
<td>Data characteristics and Statistical presentation</td>
<td></td>
</tr>
<tr>
<td>u = unpublished</td>
<td>intention to treat</td>
<td>adequate sample size?</td>
<td></td>
<td>External Validity: Generalisability of patients and model?</td>
<td></td>
</tr>
<tr>
<td>s = unpublished sought, not used</td>
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</tbody>
</table>
Trials Contributing Data to the Review

<table>
<thead>
<tr>
<th>Trial (1)</th>
<th>Methods (2)</th>
<th>Participants (3)</th>
<th>Comparison Groups (4)</th>
<th>Outcomes (5)</th>
<th>Notes</th>
</tr>
</thead>
</table>
### Controlled Trials Contributing Data to The Review

<table>
<thead>
<tr>
<th>Trial (1)</th>
<th>Methods (2)</th>
<th>Participants (3)</th>
<th>Comparison Groups (4)</th>
<th>Outcomes (5)</th>
<th>Notes/Statistics (6)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Melzack 1983 (p)</td>
<td>Double-blind RCT with an adequate allocation concealment using the sealed envelope method. Researcher selected suitable candidates from referrals to physiotherapy dept. ALTENS (4-8Hz) as a standardized intervention. with electrode placement over the pain site and one on the lateral aspect of the thigh x 30 minutes x up to 10 treatments (average of 5.1 treatments) over a two-week period</td>
<td>41 subjects 19M/22F Average age 46.3 years Source - Canada Physiotherapy Dept. average length of pain 36.2 weeks Subjects ambulant and intelligent Adequate source population no details of previous surgery</td>
<td>1. ALTENS (n=20) 2. Mechanical massage as a control (n=21) 3. no placebo control group. 4. all participants had standard exercises for Low Back Pain after treatment.</td>
<td>Appropriate and valid outcome measures for pain and activity which showed TENS to be more effective than mechanical massage for pain relief and also gave an increased range of movement  no side effects  no follow up data and statistical presentations satisfactory model validity satisfactory</td>
<td>An acceptable trial with participants meeting the inclusion criteria and internal, external and model validity satisfactory. All subjects also exercised after treatment? effect of this on outcome. Initial outcome at 2 weeks: % improved ALTENS = 85% CONTROL = 38% Difference = 47%</td>
</tr>
</tbody>
</table>

Outcome measured by McGill Pain Questionnaire (MPQ) and two Range Of Motion (ROM) tests for activity. Small sample size - low power
### Controlled Trials Contributing Data to The Review

<table>
<thead>
<tr>
<th>Trial (2)</th>
<th>Methods (2)</th>
<th>Participants (3)</th>
<th>Comparison Groups (4)</th>
<th>Outcomes (5)</th>
<th>Notes/Statistics (6)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gemignani 1991 (p)</td>
<td>Double-blind RCT with allocation concealment using table of random numbers and the paired/unpaired method</td>
<td>20 subjects (10 per group) 10M/10F Age 24-59 Italy: University of Pisa</td>
<td>1. ALTENS (n=10) 2. sham TENS (n=10) and seen as a credible placebo</td>
<td>Significant or trend difference in favour of ALTENS regarding pain less obvious in stiffness. appropriate pain and activity measurements assessed by the blinded evaluator no side effects recorded no follow up % improved as ALTENS = 90% PLACEBO = 40% Difference = 50%</td>
<td>a pilot study A good response to real treatments, satisfactory response to placebo no further studies carried out Initial outcome at 3 weeks:</td>
</tr>
<tr>
<td>(m) further information sought and received</td>
<td>ALTENS (5Hz) as a standardized intervention, plus a sham placebo control, with electrode placement to low back acupuncture points x 20 minutes x 10 treatments. Outcomes measured by Visual Analogue Scales and ROM test - Schober's test.</td>
<td>All diagnosed with Ankylosing Spondylitis and lumbar pain and stiffness of at least 1 month (2-60 months) - no previous surgery indicated not clear how ‘blind’ patients were.</td>
<td>baseline matching satisfactory</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>small sample size - low power</td>
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<td></td>
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### Controlled Trials Contributing Data to The Review

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<tr>
<td>Marchand 1993 (p)</td>
<td>A RCT with a partial allocation concealment -not described as double-blind but ?single-blind</td>
<td>42 subjects 20M/22F</td>
<td>1. TENS (n=14)</td>
<td>Appropriate and valid outcome measures for pain and unpleasantness which showed TENS to be significantly more effective than placebo TENS for pain at 1 week but not at long-term follow-up, and not more effective than placebo in reducing unpleasantness - but the starting values were lower in TENS group anyway?</td>
<td>An acceptable trial with participants meeting the inclusion criteria and internal, external and model validity satisfactory. Follow up at 1 week, 3 and 6 months. Initial outcome at 10 weeks: No of patients improved not given Results given as score changes i.e. reduction in VAS pain scores: TENS = 43% PLACEBO = 18% Difference =25%</td>
</tr>
<tr>
<td>(s) further information sought</td>
<td>Patients recruited by medical referral and local advertising with clinical exclusion criteria after Nachemson (1980)</td>
<td>Average age 36 years</td>
<td>2. a credible placebo TENS (n=12)</td>
<td>no side effects shown</td>
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<tr>
<td></td>
<td>TENS (100Hz) as a standardized intervention x 30 minutes x 20 treatments with a placebo and a control, electrode placement according to the appropriate dermatome involved</td>
<td>Source - University of Quebec Pain Lab. Canada</td>
<td>3. no treatment control group (n=16)</td>
<td>no activity data given</td>
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<td></td>
<td>Average length of pain 9 years</td>
<td>Adequate source population but ? biased by self-referrals</td>
<td>4. all groups had good baseline matching - no details of previous surgery</td>
<td>data and statistical presentations satisfactory</td>
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<tr>
<td></td>
<td>Outcome measured by VAS scores for pain intensity and unpleasantness small sample size - low power</td>
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<tr>
<td>Thorsteinsson</td>
<td>A RCT cross-over design - 3 real treatments and 3 placebo over 3 days; adequate allocation concealment; randomised by medical statistics department; a double-blind trial with no washout period; TENS (15-180 Hz) as a non-standardized intervention with output/frequencies adjusted for each patient x 20 minutes x 3 treatments with electrode placement applied over 3 predetermined sites Outcome measured by NRS 4 point scale (-1 to +2) for pain plus personality assessments (MMPI) average sample size</td>
<td>33 LBP subjects Dept of Phys Med Mayo USA 11M/22F Average age 48.6 years Source - 30 had had previous surgery (1-10 operations) Adequate source population of post-surgery cases</td>
<td>1. TENS (n=33) 2. cross-over placebo adequate baseline matching with 30 post-surgery cases</td>
<td>Real TENS more effective as improved at 48.7% to 32% placebo valid outcome measurement techniques side effects = allergic reactions and aggravation of pain n=5 48 subjects on home care followed up by questionnaire at 3 months and 6 months with 56.25% and 43.75% respectively still using the modality data and statistical presentations satisfactory</td>
<td>Low model validity - too many variables best results from TENS applied over the site of the low back pain rather than over a related nerve trunk or unrelated nerve trunk Initial outcome at 3 days: % improved TENS = 48.7% CONTROL =32.3% Difference 16.4%</td>
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</table>
| Deyo 1990 | A RCT with an allocation concealment by sealed envelopes and random numbers not described as double-blind - blind to subject | 145 subjects (125 after dropouts) - including 42 post surgery or chymopapain therapy subjects - 19 allocated to the TENS group alone (61%) in the ratios of (19:3:10:10) | 1. TENS (n=31) @ 80-100 or 2-4Hz x 45 minutes x 42 treatments | Appropriate and valid outcome measures for pain and activity - showed improvement in all groups but no clinically or statistically significant treatment differences between the four. At 2 months follow-up scores back near to baseline. | A good sample size trial with participants meeting the inclusion criteria and internal and external validity satisfactory but too many variables e.g. 23% TENS 77% ALTENS, variable electrode placements, plus additional hot packs/heating pads etc and the uneven post-surgery matching.
| (p) further information sought | Mixture of TENS and ALTENS as modulated waveforms - not as a standardized intervention - 4 groups as TENS/ALTENS; Sham TENS, TENS with exercise and Sham TENS with exercise with electrode placement initially over area of pain and then moved to optimise pain control | Average age 51.4 years Source -San Antonio USA median length of pain 4.1 years as a self-referred source population | 2. TENS + exercise (n=34) | one third reported minor side effects as skin irritation data and statistical presentations satisfactory | Initial outcome at 4 weeks: No of patients improved not given. Results given as VAS pain score changes: TENS = 47% SHAM TENS = 42% |
| (s) | Subjects recruited by advert/ heavily screened before trial | N.B. all groups also had hot packs/pads a mean of 23 days x 45mins | 3. Sham TENS (n=31) and no exercise | To many groups and variables for a satisfactory model validity |
| | Outcome measured by VAS and ROM/SLR | | 4. Sham TENS (n=29) + exercise | | |
## Controlled Trials Contributing Data to The Review

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</thead>
<tbody>
<tr>
<td>Jeans (1979)</td>
<td>A Double-blind RCT with no details of allocation concealment or randomisation method</td>
<td>6 LBP subjects M/F not known</td>
<td>1. TENS (n=6) @ 60Hz x 8 treatments</td>
<td>Appropriate and valid outcome measures for pain which showed a 40% reduction in pain scores with TENS at local pain area points and 10% at other points</td>
<td>An acceptable pilot trial but with very low numbers for LBP (6), many variables i.e. 4 treatment conditions with 16 subjects and difficult to extract the relevant data.</td>
</tr>
<tr>
<td></td>
<td>(p) TENS (60Hz) as a standardized intervention with electrode placement over local pain; distal trigger or acupuncture points; sham at site of pain; and distant nonrelevant points x 2/day x 4 days.</td>
<td>Age 33-76 years mean = 47.4</td>
<td>no details of length of treatments</td>
<td>2. control = dead machine (n=4)</td>
<td>Initial outcome at 4 days:</td>
</tr>
<tr>
<td></td>
<td>(s) further information sought</td>
<td>16 subjects in trial 6=LBP - no further details of source population or inclusion exclusion criteria</td>
<td>4 modes of application as above</td>
<td>no side effects reported</td>
<td>% change in scores TENS = 33.3% CONTROL =10% Difference =30%</td>
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<td>follow up of LBP subjects showed gradual decreases in pain intensity and radiating pain over a period of a few weeks</td>
<td>data and statistical presentations satisfactory</td>
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<td>Outcome measured by McGill Pain Questionnaire</td>
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<td>model validity satisfactory</td>
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<td>small sample size - low power</td>
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<tr>
<td>Abram (1983) (p)</td>
<td>an uncontrolled cross-over trial of electroacupuncture, placebo electro-acupuncture and ALTENS x 3 different treatments x 2 sessions x 20 minutes each @ 2Hz x 48 hours apart = 6 treatments in total over 1. acupuncture points, 2. non-acupuncture points and 3. ALTENS over areas of maximum pain/tenderness no allocation concealment or blinding though sessions were randomly arranged - no further details</td>
<td>5 subjects with low back pain USA treatment setting unclear 4M/1F age 19-68 treatment failures from other modalities including surgery but no other details</td>
<td>cross over trial as 1. EAP 2. Placebo 3. ALTENS no control group no baseline matching or group comparability</td>
<td>Pain VAS scale as mean pain ratings no significant differences in the three ratings no activity assessments no blinding of subjects or observers no side effects data presentation satisfactory low model validity</td>
<td>pilot study only with no significant differences in the three modes of treatment but this indicating that low frequency high intensity electrical stimulation provides analgesia which persists over many hours no follow up after 48 hours Initial outcome at 2 weeks: % improved = 40% not improved = 60%</td>
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### Uncontrolled Trials Contributing Data to The Review

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<td>Andersson (1976)</td>
<td>an uncontrolled cross-over trial of TENS/ALTENS</td>
<td>12 patients (9 post surgery x1 or more) Sweden selected from an orthopaedic ward</td>
<td>no placebo control group</td>
<td>outcome measurements satisfactory for pain</td>
<td>3 week follow up - no lasting improvements recorded</td>
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<td></td>
<td>intervention not standardized different number of treatments (ALTENS @ 2Hz x 1-23; TENS @ 50-100Hz x 3-8), groups, and sites of application (both segmentally and non-segmentally related to the region of pain) for 55-60 minutes, plus analgesics and physio. not randomised no blinding no control</td>
<td>5M/7F age 37-73 yrs severe chronic back pain with multiple pathology no comparability of source population</td>
<td>TENS (1-8) v ALTENS (1-23 sessions) no baseline matching no group comparability</td>
<td>no wash out period no blinding no significant side effects data presentation satisfactory poor model validity - too many variables and probably too few treatments to evaluate the outcomes satisfactorily</td>
<td>2Hz treatment gave poor results (but 7 patients had 5 or less treatments mode = 3), 100Hz better (8 patients had 5 or less treatments mode = 3) but only a short-term effect i.e. 30 minutes</td>
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<tr>
<td></td>
<td>VRS measurement for pain no valid activity assessment</td>
<td>pilot study size</td>
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<td>Initial outcome (at unspecified time): ALTENS % improved = 9% not improved = 91%</td>
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### Notes/Statistics

- **TENS**: % improved = 58%
- **not improved = 42%**
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<tr>
<td>Brill (1985) (p)</td>
<td>an uncontrolled study of 24 hour burst TENS @ 100Hz x 2 weeks at unspecified locations and conventional TENS also used by some patients</td>
<td>129 patients no details of gender or ages Back school USA severe back pain unable to enter back school programme eligibility and exclusion criteria simply stated adequate sample size</td>
<td>no control group no baseline matching or details of post-surgery cases in the numbers</td>
<td>inadequate pain and activity measurements no baseline matching or details of post-surgery cases in the numbers</td>
<td>at 12 months follow up - 80% had returned to normal activity a full trial Initial outcome at 2 weeks: % improved = 31% not improved = 69% Improvement at 1 year: % improved = 80% not improved = 20%</td>
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<td>Cassuto</td>
<td>an uncontrolled trial of high frequency TENS @ 15K Hz. on self selected patients with mixed pathologies and encompassed local trigger points</td>
<td>10 Sweden Hospital pain clinic no placebo control</td>
<td>VAS scores for pain showed a significant 62% reduction in scores</td>
<td>VAS scores for pain showed a significant 62% reduction in scores</td>
<td>pilot study numbers no follow up after treatment month</td>
</tr>
<tr>
<td>(1993)</td>
<td></td>
<td>no details of gender or ages</td>
<td>8 out of 10 patients had good pain relief</td>
<td>8 out of 10 patients had good pain relief no side effects recorded</td>
<td>medication allowed further information sought</td>
</tr>
<tr>
<td>(p)</td>
<td>VAS scale for pain assessment before treatment and after daily treatment</td>
<td>chronic long standing neck/back pain no details of conventional TENS</td>
<td>no activity assessment</td>
<td>no activity assessment data presentation satisfactory</td>
<td>Initial outcome at 1 month: % improved = 80% not improved = 20%</td>
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<td>(m)</td>
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<tr>
<td>Cheng (1987) (p)</td>
<td>an uncontrolled trial to compare ALTENS vs. electroacupuncture (EAP) for chronic back pain</td>
<td>24 subjects no gender or age details pain clinic Canada above 4 weeks of pain adequate source population - no multiple surgery small sample size of back pain subjects</td>
<td>ALTENS vs. EAP no placebo control group baseline matching and group comparable</td>
<td>appropriate outcome measures as VAS for pain and activity no blinding of subjects, observers operators, no side effects described Data presentation and statistics good no apparent differences between ALTENS/EAP after trial but ALTENS better at follow up. low internal, external and model validity - using a novel approach with 'Codetron' and telephone follow up</td>
<td>telephone follow up at 4 and 8 months of 75% of ALTENS, 85% of EAP showing ALTENS outperforming EAP Initial outcome at an unspecified time: % pain improved ALTENS = 96% EAP = 95% follow-up % improved ALTENS = 89% EAP = 41% % improved activity ALTENS 92% EAP 100%; follow up % improved ALTENS = 93%, EAP = 39%</td>
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<tr>
<td>Coletta (1988)</td>
<td>an uncontrolled trial of TENS vs. TENS and local etofenamate ointment</td>
<td>30 (15:15) 19M/11F</td>
<td>no control group</td>
<td>outcome measures satisfactory for pain and activity</td>
<td>no follow up pilot study only</td>
</tr>
<tr>
<td>(p)</td>
<td>not a standardised intervention; varying frequencies i.e. 30 - 100Hz x 10 treatments x length of treatment not given, applied to peri-articular areas of trigger points</td>
<td>Rehabilitation Unit Ancona Italy</td>
<td>no randomisation or baseline matching</td>
<td>TENS with etofenamate better than TENS alone for pain and shorter treatment period</td>
<td>Initial outcome at 20 days: % pain improved on TENS = 73% TENS + etofen = 100%</td>
</tr>
<tr>
<td>described as a RCT but no placebo control</td>
<td>source population not described - no details of previous surgery</td>
<td>no details of group compatibility as various spinal pain syndromes</td>
<td>some skin reactions</td>
<td>% activity improved on TENS = 40% TENS + etofen = 87%</td>
<td></td>
</tr>
<tr>
<td>no details of randomisation or blinding techniques described</td>
<td>no inclusion exclusion criteria</td>
<td>low model validity</td>
<td>data and statistics satisfactory but no binary measurements</td>
<td>N.B. needs further studies of adequate power to confirm these interesting findings.</td>
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<tr>
<td>Davis (1975) (p)</td>
<td>an uncontrolled study of TENS at the lowest setting agreeable to patient for 3-4 days using large dermatome electrodes for wide cutaneous stimulation no details of electrical parameters, randomisation, blinding or assessment measures</td>
<td>16 low back pain following spinal cord injury - 5 post-cordotomies Age 23-68 Spinal cord injury service USA no details of baseline matching or inclusion exclusion criteria small sample size</td>
<td>no control group</td>
<td>no details of outcome measures, blinding or side effects</td>
<td>pilot study size no follow up after 1 month Initial outcome at 4 weeks: % improved = 50% not improved = 50%</td>
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<tr>
<td>Denning (1988) (p)</td>
<td>a retrospective report by questionnaire of TENS usage in 182 patients of which 100 replies were used no randomisation or blinding no details of electrical parameters or no of treatments, advised to wear 8 hours/day (presumably as conventional TENS) for 1 - 47 months, average = 17 months with electrodes placed at the 'most appropriate position'</td>
<td>182 LBP patients (100 replied to the questionnaire) Royal National Hospital UK 2nd or 3rd referral after other conventional methods had failed - no details of previous surgery</td>
<td>TENS group no control no baseline matching group comparable</td>
<td>VAS pain measurement 76 (41%) of original responders obtained long-term improvement however 45% did not return the questionnaire so it could be more? no blinding skin irritation to tape and gel and electrodes cost effective data presentation and statistics satisfactory</td>
<td>retrospective study over 4 years to analyse the usage and effectiveness of TENS in 100 low back pain responders to the questionnaire Initial outcome of 182 subjects at 2 weeks: % improved = 86.8 not improved = 13.2% Long term outcome of 100 subjects (up to 4 years reviewed): % improved = 41%</td>
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<tr>
<td>Eriksson (1979) (p)</td>
<td>an uncontrolled study of TENS and ALTENS given as a fixed schedule, using 10-100Hz and 1-4Hz as pulse burst or continuous mode, over a one to two week period initially x 3/day using several electrode placements, within or around the painful area or over nerve branches innervating the painful dermatome or over the corresponding myotome. no standardisation of intervention, blinding, randomisation or placebo controls VAS assessment for pain</td>
<td>27 low back pain subjects in a study of 123 consecutively referred with chronic pain to a pain treatment group in Sweden - which also included many who had previous surgery no details of baseline matching no inclusion/exclusion criteria</td>
<td>TENS or ALTENS no placebo control group</td>
<td>VAS scale for measuring improvement in pain outcome 18 out of 27 improved = 66% data presentation and statistics satisfactory side effects as 15% with skin problems data presentation and statistics satisfactory</td>
<td>a 2 year follow up pilot study numbers for back pain Initial outcome at 2 weeks: % improved = 66% not improved = 34% % still using the modality at 3 months follow up = 66% no further breakdown of follow up data possible</td>
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<tr>
<td>Ersek (1976) (p)</td>
<td>an uncontrolled study of 35 consecutive patients of which 13 were low back pain using ALTENS at 4HZ in continuous mode, for 5-10 minutes with electrodes placed directly over the area of pain, x an unknown number of treatments, no randomisation, blinding or credible outcome assessment measures other than a % rating for pain relief</td>
<td>13 subjects with LBP - 2 with previous surgery, surgical outpatients, emergency or wards, USA</td>
<td>no placebo control group, each patient served as own control</td>
<td>all 13 patients experienced at least a 50% or more improvement in pain relief, overall improvement = 55%, as 6 @ 50-75%, 4 @ 76-89%, 2 @ 90-99%, 1 @ 100%</td>
<td>a pilot study as far as back pain subjects concerned, telephone follow up attempted during the 7 months trial period - no further details, Initial outcome (at unspecified time): % improved as 100% not improved as 0%</td>
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<tr>
<td>Fargas-Babjak (1992)</td>
<td>an uncontrolled trial using a novel form of ALTENS (Codetron); with a randomised stimulation at 4,1,4 and 200Hz for 30 minutes x 3-10 treatments using 7 electrodes on local pain areas - not specified</td>
<td>38 subjects in Part 1 of the trial with chronic low back pain 6 had previous surgery</td>
<td>no placebo control group</td>
<td>pain assessed at 6 levels no side effects recorded data presentation and statistics satisfactory low model validity</td>
<td>no follow up pilot study only - to test effectiveness of a new electrostimulation units delivering a strong acupuncture-like stimulation in a random order Initial outcome (at unspecified time): % improved = 81.5% not improved = 18.5%</td>
</tr>
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- **Trial**: Fargas-Babjak (1992)
- **Methods**: An uncontrolled trial using a novel form of ALTENS (Codetron); with a randomised stimulation at 4,1,4 and 200Hz for 30 minutes x 3-10 treatments using 7 electrodes on local pain areas - not specified.
- **Participants**: 38 subjects in Part 1 of the trial with chronic low back pain 6 had previous surgery.
- **Comparison Groups**: No placebo control group.
- **Outcomes**: Pain assessed at 6 levels no side effects recorded data presentation and statistics satisfactory low model validity.
- **Notes/Statistics**: No follow up pilot study only - to test effectiveness of a new electrostimulation units delivering a strong acupuncture-like stimulation in a random order. Initial outcome (at unspecified time): % improved = 81.5% not improved = 18.5%.

---

- **Pain** outcomes measured by a modified VAS.
- **No** blinding
- **No** activity assessment
- **Pain Clinic Canada**
- **Chronic low back pain patients** over a two year period with use of home care units.
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<tr>
<td>Fox (1976) (p)</td>
<td>an uncontrolled cross-over trial of TENS vs. acupuncture (2:2) as a standardised intervention, with TENS given @ 60Hz in 3 second bursts for 30 minutes over 4 weeks, at local and distal acupuncture points on the bladder meridian (B24, B26, B62)</td>
<td>12 - 8 had previous surgery Age 30-72 7M/5F</td>
<td>no placebo control group</td>
<td>appropriate and valid outcome measurements Pain relief &gt;33% in 75% of acupuncture and 66% of TENS no side effects recorded data and statistical presentation satisfactory acupuncture and TENS claimed to be equally effective but acupuncture slightly better? low model validity with 2 treatments and crossover without washout</td>
<td>pilot study 4 months follow up with 4 out of 8 patients reporting pain levels still reduced (4 lost to follow up) no further information</td>
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| Fried (1984) | a retrospective review of TENS - no standardisation of intervention with patient selection of treatment parameters and sites of electrode placement TENS given in addition to standard treatments such as ultrasound, counselling etc no randomisation, blinding or outcome assessment descriptions a set of observations | 460 low back pain subjects among 846 mixed pathologies - no details of previous surgery rehabilitation centre Canada no inclusion/exclusion criteria adequate source population bit no baseline details good sample size | no placebo control group no baseline matching | 83.8% improved 44.6% free of disability 36.2% capable of modified work no valid outcome measurements used based on return to work, partial return, disability no side effects reported data presentation satisfactory | review of effectiveness of clinical use of TENS in a good number of subjects over 4 years 6 months follow up outcomes only - no initial outcome details given 
Outcome at 6 months: % improved = 83.8% not improved = 16.2% |
## Uncontrolled Trials Contributing Data to The Review

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<thead>
<tr>
<th>Trial (1)</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Gunn (1975) (p)</td>
<td>a retrospective review of 100 low back pain subjects, but not all with pain lasting more than 8 weeks; treated with TENS @ 70-100 Hz, with a continuous waveform, for 20 minutes daily x 3 weeks at bilateral local and distal acupuncture points; (but not using ALTENS frequencies &lt;3Hz) no standardisation of intervention, randomisation or blinding but therapists counselled against bias no validated pain/activity outcome assessment measure</td>
<td>100 (96 - 4 dropouts) &lt;20 - &gt;60 90% Male British Columbia Rehabilitation clinic adequate sample size but with multiple low back pathology 14 previous surgery or fractures and poor experimental design</td>
<td>no placebo control group TENS vs. historical standard control group given an exercise regimen no baseline matching and group not comparable</td>
<td>80% improvement comparable to standard measures of 85% at 8 weeks but less invasive? but also with 37 refractory cases benefiting from the TENS regime some reduction in analgesics some activity assessment as return to work or not low model validity no statistical analysis or comparisons some skin side effects</td>
<td>a review with a 3 months follow up but no statistical data Initial outcome at 8 weeks: % improved = 80% not improved =20%</td>
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<tr>
<td>Indeck</td>
<td>an uncontrolled study with no details of standardisation of intervention, electrical parameters, randomisation or blinding</td>
<td>90 subjects (40 in-patients 50 out-patients)</td>
<td>no placebo control group</td>
<td>in-patients = 50% improved</td>
<td>no follow up</td>
</tr>
<tr>
<td>(1975)</td>
<td>electrode placement to various trigger zone areas, acupuncture sites or peripheral nerves for up to 24 hours/treatment</td>
<td>pain ward USA chronic back pain 1-23 years many (?) no.) had previous surgery with an average of 3.5 surgical procedures</td>
<td>no experimental design</td>
<td>out-patients = 40% improved</td>
<td>a reasonably sized trial but few details of methodology</td>
</tr>
<tr>
<td>(p)</td>
<td>VAS assessment for pain no details of activity assessments</td>
<td>no details of selection</td>
<td>no details of outcome measures</td>
<td>some skin irritation</td>
<td>Initial outcome at 2 weeks:</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>data presentation satisfactory but no relevant statistics</td>
<td>% improved = 44%</td>
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<td>not improved = 56%</td>
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<tr>
<td>Johnson</td>
<td>a retrospective study of long term TENS for pain relief - over a ten year period</td>
<td>430 subjects with low back pain out of a total of 1582 subjects reviewed at Newcastle Pain Relief Clinic UK</td>
<td>no control groups</td>
<td>an overall 58.6% success rate with mixed pathologies</td>
<td>a retrospective study of long term use of TENS</td>
</tr>
<tr>
<td>(1992)</td>
<td>no details of electrical parameters given</td>
<td>no details of previous surgery given</td>
<td></td>
<td>288 out of 430 patients with back pain continued with long term use of the modality - most patients not responding to TENS (during a home trial) returned the stimulators at the first follow-up appointment</td>
<td>no further analyses given - therefore the Outcome statistics are based on the 150 out of 430 obtaining long term relief</td>
</tr>
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<tr>
<td>Laitinen (1976) (p)</td>
<td>an uncontrolled comparative trial between acupuncture and TENS x 2-10 treatments x weekly sessions with TENS at 50Hz for 20 minutes with bilateral electrode or needle placements at one point along the course of the nerve trunk affected, and one point at a dermatome proximal to the affected segment. no randomisation or blinding described VRS assessments by doctor and by patient for pain levels</td>
<td>100 (50:50) 33 had previous surgery chronic LBP mean age = 47 Physical Med Dept Finland adequate source population length of LBP av. = 4.1 years no inclusion/exclusion criteria</td>
<td>TENS vs. Acupuncture 50:50 details of baseline matching e.g. TENS group had more post-surgery cases, more patients unfit to work, longer duration of symptoms and differences in baseline pain levels and no. of treatments</td>
<td>initial medical assessment of pain = 58% improved on Acupuncture 46% on TENS ; (patients assessment = 65% acupuncture 55% TENS) with 21% having pain relief for at least 6 months - (33% for the acupuncture group) vague VRS outcome measures and no activity measures no side effects reported data and statistics difficult to interpret - two sets of outcome measures for initial and long term - low model validity</td>
<td>good follow-up at 2 and at 6 months (postal inquiry) Initial outcome at 3-5 weeks: % improved = 46% not improved =54%</td>
</tr>
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<tr>
<td>Lamp (1987) (p)</td>
<td>a 5-day cross-over study of TENS for back pain using either conventional TENS at 85Hz or as a biphasic waveform with an interpulse interval at 273Hz x 5 treatments (2:3) for 20-60 minutes each + home treatment as required - with various electrode placement sites as pain located 1&quot; to 2&quot; below electrodes or pain centered within a 4 electrode arrangement. in addition to standard therapies - ultrasound, heat and cold but no electrical modalities no randomisation or blinding VAS scale for pain</td>
<td>65 subjects - no other data given including previous surgery Phys Ther Clinic USA LBP secondary to musculo-skeletal disorder adequate source population and sample size</td>
<td>no placebo control group each patient acting as his own control</td>
<td>VAS scale of pain outcome measure low model validity - 20 different TENS units used biphasic more acceptable to patients but no better pain relief % improvement data available on only 51 patients including 6 poor-responders</td>
<td>comparison of biphasic with ‘standard’ TENS pain relief for approx 1 hour 88% considered it useful Initial outcome at 5 days: % improved = 88.2% not improved = 11.8%</td>
</tr>
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<tr>
<td>Ledergerber (1979)</td>
<td>an uncontrolled trial of a novel ALTENS system vs. TENS; ALTENS at 6Hz on a high frequency carrier wave of 20KHz and TENS as a 10-100Hz continuous waveform x 5-6 treatments with variable bilateral electrode placements e.g. over the area of pain, trigger points or acupuncture points - using specific -ve and +ve electrode placement - until maximum pain relief obtained no further details of experimental design described - no randomisation, blinding or outcome measures</td>
<td>74 LBP subjects California Obs/Gynae unit USA</td>
<td>no placebo control group</td>
<td>no details of outcome measures given low model validity with too many variables</td>
<td>2 year follow up with good data as 1. ALTENS = 55% long term pain relief for moderate pain 2. TENS = 72% long term relief for severe pain Initial outcome at 2-3 weeks: ALTENS % improved = 25% not improved = 75% TENS % improved = 16.6% not improved = 83.4%</td>
</tr>
</tbody>
</table>

novel ALTENS used for moderate pain and TENS for severe pain
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<tr>
<td>Lerner 1981 (p)</td>
<td>A double-blind retrospective case-control comparative study with few details of allocation concealment, randomisation or blinding</td>
<td>40 subjects (18 had 1 or more previous surgeries)</td>
<td>1. ALTENS (n=20)</td>
<td>Active ALTENS subjects experienced an average pain reduction 37.26% greater than the placebo group</td>
<td>A retrospective study with few technical and experimental design details given</td>
</tr>
<tr>
<td>(s) further information sought but not obtained</td>
<td>ALTENS (0.5Hz) as a standardized intervention treating 16 various acupuncture points x two six second treatments with microstimulation x 3/week x 2 weeks - with few technical details</td>
<td>42%M/58%F Age 19-63 years 63% (25) LBP</td>
<td>2. placebo as dead battery - control (n=20)</td>
<td>outcome measures not a standard procedure</td>
<td>Initial outcome at 2 weeks:</td>
</tr>
<tr>
<td></td>
<td>Source - selected retrospectively from 201 cases on the basis of the Chronic Pain Characteristic Profile over a 12 months period in a chiropractic clinic USA</td>
<td>no details of baseline matching</td>
<td>no side effects</td>
<td>2 months follow up - 75.22% pain reduction with 6.3% in the placebo group</td>
<td>% improved ALTENS =75% CONTROL =10% Difference =65%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>satisfactory data and statistical presentations</td>
<td>low model validity</td>
<td></td>
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<tr>
<td>Loeser</td>
<td>an uncontrolled trial of TENS using patient selected frequencies of 10-150 Hz with a variable length and number of treatments</td>
<td>61 patients with back pain (out of a larger trial of 198 subjects) ages 16-83</td>
<td>no placebo control group</td>
<td>outcome measures not described</td>
<td>follow up to 1 year long-term relief (over 1 year) = 13%</td>
</tr>
<tr>
<td>(1975)</td>
<td>electrode placement initially over the area of pain but then adjusted and moved to other local or distal regions giving maximum pain relief</td>
<td>Dept of Neurosurgery USA</td>
<td>no details of baseline matching or group comparability</td>
<td>no blinding described</td>
<td>Initial outcome (at unspecified time): % improved = 77% not improved = 33%</td>
</tr>
<tr>
<td>(p)</td>
<td>no standardisation of the treatment intervention</td>
<td>no further details of subject source, comparability or previous surgery</td>
<td></td>
<td>some mild side effects as skin irritation</td>
<td></td>
</tr>
<tr>
<td></td>
<td>no randomisation, blinding or description of outcome measures used</td>
<td>no inclusion/exclusion criteria</td>
<td></td>
<td>data satisfactory</td>
<td></td>
</tr>
<tr>
<td></td>
<td>fair sample size</td>
<td></td>
<td></td>
<td>low model validity using patient preferences</td>
<td></td>
</tr>
</tbody>
</table>

- **Methods**
  - TENS: Transcutaneous Electrical Nerve Stimulation
  - Frequencies: 10-150 Hz
  - Variable length and number of treatments
- **Participants**
  - 61 patients with back pain
  - Ages: 16-83
- **Outcomes**
  - Initial outcome (at unspecified time):
    - % improved = 77%
    - Not improved = 33%
- **Notes/Statistics**
  - Follow up to 1 year
  - Long-term relief (over 1 year) = 13%
Uncontrolled Trials Contributing Data to The Review

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<tbody>
<tr>
<td>Long (1974)</td>
<td>an uncontrolled study of TENS with patient selected electrical parameters x 3 hours x 3-4 sessions with various non-specific electrode placements with further treatment x 1 month</td>
<td>99 LBP out of 400 with mixed pathologies USA</td>
<td>no placebo control group apart from the pilot study which was abandoned because of lack of placebo response</td>
<td>outcome measures not described</td>
<td>one year follow up with 74% improved</td>
</tr>
<tr>
<td>(p)</td>
<td>no standardisation of intervention</td>
<td>subjects with chronic low back pain not responsive to previous treatments and considered difficult pain management problems</td>
<td>low model validity - patient selected treatment</td>
<td>84% with initial improvement</td>
<td>Initial outcome at 4 weeks:</td>
</tr>
<tr>
<td></td>
<td>no randomisation, blinding or validated pain/activity outcome measures described</td>
<td>no details of baseline matching or previous surgery</td>
<td>skin irritation a problem</td>
<td>data presentation satisfactory</td>
<td>% improved = 84%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>not improved = 16%</td>
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<tbody>
<tr>
<td>Long (1979)</td>
<td>an uncontrolled study of TENS which follows on from Long's study of 1974 study</td>
<td>50 low back pain subjects Pain clinic USA</td>
<td>no placebo control group</td>
<td>20 out of the 50 with low back pain improved at one month</td>
<td>19 out of 50 still improved at 1 year follow up = 38%</td>
</tr>
<tr>
<td></td>
<td>all subjects had a 1 month trial and then up to 1 year of home use</td>
<td>subjects selected by the authors as representative of this group of patients with 34 out of 50 with more than 2 lumbar surgery interventions</td>
<td>no side effects described</td>
<td>no side effects described</td>
<td>Initial outcome at 4 weeks: % improved = 40% not improved = 60%</td>
</tr>
<tr>
<td></td>
<td>no details of electrode placements or electrical parameters given in this paper</td>
<td>no inclusion/exclusion criteria described</td>
<td>data presentation satisfactory</td>
<td>data presentation satisfactory</td>
<td></td>
</tr>
<tr>
<td></td>
<td>no standardisation of intervention, randomisation or blinding techniques described</td>
<td></td>
<td>low model validity</td>
<td>low model validity</td>
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<tr>
<td></td>
<td>pain intensity measured on a NRS scale of 0-4</td>
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<tr>
<td>Lundeberg (1984)</td>
<td>a trial of TENS and ALTENS with subjects randomised to 1 of 6 groups in series: i.e. one treatment each of 20Hz; 100Hz; high frequency TENS; low frequency TENS or placebo stimulation x 45 minutes x 2/week for 3 weeks = 5 treatments + one placebo = 6 treatments for each patient - with electrode placement in the pain area or other points if necessary, then two days later by 1G of aspirin for comparison not a standardised intervention - too many variables no blinding described</td>
<td>19 LBP subjects out of 60 with mixed pathologies unresponsive to recognised therapy</td>
<td>no placebo control group as such - each subject having one session of placebo and 5 different treatments with a 2-4 day washout period in between each treatment.</td>
<td>difficult to assess because of the number of variables in LBP low frequency is the most effective vibratory stimulation is as effective as TENS no side effects described data presentation satisfactory</td>
<td>no follow up described pilot study numbers for LBP subjects Initial outcome at 3 weeks: % improved = 79% not improved = 21%</td>
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<tr>
<td>Magbagbeola (1987)</td>
<td>an uncontrolled trial of TENS and ALTENS at various frequencies 5-30Hz (mode not described) x 6-8 electrodes x 30 minutes x 10-15 treatments at low back trigger points</td>
<td>40(60) Pain Clinic Saudi-Arabia</td>
<td>TENS/ALTENS</td>
<td>outcome measures not described</td>
<td>no follow up indicated</td>
</tr>
<tr>
<td></td>
<td>use of analgesic discouraged during the trial</td>
<td></td>
<td></td>
<td>15% cured</td>
<td>a small study with a large 38% dropout from 60 to 40 subjects</td>
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<tr>
<td></td>
<td>not a standardised intervention</td>
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<td></td>
<td>75% improved</td>
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<td></td>
<td>no randomisation or blinding</td>
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<td>10% failed</td>
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<td></td>
<td>pain/activity outcome measures not described</td>
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<td>no side effects</td>
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<td></td>
<td></td>
<td>data presentation satisfactory within the confines of a Outcome</td>
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<td>low model validity - too many electrical variables</td>
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<tr>
<td>McDonnell (1980) (p)</td>
<td>an uncontrolled trial of conventional TENS over 4 weeks using frequencies of 10-100Hz in continuous mode at low intensity; no details of the number of treatments, their length or electrode placement described. no details of the standardisation of the intervention, randomisation, blinding, inclusion/exclusion criteria or outcome measures used</td>
<td>88 (including 60 post-surgical) chronic LBP subjects out of a larger trial of 268 with mixed pathologies not responding to conventional treatments Neurosurgery unit USA no other details of source population or baseline matching a good sample size</td>
<td>no placebo control group</td>
<td>Initial outcomes as 61% improved overall - but no breakdown for low back pain subjects follow-up gives a breakdown for low back pain subjects as 48% overall reflecting a similar percentage response compared with the entire group no details of outcome measures, blinding or side effects described little data given</td>
<td>Initial overall outcome at 4 weeks: % improved = 61% not improved = 39% Outcome for LBP at 3 months - 4 years follow-up: % improved = 48% not improved = 52%</td>
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<tr>
<td>Melzack (1975)</td>
<td>an uncontrolled trial of TENS and ALTENS with some treatments at 60Hz and some at 3 or 10Hz x 20 minutes x a variable number of treatments from 1-8 x 1-3/wk at variable near acupuncture points or near trigger points or distal points or innervating peripheral nerves depending on response</td>
<td>15 LBP out of a trial of 53</td>
<td>some subjects acted as their own control in one of two unvalidated methods</td>
<td>60% mean reduction in pain in 12 out of 15 subjects using valid outcome measures</td>
<td>pilot study numbers</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>no blinding</td>
<td></td>
<td>6-18 months follow up for some subjects with 56% reporting pain still less</td>
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<td></td>
<td></td>
<td></td>
<td>no side effects described</td>
<td>data presentation good statistics poor</td>
<td>Initial outcome at 1-3 weeks with a % improvement &gt;33%; % improved = 80%; not improved = 20%</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>adequate source population but no inclusion/exclusion criteria</td>
<td>low model validity with too many variables</td>
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<tbody>
<tr>
<td>Melzack (1980) (p)</td>
<td>a cross-over design trial of continuous ALTENS at 3Hz x 30 minutes x 4 (2:2) treatments as a standardised intervention vs. ice massage at 1-2 week intervals with electrodes/ice placement at local midline back and distal leg points</td>
<td>44 LBP subjects 32M/21F 18-73F mean duration 7.4yrs and mainly post-surgery patients Pain Clinic Canada</td>
<td>ALTENS vs. ice massage no placebo control group no baseline matching or group comparability</td>
<td>no significant differences between ice packs and TENS at 3Hz data presentation satisfactory reliable pain assessment measures no side effects described</td>
<td>pilot study numbers 30 subjects followed up 1-12 months later with 14 (32%) still using TENS and 5 (11%) using ice massage Initial outcome at 2 weeks &gt;33%: % improved = 68.2% not improved = 31.8%</td>
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<tr>
<td>Meyler (1994)</td>
<td>an uncontrolled trial of TENS at 50-100Hz x 60 minutes x 3/day x 2-4 weeks with electrode placement on or around the painful area or proximally along the involved nerve to the area</td>
<td>22 subjects (from a larger multipathology study of 211) with chronic intractable LBP</td>
<td>no placebo control group</td>
<td>outcome measures as % alleviation scores with a 68% reduction in pain side effects of skin irritation in 22% subjects</td>
<td>pilot study numbers for LBP 6 months follow up = 69% still improved Initial outcome at 2-4 weeks with an improvement &gt;50%: % improved = 50% not improved = 50%</td>
</tr>
</tbody>
</table>

- no standardisation of the intervention - patients controlled electrical parameters
- no details of randomisation or blinding described
- % scoring for outcome measurement of pain intensity/alleviation and physical examinations
- Pain Clinic Netherlands
- no further details of baseline matching, previous surgery or inclusion/exclusion criteria
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</thead>
<tbody>
<tr>
<td>Moore (1983)</td>
<td>an uncontrolled trial of TENS and ALTENS in sequence at 10-100HZ x 30 minutes followed by 1-4 Hz x 30 minutes - daily over a 12 day period - as a standardised intervention but applied at various local pain, trigger or distal acupuncture point locations depending on response</td>
<td>58 patients with back pain out of 98 subjects - site not specified age 19-81 years Pain clinic USA chronic LBP 6/12 - 20 years</td>
<td>no placebo control group</td>
<td>outcome measured by % reduction in pain relief of at least 50% at the 12 day end period with 40 out of 58 subjects reporting relief no blinding 69% reduction on average minimal side effects minimal data and statistical presentation low model validity - too many electrical parameters, sites of application and patient control of treatment</td>
<td>follow up at 6 weeks, 6 months, 1 year and 2 years but no specific breakdown for LBP subjects. fair trial size Initial outcome at 12 days &gt;50%: % improved = 69% not improved = 31%</td>
</tr>
<tr>
<td></td>
<td>some patients rented TENS machines for further use no details of selection, randomisation or blinding</td>
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<tr>
<td></td>
<td>outcome measurements as a % of pain reduction</td>
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496
<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td>Procacci (1982)</td>
<td>an uncontrolled trial of continuous TENS at 50Hz x 15 minutes x 10 treatments as a standardised intervention to local or scar trigger points if present or to the area of pain</td>
<td>108 subjects - 24 had previous surgery 34M/74F age 27-81</td>
<td>no placebo control group</td>
<td>all patients examined experienced varying degrees of pain relief as follows 48% had long lasting pain control at 2 months 52% had temporary pain relief</td>
<td>good sample size with impressive results in all subjects after 10 treatments follow up at 2 months with 48% improved <strong>Initial outcome at 10 days:</strong> % improved = 52% not improved = 48%</td>
</tr>
<tr>
<td>(p)</td>
<td>no details of randomisation, matching or blinding</td>
<td>Pain centre Italy</td>
<td>detailed listing of LBP pathologies</td>
<td>no details of outcome measures apart from clinical examination</td>
<td></td>
</tr>
<tr>
<td></td>
<td>no details of outcome measures apart from clinical examination</td>
<td>no inclusion/exclusion criteria described</td>
<td>a variable source population</td>
<td>no blinding</td>
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<tr>
<td></td>
<td></td>
<td>good sample size</td>
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### Uncontrolled Trials Contributing Data to The Review

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<tbody>
<tr>
<td>Richardson (1981)</td>
<td>an uncontrolled trial of TENS with electrode placement over the area of pain, no other details of trial methodology or the electrical parameters used or the number of treatments x 3 days.</td>
<td>39 subjects 17M/22F</td>
<td>no placebo control group</td>
<td>41% of subjects had an initial relief of pain &gt;50% lasting up to 2 months i.e. 6 (42%) of the 15 nonsurgical and 9 (39%) out of the 23 postsurgical subjects obtained relief 40% had increased pain or other side effects of inappropriate sensation or behaviour</td>
<td>no long term benefit obtained at the 1 year follow-up Initial outcome at 3 days - 3 months: % improved = 41% not improved = 59%</td>
</tr>
</tbody>
</table>

apart from a description of the numerous but valid outcome measures

Neurosurgical Unit USA
15 nonsurgical and 24 postsurgical patients (average 1.8 lumbar laminectomies)
no details of baseline matching
Uncontrolled Trials Contributing Data to The Review

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<tr>
<td>Shealy (1974) (p)</td>
<td>a retrospective study of 200 patients with chronic LBP and/or sciatica (taken from a larger study of 750 subjects) treated with TENS, with electrode placement either side of the pain, with occasional use of distal points, for 1-24 hours</td>
<td>200 Neurosurgery clinic</td>
<td>no placebo control group</td>
<td>115 (57.5%) improved 85 (42.5%) not improved</td>
<td>large sample with a 25% long term improvement</td>
</tr>
<tr>
<td></td>
<td>no details of source population, previous surgery or baseline matching</td>
<td>a large sample study</td>
<td></td>
<td>no details of outcome measures used</td>
<td>better results with low back pain alone than with sciatica</td>
</tr>
<tr>
<td></td>
<td>no details of electrical parameters or outcome measures described</td>
<td></td>
<td></td>
<td>no details of side effects</td>
<td>Initial outcome at unspecified time:</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>low model validity</td>
<td>% improved = 57.5% not improved = 42.5%</td>
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<tr>
<td>Sodipo (1981)</td>
<td>a cross-over trial of TENS (25 minutes) vs. acupuncture (5 minutes) given at weekly intervals - no details of electrical parameters given</td>
<td>12 7M/5F Ages 29-55 Pain Clinic Nigeria</td>
<td>no placebo control group no details of baseline matching or details of any wash-out period</td>
<td>satisfactory pain outcome measurements with 50-75% improvement and no differences between the two treatments no blinding described no side effects described</td>
<td>a pilot study no follow-up indicated TENS potentially more practical than acupuncture Initial outcome: % improved = 58% not improved = 42%</td>
</tr>
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<tr>
<td>Thurin</td>
<td>an uncontrolled study of TENS with no details of electrical parameters used, electrode placements to the local trigger points, applied daily for 20-25 minutes</td>
<td>17 chronic LBP subjects some with sciatica GP practice Australia</td>
<td>no placebo control group</td>
<td>15 (88%) improved 2 (12%) not improved</td>
<td>no follow-up indicated pilot study numbers</td>
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<tr>
<td>Tulgar (1991a)</td>
<td>an uncontrolled comparative study of three different waveforms used in TENS @ 70Hz continuous, burst at 100Hz x 2 bursts/second, modulated at 90-55Hz x 3 treatments (1 of each mode) x 30 minutes</td>
<td>12 patients with LBP and/or sciatica out of a larger (27) multipathology group 7M/5F Pain Clinic UK no details of randomisation or baseline matching</td>
<td>no placebo control groups 3 different wave forms as continuous vs. burst vs., modulated</td>
<td>11 (92%) patients improved 1 (8%) not improved patients preferred burst mode or frequency modulation all 12 patients given 1 session of each of the three treatments and reported lower VAS scores after treatment</td>
<td>pilot study numbers majority of LBP subjects preferred frequency modulation wave-forms no follow up <strong>Initial outcome:</strong> % improved = 92% not improved = 8%</td>
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<td>(p)</td>
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<tr>
<td>Tulgar (1991b)</td>
<td>a comparative study of different wave forms used as TENS, i.e. continuous @ 70Hz, burst @ 90Hz x 1.3 bursts/second, frequency modulation @ 90-55Hz and 60-20Hz x 20 minutes x 4 treatments followed by 3 months of home use using the most effective electrical parameters for that patient electrode placement for optimal distribution of paraesthesia? double-blind only regarding the different active wave forms VAS scale for pain assessment no activity assessments</td>
<td>8 patients with LBP out of a multipathology group of 14 Pain Clinic UK experimental setting no details of source population, previous surgery or baseline matching</td>
<td>no placebo control groups continuous, burst and frequency modulation groups</td>
<td>good results in 5 out of 8 LBP patients valid outcome measures satisfactory data presentation low model validity - too many electrical parameters and multipathology</td>
<td>a comparative study of different wave forms as a pilot study size At 3 months follow up on 5 out of 8 subjects with all 5 claiming long-term pain relief Initial outcome at 4 days: % improved = 62.5% not improved = 37.5%</td>
</tr>
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<tr>
<td>Van Doorn (1981)</td>
<td>an uncontrolled trial of TENS - with no details of the electrical parameters or assessment measures used</td>
<td>41 LBP subjects out of a larger multipathology trial of 182 which included previous surgery (1975-81) Pain Group Holland</td>
<td>no placebo control group</td>
<td>36 out of 41 LBP (88%) patients improved at 3 months but no other details of outcome measures, blinding, side effects etc</td>
<td>up to three years follow-up with 48% still using the modality Initial outcome at up to 3 months: % improved = 88% not improved = 12%</td>
</tr>
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<tr>
<td>Walmsley (1979) (p)</td>
<td>an uncontrolled trial of continuous variable TENS at 25-300Hz x 20 minutes x 4+ sessions (total number of treatments not given) with electrode placements at variable low resistance local and distal (?) acupuncture points determined by the use of a Neurometer no randomisation or blinding described McGill Pain Questionnaire</td>
<td>10 subjects 4M/6F Physiotherapy Unit Canada all subjects had had active treatment and 3 were postsurgery no other details of source population or baseline matching</td>
<td>no placebo control group</td>
<td>64% reduction in pain in 60% (6) of patients using a valid outcome measure 100Hz gave more profound relief side effects - 30% had increased pain, 40% had other adverse reactions low model validity - variable electrode placements and patient controlled frequencies some inconsistencies in the statistics</td>
<td>a pilot study no follow-up indicated Initial outcome at 2 weeks: % improved = 60% not improved = 40%</td>
</tr>
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<tr>
<td>Wynn-Parry 1988 (p)</td>
<td>an uncontrolled prospective study of TENS as part of a rehabilitation programme using a variety of pain relief techniques</td>
<td>101 subjects</td>
<td>1. TENS (n=101) x 8 hours daily for 2 weeks = continuous use if necessary</td>
<td>no details of outcome measures with 58% of subjects showing complete or substantial relief of pain overall</td>
<td>2 years follow up with 60% of those improved still finding relief from TENS = 34.8% Initial outcome: % improved =58% not improved = 42%</td>
</tr>
<tr>
<td>no further information sought</td>
<td>no details of a standardized intervention, electrical parameters or electrode placements includes 72 post surgery subjects</td>
<td>no further details</td>
<td>2. no placebo control group.</td>
<td>with 60% of this group finding TENS the most successful modality and with 19% of those unimproved finding some benefit from TENS with an exercise programme second best</td>
<td>Adequate source population</td>
</tr>
<tr>
<td></td>
<td>no details of outcome measures no blinding or randomisation average sample size</td>
<td>average length of pain 10 years</td>
<td></td>
<td>no side effects described satisfactory statistics low model validity</td>
<td></td>
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</tbody>
</table>

Source: if necessary substantial relief of pain
### EXCLUDED Controlled Trials not Contributing Data to The Review: NO FURTHER INFORMATION

<table>
<thead>
<tr>
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<tr>
<td>Field 1991 (p)</td>
<td>no details of the allocation concealment method - described as a double-blind trial with a random allocation/cross over after 1 month TENS - no details of frequency used only as pulse burst and as conventional TENS with electrode placement not described</td>
<td>20 subjects</td>
<td>1. TENS(n=20)</td>
<td>Appropriate and valid outcome measures for pain and disability which showed no differences between conventional TENS and pulse-burst TENS no side effects no follow up no data or statistics</td>
<td>pilot study - no further details Initial outcome: no data</td>
</tr>
<tr>
<td>(s) further information sought</td>
<td></td>
<td>M/F not known Ages 16-65 years Source - new referrals pain clinic UK average length of pain not known no details of Hz, length or number of treatments 3. no placebo control group. no randomisation details no inclusion/exclusion criteria given no baseline matching</td>
<td>2. Burst TENS (n=20)</td>
<td>3. no placebo control group. no randomisation details no inclusion/exclusion criteria given no baseline matching</td>
<td>3. no placebo control group. no randomisation details no inclusion/exclusion criteria given no baseline matching</td>
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Initial outcome:
- no data
### EXCLUDED Uncontrolled Trials not Contributing Data to The Review

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<tbody>
<tr>
<td>Barr (1987) (p) abstract</td>
<td>uncontrolled trial of Sham TENS vs. continuous TENS vs. pulsed TENS</td>
<td>17 patients mean age 75.2 ± 10.3 years residents of old peoples home USA</td>
<td>control - sham TENS (no details) vs. continuous at 60 Hz and burst at 100Hz no randomisation or matching</td>
<td>pain outcome measured by VAS with conventional TENS giving a 13% reduction in pain and pulse burst TENS 18% reduction in pain and control no significant change ANOVAR pre-and post treatment but after each treatment? or after a course of treatment Outcome of conclusions of doubtful validity but no data</td>
<td>excluded from the review as subjects not described with low back pain pilot study only no data presented no experimental details</td>
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<tbody>
<tr>
<td>Bates (1980)</td>
<td>uncontrolled trial of TENS in a self selected group of patients</td>
<td>36 LBP subjects out of 235 mixed pathology group UK</td>
<td>no control group</td>
<td>no accepted pain measurement technique</td>
<td>2 years follow up some patients excluded at practitioners discretion</td>
</tr>
<tr>
<td></td>
<td>variable frequencies usually between 20 and 70 Hz but no standardization of treatment</td>
<td>a selected group from a Neurological Hospital who had not responded to other treatments</td>
<td></td>
<td>a subjective assessment of pain levels</td>
<td>excluded from the review as we do not now how many of the 36 LBP patients fared</td>
</tr>
<tr>
<td></td>
<td>no randomisation no blinding</td>
<td></td>
<td></td>
<td>side effects - 3 allergic to adhesive tape</td>
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</tr>
<tr>
<td></td>
<td>no pain measurements or activity assessments</td>
<td></td>
<td></td>
<td>insufficient data on the low back pain patients to know how they responded to the treatment</td>
<td></td>
</tr>
<tr>
<td></td>
<td>verbal report back and noting reduction in analgesics</td>
<td></td>
<td></td>
<td>only 29 patients carried on the treatment for more than one week</td>
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<tr>
<td>Chilton (1993)</td>
<td>3 case studies of TENS</td>
<td></td>
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<td>3 case studies only therefore excluded from the review</td>
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<tr>
<td>Deyo (1990) (p)</td>
<td>double-blind</td>
<td>145 subjects</td>
<td>assessment of efficiency of blinding of patient and practitioner to TENS and exercise</td>
<td></td>
<td>excluded from the review as assessment of blinding and not pain control for chronic low back pain</td>
</tr>
<tr>
<td></td>
<td>no assessment for pain control or activity</td>
<td>mean age 51.4 years</td>
<td>ALTENS vs. sham TENS/ALTENS</td>
<td></td>
<td>a very good discussion of blinding</td>
</tr>
<tr>
<td></td>
<td>randomized</td>
<td>58% female</td>
<td>USA</td>
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### Trial Methods

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<tr>
<td>Hery (1987)</td>
<td>TENS vs. Epidural no other details of methodology</td>
<td>100 India low back pain of variable pathology</td>
<td>no placebo control group no details of baseline matching</td>
<td>assessed clinically for pain relief a significant relief of pain obtained with TENS but no statistics given</td>
<td>trial suggests TENS more effective than epidural but no further details trial abstract excluded from this review due to lack of statistical data</td>
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<tr>
<td>Hsieh (1992) (p)</td>
<td>a randomised trial of TENS as Transcutaneous Muscular Stimulation - at 37Hz for 8hours x 3 weeks, as a standardised intervention but not double blind, and as a four way comparison with chiropractic, massage and corset validated pain and activity assessments</td>
<td>10 patients out of a total of 85 in the trial had TMS a combination of acute and chronic low back pain subjects</td>
<td>a 4 way comparison of chiropractic, massage, corset and TMS no placebo control group</td>
<td>appropriate outcome measures but no relevant statistics given to assess the value of TMS low model validity - too many variables of treatment and no placebo control</td>
<td>pilot study numbers for TMS with no binary statistics unsuitable for inclusion in the review</td>
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<tr>
<td>Jarzem (1997)</td>
<td>This study is described, as a randomised double-blind study of conventional, Nu-Wavefor, Acupuncture-type and sham therapies but insufficient data is available in this unpublished paper to include in the review. Information sought on: Allocation concealment Electrical parameters Numbers of subjects improved/ not improved in the four groups Long term evaluation Estimation of trial numbers Details of exercise and other treatment given simultaneously</td>
<td>324 subjects Age 18-70 mean duration of LBP @ 6 years Canada</td>
<td>4 groups TENS ALTENS NU-WAVE SHAM</td>
<td>Appropriate outcome measures used but unable to extract data suitable for inclusion in the meta-analysis Drop-outs evaluated No side effects recorded</td>
<td>A full scale trial with good methodology Unable to include this study in the meta-analysis until more data is available No follow up after 4 weeks N.B. This is a potentially most important study in view of the negative results described at conference and further information is urgently required</td>
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<tr>
<td>Johansson (1980) (p)</td>
<td>an uncontrolled trial of TENS as a standardised intervention using 80-100Hz frequency x 3-6 times a day for 2-4 days (6-24 treatments) for 2 minutes/session no randomisation or blinding VAS for pain outcomes before and after treatment</td>
<td>72 patients with multiple pathology and chronic pain 43M /29F University Hospital Sweden</td>
<td>no control group</td>
<td>50% overall improvement in pain relief but no statistics to identify subgroups age, sex and pain severity not predictors of efficacy of treatment</td>
<td>no follow up insufficient data to include in this review</td>
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<tr>
<td>Johnson (1993) (p)</td>
<td>a prospective study of responses to TENS at various frequencies and modes, 7days/week @ 4hours/day = 24 treatments</td>
<td>29 subjects with pain</td>
<td>no control groups</td>
<td>66% pain relief with 75% relief in chronic low back pain (3 out of 4 subjects) side effects = 10% skin rashes</td>
<td>4 months follow up too many variables and too few relevant subjects to be included in this review - albeit an interesting paper</td>
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</thead>
<tbody>
<tr>
<td>Lehmann (1983) (p)</td>
<td>a trial of subthreshold continuous TENS (60Hz); EAP(2-4Hz) and a placebo group (18:17:18) as a standardised interventions x 15 treatments over 3 weeks</td>
<td>54 (40 valid) patients with back pain screened by Ortho clinic USA</td>
<td>TENS; EAP; placebo</td>
<td>Outcome measures as VAS for pain assessment plus other observations subthreshold TENS ineffective; EAP better. no side effects recorded poor data presentation and complex statistical analysis of A of V.</td>
<td>pilot study numbers follow up indicated but not reported data does not seem to add up - with over reporting influencing outcome? no outcome statistics possible from the data given so this trial excluded from the review</td>
</tr>
</tbody>
</table>

<p>| | | | | | |
| | | | | | |
| | | 13F/27M age 20-59 | | | |
| | | 21 out of the 40 post lumbar surgery no further details of baseline matching | | | |
| | | VAS for pain outcome measures ROM assessments and many other subjective assessments | | | |</p>
<table>
<thead>
<tr>
<th>Trial (1)</th>
<th>Methods (2)</th>
<th>Participants (3)</th>
<th>Comparison Groups (4)</th>
<th>Outcomes (5)</th>
<th>Notes/Statistics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lehmann</td>
<td>a repeat of their 1983 trial subthreshold TENS, EAP and placebo with ‘dead battery’</td>
<td>54 (40)</td>
<td>TENS EAP Placebo</td>
<td>10 outcome measures</td>
<td>a repeat of their 1983 trial but with no new information to present a statistical outcome so therefore excluded from this review</td>
</tr>
<tr>
<td>(1986)</td>
<td>EAP patients treated on an individual basis i.e. not always given the same treatment no blinding some matching described</td>
<td>heavily selected for trial high dropout rate</td>
<td>control unsatisfactory since subjects not blinded</td>
<td>no significant differences between the three groups EAP slightly better subthreshold TENS no better than placebo extensive valid examination and assessment extensive A of V analysis</td>
<td></td>
</tr>
<tr>
<td>(p)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
## EXCLUDED Uncontrolled Trials not Contributing Data to The Review

<table>
<thead>
<tr>
<th>Trial (1)</th>
<th>Methods (2)</th>
<th>Participants (3)</th>
<th>Comparison Groups (4)</th>
<th>Outcomes (5)</th>
<th>Notes/Statistics (6)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Linzer (1976) (p)</td>
<td>an uncontrolled trial of variable, patient determined TENS at 14-360Hz to determine electrical stimulation parameters and electrode locations</td>
<td>a selected subgroup of 23 (10 subjects with LBP) from a larger multipathology study of 100 Dept of Neurosurgery USA</td>
<td>no placebo control group</td>
<td>70% of these selected patients with low back pain improved on TENS</td>
<td>no follow up indicated pilot study size Initial outcome: % improved = 70% not improved = 30% which represents a selected subgroup of responders from a larger trial therefore this study was not included in this review</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

- **Participants:**
  - a selected subgroup of 23 (10 subjects with LBP) from a larger multipathology study of 100 Dept of Neurosurgery USA

- **Comparison Groups:**
  - no placebo control group

- **Outcomes:**
  - 70% of these selected patients with low back pain improved on TENS

- **Notes/Statistics:**
  - no follow up indicated pilot study size
  - Initial outcome: % improved = 70% not improved = 30% which represents a selected subgroup of responders from a larger trial
  - therefore this study was not included in this review
**EXCLUDED** Uncontrolled Trials not Contributing Data to The Review

<table>
<thead>
<tr>
<th>Trial (1)</th>
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<th>Participants (3)</th>
<th>Comparison Groups (4)</th>
<th>Outcomes (5)</th>
<th>Notes/Statistics (6)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Long (1975) (p)</td>
<td>a secondary reviews of Long’s (1974) study - systematically reviewed earlier in the main body of this study</td>
<td>as (1974)</td>
<td>as (1974)</td>
<td>as (1974)</td>
<td>a review of Long’s (1974) study previously included earlier therefore this paper excluded from the review</td>
</tr>
</tbody>
</table>
## EXCLUDED Uncontrolled Trials not Contributing Data to The Review

<table>
<thead>
<tr>
<th>Trial (1)</th>
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<th>Outcomes (5)</th>
<th>Notes/Statistics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moore And Shurman (1997) (p)</td>
<td>This was a preliminary and experimental study of 24 patients which compared neuromuscular electrical stimulation, transcutaneous electrical nerve stimulation, a combination of both of these treatment and a placebo, using a cross-over design in the treatment of multipathology chronic back pain subjects. Inclusion and exclusion criteria were satisfactory and good pain outcome assessments were made but we were unable to extract the data for pooling in the meta-analysis. There were no indications that assessors were blinded.</td>
<td>28 subjects 4 dropouts 16F/8M 26-80 years Pain clinic USA 2-10 years history multipathology 63% LBP</td>
<td>The treatments were self administered, using a standardised intervention of 2 x 300 minutes each of the four treatments, with a 2-day wash out period between each treatment and used variable electrode placement.</td>
<td>Pain assessments with VAS and McGill PPI No activity assessments No indication that assessors were blind Drop-out analysed No side effects recorded</td>
<td>This experimental 14-day pilot study used 4 different modes of treatment for each subject, unable to extract LBP data from rest, does not reflect clinical utility and was therefore not suitable for inclusion in this review. There was no follow up assessments after 4 days.</td>
</tr>
</tbody>
</table>
**EXCLUDED Uncontrolled Trials not Contributing Data to The Review**

<table>
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<tr>
<th>Trial (1)</th>
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<th>Notes/Statistics (6)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pontinen (1979)</td>
<td>an uncontrolled trial of acupuncture vs. TENS with no details of electrical parameters, number of treatments or methodology, electrodes applied along the sciatic nerve outcome assessment by patient questionnaire and clinical follow-up</td>
<td>66 out of 70 - all subjects had had previous physical treatment with 12 being post-op Acupuncture research unit Finland no baseline matching, inclusion/exclusion criteria</td>
<td>no placebo control group acupuncture vs. TENS - but no details of numbers in each group</td>
<td>83.3% of acute patients improved 60.1% of chronic patients improved - but no details given of which subjects responded to acupuncture vs. TENS no further details to permit an assessment of the outcome statistics no side effects recorded low model validity</td>
<td>no follow-up indicated not suitable for inclusion in this review because of the lack of methodological details and suitable data for statistical evaluation of patient responses to TENS or acupuncture</td>
</tr>
</tbody>
</table>
### EXCLUDED Uncontrolled Trials not Contributing Data to The Review

<table>
<thead>
<tr>
<th>Trial (1)</th>
<th>Methods (2)</th>
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<th>Notes/Statistics (6)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pope (1994)</td>
<td>a comparative trial of 4 treatment groups for low back pain as manipulation, a modulated burst transcutaneous muscular stimulation (TMS) at 47Hz x 8hours a day x 21 treatments, massage and corset. no details of randomisation, blinding, matching or crossover methodologies VAS and numerous activity assessments</td>
<td>164 subjects with subacute back pain attending for chiropractic treatment and via advertising well described inclusion/exclusion criteria</td>
<td>no placebo control group manipulations vs. massage vs. corset vs. TMS as unequal groups of 70:31:31:31: baseline matching satisfactory</td>
<td>significant drops in VAS for pain in all groups with no significant differences between the treatment groups some minor statistics but no binary outcome data - difficult to understand the data and the conclusions no blinding no follow-up described low model validity with too many variables</td>
<td>12% dropout good activity assessments as expected from chiropractic insufficient data given to assess the numbers of subjects responding to the four treatments and therefore this study is not considered suitable for inclusion in the review</td>
</tr>
</tbody>
</table>
### EXCLUDED Uncontrolled Trials not Contributing Data to The Review

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</tr>
</thead>
<tbody>
<tr>
<td>Richard-son (1980)</td>
<td>uncontrolled trial of TENS with no details of electrical parameters or trial methodology</td>
<td>47 LBP patients (mean age 41.5) out of a larger multipathology trial</td>
<td>no placebo control group</td>
<td>physical and social interactions increased as an initial response to TENS but no details of number of patients improved</td>
<td>1 year follow up showed no long term effectiveness of TENS</td>
</tr>
<tr>
<td>(p)</td>
<td>detailed description of physical, social interactions and pain behaviour outcome measurements</td>
<td>Neurosurgical unit USA</td>
<td>functional LBP vs. organic LBP vs. mixed LBP vs. other chronic pain</td>
<td>initial response by all patients attributed to the 'placebo' effect</td>
<td>no binary outcome measures obtainable from the paper therefore this trial not included in the review</td>
</tr>
</tbody>
</table>
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</tr>
</thead>
<tbody>
<tr>
<td>Rutkowski</td>
<td>an uncontrolled trial of electrostimulation using needles as electrodes at 1-2.5 Hz</td>
<td>367 Pain relief clinic Poland</td>
<td>no placebo control group</td>
<td>80% improved 20% not improved using a basic pain assessment technique</td>
<td>208 subjects followed up 6-36 months later with 70% maintaining their improvement this study used needles as electrodes rather than surface electrodes so therefore this paper was excluded from the review</td>
</tr>
<tr>
<td>(1977) (p)</td>
<td>no blinding, randomisation, or baseline matching</td>
<td>mixed LBP pathologies with 0.5-20 years history</td>
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</tr>
<tr>
<td></td>
<td>NRS (%) for pain no activity assessments</td>
<td></td>
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</tr>
</tbody>
</table>

525
**EXCLUDED Uncontrolled Trials not Contributing Data to The Review**

<table>
<thead>
<tr>
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<th>Outcomes (5)</th>
<th>Notes/Statistics (6)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Schuster (1980) (p)</td>
<td>a comparative study of TENS and post-operative narcotic analgesia after low back pain surgery using TENS at 25-100 Hz applied either side of the incision line continuously for 18-24 hours and then as required - no details of other electrical parameters given no details of randomisation, blinding or outcome measures</td>
<td>52 (26:26) subjects from a larger group of 147 20M/ 24F Pain Clinic USA adequate baseline matching small sample size</td>
<td>no placebo control group control group of post-op medication</td>
<td>analgesic use in control group much higher then the TENS group in the first 72 hours post-op no side effects recorded data presentation satisfactory</td>
<td>low sample size no follow up no binary outcome measures so not suitable for inclusion in this review</td>
</tr>
</tbody>
</table>
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</tr>
</thead>
<tbody>
<tr>
<td>Thorsteinsson (1978)</td>
<td>replication of the 1977 paper</td>
<td></td>
<td></td>
<td></td>
<td>excluded - a replication of the 1977 paper</td>
</tr>
<tr>
<td>Thorsteinsson (1987) (p)</td>
<td>a replication of the 1977 paper</td>
<td></td>
<td></td>
<td></td>
<td>excluded from the review - as this paper is a replication of the 1977 study</td>
</tr>
<tr>
<td>Trial (1)</td>
<td>Methods (2)</td>
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<td>Comparison Groups (4)</td>
<td>Outcomes (5)</td>
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</tr>
<tr>
<td>Timm (1994)</td>
<td>a randomised trial of a wide range of different treatments including TENS at 100Hz (which was included with hot packs and ultrasound) applied during normal working days for 8 weeks</td>
<td>250 subjects LBP after L5 laminectomy</td>
<td>no placebo control group</td>
<td>extensive and appropriate activity/pain assessments and cost analysis</td>
<td>extensive activity and pain status assessments with 1 year tracking</td>
</tr>
<tr>
<td></td>
<td></td>
<td>50 allocated to physical activity treatment group <em>Physical Therapy Dept USA</em></td>
<td>comparison of several different active and passive therapies which did not include TENS on its own</td>
<td>physical agents including TENS in the regimen had no significant effect</td>
<td>TENS treatment (on its own) was not examined therefore this trial is excluded from the review</td>
</tr>
<tr>
<td></td>
<td></td>
<td><em>adequate and comparable source population and sample size</em></td>
<td><em>adequate baseline matching</em></td>
<td><em>exercise was the only effective treatment of lumbar mobility</em></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td><em>Oswestry and other procedures used to assess pain and activity status</em></td>
<td>no blinding</td>
<td><em>good data and analysis</em></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td><em>low model validity - too many variables</em></td>
<td></td>
</tr>
</tbody>
</table>
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<tr>
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<th>Outcomes (5)</th>
<th>Notes/Statistics (6)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wolf</td>
<td>an uncontrolled trial of continuous TENS at 50-100Hz variable (patient determined) x 30-45 minutes x 3-5 treatments</td>
<td>mixed pathologies - low back pain subjects not clearly identified</td>
<td>no placebo control group</td>
<td>improvements as radiculopathy 47% musculo-skeletal 61%</td>
<td>1 month follow-up for 25 subjects</td>
</tr>
<tr>
<td>(1981)</td>
<td>25 patients x 1 month x 2-3 daily for 1 hour</td>
<td>MULTICENTRED STUDY USA</td>
<td>35% non responders</td>
<td>30% of subjects had only 1 treatment</td>
<td></td>
</tr>
<tr>
<td>(p)</td>
<td>electrode placements at various local and distal sites - not as a standardised intervention</td>
<td>multiple previous treatments, no details of exact diagnoses</td>
<td>no clear correlation between electrode placements and pain relief</td>
<td>no side effects described</td>
<td>this study was excluded from the review because of the poor identification of low back pain subjects and the lack of binary data</td>
</tr>
<tr>
<td></td>
<td>no randomisation or blinding described</td>
<td>VAS and McGill Pain Questionnaire</td>
<td>low model validity with too many variables</td>
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</table>
APPENDIX

B(iii)

Quality Documents

(iii) Quality documentation
Assessing the Quality of a Randomized Controlled Trial:


J Gordon Gadsby November 1996
Assessing the Quality of a Randomized Controlled Trial:

There are a number of reasons for attempting to develop a useful technique for assessing the quality of a randomized control trial. For example, in many instances small and inconclusive studies have been reported to show no effect of a therapy that seemed promising enough to warrant independent studies. It is conceivable that useful clinical effects might be better understood and accepted if one could combine the data from several well-designed studies. On the other hand, large studies sometimes have conflicting conclusions. Is this the result of the inclusion of different patients, employment of different therapies, improper control of bias, or improper analysis of the results? Valid resolution of conflicting conclusions would be facilitated by an assessment of quality (Chalmers 1981).

On this basis, the six randomized controlled trials meeting the inclusion criteria for this systematic review and meta analysis were rated for experimental design quality using the Reeve et al. (1995) scale, a modification of a scale originally published by Chalmers et al (1981). Reeve's (1995) modified scale was first used in a Technology Assessment of Transcutaneous Electrical Nerve Stimulation by the Canadian Coordinating Office for Health Technology Assessment and is illustrated below. In this, each trial is rated along a number of dimensions, and a total score accumulated. The range of the scale is from 0 (low quality) to 60 (high quality). From the original 0 to 100 scale published by Chalmers et al, only the elements evaluating study design were used: selection and description of subjects, withdrawals and reasons for withdrawals, definition of therapeutic regime, use of placebo, blinding, randomization, compliance and outcome measures. In addition, the scale was revised to include inclusion and exclusion criteria, and an indication whether the procedure of administering TENS and the placebo were identical. This modified scale has 16 elements (Reeve 1995).

On completion of the quality assessment form for each of the six studies, an index of experimental design quality for each RCT was then calculated, by dividing the total score obtained by the total possible score (normally 60 but 57 for this review as the compliance section was non-applicable in this instance) for inclusion in the systematic review report.
Table 1. The Modified Chalmers et al. (1981) by Reeve et al (1995) system for evaluating the methodological quality of a randomized controlled trial.

<table>
<thead>
<tr>
<th>Item</th>
<th>Possible Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Description of selection of subject was adequate</td>
<td>3</td>
</tr>
<tr>
<td>2. Description of patients screened was provided</td>
<td>3</td>
</tr>
<tr>
<td>3. Inclusion criteria for study included</td>
<td>1.5</td>
</tr>
<tr>
<td>4. Exclusion criteria for study included</td>
<td>1.5</td>
</tr>
<tr>
<td>5. Withdrawals and reason for withdrawal were described</td>
<td>3</td>
</tr>
<tr>
<td>6. Therapeutic regimen was defined</td>
<td>3</td>
</tr>
<tr>
<td>7. Appearance of TENS unit and placebo unit was identical</td>
<td>1.5</td>
</tr>
<tr>
<td>8. Procedure for administering TENS and placebo was identical</td>
<td>1.5</td>
</tr>
<tr>
<td>9. Randomization was blinded</td>
<td>10</td>
</tr>
<tr>
<td>10. Patients were blinded to treatment group</td>
<td>8</td>
</tr>
<tr>
<td>11. Practitioners were blinded to treatment group</td>
<td>8</td>
</tr>
<tr>
<td>12. Number of subjects needed in trial was estimated a priori</td>
<td>3</td>
</tr>
<tr>
<td>13. Adequacy of randomisation was evaluated</td>
<td>3</td>
</tr>
<tr>
<td>14. Adequacy of blinding was evaluated</td>
<td>3</td>
</tr>
<tr>
<td>15. Compliance with treatment was assessed</td>
<td>3</td>
</tr>
<tr>
<td>16. Measure of outcome of the active therapy was made</td>
<td>3</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>60</strong></td>
</tr>
<tr>
<td>Table 2: Trial Author: .............................................</td>
<td>Quality Index  =</td>
</tr>
<tr>
<td>------------------------------------------------------------</td>
<td>-----------------</td>
</tr>
<tr>
<td>1. Description of selection of subject was adequate</td>
<td></td>
</tr>
<tr>
<td>........1. Adequate</td>
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<tr>
<td>........2. Fair</td>
<td></td>
</tr>
<tr>
<td>........3. Inadequate</td>
<td></td>
</tr>
<tr>
<td>2. Description of patients screened was provided</td>
<td></td>
</tr>
<tr>
<td>........1. Yes</td>
<td></td>
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<tr>
<td>........2. Partial</td>
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<tr>
<td>........3. No</td>
<td></td>
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<tr>
<td>........4. Unknown</td>
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<tr>
<td>3. Inclusion criteria for study included</td>
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<tr>
<td>........1. Yes</td>
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<tr>
<td>........1. Yes</td>
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<td>........2. Partial</td>
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<td>........3. No</td>
<td></td>
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<tr>
<td>5. Withdrawals and reason for withdrawal were described</td>
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<tr>
<td>........1. List given</td>
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<tr>
<td>........2. No withdrawals</td>
<td></td>
</tr>
<tr>
<td>........3. No list</td>
<td></td>
</tr>
<tr>
<td>........4. Unknown</td>
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<tr>
<td>........5. &gt;15% withdrawals for long-term studies and &gt; 10% for studies lasting less than 3 months</td>
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<tr>
<td>6. Therapeutic regimen was defined</td>
<td></td>
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<tr>
<td>........1. Adequate</td>
<td></td>
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<tr>
<td>........2. Fair</td>
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<td>........3. Inadequate</td>
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<tr>
<td>7. Appearance of TENS unit and placebo unit was identical</td>
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<tr>
<td>........1. Same</td>
<td></td>
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<tr>
<td>........2. Different</td>
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<tr>
<td>........3. Unstated</td>
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<tr>
<td>8. Procedure for administering TENS and placebo was identical</td>
<td></td>
</tr>
<tr>
<td>........1. Same</td>
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</tr>
<tr>
<td>........2. Different</td>
<td></td>
</tr>
<tr>
<td>........3. Unstated</td>
<td></td>
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<tr>
<td>9. Randomization was blinded and described</td>
<td></td>
</tr>
<tr>
<td>........1. Yes</td>
<td></td>
</tr>
<tr>
<td>........2. Partial</td>
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<tr>
<td>........3. No</td>
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<td>........4. Unknown</td>
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</tr>
<tr>
<td>10. Patients were blinded to treatment group</td>
<td></td>
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<tr>
<td>........1. Yes</td>
<td></td>
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<tr>
<td>........2. No</td>
<td></td>
</tr>
<tr>
<td>........3. Unknown</td>
<td></td>
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<tr>
<td>........4. N.A.</td>
<td></td>
</tr>
</tbody>
</table>
11. Practitioners were blinded to treatment group
   .............1. Yes
   .............2. Partial
   .............3. No
   .............4. Unknown
   .............5 N.A.
12. Number of subjects needed in trial was estimated a priori
   .............1. Yes
   .............2. No
   .............3. Unknown
13. Adequacy of randomisation was evaluated
   .............1. Yes
   .............2. Partial
   .............3. No
   .............4. Unknown
14. Adequacy of blinding was evaluated
   .............1. Yes
   .............2. Partial
   .............3. No
   .............4. Unknown
   .............5 N.A.
15. Compliance with treatment was assessed
    .............1. Yes
    .............2. Partial
    .............3. No
    .............4. Unknown
    .............5 N.A.
16. Measure of outcome of the active therapy was made
    .............1. Yes
    .............2. Partial
    .............3. No

**TOTAL SCORE**

**Summary:**

Total score = points out of a maximum of 57 points in this study

Quality Index = \( \frac{1}{57} \) =

(Quality Index = . )
Table 3. Quality Score sheet: experimental design - scoring method

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<tr>
<th>Category</th>
<th>Description</th>
<th>Score</th>
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</tr>
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<td>2. Adequate</td>
<td>Fair = 2</td>
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</tr>
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<td>3. Adequate</td>
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<td>3 points max</td>
</tr>
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<td>4. Adequate</td>
<td>Adequate = 3</td>
<td>3 points max</td>
</tr>
<tr>
<td>5. Adequate</td>
<td>Partial = 2</td>
<td>3 points max</td>
</tr>
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<td>6. Adequate</td>
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<td>8. Adequate</td>
<td>Yes = 3</td>
<td>3 points max</td>
</tr>
<tr>
<td>9. Adequate</td>
<td>Partial = 2</td>
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</tr>
<tr>
<td>10. Adequate</td>
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<td>27. Adequate</td>
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535
11. Practitioners were blinded to treatment group = 8 points max
   
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12. Number of subjects needed in trial was estimated a priori = 3 max
   
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</tr>
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13. Adequacy of randomisation was evaluated = 4 points max
   
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<th>Unknown</th>
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<td>3</td>
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14. Adequacy of blinding was evaluated = 3 points max
   
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<th>No</th>
<th>Unknown</th>
<th>N.A.</th>
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<td>0</td>
<td>3</td>
</tr>
</tbody>
</table>

15. Compliance with treatment was assessed = 3 points max
   
<table>
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<th>Unknown</th>
<th>N.A.</th>
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16. Measure of outcome of the active therapy was made = 3 points max
   
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<th>Unknown</th>
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<td>0</td>
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</table>

---

NB:

1. The maximum score possible on the above rating scale would be = 60 points which then gives a Quality Index of \( \frac{60}{60} = 1 \) = (Quality Index = 1)

2. In the TENS/ALTENS study item 15 on compliance is Not Applicable in this instance as all treatments were practitioner supervised, so the maximum score possible on the above rating scale = 57 points which gives a Quality Index of \( \frac{57}{57} = 1 \) and would be shown in the text/tables as (Quality Index = 1).
Some comments based on Chalmers 1981 guidelines on completion of form:

1. Description of selection of subject was adequate:
   were the subjects described in such a way that the reader obtains a clear picture of the patients studied?

2. Description of patients screened was provided:
   was there a description of the eligible population not accepted for the trial and specific reasons given for their noneligibility?

3. Inclusion criteria for study included:
   were the inclusion criteria adequately described?

4. Exclusion criteria for study included:
   were the exclusion criteria adequately described?

5. Withdrawals and reason for withdrawal were described:
   were dropouts listed by diagnosis, treatment and reason for withdrawal? whether withdrawal occurred as a result of patient or investigator initiative? RCT’s that do not mention withdrawals, or those with withdrawals exceeding 10% within a 3 month trial or 15% for longer than 3 months should be carefully scrutinised.

6. Therapeutic regimen was defined:
   were descriptions of the experimental, placebo and all ancillary therapies complete enough to allow proper interpretation of the results and replication in other studies or practice? were descriptions of timing and amount of therapies and other allowable therapies described?

7. Appearance of TENS unit and placebo unit was identical:
   were the TENS units identical in appearance?

8. Procedure for administering TENS and placebo was identical:
   were the treatment procedures for active and placebo TENS identical?

9. Randomization was blinded:
   was the randomisation procedure described and adequate e.g as a procedure by consecutively numbered opaque envelopes, telephone assignment etc?

10. Patients were blinded to treatment group:
    were patients blinded to the treatment group with adequate information?

11. Practitioners were blinded to treatment group:
    were practitioners administering or responsible for the patients blinded to the treatments

12. Number of subjects needed in trial was estimated a priori:
    was a prior estimate of the number of patients required for the trial done?

13. Adequacy of randomisation was evaluated:
    were the pretreatment characteristics of the groups measured e.g. demographic comparisons and the distribution of known prognostic features by treatment category shown i.e. proportions of post-surgery to non-surgery cases etc.

14. Adequacy of blinding was evaluated:
    were physicians and patients quizzed at the end of the study to determine whether or not they have guessed the treatment involved... the data may be important in interpretation of the results?

15. Compliance with treatment was assessed: not applicable in this review:

16. Measure of outcome of the active therapy was made:
    were validated outcome measures for pain relief, activity assessment, functional status or return to work described
<table>
<thead>
<tr>
<th>Question</th>
<th>Score</th>
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</thead>
<tbody>
<tr>
<td>1. Description of selection of subject was adequate</td>
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<tr>
<td>Adequate</td>
<td></td>
</tr>
<tr>
<td>Fair</td>
<td></td>
</tr>
<tr>
<td>Inadequate</td>
<td></td>
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<td>2. Description of patients screened was provided</td>
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<td>Yes</td>
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<td></td>
</tr>
<tr>
<td>Partial</td>
<td></td>
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<tr>
<td>No</td>
<td></td>
</tr>
<tr>
<td>5. Withdrawals and reason for withdrawal were described</td>
<td>3</td>
</tr>
<tr>
<td>List given</td>
<td></td>
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<tr>
<td>No list</td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
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<tr>
<td>&gt;15% withdrawals for long-term studies and &gt; 10% for studies lasting less than 3 months</td>
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<tr>
<td>6. Therapeutic regimen was defined</td>
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<td>Adequate</td>
<td></td>
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<tr>
<td>Fair</td>
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<tr>
<td>Inadequate</td>
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<tr>
<td>7. Appearance of TENS unit and placebo unit was identical</td>
<td>1.5</td>
</tr>
<tr>
<td>Same</td>
<td></td>
</tr>
<tr>
<td>Different</td>
<td></td>
</tr>
<tr>
<td>Unstated</td>
<td></td>
</tr>
<tr>
<td>8. Procedure for administering TENS and placebo was identical</td>
<td>1.5</td>
</tr>
<tr>
<td>Same</td>
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<tr>
<td>Different</td>
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<tr>
<td>9. Randomization was blinded and described</td>
<td>10</td>
</tr>
<tr>
<td>Yes</td>
<td></td>
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<td>Partial</td>
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<td>10. Patients were blinded to treatment group</td>
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<td>No</td>
<td></td>
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<tr>
<td>Unknown</td>
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<tr>
<td>N.A.</td>
<td></td>
</tr>
</tbody>
</table>
11. Practitioners were blinded to treatment group
..... 1. Yes
..... √ 2. Partial
..... 3. No
..... 4. Unknown
..... 5 N.A.

12. Number of subjects needed in trial was estimated a priori
..... 1. Yes
..... √ 2. No
..... 3. Unknown

13. Adequacy of randomisation was evaluated
..... 1. Yes
..... √ 2. Partial
..... 3. No
..... 4. Unknown

14. Adequacy of blinding was evaluated
..... 1. Yes
..... 2. Partial
..... 3. No
..... √ 4. Unknown
..... 5 N.A.

15. Compliance with treatment was assessed
..... 1. Yes
..... 2. Partial
..... 3. No
..... 4. Unknown
..... 5 N.A.

16. Measure of outcome of the active therapy was made
..... √ 1. Yes
..... 2. Partial
..... 3. No

TOTAL SCORE = 33.5

Summary:

Total score = 33.5 points out of a maximum of 57 points in this study

Quality Index = 33.5 / 57 = .55

Quality Index = 0.59
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<td>• 2. Fair</td>
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<tr>
<td>• 3. Inadequate</td>
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<tr>
<td>2. Description of patients screened was provided</td>
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</tr>
<tr>
<td>• 1. Yes</td>
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</tr>
<tr>
<td>• 2. Partial</td>
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<td>3. Inclusion criteria for study included</td>
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<tr>
<td>• 1. Yes</td>
<td></td>
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<tr>
<td>• 2. Partial</td>
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<tr>
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<tr>
<td>• 2. No withdrawals</td>
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<tr>
<td>• 3. No list</td>
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<tr>
<td>• 5. &gt;15% withdrawals for long-term studies and &gt; 10% for studies lasting less than 3 months</td>
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<td>6. Therapeutic regimen was defined</td>
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<td>• 2. Fair</td>
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<tr>
<td>7. Appearance of TENS unit and placebo unit was identical</td>
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</tr>
<tr>
<td>• 1. Same</td>
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</tr>
<tr>
<td>• 2. Different</td>
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<tr>
<td>8. Procedure for administering TENS and placebo was identical</td>
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<td>• 2. Different</td>
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<td>• 4. N.A.</td>
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</table>
11. Practitioners were blinded to treatment group
   1. Yes
   2. Partial
   3. No
   4. Unknown
   5. N.A.
12. Number of subjects needed in trial was estimated a priori
   1. Yes
   2. No
   3. Unknown
13. Adequacy of randomisation was evaluated
   1. Yes
   2. Partial
   3. No
   4. Unknown
14. Adequacy of blinding was evaluated
   1. Yes
   2. Partial
   3. No
   4. Unknown
   5. N.A.
15. Compliance with treatment was assessed
   1. Yes
   2. Partial
   3. No
   4. Unknown
   5. N.A.
16. Measure of outcome of the active therapy was made
   1. Yes
   2. Partial
   3. No

TOTAL SCORE = 40

Summary:

Total score = 40 points out of a maximum of 57 points in this study

Quality Index = 40 / 57 = 0.70

Quality Index = 0.70
1. Description of selection of subject was adequate  
   ✓ 1. Adequate  
   .... 2. Fair  
   .... 3. Inadequate

2. Description of patients screened was provided  
   ✓ 1. Yes  
   .... 2. Partial  
   .... 3. No  
   .... 4. Unknown

3. Inclusion criteria for study included  
   ✓ 1. Yes  
   .... 2. Partial  
   .... 3. No

4. Exclusion criteria for study included  
   ✓ 1. Yes  
   .... 2. Partial  
   .... 3. No

5. Withdrawals and reason for withdrawal were described  
   ✓ 1. List given  
   .... 2. No withdrawals  
   .... 3. No list  
   .... 4. Unknown  
   .... 5. >15% withdrawals for long-term studies and > 10% for studies lasting less than 3 months

6. Therapeutic regimen was defined  
   ✓ 1. Adequate  
   .... 2. Fair  
   .... 3. Inadequate

7. Appearance of TENS unit and placebo unit was identical  
   ✓ 1. Same  
   .... 2. Different  
   .... 3. Unstated

8. Procedure for administering TENS and placebo was identical  
   ✓ 1. Same  
   .... 2. Different  
   .... 3. Unstated

9. Randomization was blinded and described  
   ✓ 1. Yes  
   .... 2. Partial  
   .... 3. No  
   .... 4. Unknown

10. Patients were blinded to treatment group  
    ✓ 1. Yes  
    .... 2. No  
    .... 3. Unknown  
    .... 4. N.A.
11. Practitioners were blinded to treatment group
   - 1. Yes  
   - 2. Partial  
   - 3. No  
   - 4. Unknown  
   - 5. N/A  

12. Number of subjects needed in trial was estimated a priori
   - 1. Yes  
   - 2. No  
   - 3. Unknown  

13. Adequacy of randomisation was evaluated
   - 1. Yes  
   - 2. Partial  
   - 3. No  
   - 4. Unknown  

14. Adequacy of blinding was evaluated
   - 1. Yes  
   - 2. Partial  
   - 3. No  
   - 4. Unknown  
   - 5. N/A  

15. Compliance with treatment was assessed
   - 1. Yes  
   - 2. Partial  
   - 3. No  
   - 4. Unknown  
   - 5. N/A  

16. Measure of outcome of the active therapy was made
   - 1. Yes  
   - 2. Partial  
   - 3. No  

TOTAL SCORE = 48

Summary:

Total score = 48 points out of a maximum of 57 points in this study

Quality Index = 48/57 = 0.84

Quality Index = 0.84
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</tr>
<tr>
<td></td>
<td>1. Adequate</td>
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</tr>
<tr>
<td></td>
<td>2. Fair</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3. Inadequate</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Description of patients screened was provided</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>1. Yes</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2. Partial</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3. No</td>
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<td>Inclusion criteria for study included</td>
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<td></td>
<td>1. Yes</td>
<td></td>
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<tr>
<td></td>
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<td>Withdrawals and reason for withdrawal were described</td>
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<tr>
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<td>2. No withdrawals</td>
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<td>3. No list</td>
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<tr>
<td></td>
<td>4. Unknown</td>
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<tr>
<td></td>
<td>5. &gt;15% withdrawals for long-term studies and &gt; 10% for studies</td>
<td></td>
</tr>
<tr>
<td></td>
<td>lasting less than 3 months</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>Therapeutic regimen was defined</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>1. Adequate</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2. Fair</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3. Inadequate</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>Appearance of TENS unit and placebo unit was identical</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>1. Same</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2. Different</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3. Unstated</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>Procedure for administering TENS and placebo was identical</td>
<td>1.5</td>
</tr>
<tr>
<td></td>
<td>1. Same</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2. Different</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3. Unstated</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>Randomization was blinded and described</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>1. Yes</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2. Partial</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3. No</td>
<td></td>
</tr>
<tr>
<td></td>
<td>4. Unknown</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>Patients were blinded to treatment group</td>
<td>8</td>
</tr>
<tr>
<td></td>
<td>1. Yes</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2. No</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3. Unknown</td>
<td></td>
</tr>
<tr>
<td></td>
<td>4. N.A.</td>
<td></td>
</tr>
</tbody>
</table>
11. Practitioners were blinded to treatment group
   ...1. Yes
   ...2. Partial
   ...3. No
   ...4. Unknown
   ...5 N.A.
12. Number of subjects needed in trial was estimated a priori
   ...1. Yes
   ...2. No
   ...3. Unknown
13. Adequacy of randomisation was evaluated
   ...1. Yes
   ...2. Partial
   ...3. No
   ...4. Unknown
14. Adequacy of blinding was evaluated
   ...1. Yes
   ...2. Partial
   ...3. No
   ...4. Unknown
   ...5 N.A.
15. Compliance with treatment was assessed
   ...1. Yes
   ...2. Partial
   ...3. No
   ...4. Unknown
   ...5 N.A.
16. Measure of outcome of the active therapy was made
   ...1. Yes
   ...2. Partial
   ...3. No

TOTAL SCORE = 31.5

Summary:

Total score = 31.5 points out of a maximum of 57 points in this study

Quality Index = 31.5/57 = 0.55

Quality Index = 0.55
1. Description of selection of subject was adequate
   ...✓.1. Adequate
   .......2. Fair
   .......3. Inadequate
2. Description of patients screened was provided
   ...✓.1. Yes
   .......2. Partial
   .......3. No
   .......4. Unknown
3. Inclusion criteria for study included
   ...✓.1. Yes
   .......2. Partial
   .......3. No
4. Exclusion criteria for study included
   ...✓.1. Yes
   .......2. Partial
   .......3. No
5. Withdrawals and reason for withdrawal were described
   .......1. List given
   .......2. No withdrawals
   .......✓.3. No list
   .......4. Unknown
   .......5. >15% withdrawals for long-term studies and > 10% for studies
         lasting less than 3 months
6. Therapeutic regimen was defined
   ...✓.1. Adequate
   .......2. Fair
   .......3. Inadequate
7. Appearance of TENS unit and placebo unit was identical
   .......1. Same
   .......✓.2. Different
   .......3. Unstated
8. Procedure for administering TENS and placebo was identical
   ...✓.1. Same
   .......2. Different
   .......3. Unstated
9. Randomization was blinded and described
   .......1. Yes
   .......✓.2. Partial
   .......3. No
   .......4. Unknown
10. Patients were blinded to treatment group
    ...✓.1. Yes
       .......2. No
       .......3. Unknown
       .......4. N.A.
11. Practitioners were blinded to treatment group
   ... 1. Yes
   ... 2. Partial
   ... 3. No
   ... 4. Unknown
   ... 5 N.A.
12. Number of subjects needed in trial was estimated a priori
   ... 1. Yes
   ... 2. No
   ... 3. Unknown
13. Adequacy of randomisation was evaluated
   ... 1. Yes
   ... 2. Partial
   ... 3. No
   ... 4. Unknown
14. Adequacy of blinding was evaluated
   ... 1. Yes
   ... 2. Partial
   ... 3. No
   ... 4. Unknown
   ... 5 N.A.
15. Compliance with treatment was assessed
   ... 1. Yes
   ... 2. Partial
   ... 3. No
   ... 4. Unknown
   ... 5 N.A.
16. Measure of outcome of the active therapy was made
   ... 1. Yes
   ... 2. Partial
   ... 3. No

TOTAL SCORE = 32.5

Summary:

Total score = 32.5 points out of a maximum of 57 points in this study

Quality Index = 32.5/57 = 0.57

Quality Index = 0.57
1. Description of selection of subject was adequate
   ⚡1. Adequate
   ⚠2. Fair
   ⚠3. Inadequate
2. Description of patients screened was provided
   ⚠1. Yes
   ⚡2. Partial
   ⚠3. No
   ⚠4. Unknown
3. Inclusion criteria for study included
   ⚡1. Yes
   ⚠2. Partial
   ⚠3. No
4. Exclusion criteria for study included
   ⚠1. Yes
   ⚠2. Partial
   ⚠3. No
5. Withdrawals and reason for withdrawal were described
   ⚠1. List given
   ⚠2. No withdrawals
   ⚡3. No list
   ⚠4. Unknown
   ⚠5. >15% withdrawals for long-term studies and > 10% for studies lasting less than 3 months
6. Therapeutic regimen was defined
   ⚡1. Adequate
   ⚠2. Fair
   ⚠3. Inadequate
7. Appearance of TENS unit and placebo unit was identical
   ⚡1. Same
   ⚠2. Different
   ⚠3. Unstated
8. Procedure for administering TENS and placebo was identical
   ⚡1. Same
   ⚠2. Different
   ⚠3. Unstated
9. Randomization was blinded and described
   ⚡1. Yes
   ⚠2. Partial
   ⚠3. No
   ⚠4. Unknown
10. Patients were blinded to treatment group
    ⚡1. Yes
    ⚠2. No
    ⚠3. Unknown
    ⚠4. N.A.
11. Practitioners were blinded to treatment group
   ✓ 1. Yes
   2. Partial
   3. No
   4. Unknown
   5. N.A.

12. Number of subjects needed in trial was estimated a priori
   ✓ 1. Yes
   2. No
   3. Unknown
   4. Unknown

13. Adequacy of randomisation was evaluated
   ✓ 1. Yes
   2. Partial
   3. No
   4. Unknown
   5. N.A.

14. Adequacy of blinding was evaluated
   ✓ 1. Yes
   2. Partial
   3. No
   4. Unknown
   5. N.A.

15. Compliance with treatment was assessed
   ✓ 1. Yes
   2. Partial
   3. No
   4. Unknown
   5. N.A.

16. Measure of outcome of the active therapy was made
   ✓ 1. Yes
   2. Partial
   3. No

**TOTAL SCORE = 40.5**

**Summary:**

Total score = 40.5 points out of a maximum of 57 points in this study

Quality Index = 40.5/57 = 0.71

Quality Index = **0.71**
APPENDIX

B(iv)

Sensitivity Testing

(iva) Comparison 1

(ivb) Comparison 3

(ivc) A Cumulative Meta-analysis

(ivr) A new model of meta-analysis of non RCT's
Appendix B (iv)

Metaview Charts: Sensitivity testing by exclusion

1. Comparison 1: - original meta-analysis

Review: The effectiveness of TENS in chronic low back pain
Comparison: TENS/ALTENS vs Placebo in chronic back pain
Outcome: TENS vs Placebo in pain reduction - Comparison 1.

<table>
<thead>
<tr>
<th>Study</th>
<th>Expt n/N</th>
<th>Ctrl n/N</th>
<th>Peto OR (95% CI Fixed)</th>
<th>Weight %</th>
<th>Peto OR (95% CI Fixed)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DeyoWalsh 1990</td>
<td>30 / 65</td>
<td>25 / 60</td>
<td>1.02 [0.59, 2.24]</td>
<td>9.2</td>
<td></td>
</tr>
<tr>
<td>Jeans 1979</td>
<td>7 / 14</td>
<td>1 / 14</td>
<td>1.00 [0.00, 6.24]</td>
<td>0.0</td>
<td></td>
</tr>
<tr>
<td>Marchand 1993</td>
<td>6 / 14</td>
<td>2 / 12</td>
<td>1.00 [0.00, 6.24]</td>
<td>0.0</td>
<td></td>
</tr>
<tr>
<td>Thorstensson 1977</td>
<td>16 / 33</td>
<td>11 / 33</td>
<td>1.00 [0.00, 6.24]</td>
<td>0.0</td>
<td></td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>54 / 118</td>
<td>39 / 109</td>
<td></td>
<td>100.0</td>
<td>1.52 [0.99, 2.55]</td>
</tr>
</tbody>
</table>

2. Comparison 1: - excluding Jeans 1979

Review: The effectiveness of TENS in chronic low back pain
Comparison: TENS/ALTENS vs Placebo in chronic back pain
Outcome: TENS vs Placebo in pain reduction - Comparison 1.

<table>
<thead>
<tr>
<th>Study</th>
<th>Expt n/N</th>
<th>Ctrl n/N</th>
<th>Peto OR (95% CI Fixed)</th>
<th>Weight %</th>
<th>Peto OR (95% CI Fixed)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DeyoWalsh 1990</td>
<td>30 / 65</td>
<td>25 / 60</td>
<td>1.02 [0.59, 2.24]</td>
<td>9.2</td>
<td></td>
</tr>
<tr>
<td>Marchand 1993</td>
<td>6 / 14</td>
<td>2 / 12</td>
<td>1.00 [0.00, 6.24]</td>
<td>0.0</td>
<td></td>
</tr>
<tr>
<td>Thorstensson 1977</td>
<td>16 / 33</td>
<td>11 / 33</td>
<td>1.00 [0.00, 6.24]</td>
<td>0.0</td>
<td></td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>52 / 112</td>
<td>38 / 105</td>
<td></td>
<td>100.0</td>
<td>1.53 [0.89, 2.62]</td>
</tr>
</tbody>
</table>

3. Comparison 1: - excluding Jeans 1979 and Marchand 1993

Review: The effectiveness of TENS in chronic low back pain
Comparison: TENS/ALTENS vs Placebo in chronic back pain
Outcome: TENS vs Placebo in pain reduction - Comparison 1.

<table>
<thead>
<tr>
<th>Study</th>
<th>Expt n/N</th>
<th>Ctrl n/N</th>
<th>Peto OR (95% CI Fixed)</th>
<th>Weight %</th>
<th>Peto OR (95% CI Fixed)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DeyoWalsh 1990</td>
<td>30 / 65</td>
<td>25 / 60</td>
<td>1.02 [0.59, 2.24]</td>
<td>9.2</td>
<td></td>
</tr>
<tr>
<td>Thorstensson 1977</td>
<td>16 / 33</td>
<td>11 / 33</td>
<td>1.00 [0.00, 6.24]</td>
<td>0.0</td>
<td></td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>46 / 98</td>
<td>36 / 93</td>
<td></td>
<td>100.0</td>
<td>1.39 [0.79, 2.46]</td>
</tr>
</tbody>
</table>

4. Comparison 1: using a Random Effects model

Review: The effectiveness of TENS in chronic low back pain
Comparison: TENS/ALTENS vs Placebo in chronic back pain
Outcome: TENS vs Placebo in pain reduction - Comparison 1.

<table>
<thead>
<tr>
<th>Study</th>
<th>Expt n/N</th>
<th>Ctrl n/N</th>
<th>OR (95% CI Random)</th>
<th>Weight %</th>
<th>OR (95% CI Random)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DeyoWalsh 1990</td>
<td>30 / 65</td>
<td>25 / 60</td>
<td>1.02 [0.59, 2.24]</td>
<td>9.2</td>
<td>1.02 [0.59, 2.24]</td>
</tr>
<tr>
<td>Jeans 1979</td>
<td>7 / 14</td>
<td>1 / 14</td>
<td>1.00 [0.00, 6.24]</td>
<td>0.0</td>
<td>1.00 [0.00, 6.24]</td>
</tr>
<tr>
<td>Marchand 1993</td>
<td>6 / 14</td>
<td>2 / 12</td>
<td>1.00 [0.00, 6.24]</td>
<td>0.0</td>
<td>1.00 [0.00, 6.24]</td>
</tr>
<tr>
<td>Thorstensson 1977</td>
<td>16 / 33</td>
<td>11 / 33</td>
<td>1.00 [0.00, 6.24]</td>
<td>0.0</td>
<td>1.00 [0.00, 6.24]</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>54 / 118</td>
<td>39 / 109</td>
<td></td>
<td>100.0</td>
<td>1.52 [0.89, 2.61]</td>
</tr>
</tbody>
</table>
### 1. Comparison 3: - original meta-analysis

**Review:** The effectiveness of TENS in chronic low back pain
**Comparison:** TENS/ALTENS vs Placebo in chronic back pain

<table>
<thead>
<tr>
<th>Study</th>
<th>Exp nN</th>
<th>Ctrl nN</th>
<th>Peto OR (95%CI Fixed)</th>
<th>Weight %</th>
<th>Peto OR (95%CI Fixed)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deyo/Walsh 1990</td>
<td>30 / 65</td>
<td>25 / 60</td>
<td>3.3 (1.8-5.7)</td>
<td>44.3</td>
<td>1.20 (0.59-2.24)</td>
</tr>
<tr>
<td>Gemignani 1991</td>
<td>9 / 10</td>
<td>4 / 10</td>
<td>7.1 (4.2-11.8)</td>
<td>10.4</td>
<td>0.57 (0.28-1.17)</td>
</tr>
<tr>
<td>Marchand 1993</td>
<td>6 / 14</td>
<td>2 / 12</td>
<td>8.5 (4.5-16.2)</td>
<td>1.75</td>
<td>1.30 (0.73-2.36)</td>
</tr>
<tr>
<td>Melzack/Vetere 1983</td>
<td>17 / 20</td>
<td>8 / 21</td>
<td>6.8 (4.0-11.4)</td>
<td>1.43</td>
<td>1.30 (0.73-2.36)</td>
</tr>
<tr>
<td>Thorsensson 1977</td>
<td>16 / 33</td>
<td>11 / 33</td>
<td>23.2 (12.2-44.2)</td>
<td>1.85</td>
<td>0.70 (0.49-1.02)</td>
</tr>
<tr>
<td>Total (95%CI)</td>
<td>80 / 148</td>
<td>51 / 140</td>
<td></td>
<td>100.0</td>
<td>2.11 (1.32-3.38)</td>
</tr>
</tbody>
</table>

Chi-square 8.52 (df=5) Z=3.13

1 2 3 4 5 10 Treatment worse Treatment better

### 2. Comparison 3: - excluding Jeans 1979

**Review:** The effectiveness of TENS in chronic low back pain
**Comparison:** TENS/ALTENS vs Placebo in chronic back pain

<table>
<thead>
<tr>
<th>Study</th>
<th>Exp nN</th>
<th>Ctrl nN</th>
<th>Peto OR (95%CI Fixed)</th>
<th>Weight %</th>
<th>Peto OR (95%CI Fixed)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deyo/Walsh 1990</td>
<td>30 / 65</td>
<td>25 / 60</td>
<td>45.8 (23.1-90.6)</td>
<td>45.8</td>
<td>1.20 (0.59-2.24)</td>
</tr>
<tr>
<td>Gemignani 1991</td>
<td>9 / 10</td>
<td>4 / 10</td>
<td>7.1 (4.2-11.8)</td>
<td>7.1</td>
<td>1.20 (0.59-2.24)</td>
</tr>
<tr>
<td>Marchand 1993</td>
<td>6 / 14</td>
<td>2 / 12</td>
<td>8.5 (4.5-16.2)</td>
<td>8.5</td>
<td>1.30 (0.73-2.36)</td>
</tr>
<tr>
<td>Melzack/Vetere 1983</td>
<td>17 / 20</td>
<td>8 / 21</td>
<td>6.8 (4.0-11.4)</td>
<td>6.8</td>
<td>1.30 (0.73-2.36)</td>
</tr>
<tr>
<td>Thorsensson 1977</td>
<td>16 / 33</td>
<td>11 / 33</td>
<td>23.9 (12.2-44.2)</td>
<td>23.9</td>
<td>1.85 (0.70-4.91)</td>
</tr>
<tr>
<td>Total (95%CI)</td>
<td>78 / 142</td>
<td>50 / 136</td>
<td></td>
<td>100.0</td>
<td>2.14 (1.33-3.45)</td>
</tr>
</tbody>
</table>

Chi-square 8.43 (df=4) Z=3.13

1 2 3 4 5 10 Treatment worse Treatment better

### 3. Comparison 3: - excluding Jeans 1979 and Marchand 1993

**Review:** The effectiveness of TENS in chronic low back pain
**Comparison:** TENS/ALTENS vs Placebo in chronic back pain

<table>
<thead>
<tr>
<th>Study</th>
<th>Exp nN</th>
<th>Ctrl nN</th>
<th>Peto OR (95%CI Fixed)</th>
<th>Weight %</th>
<th>Peto OR (95%CI Fixed)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deyo/Walsh 1990</td>
<td>30 / 65</td>
<td>25 / 60</td>
<td>49.3 (25.7-94.3)</td>
<td>49.3</td>
<td>1.20 (0.59-2.24)</td>
</tr>
<tr>
<td>Gemignani 1991</td>
<td>9 / 10</td>
<td>4 / 10</td>
<td>9.1 (5.6-14.5)</td>
<td>9.1</td>
<td>1.30 (0.73-2.36)</td>
</tr>
<tr>
<td>Melzack/Vetere 1983</td>
<td>17 / 20</td>
<td>8 / 21</td>
<td>15.9 (9.1-27.7)</td>
<td>15.9</td>
<td>1.30 (0.73-2.36)</td>
</tr>
<tr>
<td>Thorsensson 1977</td>
<td>16 / 33</td>
<td>11 / 33</td>
<td>25.7 (12.2-54.5)</td>
<td>25.7</td>
<td>1.85 (0.70-4.91)</td>
</tr>
<tr>
<td>Total (95%CI)</td>
<td>69 / 132</td>
<td>45 / 126</td>
<td></td>
<td>100.0</td>
<td>1.94 (1.18-3.37)</td>
</tr>
</tbody>
</table>

Chi-square 6.16 (df=3) Z=2.62

1 2 3 4 5 10 Treatment worse Treatment better

### 4. Comparison 3: using a Random Effects model

**Review:** The effectiveness of TENS in chronic low back pain
**Comparison:** TENS/ALTENS vs Placebo in chronic back pain

<table>
<thead>
<tr>
<th>Study</th>
<th>Exp nN</th>
<th>Ctrl nN</th>
<th>OR (95%CI Random)</th>
<th>Weight %</th>
<th>OR (95%CI Random)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deyo/Walsh 1990</td>
<td>30 / 65</td>
<td>25 / 60</td>
<td>3.15 (1.20-8.24)</td>
<td>3.15</td>
<td>1.20 (0.59-2.44)</td>
</tr>
<tr>
<td>Gemignani 1991</td>
<td>9 / 10</td>
<td>4 / 10</td>
<td>8.3 (5.0-13.7)</td>
<td>8.3</td>
<td>1.20 (0.59-2.44)</td>
</tr>
<tr>
<td>Marchand 1979</td>
<td>2 / 6</td>
<td>1 / 4</td>
<td>6.4 (4.1-10.1)</td>
<td>6.4</td>
<td>1.20 (0.59-2.44)</td>
</tr>
<tr>
<td>Melzack/Vetere 1983</td>
<td>6 / 14</td>
<td>2 / 12</td>
<td>12.5 (5.0-30.9)</td>
<td>12.5</td>
<td>1.20 (0.59-2.44)</td>
</tr>
<tr>
<td>Thorsensson 1977</td>
<td>16 / 33</td>
<td>11 / 33</td>
<td>16.3 (9.1-30.1)</td>
<td>16.3</td>
<td>1.20 (0.59-2.44)</td>
</tr>
<tr>
<td>Total (95%CI)</td>
<td>80 / 148</td>
<td>51 / 140</td>
<td></td>
<td>100.0</td>
<td>2.68 (1.23-5.82)</td>
</tr>
</tbody>
</table>

Chi-square 8.84 (df=5) Z=2.48

1 2 3 4 5 10 Treatment worse Treatment better

---

**Appendix B (iv):** Metaview Charts: Sensitivity testing by exclusion

1. **Comparison 3:**
   - **Original meta-analysis**
   - **Excluding Jeans 1979**
   - **Excluding Jeans 1979 and Marchand 1993**
   - **Using a Random Effects model**
# Metaview Charts: A Cumulative Meta-analysis

## 1. Comparison 1: 1977 - 1993 - 4 studies (TENS vs. Placebo)

### Review: O11 The effectiveness of TENS in LBP Cumulative MA

<table>
<thead>
<tr>
<th>Study</th>
<th>Exp t n/N</th>
<th>Ctrl n/N</th>
<th>Peto OR (95% CI Fixed)</th>
<th>Weight %</th>
<th>Peto OR (95% CI Fixed)</th>
</tr>
</thead>
<tbody>
<tr>
<td>x Thorstenson 1977</td>
<td>0 / 0</td>
<td>0 / 0</td>
<td>0.0</td>
<td>0.0</td>
<td>Not Estimable</td>
</tr>
<tr>
<td>Jean 1979</td>
<td>18 / 39</td>
<td>12 / 37</td>
<td>20.0</td>
<td>1.76 [0.71,4.40]</td>
<td></td>
</tr>
<tr>
<td>Deyo/Walsh 1990</td>
<td>33 / 70</td>
<td>25 / 68</td>
<td>36.8</td>
<td>0.53 [0.78,2.99]</td>
<td></td>
</tr>
<tr>
<td>Marchand 1993</td>
<td>39 / 84</td>
<td>27 / 80</td>
<td>43.1</td>
<td>1.69 [0.91,3.15]</td>
<td></td>
</tr>
<tr>
<td>Total (95%)</td>
<td>90 / 193</td>
<td>64 / 185</td>
<td></td>
<td>100.0</td>
<td>1.64 [1.09,2.47]</td>
</tr>
</tbody>
</table>

Chi-square: 0.08 (df=2) Z=2.37

---

## 2. Comparison 3: 1977 - 1993 - 6 studies (AL)TENS vs Placebo)

### Review: O11 The effectiveness of TENS in LBP Cumulative MA

<table>
<thead>
<tr>
<th>Study</th>
<th>Exp. t n/N</th>
<th>Ctrl n/N</th>
<th>Peto OR (95% CI Fixed)</th>
<th>Weight %</th>
<th>Peto OR (95% CI Fixed)</th>
</tr>
</thead>
<tbody>
<tr>
<td>x Thorstenson 1977</td>
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<td>0 / 0</td>
<td>0.0</td>
<td>0.0</td>
<td>Not Estimable</td>
</tr>
<tr>
<td>Jean 1979</td>
<td>18 / 39</td>
<td>12 / 37</td>
<td>8.3</td>
<td>1.76 [0.71,4.40]</td>
<td></td>
</tr>
<tr>
<td>MelzackVetere 1987</td>
<td>35 / 59</td>
<td>20 / 58</td>
<td>14.8</td>
<td>2.69 [1.30,5.54]</td>
<td></td>
</tr>
<tr>
<td>Deyo/Walsh 1990</td>
<td>50 / 90</td>
<td>33 / 83</td>
<td>22.5</td>
<td>2.09 [1.17,3.76]</td>
<td></td>
</tr>
<tr>
<td>Marchand 1993</td>
<td>65 / 114</td>
<td>39 / 111</td>
<td>28.3</td>
<td>2.40 [1.42,4.05]</td>
<td></td>
</tr>
<tr>
<td>Total (95%)</td>
<td>227 / 402</td>
<td>141 / 394</td>
<td></td>
<td>100.0</td>
<td>2.29 [1.74,3.03]</td>
</tr>
</tbody>
</table>

Chi-square: 0.64 (df=4) Z=5.85

---

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Appendix B (iv)

Metaview Charts:

1. A new model of meta-analysis of non-RCTs: pooled against a standard placebo: All TENS and ALTENS trials with data.

<table>
<thead>
<tr>
<th>Study</th>
<th>Exp. n/N</th>
<th>Ctrl n/N</th>
<th>Peto OR (95%CI Fixed)</th>
<th>Weight %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abram 1983</td>
<td>2 / 5</td>
<td>2 / 5</td>
<td>0.2</td>
<td>1.00 [0.09, 11.03]</td>
</tr>
<tr>
<td>Anderson 1976</td>
<td>8 / 24</td>
<td>9 / 24</td>
<td>0.8</td>
<td>0.84 [0.26, 2.70]</td>
</tr>
<tr>
<td>Brill 1985</td>
<td>40 / 129</td>
<td>47 / 129</td>
<td>4.3</td>
<td>0.79 [0.47, 1.31]</td>
</tr>
<tr>
<td>Castufo 1993</td>
<td>8 / 10</td>
<td>4 / 10</td>
<td>0.4</td>
<td>4.67 [0.85, 27.56]</td>
</tr>
<tr>
<td>Cheong 1987</td>
<td>23 / 24</td>
<td>9 / 24</td>
<td>0.8</td>
<td>13.07 [3.99, 42.86]</td>
</tr>
<tr>
<td>Coletta 1988</td>
<td>11 / 15</td>
<td>5 / 15</td>
<td>0.6</td>
<td>4.73 [1.15, 19.38]</td>
</tr>
<tr>
<td>Davis 1975</td>
<td>8 / 16</td>
<td>6 / 16</td>
<td>0.6</td>
<td>1.64 [0.41, 6.47]</td>
</tr>
<tr>
<td>Denning 1988</td>
<td>156 / 182</td>
<td>66 / 182</td>
<td>6.4</td>
<td>8.41 [5.52, 12.63]</td>
</tr>
<tr>
<td>Eriksson 1979</td>
<td>18 / 27</td>
<td>10 / 27</td>
<td>1.0</td>
<td>3.21 [1.11, 9.23]</td>
</tr>
<tr>
<td>Ersek 1976</td>
<td>13 / 13</td>
<td>5 / 13</td>
<td>0.4</td>
<td>16.08 [3.14, 82.36]</td>
</tr>
<tr>
<td>Fargas-Babjak 1992</td>
<td>31 / 38</td>
<td>14 / 38</td>
<td>1.4</td>
<td>6.22 [2.51, 15.44]</td>
</tr>
<tr>
<td>Fox 1976</td>
<td>8 / 12</td>
<td>4 / 12</td>
<td>0.5</td>
<td>3.59 [0.75, 17.19]</td>
</tr>
<tr>
<td>Fried 1984</td>
<td>385 / 460</td>
<td>167 / 460</td>
<td>16.3</td>
<td>7.19 [5.29, 9.36]</td>
</tr>
<tr>
<td>Gunn 1979</td>
<td>75 / 54</td>
<td>34 / 54</td>
<td>3.4</td>
<td>5.93 [3.33, 10.57]</td>
</tr>
<tr>
<td>Indeck 1975</td>
<td>40 / 50</td>
<td>32 / 50</td>
<td>3.2</td>
<td>1.45 [0.80, 2.62]</td>
</tr>
<tr>
<td>Johnson 1992</td>
<td>150 / 430</td>
<td>156 / 430</td>
<td>14.6</td>
<td>0.94 [0.71, 1.24]</td>
</tr>
<tr>
<td>Lathen 1976</td>
<td>23 / 50</td>
<td>18 / 50</td>
<td>1.8</td>
<td>1.51 [0.63, 3.53]</td>
</tr>
<tr>
<td>Lamp 1987</td>
<td>45 / 51</td>
<td>19 / 51</td>
<td>1.8</td>
<td>8.87 [3.80, 19.27]</td>
</tr>
<tr>
<td>Leedergerber 1979</td>
<td>14 / 74</td>
<td>27 / 74</td>
<td>2.2</td>
<td>0.42 [0.20, 0.86]</td>
</tr>
<tr>
<td>Leman/Krish 1981</td>
<td>15 / 20</td>
<td>2 / 20</td>
<td>0.7</td>
<td>13.37 [3.88, 46.13]</td>
</tr>
<tr>
<td>Lounie 1985</td>
<td>47 / 61</td>
<td>22 / 61</td>
<td>2.2</td>
<td>5.33 [2.56, 10.67]</td>
</tr>
<tr>
<td>Long 1974</td>
<td>53 / 99</td>
<td>36 / 99</td>
<td>3.5</td>
<td>7.17 [4.06, 12.64]</td>
</tr>
<tr>
<td>Long 1979</td>
<td>20 / 50</td>
<td>18 / 50</td>
<td>1.8</td>
<td>1.18 [0.53, 2.64]</td>
</tr>
<tr>
<td>Lundeberg 1984</td>
<td>15 / 19</td>
<td>7 / 19</td>
<td>0.7</td>
<td>5.38 [1.51, 16.16]</td>
</tr>
<tr>
<td>Magdabogdo 1987</td>
<td>36 / 40</td>
<td>15 / 40</td>
<td>1.4</td>
<td>9.43 [3.81, 23.32]</td>
</tr>
<tr>
<td>McDonnell 1980</td>
<td>54 / 88</td>
<td>32 / 88</td>
<td>3.3</td>
<td>2.70 [1.04, 6.86]</td>
</tr>
<tr>
<td>Mecarack 1975</td>
<td>12 / 15</td>
<td>5 / 15</td>
<td>0.6</td>
<td>6.28 [1.52, 25.97]</td>
</tr>
<tr>
<td>Melarack 1982</td>
<td>30 / 40</td>
<td>15 / 40</td>
<td>1.5</td>
<td>4.50 [1.87, 10.83]</td>
</tr>
<tr>
<td>Meyler 1994</td>
<td>22 / 44</td>
<td>16 / 44</td>
<td>1.6</td>
<td>1.73 [0.75, 3.84]</td>
</tr>
<tr>
<td>Moore 1963</td>
<td>40 / 54</td>
<td>21 / 54</td>
<td>2.2</td>
<td>3.68 [1.78, 7.80]</td>
</tr>
<tr>
<td>Piacun 1982</td>
<td>56 / 108</td>
<td>39 / 108</td>
<td>4.0</td>
<td>1.89 [1.03, 3.23]</td>
</tr>
<tr>
<td>Richardson 1981</td>
<td>16 / 39</td>
<td>14 / 39</td>
<td>1.4</td>
<td>1.24 [0.50, 3.07]</td>
</tr>
<tr>
<td>Sheavy 1974a</td>
<td>115 / 273</td>
<td>73 / 270</td>
<td>7.4</td>
<td>2.86 [1.57, 5.34]</td>
</tr>
<tr>
<td>Siddiq 1981</td>
<td>7 / 12</td>
<td>4 / 12</td>
<td>0.5</td>
<td>2.62 [0.54, 12.64]</td>
</tr>
<tr>
<td>Thurn 1980</td>
<td>15 / 17</td>
<td>6 / 17</td>
<td>0.6</td>
<td>8.81 [2.25, 34.42]</td>
</tr>
<tr>
<td>Tulgar 1991a</td>
<td>11 / 12</td>
<td>4 / 12</td>
<td>0.4</td>
<td>10.96 [2.15, 54.77]</td>
</tr>
<tr>
<td>Tulgar 1991b</td>
<td>5 / 8</td>
<td>3 / 8</td>
<td>0.3</td>
<td>5.50 [0.38, 17.03]</td>
</tr>
<tr>
<td>Van Doorn 1981</td>
<td>36 / 41</td>
<td>15 / 41</td>
<td>1.4</td>
<td>8.60 [3.44, 20.89]</td>
</tr>
<tr>
<td>Woosley 1979</td>
<td>6 / 10</td>
<td>4 / 10</td>
<td>0.4</td>
<td>2.14 [0.39, 11.81]</td>
</tr>
<tr>
<td>Wynn Parry 1983</td>
<td>43 / 101</td>
<td>37 / 101</td>
<td>3.6</td>
<td>1.28 [0.73, 2.25]</td>
</tr>
</tbody>
</table>

Total (95%CI) | 1744 / 2826 | 1022 / 2826 | * | 100.0 | 2.91 [2.61, 3.23] |

Chi-squared = 286.69 (df=39); Z=19.63

<table>
<thead>
<tr>
<th>Treatment worse</th>
<th>Treatment better</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 2 3 4 5 6 7 8</td>
<td>9 10</td>
</tr>
</tbody>
</table>
## 2. A new model of meta-analysis of non-RCTS: pooled against a standard placebo: All ALTENS trials with appropriate data.

### Review: O20 new model of meta-analysis of non-RCTS

**Comparison:** TENALTENS vs Standard Placebo  
**Outcome:** ALTENS - improvement in pain

<table>
<thead>
<tr>
<th>Study</th>
<th>N Altens</th>
<th>N Ctrl</th>
<th>Peto OR (95%CI Fixed)</th>
<th>Weight</th>
</tr>
</thead>
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<td>Abram 1983</td>
<td>275</td>
<td>275</td>
<td>3.3 [0.99, 11.03]</td>
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</tr>
<tr>
<td>Anderson 1976</td>
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<td>112</td>
<td>5.1 [0.23, 0.16]</td>
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</tr>
<tr>
<td>Cheng 1987</td>
<td>92</td>
<td>92</td>
<td>13.5 [3.09, 4.86]</td>
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</tr>
<tr>
<td>Erwae 1976</td>
<td>151</td>
<td>151</td>
<td>7.1 [3.14, 8.36]</td>
<td></td>
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<tr>
<td>Fargas-Bajak 1992</td>
<td>38</td>
<td>38</td>
<td>23.1 [2.51, 15.44]</td>
<td></td>
</tr>
<tr>
<td>Ledergerber 1979</td>
<td>20</td>
<td>20</td>
<td>10.7 [0.17, 2.36]</td>
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<td>Lerman/Krahn 1991</td>
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<td>22.4 [3.86, 13.1]</td>
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<tr>
<td>Meizack 1980</td>
<td>30</td>
<td>40</td>
<td>24.7 [8.7, 10.8]</td>
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</tr>
<tr>
<td>Total (95%CI)</td>
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<tr>
<td>Chi-square 27.75 (df=7)</td>
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</tbody>
</table>

### 3. A new model of meta-analysis of non-RCTS: pooled against a standard placebo: All TENS trials with appropriate data -

### Review: O20 new model of meta-analysis of non-RCTS

**Comparison:** TENALTENS vs Standard Placebo  
**Outcome:** TENS - improvement in pain

<table>
<thead>
<tr>
<th>Study</th>
<th>N Altens</th>
<th>N Ctrl</th>
<th>Peto OR (95%CI Fixed)</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anderson 1976</td>
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<td>12</td>
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</tr>
<tr>
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<td>47/129</td>
<td>47/129</td>
<td>5.1 [0.47, 13.3]</td>
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</tr>
<tr>
<td>Cassuto 1993</td>
<td>8/10</td>
<td>8/10</td>
<td>5.1 [0.47, 13.3]</td>
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</tr>
<tr>
<td>Colletta 1988</td>
<td>11/5</td>
<td>11/5</td>
<td>4.87 [0.85, 27.66]</td>
<td></td>
</tr>
<tr>
<td>Davis 1975</td>
<td>8/16</td>
<td>8/16</td>
<td>4.73 [1.15, 19.38]</td>
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</tr>
<tr>
<td>Dening 1988</td>
<td>158/182</td>
<td>66/182</td>
<td>7.6 [4.52, 12.83]</td>
<td></td>
</tr>
<tr>
<td>Fox 1976</td>
<td>8/12</td>
<td>8/12</td>
<td>7.19 [3.52, 3.64]</td>
<td></td>
</tr>
<tr>
<td>Fried 1984</td>
<td>385/400</td>
<td>167/400</td>
<td>4.1 [3.33, 10.57]</td>
<td></td>
</tr>
<tr>
<td>Gun 1975</td>
<td>75/94</td>
<td>34/94</td>
<td>17.5 [0.71, 4.24]</td>
<td></td>
</tr>
<tr>
<td>Johnson 1992</td>
<td>150/430</td>
<td>156/430</td>
<td>17.5 [0.71, 2.46]</td>
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</tr>
<tr>
<td>Laten 1976</td>
<td>23/50</td>
<td>18/50</td>
<td>2.2 [0.68, 3.31]</td>
<td></td>
</tr>
<tr>
<td>Lamp 1987</td>
<td>45/51</td>
<td>19/51</td>
<td>5.87 [3.90, 19.27]</td>
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<tr>
<td>Ledergerber 1979</td>
<td>8/54</td>
<td>20/54</td>
<td>1.9 [0.36, 0.52]</td>
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<td>47/61</td>
<td>22/61</td>
<td>1.9 [0.36, 0.52]</td>
<td></td>
</tr>
<tr>
<td>Long 1974</td>
<td>83/99</td>
<td>36/99</td>
<td>4.2 [0.17, 4.06]</td>
<td></td>
</tr>
<tr>
<td>Long 1979</td>
<td>20/50</td>
<td>18/50</td>
<td>4.2 [0.17, 4.06]</td>
<td></td>
</tr>
<tr>
<td>McDonnell 1980</td>
<td>54/88</td>
<td>32/88</td>
<td>4.2 [0.17, 4.06]</td>
<td></td>
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<td>Meyer 1994</td>
<td>22/44</td>
<td>16/44</td>
<td>4.1 [0.17, 4.06]</td>
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<tr>
<td>Procaccio 1982</td>
<td>56/108</td>
<td>519/108</td>
<td>4.2 [1.10, 2.32]</td>
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</tr>
<tr>
<td>Richardson 1981</td>
<td>16/39</td>
<td>14/39</td>
<td>1.7 [0.24, 0.30]</td>
<td></td>
</tr>
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<td>Shealy 1974a</td>
<td>115/200</td>
<td>73/200</td>
<td>8.8 [1.57, 3.43]</td>
<td></td>
</tr>
<tr>
<td>Sidipo 1981</td>
<td>7/12</td>
<td>4/12</td>
<td>0.6 [0.54, 12.64]</td>
<td></td>
</tr>
<tr>
<td>Troen 1982</td>
<td>15/17</td>
<td>6/17</td>
<td>0.7 [0.22, 0.34]</td>
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</tr>
<tr>
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<td>11/12</td>
<td>4/12</td>
<td>0.7 [0.22, 0.34]</td>
<td></td>
</tr>
<tr>
<td>Tulgar 1991b</td>
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<td>3/8</td>
<td>0.4 [0.25, 0.18]</td>
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</tr>
<tr>
<td>Walsmy 1979</td>
<td>6/10</td>
<td>4/10</td>
<td>0.5 [0.21, 0.38]</td>
<td></td>
</tr>
<tr>
<td>Wynn Parry 1988</td>
<td>43/101</td>
<td>37/101</td>
<td>4.3 [0.73, 2.25]</td>
<td></td>
</tr>
<tr>
<td>Total (95%CI)</td>
<td></td>
<td></td>
<td>1427/2364</td>
<td>100.0</td>
</tr>
<tr>
<td>Chi-square 236.19 (df=25)</td>
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</tbody>
</table>

554
APPENDIX B(v)

(v) Amended Cochrane Glossary
GLOSSARY

Extracted from The Cochrane Library Glossary (1997) together with definitions specific to this thesis.

**Absolute risk reduction (ARR)**
The absolute arithmetic difference in outcome rates. Usually reported as a percentage and calculated as CER - EER (CER=control group event rate; EER=experimental group event rate). See also risk difference.

**Allocation concealment**
See concealment of allocation.

**ALTENS - acupuncture-like transcutaneous electrical nerve stimulation**
A type of TENS using low frequency high intensity stimulation and based on acupuncture needle stimulation.

**Ankylosing spondylitis**
A chronic inflammatory disease of unknown origin and a cause of low back pain that tends to affect young men.

**Applicability (synonyms: external validity, generalisability, relevance, transferability)**
The degree to which the results of an observation, study or review hold true in other settings.

**Attrition bias**
Systematic differences between comparison groups in withdrawals or exclusions of participants from the results of a study. For example, patients may drop out of a study because of side effects of the intervention. Excluding these patients from the analysis could result in an overestimate of the effectiveness of the intervention.

**Bayesian analysis**
An approach that can be used in single studies or meta-analysis which incorporates a prior probability distribution based on subjective opinion and objective evidence, such as the results of previous research. Bayesian analysis uses Bayes' theorem to update the prior distribution in light of the results of a study, producing a posterior distribution. Statistical inferences (point estimates, confidence intervals, etc.) are based on this posterior distribution. The posterior distribution also acts as the prior distribution for the next study. This approach has many attractive features, but is controversial because it depends on opinions, and frequently they will vary considerably.
Bayes' theorem
A probability theorem used to obtain the probability of a condition in a
group of people with some characteristic (e.g. exposed to an
intervention of interest, or with a specified result on a diagnostic test)
on the basis of the overall rate of that condition (the prior probability)
and the likelihood's of that characteristic in people with and without
the condition.

Bias
A systematic error or deviation in results or inferences. In studies of
the effects of healthcare bias can arise from systematic differences in
the groups that are compared (selection bias), the care that is
provided, or exposure to other factors apart from the intervention of
interest (performance bias), withdrawals or exclusions of people
entered into the study (attrition bias) or how outcomes are assessed
(detection bias). Bias does not necessarily carry an imputation of
prejudice, such as the investigators' desire for particular results. This
differs from conventional use of the word in which bias refers to a
partisan point of view. Many varieties of bias have been described
[489]. See also methodological quality, validity.

Blinding (synonym: masking)
Keeping secret group assignment (e.g. to treatment or control) from
the study participants or investigators. Blinding is used to protect
against the possibility that knowledge of assignment may affect
patient response to treatment, provider behaviours (performance bias)
or outcome assessment (detection bias). Blinding is not always
practical (e.g. when comparing surgery to drug treatment). The
importance of blinding depends on how objective the outcome
measure is; blinding is more important for less objective outcome
measures such as pain or quality of life. See also single blind, double
blind and triple blind.

Breslow-Day test
A statistical test for the homogeneity of odds ratios.

Case study (synonyms: anecdote, case history, single case report)
An uncontrolled observational study involving an intervention and
outcome for a single person.

Case-control study (synonyms: case referent study, retrospective
study)
A study that starts with identification of people with the disease or
outcome of interest (cases) and a suitable control group without the
disease or outcome. The relationship of an attribute (intervention,
exposure or risk factor) to the outcome of interest is examined by
comparing the frequency or level of the attribute in the cases and
controls. For example, to determine whether thalidomide caused birth
defects a group of children with birth defects (cases) could be compared to a group of children without birth defects (controls). The groups would then be compared with respect to the proportion exposed to thalidomide through their mothers taking the tablets. Case-control studies are sometimes described as being retrospective as they are always performed looking back in time.

**CD-ROM (Compact Disc - Read Only Memory)**
A computer storage medium. A CD-ROM can contain a database of information (e.g. MEDLINE, or the Cochrane Controlled Trials Register) that may be searched either on a personal computer or a computer linked to a network.

**CDSR**
See Cochrane Database of Systematic Reviews.

**CER**
Control group event rate

**Chi-square test**
Any statistical test based on comparison of a test statistic to a chi-square distribution. The Mantel-Haenszel test is a well-known chi-square test.

**CI**
See Confidence interval

**Citizens’ Jury**
A Citizens’ Jury is a way of involving the public in making decisions, which affect their communities. It is a small group of people randomly picked to reflect the local population. They are given information about a potential topic, hear evidence from witnesses and cross-examine them. The jurors discuss the matter and reach a decision. The body that has sponsored the Jury must then take the recommendations seriously and, if they are not carried out, must say why.

**CL**
See Cochrane Library

**Clinical effectiveness**
The extent to which a treatment produces the desired outcome in patients - i.e. whether or not it works. This should be measured by high quality studies, e.g. randomised controlled trials

**Clinical trial (synonyms: therapeutic trial, intervention study)**
A trial that tests out a drug or other intervention to assess its effectiveness and safety. This general term encompasses randomised controlled trials and controlled clinical trials.
Cochrane Centres
An entity in the *Cochrane Collaboration* with responsibility for helping to co-ordinate and support the Collaboration. Responsibilities include: maintaining a directory of people contributing to the *Cochrane Collaboration*; helping to establish Collaborative Review Groups; organising workshops, seminars and annual colloquia to support and guide the development of the *Cochrane Collaboration*. Each Centre is responsible for providing support within a specified geographic area. Details of Centre responsibilities and a list of the Centre responsible for any given country are available in *CDSR*.

Cochrane Collaboration
An international organisation that aims to help people make well informed decisions about health by preparing, maintaining and ensuring the accessibility of systematic reviews of the benefits and risks of healthcare interventions.

Cochrane Collaboration Handbook
Guidelines for preparing and maintaining *Cochrane Reviews*. Information about the Collaboration that was previously contained in Sections I to V of the Handbook is now maintained and published as a module in *CDSR*. The Handbook is published in the *Cochrane Library* and it can be downloaded from FTP servers at the Australasian, Canadian and UK *Cochrane Centres*.

Cochrane Controlled Trials Register (CCTR)
A database of references to controlled trials in health care. Cochrane groups and other organisations have been invited to contribute their specialised registers, and these registers, together with references to clinical trials identified on *MEDLINE*, form The Cochrane Controlled Trials Register (CCTR).

Cochrane Database of Systematic Reviews (CDSR)
The major product of the *Cochrane Collaboration*. It brings together all the currently available *Cochrane Reviews* and is updated quarterly. It also contains information about the Collaboration. Collaborative Review Groups submit modules of edited reviews and other information to the Parent Database for inclusion in the *CDSR*. See *Cochrane Library*.

Cochrane Library (CL)
A collection of databases, published on disk and CD-ROM and updated quarterly, containing the *Cochrane Database of Systematic Reviews*, the *Cochrane Controlled Trials Register*, the *Database of Abstracts of Reviews of Effectiveness*, the *Cochrane Review Methodology Database*, and information about the *Cochrane Collaboration*.
Cochrane Review
A Cochrane Review is a systematic, up-to-date summary of reliable evidence of the benefits and risks of healthcare. Cochrane Reviews are intended to help people make practical decisions. For a review to be called a "Cochrane Review" it must be in the Parent Database maintained by the Cochrane Collaboration. The Parent Database is composed of modules of reviews submitted by Collaborative Review Groups (CRGs) registered with the Cochrane Collaboration. The editorial team of the CRG, as described in the CRG module referees the reviews contributed to one of the modules making up the Parent Database. Reviewers adhere to guidelines published in the Cochrane Handbook. The specific methods used in a Review are described in the text of the review. Cochrane Reviews are prepared using Review Manager software provided by the Collaboration and adhere to a structured format that is described in the Handbook.

Cochrane Review Methodology Database (CRMD)
A bibliography of articles and books about methodological issues relevant to summarising evidence of the effects of healthcare. It is published in the Cochrane Library.

Cointervention
In a randomised controlled trial, the application of additional diagnostic or therapeutic procedures to members of either or both the experimental and the control groups.

Collaborative Review Group (CRG)
The primary working entity (organisational unit) of the Cochrane Collaboration. CRGs are made up of individuals sharing an interest in a particular healthcare problem or type of problem. The main purpose of a CRG is to prepare and maintain systematic reviews of the effects of health care within the scope of the Group. Members participate in the Group not only by preparing Cochrane Reviews but also by hand-searching journals or other activities that help the Group to fulfil its aim. Each CRG is co-ordinated by an editorial team, responsible for regularly updating and submitting to the Parent Database an edited module of Reviews and information about the Group.

Concealment of allocation
The process used to prevent foreknowledge of group assignment in a randomised controlled trial, which should be seen as distinct from blinding. The allocation process should be impervious to any influence by the individual making the allocation by having the randomisation process administered by someone who is not responsible for recruiting participants; for example, a hospital pharmacy, or a central office. Using methods of assignment such as date of birth and case record numbers (see quasi random allocation) are open to manipulation. Adequate methods of allocation concealment include: centralized randomisation schemes;
randomisation schemes controlled by a pharmacy; numbered or coded containers in which capsules from identical-looking, numbered bottles are administered sequentially; on-site computer systems, where allocations are in a locked unreadable file; and sequentially numbered opaque, sealed envelopes.

**Conference abstracts**
Short summaries of presentations at conferences. May be published as proceedings.

**Confidence interval (CI)**
Confidence intervals quantify the uncertainty in clinically useful measures. The range within which the "true" value (e.g. size of effect of an intervention) is expected to lie with a given degree of certainty (e.g. 95% or 99%) i.e. the range of values within which we can be 95%(or 99%) sure that the true value lies for the whole population of patients from whom the study patients were selected. The CI for a measure like a number needed to treat (NNT) narrows as the number of patients on which it is based increases. Confidence intervals are usually preferred to $P$ values because the former tell us about the strength of evidence, whereas the latter merely test the evidence against a null hypothesis. 

Note: Confidence intervals represent the probability of random errors, but not systematic errors (bias).

**Confounding**
A situation in which a measure of the effect of an intervention or exposure is distorted because of the association of exposure with other factor(s) that influence the outcome under study.

**Contamination**
In clinical trials, the inadvertent application of the intervention being evaluated to people in the control group or inadvertent failure to apply the intervention to people assigned to the intervention group.

**Contingency table**
A tabular cross-classification of data such that subcategories of one characteristic are indicated horizontally (in rows) and subcategories of another characteristic are indicated vertically (in columns). Tests of association between the characteristics can be readily applied. The simplest contingency table is the fourfold, or $2 \times 2$ table, which is used in clinical trials to compare dichotomous outcomes, such as death, for an intervention and control group or two intervention groups.

**Control**
1. In clinical trials comparing two or more interventions, a control is a person in the comparison group that receives a placebo, no intervention, usual care or another form of care.
2. In case-control studies a control is a person in the comparison group without the disease or outcome of interest.
3. In statistics control means to adjust for or take into account extraneous influences or observations.
4. Control can also mean programs aimed at reducing or eliminating the disease when applied to communicable (infectious) diseases.

**Controlled clinical trial**
Refers to a study that compares one or more intervention groups to one or more comparison (control) groups. Whilst not all controlled studies are randomised, all randomised trials are controlled.

**Co-ordinator** (of a Collaborative Review Group) (Previously known as Administrator)
The key person in managing and supporting a Collaborative Review Group (CRG) on a day to day basis. Most CRGs have a full-time co-ordinator working from an editorial base. Responsibilities of a co-ordinator include: co-ordinating the activities of the CRG; fostering liaison and communication between editors and reviewers; setting up and maintaining a trials register; producing newsletters; providing reviewers with the relevant software (RevMan), manuals and support to do their reviews; transferring reviews to the Parent Database via the Module Manager (ModMan) software, for inclusion in the Cochrane Database of Systematic Reviews. Coordinators come from a variety of backgrounds, and whilst some also prepare systematic reviews in addition to their work as co-ordinator, many do not.

**Critical appraisal**
The process of assessing and interpreting evidence by systematically considering its validity, results and relevance.

**Cross-over trial**
A type of clinical trial comparing two or more interventions in which the participants, upon completion of the course of one treatment are switched to another. For example, for a comparison of treatments A and B, half the participants are randomly allocated to receive them in the order A, B and half to receive them in the order B, A. A problem with this design is that the effects of the first treatment may carry over into the period when the second is given.

**Cumulative meta-analysis**
In cumulative meta-analysis studies are added one at a time in a specified order (e.g. according to date of publication or quality) and the results are summarised as each new study is added. In a graph of a cumulative meta-analysis each horizontal line represents the summary of the results as each study is added, rather than the results of a single study.

**Database**
A collection of organised information, usually held on a computer. In some ways a database is similar to a filing system, but with important
advantages: the information can be revised and kept up to date easily, and the computer can retrieve information from it very quickly. Electronic databases such as MEDLINE, EMBASE and the CDSR can be distributed on disk, CD-ROM or via the Internet.

**Database of Abstracts of Reviews of Effectiveness (DARE)**
A collection of structured abstracts and bibliographic references of systematic reviews of the effects of healthcare. See the Cochrane Library.

**Degrees of freedom**
The number of independent comparisons that can be made between the members of a sample. It refers to the number of independent contributions to a sampling distribution (such as chi-square distribution). In a contingency table it is one less than the number of row categories multiplied by one less than the number of column categories; e.g. a 2 x 2 table comparing two groups for a dichotomous outcome, such as death, has one degree of freedom.

**Detection bias (synonym: ascertainment bias)**
Systematic differences between comparison groups in how outcomes are ascertained, diagnosed or verified.

**Dichotomous data (synonym: binary data)**
Observations with two possible categories such as dead/alive, smoker/non-smoker, present/not present.

**Double blind (synonym: double masked)**
Neither the participants in a trial nor the investigators (outcome assessors) are aware of which intervention the participants are given. The purpose of blinding the participants (recipients and providers of care) is to prevent performance bias. The purpose of blinding the investigators (outcome assessors, who might also be the care providers) is to protect against detection bias. See also blinding, single blind, triple blind, concealment of allocation.

**Editor (of a Collaborative Review Group)**
A member of the editorial team, often not located at the editorial base, who not only prepares and maintains one or more systematic reviews as a member of a CRG, but also has responsibilities to support the coordinating editor in editing systematic reviews prepared by others, and in fostering the smooth running of the Group.

**Editorial base**
Collaborative Review Groups have an editorial base where the coordinating editor, the co-ordinator, secretarial support, and the Group’s trials register are located, and to which reviewers are encouraged to come to work on their reviews.
**Editorial process**
The process by which each individual CRG decides on the criteria for editing and including reviews in its edited module for inclusion in the *Cochrane Database of Systematic Reviews*. Protocols may also be reviewed both by the editors (internal review) and by external peer reviewers. See also referee process.

**Editorial team (of a Collaborative Review Group)**
Normally consists of a co-ordinator, several editors and a secretary.

**EER**
Experimental group event rate

**Effect size**
1. A generic term for the *estimate of effect* for a study.
2. A dimensionless measure of effect that is typically used for *continuous data* when different scales (e.g. for measuring pain) are used to measure an outcome and is usually defined as the difference in means between the intervention and control groups divided by the standard deviation of the control or both groups. See standardised mean difference.

**Effectiveness**
The extent to which a specific intervention, when used under ordinary circumstances, does what it is intended to do. Clinical trials that assess effectiveness are sometimes called management trials. See also intention-to-treat.

**Efficacy**
The extent to which an intervention produces a beneficial result under ideal conditions. Clinical trials that assess efficacy are sometimes called explanatory trials and are restricted to participants who fully co-operate.

**EMBASE (Excerpta Medica database)**
A European-based electronic *database* of pharmacological and biomedical literature covering 3,500 journals from 110 countries. Years of coverage - 1974 to present.

**Empirical**
Empirical results are based on experience (or observation) rather than on reasoning alone.

**Estimate of effect (synonym: treatment effect)**
In studies of the effects of healthcare, the observed relationship between an intervention and an outcome expressed as, for example, a number needed to treat, odds ratio, risk difference, relative risk, standardised mean difference, or weighted mean difference.
**Event rate**
The proportion of participants in a group in whom an event is observed. Thus, if out of 100 patients the event (e.g. a stroke) is observed in 32, the event rate is 0.32.

**Expected date (of a Cochrane Review)**
The time by which a user of CDSR can expect to have access to a completed review. It appears on the title page of a protocol in CDSR, and is the date by which the review is expected to have been completed and gone through the editorial process of the CRG responsible for the module in which the review is found.

**External peer reviewer (of a Cochrane Review)**
A person with relevant content, methodological or user expertise who critically examines reviews in her/his area of expertise.

**External validity (synonyms: external validity, generalisability, relevance, transferability)**
The degree to which the results of an observation hold true in other settings. See also validity.

**Extramural**
Outside (the walls or boundaries of) a place or institution. Refers to "external" sources of support (such as funding) as opposed to "internal" (intramural) support.

**F-test (synonym: variance ratio test)**
A statistical test of the hypothesis that two population variances are the same. The t test is based on the assumption that this is the case.

**Fixed effect model**
A statistical model that stipulates that the units under analysis (e.g. people in a trial or study in a meta-analysis) are the ones of interest, and thus constitute the entire population of units. Only within-study variation is taken to influence the uncertainty of results (as reflected in the confidence interval) of a meta-analysis using a fixed effect model. Variation between the estimates of effect from each study (heterogeneity) does not effect the confidence interval in a fixed effect model. See random effects model.

**Funnel plot**
A graphical display of sample size plotted against effect size that can be used to investigate publication bias. When many studies have been located that estimate the same effect, the distribution of points should resemble a funnel shape with a widening in the spread of effect sizes as sample size decreases. A gap on one side of the wide part of the funnel indicates that some studies have not been published or located. Funnel plots are not presently available in the Cochrane software.
Generalisability (synonyms: applicability, external validity, relevance, transferability)

Generalisability is the degree to which the results of a study or systematic review can be extrapolated to other circumstances, in particular to routine health care situations.

Gold standard

The method, procedure or measurement that is widely accepted as being the best available against which new interventions should be compared. It is particularly important in studies of the accuracy of diagnostic tests. For example, handsearching is sometimes used as the gold standard for identifying trials against which electronic searches of databases such as MEDLINE are compared.

Handbook

See Cochrane Collaboration Handbook

Handsearching

Handsearching within the Cochrane Collaboration refers to the planned searching of a journal page by page (i.e. by hand), including editorials, letters, etc., to identify all reports of randomised controlled trials. Normally a person would start by handsearching the current year of a journal, and work backwards to 1948 (or volume 1 if after 1948). Once a trial is found, it is coded appropriately using definitions agreed within the Cochrane Collaboration and published in CDSR. All the identified trials, regardless of the topic, are sent to the Baltimore Cochrane Center, for forwarding to the US National Library of Medicine for re-tagging on MEDLINE, and trials that are within the scope of a Collaborative Review Group or Field go into their specialised register of trials. A handsearching manual is available through the Baltimore Cochrane Center, and should be read before handsearching is commenced. A journal handsearch registration form must be completed for each journal title, and sent to Baltimore to avoid duplication of effort.

Heterogeneity

In systematic reviews heterogeneity refers to variability or differences between studies in the estimates of effects. A distinction is sometimes made between "statistical heterogeneity" (differences in the reported effects), "methodological heterogeneity" (differences in study design) and "clinical heterogeneity" (differences between studies in key characteristics of the participants, interventions or outcome measures). Statistical tests of heterogeneity are used to assess whether the observed variability in study results (effect sizes) is greater than that expected to occur by chance. However, these tests have low statistical power. See also homogeneity.

Homogeneity

In systematic reviews homogeneity refers to the degree to which the
results of studies included in a review are similar. "Clinical homogeneity" means that, in trials included in a review, the participants, interventions and outcome measures are similar or comparable. Studies are considered "statistically homogeneous" if their results vary no more than might be expected by the play of chance. See heterogeneity.

**Index Medicus**
Catalogue of the United States National Library of Medicine (NLM), and a periodical index to the medical literature. Available in printed form, or electronically as MEDLINE.

**Individual patient data**
In systematic reviews this term refers to the availability of raw data for each study participant in each included trial, as opposed to aggregate data (summary data for the comparison groups in each study). Reviews using individual patient data require collaboration of the investigators who conducted the original trials, who must provide the necessary data.

**Intention-to-treat**
An intention-to-treat analysis is one in which all the participants in a trial are analysed according to the intervention to which they were allocated, whether they received it or not. Intention-to-treat analyses are favoured in assessments of effectiveness as they mirror the non-compliance and treatment changes that are likely to occur when the intervention is used in practice, and because of the risk of attrition bias when participants are excluded from the analysis.

**Intramural**
Within (the walls or boundaries of) a community or institution (e.g. a university). Used to distinguish from "external" (extramural) sources of support (such as funding).

**Log-odds ratio**
The (natural) log of the odds ratio. It is used in statistical calculations and in graphical displays of odds ratios in systematic reviews.

**Mantel-Haenszel test**
A summary chi-square test for stratified data and used when collecting for confounding. In meta-analyses the Mantel-Haenszel test is used to analyse data stratified (grouped) by study.

**Mean (synonyms: arithmetic mean, average)**
The average value, calculated by adding all the observations and dividing by the number of observations.

**MEDLINE (MEDlars on-line)**
An electronic database produced by the United States National
Library of Medicine. It indexes millions of articles in selected (about
3,700) journals. It is available through most medical libraries, and can
be accessed on CD-ROM, the Internet and by other means. Years of
coverage - 1966 to present.

MeSH headings (Medical Subject Headings)
Terms used by the United States National Library of Medicine to index
articles in Index Medicus and MEDLINE. Designed to reduce problems
that arise from, for example, differences in British and American
spelling. The MeSH system has a tree structure in which broad
subject terms branch into a series of progressively narrower subject
terms.

Meta-analysis
The use of statistical techniques in a systematic review to integrate
the results of the included studies. Also used to refer to systematic
reviews that use meta-analysis.

MetaView
Software incorporated in RevMan and CDSR that does statistical
analyses and prepares tabular and graphical displays of the results of
the studies included in a review.

Methodological quality (synonyms: validity, internal validity)
The extent to which the design and conduct of a trial are likely to have
prevented systematic errors (bias). Variation in quality can explain
variation in the results of trials included in a systematic review. More
rigorously designed (better 'quality') trials are more likely to yield
results that are closer to the 'truth'. See also external validity,
validity.

Minimisation
A method of allocation used, particularly in small trials, to provide
comparison groups that are closely similar for several variables. It
can be done with or without a component of randomisation. It is best
performed centrally with the aid of a computer program to ensure
allocation concealment.

ModMan (Module Manager)
Software developed by the Cochrane Collaboration to allow
Collaborative Review Groups to assemble and manage their edited
protocols and reviews. ModMan also contains information about the
Collaborative Review Group.

ModMan is used by Collaborative Review Group coordinators to edit
and update modules that are sent electronically, at quarterly intervals,
to the Parent Database for inclusion in the CDSR. A variation of the
ModMan software is also used by other Cochrane entities to prepare
modules for CDSR.
other Cochrane entities to prepare modules for CDSR.

Module
Edited protocols and reviews, and information about a Collaborative Review Group, is referred to as the Group's module. This module is transferred electronically using ModMan to the Parent Database at quarterly intervals, for inclusion in the CDSR. Other Cochrane entities also produce modules for inclusion in the Parent Database and CDSR.

Negative study
A term used to refer to a study that does not have "statistically significant" (positive) results indicating a beneficial effect of the intervention being studied. The term can generate confusion because it refers to both statistical significance and the direction of effect, studies often have multiple outcomes, the criteria for classifying studies as "negative" are not always clear and, in the case of studies of risk or undesirable effects, "negative" studies are ones that do not show a harmful effect.

Null hypothesis
The statistical hypothesis that one variable (e.g. whether or not a study participant was allocated to receive an intervention) has no association with another variable or set of variables (e.g. whether or not a study participant died), or that two or more population distributions do not differ from one another. In simplest terms, the null hypothesis states that the results observed in a study are no different from what might have occurred as a result of the play of chance.

Number needed to treat (NNT)
The number of patients who need to be treated to prevent one more adverse/bad outcome event. Specifies the treatment, its duration, and the adverse event being prevented. Reported as a whole number, calculated as 1/ARR, rounded to the next highest whole number, and accompanied by its 95% confidence interval (CI). It is the inverse of the risk difference.

Odds ratio (OR)
When used to summarize an overview or for individual studies in treatment, diagnosis, causation, or prognosis, an odds ratio describes the odds of an experimental patient having an adverse event relative to a control patient i.e. the ratio of the odds of an event in the experimental (intervention) group to the odds of an event in the control group. Odds are the ratio of the number of people in a group with an event to the number without an event. Thus, if a group of 100 people had an event rate of 0.20, 20 people had the event and 80 did not, and the odds would be 20/80 or 0.25. An odds ratio of one indicates no difference between comparison groups. For undesirable outcomes an OR that is less than one indicates that the intervention was effective.
in reducing the risk of that outcome. When the event rate is small, odds ratios are very similar to relative risks.

Open clinical trial
1. A clinical trial in which the investigator is aware which intervention is being given to which participant (random allocation may or may not be used).
2. A clinical trial in which the investigator decides which intervention is to be given (non-random allocation). Also called open label design.
3. A clinical trial with an open sequential design.

Ordinal data
Data that are classified into more than two categories where there is a natural order to the categories; for example, non-smokers, ex-smokers, light smokers and heavy smokers. Ordinal data are often reduced to two categories to simplify analysis and presentation, which may result in a considerable loss of information.

Performance bias
Systematic differences in care provided apart from the intervention being evaluated. For example, if patients know they are in the control group they may be more likely to use other forms of care, patients who know they are in the experimental (intervention) group may experience placebo effects, and care providers may treat patients differently according to what group they are in. Blinding of study participants (both the recipients and providers of care) is used to protect against performance bias.

Peto method
A way of combining odds ratios that has become widely used in meta-analysis. The calculations are straightforward and understandable, but this method produces biased results in some circumstances. It is a fixed effect model.

Peto odds ratio
An approximation to the exact odds ratios which are used when doing a meta-analysis using the Peto method. In some circumstances the Peto odds ratio can differ substantially from the exact odds ratio.

Placebo
An inactive substance or procedure administered to a patient, usually to compare its effects with those of a real drug or other intervention, but sometimes for the psychological benefit to the patient through a belief that s/he is receiving treatment. Placebos are used in clinical trials to blind people to their treatment allocation. Placebos should be indistinguishable from the active intervention to ensure adequate blinding.
Placebo effect
A favourable response to an intervention, regardless of whether it is the real thing or a placebo, attributable to the expectation of an effect, i.e. the power of suggestion. The effects of many healthcare interventions are attributable to a combination of both placebo and "active" (non-placebo) effects.

Point estimate
The results (e.g. mean, weighted difference, odds ratio, relative risk or risk difference) obtained in a sample (a study or a meta-analysis) which are used as the best estimate of what is true for the relevant population from which the sample is taken. A confidence interval is a measure of the uncertainty (due to the play of chance) associated with that estimate.

Positive study
A term used to refer to a study with results indicating a beneficial effect of the intervention being studied. The term can generate confusion because it can refer to both statistical significance and the direction of effect, studies often have multiple outcomes, the criteria for classifying studies as negative or positive are not always clear and, in the case of studies of risk or undesirable effects, "positive" studies are ones that show a harmful effect.

Precision
1. A measure of the likelihood of random errors in the results of a study, meta-analysis or measurement. Confidence intervals around the estimate of effect from each study are a measure of precision, and the weight given to the results of each study in a meta-analysis (typically the inverse of the variance of the estimate of effect) is a measure of precision (i.e. the degree to which a study influences the overall estimate of effect in a meta-analysis is determined by the precision of its estimate of effect).
2. The proportion of relevant citations located using a specific search strategy, i.e. the number of relevant studies (meeting the inclusion criteria for a trials register or a review) divided by the total number of citations retrieved.

Primary study (synonyms: included study, original study)
"Original research" in which data are first collected; a study included in a systematic review. The term primary research is sometimes used to distinguish it from "secondary research" (reanalysis of previously collected data), meta-analysis, and other ways of combining studies (such as economic analysis and decision analysis).

Prospective study
In evaluations of the effects of healthcare interventions, a study in
synonym for cohort study. See retrospective study.

**Protocol**
The plan or set of steps to be followed in a study. A protocol for a systematic review should describe the rationale for the review; the objectives; and the methods that will be used to locate, select and critically appraise studies, and to collect and analyse data from the included studies.

**Publication bias**
A bias in the published literature where the publication of research depends on the nature and direction of the study results. Studies in which an intervention is not found to be effective are sometimes not published. Because of this, systematic reviews that fail to include unpublished studies may overestimate the true effect of an intervention.

**P-value**
The probability (ranging from zero to one) that the observed results in a study, or results more extreme, could have occurred by chance. In a meta-analysis the P-value for the overall effect assesses the overall statistical significance of the difference between the treatment and control groups, whilst the P-value for the heterogeneity statistic assesses the statistical significance of differences between the effects observed in each study.

**Quality**
See methodological quality.

**Quality score**
A value assigned to represent the validity of a study either for a specific criterion, such as allocation concealment, or overall. Quality scores can be use letters (A, B, C) or numbers. An advantage of using letters is that the order of best to worst may be more obvious than for numbers.

**Quasi-random allocation**
A method of allocating participants to different forms of care that is not truly random; for example, allocation by date of birth, day of the week, medical record number, month of the year, or the order in which participants are included in the study (e.g. alternation).

**Quasi-randomised trial**
A trial using a quasi-random method of allocating participants to different forms of care. There is a greater risk of selection bias in quasi-random trials where allocation is not adequately concealed compared with randomised controlled trials with adequate allocation concealment.
Random
Governed by chance. See randomisation.

Random allocation
A method that uses the play of chance to assign participants to comparison groups in a trial, e.g. by using a random numbers table or a computer-generated random sequence. Random allocation implies that each individual or unit being entered into a trial has the same chance of receiving each of the possible interventions. It also implies that the probability that an individual will receive a particular intervention is independent of the probability that any other individual will receive the same intervention. See also concealment of allocation, quasi-random allocation, randomisation.

Random effects model
A statistical model sometimes used in meta-analysis in which both within-study sampling error (variance) and between-studies variation are included in the assessment of the uncertainty (confidence interval) of the results of a meta-analysis. See Fixed effect model. If there is significant heterogeneity among the results of the included studies, random effects models will give wider confidence intervals than fixed effect models.

Random error (synonym: sampling error)
Error due to the play of chance. Confidence intervals and P-values represent the probability of random errors, but not systematic errors (bias).

Random selection (synonym: random sampling)
A method of obtaining a representative, unbiased group of people from a larger population. Random selection which is not related to how participants are allocated to comparison groups is frequently used in cross-sectional and cohort studies, which are not randomised controlled trials, and it is frequently not used in randomised controlled trials. In older trial reports, however, the term is occasionally used instead of random allocation or randomisation.

Randomisation (spelled randomization in US English)
Method used to generate a random allocation sequence, such as using tables of random numbers or computer-generated random sequences. The method of randomisation should be distinguished from concealment of allocation because of the risk of selection bias despite the use of randomisation, if there is not adequate allocation concealment. For instance, a list of random numbers may be used to randomise participants, but if the list is open to the individuals responsible for recruiting and allocating participants, those individuals can influence the allocation process, either knowingly or unknowingly.
Randomisation blinding
See concealment of allocation.

Randomised controlled trial (RCT) (Synonym: randomised clinical trial)
An experiment in which investigators randomly allocate eligible people into (e.g. treatment and control) groups to receive or not to receive one or more interventions that are being compared. The results are assessed by comparing outcomes in the treatment and control groups. NOTE: when using randomized controlled trial as a search term (publication type) in MEDLINE use the US spelling (randomized).

RCT
See randomised controlled trial.

Referee process
System by which a review goes out to editors and also sometimes one or more external parties with content, methodological or user expertise. These people are sometimes called external peer reviewers or referees. See also editorial process.

Relative Risk (RR) (synonym: risk ratio)
The ratio of risk in the intervention group to the risk in the control group. The risk (proportion, probability or rate) is the ratio of people with an event in a group to the total in the group. A relative risk of one indicates no difference between comparison groups. For undesirable outcomes an RR that is less than one indicates that the intervention was effective in reducing the risk of that outcome.

Relative Risk Reduction (RRR)
The proportional reduction in outcome rates between control and experimental patients in a trial. Reported as a percentage, calculated as (CER – EER)/CER, and accompanied by its 95% confidence interval (CI).

Reliability
Refers to the degree to which results obtained by a measurement procedure can be replicated. Lack of reliability can arise from divergences between observers or measurement instruments, or instability in the attribute being measured.

Review
1. A systematic review.
2. A review article in the medical literature which summarises a number of different studies and may draw conclusions about a particular intervention. Review articles are often not systematic. Review articles are also sometimes called overviews.
3. To referee a paper, referee, referee process, external peer reviewer.
Reviewer
Somebody responsible for preparing and, in the case of Cochrane Reviews, keeping up-to-date a systematic review. Reviewer is also sometimes used to refer to an external peer reviewer, or referee.

Review Manager (RevMan)
Software developed for the Cochrane Collaboration to assist reviewers in preparing Cochrane Reviews. Reviewers enter their protocols and reviews into RevMan, from which they can be imported into ModMan by a Collaborative Review Group co-ordinator for inclusion in the Parent Database and CDSR as part of the Group's edited module.

Review protocol
See protocol.

Risk difference (RD) (synonym: absolute risk reduction)
The absolute difference in the event rate between two comparison groups. A risk difference of zero indicates no difference between comparison groups. For undesirable outcomes an RD that is less than zero indicates that the intervention was effective in reducing the risk of that outcome.

Search strategy
1. The methods used by a Collaborative Review Group (CRG) to identify trials within the Group's scope. This includes handsearching relevant journals, searching electronic databases, contacting drug companies, other forms of personal contact and checking reference lists. CRGs must describe their search strategy in detail in the Group's module. Reviewers can refer to the Group's search strategy when preparing a Cochrane Review, and if necessary supplement this with a description of their own additional searches.
2. The methods used by a reviewer to locate relevant studies, including the use of a CRG's trials register.
3. The combination of terms used to identify studies in an electronic database such as MEDLINE.

Selection bias
1. In assessments of the validity of studies of healthcare interventions, selection bias refers to systematic differences between comparison groups in prognosis or responsiveness to treatment. Random allocation with adequate concealment of allocation protects against selection bias. Other means of selecting who receives the intervention of interest, particularly leaving it up to the providers and recipients of care, are more prone to bias because decisions about care can be related to prognosis and responsiveness to treatment.
2. Selection bias is sometimes used to describe a systematic error in reviews due to how studies are selected for inclusion. Publication bias is an example of this type of selection bias.
3. Selection bias, confusingly, is also sometimes used to describe a
systematic difference in characteristics between those who are selected for study and those who are not. This affects the generalisability (external validity) of a study but not its (internal) validity.

**Sensitivity analysis**
An analysis used to determine how sensitive the results of a study or *systematic review* are to changes in how it was done. Sensitivity analyses are used to assess how robust the results are to uncertain decisions or assumptions about the data and the methods that were used.

**Sequential trial**
A trial in which the data are analysed after each patient's results become available, and the trial continues until a clear benefit is seen in one of the comparison groups, or it is unlikely that any difference will emerge. The main advantage of sequential trials is that they will be shorter than fixed length trials when there is a large difference in the effectiveness of the interventions being compared. Their use is restricted to conditions where the outcome is known relatively quickly.

**Single blind (synonym: single masked)**
The investigator is aware of the treatment/intervention the participant is getting, but the participant is unaware. See also *blinding*, double blind, *triple blind*.

**Statistical power**
The probability that the *null hypothesis* will be rejected if it is indeed false. In studies of the effectiveness of healthcare interventions, power is a measure of the certainty of avoiding a false negative conclusion that an intervention is not effective when in truth it is effective. The power of a study is determined by how large it is (the number of participants), the number of events (e.g. strokes) or the degree of variation in a continuous outcome (such as weight), how small an effect one believes is important (i.e. the smallest difference in outcomes between the intervention and the control groups that is considered to be important), and how certain one wants to be of avoiding a false positive conclusion (i.e. the cut-off that is used for *statistical significance*).

**Statistical significance**
An estimate of the probability of an association (effect) as large or larger than what is observed in a study occurring by chance, usually expressed as a *P*-value. For example, a *P*-value of 0.049 for a *risk difference* of 10% means that there is less than a one in 20 (0.05) chance of an association that is as large or larger having occurred by chance and it could be said that the results are "statistically significant" at *P* = 0.05. The cut-off for statistical significance is usually taken at 0.05, but sometimes at 0.01 or 0.10. These cut-offs
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**Systematic review (synonym: systematic overview)**

A *review* of a clearly formulated question that uses systematic and explicit methods to identify, select and critically appraise relevant research, and to collect and analyse data from the studies that are included in the review. Statistical methods (*meta-analysis*) may or may not be used to analyse and summarise the results of the included studies. See also *Cochrane Review*.

**TENS - Transcutaneous electrical nerve stimulation**

Transcutaneous electrical nerve stimulation: a method of pain control by the application of electric pulses to the nerve endings usually at a high frequency and a low intensity. This is done through carbon rubber electrodes that are placed on the skin and attached to a stimulator by flexible wires. The electric impulses generated are similar to those of the body, but different enough to block transmission of pain signals to the brain. TENS is non-invasive and non-addictive, with no known side effects. It is contraindicated in patients with a demand-type cardiac pacemaker.

**Trials register**

In the *Cochrane Collaboration*, this is a *database* of bibliographic references to *randomised controlled trials* and *controlled clinical trials* relevant to a *Collaborative Review Group* or *Field*, that is maintained at the *editorial base*. Software such as *ProCite* or *Reference Manager* is used to manage the database. Once a relevant report of a trial is identified, it is photocopied, coded and entered onto the register. Wherever possible, relevant trial reports are downloaded directly into the register from an electronic database such as *MEDLINE*. Information about unpublished and ongoing trials is also included in trials registers.

**Triple blind (synonym: triple masked)**

An expression that is sometimes used to indicate that knowledge of which study participants are in which comparison group is kept secret from the statistician doing the analysis as well as from the study
participants and investigators (outcome assessors). See also *blinding*, single blind, double blind.

**Validity (synonym: internal validity)**
Validity is the degree to which a result (of a measurement or study) is likely to be true and free of *bias* (systematic errors). Validity has several other meanings, usually accompanied by a qualifying word or phrase; for example, in the context of measurement, expressions such as "construct validity", "content validity" and "criterion validity" are used. The expression "internal validity" is sometimes used to distinguish validity (the extent to which the observed effects are true for the people in a study) from *external validity* or *generalisability* (the extent to which the effects observed in a study truly reflect what can be expected in a target population beyond the people included in the study). See also *methodological quality*, *random error*.

**Variable**
Any quantity that varies. A factor that can have different values.

**Variance**
A measure of the variation shown by a set of observations, defined by the sum of the squares of deviations from the mean, divided by the number of *degrees of freedom* in the set of observations.

**Washout period**
The stage in a *cross-over trial* when treatment is withdrawn before the second treatment is given. Washout periods are usually necessary because of the possibility that the intervention administered first can affect the outcome variable for some time after treatment ceases. A *run-in period* before a trial starts is sometimes called a washout period if treatments that participants were using before entering the trial are discontinued.

**Weighted mean difference (in meta-analysis)**
A method of *meta-analysis* used to combine measures on continuous scales (such as weight), where the mean, standard deviation and sample size in each group are known. The weight given to each study (e.g. how much influence each study has on the overall results of the meta-analysis) is determined by the precision of its estimate of effect and, in the statistical software in *RevMan* and *CDSR*, is equal to the inverse of the *variance*. This method assumes that all of the trials have measured the outcome on the same scale. See also *standardised mean difference*.