Low back pain: the acute management of patients with chronic (longer than 6 weeks) non-specific low back pain

Full guideline – Consultation version

September 2008

National Collaborating Centre for Primary Care

NOTE: Please reference the page number and line number for each comment made during consultation.

Citation

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APPENDICES (these are presented as separate files)

Preface

To be added for final version.

Key priorities for implementation

A number of key priority recommendations have been identified for implementation listed below. These recommendations are considered by the GDG to have the most significant impact on patients' care and patients' outcomes.

The criteria the GDG used to select these key priorities for implementation included whether a recommendation is likely to:

- have a high **impact** on patients' outcomes in particular pain, disability or psychological distress.
- have a **high impact** on reducing variation in the treatment offered to patients
- lead to a **more efficient** use of NHS resources
- enable patients to **reach important points in the care pathway more rapidly**
- promote patient choice.

- Consider offering a course of manual therapy including spinal manipulation of up to 9 sessions over up to 12 weeks[1].
- Consider offering a course of acupuncture needling comprising up to 10 sessions over a period of up to 12 weeks[1].
- Consider offering a structured exercise programme tailored to the individual[1].
- Offer supervised group exercise programmes in preference to one-to-one supervised exercise programmes.
- Consider referral for a combined physical and psychological treatment programme for patients who have high disability and/or significant psychological distress after having received less intensive treatments.
- Do not offer X-ray of the lumbar spine for the management of non-specific low back pain.
- MRI for non-specific low back pain should only be performed within the context of a referral for an opinion on spinal fusion.

[1] A choice of any of these therapies may be offered, taking into account patient preference.

- Consider referral for an opinion on spinal fusion for people who have completed a comprehensive package of care including a combined physical and psychological treatment programme and who have persistent severe non-specific low back pain for which the patient would consider surgery.
- Do not offer injections of therapeutic substances into the back.

Guideline recommendations

All recommendations are repeated within the relevant chapter. Please make comments on the recommendations within the chapter.

1.1 Assessment

Hyperlink to Assesment chapter

1.1.1 Do not offer X-ray of the lumbar spine for the management of non-specific low back pain.

1.1.2 Consider MRI (magnetic resonance imaging) when a diagnosis of spinal malignancy, sepsis, fracture, cauda equina syndrome or inflammatory disease is suspected.

1.1.3 MRI for non-specific low back pain should only be performed within the context of a referral for an opinion on spinal fusion.

1.2 Information, education and patient treatment preferences

Hyperlink to Information, education and patient treatment preferences chapter

1.2.1 Use educational materials consistent with this guideline to support other treatments.

1.2.2 Include an educational component consistent with this guideline as part of other interventions.

1.2.3 Do not offer stand-alone formal education programmes.

1.2.4 Take into account the patient's expectations and preferences when considering recommended treatments.

1.2.5 The patient's expectations and preferences should not be used to predict the response to treatments.

1.3 Exercise

Hyperlink to Exercise chapter

1.3.1 Advise people with low back pain that maintaining a physically active lifestyle is likely to be beneficial.

1.3.2 Advise all people with low back pain to exercise.

1.3.3 Consider offering a structured exercise programme tailored to the individual[2].

1.3.4 Offer supervised group exercise programmes in preference to one-to-one supervised exercise programmes.

1.4 Manual therapies

Hyperlink to Manual therapies chapter

1.4.1 Consider offering a course of manual therapy including spinal manipulation of up to 9 sessions over up to 12 weeks[3].

[2] A choice of an exercise programme, a course of manual therapy (see section 1.4.1) and a course of acupuncture (see section 1.8.1) may be offered, taking into account patient preference.
[3] A choice of an exercise programme (see section 1.3.3), a course of manual therapy and a course of acupuncture (see section 1.8.1) may be offered, taking into account patient preference.

1.5 Other non-pharmacological therapies

Hyperlink to Other non-pharmacological therapies chapter

Electrotherapy modalities

1.5.1 Do not offer laser therapy.

1.5.2 Do not offer interferential therapy.

1.5.3 Do not offer therapeutic ultrasound.

Transcutaneous nerve stimulation (TENS)

1.5.4 Do not offer transcutaneous electrical nerve simulation (TENS) routinely.

Lumbar supports

1.5.5 Lumbar supports are not recommended.

Traction

1.5.6 Do not offer traction because of the increased risk of aggravating symptoms.

1.6 Combined physical and psychological intervention

Hyperlink to Combined physical and psychological interventions chapter

1.6.1 Consider referral for a combined physical and psychological treatment programme for patients who have high disability and/or significant psychological distress after having received less intensive treatments.

1.7 Pharmacological therapies

Hyperlink to Pharmacological therapies chapter

NSAIDs/COX-2 inhibitors

1.7.1 Advise the person to take regular paracetamol as the first medication option.

1.7.2 Consider offering non-steroidal anti-inflammatory drugs (NSAIDs) for short-term use when paracetamol is ineffective.

1.7.3 Give due consideration to the risk of side effects from NSAIDs in older people, and other patients at high risk of experiencing side effects.

1.7.4 When offering treatment with an oral NSAID/COX-2 inhibitor, the first choice should be either a standard NSAID or a COX-2 inhibitor (other than etoricoxib 60 mg). In either case, these should be co-prescribed with a PPI, choosing the one with the lowest acquisition cost[4].

Opioids

1.7.5 Consider offering strong opioids for short-term use to people in severe pain.

1.7.6 Consider referral for specialist assessment for people who may require prolonged use of strong opioids.

1.7.7 Give due consideration to the risk of opioid dependence and side effects

1.7.8 Offer an NSAID or opioid depending upon the individual risk of side effects and patient preference.

1.7.9 Consider offering mild opioids when regular paracetamol alone is ineffective.

1.7.10 Base decisions on continuation of mild opioids on individual response.

[4] This recommendation is from 'Osteoarthritis: the care and management of osteoarthritis in adults' (NICE clinical guideline 59).

Antidepressants

1.7.11 Do not offer selective serotonin reuptake inhibitors (SSRIs) for treating pain.

1.7.12 Consider offering a trial of tricyclic antidepressants.

1.7.13 Start tricyclic antidepressants at a low dosage and increase up to the maximum antidepressant dose until therapeutic effect is achieved or unacceptable side effects prevent further increase. People starting on a tricyclic antidepressant should be reviewed at least monthly.

1.8 Invasive procedures

Hyperlink to Invasive procedures chapter

1.8.1 Consider offering a course of acupuncture needling comprising up to 10 sessions over a period of up to 12 weeks[5].

1.8.2 Do not offer injections of therapeutic substances into the back.

1.9 Referral for surgery

Hyperlink to Referral for surgery chapter

1.9.1 Consider referral for an opinion on spinal fusion for people who have completed a comprehensive package of care including a combined physical and psychological treatment programme and who have persistent severe non-specific low back pain for which the patient would consider surgery.

1.9.2 People who have psychological distress should receive appropriate treatment for this before referral for spinal fusion.

[5] A choice of an exercise programme (see section 1.3.3), a course of manual therapy (see section 1.4.1) and a course of acupuncture may be offered, taking into account patient preference.

1.9.3 If spinal fusion is being considered, refer the patient to a specialist surgical service.

1.9.4 Due consideration should be given to possible risks of spinal fusion.

1.9.5 Do not refer people for intradiscal electrothermal therapy (IDET), percutaneous intradiscal radiofrequency thermocoagulation (PIRFT) or radiofrequency facet joint denervation.

2 Introduction

2.1 Background

Low back pain is a common disorder. Nearly everyone is affected by it at some time. For most people affected by low back pain substantial pain or disability is short lived and they soon return to normal activities; regardless of any advice or treatment they receive. A small proportion, however, develop chronic pain and disability. Once back pain has been present for greater than one year few people with long-term pain and disability return to normal activities. It is this group who account for the majority of the health and social costs associated with low back pain.

Guidelines and consensus statements internationally are consistent in their overall approach to the management of acute low back; that is back pain of less than six weeks duration (Koes, B. W., van Tulder, M. W., Ostelo, R. et al , 2001). What has been less clear is how those patients whose spinal pain and disability persists for longer than six weeks should be managed in order to prevent long-term disability. Appropriate management of people in this group has the potential to reduce the number of people with disabling long-term back pain; and consequentially to reduce the cost of back pain to society. Thus, the focus of this guideline is on treatment of people with low back pain that has been present for more than six weeks, but for less than 12 months. This guideline does not address the management of people with long-term severe disabling low back pain.

Non-specific low back pain

Non-specific low back pain is pain muscle tension or stiffness affecting the lower back for which there is not a recognised patho-anatomic cause. The lower back is commonly defined as the area bounded by the bottom of the rib cage and the buttock creases. Some people with non-specific low back pain may also feel pain in their upper legs; but the low back pain usually predominates. The syndrome of radicular pain due to nerve root compression (sometimes called sciatica) is a different clinical syndrome; its management is not part of this guideline. The management of the syndrome of cauda equina compression causing widespread neurological damage requires emergency treatment and is not part of this guideline.

If caudia equina syndrome is suspected an immediate referral for a surgical opinion is needed.

The diagnosis of non-specific low back pain is dependent on the clinician being satisfied that there is not a specific cause for their patient's pain. Where the clinician has grounds to be concerned that there is a specific cause for their patient's low back pain they should arrange the relevant investigations [box 1]. The diagnosis of specific causes of low back pain, however, is beyond the remit of this guideline.

Box 1 Specific causes of low back pain

Malignancy

Infection

Osteoporotic Collapse

Fracture

Rheumatoid arthritis

Ankylosing Spondylitis or other inflammatory disorders

Conventionally low back pain is categorised according to its duration as acute (<6 weeks), sub-acute (6 weeks - 12 weeks) and chronic (>12 weeks) (Spitzer, W. O. and Leblanc, F. E., 1987). Since many people affected by low back pain find that their symptoms wax and wane it may not always be appropriate to use such a rigid classification system.(Croft, P. R., Macfarlane, G. J., Papageorgiou, A. C. et al , 1998)

Epidemiology of low back pain.

Estimates for the prevalence of low back pain vary considerably between studies; estimates for low back pain range up to 33% for point prevalence, 65% for one year prevalence, and 84% for lifetime prevalence.(Walker, B. F., 2000) There is no convincing evidence that age affects the prevalence of back pain. (Airaksinen, O., Brox, J. I., Cedraschi, C. et al , 2006)

There are few epidemiological data that are directly relevant to the target population for these guidelines. Published data do not distinguish between low back pain persisting for greater than one year and less than one year.

Annually, back pain probably affects a third of the population; around 20% of those affected, one in fifteen of the population, will see their general practitioner for advice(Macfarlane, G. J., Jones, G. T., and Hannaford, P. C., 2006). This results in 2.6 million people seeking advice about of back pain from their GP each year(Arthritis Research Campaign., 2002).

One year after a first episode of back pain 62% of people still have pain and 16% of those initially unable to work are not working after one year (Hestbaek, L., Leboeuf-Yde, C., and Manniche, C., 2003). Typically pain and disability improve rapidly during the first month; (58% reduction from initial scores for both pain and disability) with little further improvement being observed after three months(Pengel, L. H., Herbert, R. D., Maher, C. G. et al , 2003). Estimates for the adult population burden of chronic back pain include; 11% for disabling back pain in the previous three months, 23% for low back pain lasting more than three months and, 18% for at least moderately troublesome pain in the previous month (Andersson, H. I., Ejlertsson, G., Leden, I. et al , 1993; Cassidy, J. D., Carroll, L. J., and Cote, P., 1998; Parsons, S., Breen, A., Foster, N. E. et al , 2007).

Cost of back pain.

The direct and indirect financial costs of low back pain are substantial in all developed countries. Estimates for the cost of back pain in different health and social systems are not directly comparable (Dagenais, S., Caro, J., and Haldeman, S., 2008). The most recent UK cost of illness study for the UK is based on 1998 treatments. (Maniadakis, N. and Gray, A., 2000) The economic climate has changed and there has been inflation since then. It is difficult to estimate effect of the first two of these factors on current cost of LBP. The UK retail price index, however, increased by 28.8% in the ten years to July 2008 (Office for National Statistics., 2008). http://www.statistics.gov.uk/downloads/theme_economy/RP04.pdf accessed 15.09.08). suggesting that current direct health care costs are likely to be substantially greater than the published figures.

The 1998 estimate direct health care costs were estimated at £1,632M, of which £565M was the cost of non-NHS direct health care costs (Maniadakis, N. and Gray, A., 2000). These large non-NHS costs are mainly accounted for by the use of private therapists (acupuncturists, chiropractors, occupational therapists, osteopaths, physiotherapists and others). This large private sector involvement in the care of back pain is unusual within the UK health care system. Although NICE guidance is developed for the NHS these guidelines may also be relevant to purchasing decisions made by individuals with back pain and private insurers.

The indirect costs of low back pain, due to lost production are larger. Using the more conservative friction method the 1998 estimate came to £3,440M, whilst a human capital approach yielded a cost of £9,090M. (Maniadakis, N. and Gray, A., 2000)
Management

Diagnosis

For patients presenting with a new episode, or exacerbation, of low back pain consideration needs to be given to the possibility that there is a specific cause for their pain. For acute back pain, malignancy, infection, osteoporotic and non-osteoporotic fractures need to be considered. Malignancy is commoner in older people and those with a past history of tumours known to metastasise to bone (e.g. breast, lung and prostate). Infection should be considered in those who may have an impaired immune system, e.g. people living with HIV, or who are systemically unwell. Osteoporotic fractures typically affect older people (women more than men) and those with other chronic illnesses. Apart from osteoporotic fratures in older people these are all uncommon; very few patients presenting with back pain will need further investigation before making a diagnosis of acute non-specific low back pain. The general approach to the treatment for acute non-specific low back pain is advice to stay active and to avoid best rest, plus pain reliving medications such as NSAIDs.(Koes, B. and van Tulder, M., 2006)

For those with pain that continues for longer than six weeks or who further deteriorate between six weeks and one year the possibility of a specific cause needs to be re-considered. In addition to the specific causes of acute low back pain the possibility of chronic inflammatory conditions such as ankylosing spondylitis or rheumatoid arthritis needs to be considered.

Objective for treatment of non-specific low back pain

The overall objective of treatment of non-specific low back pain lasting six weeks to one year is to ensure that an episode of low back pain does not result in long term withdrawal from normal activities, including sickness absence from paid employment. More severe pain and back pain related disability, and psychological distress predict a poor long term outcome for people with non-specific back pain.(Pincus, T., Santos, R., Breen, A. et al , 2008) It is improving these outcomes (pain, disability and distress) that are the focus for the management of non-specific low back pain and thus the focus of this guideline.

Available treatments for non-specific low back pain

There are a plethora of treatments available for the treatment of non-specific low back pain. Not all of the treatments used have a strong theoretical underpinning. The differences and similarities between different therapeutic approaches is not always clearly explicated in the literature. Furthermore, for many of the individual treatment approaches used any therapeutic benefit is the result both of the specific treatment modality used and the non-specific effects of the therapist delivering the treatment. For therapist delivered interventions the guideline development group took the pragmatic decision that it was the effect of the package of care delivered by the therapist or therapists that is of interest rather than the individual components of the treatment package. Broadly speaking the treatments that have been used for non-specific low back pain are;

Combined physical and psychological interventions (CPP)

These includes the components seen in some types of back school and multidisciplinary rehabilitation programmes

Education/information

Including advice from practitioners regarding exercise and/or causes of back pain, formal education sessions, and written educational material.

Exercise

Including group and individual supervised exercise both land and water based

Invasive procedures

Including acupuncture, electro-acupuncture, nerve blocks, neuroreflexotherapy,

percutaneous electrical nerve stimulation (PENS), injection of therapeutic substance into the spine.

Manual therapies
Including manipulation, massage, mobilisation

Passive non-pharmacological interventions
Including, interferential, laser, lumbar supports, transcutaneous electrical nerve stimulation, traction, ultrasound,

Pharmacological interventions
Including antidepressants, non-steroidal anti-inflammatory drugs (NSAIDs), opioids, and paracetamol, ,

Psychological interventions
These including a variants of cognitive behavioural therapy and self management

Surgical referral
For this guideline the evidence supporting different therapeutic approaches and the evidence on the decision making process for selecting therapeutic approaches has been reviewed.

2.2 Aim of the guideline

Clinical guidelines are defined as 'systematically developed statements to assist practitioner and patient decisions about appropriate healthcare for specific clinical circumstances'.

This guideline gives recommendations to clinicians and others about clinical assessment, pharmacological and non-pharmacological treatments and referral to surgery .

2.3 How the guideline is set out

The recommendations for all the topics in each clinical chapter are listed at the start of the chapter. Both the evidence statements and narratives of the research studies on which our recommendations are based are found within each topic section. The

evidence statements follow the narrative for each topic. Also included in each chapter is a brief explanation of why the GDG made the specific recommendations. The evidence tables with details of the research studies that describe the studies reviewed are found in Appendices C.

Unless otherwise indicated, recommendations are relevant for individuals with non specific low back pain.

2.4 Scope

The guideline was developed in accordance with a scope given by the National Institute for Health and Clinical Excellence (NICE, 'the Insititute'). The scope set the remit of the guideline and specified those aspects of the management of low back pain to be included and excluded. The scope was published in May 2007 and is reproduced here in Appendix A.

Whom the guideline is intended for

This guideline is of relevance to those who work in or use the National Health Service (NHS) in England and Wales:

- Primary and secondary care settings dealing with assessment, treatment and management of non-specific low back pain in adults.
- People with non-specific low back pain who are considering purchasing treatment privately may also find these guidelines useful when choosing treatment options

Areas outside the remit of the guideline

- Individuals who have LBP because of specific spinal pathologies, including:
  - Malignancy
  - Infection
  - Osteoporotic Collapse
  - Fracture
  - Rheumatoid arthritis
  - Ankylosing Spondylitis or other inflammatory disorders
  - (Cauda eqina compression)
- People with radiculopathy and/or nerve root pain.
- Children under the age of 18 years

- People with acute LBP (less than 6 weeks duration)
- People with non-specific LBP of greater than 12 months duration.

2.5 Responsibility and support for guideline development

2.5.1 The National Collaborating Centre for Primary Care (NCC-PC)

The NCC-PC is a partnership of primary care professional associations and was formed as a collaborating centre to develop guidelines under contract to NICE. It is entirely funded by NICE. The NCC-PC is contracted to develop four guidelines at any one time, although there is some overlap at start and finish. Unlike many of the other centres which focus on a particular clinical area, the NCC-PC has a broad range of topics relevant to primary care. However, it does not develop guidelines exclusively for primary care. Each guideline may, depending on the scope, provide guidance to other health sectors in addition to primary care.

The Royal College of General Practitioners (RCGP) acts as the host organisation. The Royal Pharmaceutical Society and the Community Practitioners and Health Visitors' Association are partner members with representation from other professional and lay bodies on the Board. The RCGP holds the contract with the Institute for the NCC-PC.

2.5.2 The development team

The development team had the responsibility for this guideline throughout its development. They were responsible for preparing information for the Guideline Development Group (GDG), for drafting the guideline and for responding to consultation comments. The development team working on this guideline consisted of the:

- **Guideline lead**
  who is a senior member of the NCC-PC team who has overall responsibility for the guideline
- **Information scientist**
  who searched the bibliographic databases for evidence to answer the questions posed by the GDG

- **Reviewer (Health Services Research Fellow**)
  who appraised the literature and abstracted and distilled the relevant evidence for the GDG
- **Health economist**
  who reviewed the economic evidence, constructed economic models in selected areas and assisted the GDG in considering cost effectiveness
- **Project manager**
  who was responsible for organising and planning the development, for meetings and minutes and for liaising with the Institute and external bodies
- **Clinical advisor**
  A clinician with an academic understanding of the research in the area and its practical implications to the service, who advised the development team on searches and the interpretation of the literature
- **Chair**
  who was responsible for chairing and facilitating the working of the GDG meetings

Applications were invited for the post of Clinical Advisor, who was recruited to work on average, a half a day a week on the guideline. The members of the development team attended the GDG meetings and participated in them. The development team also met regularly with the Chair of the GDG and the Clinical Advisor during the development of the guideline to review progress and plan work.

2.5.3 The Guideline Development Group (GDG)

A Chair was chosen for the group and his primary role was to facilitate and chair the GDG meetings.

Guideline Development Groups (GDGs) are working groups consisting of a range of members with the experience and expertise needed to address the scope of the guideline. Nominations for GDG members were invited from the relevant stakeholder organisations which were sent the draft scope of the guideline with some guidance on the expertise needed. Two patient representatives and nine healthcare professionals were invited to join the GDG.

Nominees who were not selected for the GDG were invited to act as Expert Peer Reviewers and were sent drafts of the guideline by the Institute during the consultation periods and invited to submit comments using the same process as stakeholders.

Each member of the GDG served as an individual expert in their own right and not as a representative of their nominating organisation, although they were encouraged to keep the nominating organisation informed of progress.

In accordance with guidance from NICE, all GDG members' interests were recorded on a standard declaration form that covered consultancies, fee-paid work, share-holdings, fellowships, and support from the healthcare industry. Details of these can be seen in Appendix F.

The names of GDG members appear listed below.

Full GDG members

- Professor Martin Underwood(Chair)
  Professor of Primary Care Research
  Warwick Medical School, University of Warwick
- Professor Paul Watson (Clinical Advisor)
  Professor of Pain Management and Rehabilitation
  Department of Health Sciences, University of Leicester
- Mrs Elaine Buchanan
  Consultant Physiotherapist, Nuffield Orthopaedic Centre, Oxford
- Dr Paul Coffey
  General Practitioner, Eynsham Medical Group, Whitney, Oxon
- Mr Peter Dixon
  Chiropractor Chairman General Chiropractic Council, London
- Mrs Christine Drummond
  Patient representative
- Mrs Margaret Flanagan
  Nurse Clinician, Western Avenue Medical Centre, Chester
- Professor Charles Greenhough
  Consultant Spinal Surgeon, James Cook University, Middlesborough

- Dr Mark Griffiths,
  Consultant Clinical Psychologist
  Halton & St Helens PCT, Cheshire
- Dr Jacqueline Halliday Bell
  Medical Inspector Health and Safety Executive, Birmingham
- Dr Dries Hettinga
- Patient representiative
  Mr Steven Vogel
  Vice Principal (Research and Quality), British School of Osteopathy, London
- Dr David Walsh
  Associate Professor, Kings Mill Hospital, Sutton in Ashfield

Members of the GDG from the NCC-PC were:

- Gill Ritchie
  Guideline Lead , NCC-PC
- Pauline Savigny
  Health Services Research Fellow, NCC-PC
- Nicola Brown
  Health Services Research Fellow, NCC-PC (from May 2007 to October 2007)
- Stefanie Kuntze
  Health Economist, NCC-PC
- David Hill
  Project Manager, NCC-PC
- Chris Rule
  Project Manager, NCC-PC (from August 2006 to September 2007)
- Marian Cotterell
  Information Scientist , NCC-PC

Co-opted GDG Members

- Dr Michael Cummings

- Medical Director, British Medical Acupuncture Society

- Mr Ray Langford
  Clinical Specialist Occupational Therapist, St Helens, Knowsley Hospitals NHS Teaching Trust

Observers

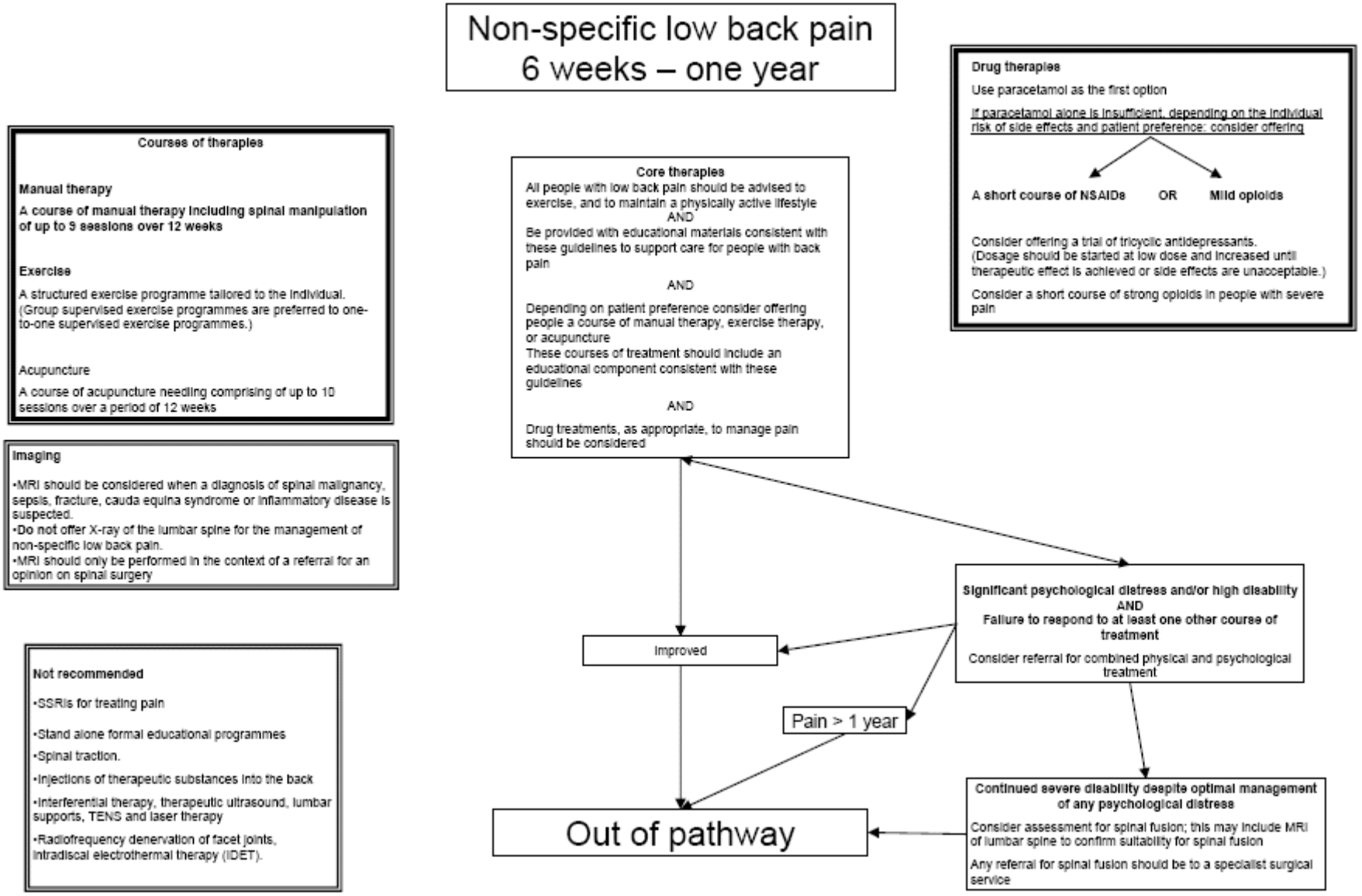
- Ms Colette Marshall
  Commissioning Manager, National Institute for Health and Clinical Excellence (until August 2007)
- Ms Sarah Willett
  Commissioning Manager, National Institute for Health and Clinical Excellence (from December 2007)

2.5.4 Guideline Development Group meetings

The GDG met at 5 to 6 weekly intervals for 16 months to review the evidence identified by the development team, to comment on its quality and relevance, and to develop recommendations for clinical practice based on the available evidence. The recommendations were agreed by the full GDG.

2.6 Care pathway

A clinical care pathway has been developed to indicate the key components in the treatment and management of non-specific LBP in adults.


Non-specific low back pain
6 weeks – one year
Courses of therapies
Manual therapy
A course of manual therapy including spinal manipulation of up to 9 sessions over 12 weeks
Exercise
A structured exercise programme tailored to the individual. (Group supervised exercise programmes are preferred to one-to-one supervised exercise programmes.)
Acupuncture
A course of acupuncture needling comprising of up to 10 sessions over a period of 12 weeks
Core therapies
All people with low back pain should be advised to exercise, and to maintain a physically active lifestyle
AND
Be provided with educational materials consistent with these guidelines to support care for people with back pain
AND
Depending on patient preference consider offering people a course of manual therapy, exercise therapy, or acupuncture
These courses of treatment should include an educational component consistent with these guidelines
AND
Drug treatments, as appropriate, to manage pain should be considered
Drug therapies
Use paracetamol as the first option
If paracetamol alone is insufficient, depending on the individual risk of side effects and patient preference: consider offering
A short course of NSAIDs
OR
Mild opioids
Consider offering a trial of tricyclic antidepressants. (Dosage should be started at low dose and increased until therapeutic effect is achieved or side effects are unacceptable.)
Consider a short course of strong opioids in people with severe pain
Imaging
•MRI should be considered when a diagnosis of spinal malignancy, sepsis, fracture, cauda equina syndrome or inflammatory disease is suspected.
•Do not offer X-ray of the lumbar spine for the management of non-specific low back pain.
•MRI should only be performed in the context of a referral for an opinion on spinal surgery
Not recommended
•SSRIs for treating pain
•Stand alone formal educational programmes
•Spinal traction.
•Injections of therapeutic substances into the back
•Interferential therapy, therapeutic ultrasound, lumbar supports, TENS and laser therapy
•Radiofrequency denervation of facet joints, intradiscal electrothermal therapy (IDET).
Improved
Significant psychological distress and/or high disability
AND
Failure to respond to at least one other course of treatment
Consider referral for combined physical and psychological treatment
Pain > 1 year
Continued severe disability despite optimal management of any psychological distress
Consider assessment for spinal fusion; this may include MRI of lumbar spine to confirm suitability for spinal fusion
Any referral for spinal fusion should be to a specialist surgical service
Out of pathway

1

2.7 Research recommendations

What is the clinical and cost effectiveness of using screening protocols to target treatments for patients with non-specific low back pain?

Why this is important.

There is much evidence from cross sectional and longitudinal studies that people with poorer physical function and in particular psychological factors such as elevated fear of activity, psychological distress and distorted cognitions about back pain are more disabled by their pain and are more likely to have a poor outcome from treatment. It is suggested by some researchers that screening to identify those who have a profile suggestive of poor outcome and referring them to combined physical and psychological therapies at an early stage will improve outcome.

There is one randomised controlled trail (RCT) which demonstrated the value of screening in improving outcome with respect to return to work. There is no UK study to date which has demonstrated that targeting treatments based on a risk factor profile leads to improved outcome or cost effectiveness.

How can education be effectively delivered for people with chronic non-specific low back pain?

Why is this important?

Improved understanding of low back pain and its management are identified as key components of care both by patients and by healthcare professionals. These guidelines emphasise the importance of patient choice, and people can only effectively exercise choice if they have an adequate understanding of the available options. Extensive research literature addresses the education of adults using a wide variety of techniques, but studies of patient education in low back pain have focused almost exclusively on written information. Little evidence is available as to whether such materials are the most effective way to deliver educational goals. Interdisciplinary projects combining educational and healthcare research methodologies should:

- Identify appropriate goals and techniques for the education of people with low back pain.
- Determine efficacy in achieving educational goals.
- Determine effects on clinical outcomes including pain, distress and disability.

What is the effectiveness and cost effectiveness of sequential interventions (manual therapy, exercise and acupuncture) compared with single interventions on pain, functional disability and psychological distress, in people with chronic non-specific back pain of between six weeks and one year?

Why is this important?

There is evidence that individually manual therapy, exercise and acupuncture are cost effective management options compared to usual care for chronic non-specific low back pain. There are substantial cost implications for those who do not respond to initial therapy and receive multiple back care interventions. It is unclear whether there is added health gain for this subgroup from either multiple or sequential use of therapies. There is also a need for further research to determine the characteristics of people with back pain who respond differentially to manual therapy, exercise or acupuncture.

Research should:

- Test the effect of sequencing manual therapy, exercise and acupuncture in the management of chronic non-specific low back pain.
- Determine the cost effectiveness of providing more than one of these interventions to people with chronic non-specific low back pain.
- Investigate whether subgroups of people with chronic non-specific low back pain respond differently to acupuncture, exercise or manual therapy.

What is the effectiveness and cost effectiveness of psychological treatments for non-specific low back pain greater than six weeks?

Why this is important

The effectiveness and cost effectiveness of psychological treatments for non-specific low back pain is not known. Data from RCTs of people with a mixture of painful disorders, and other research, suggest that they help non-specific low back pain; but there are few robust back pain specific data.

Research should:

- Use RCTs to test the effect of adding psychological treatment to other treatments for non-specific low back pain.
- Test individual and/or group treatments.
- Clearly describe, and justify the psychological treatments tested; these should have a robust theoretical justification.

If possible the comparative effectiveness and cost effectiveness of different psychological treatments should be tested, e.g. group versus individual treatment, or treatment approaches grounded in different theoretical paradigms.

Outcomes of interest include: pain, disability, psychological distress, self-efficacy, coping strategies, quality of life, costs and social engagement.

2.8 Acknowledgements

We gratefully acknowledge the contributions of Joanne Lord (NICE) for her advice and work on the health economic modeling. Anne Morgan for her work on the cost effectiveness and clinical evidence reviews. Chris Rule for project managing the guideline through the scoping and development phases. Chris Tack for his work on the guideline scope and developing the clinical questions this guideline should address; Angela Cooper, Neill Calvert; Julie Neilson and Katrina Sparrow from the NCC-PC for their help and advice with regard to the clinical and cost effectiveness reviews. Finally we are also very grateful all those who advised the development team and GDG and so contributed to the guideline process.

We would also like to acknowledge the contributions of the expert peer reviewers, namely

- To be added for final version

2.9 Glossary

Acupuncture	Acupuncture refers to the insertion of a solid needle into any part of the human body for disease prevention, therapy or maintenance of health. There are various other techniques often used with acupuncture, which may or may not be invasive. From: Acupuncture Regulation Working Group report published in September 2003
Alexander Technique	A discipline of physical movement that has a focus of self perception of movement
Autotraction	Traction performed by utilising the patient's own body weight (for example by suspension via the lower limb) or through movement.
CBT	Cognitive behavioural therapy
Chiropractic treatment	The diagnosis, treatment and prevent of mechanical disorders of the musculoskeletal system, and the effects of these disorders on the functions of the nervous system and general health. There is an emphasis on manual treatments including spinal adjustment and other joint and soft-tissue manipulation. (World Federation of Chiropractic 2001)
Cost effectiveness	The cost-effectiveness acceptability curve (CEAC) is a

acceptability curve (CEAC)	method for summarising the uncertainty in estimates of cost-effectiveness. The CEAC, derived from the joint distribution of costs and effects, illustrates the (Bayesian) probability that the data are consistent with a true cost-effectiveness ratio falling below a specified ceiling ratio. (Fenwick et al., 2006 BMC)
Cost-benefit analysis	A type of economic evaluation where both costs and benefits of healthcare treatment are measured in the same monetary units. If benefits exceed costs, the evaluation would recommend providing the treatment.
Cost-consequences analysis	A type of economic evaluation where various health outcomes are reported in addition to cost for each intervention, but there is no overall measure of health gain.
Cost-effectiveness analysis	An economic study design in which consequences of different interventions are measured using a single outcome, usually in 'natural' units (for example, life-years gained, deaths avoided, heart attacks avoided, cases detected). Alternative interventions are then compared in terms of cost per unit of effectiveness.
Cost-effectiveness model	An explicit mathematical framework, which is used to represent clinical decision problems and incorporate evidence from a variety of sources in order to estimate the costs and health outcomes. See also Markov model.
Cost-minimisation analysis	An economic evaluation that finds the least costly alternative therapy after the proposed interventions has been demonstrated to be no worse than its main comparator(s) in terms of effectiveness and toxicity.
Cost-utility analysis	A form of cost-effectiveness analysis in which the units of

	effectiveness are quality-adjusted life-years (QALYs).
CPP	Combined physical and psychological interventions
Decision analysis	A systematic way of reaching decisions, based on evidence from research. This evidence is translated into probabilities, and then into diagrams or decision trees which direct the clinician through a succession of possible scenarios, actions and outcomes.
Decision problem	A clear specification of the interventions, patient populations and outcome measures and perspective adopted in an evaluation, with an explicit justification, relating these to the decision which the analysis is to inform.
Discounting	Costs and benefits incurred today have a higher value than costs and benefits occurring in the future. Discounting health benefits reflects individual preference for benefits to be experienced in the present rather than the future. Discounting costs reflects individual preference for costs to be experienced in the future rather than the present. For NICE economic evaluations, health outcomes will be discounted at 3.5% and costs at 3.5% per annum, following the recommendations of the UK Treasury.
Dominance	An intervention is said to be dominant if there is an alternative intervention that is both less costly and more effective. See also extended dominance.
Economic evaluation	Comparative analysis of alternative health strategies (interventions or programmes) in terms of both their costs and consequences.

Extended dominance	An intervention is extendedly dominated when it can be dominated by a combination of two alternative interventions (i.e. if x% of the population are treated with intervention A, and y% are treated with intervention C, the overall result will be an intervention strategy that is both cheaper and more effective than intervention B). See also dominance.
Extrapolation	In data analysis, predicting the value of a parameter outside the range of observed values.
Facet Joint denervation	Removal of nerve supply to the synovial joints between zygapophyses or articular processes of the vertebrae, usually by heating, cutting or crushing the axons
Facet joint injection	Injection of therapeutic substances into the facet joint
Health economics	The study of the allocation of scarce resources among alternative healthcare treatments. Health economists are concerned with both increasing the average level of health in the population and improving the distribution of healthcare resources.
Health-related quality of life	A combination of an individual's physical, mental and social well-being; not merely the absence of disease.
Hydrotherapy	An exercise treatment conducted within a specially designed pool so that water supports the patients body weight.
ICER	Incremental cost effectiveness ratio – this is the difference between the mean costs in the population of interest divided by the difference in the mean outcomes in the population of interest

Incremental Cost effectiveness ratio	Is the difference in costs between two interventions being compared divided by the difference in effect of the two interventions. For instance if A and B are being compared Cost of A – costs of B divided by effects of A- effects of B.
Interferential therapy	An electrical treatment that uses two of medium frequency currents, simultaneously, so that their paths. Where they cross a beat frequency is generated which mimics a low frequency stimulation
Intra-Discal Electrothermal Therapy (IDET)	Use of a heating wire passed through a hollow needle into the Lumbar disc intended to seal any ruptures in the disc
Laser therapy	The use of lasers to generate heat and non-heat energy within the body.
Life-year	A measure of health outcome that shows the number of years of remaining life expectancy.
Life-years gained	Average years of life gained per person as a result o fan intervention.
Lumbar supports	External devices designed to reduce spinal mobility, e.g. corsets
Manipulation	Small amplitude high velocity movement at the limit of joint range taking the joint beyond the available range of movement
Markov model	A modelling technique used when a greater number of health states needs to be considered. They are particularly useful for disease in which events can occur repeatedly over time.
McKenzie	A physiotherapy approach to treating back pain which

	uses specific (extension) exercises and some manual therapy.
Mobilisation	joint movement within the available range of motion
MRI	Magnetic resonance imaging A special imaging techniques used to image internal structures of the body, particularly the soft tissues.
Neuroreflexotherapy	temporary implantations of epidermal devices into trigger points at the site of each subject's clinically involved dermatomes on the back and into referred tender points in the ear"
Non-specific low back pain	pain muscle tension or stiffness affecting the lower back for which there is not a recognised patho-anatomic cause
NSAIDS	Non-steroidal anti-inflammatory drugs
Opportunity cost	The opportunity cost of investing in a healthcare intervention is the other healthcare programmes that are displaced by its introduction. This may be best measured by the health benefits that could have been achieved had the money been spent on the next best alternative healthcare intervention.
Osteopathy	Osteopaths specialise in the diagnosis, treatment, prevention and rehabilitation of certain musculoskeletal conditions. Osteopathic manual therapy, including manipulation, is an important part of most treatment. Consultations are conceptualised within a bio-psychosocial model of patient centred care, which includes offering guidance on diet, lifestyle, and exercise. Diagnosis involves the use of a combination of specific osteopathic methods and conventional medical examination procedures. A four to five-year degree or

	masters programme is underpinned by extensive clinical training. By law, osteopaths must be registered by the General Osteopathic Council (GOsC) which has a statutory duty to regulate, develop and promote the practice of osteopathy in the UK. Although most osteopaths work in private practice, there are numerous examples of NHS commissioning for osteopathy across the UK
Percutaneous Electrical Nerve Stimulation (PENS)	The electrical stimulation, using needles inseterd into the skin, of sensory nerves serving pain generating structures
Prepared Patient Information	prepared patient information booklets as opposed to written report of verbal information given during the consultation.
Probabilistic sensitivity analysis	Probability distributions are assigned to the uncertain parameters and are incorporated into evaluation models based on decision analytical techniques (for example, Monte Carlo simulation).
Prolotherapy	Injections of irritant solutions to strengthen lumbosacral ligaments
Quality adjusted life-years (QALYS)	An index of survival that is adjusted to account for the person's quality of life during this time. QALYs have the advantage of incorporating changes in both quantity (longevity/mortality) and quality (morbidity, psychological, functional, social and other factors) of life. Used to measure benefits in cost-utility analysis, QALYS are calculated by estimating the number of years of life gained from a treatment and weighting each year with a quality-of-life score between zero and one.
radiofrequency facet	The use of radio-frequency energy to generate heat to

joint denervation	destroy nerves suppling the lumbar facet jpints
RMDQ	Roland Morris Disability Questionnaire
Spinal Fusion	A procedure that involves fusing together two or more vetebrae in the spine using either bone grafts or metal rods
Spinal fusion	Any, of a number of surgical techniques to reduce movement between two lumbar vertebrae
SSRI	Selective Serotonin reuptake inhibitor. A class of drug that are used as an antidepressant.
TENS	Transcutaneous electrical nerve stimulation. A method of producing electroanalgesia through electrodes applied to the skin.
The Back Book	A widely used advice booklet for people with back pain.
Therapeutic ultrasound	The use of, externally apllied sound waves to generate heat within specific parts of the body
Time horizon	The time span used in the NICE appraisal that reflects the period over which the main differences between interventions in health effects and use of healthcare resources are expected to be experienced, and taking into account the limitations of supportive evidence.
Traction	The use of externally applied force to stretch and mobilise the spine
Usual Care	Typical advice and other treatments offered in within general practice
Utility	This concept is applied in health care to mean the individual's valuation of their state of well-being deriving from the use of health care interventions. In brief, utility is

	a measure of the preference for, or desirability of, a specific level of health status or specific health outcome.
VAS	Visual analogue score - a score for measuring pain
Willingness to pay (WTP)	WTP refers to the amount that a decision maker is willing to pay for an additional unit of outcome (e.g. an additional QALY). If the WTP is higher than the ICER, the intervention is cost effective. If not, the intervention is not cost effective.

1

3 Methods

3.1 Introduction

This chapter sets out in detail the methods used to generate the recommendations for clinical practice that are presented in the subsequent chapters of this guideline. The methods are in accordance with those set out by the the Institute in 'The guidelines manual'. April 2006. London: National Institute for Health and Clinical Excellence. Available from: www.nice.org.uk/guidelinesmanual. *The Guideline Development Process – an overview for stakeholders, the public and the NHS* describes how organisations can become involved in the development of a guideline.

3.2 Developing key clinical questions (KCQs)

The first step in the development of the guideline was to refine the guideline scope into a series of key clinical questions (KCQs). These KCQs formed the starting point for the subsequent review and as a guide to facilitate the development of recommendations by the Guideline Development Group (GDG).

The KCQs were developed by the GDG and with assistance from the methodology team. The KCQs were refined into specific evidence-based questions (EBQs) specifying interventions to search and outcomes to be searched for by the methodology team and these EBQs formed the basis of the literature searching, appraisal and synthesis.

The total list of KCQs identified is listed in Appendix B. The development team, in liaison with the GDG, identified those KCQs where a full literature search and critical appraisal were essential.

3.3 Literature search strategy

Systematic literature searches are undertaken to identify published evidence to answer the clinical questions identified by the methodology team and the GDG. The information scientist developed search strategies for each question, with guidance from the GDG, using relevant MeSH (medical subject headings) or indexing terms,

and free text terms. Searches were conducted between May 2007 and May 2008. Update searches for all questions were carried out in July 2008 to identify any recently published evidence. Full details of the sources and databases searched and the strategies are available in Appendix G. **To ADD**

An initial scoping search for published guidelines, systematic reviews, economic evaluations and ongoing research was carried out on the following databases or websites: National Library for Health (NLH) Guidelines Finder, National Guidelines Clearinghouse, Scottish Intercollegiate Guidelines Network (SIGN), Guidelines International Network (GIN), Canadian Medical Association (CMA) Infobase (Canadian guidelines), National Health and Medical Research Council (NHMRC) Clinical Practice Guidelines (Australian Guidelines), New Zealand Guidelines Group, BMJ Clinical Evidence, Cochrane Database of Systematic Reviews (CDSR), Database of Abstracts of Reviews of Effects (DARE) and Heath Technology Assessment Database (HTA), NHS Economic Evaluations Database (NHSEED), National Research Register and Current Controlled Trials

For each clinical question the following bibliographic databases were searched from their inception to the latest date available: Database of Systematic Reviews (CDSR), Database of Abstracts of Reviews of Effects (DARE), Health Technology Database (HTA), MEDLINE, EMBASE, CINAHL, CENTRAL (Cochrane Controlled Trials Register) and PsycINFO . When appropriate to the question AMED was also searched.

The search strategies were developed in MEDLINE and then adapted for searching in other bibliographic databases. Methodological search filters designed to limit searches to systematic reviews or randomised controlled trials were used. These were developed by the Centre for Reviews and Dissemination (CRD) and The Cochrane Collaboration. For all other questions, no restriction was placed on study design.

The economic literature was identified by conducting searches in NHS Economic Evaluations Database (NHSEED) and in MEDLINE and EMBASE using an economics search strategy developed by ScHARR at the University of Sheffield.

Databases of the results of the searches for each question or topic area were created using the bibliographic management software Reference Manager.

3.4 Identifying the evidence

After the search of titles and abstracts was undertaken, full papers were obtained if they appeared to address the KCQ. The highest level of evidence was sought. The Guideline Development Group agreed that only randomized controlled trials and systematic reviews (of randomized controlled trials) should be considered for selection. Observational studies and surveys were felt appropriate for only one KCQ on adverse events of manual therapy. Expert consensus was used when randomised control trials were not available. Following a critical review of the full text paper, articles not relevant to the subject in question were excluded. Studies that did not report on relevant outcomes were also excluded. On the advice of the GDG randomised controlled trials that reported outcomes on less than 20 participants in each intervention arm were excluded as these have insufficient power. Studies including participants with low back pain for longer than 1 year were accepted if the information provided in the paper suggested participants had recurring pain but were not suffering from chronic severe disabling low back pain. Usual care was the chosen comparator in most KCQ, and the GDG agreed to define it as usual care provided by GPs. Studies were selected with this definition in mind, and where there was doubt about whether a study's specific comparator was relevant the GDG was consulted and made the final decision.

3.5 Critical appraisal of the evidence

From the papers retrieved, the Health Service Research Fellow (HSRF) synthesised the evidence for each question or questions into a narrative summary. These form the basis of this guideline. Each study was critically appraised using the Institute's criteria for quality assessment and the information extracted for included studies is given in Appendix C. Background papers, for example those used to set the clinical scene in the narrative summaries, were referenced but not extracted.

3.5.1 Choice of outcomes

Primary outcomes of interest were pain scores, disability score and psychological distress. As far as possible validated tools for measuring those outcomes were sought, however whatever instrument used was reported in the extraction with as much information as was reported in the paper. Studies reporting on outcomes other than these were excluded. Secondary outcomes were safety and adverse events.

3.6 Economic analysis

The essence of economic evaluation is that it provides a balance sheet of the benefits and harms as well as the costs of each option. A well conducted economic evaluation will help to identify, measure, value and compare costs and consequences of alternative policy options. Thus the starting point of an economic appraisal is to ensure that healthcare interventions are clinically effective and then also cost effective. Although NICE does not have a threshold for cost effectiveness, interventions with a cost per quality adjusted life year of up to £20,000 are deemed cost effective, those between £20-30,000 may be cost effective and those above £30,000 are unlikely to be judged cost effective. If a particular treatment strategy were found to yield little health gain relative to the resources used, then it could be advantageous to re-deploy resources to other activities that yield greater health gain.

To assess the cost effectiveness of different management strategies in people with non specific low back pain a comprehensive systematic review of the economic literature relating to low back pain patients was conducted. For selected components of the guideline original cost effectiveness analyses were performed. The primary criteria applied for an intervention to be considered cost effective were either:

- the intervention dominated other relevant strategies (that is it is both less costly in terms of resource use and more clinically effective compared with the other relevant alternative strategies); or
- the intervention cost less than £20,000 per quality-adjusted life-year (QALY) gained compared with the next best strategy (or usual care).

3.6.1 Health economic evidence reviews

Identified titles and abstracts from the economic searches were reviewed by a single health economist and full papers obtained as appropriate. No criteria for study design were imposed a priori. In this way the searches were not constrained to randomised controlled trials (RCTs) containing formal economic evaluations.

Studies were included in the cost-effectiveness evidence review if:

- The study population meets the inclusion criteria for the review of clinical evidence as set out in the NICE scope document and as agreed by the GDG
- An incremental cost-effectiveness analysis is performed with results presented as cost per Quality Adjusted Life Year (QALY)
- The study and costing perspective is that of the UK health service

If no studies were found which met all of the above criteria, then studies which met some of the criteria such as non-UK cost per QALY studies, or studies which take a broader costing perspective, or non-QALY cost-effectiveness analyses were considered for review and presentation to the GDG.

The full papers were critically appraised by the health economist using a standard validated checklist. A general descriptive overview of the studies, their quality, and conclusions was presented and summarised in the form of a narrative review (see also Appendix D for the full extractions and reasons for exclusion).

Each study was categorised as one of the following: cost effectiveness analysis or cost utility analysis (i.e. cost effectiveness analysis with effectiveness measured in terms of QALYs or life year gained). Some studies were categorised as ‘cost consequences analyses’ or ‘cost minimisation analyses’. These studies did not provide an overall measure of health gain or attempt to sythesise costs and benefits together. Such studies were considered as partial economic evaluations.

3.6.2 Cost effectiveness modelling

Combined physical and psychological interventions (CPP) was selected for further economic analysis as there was likelihood that the recommendation made would substantially change clinical practice in the NHS and have important consequences for resource use.

The question asked was whether an intensive CPP intervention was cost effective when compared with a monotherapy such as exercise. One crucial aspect of the model was to reduce progression to chronic disability of up to one year. This was done by separating people with a poor prognosis and evaluating whether treating these more intensively was beneficial or not. The model is a cost utility analysis as costs and QALYs were used as model outcomes. Return to work was an intermediary outcome and taken from trial data. Univariate and probabilistic senstitivity analysis was carried out in order to estimate the uncertainty of the results.

The full report for this analysis is included in Appendix E of this guideline. The GDG was consulted during the construction and interpretation of the model to ensure that appropriate assumptions, model structure and data sources were used. All models were done in accordance to the NICE reference case outlined in the 'The guidelines manual'. April 2006. London: National Institute for Health and Clinical Excellence. Available from: www.nice.org.uk

3.7 Assigning levels to the evidence

The evidence levels and recommendation are based on the Institute's technical manual 'The guidelines manual'. April 2006. London: National Institute for Health and Clinical Excellence. Available from: www.nice.org.uk/guidelinesmanual. Evidence levels for included studies were assigned based upon Table 1.

Table 1 Levels of evidence

Level of evidence	Type of evidence
1++	High-quality meta-analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias
1+	Well-conducted meta-analyses, systematic reviews of RCTs, or RCTs with a low risk of bias
1–	Meta-analyses, systematic reviews of RCTs, or RCTs with a high risk of bias
2++	High-quality systematic reviews of case–control or cohort studies High-quality case–control or cohort studies with a very low risk of confounding, bias or chance and a high probability that the relationship is causal
2+	Well-conducted case–control or cohort studies with a low risk of confounding, bias or chance and a moderate probability that the relationship is causal
2–	Case–control or cohort studies with a high risk of confounding, bias, or chance and a significant risk that the relationship is not causal
3	Non-analytical studies (for example, case reports, case series)
4	Expert opinion, formal consensus

3.8 Forming recommendations

In preparation for each meeting, the narrative and extractions for the questions being discussed were made available to the GDG one week before the scheduled GDG meeting. These documents were available on a closed intranet site and sent by post to those members who requested it.

GDG members were expected to have read the narratives and extractions before attending each meeting. The GDG discussed the evidence at the meeting and agreed evidence statements and recommendations. Any changes were made to the electronic version of the text on a laptop computer and projected onto a screen until the GDG were satisfied with these.

All work from the meetings was posted on the closed intranet site following the meeting as a matter of record and for referral by the GDG members.

3.9 Areas without evidence and consensus methodology

The table of clinical questions in Appendix B indicates which questions were searched.

In cases where evidence was sparse, the GDG derived the recommendations via informal consensus methods, using extrapolated evidence where appropriate. All details of how the recommendations were derived can be seen in the 'Evidence to recommendations' section of each of the chapters.

3.10 Consultation

The guideline has been developed in accordance with the Institute's guideline development process. This has included allowing registered stakeholders the opportunity to comment on the scope of the guideline and the draft of the full and short form guideline. In addition, the draft was reviewed by an independent Guideline Review Panel (GRP) established by the Institute.

The comments made by the stakeholders, peer reviewers and the GRP were collated and presented for consideration by the GDG. All comments were considered systematically by the GDG and the development team recorded the agreed responses.

3.11 Relationships between the guideline and other national guidance

3.11.1 Related NICE Guidance

It was identified that this guideline intersected with the following NICE guidelines published or in development. Cross reference was made to the following guidance as appropriate.

Guidelines

- .Osteoarthritis: the care and management of osteoarthritis in adults (NICE clinical guideline 59), 2008.

Public health intervention guidance

- Four commonly used methods to increase physical activity: brief interventions in primary care, exercise referral schemes, pedometers and community-based exercise programmes for walking and cycling. (NICE public health guidance 2), 2006
- Management of long term sickness and incapacity for work. NICE public health guidance (publication expected March 2009).

Through review of published guidance, personal contact and commenting on guideline scope, endeavours were made to ensure that boundaries between guidance were clear and advice was consistent.

4 Assessment of non-specific low-back pain

4.1 Introduction

Initial assessment serves to clarify the diagnosis of non-specific low back pain. These guidelines apply only to non-specific low back pain present for between six weeks and one year. Specific causes of low-back pain will normally have been excluded early in an episode of back pain.

The diagnosis of non-specific low back pain is dependent on the clinician being satisfied that there is not a specific cause for their patient's pain. Where the clinician has grounds to be concerned that there is a specific cause for their patient's low back pain they should arrange the relevant investigations [box 1]. The diagnosis of specific causes of low back pain, however, is beyond the remit of this guideline.

Box 1 Specific causes of low back pain

Malignancy

Infection

Osteoporotic Collapse

Fracture

Rheumatoid arthritis

Ankylosing Spondylitis or other inflammatory disorders

The syndrome of radicular pain due to nerve root compression (sometimes called sciatica) is a different clinical syndrome; its management is not part of this guideline. The management of the syndrome of cauda equine compression causing widespread neurological damage requires emergency treatment and is not part of this guideline.

The guidance on this chapter addresses the assessment of people diagnosed with non-specific low back pain it does not address the investigation of people in whom a specific cause of back pain is suspected.

4.2 Recommendations for assessment

Hyperlink to related evidence statements

4.2.1 Do not offer X-ray of the lumbar spine for the management of non-specific low back pain.

4.2.2 Consider MRI (magnetic resonance imaging) when a diagnosis of spinal malignancy, sepsis, fracture, cauda equina syndrome or inflammatory disease is suspected.

4.2.3 MRI for non-specific low back pain should only be performed within the context of a referral for an opinion on spinal fusion.

4.3 X-ray and MRI

Clinical question: what is the effectiveness of performing x-ray or MRI compared with no investigation to improve pain, functional disability or psychological distress?

Clinical question: what is the effectiveness of performing X-ray compared with MRI, to improve pain, functional disability or psychological distress?

4.3.1 Clinical evidence

Literature searching retrieved a total of 873 papers for this question of which 15 were ordered. Twelve were excluded and three were included; two investigated X-ray versus no X-ray (Kendrick, D., Fielding, K., Bentley, E. et al , 2001; Kerry, S., Hilton, S., Patel, S. et al , 2000) while the third investigated MRI vs. delayed MRI (Gilbert,

F. J., Grant, A. M., Gillan, M.-G. C. et al , 2004). No studies were found that compared MRI with no MRI. Due to the nature of the intervention, none of these studies blinded participants to treatment allocation. The primary outcomes of interest were pain, disability and psychological distress. Secondary outcomes were harms, recovery, costs, patient satisfaction and reassurance.

4.3.1.1 X-ray versus no X-ray

The first RCT (Kendrick, D., Fielding, K., Bentley, E. et al , 2001) recruited patients aged 20-55 years with low back pain of at least 6 weeks duration (median duration of LBP was 10 weeks). A total of 421 participants were randomised to the intervention, x-ray of lumbar spine (n=210) or the control group (n=211) who received usual care, patients were then followed up at 3 and 9 months. At three months, more patients randomised to receive radiography still had pain compared with those who received usual care, OR=1.26 (95% CI 1.0 to 1.60). Patients randomised to radiography also had higher median Roland Morris Disability Questionnaire (RMDQ) scores (Z score = -1.93, P=0.05) and lower median health status scores (Z score = -2.32, P=0.02) compared with those randomised to usual care. At the nine month follow-up, there were no significant differences between the groups except for the outcome of median satisfaction with consultation. Patients randomised to radiography were more satisfied than those in the usual care group (Z score = -2.69, P<0.01) (Kendrick, D., Fielding, K., Bentley, E. et al , 2001) .

This was a high quality RCT with a very low risk of bias.

The second study (Kerry, S., Hilton, S., Patel, S. et al , 2000) recruited patients to either an RCT or observational study. Patients recruited to the RCT were aged between 16 and 64 who had consulted with low back pain at first presentation. Duration of low back pain was as follows: < 1 week (30% not referred for X-ray vs. 22% referred for X-ray), 1-8 weeks (49% vs. 42%), 8 weeks – 6 months (5% for both groups) and > 6 months (16% vs. 31%). A total of 153 patients were randomised to either be referred for X-ray (n=73) or to not be referred for X-ray (n=80) and were followed up at 6 weeks and one year. No differences were found between the two groups at either follow-up point for the following outcomes: RMDQ score, satisfaction, depression or anxiety (measured using the Hospital Anxiety and

Depression Scale -HADS). No differences were found for any of the components of the SF-36 scale (physical functioning, physical role, bodily pain, general health, vitality, social functioning or emotional role) except for the mental health subscale where patients referred for X-ray had improved scores at both 6 weeks and 1 year compared with those not referred for X-ray (adjusted mean difference at 6 weeks = -8 (95% CI -14 to -1), adjusted mean difference at 1 year = -8 (95% CI -15 to -2)) (Kerry, S., Hilton, S., Patel, S. et al , 2000) .

This was a well conducted RCT with a low risk of bias.

4.3.1.2 MRI vs. no MRI

No trials were found that compared MRI with no MRI, however, one randomised controlled trial was included that compared 'early' imaging with 'delayed selective' imaging (Gilbert, F. J., Grant, A. M., Gillan, M.-G. C. et al , 2004). This trial recruited patients with low back pain and/or sciatica for whom there was clinical uncertainty about the need for imaging. Duration of low back pain was as follows: < 3 months, (21% early vs. 14% delayed) 3-12 months (40% early vs. 43% delayed) and >12 months (38% early vs. 42% delayed). A total of 782 patients were randomised to either 'early' imaging (n=393) whereby MRI or CT scan was given as soon as practicable (82.4% received MRI), or to the 'delayed selective' imaging group (n=389) whereby patients were not imaged unless there was a change in their condition or a decision to perform surgery (24% had MRI). Patients were followed up at eight and 24 months. 'Early' imaging was found to be associated with a significant improvement in pain (measured using Aberdeen Low Back Pain (ALBP) score) and the bodily pain subscale of the SF-36 score compared with 'delayed selective' imaging at both the eight and 24 month follow up points: At 24 months, the adjusted difference in means for the outcome of pain (ALBP score) was -3.62 (95% CI -5.92 to -1.32) and for the outcome of bodily pain (SF-36) was 5.14 (95% CI 1.61 to 8.67). 'Early' imaging was also associated with a significant improvement in the EQ-5D score at 8 months but not at 24 months (adjusted difference in means = 0.057 (95% CI 0.013 to 0.101)) and a significant improvement in the vitality subscale

of the SF-36 at eight months but not 24 months (adjusted difference in means = 4.28 (95% CI 1.52 to 7.05)) (Gilbert, F. J., Grant, A. M., Gillan, M.-G. C. et al , 2004).

This was a high quality RCT with a very low risk of bias.

4.3.1.3 X-ray Vs MRI

Literature searching retrieved a total of 873 papers for this question of which 15 were ordered. Fourteen were excluded and one was included (Jarvik, Jeffrey G., Hollingworth, William, Martin, Brook et al , 2003) that compared the effectiveness of lumbar spine radiographs with lumbar spine rapid MRI.

This North American trial recruited patients aged 18 years or more with low back pain with or without leg pain whose primary care physicians had ordered that their low back be evaluated by radiograph. A total of 380 patients were randomised to receive either lumbar spine radiograph (n=190) or lumbar spine rapid MRI (n=190) and were followed up at three and 12 months after randomisation. After 12 months, those randomised to the MRI group were significantly more reassured (on a five point scale) than those randomised to receive X-ray (difference = -0.68, 95% CI -1.00 to -0.35). No differences were found between the two groups for the following outcomes: pain, SF-36 score and patient satisfaction. Patients randomised to receive MRI had better modified RMDQ scores at the three-month follow-up point than those who received X-ray (difference = -1.8, 95% CI -3.47 to -0.19) however, there was no significant difference between the two groups at the 12 month follow-up point (Jarvik, Jeffrey G., Hollingworth, William, Martin, Brook et al , 2003) .

This was a high quality RCT with a very low risk of bias.

4.3.2 Health economics

The search retrieved 393 papers of which 11 papers were ordered. Of these, six papers were subsequently excluded and five included and formally reviewed. One study compared x-ray with no x-ray (Kendrick, D., Fielding, K., Bentley, E. et al ,

2001). Two studies investigated the cost effectiveness of rapid MRI testing compared to x-ray (Hollingworth, William, Gray, Darryl T., Martin, Brook, I et al , 2003; Jarvik, Jeffrey G., Hollingworth, William, Martin, Brook et al , 2003). A further two studies were found: one comparing immediate referral for x-ray versus no referral for x-ray (Kerry, S., Hilton, S., Patel, S. et al , 2000), the other early versus delayed imaging, with the choice between CT and MRI(Gilbert, F. J., Grant, A. M., Gillan, M.-G. C. et al , 2004).

4.3.2.1 X-ray vs no x-ray

One study report was included (Kendrick, D., Fielding, K., Bentley, E. et al , 2001) that was based on a randomised unblinded controlled trial in a primary care setting of 421 subjects and an preference arm of 55 participants with low back pain of a median duration of ten and eleven weeks respectively. In the randomised arm, 210 patients were offered radiography of the lumbar spine whilst the control group received usual care without radiography.

A good quality cost effectiveness analysis (CEA) was undertaken from a societal perspective comprising costs to the NHS, patient and society; however, direct costs were reported separately and serve as an indication for a service perspective. A time horizon of nine months was used. Probabilistic sensitivity analysis (PSA) was carried out in order to quantify the uncertainty around the cost effectiveness estimate.

The trial found that the intervention was not associated with an improvement in health outcomes, including pain, disability, and health status or sickness absence. Health status scores were lower in the x-ray group at three months, but showed no difference at nine months. Participants in the preference group did not have better outcomes than those randomised to a group. However, patient satisfaction was measured and shown to be higher at nine months in the intervention group, with a mean difference of 2.1 units on the satisfaction score.

The intervention was associated with higher direct costs at 3 and 9 months and higher total resource use at 9 months. Between the groups, the mean direct cost difference was £41.04. This alone led to an ICER of £19.54 per one additional unit satisfaction.

The authors also performed a simple cost benefit analysis where patients' willingness to pay was elicited. They found that patients valued the reassurance gained from a radiograph at £30 and the perceived risk of radiation at £43.

The authors report that at willingness to pay (WTP) threshold of £30 per additional unit satisfaction there was a 90% chance that radiography will be cost effective.

The authors conclude that, from the cost effectiveness analysis, this intervention is not cost effective. With regard to the satisfaction, it is argued that at zero prices at the point of consumption demand is likely to be high for commodities, and therefore the increase in satisfaction was unsurprising. The cost benefit analysis indicated that lumbar spine radiography is associated with a net economic loss at nine months follow up.

4.3.2.2 Rapid MRI Versus X-RAY

Two papers from the US investigated the cost effectiveness of rapid MRI testing compared to x-ray(Hollingworth, William, Gray, Darryl T., Martin, Brook, I et al , 2003; Jarvik, Jeffrey G., Hollingworth, William, Martin, Brook et al , 2003).

Jarvik et al. performed a CEA alongside a randomised controlled trial in 380 participants. Patients with low back pain for whom the primary physician had ordered a radiographic evaluation were randomised to either receive lumbar spine evaluation by rapid MRI or radiograph. They took a societal perspective and used a time horizon of three and 12 months. Probabilistic Sensitivity Analysis (PSA) was performed to estimate the magnitude of uncertainty.

For rapid MRI, there was a statistically insignificant difference of an additional $470 from a health service perspective and of $321 from a societal perspective. There were no significant differences in clinical outcomes (RMDQ, pain score and SF-36), however, patients and physicians alike preferred MRI scanning to X-ray. The ICER was not reported since the ratio statistic was undefined as the denominator was zero.

One US study (Hollingworth, William, Gray, Darryl T., Martin, Brook, I et al , 2003) conducted a cost utility analysis (CUA) that compared x-ray versus rapid MRI

imaging in low back pain patients. Their decision analytic model took a third party payer perspective, using a time horizon of 20 years and a discount rate of 3% (0-7%). Quality adjusted life years (QALYs) and cost per case detected were used as outcome measures. They performed univariate sensitivity analysis.

The model calculated that there was an incremental cost difference of $135 in the cost per case detected model, and of $128 in the cost per QALY model. This small difference was due to palliative treatment alterations in detected cases as following diagnosis. Thus, MRI was more expensive, which was thought to be largely due to the low prevalence of cancer related disease and comparatively poor specificity. MRI detects <1 extra case of cancer per 1,000 patients screened and generates 0.00043 QALYs. Only 10% of this incremental effectiveness was due to reduced morbidity from cancer related back pain. The remaining 90% arose from the avoidance of the radiation induced tumours inherent in the x-ray strategy. Overall, the estimated incremental cost per QALY was $296,176.

In Jarvik's (Jarvik, Jeffrey G., Hollingworth, William, Martin, Brook et al , 2003) study, uncertainty was high, and as a result the non parametric bootstrap replications of the ICER were highly dispersed on the cost effectiveness plane (CE plane). The Hollingworth model seemed very robust in univariate sensitivity analysis. The ICER was most sensitive to probability of x-ray induced cancers (no risk $2.8m/QALY; high risk=19 in 100 000 $153,421/Qaly). Discount rate was also influential as these induced cancers only manifest after about 20 years. Baseline prevalence and specificity and sensitivity changes in MRI scanning were also important: with higher specificity (0.97), ICER falls to $98,681/QALY. Survival, QoL or treatment costs did not greatly influence the result.

Jarvik et al. conclude that, while the intervention resulted in nearly identical health outcomes for LBP patients, costs for MRI are likely to be significantly higher than x-ray. There is also a larger number of spine operations associated with MRI scanning. The authors concluded that early MRI scanning should not be recommended. As for the diagnostic benefits, disk and facet joint degenerations were very common in both groups; there was no evidence of infection, tumour, inflammatory spondylitis in any one patient.

Hollingworth et al. conclude that routine use of (rapid) MRI is not to be recommended for cancer detection in LBP patients. Only in a population where the prevalence is raised to 5%, rapid MRI scanning becomes cost effective ($8,816/QALY).

4.3.2.3 Immediate referral versus no referral for X-Ray

One HTA was included (Kerry, S., Hilton, S., Patel, S. et al , 2000) that was based on an RCT of 153 subjects and an observational study arm of 506 patients. In the RCT they allocated patients who consulted their general practitioner with low back pain and who had not consulted in the previous four weeks randomly to immediate referral for x-ray or not. Alongside the trial they carried out a cost minimisation analysis (CMA). A cost effectiveness analysis (CEA) was also done using the EuroQol (EQ-5D) as basis for the effectiveness measure. Time horizon was six weeks interim and one year. The perspective taken was societal, but costs to service provision were reported separately. For the CMA univariate sensitivity analysis was undertaken, whilst the uncertainty of the results of the CEA was shown in a cost effectiveness acceptability curve (CEAC).

Patients referred for X-ray had higher costs in the short term than patients who are not. A difference that was interpreted to be almost entirely due to the cost of the X-ray itself. Using the RCT data, the CMA resulted in a significant difference in NHS costs at three months (£41.90) but not at 12 months. This may be due to higher consultation rates in the control group that offset initial x-ray costs in the intervention group. However, in the observational arm of the trial (n=506) there were significantly higher costs in intervention group both at 3 and 12 months. The CEA found a mean difference of £42 in direct NHS costs at six weeks.

There are no effectiveness results to report for the CMA as this is not applicable for this design. The RCT did not show a statistically significant difference on the physical subscales of the SF-36, EuroQol, HADS[6] or RMDQ both after six weeks and one year). There was some effectiveness improvement of 8 percentage points in the mean SF-36 Mental Health scores for patients who where referred for x-ray

[6] Hospital Anxiety and Depression Scale

compared to those who were not, after adjustment for age, sex and length of episode at six weeks which was used for the cost effectiveness analysis. The cost effectiveness of early GP referral of LBP patients for x-ray was £5.25 per percentage point gain in SF-36 mental health dimension.

For the CMA, a univariate sensitivity analysis was undertaken and unit costs varied -50%, +100% and revealed highest sensitivity to changes in costs for radiography. For the CEA the bootstrapped replicates were plotted on the CE plane. The six week points lie mainly within the north east (NE) quadrant, where the early referral for x-ray is both more costly and more effective than delayed referral or no referral. However, many points lie in the north west (NW) quadrant, where the intervention is more costly and less effective (dominated). At 12 months the points are spread across all four quadrants. At the traditional 95% confidence level, immediate referral for x-ray is cost effective given a WTP of £93 or more per percentage point improvement in SF-36 mental health scale at six weeks or to pay £10 or more at 12 months.

The one percentage point improvement in mental health scores at six weeks at a cost of £93 must still be offset by the potential cost of radiation and the potential benefit of a reduction in the probability of failing to detect serious disease as neither were included formally in the evaluation. It cannot be concluded that this intervention is a worthwhile use of NHS resources.

4.3.2.4 Early versus delayed imaging (CT or MRI)

The last HTA included for this question was by Gilbert et al. (Gilbert, F. J., Grant, A. M., Gillan, M.-G. C. et al , 2004). A cost utility analysis (CUA) was conducted alongside an RCT of 782 participants with acute, sub acute and chronic LBP who were referred by their GP to an orthopaedic specialist or neurosurgeon because of symptomatic lumbar spine disorders. Patients were randomised to either receive an imaging test early (as soon as practical) or delayed and only if clear indication develops. The imaging test used (CT or MRI) was at the discretion of the specialist.

The CUA used a societal perspective and had a time horizon of 24 months and comprised patient management costs and costs incurred by patients. They used a

discount rate of 6% and discounted costs only. Probabilistic sensitivity analysis (PSA) was carried out.

Early imaging was found more costly and slightly more effective. The incremental cost difference between early imaging and delayed was £61. The intervention further generated a difference of 0.07 QALYs. This results in an ICER of £870 per QALY.

PSA resulted in a CEAC showing that there is 90% chance that the intervention is cost effective at base case when the WTP equals £30,000.

The authors conclude that early imaging may be cost effective given similar WTP thresholds prevailing in NHS framework when compared with delayed imaging. They state that there is some uncertainty surrounding the underlying assumptions. The authors highlighted that the small increment in quality of life in this population would need to be weighed against competing indications for the sparsely available imaging resource.

4.3.3 Evidence statements for Xray and MRI

Evidence statements	Evidence into recommendations
4.3.3.1 *One RCT showed that X-ray was associated with more pain, higher disability scores and lower health status scores compared with no treatment after 3 months. There were no differences in work absenteeism, pain, EuroQol score or satisfaction with care. At 9 month follow up, the only difference between the two outcomes was higher satisfaction of care for the X-ray treatment group.(1++) (Kendrick, D., Fielding, K., Bentley, E. et al , 2001)* *4.3.3.2* *One RCT found that X-ray improved SF-36 mental health subscale scores at 6 weeks and 1 year compared with no treatment. There were no differences between the groups for the outcomes of disability, depression, anxiety, satisfaction or any other SF-36 subscale at 6 weeks or 1 year (1+).(Kerry, S., Hilton, S., Patel, S. et al , 2000))* *4.3.3.3* *No randomised controlled trials were identified that compared MRI with no MRI.* *4.3.3.4* *One RCT compared 'early' imaging with 'delayed selective' imaging. At 8 months ,*	No evidence of a clinical or cost benefit was found but there is some evidence that patients gain some satisfaction from having an MRI. There is evidence of harm with use of x-ray. The only applicable benefit of MRI for non-specific low back pain is in identifying those patients who may benefit from surgery. Greater satisfaction with MRI was shown but the GDG felt that clinical examination and assessment was of similar benefit in terms of satisfaction.

	'early imaging' was associated with improvement in pain and the social functioning, vitality and bodily pain subscales of the SF-36. Early imaging showed no benefit for the following outcomes; EQ-5D score physical functioning, mental health or general health perception subscales of the SF-36. At 24 months, 'early imaging' was associated with improvement in the EQ-5D score and the bodily pain subscale of the SF-36. No differences were found between groups for the other SF-36 subscales.(1++)(Gilbert, F. J., Grant, A. M., Gillan, M.-G. C. et al , 2004))	
4.3.3.5	*One RCT comparing X-ray with MRI found that MRI was associated with an improvement in disability compared with X-ray at 3 month follow-up. At 12 months follow-up, MRI was associated with an improvement in patient reassurance. There was no difference between groups for the outcomes of disability, SF-36 score, satisfaction or time off work.(1++)(Jarvik, Jeffrey G., Hollingworth, William, Martin, Brook et al , 2003)*	
Cost-effectiveness		
4.3.3.6	*One HTA was found that compared X-ray vs. no x-ray. There was no improvement in health outcomes, including pain, disability or*	

	health status. However, the intervention was associated with higher costs. Patient preference had a mean difference of 2.1 units on the satisfaction scale at nine months follow up. However, when patients' valuation of the benefit from reassurance and risk of radiation was weighed in a cost benefit analysis, it was concluded that the intervention was associated with a net economic loss. (Kendrick, D., Fielding, K., Bentley, E. et al , 2001)	
4.3.3.7	*Two US studies were found that compared rapid MRI with x-ray, one was carried out alongside an RCT and the other used a decision analytic approach. The latter took into account the long term risks and benefits from detecting causal malignancies and radiation induced cancer. The analyses concluded that early use of rapid MRI scanning and routine use of rapid MRI scanning for cancer detection in a general low back pain population was not cost effective(Hollingworth, William, Gray, Darryl T., Martin, Brook, I et al , 2003; Jarvik, Jeffrey G., Hollingworth, William, Martin, Brook et al , 2003)*	

1

5 Information, education and patient treatment preferences

5.1 Recommendations for information, education and patient treatment preferences

5.1.1 Use educational materials consistent with this guideline to support other treatments.

5.1.2 Include an educational component consistent with this guideline as part of other interventions.

5.1.3 Do not offer stand-alone formal education programmes.

5.1.4 Take into account the patient's expectations and preferences when considering recommended treatments.

5.1.5 The patient's expectations and preferences should not be used to predict the response to treatments.

5.2 Information

Clinical question: what is the effectiveness of prepared patient information material compared to no information or alternative information on pain, functional disability or psychological distress?

5.2.1 Clinical evidence

Literature searching retrieved 256 papers, of which 6 were ordered. For the purpose of this question, prepared patient information was defined as prepared patient

information booklets as opposed to written report of verbal information given during the consultation. Three RCTs were ultimately included, all comparing prepared written information. Two compared a booklet/leaflet to usual care, and one compared a novel booklet to a traditional booklet. Outcomes of interest were pain, disability and psychological distress.

One randomised controlled trial compared a novel educational booklet with a traditional booklet for patients seeking treatment in primary care for low back pain (Burton, A. K., Waddell, G., Tillotson, K. M. et al , 1999) . Patients visiting one of five participating GP practices or one participating osteopathic centre were recruited. They had to be aged between 17 and 70, be originally seeking treatment for a new episode of acute or recurrent nonspecific low back pain, with a present duration of pain less than three months. They should not have sought healthcare or lost any time from work as a result of back pain during the three months preceding the episode. Patients with possible serious spinal disease or nerve root pain were excluded alongside patients with primary psychiatric illness or a history of alcohol or drug abuse.

A total of 83 patients were randomised into the experimental group and 79 were randomised into the control group. The intervention and control consisted of booklets, both professionally produced and commercially available in the UK, and of similar size and presentation. Patients in the experimental group received ‘The Back Book‘, where the main aim is to change beliefs and behaviour. The main messages included in it are that the spine is strong, that there are a number of treatments that can help to control the pain but that lasting relief depends on the patients’ own effort, that recovering depends on getting the back moving and working again and restoring normal function and fitness. The booklet also emphasises positive attitudes towards back pain. Patients in the control group were given the Handy Hints booklet, produced by a patient-support group. The booklet included traditional biomedical concepts of spinal anatomy, injury and damage. Messages included in the booklet were that activity should be avoided when in pain and that GPs may advise bedrest. The booklet describes possible further investigations and surgery, thereby reinforcing the message that back pain is a medical problem and that there is little that the patient can do. Pain is emphasised rather than activity, thereby giving the

implicit message that restoring activity and function must await relief of pain. The booklet encourages patients to be passive. The physicians caring for both groups were instructed to provide usual information and advice in addition to handing out the booklets.

Results showed the Back Book had no effect on pain, and disability improved more in the experimental group than in the control group at 2 weeks, 3 months and 1 year follow-up, but the differences in the means were not statistically significant. Overall, results suggested that The Back Book may be a useful adjunct to the management of low back pain in primary care.

This was a RCT with a high risk of bias

A randomised controlled factorial trial (Little, P., Roberts, L., Blowers, H. et al , 2001) assessed the effectiveness of a booklet compared to the usual care advice to mobilise and use simple analgesia.

Consecutive patients seeking treatment from six practices in southern England were randomised to receive either a booklet, advice to exercise, both or neither. Patients had to be seeking treatment for a new episode of back pain (ie pain for < 3months or an exacerbation of chronic low back pain) and had to be aged between 16 and 80. Stable chronic back pain requiring repeat prescriptions, major psychiatric illness, dementia, progressive or multilevel neurologic deficit, cauda equina syndrome, previous history of cancer or prolonged use of oral steroid, pregnancy or inability to walk 50 yards were all exclusion criteria.

A total of 311 patients were randomised into the control group (n=78), the booklet group (n=81), the advice to exercise group (n=75) and the booklet and advice to exercise group (n=77). All groups received advice to keep mobile, to minimise bedrest and to take simple analgesia. Patients in the booklet group additionally received the Back Home booklet and the physician endorsed the booklet by supporting the information enclosed and asked the patient to read the booklet carefully. Patients in the exercise group were given advice to exercise as soon as back pain allowed and to aim for regular exercise 3 times a week.

Results showed that compared to usual care, a booklet was associated with reductions in a combined pain/function score at 1 week follow-up. Similarly the Aberdeen pain and function scale was lower in the booklet group. No significant difference between groups in pain/function score was found at 3 weeks follow-up.

This was a RCT with a high risk of bias

A single-blind randomized controlled trial (Roberts, Lisa, Little, Paul, Chapman, Judith et al , 2002) tested the effectiveness of a patient information leaflet on knowledge, attitude, behaviour and function compared with the usual GP management of back pain. Patients visiting 51 participating GPs from 26 practices in southern England were invited to enter the trial. They had to be aged between 16 and 60 years, not have had low back pain in the previous six months, have back pain severe enough to warrant at least three days off work or an equivalent, and be able to read and understand English. Exclusion criteria included the presence of “red flag” signs or symptoms, previous formal instructions in back pain management, past treatment from private practitioners such as physiotherapist, osteopaths or chiropractors before the 2nd assessment, pregnancy, or ongoing litigation.

Participating practices were randomly allocated to either the control or experimental group within pairs of practices matched for location and number of participating GPs in the practice. A total of 35 patients were entered into the experimental group, and 28 patients were recruited into the control group. GPs in the control group continued providing their usual management and advice for patients. The GPs in the experimental group also gave the patient a copy of the Back Home leaflet, verbally reinforcing the content. Participants were followed up at home within two working days, two weeks, and then three months, six months and one year. Outcomes of interest were knowledge, attitude, observable behaviour and function. Results suggest that written advice for patient may change aspects of knowledge and behaviour (at three months), however no effect on function was observed.

This was a RCT with a high risk of bias

5.2.2 Health economics

No economic evaluations were identified for prepared patient information.

5.2.3 Evidence statements for prepared patient information

Hyperlink to related recommendations

Evidence statements		Evidence to recommendations
5.2.3.1	*One RCT compared a novel educational booklet (Back Book) with a traditional booklet and found the Back Book to have no effect on pain, and a non significant effect on disability at 1 year follow-up(1-) (Burton, A. K., Waddell, G., Tillotson, K. M. et al , 1999)*	Two small and one reasonable sized study, using two different booklets, did not show an effect on pain, disability or psychological distress. No cost effectiveness studies were found. No evidence of statistically significant benefit was found. However the GDG agreed that educational materials may have a role. Any education materials used should be based on, and consistent with, the recommendations made within this guideline.
5.2.3.2	*One RCT compared a booklet with usual care and found a significant reduction in pain and function at 1 week in the booklet group, but no significant difference in pain or function between groups after 3 weeks (1-)(Little, P., Roberts, L., Blowers, H. et al , 2001)*	
5.2.3.3	*One RCT compared a leaflet to usual care and found no effect on function up to 1 year after intervention (1-) (Roberts, Lisa, Little, Paul, Chapman, Judith et al , 2002)*	

5.2.3.4 No cost effectiveness studies were found.	

5.3 Education

Clinical question: what is the effectiveness of group structured education programmes compared to usual care/other interventions on pain, functional disability or psychological distress?

5.3.1 Clinical evidence

Literature searching retrieved 1805 papers. 43 papers were ordered and seven ultimately included; one consisted of mainly educational programmes and six were education and exercise programmes (including one systematic review).

Few, if any, of the RCTs identified tested interventions that were purely educational. The interventions typically had some other elements, such as exercise or elements of a cognitive behavioural approach, as part of the intervention. For this question GDG agreed to consider those interventions where the predominant component was educational as the best evidence. Since running the searches an additional randomised controlled trial was published (Little, P., Lewith, G., Webley, F. et al , 2008), and the GDG thought it ought to be included in the evidence review.

5.3.1.1 Mainly educational programmes

One randomised controlled trial (Storheim, Kjersti, Brox, Jens, I, Holm, Inger et al , 2003) compared intensive group training to cognitive intervention, and to usual care control group. Participants had to be sick listed from a permanent job for eitght to12 weeks due to non specific LBP with no sick leave due to LBP during a period of 12 weeks before the current sick listing period.

A total of 93 patients were randomised in the intensive group training (n=30), a cognitive intervention group (n=34) or a control group (n=29). Patients in the

cognitive intervention received a consultation between a specialist in physical medicine and a physical therapist. The consultations included explanation of pain mechanisms; discussion of original questionnaire; functional examination; instruction in activation of deep stabilising muscles and advice on how to use it functionally; instruction in the squat technique when lifting is required; how to cope with new attacks and reassure and emphasise that it is safe to move and to use the back without restriction. The GDG therefore considered the intervention to be mainly educational (and thus relevant for this question) despite its psychological title. Patients in the intensive group training arm received biweekly sessions for 15 weeks, with the exercise being a modified Norwegian Aerobic Fitness Model focusing on ergonomic principles and functional tasks and movement. Patients in the control group received usual care, consisting of treatment by their GP with no restrictions of treatment or referrals. Outcomes of interest were pain, disability and sick listing. At 18 weeks follow-up the cognitive group showed significant reduction in disability, emotional distress, general health and life satisfaction.

This was a well conducted RCT with a low risk of bias

5.3.1.2 Educational-Exercise programmes

A systematic review aimed to determine if back schools were more effective than other treatment or no treatment for patients with non-specific LBP (Heymans, M. W., Van-Tulder, M. W., Esmail, R. et al , 2004). A back school was defined as an educational and skills acquisition programme, including exercises, in which all lessons were given to groups of patients and supervised by a paramedical therapist or medical specialist. Nineteen studies were included. Overall the methodological quality was low with only 6 high quality trials.

The results indicate that there is moderate evidence suggesting that back schools have better short and intermediate term effects on pain and functional status than other treatments for patients with recurrent and chronic LBP (five trials; 1095 patients). There is also moderate evidence suggesting that back schools for chronic LBP in an occupational setting are more effective than other treatments (exercises, manipulation, myofascial therapy, advice; three trials. 764 patients) and placebo or

waiting list controls (two trials; 186 patients) on pain, functional status and return to work during short and intermediate term follow-up.

This was a high quality systematic review with a very low risk of bias.

One RCT assessed back rehabilitation groups (BRG) in a UK outpatient setting (Callaghan, M. J., 1994).The author compared patients in an 8-session BRG (n=30) to a control group (n=20), and compared the 8-session BRG with a 4-session BRG (n=30). The 8-session group had twice weekly 45 minute sessions consisting of an educational element and an exercise element. Education was given via lectures and patients received a written home exercise programme. Examples of exercises included sit-ups, extension in lying, exercise bike, hip/knee rolling and jogging. The 4-session group had 4 twice weekly 45 minute sessions and it consisted of a shorter version of the 8-session programme. The controls were seen twice weekly for 45 minutes for 4 weeks (same as 8-session group) and were given abdominal exercises because this is a frequently prescribed exercise for back pain but would not affect lumbar ranges of movement. Results showed that both 8-session and 4-session improved pain outcomes at end of treatment more than controls (limited exercises only and discussion of pain with physiotherapist), but that there is no statistical difference in outcome between a BRG of 4 sessions and one of 8 sessions at end of treatment. Randomisation was not described, no statistical power was reported, no primary outcome was specified and no comparative follow-up data were available.

This was a RCT with a high risk of bias

Three-year follow-up results from an original study (Lønn, J. H., Glomsrød, B., Soukup, M. G. et al , 1999) were presented (Glomsrod, B., Lonn, J. H., Soukup, M. G. et al , 2001). The original study was an RCT for an active back school (ABS) (n=43) versus controls (n=38) who received “no treatment”, and was included in the Cochrane systematic review of back schools by Heymans et al (2004). At 3 years the number followed up in the intervention group was n=37 and in the controls n=35. ABS included 20 sessions of 1 hour each in 13 weeks, consisting of education (anatomy, biomechanics, pathology, ergonomic principles) and exercise (ergonomic, functional, strength and stretching exercises of upper body, pelvis and leg muscles

and joints, simulation of home and work activities). Controls were allowed to choose any treatment (or no treatment) for LBP in the follow-up period. Results show that both the active back school participants and controls improved over 3 years, the differences between the groups with regard to pain and low back function were significantly in favour of the active back school group. The study did not calculate a statistical power for the primary outcome. Randomisation was poorly addressed but dropouts were relatively low at 3 years.

This was a well conducted RCT with a low risk of bias.

One randomised controlled trial (Heymans, Martijn W., de-Vet-Henrica, C. W., Bongers, Paulien M. et al , 2006) compared two types of back school, a high intensity (HI) and a low intensity (LI), with usual care (UC) in Dutch workers (n=299) who had been on sick leave for 3 weeks due to LBP. Usual care was provided by an occupational physician (OP). LI consisted of 4 physiotherapy-led group sessions once a week for 4 weeks. Each session had an educational part (30 mins) and a practical part (90 mins) guided by written information and a standardised exercise programme. Exercises consisted of strength training and home exercises. HI was conducted twice a week for 8 weeks. It consisted of 16 physiotherapy-led sessions each lasting 1 hour. As well as exercises and education as for low intensity, principles of CBT were applied and the physiotherapist promoted a time contingent increase in level of activity. The primary outcome of the study was sick-leave days. Secondary outcomes were pain and disability. At 6 months patients in all three groups had improved from baseline but there were no statistically significant differences between the back school groups and between back school groups and usual care group.

This was a well conducted RCT with a low risk of bias.

An exercise and education intervention, using a CBT approach was compared to usual care supplemented with education materials in a randomised controlled trial (Johnson, Ruth E., Jones, Gareth T., Wiles, Nicola J. et al , 2007). Patients (age 18 to 65) were recruited into the trial if, three months after visiting their GP they still reported persistent disabling LBP. They were excluded if: they had had a

consultation in the 6 months before visiting their GP for the current episode. The intervention group attended a community-based treatment program using a CBT approach, consisting of eight 2-hour group sessions over a 6-week period. Each group comprised between 4 and 10 participants and was led by 2 physiotherapists. Both the intervention and control groups were mailed an education pack consisting of leaflets and audio material. The primary outcome was disability as measured by the RMDQ and pain as measured on a VAS. At 12 months after recruitment both groups showed substantial improvement in disability and pain but there were no statistically significant differences between the groups. Follow up in this study was high (84% at 12 months post recruitment) while compliance with treatment was lower (63% of subjects allocated to the intervention attended at least half (4 of 8) of the sessions.

This was a well conducted RCT with a low risk of bias

One randomised controlled trial assessed the clinical effectiveness of Alexander technique lessons, exercise and massage for chronic and recurrent back pain (Little, P., Lewith, G., Webley, F. et al , 2008). Participants were recruited from 64 general practices in the UK. Participants (aged 18 to 65) had to have presented in primary care with low back pain more than 3 months previously, score 4 or more on the Roland Morris Disability Questionnaire, have current low back pain for more than 3 weeks. Exclusion criteria included previous experience of Alexander Technique, clinical indicators of serious spinal disease, current nerve root pain, previous spinal surgery, pending litigation, history of psychosis or major alcohol misuse, and perceived inability to walk 100m.

A total of 579 participants were included in the study: of these 72 received normal care; 73 received six lessons in Alexander Technique; 73 received 24 lessons in Alexander Technique; 72 received exercise; 72 received exercise and massage; 71 received exercise and 6 lessons of Alexander Technique; 71 received exercise and 24 lessons in Alexander Technique. The Alexander Technique and Exercise treatments were compared to each other and to normal care. Outcomes were the RMDW, number of days of pain in the past four weeks, quality of life, Von Korff scale and the Deyo ‘troublesomeness’ scale. These outcomes were measured at baseline, 3 months and 1 year.

Results showed significant changes in the RMDQ score and days in pain at three months for all groups compared to the control group. Exercise and lessons in the Alexander Technique were still effective at one year compared to the control group. The overall conclusion was that structured programmes of Alexander Technique and exercise compared to usual care were effective at reducing pain and functional disability.

This was a well conducted RCT with a low risk of bias

One randomised controlled trial was designed to evaluate the clinical effectiveness of spinal manipulative therapy (High velocity low amplitude (HVLA)) alone for chronic LBP when compared to two alternative treatment groups, manipulation mimic (High velocity low force(HVLF)) and a back education programme (BEP) (Triano, J. J., McGregor, M., Hondras, M. A. et al , 1995). A total of 209 participants were included. In the HVLA group therapy was applied to the lumbar and pelvic site or sites that defined the area of lesion. In the HVLF group the mimic therapy was also applied to the lumbar and pelvic site. The BEP was intended as a contrast for the physical contact between provider and patient that is offered by HVLA and HVLF. Elements of BEP included anatomic and biomechanical information of spinal function and hygiene and patients received written information to reinforce presentation information. Treatment sessions were carried out during a 2 week interval. Daily sessions were held, on the basis of a 6-day/week clinic schedule. Physician-patient time for each group was the same. All three groups improved with regard to pain, disability and depression after treatment. However, at 2 weeks there were no statistically significant differences in improvements between the three treatment groups in any of the primary outcomes. This study had low power to detect clinically significant differences and less than 70% of patient data were available for final analysis due to dropouts and eliminated data.

This was a RCT with a high risk of bias.

5.3.2 Health economics

No economic evaluations were identified for educational programmes

5.3.3 Evidence statements for education programmes

Hyperlink to related recommendations

Evidence statements		Evidence to recommendations
5.3.3.1	*1 RCT consisting of a mainly educational programme showed an association with decreased disability, sick leave and improved general health.(1+)(Storheim, Kjersti, Brox, Jens, I, Holm, Inger et al , 2003)*	One small study was found that suggests that standalone educational programmes may be helpful. The GDG agreed this provided insufficient evidence to recommend educational programmes as a standalone intervention.
5.3.3.2	*A systematic review on Back Schools reported moderate evidence of better short and intermediate term effects on pain and functional status than other treatment. In an occupational setting, there was moderate evidence that Back Schools were more effective than other treatment, placebo and waiting list control on pain, functional status and return to work in short and intermediate term effects.(1++)(Heymans, M. W.,*	One positive study for educational/exercise programme was found. The GDG agreed that education should be included as a part of other interventions being offered. The content and delivery of education varied greatly between the studies so that it was not possible to make a recommendation regarding the content of the educational component. The GDG considered that this be considered for a research recommendation.

	Van-Tulder, M. W., Esmail, R. et al , 2004)	
5.3.3.3	*One RCT on Back Schools found pain and disability to be significantly improved in the intervention group after 3 years (1+)(Glomsrod, B., Lonn, J. H., Soukup, M. G. et al , 2001), Another RCT on Back Schools found no significant differences in pain and disability between 2 back school groups of different intensity and between back school groups and usual care.(1+)(Heymans, Martijn W., de-Vet-Henrica, C. W., Bongers, Paulien M. et al , 2006)*	
5.3.3.4	*One RCT compared Back Rehabilitation Groups (2 intensity levels) to controls. After treatment pain was significantly decreased in the BRG compared to controls, but there was no significant difference between the 2 intensity levels.(1-)(Callaghan,*	

	M. J., 1994)	
5.3.3.5	*One well-conducted RCT compared an education-exercise intervention to usual care with education. At 12 months follow-up no significant difference in pain and disability between intervention and controls observed.(1+)(Johnson, Ruth E., Jones, Gareth T., Wiles, Nicola J. et al , 2007)]*	
5.3.3.6	*One RCT compared Alexander Technique and exercise to usual care. At 3 months exercise and lessons in the Alexander Technique significantly reduced functional disability and days of pain compared to normal care. At 1 year follow-up Exercise and Alexander Technique lessons still reduced disability, but exercise did not significantly affect days in pain anymore. (1+) (Little, P., Lewith, G., Webley, F. et al , 2008)*	

5.3.3.7	*One RCT compared manual therapy to a back education programme and found no significant difference in pain disability or depression between groups after 2 weeks.91-)(Triano, J. J., McGregor, M., Hondras, M. A. et al , 1995)*	
5.3.3.8	*No economic evaluations were identified*	

5.4 Patient Preference

Clinical question: is patient preference or expectations of treatments effective at identifying which patients may gain the greatest benefit from either general or specific treatments?

5.4.1 Clinical evidence

Literature searching retrieved 423 papers of which 17 were ordered for this question. None of these were randomised controlled trials of the effect of patient preferences or expectations, therefore all the studies were excluded.

5.4.2 Health economics

No economic evaluations were identified for patient preference of treatments.

5.4.3 Evidence statements for patient preference and expectations of treatments

Hyperlink to related recommendations

Evidence statements	Evidence to recommendations
5.4.3.1 *No suitable RCTs were identifed* *5.4.3.2* *This question is unsuitable for health economic evaluation. A search alongside the clinical literature did not identify economic papers*	The evidence presented was based on observational arms within RCTs. The group considered these to be similar, in terms of quality, as cohort studies which had been excluded from the searches conducted. As not all the evidence of a similar quality was reviewed for this question the group decided the studies reviewed for this question should be excluded and that the NICE guidance on patient centred care be used. The final recommendation was based on group consensus and generic NICE guidance on patient centred care.

6 Exercise

6.1 Recommendations for exercise

6.1.1 Advise people with low back pain that maintaining a physically active lifestyle is likely to be beneficial.

6.1.2 Advise all people with low back pain to exercise.

6.1.3 Consider offering a structured exercise programme tailored to the individual[7].

6.1.4 Offer supervised group exercise programmes in preference to one-to-one supervised exercise programmes.

6.2 Exercise Advice

Clinical question: what is the effectiveness of advice to maintain normal physical activity/general exercise levels compared with no advice or advice to rest on pain, functional disability or psychological distress?

Clinical question: what is the effectiveness/cost effectiveness of advice to increase self directed physical activity/general exercise compared with no advice or advice to rest on pain, functional disability or psychological distress?

6.2.1 Clinical evidence

Literature searching did not identify any randomised controlled trials that compared advice to maintain normal physical activity/general exercise levels compared with no advice or advice to rest. Similarly literature searching did not identify any studies that examined the effectiveness of advice to increase self directed physical activity/general exercise compared with no advice or advice to rest.

[7] A choice of an exercise programme, a course of manual therapy (see section 1.4.1) and a course of acupuncture (see section 1.8.1) may be offered, taking into account patient preference.

For further guidance on exercise refer to:

Four commonly used methods to increase physical activity (NICE Public Health Intervention Guidance 2).(National Institute for Health and Clinical Excellence, 2006)

6.2.2 Health economics

No economic evaluations were identified for exercise advice.

6.2.3 Evidence statements for exercise advice

Hyperlink to related recommendations

Evidence statements	**Evidence to recommendations**
6.2.3.1 Literature searching did not identify any RCTs in adults with non-specific low back pain of greater than six weeks and less than 1 year that examined advice to increase self directed physical activity and / or general exercise as a single intervention compared with no advice or advice to rest.	No RCT data was found to tell whether advice to exercise or advice not to rest on its own is beneficial or not. It is usual practice to advise people to be as active as possible, or at least maintain normal activity and the consensus view was to stay active. The GDG agreed that advice to keep active should be made, however advice alone is not sufficient. It was agreed that this guidance should cross refer to NICE physical activity guidance

1

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6.3 Exercise Programmes

Clinical question: what is the effectiveness of general supervised exercise programmes or specific exercise training programmes (individual and group) compared with usual care on pain, functional disability or psychological distress?

6.3.1 Clinical evidence

Literature searching retrieved 1195 papers, of which 59 were ordered. Seven were ultimately included. 1 Cochrane review, 1 RCT on yoga, 1 on hydrotherapy/spa therapy and 4 on exercise programmes.

A systematic review (Hayden, J. A., van Tulder, M. W., Malmivaara, A. et al , 2005) evaluated the effectiveness of exercise therapy in adult nonspecific acute, subacute and chronic low back pain versus no treatment and other conservative treatments. The Cochrane Central Register of Controlled Trials, MEDLINE, EMBASE, PsychInfo, and CINAHL databases to October 2004 were searched, alongside citation searches and bibliographic reviews of previous systematic reviews. The aim was to identify randomised controlled trials involving participants with nonspecific low back pain comparing exercise therapy to no treatment/placebo/sham, another conservative therapy or another exercise group. Outcomes of interest were self-reported pain intensity, function, global improvement and return-to-work. Pooled analysis of 4 trials of subacute patient populations suggest that there is insufficient evidence to support or refute the effectiveness of exercise therapy for reducing pain intensity and improving function. Meta analysis of functional and pain outcomes from 20 and 23 studies respectively involving chronic low back pain patient populations suggests exercise therapy is slightly effective at decreasing pain and improving function relative to other comparisons (no-treatment, sham, placebo or other conservative treatment). People involved in the studies on chronic low back pain may have had co-interventions during the study period.

This was a high quality systematic review with a very low risk of bias.

The United Kingdom back pain exercise and manipulation (UK BEAM) trial (UK Back pain exercise and manipulation (UKBEAM) Trial Team., 2004) aimed to estimate the effectiveness of adding exercise, spinal manipulation or a combination of both to the standard care in general practice. Patients recruited from participating centres had to be aged 18-65 and have had pain everyday for the 28 days before randomisation (or 21 out of 28 days before randomisation and 21 out of 28 days before that). They also had to agree to avoid physical treatment other than trial treatments for 3 months. Exclusion criteria included cancer, osteoporosis, ankylosing spondylitis, cauda equina compression, previous spinal surgery, anticoagulant treatment and cardiovascular disease or hypertension.

A total of 1334 patients were included in the study, with 310 randomised to the exercise group and 338 were randomised to a ‘Best Usual Care’ control group. All patients received advice to continuing normal activities and avoiding rest, and were provided with copies of ‘The Back Book’ . Following an initial individual assessment participants randomised to the Exercise programme attended group classes incorporating cognitive behavioural principles after. The programme was delivered by trained physiotherapists, and the participants were invited to attend up to eight 60-minute sessions over four to eight weeks, and a “refresher” class at 12 weeks after randomisation.

Results showed that compared to Best Care, the exercise programme produced statistically significant improvements in mean Roland disability score at three months only, in mean Von Korff disability and pain scores and back beliefs score at both three and 12 months, and in mean SF-36 physical score and fear avoidance beliefs physical score at three months only. Mean SF-36 mental score did not differ.

This was a high quality RCT with a very low risk of bias

One randomised controlled trial (Kuukkanen, T. and Mälkiä, E., 2000; Kuukkanen, Tiina, Mälkiä, Esko, Kautiainen, Hannu et al , 2007) assessed the effectiveness of a home exercise programme on patients with nonspecific low back pain. Patients were

recruited from eight regional occupational healthcare centres in central Finland and referred to physicians in a hospital in central Finland. Inclusion criteria included a local place of residence, age between 20 and 55, employment and no sick leave exceeding a total of three months during the previous year, disabling LBP over three years, pain at rest or with stress and localisation to lumbar area or buttocks. Exclusions included need for surgery, pregnancy, history of back disease (cancer, fracture, spondylarthritis ancylopoetica or infection), substance abuse and somatic or psychiatric disorder preventing patients from exercising.

A total of 57 patients were randomly allocated to a home exercise programme group (n=29) or a control group (n=28). Patients in the home exercise programmed received a three month programme consisting of three progressive monthly programmes. The physiotherapist instructed the patients on the exercises, which aimed to improve the function of abdominals, back extensors, upper and lower limbs muscles, and established the optimal function of the spine. The progression of the programme was based on weekly tests, which the home exercise group performed independently. A physiotherapist supervised the exercise programmes once a month in an exercise room. The programmes were carried out at home, without extra equipment, with 10min warm-up and cool-down periods. The load of each exercise movement was individually adjusted according to the repetition maximum. The exercises were performed as three to four sets of 15-20 repetitions. The goal was for subjects to attempt exercises every day, and to record this in their diaries. Patients in the control group did not alter physical activity levels or participate in any exercise programme during the study.

Results showed that pain intensity and functioning decreased significantly in all subjects during the study period, and that for patients in the home exercise group those values remained below baseline values in the 12 months follow-up. After five years pain intensity was significantly lower ($p<0.01$) in the home exercise group. Functioning also decreased in that group over the five years period, but there were no statistical difference between the groups ($p<0.27$). The overall conclusion is that the study indicates that supervised controlled home exercises lead to reduced LBP and that positive effects were preserved over five years.

This was a RCT with a high risk of bias

One randomised controlled trial involved hospital employees with chronic low back pain (Maul, I., Läubli, T., Oliveri, M. et al , 2005). Potential candidates were recruited amongst employees of a large university hospital (Switzerland) who returned a modified version of the Nordic Questionnaire on LBP. Inclusion criteria included over 30 days of low back pain in the previous 12 months, an age between 20 and 55 and the ability to read and write German or Italian. Exclusions included cardiovascular or metabolic diseases, progressive radicular neurological defects, inflammatory disease of the spine, previous spinal surgery, pregnancy and regular strength training within the last six months.

A total of 97 patients were allocated to the Exercise group, and 86 were allocated to the comparison group. All patients attended a back school which consisted of three sessions, each lasting one hour and giving information about functional anatomy of the spine, correct lifting techniques, how to use mental stress coping strategies and giving advice on sports activities. Patients in the exercise programme groups received in addition exercises based on concepts of medical training therapy and sequence exercise training. The programme consisted of three phases of individual training, each lasting four weeks with sessions two or three times a week. Each training session was supervised by a physiotherapist.

Results showed that in addition to back school, supervised physical training effectively improved functional capacity in terms of muscular endurance and isokinetic strength during a six months follow-up. Furthermore, self-rated pain and disability significantly decreased during a one-year follow-up.

This was a RCT with a high risk of bias

One randomised controlled trial aimed to determine the effectiveness of graded activity as part of a multistage return-to-work programme (Steenstra, I. A., Anema, J. R., Bongers, P. M. et al , 2006). A total of 112 workers absent from work for >8weeks due to LBP were randomised to either graded activity (n=55) or usual (n=57). Inclusion criteria were sick leave for >8 weeks and no plans to return to work within a week, inclusion in the multistage RTW back pain management programme at two to six weeks of sick-leave, age between 18 and 65 and ability to read and write in Dutch. Exclusion criteria were specific cause to the LBP, coexisting cardiovascular,

psychiatric contraindications or juridical procedures pregnancy, sick leave due to LBP less than a month prior to current episode. Outcomes were return-to-work, pain intensity and functional status.

Workers in the graded activity group received an individual, submaximal, gradually increasing exercise programme, with an operant-conditioning behavioural approach. This was based on findings from patient history, physical examination, functional capacity evaluation, the demands from the patients' work and the patients' expectations on time to return to work. The entire programme consisted of 26 one-hour sessions maximum, with a frequency of 2 sessions a week. Workers in the usual care group received care following the Dutch occupational physician guidelines for low back pain. Patients were followed-up at 12 weeks and 26 weeks. Results showed that graded activity did not improve pain or functional status clinically significantly.

This was a RCT with a high risk of bias

Hydrotherapy/Spa therapy studies:

One randomised controlled trial investigated the claimed benefits of group hydrotherapy for subjects with chronic low back pain (McIlveen, B. and Robertson, V. J., 1998). Following publication of an article about the study in the local newspaper, subjects referred for hydrotherapy by their GP or physiotherapist contacted a large community care centre in Australia. Patients were then assessed for suitability and were excluded if they couldn't read or write in English, had spondylolisthesis, had had previous lower limb joint replacement surgery or were receiving work or traffic injury-related compensation insurance. Other exclusion criteria were uncontrolled hypertension, severe postural hypotension, left heart failure, exercise induced angina, lung vital capacity of less than 1.5 litres, faecal or urinary incontinence, an allergy to chlorine, severe limiting airways disease, early pregnancy (ie 1st trimester), and a tendency to antisocial behaviour such as can occur with a head injury,.

A total of 56 subjects were randomly assigned to the hydrotherapy group, and 53 were assigned to a control group (delayed hydrotherapy). Patients in the hydrotherapy group participated in 60-min group hydrotherapy sessions twice weekly for 4 weeks. Each session was led by experienced pool volunteers with additional

training in delivering the prescribed 20 spinal exercises. Ten repetitions of each prescribed exercise were included in each session. Prescribed exercises included walking in water, marching on the spot, swinging the legs backwards and forward in the water, bicycling the legs and pushing and pulling a kickboard with the hands. Patients in the control group were placed on the existing 4-week waiting list for hydrotherapy. Both groups were reminded not to start any other treatment, medication or exercise programmed for their low back pain during this period. Outcomes were range of flexion, extension, pain and function.

Results showed that patients in hydrotherapy group significantly improved in function (measured by the Oswestry Disability Index). However the differences between subjects in the experimental and control groups were not significant for the other measures of pain or the ranges of flexion and extension.

This was a RCT with a high risk of bias

Yoga therapies:

One randomised controlled trial aimed to determine whether yoga is more effective than conventional exercise or a self-care book for patients with chronic low back pain (Sherman, Karen J., Cherkin, Daniel C., Erro, Janet et al , 2005). Patients from a non-profit integrated healthcare system in the USA were recruited. Letters describing the study were mailed to patients matching the inclusion criteria (based on the available electronic records). The study was also advertised in the consumer magazine. Patients had to be aged between 20 and 64, have visited a primary care provider for treatment for back pain 3-15 months before the study (according to electronic records), and have the ability to read and understand English. Exclusion criteria were sciatica, previous back surgery, spinal stenosis, pregnancy, cancer, spondylolisthesis, fractured bones, dislocated joints, concurrent treatment for back pain, participation in yoga or exercise training for back pain in the previous year, current litigation, unstable medical or severe psychiatric conditions and contraindications or schedules that preclude class participation.

A total of 101 patients were randomly assigned to the yoga group (n=36), the exercise group (n=35) or a self-care booklet group (n=30). The yoga and exercise classes were developed specifically for the study and consisted of 12 weekly 75min

classes designed to benefit people with chronic low back pain. Participants were also asked to practice daily at home. Patients in the yoga group performed viniyoga, which emphasises safety and is relatively easy to learn. All sessions emphasised the use of postures and breathing, and each session had a specific focus: relaxation; strength-building, flexibility, and large-muscle movement; asymmetric poses; strengthening the hip muscles; lateral bending; integration; and customising personal practice. The postures selected from a core of 17 relatively simple postures. Each class included a question and answer period, an initial and final breathing exercise, five-12 postures, and a guided deep relaxation. Patients in the exercise group followed a specifically-designed 12-session class series. Each session consisted of an educational talk, a warm-up to increase the heart rate, repetitions of a series of seven aerobics exercises and 10 strengthening exercises that emphasised leg, hip, abdominal and back muscles. Over the course of the 12-weeks series, the number of reps of each aerobic and strength exercise increased from eight to 30 in increments of two. The strengthening exercises were followed by 12 stretches for the same muscle groups. Classes ended with a short, unguided period of deep slow breathing. Patients in the self-care book group were mailed a copy of the Back Pain Helpbook, an evidence-based book that emphasised such self-care strategies as adoption of comprehensive fitness and strength programme, appropriate lifestyle modification and guidelines for managing flare-ups.

Results showed that after adjustment for baseline values, back-related function in the yoga group was superior to the book and exercise groups at 12 weeks. No significant difference in “bothersomeness” of pain was found between any two groups at 12 weeks. At 26 weeks, back-related function in the yoga group was superior to the book group. At 26 weeks, pain bothersomeness was also better in the yoga group than in the book group. Overall, yoga was more effective than a self-care book for improving function and reducing chronic low back pain and the benefits persisted for at least several months.

This was a well conducted RCT with a low risk of bias

6.3.2 Health economics

Literature searching retrieved 208 papers of which two were ordered for this question. Only one was included: this was a UK-based cost-effectiveness study of four interventions for treatment of low back pain, two of which included exercise programmes.

An economic evaluation was conducted alongside the UK back pain exercise and manipulation randomised trial (UK Back pain exercise and manipulation (UKBEAM) Trial Team, 2004) to assess the cost effectiveness of adding spinal manipulation, exercise classes or manipulation followed by exercise ("combined treatment") to "best care" in general practice for patients consulting with low back pain. The study recruited 1334 patients aged between 18 and 65 years if they had experienced pain every day for the 28 days before randomisation or for 21 out of the 28 days before randomisation and 21 out of the 28 days before that. In addition, they had to have a score of four or more on the RMDQ at randomisation.

The four treatment groups were 1) best care, which included active management and providing The Back Book to patients, 2) best care + an exercise programme of up to nine classes over 12 weeks, 3) best care + spinal manipulation package of eight sessions over 12 weeks and 4) combined treatment, which included best care + six weeks of manipulation followed by six weeks of exercise. The main outcome measures were healthcare costs, quality adjusted life years (QALYs), and cost per QALY over 12 months. The number of QALYs gained over 12 months was estimated using EQ-5D questionnaire data which was collected as part of the trial. The costing perspective was that of the UK health service. Healthcare resources included those for: the spinal manipulation package, the exercise programme, hospital inpatient stays, outpatient attendances, and general practice consultations. These resources were costed using published national averages for England. Private care was costed using information from a major insurance provider. Costs were reported in pounds sterling at 2000/2001 prices. Costs were not discounted since the focus was on effects over only one year.

To cover scenarios in which either exercise or manipulation was not available ICERs were calculated to compare best care with manipulation alone or exercise alone.

Sensitivity analysis examined the impact on costs if the NHS purchased private care for some or all of the patients. The justification for this is that in the short term it might be difficult to make all manipulation or combined treatment available within the NHS: there are insufficient numbers of trained practitioners in the NHS to meet demand and it would take a few years to train people up within the NHS.

Results (base case)

The mean cost (Standard Deviation) of best care was £346 (£602). best care+exercise cost £140 more than best care Relative to best care, best care+exercise generated an additional 0.017 (-0.017 to 0.051).

At base case,best care + exercise was dominated by combined therapy: it cost more and generated fewer QALYs over the 12 month period. With all options available, the combination package was the most cost effective strategy. However, if manipulation is not available (n=668) exercise generates 0.017 more QALYs per patient than best care at an additional cost of £140 per patient yielding an ICER of £8,235 per QALY, which is an acceptable value for money under current guidelines. The GDG felt that from the evidence presented for some patients exercise alone would be an appropriate option . *Sensitivity analysis*

The study reported the results of three sensitivity analyses. First, statistical outliers were excluded (n=51). Second, the effects on unit costs of a scenario in which the NHS buys half of the manipulation sessions from the private sector, NHS costs were replaced with private costs for manipulation that took place in a private setting was examined.And in the third analysis the scenario was one where the NHS buys all manipulation from the private sector when private costs were used for all manipulation within the trial. The results did not change the finding of the base line analysis where manipulation was found to be most favourable.

6.3.3 Evidence statements for general or specific exercise programmes

Hyperlink to related recommendations

Evidence statements	Evidence to recommendations
6.3.3.1 *A systematic review evaluated the effectiveness of exercise therapy and found Insufficient evidence to support or refute the effectiveness of exercise in patients with subacute low back pain. In patients with chronic low back pain, exercise therapy was found to be slightly effective at decreasing pain and improving function relative to other comparisons (no treatment, sham, placebo, other conservative treatments) (1++) (Hayden, J. A., van Tulder, M. W., Malmivaara, A. et al , 2005)* 6.3.3.2 *One large well-conducted RCT evaluated the effectiveness of adding exercise, spinal manipulation package or a combination of both to Best Care in general practice. Relative to best care exercise significantly*	There is evidence for clinical effectiveness of structured exercise programmes. There is evidence of improved function and reduced disability and reduced pain. No evidence was found of an effect on psychological distress. The size of effect however, is generally small. Most of the recent studies have used advice to remain active as part of a controlled intervention. There is variance on intensity of exercise within the trials. There is evidence of cost effectiveness of exercise alone compared to best care in general practice. The GDG were also presented with the economics of the combined treatment option as once manipulation is included in the analysis, the exercise alone option is dominated by the manipulation (either alone or in combination with exercise) treatment options. In a probabilistic analysis, best care plus exercise alone had a less than 10% chance of being the most cost-

	improved disability and pain at 3 months but not at 12 months follow-up. No effect on mental health was observed(1++) (UK Back pain exercise and manipulation (UKBEAM) Trial Team., 2004)	effective treatment option at the £20,000 per QALY threshold. However, if manipulation is not available, providing exercise interventions in addition to usual care is likely to be a cost effective use of NHS resources. The GDG felt that this evidence was not sufficient to justify not making an exercise programme available for people for whom manipulation was not suitable or who preferred exercise. This meant that exercise alone would remain an option for this patient population.
6.3.3.3	*One RCT assessed the effectiveness of a home exercise programme and found that after 5 years, pain intensity was significantly lower in the exercise group. No significant difference in function was found after 5 years (1-) (Kuukkanen, T. and Mälkiä, E., 2000; Kuukkanen, Tiina, Mälkiä, Esko, Kautiainen, Hannu et al , 2007)*	
6.3.3.4	*One RCT compared the effectiveness of adding exercise to a back school and found that exercise was associated with significantly reduced pain and disability after 1 year*	

	follow-up (1-) (Maul, I., Läubli, T., Oliveri, M. et al , 2005)	
6.3.3.5	*One RCT evaluated the effectiveness of hydrotherapy and found it was associated with a significant difference in function at 4 weeks. No significant difference in pain was found (1-) (McIlveen, B. and Robertson, V. J., 1998)*	
6.3.3.6	*One RCT compared yoga, exercise and a self-care book. At 12 and 26 weeks, function was significantly better in the yoga group than in the booklet group (1+) (Sherman, Karen J., Cherkin, Daniel C., Erro, Janet et al , 2005)*	
6.3.3.7	*One RCT compared graded activity to usual care and showed that at 26 weeks graded activity did not improve pain or function significantly (1-) (Steenstra, I. A., Anema, J. R., Bongers, P. M. et al , 2006)*	

Cost-effectiveness *6.3.3.8* *One health economics analysis was found in the literature. This was a cost per QALY analysis based on the clinical and resource use outcomes from the UK BEAM clinical trial. It compared exercise and manipulation (alone or in combination) added to best care. The base case analysis took an UK NHS costing perspective. This analysis suggested that the cost-effectiveness of the included exercise programme when added to best care had an ICER of £8,300 compared to best care alone, and there was about a 60% chance that the estimated ICER was less than £20,000 per QALY (UK Back pain exercise and manipulation (UKBEAM) Trial Team, 2004).*	

6.4 Group vrs Specific Exercise

Clinical question: what is the effectiveness of general or specific group exercise programmes compared with general or specific individual exercise programmes on pain, functional disability or psychological distress?

6.4.1 Clinical evidence

Literature searching retrieved 1195 papers (same search as for section 6.3.1), and 2 studies were ultimately included.

A systematic review was undertaken aiming to identify particular exercise intervention characteristics that decrease pain and improve function in adults with non specific chronic low back pain (Hayden, J. A., van-Tulder, Maurits W., and Tomlinson, G., 2005). The MEDLINE, EMBASE, PsychInfo and CINAHL databases were searched (up to October 2004) as well as the Cochrane Central Register of Controlled Trials. Randomised controlled trials investigating exercise therapy as an intervention for non-specific low back pain were selected, regardless of the comparison group or groups. Outcomes of interest were pain, function, return to work or absenteeism, global improvement.

They characterised the exercise interventions by the exercise programme design, delivery type, dose or intensity, and then carried out a Bayesian multivariate random-effects meta-regression on 43 trials of 72 exercise treatment and 31 comparison groups. The dose of each exercise intervention was dichotomized to aid interpretation; high dose exercises were those with 20 or more hours of intervention time.

Results suggested that the most effective strategy seemed to be individually designed exercise programmes delivered in a supervised format (for example home exercises with regular therapist follow-up) and encouraging adherence to achieve high dosage.

This was a well conducted systematic review with a low risk of bias.

A randomised controlled trial (Mannion, A. F., Müntener, M., Taimela, S. et al , 2001) examined the efficacy of 3 active therapies for patients with chronic low back pain. Patients were recruited following advertisement in the local media. Inclusion criteria included an age of less than 65, low back pain for over three months with or without referred pain (non-radicular) serious enough to require attention or absences from work, willingness to comply with the randomly assigned treatment. Patients were excluded if they had constant or persistent severe pain, were pregnant, had previous spinal surgery, had current nerve root entrapment accompanied by neurological deficit or had spinal cord compression. Other exclusion criteria included tumours, severe structural deformity, severe instability; severe osteoporosis, inflammatory disease of the spine, spinal infection, severe cardiovascular or metabolic disease, and acute infection.

A total of 148 patients were randomised to receive active physiotherapy (n=49), group aerobics classes (n=50) or muscle reconditioning through devices (n=49). Patients in the active physiotherapy group had half-hour individual physiotherapy sessions focusing on improving functional capacity using strengthening, coordination and aerobics exercises, and with instructions on ergonomic principles and home exercises. Patients in the aerobics group took part in low impact aerobics classes lasting 1hr, comprising exercises to music, with a maximum of 12 patients per group. A warm-up of 10-20 min, involving whole-body stretching and low-impact aerobics exercises, was followed by 20-30min of specific trunk and leg muscle exercises. The last 15 min of the class comprised cool-down and stretching/relaxation exercises. Patients in the devices group had 1-hr sessions for muscle reconditioning using training machines/devices, in groups of two or three. Four exercises devices provided progressive, isoinertial loading to the trunk in the three cardinal planes. Each session was preceded by a 5-10min of aerobic warm-up and

relaxation/stretching exercises were carried out before and after the use of each device.

Results showed no difference between therapies in terms of efficiency at reducing pain intensity and frequency for up to 1 year after therapy. However there was a slight but significant difference between the pattern of change in disability for the individual physiotherapy group compared to the aerobics group: patients in the physiotherapy group had an increase in disability between the end of therapy and the 6 months follow-up, whereas during the same period the aerobics group showed a further reduction. There was also a slight but significant difference between the pattern of change in psychological disturbance for the physiotherapy group compared with that of the aerobics group; in the aerobics group the Modified Somatic Perceptions Questionnaire (MSPQ) and ZUNG scores declined after therapy, then increased towards pre-therapy values over the following 12 months, whilst the physiotherapy group showed no change after therapy, an increase at 6 months and then a reduction to pre-therapy values after 12 months.

This was a well conducted RCT with a low risk of bias

6.4.2 Health economics

No economic evaluations were identified for group or individual exercise programmes.

6.4.3 Evidence statements for group or individual exercise programmes.

Hyperlink to related recommendations

Evidence statements		Evidence to recommendations
6.4.3.1	*One systematic review carried out Bayesian multivariate analysis to identify specific exercise*	There no evidence that one to one based exercise is better than group exercise. The GDG considered that group

	characteristics to improve pain and function, and found that individually designed exercise programmes offered in a supervised setting appeared most effective (1+) (Hayden, J. A., van-Tulder, Maurits W., and Tomlinson, G., 2005)	treatment is also more likely to be cost effective than one to one treatment.
6.4.3.2	*One RCT examined the efficacy of active physiotherapy, group aerobic classes and muscle reconditioning through devices. Results showed no significant difference in pain intensity and frequency between groups at 1 year follow-up. Slight but significant differences in patterns of change between the active physiotherapy and aerobic groups were observed for disability and psychological disturbance (1+) (Mannion, A. F., Müntener, M., Taimela, S. et al , 2001)*	
6.4.3.3	*No cost effectiveness studies were found*	

7 Manual therapies

7.1 Introduction

The manual therapies reviewed were manipulation (a small amplitude high velocity movement at the limit of joint range taking the joint beyond the passive range of movement), mobilisation (joint movement within the available range of motion) and massage (manual manipulation of soft tissues). The manual therapies of mobilisation and massage are performed by a wide variety of practitioners. Manipulation **can be** performed by **chiropractors or o**steopaths**,** and by **doctors or** Physiotherapists who have undergone specialist post-graduate training in manipulation.

Evidence of adverse events of manipulation showed that there was little risk of severe adverse events for those with non-specific low back pain. A recent large study found similar increased risks of vertebro artery dissection and stroke for people under 45 attending chiropractic as those people consulting a family physician (Cassidy, J. D., Boyle, E., Cote, P. et al , 2008).

7.2 Recommendations for manual therapies

7.2.1 Consider offering a course of manual therapy including spinal manipulation of up to 9 sessions over up to 12 weeks[8].

7.3 Manual Therapies -Effectiveness

Clinical question: what is the effectiveness of manual therapies compared with usual care on pain, functional disability or psychological distress?

[8] A choice of an exercise programme (see section 1.3.3), a course of manual therapy and a course of acupuncture (see section 1.8.1) may be offered, taking into account patient preference.

7.3.1 Clinical evidence

Literature searching retrieved 1482 papers of which 47 were ordered. Studies were categorised according to whether the intervention included spinal manipulation/mobilisation or massage/soft tissue manipulation. A total of 8 RCTs on manipulation/mobilisation techniques and 1 systematic review on massage therapy were included.

Although systematic reviews were identified and ordered for this question, they were ultimately excluded because of the heterogeneity between the included studies; studies varied on the patient population (mainly the duration of the low back pain episode), the interventions and comparators used. This meant that only a handful of RCTs within the systematic reviews were relevant to our population and guideline. The relevant RCTs were therefore instead extracted independently.

7.3.1.1 Spinal Manipulation/Mobilisation

The United Kingdom back pain exercise and manipulation (UK BEAM) trial (UK Back pain exercise and manipulation (UKBEAM) Trial Team., 2004) aimed to estimate the effectiveness of adding exercise, spinal manipulation to best usual care in general practice. Patients recruited from participating centres had to be aged 18-65 and have had pain everyday for the 28 days before randomisation (or 21 out of 28 days before randomisation and 21 out of 28 days before that). They also had to agree to avoid physical treatment other than trial treatments for 3 months. Exclusion criteria included cancer, osteoporosis, ankylosing spondylitis, cauda equina compression, previous spinal surgery, anticoagulant treatment and severe cardiovascular disease or inadequately controlled hypertension.

A total of 1334 patients were included in the study, with 353 randomised to a manipulation group and 338 to a ‘Best Usual Care’ control group. All patients received advice to continuing normal activities and avoiding rest, and copies of The Back Book were made available to them. Patients in the spinal manipulation package group received treatment using techniques agreed by professional representatives of chiropractic, osteopathy and physiotherapy following open

consultation in the UK . Following initial assessment, manipulators chose from the agreed manual and non-manual treatment options. High-velocity thrusts were used on most patients at least once. Patients were invited to attend up to eight 20-minute sessions, if necessary over 12 weeks. Patients in the control group (the best care alone group) only received the advice everyone was given.

Results showed that relative to "best usual care", spinal manipulation improved back function by a small to moderate margin at 3 months and by a smaller but still significant margin at 1 year. It also improved disability and pain and general physical health.

This was a high quality RCT with a very low risk of bias

One randomised controlled trial aimed to determine whether osteopathic care, including manipulative therapy, would benefit patients with non-specific low back pain more than would standard allopathic care (Andersson, G. B., Lucente, T., Davis, A. M. et al , 1999). Triage nurses at a Health Maintenance Organisation in the USA identified eligible patients (i.e patients aged 20-59 years and with low back pain between 3 weeks and 6 months). Exclusion criteria included, but were not restricted to, nerve-root compression, systemic inflammatory disorder, cancer, known psychiatric or psychological illness, pregnancy, ongoing litigation and manipulative treatment in previous three weeks.

A total of 178 patients were randomized into either the osteopathic treatment group (n=93) or the standard allopathic treatment group (n=85). Patients in the osteopathic treatment group received osteopathic manipulation to areas the osteopath determined to be related to the back pain. A variety of techniques were used, including thrust (manipulation), muscle energy, counterstrain, articulation, and myofascial release. The treating physician chose the techniques used. Treatment was given during four weekly visits and then through four more visits at intervals of two weeks. Standard care was provided by a physician. Treatment included analgesics, anti-inflammatory medication, active physical therapy, or therapies such as ultrasonography, diathermy, hot or cold packs, use of a corset, or TENS. No information was given on the frequency of use of the potential different interventions in the standard care group. All patients viewed a 10-minute educational video on

back pain. The outcomes of interest were pain and function and patients were followed-up for 12 weeks.

No difference in clinical outcome between standard care and osteopathic care was observed.

This was a RCT with a high risk of bias.

One randomised controlled trial included patients recruited from two Seattle-area primary care clinics (Cherkin, D. C., Deyo, R. A., Battié, M. et al , 1998). Patients had to have been aged 20-64 and have low back pain persisting 7 days after visiting their primary care physician. A total of 321 patients were randomly assigned to the McKenzie method of physical therapy (n=133), chiropractic manipulation (n=122), or a minimal interventions (provision of an educational booklet) (n=66). In the McKenzie approach, patients were placed in one of three broad categories (derangement, dysfunction and postural syndrome). The most common method of chiropractic manipulation was used (short-lever, high velocity thrust); no other physical treatments were permitted. Patients in the chiropractic manipulation and physical therapy groups received up to 9 sessions over 5 weeks. The minimal intervention group received an educational booklet to minimise potential disappointment with not receiving treatment. The booklet discussed causes of back pain, prognosis, appropriate use of imaging studies and specialists and activities for promoting recovery and preventing recurrences. Patients were followed-up at four weeks, 12weeks, one year and two years. Results suggest there are no clear advantages of chiropractic manipulation over physical therapy. Patients receiving these treatments had only marginally better outcomes than those receiving the minimal intervention of an educational booklet

This was a well conducted RCT with a low risk of bias.

One randomised controlled trial randomly allocated patients to one of 4 treatments: manipulation (n=116), physiotherapy (n=114), corset (n=109) and analgesics (n=113) (Doran, D. M. and Newell, D. J., 1975). To be included, patients had to be aged 20-50 years, have painful limitation of movement in the lumbar spine and be suitable for any of the 4 treatments. Exclusion criteria included pregnancy, significant root pain in legs, abnormal reflexes, osteoarthrosis of the hip joint, osteoporosis,

previous manipulation and spondylolysis, spondylolisthesis or systemic disease. The techniques used on patients in the manipulation group were at the discretion of the manipulator. Ancillary osteopathic procedures such as mobilising and soft-tissue techniques could be included. A minimum of two treatments were given each week, and an average of six treatments per patient was actually given. Patients in the physiotherapy group could receive any treatment within the usual practice of the department except manipulation. The therapist could vary the treatment in an attempt to give patients maximum benefit with a planned minimum of two treatments each week. This resulted in an average of 7.3 physiotherapy treatments per patient. For patients in the corset group, any corset applied on the day of entry to the trial was acceptable. Each hospital decided in advance which type it would use throughout the trial. Patients in the control group (analgesic group), were given a course of 2 paracetamol tablets every four hours. The main outcome was pain.

Results showed no important differences among the four groups of patients, and the authors concluded that there was no strong reason to recommend manipulation over physiotherapy or corset.

This was a RCT with a high risk of bias

One randomised controlled trial compared the effectiveness of a spinal stabilisation rehabilitation programme, manual therapy and a minimal intervention package (an education booklet) acting as the control intervention (Goldby, Lucy. Jane., Moore, Ann. P., Doust, Jo. et al , 2006). Patients were recruited from a UK hospital physiotherapy department; they had to have chronic low back disorder with the current episode lasting a minimum of 12 weeks, had to be aged between 18 and 65 years and be able to read and write English. Exclusion criteria included nonmechanical pain, spinal stenosis, spondylolisthesis, inflammatory joint disease, present or past metastatic disease, pregnancy or over two past operative interventions for low back pain.

A total of 213 patients received either manual therapy (n=89), a 10-week spinal stabilisation rehabilitation program (n=84), or a minimal intervention group (n=40). Patients in the 10-week spinal stabilisation rehabilitation program received functionally progressive exercise class that emphasised the selective retraining of

the transversus abdominis, multifidus, the pelvic floor and diaphragm muscles, while inhibiting global muscle substitution mechanisms. A video illustrating the effect of the muscles on the stability of the spine was shown at the beginning of each class. Each of the 10 weekly class lasted 1 hour. Patients in the manual therapy group were also treated by physiotherapists, who were not allowed to prescribe any exercise for the transversus abdominis, multifidus, the pelvic floor and diaphragm muscles. Nor were they allowed to prescribe any electrophysical methods. Any other form of exercise or manual procedure within the remit of musculoskeletal physiotherapy was allowed. They received a maximum of 10 interventions. Patients in the control group (educational booklet) were given the educational booklet “Back in Action” and explained the contents. They were then discharged and booked to attend the Back School, which patients in all groups attended and consisted of one group-specific three-hour questions and answer session.

Results suggest that manual therapy provides pain relief, but not simultaneous reduction in disability and handicap. Both spinal stabilisation and manual therapy were significantly effective in pain reduction compared to an active control.

This was a RCT with a high risk of bias because of high treatment dropouts and loss to follow-up.

A randomised controlled trial compared the effectiveness of medical and chiropractic care for low back pain in patients in managed care (Hurwitz, Eric L., Morgenstern, Hal, Harber, Philip et al , 2002; Hurwitz, Eric L., Morgenstern, Hal, Kominski, Gerald F. et al , 2006). Those included had to be aged 18 or over, be a member of the health maintenance organisation, present with a complaint of low back pain with or without leg pain and not had received treatment for low back pain within the previous month.

Patients were randomly assigned to either Medical care only (n = 170), Chiropractic care only (n = 169), Medical care with physical therapy (n = 170) or Chiropractic care and physical modalities (n = 172). Patients in the medical care only group received one or more of the following: instruction in proper back care and strengthening and flexibility exercises, prescriptions for pain killers, muscle relaxants, anti-inflammatory agents, and other medications use to reduce or eliminate pain or discomfort, and

recommendations regarding bed rest, weight loss, and physical activities. Patients in the Chiropractic care only group received spinal manipulation or another spinal-adjusting technique (eg mobilization), instruction in strengthening and flexibility exercises, and instruction in proper back care. Medical Care with Physical therapy patients received medical care, instruction in proper back care plus one or more of the following: heat therapy, cold therapy, ultrasound, electrical muscle stimulation, soft-tissue and joint mobilisation, traction, supervised therapeutic exercise, and strengthening and flexibility exercises. Patients in the 4th group received chiropractic care plus one or more of following: heat or cold therapy, ultrasound and electrical muscle stimulation. Frequency of medical, chiropractic and physical therapy visits were at the discretion of the medical provider, chiropractor or physical therapist assigned to the patient.

Results suggested that medical and chiropractic care alone yielded similar improvements in pain severity and disability after 6 months (and 18 months) follow-up.

This was a RCT with a high risk of bias

A randomised controlled trial compared manipulation, a manipulation mimic and a back education programme (Triano, J. J., McGregor, M., Hondras, M. A. et al , 1995). Patients with low back pain for over 50 days or with over 6 episodes in the previous year were included. Exclusion criteria included neuropathy, severe osteoporosis, fracture, osseous pathology of the spine, receiving other treatment intended to relieve back pain, workers compensation or litigation claims.

A total of 209 patients were randomised into the High-Velocity Low Amplitude group (HVLA), a High Velocity Low Force group (HVLF a HVLA mimic) or a Back Education programme. The exact number of patients assigned to each group is not clear but it was around 40 in each group. Patients receiving HVLA manipulation were placed in a lateral decubitus posture close to the leading edge of the treatment table. The free leg was flexed at the knee and pelvis to cause a relative flexion of the lumbar spine. Patients receiving the mimic manipulation, HVLF, were also manipulated at the lumbar and pelvic sites. The HVLF procedures were intended to balance the study design to account for physician contact and the physical handling

of the patient. The third group, the Back Education Programme (BEP) was intended as a contrast for the physical contact between provider and patient that is offered by HVLA and HVLF. Elements of BEP included attractive colour graphics couples with common anatomic and biomechanical information of spinal function and hygiene. Each treatment session consisted of didactic presentation conducted with physical separation between patient and provider. Exercise was described in general terms, but none were specifically recommended.

Treatment sessions were scheduled during a 2-week interval, and were held daily on the basis of a 6-day/week clinic schedule. Adherence to the scheduled interval within a 72-hour window was required for inclusion.

Results suggest the existence of clinical value to treatment according to a defined plan using manipulation. Immediate reduction of reported pain after individual treatment sessions was observed at the end of 2 weeks of treatment. Self-reported functional levels were similarly enhanced in the HVLA group versus the HVLF and BEP groups.

This was a RCT with a high risk of bias

7.3.1.2 Massage/soft-tissue mobilisation

A systematic review (Furlan, A. D., Brosseau, L., Imamura, M. et al , 2002) assessed the effects of massage therapy for non-specific low back pain. The following were searched for randomised controlled trials and controlled clinical trials: MEDLINE, HealthSTAR, CINAHL, EMBASE, dissertation abstract, Cochrane Controlled Trials Register. Patients had to be aged 18 or over, have acute (<4wks), subacute (4-12wks), chronic (>12wks) non-specific low back pain. Low back pain was defined as pain localised from costal margin or 12th rib to inferior gluteal fold. Exclusion criteria were the following: infection, neoplasm, metastasis, osteoporosis, rheumatoid arthritis, fracture, inflammatory process or radicular syndrome.

Eight RCTs were identified, 4 conducted in the USA (466 patients), 3 in Canada (235 patients) and one in Germany (190 patients). The population included in the trials was similar regarding the diagnosis of LBP but differed with respect to duration of pain, previous treatments and distribution of age. One RCT comparing massage to

inert treatment (sham laser) showed that massage was superior. The other studies compared massage to different active treatments. They showed that massage was equal to corsets and superior to self-care education. The beneficial effect of massage in patients with chronic low back pain lasted at least a year after the end of treatment.

This was a high quality systematic review with a very low risk of bias

7.3.2 Health economics

Literature searching retrieved 271 papers of which 9 were ordered for this question. In total, 8 were excluded and 1 was included: this was a UK-based cost-effectiveness study of four interventions for treatment of low back pain, two of which included manual therapy. It is described below.

An economic evaluation was conducted alongside the UK back pain exercise and manipulation randomised trial (UK Back pain exercise and manipulation (UKBEAM) Trial Team, 2004) to assess the cost effectiveness of adding spinal manipulation, exercise classes or manipulation followed by exercise ("combined treatment") to "best care" in general practice for patients consulting with low back pain. The study recruited 1334 patients aged between 18 and 65 years if they had experienced pain every day for the 28 days before randomisation or for 21 out of the 28 days before randomisation and 21 out of the 28 days before that. In addition, they had to have a score of four or more on the Roland disability questionnaire at randomisation.

The four treatment groups were 1) best care, which included active management and providing The Back Book to patients, 2) best care + an exercise programme of up to nine classes over 12 weeks, 3) best care + spinal manipulation package of eight sessions over 12 weeks and 4) combined treatment, which included best care + six weeks of manipulation followed by six weeks of exercise. The main outcome measures were healthcare costs, quality adjusted life years (QALYs), and cost per QALY over 12 months. The number of QALYs gained over 12 months was estimated using EQ-5D questionnaire data which was collected as part of the trial. A large British sample valued EQ-5D health states on a "utility" scale on which being dead scores zero and perfect health scores one. The costing perspective was that of the

UK health service. Healthcare resources included those for: the spinal manipulation package, the exercise programme, hospital inpatient stays, outpatient attendances, and general practice consultations. These resources were costed using national averages for England. Private care was costed using information from a major insurance provider. Costs were reported in pounds sterling at 2000/2001 prices. Costs were not discounted since the focus was on effects over only one year.

To cover scenarios in which either exercise or manipulation was not available ICERs were calculated to compare best care with manipulation alone or exercise alone.

Sensitivity analysis examined the impact on costs if the NHS purchased private care for some or all of the patients. The justification for this is that in the short term it might be difficult to make all manipulation or combined treatment available within the NHS: there are insufficient numbers of trained practitioners in the NHS to meet demand and it would take a few years to train people up within the NHS.

Results (base case)

The mean cost (Standard Deviation) of best care was £346 (£602). best care+manipulation cost £195 more than best care. Relative to best care, best care+manipulation generated an additional 0.041 (95% CI 0.016 to 0.066) QALYs per participant, . If exercise is not available (n=623) manipulation generates 0.041 more QALYs per patient than best care at an additional cost of £195 per patient , yielding an ICER of £4800 per QALY. The GDG felt that from the evidence presented it was not appropriate to rule out either treatment option. For some people certain therapies may not be suitable therefore manipulation alone remains an option for this population.

Sensitivity analysis

The study reported on three sensitivity analyses. 1) When statistical outliers were excluded (n=51): that is, where healthcare costs exceeded £2000, best care+manipulaton achieved extended dominance over both exercise and combined treatment, with an ICER of £3000 per additional QALY. 2) To examine the effects on unit costs of a scenario in which the NHS buys half of the manipulation sessions from the private sector, NHS costs were replaced with private costs for manipulation

that took place in a private setting. In the third analysis the scenario was one where the NHS buys all manipulation from the private sector when private costs were used for all manipulation within the trial, results were similar to the above: exercise was subject to extended dominance compared with best care.

This study shows that in the base case analysis combined spinal manipulation + exercise is the most cost effective addition to best care for low back pain in general practice in the UK (ICER=£3800 relative to best care). This combined therapy dominates the exercise programme since it generates more QALYs and costs less than the addition of exercise to best care. Therefore, if additional QALYs are valued at much less than £3800 then best care is the best strategy. If decision makers valuation of QALYs lies between £3800 and £8700 then spinal manipulation followed by exercise classes is likely to be the best therapy. And if their valuation is well above £8700 then manipulation added to best care is probably the best therapy.

7.3.3 Evidence statements for manual therapies

Hyperlink to related recommendations

Evidence statements		Evidence to recommendations
7.3.3.1	*One large and well-conducted RCT evaluated the effectiveness of adding exercise, spinal manipulation package or a combination of both to the Best care in general practice. Relative to best care,*	There is some evidence of reduction in pain and disability when used in addition to usual care. There is no evidence of benefit in psychological outcomes. Manual therapies have a modest effect and are at least equivalent to usual care. They are cost effective, although the combined treatment option was the

	spinal manipulation was found to improve back function by a small to moderate margin at 3 months and by a smaller but still significant margin at 1 year follow-up. Disability, pain and general physical health were also improved (1++) (UK Back pain exercise and manipulation (UKBEAM) Trial Team., 2004).	most cost effective in this study . The GDG felt that from the evidence presented it was not appropriate to rule out either treatment option. For some people certain therapies may not be suitable therefore manipulation alone remains an option for this population. Clarification on what comprised a 'course' of treatment was requested by the group. The number of treatments and time of delivery in the trials were checked and the recommendation was adapted to reflect this by stating up to 9 sessions over up to 12 weeks.
7.3.3.2	*One RCT compared osteopathic care (including manipulative therapy) to standard care, and found no difference in pain or function at 12 weeks follow-up (1-) (Andersson,*	There is weak evidence from one well conducted systematic review that massage provides short term pain relief. No cost effectiveness studies were found for massage. GDG agreed that this could not be recommended.

	G. B., Lucente, T., Davis, A. M. et al , 1999)	
7.3.3.3	*One well conducted RCT compared the effectiveness of the McKenzie method of physical therapy, chiropractic manipulation and the provision of an educational booklet. After a 2-year follow-up, patients who had received chiropractic manipulation had only slightly better function and symptoms than patients who received an educational booklet (1+) (Cherkin, D. C., Deyo, R. A., Battié, M. et al , 1998)*	
7.3.3.4	*One RCT*	

	compared manipulation, physiotherapy, corsets and analgesics, and found no important differences in patients' assessment of pain at 6 weeks between the 4 groups. Manipulation wasn't significantly superior to analgesics.(1-) (Doran, D. M. and Newell, D. J., 1975)	
7.3.3.5	*One well conducted RCT compared the effectiveness of a spinal stabilisation programme, manual therapy and an educational booklet, and found that manual therapy was significantly*	

	effective in pain reduction (but not disability) compared to an educational booklet at 3 months (1-) (Goldby, Lucy. Jane., Moore, Ann. P., Doust, Jo. et al , 2006)	
7.3.3.6	*One RCT compared chiropractic care to medical care, and found no difference in pain severity or disability after 6 months and 18-months (1-) (Hurwitz, Eric L., Morgenstern, Hal, Harber, Philip et al , 2002; Hurwitz, Eric L., Morgenstern, Hal, Kominski, Gerald F. et al , 2006)*	
7.3.3.7	*One RCT comparing manipulation, a*	

	manipulation mimic and a back education program found that manipulation was associated with reduced pain and improved self-reported function at the end of 2 weeks of treatment(1-)(Triano, J. J., McGregor, M., Hondras, M. A. et al , 1995))	
7.3.3.8	*One systematic review assessed the effects of massage therapy and found evidence of massage being superior to inert treatment and self-care education, but equal to corsets.(1++) (Furlan, A. D., Brosseau, L., Imamura, M. et al , 2002))*	

Cost-effectiveness-manual therapies *7.3.3.9 The cost-effectiveness of the included manipulation programme when added to best care, had an ICER of £4,756 compared to best care alone, and there was over a 95% chance that the estimated ICER was less than £20,000 per QALY. (UK Back pain exercise and manipulation (UKBEAM) Trial Team., 2004).The ICER for manipulation alone compared to combined therapy was estimated at £8,700/QALY. Using a threshold of £20,000 per QALY, manipulation alone had over a*	

	50% probability of being the most cost-effective treatment option. The combination treatment option was estimated to be the most cost-effective option about 40% of the time at the £20,000/QALY threshold. (UK Back pain exercise and manipulation (UKBEAM) Trial Team., 2004).	
7.3.3.10	*No cost effectiveness studies were found for massage*	

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7.4 Manual Therapies - Adverse Events

Clinical question: what are the effects of adverse events of manual therapies on functional disability, pain or psychological distress?

7.4.1 Clinical evidence

Literature searching retrieved 2210 papers, of which 13 were ordered. Two systematic reviews (one being an update of the other), one cohort and one survey were included. The review focussed on evidence relevant to the treatment of low back pain hence cervical manipulation was outside our inclusion criteria.

A systematic review aimed to identify adverse effects of spinal manipulation (Ernst, E., 2007). The databases MEDLINE, EMBASE, Amed, CINHAL, British Nursing Index and Cochrane Library were searched up to June 2006. Articles from the year 2000 or earlier were excluded because the review was updating a previously published one (Stevinson, Clare and Ernst, Edzard, 2002) (see below). There was no restriction on language or study design. Searches identified 32 case reports, 4 case series, 2 prospective studies, 3 case-control and 3 surveys. The case reports confirm previous reports associating upper spinal manipulation with a range of complications. The most serious problems are vertebral artery dissection as a result of overstretching of the artery during rotational manipulation of the neck. Spinal manipulation has associated with risks such as vascular accidents and nonvascular complications in a number of case series. Case-control studies suggested a causal relationship between upper spinal manipulation and the adverse effect. The survey data indicated that even serious adverse events are rarely reported in the medical literature.

It must be noted that in the review, the original complaint for which manipulation was sought is reported only for a minority of included studies, and where it is, the most frequent complaint was neck or shoulder pain.

In conclusion, spinal manipulation is commonly associated with mild to moderate adverse effects. Serious complications following manipulation of the lumbar spine are rare.

This was a well conducted systematic review with a low risk of bias

One systematic review (Stevinson, Clare and Ernst, Edzard, 2002) summarised the evidence about the risks of spinal manipulation. Searches were carried out using MEDLINE, EMBASE and the Cochrane Library in November 2001. The bibliographies of relevant papers were searched for pertinent articles.

Two reviews identified complications following spinal manipulation; these included vertebrobasilar accidents, cases of disc herniation or progression of radicular symptoms to cauda equina syndrome and other cerebral complications. Other types of complications included dislocations and fractures often accompanied by spinal cord compression. The most frequently reported injuries from cervical spinal manipulation involved arterial dissection or spasm and lesions of the brain stem. Case reports and case series of serious adverse events suggested the most common serious adverse events were cerebrovascular accidents often with permanent neurologic deficits. Retrospective surveys of neurologists reported adverse events mostly related to cerebrovascular accidents. A retrospective analysis of 26 cases of vertebral artery dissection found the suspected precipitating factor to be spinal manipulation in 11% of cases, which was less often than with sporting activity (15%).

It must be noted that in this review, the original complaint for which manipulation was sought is reported only for a minority of included studies, and where it is, the most frequent complaint was neck or shoulder pain

The conclusion was that the evidence about serious adverse events rests mostly on case reports case series and retrospective surveys. Such evidence is essentially anecdotal and it is difficult to establish cause-effect relation. It is suggested that some nonvertebral complications might be avoidable by observing contraindications for spinal manipulations. Vertebrobasilar accidents are more difficult to prevent because they tend to occur in relatively young adults without known abnormalities and there is little consensus about potential risk factors. It is finally concluded that avoiding practitioners who make use of rotatory techniques for cervical manipulation and using mobilisation (low velocity passive movement) instead of manipulation of the cervical spine might lower the risk of vertebral artery damage.

This was a well conducted systematic review with a low risk of bias.

A retrospective cohort study was identified, comparing outcomes, complications and hospital disposition for those patients who received physical therapist-administered manual therapy compared to those who did not (Cook, Chad, Cook, Amy, and Worrell, Teddy, 2008). The Nationwide Inpatient Sample databases were used (HealthCare Cost and Utilization Project in USA) from 1988 through 2005. Adults over 18 years and diagnosed with mechanical lower back pain were included. Those who had had any form of surgical procedure or pathologic fracture, tumour or other non-mechanical low back diagnosis were excluded. The sample included 150, 75 in the PT manual therapy group and 75 who did not receive PT manual therapy. The sample was generated using a randomised matching algorithm that assured close characteristics of patients in a number of categories. The 2 groups differed significantly in age ($p<0.1$) (PT manual therapy were older) but were similar in years of data collected, sex, race, household income, hospital region and modified Charlson index.

Analyses showed that those who received PT manual therapy had significantly longer lengths of hospital stay ($p<0.01$) and had significantly higher inflation-adjusted costs of care ($p<0.01$), even after controlling for demographic factors. There were no recorded instances of nervous system complications, radiculitis, myelopathy, or cauda equina for either group. Instances of sciatica were relatively low as were non-routine discharges. This study suggests that there are no more adverse events from manual therapies than when no physical therapy is given. However, the length of stay may increase.

This was a well conducted retrospective cohort study with a low risk of confounding bias or chance.

A survey of members of the Swiss Medical Association of Manual Medicine for the year 1989 analysed the frequency of complications due to manipulation of the spine (Dvorak, J., Loustalot, D., Baumgartner, H. et al , 1993). A total of 680 questionnaires were sent out, of which 63% were returned by GPs, specialists of internal medicine, rheumatologists, orthopaedic surgeons, neurologists and various other medical specialities. The results were presented stratified by location of

manipulation i.e cervical manipulation complications and thoraco-lumbar manipulation complications.

Out of a total of 342125 thoraco-lumbar manipulations, 175 patients (ratio 1:1955) reported increased pain immediately after the manipulation of the lumbar spine. The increase in pain was transient in all those cases. 17 patients (ratio 1:20125) presented in addition to increased pain a transient sensorimotor deficit with precise radicular distribution. 9 patients out of the 17 (ratio 1: 38013) developed a progressive radicular syndrome with sensorimotor deficit and radiologically verified disc herniation and had to be referred to surgery. All patients except one recovered completely after surgery. The classic high velocity low amplitude thrust was the only type of manipulation applied in all patients with complications.

The main conclusion was that side effects and complications are rare. This was a non-analytical study.

7.4.2 Evidence statements for adverse event of manual therapies

Evidence statements		Evidence to recommendations
7.4.2.1	*A systematic review on risks of spinal manipulation concluded that the evidence rested mostly on case reports case series and retrospective surveys. Nonvertebral complications could be avoided by observing contraindications for manipulation, (1+) (Stevinson, Clare and Ernst, Edzard, 2002)*	Manipulation other than for the lumbo- pelvic region is excluded from this review The GDG agreed that cervical manipulation would not generally be carried out on this population.
7.4.2.2	*A systematic review, updated by Ernst did not find any additional evidence regarding thoraco lumbar manipulation. (1+) (Ernst, E., 2007)*	No evidence was found to show any increase in serious adverse events in people with non-specific low back pain.
7.4.2.3	*A retrospective cohort study compared outcomes, complications and hospital disposition for patients who received manual therapy and for those who did not. Results suggest there are no more adverse events from manual therapies*	

	than when no manual therapy is given. (2+) (Cook, Chad, Cook, Amy, and Worrell, Teddy, 2008)	
7.4.2.4	*One survey analysed the frequency of complications due to thoraco lumbar manipulation and concluded that side effects and complications are rare.(3) (Dvorak, J., Loustalot, D., Baumgartner, H. et al , 1993)*	

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8 Other non-pharmacological therapies

8.1 Introduction

Other non-pharmocological therapies in this context are therapies in which the patient has little active involvement with the treatment. The most common treatments were suggested by the stakeholder group and a final list was developed by the GDG based upon those treatments that are commonly used in the NHS. This is not exhaustive as treatments frequently come onto the market with little or no testing and may not be commonly available on the NHS. The main treatments considered were commonly used electrotherapies, lumbar supports and spinal traction including motorised mechanical traction and autotraction. Autotraction is performed by utilising the patient's own body weight (for example by suspension via the lower limb) or through movement.

8.2 Recommendations for other non-pharmacological therapies

Electrotherapy modalities

Hyperlink to related evidence statements

8.2.1 Do not offer laser therapy.

8.2.2 Do not offer interferential therapy.

8.2.3 Do not offer therapeutic ultrasound.

Transcutaneous nerve stimulation (TENS)

Hyperlink to related evidence statements

8.2.4 Do not offer transcutaneous electrical nerve simulation (TENS) routinely.

Lumbar supports

Hyperlink to related evidence statements

8.2.5 Lumbar supports are not recommended.

Traction

Hyperlink to related evidence statements

8.2.6 Do not offer traction because of the increased risk of aggravating symptoms.

8.3 Electrotherapy Therapies

Clinical question: what is the effectiveness of electrotherapy modalities (laser therapy; interferential therapy; therapeutic ultrasound) compared with usual care or sham treatment on pain, functional disability or psychological distress?

8.3.1 Clinical evidence

Literature searching retrieved 566 papers of which 10 were ordered for this question. One systematic review for laser therapy (Yousefi, Nooraie. R., Schonstein, E., Heidari, K. et al , 2007) was included.

8.3.1.1 Laser therapy

One systematic review was included (Yousefi, Nooraie. R., Schonstein, E., Heidari, K. et al , 2007). This systematic review included 6 RCTs (n = 318 patients) that recruited people with acute (pain for four weeks or less), sub-acute (pain for one to three months) or chronic (pain for more than three months) non-specific low-back

pain. Number of participants ranged from 20 to 130, duration of therapy ranged from a single session to 4 weeks.

This review reported on two of our three primary outcomes (pain and disability) which were also the pre-specified primary outcomes of the systematic review. No RCTs that reported the third outcome of psychological distress were found. No subsequent RCTs were found. Other outcomes reported in this review were relapse, range of motion and adverse events.

Low level laser therapy was associated with a reduction in pain assessed using the visual analogue scale (VAS) compared with sham laser, weighted mean difference = -11.3 mm (95% CI -16.91 to -5.75). This was based on three RCTs (Basford, J. R., Sheffield, C. G., and Harmsen, W. S., 1999; Gur, Ali, Karakoc, Mehmet, Cevik, Remzi et al , 2003; Klein, R. G. and Eek, B. C., 1990) with a total of 126 participants who were followed up < 3 months after randomisation.

A fourth RCT (Soriano, F., 1998) found low level laser therapy to be associated with a reduction in pain assessed using the visual analogue scale (VAS) compared with sham laser after 6 month follow–up ($P < 0.001$).

A fifth RCT (Toya S, Motegi M, Inomata K et al , 1994)) found low level laser therapy to be associated with a reduction in pain assessed using a grading system compared with sham laser after one day ($P = 0.007$).

Low level laser therapy was not found to be associated with a reduction in disability compared with sham laser, standardised mean difference (SMD) = -0.14 (95% CI -0.88 to 0.59). This was based on three RCTs with a total of 126 participants who were followed up < 3 months after randomisation (Basford, J. R., Sheffield, C. G., and Harmsen, W. S., 1999; Gur, Ali, Karakoc, Mehmet, Cevik, Remzi et al , 2003; Klein, R. G. and Eek, B. C., 1990).

In a subgroup analysis according to whether an ‘adequate’ dose of laser was given (this was defined as 4 J or more (WALT-d 2005 recommendations)) low level laser therapy was found to be associated with a reduction in disability compared with sham laser when an ‘adequate dose’ was given, SMD = -0.81 (95% CI -1.36 to -0.26) based on one study (Basford, J. R., Sheffield, C. G., and Harmsen, W. S.,

1999) but not when an 'inadequate dose' was given, SMD = 0.21 (95% CI -0.26 to 0.68) based on two studies (Gur, Ali, Karakoc, Mehmet, Cevik, Remzi et al , 2003; Klein, R. G. and Eek, B. C., 1990).

A fourth RCT (Longo, L., Tamburini, A., and Monti, A., 1991) found low level laser therapy to be associated with an improvement in symptoms measured using the Ritchie Scale compared with sham laser.

Low level laser therapy was found to be associated with a reduction in percentage relapse at intermediate (3 months to one year) follow up compared with sham laser, Relative Risk = 0.43 (95% CI 0.28 to 0.65) based on two studies (Longo, L., Tamburini, A., and Monti, A., 1991; Soriano, F., 1998)).

One of these RCTs also found laser therapy to be associated with a reduction in percentage relapse at short-term (< 3 months) and long-term (> 1 year) follow-up (Longo, L., Tamburini, A., and Monti, A., 1991).

Low level laser therapy was not found to be associated with an increase in lumbar mobility compared with sham laser, SMD = 0.01 (95% CI -0.34 to 0.36) based on two studies (Basford, J. R., Sheffield, C. G., and Harmsen, W. S., 1999; Gur, Ali, Karakoc, Mehmet, Cevik, Remzi et al , 2003).

Two studies reported data on adverse events (Klein, R. G. and Eek, B. C., 1990; Toya S, Motegi M, Inomata K et al , 1994)) and neither found discomfort related to laser treatment nor an increase in pain in either group.

The authors concluded there was insufficient evidence on the efficacy of LLLT to reduce pain and disability in individuals with low back pain. However, LLLT appears to have a small effect on pain intensity and frequency in chronic low back pain sufferers when infrared wavelengths are used and if applied to painful areas for at least two weeks.

This was a high quality systematic review, however the included trials were generally small and were heterogeneous in their populations, treatments and outcome measures. The authors also highlight the need for further methodologically rigorous

RCTs evaluating different lengths of treatment, different wavelengths and different dosages.

8.3.1.2 Interferential therapy

No relevant randomized controlled trial or systematic review comparing interferential therapy with usual care or sham were identified.

8.3.1.3 Therapeutic ultrasound

No systematic reviews or randomized controlled trials comparing therapeutic ultrasound with usual care or sham were found.

8.3.2 Health economics

No economic evaluations were identified for electrotherapy modalities.

8.3.3 Evidence statements for electrotherapy modalities

Hyperlink to related recommendations

Evidence statements	Evidence to recommendations
Laser therapy *8.3.3.1 One systematic review was identified that included 6 randomised controlled trials (4 of which were small) in people with acute (< 4 weeks), sub-acute (1-3 months) or chronic (> 3 months) non-specific low back pain treated with low level laser therapy. Laser therapy was found to be*	Only weak evidence is available showing benefit for reducing pain . From the systematic review only 2 of the studies covers sub-acute LBP population. Only 1 study had a follow up of 6 months. There was also some doubt concerning the intention to treat analysis. The GDG felt that the strength or evidence was not strong enough to recommend use and that further

	associated with a reduction in pain intensity and relapse rates but not back-pain related disability or lumbar mobility compared with sham laser. Laser therapy was not found to be associated with an increase in adverse events compared with sham laser.(1++) (Yousefi, Nooraie. R., Schonstein, E., Heidari, K. et al , 2007)	research is required.
8.3.3.2	*No cost effectiveness studies were identified.*	
Interferential therapy		The decision by the GDG not to recommend interferential and ultrasound therapies is based on lack of evidence for this guideline's population of interest and consensus that these treatments did not offer benefit.
8.3.3.3	*No studies of large enough sample size comparing interferential therapy with usual care or sham were found*	
8.3.3.4	*No cost effectiveness studies were identified.*	
Therapeutic ultrasound		
8.3.3.5	*No studies of large enough sample size comparing*	

	therapeutic ultrasound with usual care or sham were found.	
8.3.3.6	*No cost effectiveness studies were identified.*	

8.4 Transcutaneous Electrical Nerve Stimulation (TENS)

Clinical question: What is the effectiveness of transcutaneous electrical nerve stimulation (TENS) compared with usual care or sham treatment on pain, functional disability or psychological distress?

8.4.1 Clinical evidence

Literature searching retrieved 566 papers for this question. 21 were ordered and 18 were excluded, three randomised controlled trials were included (Deyo, R. A., Walsh, N. E., Martin, D. C. et al , 1990; Jarzem, P. F., Harvey, E. J., Arcaro, N. et al , 2005a; Jarzem, P. F., Harvey, E. J., Arcaro, N. et al , 2005b).

One randomised controlled trial (Deyo, R. A., Walsh, N. E., Martin, D. C. et al , 1990) recruited a total of 145 patients aged 18-70 years with low back pain of at least three months' duration. Patients were randomised into one of three treatment groups (TENS alone (n=31), TENS plus exercise (n=34) or exercise alone (n=29)), or to a control group (sham TENS, n=31). The duration of treatment was four weeks; TENS sessions were undertaken at least three times a day for 45 minute periods by participants who were instructed in the use of their TENS units. After four weeks, TENS was not associated with a significant improvement in functional outcomes (overall modified Sickness Impact Profile score, Physical dimension score,

Psychosocial dimension score, or self rated activity) or pain outcomes (Self-rated improvements, VAS scores, VAS improvement scale or frequency of pain). Adverse events of minor skin irritation at the site of electrode placement were reported by one third of the subjects. One subject receiving sham TENS had a severe dermatitis four days after therapy began requiring discontinuation of treatment.

This was a well conducted RCT with a low risk of bias.

A randomised controlled trial (Jarzem, P. F., Harvey, E. J., Arcaro, N. et al , 2005a) recruited a total of 350 patients aged 18 to 70 years with continuous low back pain for at least three months duration who were randomised to one of three intervention groups (conventional TENS (n=84), acupuncture-like TENS (n=78) or Nu Wave TENS (n=79)) or to a control group (sham TENS, n=83). Patients were given identical appearing TENS stimulators and were instructed on the use of the machine. Average daily use of TENS machines was estimated at 188 minutes per day during the study period of 4 weeks. After four weeks, none of the TENS interventions were associated with an improvement in the following outcomes compared with sham TENS: Activity (McGill activity scale), Work (McGill work scale), Disability (RMDQ) or Depression (Zung scale). No data was reported on adverse events.

There were several methodological issues which may have led to bias in this trial.

A third randomised controlled trial (Jarzem, P. F., Harvey, E. J., Arcaro, N. et al , 2005b) recruited a total of fifty patients aged 18 to 70 years with continuous low back pain for at least three months duration who were randomised to one of two groups in a crossover design: The first group (Group 1) (n=25) received conventional TENS for one treatment, followed by two treatments of sham TENS (TENS, sham, sham). The second group (group 2) (n=25) received sham TENS for one treatment followed by two treatments of conventional TENS (sham, TENS, TENS). Each patient received three treatments of 20 minutes duration each. TENS was found to be associated with an improvement in the outcome of pain measured by the VAS scale compared with sham TENS (P = 0.0001) though the authors presented only their statistical analyses and not the original data, it is therefore difficult to draw conclusions from this paper.

There were several methodological issues which may have led to bias in this trial.

8.4.2 Health economics

No economic evaluations were identified for transcutaneous nerve stimulations (TENS).

8.4.3 Evidence statements for transcutaneous nerve stimulation (TENS).

Hyperlink to related recommendations

Evidence statements		Evidence to recommendations
8.4.3.1	*One RCT found that TENS was not associated with improvement in pain or function compared with sham TENS at 4 weeks (1+) (Deyo, R. A., Walsh, N. E., Martin, D. C. et al , 1990)*	Although one study was found showing an improvement in pain this was a small study using methodology that may have led to bias. There are no data on cost-effectiveness
8.4.3.2	*One RCT showed that TENS was not associated with improvement in activity, work, disability or depression compared with sham TENS at 4 weeks (1-) (Jarzem, P. F., Harvey, E. J., Arcaro, N. et al , 2005a)*	
8.4.3.3	*One small RCT found that TENS was associated with an improvement in pain compared with sham*	

	TENS after three treatments. (1-) (Jarzem, P. F., Harvey, E. J., Arcaro, N. et al , 2005b)	
8.4.3.4	*No cost effectiveness studies were identified for TENS*	

8.5 Lumbar Supports

Clinical question: what is the effectiveness of lumbar supports compared with usual care or sham treatment on pain, functional disability or psychological distress?

8.5.1 Clinical evidence

Literature searching retrieved 262 papers of which 2 were ordered for this question. One was excluded and one systematic review was included (van Duijvenbode, I., Jellema, P., van Poppel, M. N. M. et al , 2008).

One systematic review (van Duijvenbode, I., Jellema, P., van Poppel, M. N. M. et al , 2008) searched the MEDLINE, CINAHL, EMBASE and Cochrane Controlled Trials Register up to December 2006, and only included RCTs with subjects with non-specific low back pain. Specific pathologic causes for the low back pain, such as infection, neoplasm, metastasis, osteoporosis, rheumatoid arthritis, or fractures were excluded. Interventions of interest were any type of lumbar support, flexible and rigid. Studies of acute (< 6 weeks), sub-acute (6-12 weeks) and chronic (> 12 weeks) LBP were included. All trials were assessed for quality using a ten point checklist and the authors considered a study to be 'high quality' if it met five or more of the criteria. Outcomes of interest were pain, back-pain specific functional status, overall improvement and return to work.

Eight RCTs were included, involving a total of 1361 subjects. Three RCTs included only patients with chronic LBP, 4 studies included a mix of patients with acute, subacute and chronic LBP, and one did not give information about LBP duration. Number of participants ranged from 19 to 334 and duration of therapy from 3 to 8 weeks.

Results from one low quality study (Gibson, J. N. A and Ahmed, M, 2002) including people with chronic low back pain suggest limited evidence that lumbar supports are not more effective than no intervention for short term pain relief and improved functional status for patients with chronic LBP.

Out of 4 studies measuring pain as an outcome, only one low quality RCT reported a significant difference between the lumbar supports group and no intervention (Valle-Jones, J. C., Walsh, H., O'Hara, J. et al , 1992). The other three studies (Coxhead, C. E., Inskip, H., Meade, T. W. et al , 1981; Doran, D. M. and Newell, D. J., 1975); (Hsieh, C. Y., Phillips, R. B., Adams, A. H. et al , 1992), including a high quality one reported no significant difference. There is moderate evidence that lumbar supports are not more effective than no intervention for short term pain reduction for patients with a mix of (sub)acute and chronic LBP

Two low quality studies (Coxhead, C. E., Inskip, H., Meade, T. W. et al , 1981);(Doran, D. M. and Newell, D. J., 1975) (total N=790 people) measured overall improvement as the main outcome. Both studies reported no significant short term differences between groups.

Two low quality studies (Coxhead, C. E., Inskip, H., Meade, T. W. et al , 1981) (Valle-Jones, J. C., Walsh, H., O'Hara, J. et al , 1992) (total N=550) measured return to work as a main outcome. One study reported no significant difference in the short term between the groups, while the other found a significant difference in favour of the lumbar support group.

Three RCTs (Hsieh, C. Y., Phillips, R. B., Adams, A. H. et al , 1992; Penrose, K. W., Chook, K, and Stump, J. L, 1991; Valle-Jones, J. C., Walsh, H., O'Hara, J. et al , 1992) (1 high quality N=164 and 2 low quality total N=246) measured functional status as main outcome. They reported significant differences in short term functional status between the groups.

Overall, the authors concluded that the results showed there is limited evidence that lumbar supports are not more effective than no intervention for short term pain reduction and improved functional status for patients with chronic LBP. It remains unclear whether lumbar supports are more effective than no interventions for treating low back pain.

This was a well conducted systematic review with a very low risk of bias.

8.5.2 Health economics

No economic evaluations were identified for lumbar supports.

8.5.3 Evidence statements for lumbar supports

Hyperlink to related recommendations

Evidence statements	Evidence to recommendations
8.5.3.1 One systematic review of 6 randomised controlled trials in people with acute (< 6 weeks), sub-acute (6-12 weeks) or chronic (> 12 weeks) non-specific low back pain found that lumbar supports are not more effective than no intervention for short term pain relief, improved functional status and short term overall improvement for patients with chronic low back pain (1++) (van Duijvenbode, I., Jellema, P., van Poppel, M. N. M. et	Studies were not comparing lumbar supports with current usual care and therefore the GDG felt they could not make a recommendation based on these results. Included studies were also mixed populations of people with LBP. There are no data on cost-effectiveness Due to the limited evidence available the GDG's clinical opinion was that the use of lumbar supports could not be recommended.

al , 2008). *8.5.3.2 No cost effectiveness studies were identified.*	

8.6 Traction

Clinical question: what is the effectiveness of traction compared with usual care or sham treatment on pain, functional disability or psychological distress?

8.6.1 Clinical evidence

Literature searching retrieved 262 papers of which 5 were ordered for this question. Four were excluded and one systematic review was included (Clarke, Judy, van, Tulder Maurits, Blomberg, Stefan et al , 2006).

This systematic review included 25 RCTs (n=2206) that recruited male or female participants aged 18 years or older with LBP of acute, sub-acute or chronic duration with or without sciatica. Studies involving patients with LBP due to specific causes were excluded. All RCTs were assessed for quality using an 11 point quality score and the authors considered a study 'high quality' if it met six or more of the criteria.

The review reported on four primary outcomes (pain, back-pain specific functional status, global measure and return to work). A secondary outcome measure was side effects. The review did not look for the outcome of psychological distress, and neither did the included RCTs. Most of the RCTs included in this review did not provide sufficient data to allow statistical pooling, therefore, the authors conducted a qualitative analysis.

Results were separated according to whether the patients had LBP with sciatica or had LBP with or without sciatica and also by comparison.

LBP with or without sciatica

Three RCTs were included.

Two high quality RCTs (Beurskens, A. J., de Vet, H. C., Koke, A. J. et al , 1997; van der Heijden, G. J., Beurskens, A. J., Dirx, M. J et al , 1995) compared continuous traction with sham traction. One recruited a total of 25 patients with LBP > 3 months duration (van der Heijden, G. J., Beurskens, A. J., Dirx, M. J et al , 1995) while the other recruited a total of 151 patients with LBP > 6 weeks duration (Beurskens, A. J., de Vet, H. C., Koke, A. J. et al , 1997). Continuous traction was not associated with an improvement in the following outcomes compared with sham traction: pain, function, work absence, disability or overall improvement, with duration of follow-up ranging from 1-2 weeks to 6 months.

One low quality RCT (Borman, P., Keskin, D., and Bodur, H., 2003) compared physiotherapy with traction to physiotherapy alone. This study recruited a total of 42 patients with persistent LBP > 6 months duration or recurring episodes of LBP. Standard physiotherapy with traction was not found to be associated with an improvement in the following outcomes compared with standard physiotherapy only: pain, function, global recovery or satisfaction.

There was conflicting evidence on the effectiveness of autotraction. The first RCT compared autotraction plus corset with corset only (Larsson, U., Choler, U., Lidstrom, A. et al , 1980) in 82 people with lumbago-sciatica with or without neurological signs for > 2 weeks but < 3.5 months and found that autotraction was associated with an improvement in pain in the short-term (1-3 weeks) but not in the long term (3 month follow up). This study was assesssed as low quality.

The second RCT compared autotraction with usual care (bed rest and analgesics plus sham short-wave diathermy) (Lind, G., 1974) in 45 people with a history of several periods of LBP (mean duration of current episode in autotraction group = 57 days, mean duration in control group = 44 days) with or without neurological signs. Autotraction was found to be associated with an improvement in pain, change in

mean distance of pain radiation, straight leg raising, regression of neurological deficits, patient's evaluation and recovery (based on all measures) compared with control. This study was also rated as low quality.

The third RCT was the only study judged of high quality, meeting 6 of the 11 quality criteria. This trial compared autotraction with sham traction in 29 people with LBP and radiating pain of mixed duration (18 had pain > 12 weeks, 11 < 12 weeks). Autotraction was not found to be associated with an improvement in pain or physical measures compared with sham traction.

This was a well conducted systematic review. The results for studies involving mixed groups of patients with and without sciatica were quite consistent, but results were inconsistent for the effectiveness of autotraction.

8.6.2 Health economics

No economic evaluations were identified for traction.

8.6.3 Evidence statements for traction

Hyperlink to related recommendations

Evidence statements		Evidence to recommendations
8.6.3.1	*One systematic review was identified that included 25 randomised controlled trials in people with acute (< 4 weeks), sub-acute (4-12 weeks) or chronic (> 12 weeks) non-specific low back pain treated with traction. In a mixed population strong evidence was found that*	GDG agreed that there was little evidence of effectiveness and enough risk of harm to warrant a recommendation that traction should not be used. There are no data on cost-effectiveness

	continuous traction was not associated with an improvement in the outcomes of pain, function, overall improvement or work absenteeism compared with sham traction or no treatment. Limited evidence was found that physiotherapy with continuous traction did not confer benefit compared with physiotherapy alone. Nine of the twenty five trials reported data on adverse events; two stated that there were no adverse events while seven found traction to be associated with an increase pain or aggravation of symptoms compared with control. (1++) (Clarke, Judy, van, Tulder Maurits, Blomberg, Stefan et al , 2006)	
8.6.3.2	*No cost effectiveness studies were identified.*	

1

9 Psychological interventions and mixed packages of care (combined physical and psychological interventions)

9.1 Introduction

In this chapter the GDG considered the evidence for packages of care that were characterised by including both physical activity/exercise and psychological interventions. The decision for inclusion as a mixed package of care was based upon the reported content of the intervention rather than the profession of the practitioner delivering the intervention. It was difficult to determine in many studies which professions were involved in programme delivery. The intensity and duration of the interventions varied considerably between studies. Some interventions were delivered primarily by physiotherapists and others were delivered by a combination of professions. The GDG considered studies to be mixed packages of care or Complex Physical and Psychological (CPP) interventions if the content was broadly similar to that recommended in the "Recommended Guidelines for Pain Management Programmes for Adults" issued by the British Pain Society.

Psychological therapies as a monotherapy were also considered as part of this section.

The GDG recognised the heterogeneity of the types of programmes in this section. Previous reviews undertaken in the development of this guideline had suggested that intense, and by implication expensive, programmes of long duration afforded no extra benefit over brief interventions for those who were assessed and identified at low or moderate risk of a poor outcome; only those at high risk of a poor outcome benefited from intense programmes. For this reason the GDG decided to look at the literature on screening to inform which patients should be referred for intensive treatments and when. The Health Economic implication of this are also considered and have informed the treatment pathway.

9.2 Recommendations for combined physical and psychological interventions

9.2.1 Consider referral for a combined physical and psychological treatment programme for patients who have high disability and/or significant psychological distress after having received less intensive treatments.

9.3 Psychological Screening

Clinical question: is psychosocial/psychological screening effective/cost effective at identifying which patients may gain the greatest benefit from either general or specific treatments?

9.3.1 Clinical evidence

One RCT invited people to participate who had a permanent job and had been sick-listed with musculoskeletal pain for 50% of the time during the previous 8 weeks, or those who had been sick-listed with musculoskeletal pain for at least 2 months per year for the last 2 years (Haldorsen-Ellen, M. Håland, Grasdal, Astrid L., Skouen, Jan Sture et al , 2002) Of 1988 patients approached 654 were included, (1175 declined to join and 159 were excluded). Of these 391 were in the intervention groups and 263 were in the control group.

The participants were screened using a psychological questionnaire and a physiotherapy examination. to produce 3 groups according to their prognosis to return to work: good, medium and poor prognosis. These 3 groups were then randomised into 3 more groups for the type of treatment they would receive: ordinary treatment (control group), light multidisciplinary treatment and extensive multidisciplinary treatment. The outcome was the time taken to return to work. For those with a good prognosis of returning to work the type of treatment did not affect the time taken to return to work making ordinary treatment the best choice, (after 14 months 63% had returned to work). For those with a medium prognosis of returning to work, the light multidisciplinary treatment was most effective (64% had returned to work after 14 months). For those with a poor prognosis of returning to work the

extensive multidisciplinary treatment was most effective (55% had returned to work after 14 months).

This was a well conducted RCT with a low risk of bias

9.3.2 Health economics

~~No economic evaluations were identified for psychosocial screening~~

One cost benefit study (Haldorsen-Ellen, M. Håland, Grasdal, Astrid L., Skouen, Jan Sture et al , 2002) and one cost effectiveness study (Skouen, J. S., Grasdal, A. L., Haldorsen, E. M. H. et al , 2002) were found for answering whether screening for predicting outcome was cost effective. Both studies were excluded for this question. They were, however, included in the modelling to estimate the cost effectiveness of combined physical and psychological interventions. For further information please see section 9.4.

9.3.3 Evidence statements for psychosocial screening

Evidence statements		Evidence to recommendations
9.3.3.1	*One well conducted RCT used a psychosocial screening instrument in adults with non-specific back pain to identify adults with a good, medium or poor prognosis for return to work. The screening instrument also included a physical assessment. Each category was randomised to receive one of three*	The study found that people who, at baseline, had a poor prognosis who had more extensive multidisciplinary therapies were more likely to return to work; but that for those with a good prognosis a low-intensity treatment was just as effective as an intensive treatment one. There is evidence from one RCT that screening for poor prognosis for return to work aids in identifying a group who gain greater benefit from

	different treatments: ordinary, light multidisciplinary or extensive multidisciplinary. At 14 months follow up for the outcome of return to work, adults with a good prognosis did equally well in each treatment group. Adults with a medium prognosis did equally well in the light or intensive multidisciplinary treatment groups. Adults with a poor prognosis only had a similar percentage of return to work to the other prognosis groups if they received the multidisciplinary intervention.(1+) (Haldorsen-Ellen, M. Håland, Grasdal, Astrid L., Skouen, Jan Sture et al , 2002)	intensive multidisciplinary treatments compared to less intensive treatments. The GDG agreed that there is some evidence that screening for those with a poor prognosis should be considered in order to inform treatment decisions and that consideration should be given to referring this group for more intensive treatments . The GDG noted that this paper was specific to a sick listed population and the only outcome reported was return to work. The group noted that this study also Identified those who were unlikely to need complex interventions. However at present there is insufficient evidence to make recommendations for the use of any specific screening instrument. The GDG agreed that a research recommendation should be made regarding what screening tools should be used to inform treatment decisions. Health economics analysis - GDG agreed that the paper was not applicable to our population as the
9.3.3.2	*No relevant economic evaluations were identified for psychosocial screening*	

	group were those sick listed. The costing perspective is societal and not health service, also not UK and therefore not applicable for this guideline. GDG agreed to reject the economic analysis presented in this paper but that that there was sufficient evidence that those with poor prognosis may gain better outcomes from earlier assessment. Data from this paper was able to be used to inform the economic model developed for the cost effectiveness of combined packages of physical and psychological therapies

9.4 Psychological Interventions

Clinical question: what is the effectiveness of psychological interventions compared with usual care on pain, functional disability or psychological distress?

9.4.1 Clinical evidence

Literature searches retrieved 718 papers, of which 35 were ordered. A total of 2 RCTs were extracted. Two recent systematic reviews were excluded for this question: a systematic review (Ostelo, R. W. J. G., van Tulder, M. W., Vlaeyen, J. W. S. et al , 2005) was excluded because included studies were too heterogeneous (relevant studies were ordered and assessed separately). a meta-analysis (Hoffman, B. M., Papas, R. K., Chatkoff, D. K. et al , 2007) was excluded because papers included in it were too heterogeneous in interventions (some included surgery, massage, mainly combined physical and psychological interventions) and population (some were post-surgical populations).

One randomised controlled trial compared the effects of a cognitive-behaviour intervention aimed at preventing chronicity with two different forms of information (Linton, S. J. and Andersson, T., 2000). Patients aged 18-60 with <3 months cumulative sick leave during the past year were recruited from local primary care facilities and randomly assigned to a cognitive-behaviour group intervention (n=107), a pamphlet group (n=70) and an information package group (n=66). Participants in the CBT group received 6 sessions of 2 hours duration once a week for 6 weeks. The programme was carried out in groups of 6-10 people. Each session consisted of a short review of homework, an introduction to the topic for the session; structured problem-solving followed by exercise. Subsequently new skills were introduced, and participants were assigned homework. Patients in the pamphlet group received a previously evaluated pamphlet to read concerning back pain. It provided straightforward advice about the best way to cope with back pain by remaining active and thinking positively. It was aimed at preventing fear avoidance and promoting coping. Patients in the information package intervention group received a packet of information once a week for 6 weeks. The number and timing of the packages was meant to match that number of sessions the CBT group received. The material used more traditional sources of information and was based on a back school approach.

Although pain significantly improved in the CBT and pamphlet groups it did not significantly differ between groups. Fear avoidance decreased significantly in all groups but no significant between-group difference was observed.

This was a well conducted RCT with a low risk of bias.

One randomised controlled trial evaluated a cognitive-behaviour programme to enhance back pain self care (Moore, James. E., Von Korff, Michael., Cherkin, Daniel. et al , 2000). The authors evaluated a brief intervention for primary care back pain patients designed to provide accurate information about back pain. Patients enrolled in a large health maintenance organisation in the USA were invited to participate in an educational programme to improve back pain self care skills 6-8 weeks after a primary care back pain visit. Patients (n=226) were randomly assigned to a Self Care intervention (n=113) or to usual care (n=113) and were assessed at baseline, 3-, 6-, and 12-months. The intervention involved a 2-session self care group with the group leader, a psychologist experienced in pain management. Within 2 weeks of the group session each participant met individually with his or her leader for approximately 45 minutes to develop a personal self care plan. Leaders made one brief (3minute) follow up phone call to each participant to encourage continued action on the self care plan. The intervention was supplemented by educational materials (book and videos) supporting active management of back pain. The control group received usual care supplemented by a book on back pain care.

Results showed a greater reduction in average pain intensity for the self care group than the usual care group, but the difference was significant only at 6 months. The self care group showed significantly lower fear-avoidance scale scores compared to the usual care group at all follow-up periods. At 3 months, the self care group reported significantly less disability than the usual care group on the Roland Disability Questionnaire. The effect was no longer significant at 6 or 12 months. The self care group did not show more favourable mental health outcomes than the usual care group.

This was a well conducted RCT with a low risk of bias.

9.4.2 Health economics

No economic evaluations were identified for psychological therapies.

9.4.3 Evidence statements for psychological interventions

Evidence statements		Evidence to recommendations
9.4.3.1	*One RCT compared a cognitive behavioural treatment to information/pamphlet and found no significant difference in improvement in pain at 12 months follow-up (1+) (Linton, S. J. and Andersson, T., 2000).*	A number of randomised controlled trials presented were excluded by the GDG because they were not considered to be psychological interventions, or patients had had other co-interventions or were not compared with usual care. This decision was reached by consensus.
9.4.3.2	*One RCTs compared a self care intervention to usual care. The intervention was psychologist-led. Disability was significantly reduced at 3 months, and pain was significantly reduced at 6 months follow-up. No effect was found on mental health in either study (1+) (Moore, James. E., Von Korff, Michael., Cherkin, Daniel. et al , 2000)*	The GDG agreed that there is evidence in pain management literature that there is benefit from psychological interventions on distress . References to this literature were supplied and the papers reviewed but no studies could be found that showed a significant effect in patients with low back pain as the main presenting condition.
9.4.3.3	*No cost effectiveness studies were identified for psychological therapies*	There is limited evidence to support the use of psychological interventions

	on non specific low back pain. One study evaluated a brief intervention which included a 45 minute session with a psychologist which the group agreed should be included. This decision was reached by consensus. GDG considered that the study had patients who were more severely affected by their pain and therefore a recommendation should be made for this particular group. No evidence was found for longer treatments of psychological interventions delivered in the absence of concurrent or combined physical therapy. GDG decided by consensus that a recommendation be made for a combined treatment package rather than a standalone psychological intervention. The group agreed that this was an area where further research was required.

9.5 Combined Physical and Psychological Therapy

Clinical question: what is the effectiveness of combined interventions (comprising of physical and psychological therapies) compared with usual care/other interventions on pain, functional disability or psychological distress?

9.5.1 Clinical evidence

Literature searching identified 2193 papers; 47 were ordered and 11 RCTs (several with follow-up studies) were included.

One randomised controlled trial (Alaranta, H., Rytokoski, U., Rissanen, A. et al , 1994) assessed the effectiveness of an intensive physical and psychosocial training programme, described as Functional Restoration (FR) on patients with low back pain. This treatment was compared to a less intensive programme called current national type (CNT) during 15 to 20 hrs per week for 3 weeks versus 37 hours per week for 3 weeks for FR. The FR programme (n=152) consisted of cardiovascular exercises, muscular strength exercises, relaxation and rest periods, stretching and CBT group work. The CNT (n=141) consisted of a number of passive physical therapies, exercises, and back school education. The primary outcome appeared to be sick leave days. Secondary outcomes included pain and disability and psychological outcomes. Patients were aged between 30 and 47 and had pain for at least 6 months. Pain and disability improved more over 1 year in the FR group compared to the CNT group and the differences were statistically significant. Differences between the groups with regard to psychological outcomes were small. The process of randomisation was poorly reported. After randomisation and before treatment started, 85 patients (22%) were excluded because it was considered they were unfit to participate in the programmes, although the numbers excluded from each group were not reported. No sample size calculation was reported.

This was a RCT with a high risk of bias.

One randomised controlled trial (Bendix, A. F., Bendix, T., Ostenfeld, S. et al , 1995) aimed to determine if an active, multidisciplinary, intensive treatment programme

(Functional Restoration (FR) was superior to other active but less intensive programmes at 4 months. Participants (n=132), sick-listed or without a job, were randomised to one of three programmes. FR consisted of attendance at the Copenhagen Back Centre, University Hospital, for 39 hours per week (8am to 4pm) for 3 successive weeks. This was followed by 1 day a week for the next 3 weeks. It included aerobics, weight training, work simulation, relaxation, psychological group work, stretching, theoretical class and recreational activities. Physical training (PT) comprised aerobics, weight training and back school in 2- hour sessions twice a week for 6 weeks. Psychological and physical training (PPT) comprised physical training as well as pain management in 2-hour sessions twice a week for six weeks. The primary outcome was the return-to-work rate. Secondary outcomes included, among other measures, pain and function. Results showed that the FR programme was superior to the less intensive treatments and that differences between groups were statistically significant. Results on one, two and five year follow-up are reported separately (Bendix, A. E., Bendix, T., Haestrup, C. et al , 1998; Bendix, A. F., Bendix, T., Labriola, M. et al , 1998; Bendix, A. F., Bendix, T., Lund, C. et al , 1997). The follow-up periods were defined as the first Monday after three weeks of treatment, regardless of the treatment duration, plus 13 months, two years and five years respectively. They found statistically significant differences in pain scores and function scores between the three groups in favour of intensive FR at both one and two years. At five years they found a statistically significant difference in function, but not pain in favour of FR.

No sample size calculation was reported. The process of randomisation was not described.

This was a RCT with a high risk of bias

One randomised controlled trial (Bendix, A. F., Bendix, T., Vaegter, K. et al , 1996) reports on whether a 3-week, 39 hours per week, multidisciplinary programme based at the Copenhagen Back Center would affect the return-to-work rate, the number of days of sick leave used, the number of contacts with health care providers, pain and disability levels and muscle endurance in patients with chronic LBP (at least 6 months). Fifty -five participants were randomised to the intervention group and 51 to the control group. The latter could choose to go anywhere else for treatment or

choose to have no treatment. A typical day for the intervention group consisted of aerobics, weight training, work simulation, relaxation, psychological group work, stretching, theoretical class, and recreation. At study end (4 months after treatment ended) the intervention group had improved more with regard to pain and disability than the control group and the differences were statistically significant. Results from the two and five year follow-up are reported separately (Bendix, A. E., Bendix, T., Haestrup, C. et al , 1998; Bendix, A. F., Bendix, T., Labriola, M. et al , 1998). The follow-up periods were defined as the first Monday after three weeks of treatment, regardless of the treatment duration, plus two years and five years respectively. They found no statistically significant differences in pains cores or function scores between the two groups at two and five years follow-up. The study randomisation was not described and no sample size calculations are reported.

This was a RCT with a high risk of bias.

One randomised controlled trial (Bendix, T., Bendix, A., Labriola, M. et al , 2000) compared an intensive multidisciplinary functional restoration(FR) programme (n=64) with an intensive outpatient-based physical training (PT) programme (n=74). FR consisted of 3 weeks (39 hours per week) aerobic exercises, fitness machine exercises, occupational therapy, group psychology therapy, stretching exercises, back pain theory and recreational activities. PT consisted of aerobic and strengthening exercises 1.5 hours, three times per week for 8 weeks. At 1 year no difference was found between groups with regard to work capability, sick leave, health care contacts, back pain, leg pain or self-reported activities of daily living. There was a statistically significant improvement in quality of life (as measured by the individual on a 5-point scale) in favour of the FR group. This study did not specify a primary outcome, and did not present a sample size calculation. The drop out rate was relatively high.

This was a RCT with a high risk of bias

One randomised controlled trial (Corey, D. T., Koepfler, L. E., Etlin, D. et al , 1996) compared the efficacy of a limited functional restoration(FR) programme over “usual care”. The FR group (n=100) spent a maximum of 6.5 hours per day over an average of 33 days doing a multidisciplinary therapy: stretching, strengthening and endurance

building, work hardening, and education in posture and body mechanics. They also had group education and counselling. They were taught active pain management strategies, stress management and a multidimensional theory of pain. The usual care group (n=100) were discharged to the care of their physician with a letter advising proactive management including advice to encourage activity despite pain. The FR group reported less pain at 18 months compared to the usual care group and the difference was statistically significant. This study did not specify a primary outcome, and did not present a sample size calculation. The drop out rate was relatively high.

This was a RCT with a high risk of bias

A randomised controlled trial based at two London hospitals (Critchley, D. J., Ratcliffe, J., Noonan, S. et al , 2007) compared the effectiveness of three kinds of physiotherapy in participants with chronic LBP (> 12 weeks duration) at 18 months follow-up. Individual physiotherapy (IP) consisted of a combination of joint mobilizations, joint manipulation, and massage. It also included taught exercises for performing at home, and usually back care advice. Up to 12 sessions of around 30 minutes were permitted. Spinal stabilization (SS) consisted of specific muscle training followed by group exercises for SS. Up to 8 sessions of 90 minutes each were allowed. The pain management programme (PM) consisted of a combination of structured back pain education with group exercises (strengthening, stretching and light aerobic). A CBT approach was used. The program consisted of a maximum of 8 sessions of 90 minutes each.

The number of participants in each group were 71(IP), 72(SS) and 69(PM). They were over 18 years and had a good command of English. Average time since their first episode of back pain was at least 5 years. Primary outcome was the RMDQ. Secondary outcomes included pain score, EQ-5D and time off work. At 18 months all three groups had improved on the RMDQ and the pain score from baseline, and there were no significant differences between the three groups. Attrition was 17% in the IP group, 25% in the SS group and 32% in the PM group.

This was a RCT with a high risk of bias.

One randomised controlled trial (Friedrich, M., Gittler, G., Halberstadt, Y. et al , 1998) compared the effectiveness of an exercise+motivational programme (n=49) to an exercise only programme (n=49) in an RCT in participants aged 20 to 60 years. Outcomes included pain and disability at 12 months. Both groups received an individualised, gradually increased, exercise programme consisting of 10 sessions of 25 minutes each. The intervention group also took part in a motivational programme (length and duration of sessions not reported) which comprised extensive counselling, reinforcement techniques, oral and written agreements between patient and therapist, and maintaining an exercise diary to discuss with therapist. There was a statistically significant improvement in terms of pain and disability at 12 months in the motivational group compared to the exercise along group. Results from 5 years follow-up (Friedrich, M., Gittler, G., Arendasy, M. et al , 2005) showed pain intensity to be much lower for the motivational group (15 versus 45 for the control group) and the difference was statistically significant. Mean differences for the groups for disability were not reported. A regression analysis was conducted and from that the study reported that the cumulative effect in the motivational group was twice that in the control group. The study had a high risk of bias: randomisation not described, no primary outcome specified and no sample size calculation was reported. In addition, the drop out rate was high.

One randomised controlled trial (Kääpä, Eeva Helena, Frantsi, Kirsi, Sarna, Seppo et al , 2006) compared the effectiveness of a semi-intensive multidisciplinary rehabilitation (MR) for patients with chronic low back pain with individual physiotherapy in an outpatient setting in Finland. All the participants were women employed as healthcare and social care professionals with non-specific chronic LBP. The MR programme (n=59) consisted of 70 hours over 8 weeks. It comprised psychological CBT stress management, a back school programme, instruction in work ergonomics, and a physical exercise programme. The control group (n=61) received 10 hours of individual physiotherapy over 6 to 8 weeks. Each session included passive pain treatment and 15 to 20 minutes of light active exercise. In addition, they were given a home-exercise programme and advised to gradually increase their daily activities. There were no significant differences between the intervention and control group at 24 months with regard to pain intensity, disability or depression.

This was a well conducted RCT with a low risk of bias.

One randomised controlled trial (Keller, S., Ehrhardt, Schmelzer S., Herda, C. et al , 1997) compared a multidisciplinary rehabilitation (MR) programme (n=36) with a waiting list control group (n=36). The MR programme consisted of 18 2-hour group meetings (3 per week) in addition to 18 individualized training sessions (two patients with one trainer) of 30 minute duration in an outpatient setting. Treatment was administered by a multidisciplinary team including physicians and physiotherapists with training in pain management strategies, and supervised by a clinical psychologist. It included elements of education, relaxation and exercise. For ethical reasons the study investigators were not allowed to withhold the MR therapy from the controls, and therefore the control group received the same rehabilitation programme after the intervention group had finished theirs. Consequently no 6-month follow-up comparisons between the intervention and control groups could be conducted because both had received the same treatment by this time. The only comparative data results show that immediately post-treatment (before the controls were treated) pain intensity and disability were significantly reduced as a consequence of the treatment. The randomisation process was not described, no primary outcome was specified and the dropout rate was high.

This was a RCT with a high risk of bias.

One randomised controlled trial (Smeets, Rob. J. E. M., Vlaeyen, Johan. W. S., Hidding, Alita. et al , 2008) compared combined therapy (CT) of graded activity and problem solving (GAP) plus active physical training (APT) with either GAP or APT alone. Patients aged 18 to 65 with LBP > 3 months were recruited into one of three groups GAP (n=53), APT (n=58) and CT (n=51). APT included 3 sessions per week over 10 weeks. Each session consisted of 30 minutes aerobic training and 75 minutes of strength and endurance training supervised by a physiotherapist. GAP started with graded activity (GA): 3 group sessions followed by a maximum of 17 individual sessions of 30 minutes. Problem solving training (PST) was lead by a clinical psychologist and consisted of 10 sessions of 1.5 hours with a maximum of 4 patients at a time. Although patients in all three groups improved over time, at 12 months, the level of disability, main complaints, pain, depression and performance tasks did not differ significantly between treatments.

This was a well conducted RCT with a low risk of bias.

One randomised controlled trial (Tavafian, Sedigheh Sadat, Jamshidi, Ahmadreza, Mohammad, Kazem et al , 2007) compared a back school (n=50) with usual care which consisted of medication (paracetamol, NSAID, and chlordiazepoxide) (n=52) for Iranian women with LBP >90 days. Follow-up was at 3 months. The back school consisted of a four-day, five-session programme in which women were “educated” by an educator (beliefs about LBP), a clinical psychologist (coping skills) and a physical trainer (stabilizing and strengthening exercises). This group were also taking the same medication as the usual care group. The outcome of interest was quality of life as measured by the SF-36 which includes two dimensions that measure physical functioning and bodily pain. The study reports that the difference between the groups was statistically significant in favour of the back school but does not present the results of that analysis or any p values.

This was a RCT with a high risk of bias.

9.5.2 Health economics

The GDG was interested in combined physical and psychological interventions provided on an intensive and less intensive level. The literature was reviewed and further modelling considered for this question.

Evidence review

Literature searching retrieved 508 papers of which 2 were ordered. Initially included for the educational intervention question, the GDG felt it was more appropriate to use this evidence for the combined programmes covered by this question. One was included: this was a UK-based cost-effectiveness study of three interventions for treatment of low back pain. This paper was deemed useful for helping to answer the question concerning low intensity CPP (Critchley, D. J., Ratcliffe, J., Noonan, S. et al , 2007).

This cost utility analysis was conducted alongside a pragmatic randomized clinical trial to compare three types of physiotherapy commonly used to reduce disability in chronic low back pain (Critchley, D. J., Ratcliffe, J., Noonan, S. et al , 2007). The study randomized 212 patients aged 18 years or older, who had LBP of more than

12 weeks to: individual physiotherapy (n=71) in which patients were assessed and treated according to assessment findings for up to 12 sessions of around 30 minutes; spinal stabilisation (n=72) which consisted of muscle training and group exercises over a maximum of 8 sessions of 90 minutes; and pain management (n=69) which consisted of a combination of structured back pain education with group general strengthening, stretching and light aerobic exercises. A CBT approach was used. The programme consisted of a maximum of 8 sessions of 90 minutes each. For full details on the clinical results, please see section 9.4.1.

The number of QALYs gained over 18 months was estimated using EQ-5D. The costing perspective was that of the UK health service. Direct medical costs were measured by collecting public health service (NHS) utilisation data for the previous 6 months to each assessment from physiotherapy notes and from participants using the interview-based questionnaire Client Services Receipt Inventory. Units costs (£) were for 2003 to 2004, obtained from the Personal Social Services Research Unit Database, NHS reference costs, and British National Formulary. Costs and outcomes occurring during the 12- to 18-month period were each discounted at 3.5%, the current recommended rate for public sector projects.

Sensitivity analyses were conducted to investigate effects of missing data and high-cost outliers.

Results (base case)

The mean costs (Standard Deviation) of the three therapies were £474(840) for individual physiotherapy, £379(1040) for spinal stabilization and £165 (202) for pain management. Mean (Standard Deviation) QALY gains after 18 months were 0.99(0.27) for individual physiotherapy, 0.90(0.37) for spinal stabilization and 1.00 (0.28) for pain management. Overall, pain management is less costly and marginally more effective than the other interventions. Relative to spinal stabilisation, individual physiotherapy is marginally more effective with a mean incremental cost effectiveness ratio of £1055.

The cost-effectiveness acceptability curves show the probability of cost-effectiveness for the three interventions for a range of prices a health commissioner might be prepared to pay per QALY. As pain management is marginally most effective and is

associated with lowest healthcare costs, it is most likely to be cost-effective at all costs per QALY.

Sensitivity analysis

The study reported on two sensitivity analyses. 1) The exclusion of three patients (two from spinal stabilisation and one from individual physiotherapy) who incurred unusually high costs because they received spinal fusion or decompression surgery. 2) The imputation of missing EQ-5D data and cost data for all patients with endpoint clinical data.

Sensitivity analysis showed that imputing missing data made little difference to the results. However, excluding the three patients who received spinal surgery markedly reduces the associated costs of the spinal stabilization arm to £187.54(198.65), increases the incremental cost-effectiveness ratio for individual physiotherapy relative to this (£3543), and the differences in total mean public health service costs across the three groups become significant (p=0.007).

In the base case analysis a physiotherapist-led pain management programme was marginally the most effective and was associated with lowest healthcare costs, and is therefore most likely to be cost-effective at all costs per QALY. Probabilistic sensitivity analyses showed that at a ceiling of £20,000 per QALY the probability that a pain management programme is cost effective is approximately 70%. Sensitivity analysis which imputes missing values or excludes statistical outliers does not alter this result.

Discussion

After careful discussion of the uncertainty inherent in the underlying trials, the GDG decided that the presented evidence on the low intensity CPP was not sufficient to conclude that low intensity CPP would be clinically and cost effective in an NHS context.

With respect to intensive CPP interventions, there were no economic papers found to inform the GDG on cost effectiveness of such an intervention. The GDG asked whether there would be some evidence when using a broader pain management

population. A search did not find suitable papers to inform on the cost effectiveness using this population (Gobel, H., 2001; McCracken, L. M. and Turk, D. C., 2002; Thomsen, A. B., Sorensen, J., Sjogren, P. et al , 2001; Turk, D. C., 2002; Turk, D. C. and Okifuji, A., 1999; Vetter, T. R., 2007a; Vetter, T. R., 2007b).

Due to the lack of evidence for a significant benefit of intensive CPP programmes from high-quality studies, a recommendation for routine use in the NHS has to be further tested. As it remained uncertain whether such high intensity CPPs were likely to be a cost-effective use of NHS resources, further modelling was done.

9.5.2.1 Modelling the Cost-effectiveness of intensive combined psychological and physical (CPP) programmes

The question addressed by this model concerns referral to a combined programme involving psychological and physical interventions for patients with high levels of distress, judged to be at risk of developing chronic pain. There is no published cost-effectiveness evidence for these intensive CPP programmes, and the clinical evidence is limited (see 9.4.1) It was not possible to build a cost-effectiveness model based on these studies identified in the guideline review.

A decision tree model was built, based on the results from the Haldorsen study and other data and assumptions, to estimate the relative costs and health effects (QALYs) for alternative treatment strategies. Probabilistic and a number of univariate sensitivity analyses were carried out in order to quantify and estimate the uncertainty of the results. Results from the economic modelling showed that for those people with poor prognosis where a monotherapy has failed, a more intensive CPP yields more QALYs and would be most cost effective compared to no CPP.

The full write up of the model can be found in Appendix E.

9.5.3 Evidence statements for combined physical and psychological interventions

Evidence statements	Evidence to recommendations
CPP Low intensity: *9.5.3.1 One RCT compared a pain management programme to individual physiotherapy and spinal stabilisation. After 18 months no significant differences between groups was observed. (Critchley, D. J., Ratcliffe, J., Noonan, S. et al , 2007) (1-)* *9.5.3.2 One RCT compared a Back School to usual care and reports significant difference between back school and controls (although the results of that analysis are not presented). (Tavafian, Sedigheh Sadat, Jamshidi, Ahmadreza, Mohammad, Kazem et al , 2007)(1-)* CPP High intensity: *9.5.3.3 Four RCT's compared Functional Restoration*	GDG made a distinction between lower intensity combined physical and psychological therapies (CPP) and higher intensity CPP; Studies were classified as high intensity when the intervention was over at least one full day or at least five sessions a week over at least three weeks. CPP Low intensity: One well conducted study shows benefit but in non UK all female population. One UK study was identified. that had less intensive interventions for a less disabled group and demonstrated cost effectiveness (8 sessions of 90 mins). However the study had a high attrition rate and showed no significant difference between groups. GDG considered that the evidence available was not sufficient to make a recommendation for low intensity CPP. CPP High intensity: Population in the studies for more intensive interventions were more

	programmes to other interventions/usual care. Three of these RCT found significant improvements in pain and disability for patients in the FR group compared to less intensive interventions (Alaranta, H., Rytokoski, U., Rissanen, A. et al , 1994) (1-) ;(Bendix, A. F., Bendix, T., Ostenfeld, S. et al , 1995)(1-);(Bendix, A. F., Bendix, T., Lund, C. et al , 1997)(1-);(Bendix, A. F., Bendix, T., Labriola, M. et al , 1998) (1-);(Bendix, A. E., Bendix, T., Haestrup, C. et al , 1998)(1-) or usual care (Corey, D. T., Koepfler, L. E., Etlin, D. et al , 1996)(1-).	severely disabled by their condition and more were off work. Programmes within the intensive studies were usually for more than 40 hours. The format of the interventions delivered varied widely between trials and there is insufficient evidence to select one format over another but it is possible to make a statement regarding the total number of sessions delivered. The GDG discussed the methodology used and reliability of those studies showing a significant benefit in outcomes compared with the two studies achieving a higher grading methodologically which failed to show a benefit.. The GDG considered that the high quality study from a previous question on psychosocial screening which found that screening for prognosis aids in identifying who may gain greater benefit from intensive or less intensive treatments may be relevant to this question (Haldorsen). However the outcome reported was return to work. No economic evidence was found for
9.5.3.4	*No significant difference in pain or function was observed between a FR programme and physical training (Bendix, T., Bendix, A., Labriola, M. et al , 2000)(1-)*	
9.5.3.5	*Three RCTs compared multidisciplinary programmes to*	

	physiotherapy or no treatment. One study showed significantly better pain and function scores in the multidisciplinary programme (Bendix, A. F., Bendix, T., Vaegter, K. et al , 1996)(1-) ;(Bendix, A. F., Bendix, T., Labriola, M. et al , 1998)(1-) . One found no significant differences between groups for pain, disability or depression (Kääpä, Eeva Helena, Frantsi, Kirsi, Sarna, Seppo et al , 2006)(1+), and the third did not conduct statistical analysis on between-group differences (Keller, S., Ehrhardt, Schmelzer S., Herda, C. et al , 1997)(1-)	the more intensive programmes. An estimate of the cost effectiveness from the clinical studies was possible from only one study that had used an outcome measure that could be used to estimate QALYs (Smeets). This showed the QALY gain with CPP would be lower than the control. The GDG asked the methods team to go back to the Haldorsen study included for the psychosocial screening question to see if data could be used to inform their decision. The economic model presented to the GDG was based on data taken from the Haldorsen paper. The outcome measure of return to work was interpreted to mean recovery and this was converted into a suitable QALY. The prognostic indicators from the trial were used to build a decision tree which compared six strategies: 1) no CPP, 2) CPP immediately for people with poor prognosis (p/p) only, 3) CPP after a monotherapy (LMT), 4) CPP after LMT for p/p only, 5) CPP first line for p/p and after LMT for people with a good or medium (g/m) prognosis who don't respond and 6) CPP for all. At base case, comparator 4 yields
9.5.3.6	*One RCT compared an exercise + motivational programme to exercise-only. At 12 months follow-up pain and function were statistically significantly improved in the intervention group. After 5 years follow-up only pain remained statistically*	

	significantly improved in the intervention group compared to the exercise-only group. (Friedrich, M., Gittler, G., Arendasy, M. et al , 2005; Friedrich, M., Gittler, G., Halberstadt, Y. et al , 1998) (1-)	more QALYs and would be most cost effective compared to no CPP. This strategy would be to start as light programme and then onto a more intensive programme for those with a poor prognosis have not benefited from less intensive interventions The GDG agreed that from the limited clinical evidence and the economic model presented CPP should be made available to those who continue to report high levels of disability and/or psychological distress after one or more previous treatments in addition to medical care and information.
9.5.3.7	*One well conducted RCT compared a combination of physical training and graded activity with problem solving intervention to the individual treatments. No significant difference was observed between the groups at 12 months follow-up. (Smeets, Rob. J. E. M., Vlaeyen, Johan. W. S., Hidding, Alita. et al , 2008) (1+)*	
9.5.3.8	*One economic evaluation found in the base-case analysis a physiotherapist-led pain management programme is associated with lowest healthcare costs and likely to be most cost effective at all costs per QALY. Sensitivity analysis found that at a*	

	ceiling of £20k per QALY the probability that a pain management programme is cost effective is 70% (Critchley, D. J., Ratcliffe, J., Noonan, S. et al , 2007)	

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10 Pharmacological therapies

10.1 Introduction

This review considered the main drug treatments used for non-specific low back pain; opioid and non-opioid analgesics, antidepressants (tricyclic and others) and non-steroidal anti-inflammatory drugs (NSAIDs). These are mainly oral preparations. The use of injected therapeutic substances is considered elsewhere in this guideline. When considering recommending NSAIDs the prescriber should consider recommendations presented in the NICE guidance on the management of Osteoarthritis (National Institute for Health and Clinical Excellence., 2008).

The NICE osteoarthritis guideline applies specifically to people aged 45 or over who have osteoarthritis. The balance of risks and benefits may be different in people with low back pain, many of whom are aged less than 45. In particular, co-prescribing a proton pump inhibitor to reduce upper gastro-intestinal side-effects (PPI) may not always be necessary in younger people

10.2 Recommendations for pharmacological therapies

NSAIDS/COX-2

Hyperlink to related evidence statements

10.2.1 Advise the person to take regular paracetamol as the first medication option.

10.2.2 Consider offering non-steroidal anti-inflammatory drugs (NSAIDs) for short-term use when paracetamol is ineffective.

10.2.3 Give due consideration to the risk of side effects from NSAIDs in older people, and other patients at high risk of experiencing side effects.

10.2.4 When offering treatment with an oral NSAID/COX-2 inhibitor, the first choice should be either a standard NSAID or a COX-2 inhibitor (other

than etoricoxib 60 mg). In either case, these should be co-prescribed with a PPI, choosing the one with the lowest acquisition cost[9].

Opioids

Hyperlink to relevant evidence statements

10.2.5 Consider offering strong opioids for short-term use to people in severe pain.

10.2.6 Consider referral for specialist assessment for people who may require prolonged use of strong opioids.

10.2.7 Give due consideration to the risk of opioid dependence and side effects.

10.2.8 Offer an NSAID or opioid depending upon the individual risk of side effects and patient preference.

10.2.9 Consider offering mild opioids when regular paracetamol alone is ineffective.

10.2.10 Base decisions on continuation of mild opioids on individual response.

Antidepressants

Hyperlink to relevant evidence statements

10.2.11 Do not offer selective serotonin reuptake inhibitors (SSRIs) for treating pain.

10.2.12 Consider offering a trial of tricyclic antidepressants.

10.2.13 Start tricyclic antidepressants at a low dosage and increase up to the maximum antidepressant dose until therapeutic effect is achieved or unacceptable side effects prevent further increase. People starting on a tricyclic antidepressant should be reviewed at least monthly.

[9] This recommendation is from 'Osteoarthritis: the care and management of osteoarthritis in adults' (NICE clinical guideline 59).

10.3 NSAIDs

Clinical question: what is the effectiveness of oral NSAIDs compared with placebo, opioids, paracetamol or antidepressants on pain, functional disability or psychological distress?

10.3.1 Clinical evidence

Literature searching retrieved 927 papers of which 31 were ordered for this question. One of these, a systematic review, was included (Roelofs, P. D. D. M., Deyo, R. A., Koes, B. W. et al , 2008).Outcomes of interest were pain, disability, psychological distress and safety/adverse events.

The systematic review compared NSAIDs with placebo, paracetamol and opioids (Roelofs, P. D. D. M., Deyo, R. A., Koes, B. W. et al , 2008). The MEDLINE and EMBASE databases and the Cochrane Controlled Trials Register, issue 2, 2007 were searched up to June 2007. Randomised controlled trials and double-blind controlled trials were included. Subjects had to be aged 18-65 and treated for non specific LBP with or without sciatica. Studies of patients with acute (12 weeks or less) and chronic (more than 12 weeks) low back pain were included. Studies of subjects with low back pain caused by pathological entities such as infection, neoplasm, metastasis, osteoporosis, rheumatoid arthritis, or fractures were excluded. Sixty-five studies were included.

10.3.1.1 NSAIDs versus Placebo

Four studies on a chronic low back pain population were pooled (Berry, H., Bloom, B., Hamilton, E. B. et al , 1982; Birbara, C. A., Puopolo, A. D., Munoz, D. R. et al , 2003; Coats, T. L., Borenstein, D. G., Nangia, N. K. et al , 2004; Katz, N., Ju, W. D., Krupa, D. A. et al , 2003); a statistically significant effect in favour of NSAIDs was observed for the outcome of pain. The placebo group had fewer side effects than the NSAIDs group.

10.3.1.2 NSAIDs versus Paracetamol

One high quality study found limited evidence that NSAIDs are more effective for pain relief than paracetamol in patients with chronic LBP (Hickey, R. F., 1982). When

studies on acute low back pain and those on mixed populations were pooled (and one non-randomised study was also included in the meta-analysis) the paracetamol group had fewer side effects than the NSAIDs group.

10.3.1.3 NSAIDs versus Opioids

No studies comparing NSAIDs to opioids on patients with chronic low back pain were found. The systematic review compared NSAIDs to "other drugs".

The authors' overall conclusion is that NSAIDs are effective for short term global improvement in patients with chronic low back pain without sciatica, although the effects are small and that it is unclear if NSAIDs are more effective than simple analgesics and other drugs.

This was a well conducted systematic review with a low risk of bias, although few trials were included of 'chronic' low back pain (> 12 weeks duration) and in many instances it is unclear whether the studies classified as 'acute' (< 12 weeks duration of pain) are relevant to our population as the exact duration of pain is unspecified. In addition, many of the studies included were of low quality and short duration.

10.3.2 Health economics

No economic evaluations were identified for oral NSAIDS

10.3.3 Cox-2 inhibitors

For guidance on Cox-2 inhibitors refer to the NICE Guidance:

Osteoarthritis: the care and management of osteoarthritis in adults (number 59), 2008.

10.3.4 Evidence statements for NSAIDS/Cox-2

Evidence statements	**Evidence to recommendations**
	Paracetamol should normally be the

	first treatment option.
10.3.4.1 One systematic review was identified that included 65 trials in people with acute (< 12 weeks) or chronic (> 12 weeks) non-specific low back pain treated with traditional NSAIDs or COX–2 inhibitors. NSAID therapy was found to be associated with a reduction in pain intensity compared with placebo for chronic low back pain. Limited evidence was found that NSAIDs reduce pain intensity compared with paracetamol for chronic low back pain. No studies comparing NSAIDs to opioids on patients with chronic low back pain were found. NSAIDs are associated with more side effects than placebo or paracetamol. (1++) (Roelofs, P. D. D. M., Deyo, R. A., Koes, B. W. et al , 2008)	Insufficient evidence found concerning long term use of oral NSAIDS therefore recommendation should be as a short term treatment when paracetamol is ineffective option Not all traditional NSAIDs or COX-2 inhibitors are licensed for use for people with back pain. Cost effectiveness considerations: paracetamol and NSAIDs available as generics and treatment costs are expected to be similar. Effectiveness of paracetamol is good in most patients. In some patients, there are moderate to severe side effects associated with NSAIDS. The Osteoarthritis guideline found PPI cost effective for both long and short term use. Modelling was carried out for over 45 age group.
10.3.4.2 No cost effectiveness	

studies were identified for oral NSAIDS	

10.4 Opioids

Clinical question: what is the effectiveness of <u>opioids</u> compared with placebo, antidepressants, paracetamol or oral NSAIDs on pain, functional disability or psychological distress?

10.4.1 Clinical evidence

Literature searching retrieved 582 papers of which 30 were ordered for this question. Twenty-eight were excluded. Three randomised controlled trials comparing opioids with placebo were included.

The first randomised controlled trial (Katz, Nathaniel., Rauck, Richard., Ahdieh, Harry. et al , 2007) recruited opioid naïve patients with moderate to severe low back pain (pain intensity score of ≥ 50 mm using the Visual Analogue Scale (VAS)), present daily for ≥ 3 months. Subjects were recruited from 29 pain centres in the US. They had a mean age of 50 years and the most common pain aetiologies were degenerative disc disease, osteoarthritis and trauma. Three hundred and twenty five participants entered a 4 week open label titration phase in which current pain medications were terminated and patients received oxymorphone extended release (ER) 5 mg every 12 hours for 2 days. Thereafter, their dose of oxymorphone ER was gradually increased to a well-tolerated stabilised dose (one that produced a pain score of < 40 mm on the VAS). Patients were also given a mild anti- constipation agent throughout the study.

Two hundred and five subjects completed the titration phase and were randomised to either continue their dose of oxymorphone ER (n = 105) or to receive placebo (n = 100) for a period of twelve weeks. Average pain intensity scores were taken using the Visual Analogue Scale (VAS) at baseline (point of randomisation) and at final visit (12 weeks). The mean change from baseline to final pain intensity (assessed using the VAS) + / - standard deviation was found to be +10.9 +/- 24.5 mm for

oxymorphone ER and + 26.9 +/- 27.88 mm for placebo. This difference was found to be significant (least squares mean difference using ANCOVA analysis of covariance = -16.9, 95% CI -10.12 to -23.65, *P* < 0.0001).

Participants in the Oxymorphone ER group, and thie physicians rated treatment as 'Excellent' compared with placebo (*P* < 0.0001).

During the open-label titration phase, 69% of subjects experienced ≥1 adverse event and 18% of subjects discontinued treatment due to adverse events. There were fewer adverse events during the double blind treatment phase and were similar between those randomised to oxymorphone and those receiving placebo; 58% and 44% of patients experienced ≥ 1 adverse event in the oxymorphone and placebo groups respectively while 8.6% and 8.0% of patients discontinued treatment due to adverse events in the oxymorphone and placebo groups respectively.

Opioid withdrawal was measured using the Clinical Opiate Withdrawl Scale (COWS) (scores of 5-12 indicate mild opioid withdrawal) & the Adjective Rating Scale for Withdrawal (ARS) (scale of 0 to 144). One patient randomised to oxymorphone ER (COWS score of 6) and 2 patients randomised to placebo (COWS scores of 2) discontinued due to presumed opioid withdrawal. Mean COWS scores and ARS scores were slightly higher in those randomised to placebo on post-randomisation day 4 compared with those continuing their titrated dose of oxymorphone (COWS score mean +/- SD = 0.5 +/- 0.9 for oxymorphone ER, COWS score mean +/- SD = 1.1 +/-1.7 for placebo; ARS score mean +/- SD = 9.0 +/- 10.7 for oxymorphone ER and ARS score mean +/- SD = 14.0 +/- 19.5 for placebo).

This was a well conducted study with a low risk of bias. There are, however, limitations of an enriched enrolment, randomised withdrawal study design, including the potential for unblinding due to recognition of adverse events and opioid withdrawal in placebo allocated patients. The authors were aware of these factors and measured both adverse events and opioid withdrawal, neither of which were significantly different between the two groups. An additional criticism is that drop-out rates during the double-blind treatment phase were relatively high: 32% of those allocated oxymorphone did not complete the study while 53% of those allocated

placebo did not complete. In both groups the most common reason was lack of efficacy.

One randomized controlled trial (Vorsanger, Gary. J., Xiang, Jim., Gana, Theophilus. J. et al , 2008) evaluated the safety and efficacy of tramadol extended-release (ER) compared to placebo once daily in the treatment of chronic low back pain. The study was carried out across 30 centres in the USA and the design consisted of an open-label run-in followed by, without washout, a randomized controlled study design. Adults with low back pain for 6 months or more and who scored 40 or more on a pain intensity visual analogue scale received open-label tramadol ER, initiated at 100mg once daily and titrated to 300mg once daily during a 3weeks open-label run-in. Patients completing the run-in were randomized to receive tramadol ER 300mg, 200mg or placebo once daily for 12 weeks. Exclusion criteria included clinical significant fibromyalgia, history of lumbar spine surgery or chemonucleolysis, uncontrolled medical condition, TENS or spinal manipulation, difficulty swallowing tablets and previous intolerance to tramadol or other opioid analgesics.

Three hundred and eighty six participants were randomized to the Tramadol ER 300mg group (n=128), 200mg group (n=129) and a placebo group (n=129). Only tramadol ER 100mg and placebo tablets were used and they were identical in appearance and texture. Patients took 3 tablets daily, consisting of 3 active tablets (for the tramadol 300mg group), 2 active tablets and 1 placebo tablet (for the 200mg group) or 3 placebo tablets (placebo group). Patients were not allowed to use NSAIDs, corticosteroids, opioid or other analgesics during the study. Outcomes of interest were pain intensity (both current and since previous visit), patients' global assessment of study medication, RMDQ, overall quality of sleep and adverse events.

Results showed that in subjects who tolerated and obtained pain relief from tramadol, continuation of tramadol treatment for 12 weeks maintained pain relief more effectively than placebo. The authors concluded that tramadol ER was an effective treatment option in the management of chronic low back pain.

This was a well conducted RCT with a low risk of bias. There was however uncertainty with the recruitment of participants as well as a large attrition in all three groups.

A third randomised controlled trial (Webster, Lynn. R., Butera, Peter. G., Moran, Lauren. V. et al , 2006) recruited patients from 45 U.S sites between the ages of 18 and 70 with persistent low back pain (baseline Pain Intensity (PI) score ≥ 5, where 0 = no pain and 10 = severe pain) for at least 6 months requiring daily analgesics. Participants had a mean age of 48 years and 42% had used opioids in the previous month. No demographics were given for low back pain aetiologies. Patients were excluded if they had had back surgery in the previous 4 months.

Seven hundred and nineteen participants were recruited and entered into a washout period of 4-10 days. They were then randomised to placebo or to one of three intervention groups (oxycodone QID (QID = four times daily), oxytrex QID or oxytrex BID (BID = twice daily). Oxytrex is not licensed, it is a combination of oxycodone with ultra-low dose naltrexone (an opioid antagonist). For patients in the active treatment arms, the dose of oxycodone or oxytrex was titrated over a period of 1-6 weeks to achieve a pain intensity (PI) score of <= 2 to a maximum of 80 mg / day oxycodone. Patients then remained on their final dose for 12 weeks.

Oxycodone QID, oxytrex QID and oxytrex BID were all associated with a significantly greater percentage decrease in the primary endpoint of pain intensity compared with placebo at week 12 compared with baseline ($P < 0.05$).

Secondary efficacy measures included the Short-Form 12- (SF-12) and the Oswestry Disability Index (ODI) for low back pain. In all three active treatment the physical component the SF-12 score improved when compared toplacebo ($P < 0.001$, $P < 0.002$, and $P < 0.001$ for the percentage change from baseline at the end of treatment for the oxycodone QID, oxytrex QID, and oxytrex BID treatment arms, respectively).

The quality of analgesia and the global assessment of study medication (measured by the ODI and the mental component of the SF-12 respectively) were significantly improved in all 3 active treatment groups compared to placebo at the end of treatment; P values were $P < 0.001$, $P < 0.003$, and $P < 0.017$ for the oxycodone

QID, oxytrex QID, and oxytrex BID treatment arms respectively for quality of analgesia, and $P < 0.001$ for all 3 arms for global assessment of study medication.

Physical dependence, assessed using the Short Opiate Withdrawal Scale (SOWS) was significantly greater for patients randomised to receive oxycodone than placebo for days 1, 2 and 3 after discontinuation of treatment ($P < 0.001$ days 1 & 2 and $P = 0.02$ day 3) and $P = 0.07$ day 4.

SOWS scores were significantly greater for oxytrex BID than placebo for day 2 ($P = 0.01$) with trends on days 1 and 3 ($P = 0.06$ and 0.07). SOWS scores were not reported for oxytrex QID.

The following adverse events were more common with oxycodone than placebo ($P<0.05$): constipation, dizziness, somnolence, pruritus, nausea and vomiting. Adverse events were also more common for oxytrex QID and BID than placebo although not all were significantly different from placebo.

This was a well conducted study with a low risk of bias. Drop-out rates were however relatively high in all groups: 58% placebo, 51% oxycodone QID, 58% oxytrex QID and 52% oxytrex BID. The most common cause of failure to complete the treatment period for those allocated placebo was inadequate pain relief and for those allocated to the three treatment arms, adverse events. .

10.4.2 Health economics

No economic evaluations were identified for opioids.

10.4.3 Evidence statements opioids

Evidence statements	Evidence to recommendations
10.4.3.1 One randomised controlled trial in people with low back pain of > 3	There is evidence available for short term use of (oxymorphone).

	months duration found that oxymorphone extended release therapy was associated with a reduction in pain intensity compared with placebo. Incidences of opioid withdrawal after termination of therapy and adverse events were slightly higher in those randomised to receive oxymorphone compared with placebo.(1+) (Katz, Nathaniel., Rauck, Richard., Ahdieh, Harry. et al , 2007)	One study supports use of Tramadol but this has higher cost. Recommending long-term use of opioids was considered to be inappropriate as the evidence presented were all for short duration. No data were available to support use of mild opioids therefore the recommendation was made by consensus of the GDG. Where paracetamol is ineffective, the positive effect of Opioids on QoL is considered to outweigh the QoL loss and costs due to side effects. There is insufficient evidence to preferentially prescribe opioids over NSAIDS following paracetamol
10.4.3.2	*One randomised controlled trial in people with low back pain of >6 months evaluated the safety and efficacy of tramadol extended-release compared to placebo once daily. Results showed that in patients who tolerated and obtained pain relief from tramadol, continuation of treatment for 12 weeks maintained pain relief more effectively than placebo. (1+) (Vorsanger, Gary. J.,*	

	Xiang, Jim., Gana, Theophilus. J. et al , 2008)	
10.4.3.3	*A randomised controlled trial in people with low back pain of > 6 months duration found that oxycodone therapy was associated with a reduction in pain intensity compared with placebo and improvements in the quality of analgesia, global assessment of study medication and in the physical component score of the Short Form 12-Question health survey compared with placebo. Incidence of physical dependence after termination of opioid therapy and of adverse events were higher in those randomised to receive oxycodone compared with placebo.(1+) (Webster, Lynn. R., Butera, Peter. G., Moran, Lauren. V. et al , 2006)*	
10.4.3.4	*No cost effectiveness studies found for opioid*	

therapy	

10.5 Antidepressants

Clinical question : what is the effectiveness of antidepressants compared with placebo, opioids, paracetamol or oral NSAIDS on pain, functional disability or psychological distress?

10.5.1 Clinical evidence

Literature searching retrieved 265 papers of which 30 were ordered for this question. Only one, a systematic review, was included (Urquhart, D. M., Hoving, J. L., Assendelft, W.-W. J. J. et al , 2008).

The systematic review searched the MEDLINE and EMBASE database (to September 2007), PsychINFO (to June 2006) and the Cochrane Central Register of Controlled Trials 2006 (Urquhart, D. M., Hoving, J. L., Assendelft, W.-W. J. J. et al , 2008). Ten randomised, placebo-controlled trials (N = 568) of patients with chronic low back pain of > 6 months duration, treated with an oral antidepressant were included. All included trials were assessed for quality using a 22-point methodological quality checklist. Outcomes of interest were pain, function and depression.

10.5.1.1 Antidepressants versus placebo: Pain intensity

Of the seven high quality studies comparing antidepressants with placebo, five trials reported no differences in pain between treatments (Atkinson, J. H., Slater, M. A., Wahlgren, D. R. et al , 1999; Dickens, C., Jayson, M., Sutton, C. et al , 2000; Goodkin, K., Gullion, C. M., and Agras, W. S., 1990; Jenkins, D. G., Ebbutt, A. F., and Evans, C. D., 1976; Katz, Jennifer, Pennella, Vaughan Janet, Hetzel, Roderick D. et al , 2005), while two different studies by the same author reported a greater reduction in pain with the use of antidepressants (Atkinson, J. H., Slater, M. A., Wahlgren, D. R. et al , 1999; Atkinson, J. H., Slater, M. A., Williams, R. A. et al ,

1998) . Overall these findings indicate that there is conflicting evidence regarding the effect of antidepressants on pain intensity in patients with chronic low back pain. A pooled analysis of six small trials (scores of 353 people) failed to show a difference in pain relief between antidepressants and placebo for patients with chronic low back pain (WMD -0.06 (95%CI -0.26 to 0.16))

10.5.1.2 Antidepressants versus placebo: Depression

Seven high quality trials measured depression by the Beck Depression Inventory. There was considerable variability in he doses of antidepressants used between these trials, with (Jenkins, D. G., Ebbutt, A. F., and Evans, C. D., 1976) trialling 75mg/day of imipramine and (Goodkin, K., Gullion, C. M., and Agras, W. S., 1990) using 600mg/day of trazodone. The studies (491 people) compared antidepressants to placebo and reported no differences in depression. Overall these results suggest there is no consistent evidence that antidepressants reduce depressive symptoms in patients with chronic low back pain.

Only two studies could be pooled (132 people) (Dickens, C., Jayson, M., Sutton, C. et al , 2000; Goodkin, K., Gullion, C. M., and Agras, W. S., 1990), and this failed to show a difference in reduction of depression between antidepressants and placebo (standardized mean difference 0.06 (95%CI -0.29 to 0.40)). The one high quality trial that included patients with significant depressive symptoms reported conflicting results (Dickens, C., Jayson, M., Sutton, C. et al , 2000).

10.5.1.3 Antidepressants versus placebo: Functional status

Two high quality studies included functional status as outcome (Dickens, C., Jayson, M., Sutton, C. et al , 2000; Goodkin, K., Gullion, C. M., and Agras, W. S., 1990). Neither of these studies found a significant difference in functional status with the use of antidepressants compared to placebo in patients with low back pain. The pooled analysis of these two trials failed to show a difference in improvement of functional status, with a standardised mean difference of -0.06 (95%CI -0.40 to 0.29).

10.5.1.4 Antidepressant type versus placebo: Pain intensity

The pooled analysis of 2 high quality trials (Atkinson, J. H., Slater, M. A., Wahlgren, D. R. et al , 1999; Jenkins, D. G., Ebbutt, A. F., and Evans, C. D., 1976) failed to show a difference in pain relief between tricyclic antidepressants and placebo (standardised mean difference -0.12 [95%CI -0.53 to 0.29]). Similarly, SSRIs were not found to be more effective than placebo in the reduction of pain with the pooling of a further 2 high quality trials (Atkinson, J. H., Slater, M. A., Wahlgren, D. R. et al , 1999; Dickens, C., Jayson, M., Sutton, C. et al , 2000) (standardised mean difference 0.04 [95%CI -0.29 to 0.37]). The effectiveness of antidepressant type versus placebo was not assessed for other outcomes.

Overall, the authors concluded there is no clear evidence that antidepressants are more effective than placebo in the management of patients with chronic low back pain. They found no clear evidence to support the use of antidepressants to reduce pain and depression in this patient population. They emphasise however that the findings do not imply that severely depressed patients with back pain should not be treated with antidepressants.

This was a high quality systematic review with a very low risk of bias.

10.5.2 Health economics

No economic evaluations were identified for antidepressants.

10.5.3 Evidence statements for antidepressants

Evidence statements		Evidence to recommendations
10.5.3.1	*One systematic review of ten randomised controlled trials found conflicting evidence for the effect of antidepressants on pain*	One systematic review shows conflicting evidence for antidepressants to reduce pain. GDG agreed there was little risk and low cost associated with treatment. The group considered patients should

	intensity in people with low back pain of > 6 months duration. There was no consistent evidence that antidepressants reduce depression in chronic low back pain patients or that they improve function. Tricyclic antidepressants and selective serotonin reuptake inhibitors were not found to be more effective than placebo in reducing pain. (1++) (Urquhart, D. M., Hoving, J. L., Assendelft, W.-W. J. J. et al , 2008)	be offered a trial of this treatment Psychological outcomes were not considered by the review. The RCTs included in the systematic review were obtained to extract any psychological outcome data. No improvement in either anxiety or depression was found. Dosages of antidepressants given to participants in the trials were checked and presented to the GDG. Dosages given in BNF were also checked and presented. Treatment costs are expected to be similar for both paracetamol as well as antidepressants. The advice to regularly monitor those taking a trycyclic for the first time was made based on the evidence from the Depression guideline No 23. The GDG considered that further economic analysis was not necessary for the pharmaceutical agents recommended.
10.5.3.2	*No cost effectiveness studies were identified for antidepressants.*	

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11 Invasive Procedures

11.1 Recommendations for invasive procedures

11.1.1 Consider offering a course of acupuncture needling comprising up to 10 sessions over a period of up to 12 weeks[10].

11.1.2 Do not offer injections of therapeutic substances into the back.

11.2 Acupunture and other neuroreflexotherapy

Clinical question: What is the effectiveness of acupuncture (including PENS & neuroreflexotherapy) compared with usual care or sham on pain, functional disability or psychological distress?

11.2.1 Clinical evidence

Literature searching retrieved 1087 papers of which 63 were ordered for this question. 56 were excluded and 7 were included: 4 RCTs and 1 systematic review on acupuncture, 1 systematic review on neuroreflexotherapy and 1 RCT on PENS for low-back pain.

11.2.1.1 Acupuncture

One systematic review assessed the effects of acupuncture for the treatment of non-specific LBP and dry-needling for myofascial pain syndrome in the low-back region (Furlan, A. D., Van-Tulder, M. W., Cherkin, D. C. et al , 2005). The Cochrane library, MEDLINE and EMBASE databases were searched, as well as the Chinese Cochrane Centre database of clinical trials and a Japanese controlled trial database. RCTs including adults with non-specific LBP and myofascial pain syndrome in the

[10] A choice of an exercise programme (see section 1.3.3), a course of manual therapy (see section 1.4.1) and a course of acupuncture may be offered, taking into account patient preference.

low-back region were included. RCTs including subjects with LBP caused by specific pathological entities such as infection, metastatic diseases, neoplasms, osteoarthritis, rheumatoid arthritis or fractures were excluded. LBP associated with sciatica as the major symptom was also excluded. Articles evaluating acupuncture or dry-needling treatments that involve needling were included. Studies were included regardless of source of stimulation (eg hand or electrical stimulation).

With regards to acupuncture versus sham therapy 4 trials met this guideline's selection criteria. Treatment interventions varied between trials; patients received 6 x 30min over 6 weeks in one, 20 x 30min over 12 weeks in another, 8 x 30min over 4 weeks in the third trial and 12 x 30min (3 times a week) in the fourth one. The pooled analysis (N= 314) suggested evidence for pain relief at shorter-term follow-up (up to 3 months), but these effects were not maintained at the longer-term follow-ups, nor were they observed for functional outcomes. Compared to no treatment, one low-quality RCT suggested some evidence for pain relief and functional improvement for acupuncture at short-term follow-up. The included studies were very heterogeneous in terms of population, type of acupuncture administered, control groups, outcomes measures and timings of follow-up. Although the conclusions show some positive results of acupuncture, the magnitude of the effects was generally small.

This was a high quality systematic review with a very low risk of bias.

One randomised controlled trial involved participants recruited through local newspapers and some who contacted the trial centres spontaneously (Brinkhaus, B., Witt, C. M., Jena, S. et al , 2006).

Those included had to be aged 40-75, have a clinical diagnosis of chronic back pain lasting more than 6 months, have a pain intensity of 40 or more for the previous 7 days (on a 100mm VAS). They had to have only used non-steroidal anti-inflammatory drugs for the past 4 weeks. A total of 2250 patients applied to be included in the study, of those only 301met the criteria of the study, these were then randomized into three groups, at a 2:1:1 ratio to acupuncture (140 patients), minimal acupuncture (70 patients) and no treatment (74 patients) (the control group).

The participants in the acupuncture group received 12 x 30 minute sessions over 8 weeks of acupuncture which used needles of an unspecified length and which were only stimulated once during each session. Sessions occurred usually twice a week for 4 weeks and then once a week for the last 4 weeks. The treatment needled a selection of local and distant points, including (bilaterally) at least four local points from the following: Bladder 20-34; Bladder 50 to 54; Gallbladder 30; Governing vessel 3, 4, 5 and 6; extraordinary points Huatojiaji and Shiqizhuixia. If patients had local or pseudoradicular sensations at least 2 local points were acupunctured. Other acupuncture points including ear and trigger points could also be chosen individually. The participants randomized to the minimal acupuncture group also received 12 x 30 minute sessions over 8 weeks where at least 6 out of 10 predefined non-acupuncture points were needled bilaterally using a superficial insertion with fine needles (length 20-40 mm), these points were not in the lower back where participants experienced pain. The final group which received no acupuncture was told they were on a waiting list for 8 weeks, after which they received normal acupuncture, (therefore were only included in the 8 week follow up).

The results of the study showed a statistically significant difference in pain scores between the acupuncture and no acupuncture groups. However no significant difference in pain between the acupuncture and minimal acupuncture groups was found at 8, 26 and 52 weeks (the acupuncture group did have slightly better outcomes than the minimal acupuncture group).

This was a well conducted RCT with a low risk of bias.

One randomised controlled trial involved participants recruited through newspapers, magazines, radio and television (Haake, Michael, Müller, Hans Helge, Schade, Brittinger Carmen et al , 2007). Those included had to be over the age of 18 (average age of 50), have a clinical diagnosis of chronic back pain for 6 months or longer, have a Von Korff Chronic Pain Grade Scale (CPGS) grade 1 and Hanover Functional Ability Questionnaire (HFAQ) less than 70%. They had to have been therapy-free for 7 days or longer, be able to speak read and write German, and have signed written consent form. A total of 1802 participants applied to be included in the

study, of those only 1161met the criteria of the study, these were then randomized into three groups of 387 patients each to receive one of acupuncture, sham acupuncture or conventional treatment (the control group).

The participants in the acupuncture group received 10 X 30 minute sessions of verum acupuncture which used sterile disposable needles of 0.25X40mm or 0.35X50mm, with no electrical stimulation. They attended usually 2 sessions a week for 42 days. The treatment needled 14-20 fixed and additional points (from a prescribed list) chosen on the basis of traditional Chinese medicine diagnosis, including tongue diagnosis. . De qi sensation was elicited by manual stimulation. The participants randomized to the sham acupuncture group also received 10 X 30 minute sessions where 14-20 needles were inserted without stimulation 1-3mm on either side of the lateral part of the back and on the lower limbs avoiding all classical acupuncture points or meridians. The final group which received conventional treatment was also seen in 10 X 30 minute sessions which followed German guidelines of a multimodel treatment program which included physiotherapy and exercise (and other treatments) by physicians and physiotherapists. The results of the study showed a statistically significant difference in pain between the two acupuncture groups together (verum and sham) and the conventional treatment where ½ the patients receiving acupuncture benefited compared to only a ¼ who received conventional treatment. However there was no significant difference in pain scores between verum acupuncture and sham acupuncture (3.4% difference, P=0.39)

This was a well conducted RCT with a low risk of bias.

One randomised controlled trial recruited patients through their GPs (a total of 16 GP practices were involved which included 39 GPs)(Thomas, K. J., MacPherson, H., Ratcliffe, J. et al , 2005). Patients included had to be between the age of 18 and 65 (the mean age was 42) and have had non-specific low back pain for 4-52 weeks. They also had to have been assessed by their GP to check that primary care management was suitable. A total of 289 patients were identified and approached to join the study, of these 241 accepted and met the criteria. 160 were allocated to receive acupuncture and 81 were allocated to receive usual care, however 1 patient from each group dropped out, 159 actually received acupuncture (146 were followed

up at 3 months, 147 at 12 months and 123 and 24 months) and 80 received usual care (146 were followed up at 3 months, 147 at 12 months and 123 and 24 months).

Participants in the acupuncture group received 10 individualised acupuncture treatments over 3 months from one of 6 qualified acupuncturists. The usual care group received 10 NHS treatment sessions according the GPs assessment of the patients clinical need; this was a mixture of interventions, including drugs and recommended back exercises. Half the group also received physiotherapy or manipulation during the first three months. Both groups also received adjunctive care which included massage and advice on diet, rest and exercise. The results showed that acupuncture does give a greater long-term benefit compared to usual care. Acupunture was significantly more effective in reducing pain at 24 months than usual care. The study also showed that traditional acupuncture care delivered in a primary care setting was safe and acceptable to patients with non-specific low back pain.

This was a high quality RCT with a very low risk of bias.

One randomised controlled trial approached patients insured by one of the participating social health insurance funds if their physician viewed acupuncture appropriate for their chronic low back pain (Witt, Claudia M., Jena, Susanne, Selim, Dagmar et al , 2006). Those included had to be over the age of 18, have a clinical diagnosis of chronic low back pain with disease duration of more than 6 months, and have signed a written informed consent form. A total of 11630 patients met the criteria of the study, these were then randomized into three groups, 1451 to the acupuncture group, 1390 received acupuncture after a delay of 3 months and 8537 were randomised to the non-randomised acupuncture group.

Participants in the acupuncture group received up to 15 acupuncture sessions with disposable one-time needles and manual stimulation only, as well as usual care. Over the first 3 months, patients received a mean 10.4 sessions (standard deviation 3), with 74% receiving a total of 5-10 sessions. Other forms of acupuncture (e.g. laser acupuncture) were not permitted. The group receiving no acupuncture was given normal care. Participants in all three groups were allowed to use additional conventional treatments as needed. The results of the study showed that

acupuncture, in addition to usual care, gave a clinically relevant benefit for pain, function and quality of life at 3 months among patients with chronic low back pain compared to usual care alone. The authors conclude that acupuncture should be considered a viable option in the management of patients with chronic LBP.

This was a RCT with a high risk of bias.

11.2.1.2 Neuroreflexotherapy (NRT)

One systematic review (Urrútia, G., Burton, A. K., Morral, A. et al , 2004) reviewed the effectiveness of NRT for the treatment of non-specific LBP in adult patients aged 16-65. NRT was defined as “temporary implantations of epidermal devices into trigger points at the site of each subject’s clinically involved dermatomes on the back and into referred tender points in the ear”. Patients with (sub)acute LBP (2-12 weeks) and/or chronic LBP (more than 12weeks) were included.

Two RCTs comparing NRT with sham-NRT show a statistically significant short-term positive effect on chronic back pain for the main outcomes of pain, ability to perform daily activities, and functional ability, as well as secondary outcomes of return to work, side effects and medication use. The effect appeared to be rapid and remained for at least 6 weeks after intervention in most of patients treated. One RCT of NRT as a supplement to standard management protocol for LBP in routine general practice show statistically significant short term (60 days) effect on pain relief (local and referred) and ability to perform daily activities, and on duration of sick leave and consumption of resources throughout the 1 year follow-up period.

NRT appears to be a safe and effective intervention for the short term treatment of chronic non specific LBP. However the results are limited to trials conducted in one country by small number of specially trained practitioners

This was a well conducted systematic review with a low risk of bias.

11.2.1.3 Percutaneous Electrical Nerve Stimulation (PENS)

A randomised controlled trial (Hsieh, Ru Lan and Lee, Wen Chung, 2002) investigated the therapeutic effect of one shot of low-frequency PENS in patients visiting a rehabilitation clinic in Taiwan. A total of 133 patients received either (1)

medication + PENS, (2) medication +TENS or (3) medication alone (control group). The duration of low-back back pain was not a specific inclusion criteria therefore patients had low-back pain of varying duration: 56% had acute LBP (< 1week), 20% had low back pain between 1week and 3 months, and 24% had chronic low back pain (> 3months).

Participants in the control group received medication only (including NSAID, diclofenac potassium, muscle relaxant and antacid), those in the medication+PENS group received one shot PENS treatment in addition to medication, and patients in the medication +TENS group received medication and one shot of TENS treatment. Results showed that one-shot PENS produces significant immediate pain relief effect, but that due to similar pain relief and functional disability improvements at 3 days and 1 week after treatment in the 3 groups, PENS does not have additional beneficial effects over medication alone after the immediate posttreatment periods.

This was a RCT with a high risk of bias

11.2.2 Health economics

Literature searching retrieved 99 papers of which 3 were ordered for this question. In total, 2 were excluded and 1 was included. One study (Witt, Claudia M., Jena, Susanne, Selim, Dagmar et al , 2006)l was excluded only because the setting was Germany and because it took a societal perspective. In the absence of a UK-based study it would have been included.

An economic evaluation (Ratcliffe, J., Thomas, K. J., MacPherson, H. et al , 2006)was conducted alongside an RCT of acupuncture for low back pain and the aim was to evaluate the cost-effectiveness of acupuncture in the management of persistent non-specific low back pain.

The study included 241 patients between the ages of 20 and 65 years, whose current episode of back pain was at least of 4 weeks duration and no longer than 12 months.

The acupuncture group could have up to 10 acupuncture treatments over 3 months. GPs were advised that they could give any additional care they thought necessary to patients in the acupuncture group. The usual care consisted of pragmatic GP management with no restrictions on the care they received.

The main outcome measure was incremental cost per QALY gained over 2 years. The number of QALYs gained was estimated using SF-36 data collected during the trial. This was converted to a single index value (SF-6D) where 0 represents death and 1 perfect health. The costing perspective was that of the UK health service. Healthcare resources included those for: the acupuncture sessions, hospital inpatient stays, outpatient attendances, and primary care consultations. These resources were costed using national averages for England. Costs were reported in pounds sterling at 2002/2003 prices. Both costs and outcomes occurring during the 12–24-month period were discounted at 3.5%, the current recommended rate for public sector projects.

Results (base case)

The mean cost (Standard Deviation) of care for the acupuncture group was £460 (£376) compared to £345 (£550). The QALY gain for the acupuncture group over 24 months was 1.453 (0.248) compared to a mean of 1.426 (0.191) for the usual care group. The mean incremental health gain from acupuncture at 24 months was 0.027 QALYs, leading to a base case estimate of £4241 per QALY gained.

Sensitivity analysis

The study reported on three sensitivity analyses: 1) Imputing missing data relating to NHS costs or QALYs the ICER for acupuncture was £4209 at 24 months; 2) When patients who were permanently unable to work because of back pain were excluded (reason being that these patients would have higher costs and poorer outcomes) the ICER was £2104; and 3) By including lost productivity costs (from time off work with back pain) acupuncture treatment dominated usual care because of the overall cost savings from using acupuncture treatment.

This study shows that acupuncture for low back pain in primary care confers a modest health benefit for a modest increase in costs. The base case estimate is

£4241 per QALY gained. Sensitivity analysis showed acupuncture to have a more than 90% chance of being cost effective at a £20,000 cost per QALY threshold. Including patient costs and the costs of lost productivity further strengthens the economics of acupuncture: that is, using a societal costing perspective acupuncture costs less and is more effective than usual care

These results are consistent with the findings from the Witt trial (Witt, Claudia M., Jena, Susanne, Selim, Dagmar et al , 2006).

11.2.3 Evidence statements for acupuncture needling

Evidence statements	Evidence to recommendations
Acupuncture: *11.2.3.1 One systematic review reported some evidence for short-term pain relief from acupuncture compared to sham-therapy, and some evidence for pain and functional improvement from acupuncture compared to no treatment (1++) (Furlan, A. D., Van-Tulder, M. W., Cherkin, D. C. et al , 2005)* *11.2.3.2 One RCT found significant improvement in pain from acupuncture compared to no treatment, but not when comparing acupuncture and minimal acupuncture,*	There is evidence that acupuncture needling (solid needling) is beneficial in reducing pain and improving function. No evidence of effect on psychological distress was found. One paper (Thomas) consisted of population of interest, all the other papers included a population with LBP over longer duration than 12 months. The GDG agreed that it was appropriate to include those with recurring episodes of LBP which could include those whose last episode was longer than 12 months previously. Evidence suggests that seeing an acupuncturist was better than usual care but not much difference between acupuncture and sham. However, sham acupuncture is used as an

	at 52 weeks (1+) (Brinkhaus, B., Witt, C. M., Jena, S. et al , 2006)	active form of treatment by some practitioners, therefore this should be considered as a possible treatment.
11.2.3.3	*One well conducted RCT found that acupuncture was associated with an improvement in pain compared to conventional treatment, but that acupuncture didn't have an effect on pain compared to sham-acupuncture, at 6 months (1+) (Haake, Michael, Müller, Hans Helge, Schade, Brittinger Carmen et al , 2007)*	Three of the five studies describe duration of treatment as up to 10 sessions. Studies report short term benefit. A well conducted UK based cost effectiveness analysis study showed acupuncture to be a cost effective treatment. Number of treatments and duration were checked in the included studies. From this the group agreed a course comprised of up to 10 sessions over a period of up to 12 weeks. GDG considered that further research on the effects on prolonged treatment was required.
11.2.3.4	*One RCT found that acupuncture was associated with an improvement in pain, at 24 months, compared to usual care(1++) (Thomas, K. J., MacPherson, H., Ratcliffe, J. et al , 2005)*	
11.2.3.5	*One RCT showed that acupuncture was associated with significant improvements in back function, pain and quality of life, at 3 months, compared to no*	

acupuncture (1-) (Witt, Claudia M., Jena, Susanne, Selim, Dagmar et al , 2006) Neuroreflexotherapy: *11.2.3.6 One systematic review on neuroreflexotherapy showed NRT was associated with short-term improvement on pain and functional ability compared to sham-NRT, and short-term pain relief when used as supplement to standard care (1+) (Urrútia, G., Burton, A. K., Morral, A. et al , 2004)* PENS: *11.2.3.7 One RCT on PENS showed no additional beneficial effect of PENS over medication alone, at 1 week (1-) (Hsieh, Ru Lan and Lee, Wen Chung, 2002)* *Cost-effectiveness*	All the studies included in the neuroreflexotherapy review had been conducted in a healthcare setting outside of UK and all from one centre. The three RCT's included in the review also had small numbers. This treatment is currently not rountinely practised in UK. GDG agreed the evidence was not strong enough to recommend a change to current practice.

11.2.3.8	*One NHS based costs per QALY analysis indicates that we can be 90% certain that acupuncture is cost-effective compared with usual care at 24 months using £20,000/QALY as the threshold of acceptability. (Ratcliffe, J., Thomas, K. J., MacPherson, H. et al , 2006))*	

11.3 Injections

Clinical question: what is the effectiveness of injections or nerve blocks compared with usual care or sham on pain, functional disability or psychological distress?

11.3.1 Clinical evidence

Literature searching retrieved 1912 papers of which 46 were ordered for this question; 41 were excluded and 3 were included (2 systematic reviews and 1 RCT).

One systematic review of therapeutic facet joint interventions in chronic spinal pain included only one RCT relevant to our patient population (Boswell, Mark, V, Colson, James D., Sehgal, Nalini et al , 2007).The RCT is summarised below.

One randomised controlled trial (Carette, S., Marcoux, S., Truchon, R. et al , 1991) evaluated the efficacy of injections of corticosteroid into facet joints to treat chronic low back pain in a double-blind placebo-controlled trial. The design consisted of 2 phases: Phase 1 was designed to identify patients with chronic LBP whose pain was

most likely to originate in the facet joints. Phase 2 evaluated the efficacy of injections of methylprednisolone acetate or isotonic saline in to the facet joints of patients whose back pain had been documented in phase 1 to originate in those joints. Patients were selected from a rheumatology outpatient clinic and had to be aged between 18 and 65 years and had LBP for at least 6 months. Normal neurological examination results were required. Exclusion criteria were presence of back pain from not a mechanical cause (eg tumour, infection, spondylitis), previous injections into facet joints or LBP surgery, pregnancy, known allergy to local anaesthetics and presence of blood coagulation disorder. A total of 190 patients were entered in Phase 1, following which 101 were entered into Phase 2, 51 in the methylprednisolone group, and 50 in the placebo group. Patients received either 20mg (1ml) of methylprednisolone acetate mixed with 1ml of isotonic saline or 2ml of isotonic saline in each of the facet joints previously injected in Phase 1, and were followed for 6 months. Outcomes of interest were VAS score, McGill pain questionnaire, finger-to-floor distance and Sickness Impact Profile score. Results showed that after 1 month, none of the outcome measures evaluating pain, functional status and back flexion differed clinically or statistically between the 2 groups; 42% of patients who received methylprednisolone and 33% of those who received placebo reported marked or very marked improvement (95% CI for the difference -11 to 28; P=0.53). At the 6 month evaluation, the patients with methylprednisolone reported more improvement, less pain on the VAS scale, and less physical disability. The differences were reduced, however when concurrent interventions were taken into account. Moreover, only 22% of patients in the methylprednisolone group and 10% in the placebo group had sustained improvement from the first month to the 6th month (p=0.19). They concluded that injecting methylprednisolone acetate into the facet joint is of little value in the treatment of patients with chronic LBP.

This was a well conducted systematic review with a low risk of bias.

A systematic review by (Dagenais, S., Yelland, M. J., Del Mar, C. et al , 2007) aimed to assess the efficacy of prolotherapy in adults with chronic low back pain. Prolotherapy involves repeated injections of irritant solutions to strengthen lumbosacral ligaments in people with low back pain . The Cochrane library,

MEDLINE, EMBASE, CINAHL and AMED databases were searched for RCTs on prolotherapy for patients with non-specific low back pain for more than 3 months. Outcomes of interest were pain, low-back related disability, well-being and return to work. Five RCTs were included in the review, four of which are relevant to this key clinical question. They included adult patients with LBP for over 6 months. Clinical heterogeneity amongst intervention groups and control groups prevented the study results from being pooled. Treatment injections were of glucose, glycerine and phenol lignocaine, whilst control injections were either lignocaine or saline.

The authors concluded that when used alone, prolotherapy is not an effective treatment for chronic low-back pain. This was a high quality systematic review with a very low risk of bias

One randomised controlled trial (Khot, Abhay, Bowditch, Mark, Powell, John et al , 2004) investigated the use of intradiscal steroid threrapy in patients with discogenic LBP without radicular leg pain. Patients were recruited when they presented themselves to the study hospital (in the UK) with the signs and symptoms of discogenic low back pain without radicular leg pain. Other inclusion criteria were MRI findings showing degenerative disc disease and failure of at least 6 weeks of conservative treatment. Exclusions were medical conditions requiring systematic steroid therapy, sciatica, anatomical abnormalities, previous surgery and repeat injections. These patients were listed for discography, and if at discography there was concordant pain on pressurisation of a degenerate disc, the patient was randomized to the steroid or saline group, by opening a sealed envelope.

A total of 120 patients were included, 60 were injected with 1ml containing 40mg of methylprednisolone acetate, and 60 with normal saline. They were followed up to a year after the injections, in clinics and by postal questionnaire.

The study results showed that steroids are not effective in improving the clinical symptoms in this patient group (pain, disability) and that intradiscal steroid injections carried no benefit over a placebo saline injection. No information was given on the duration of low-back pain so the relevance of this RCT to this guideline and key clinical question is limited. This was a well conducted RCT with a low risk of bias

11.3.2 Health economics

No economic evaluations were identified for injection therapies or nerve blocks.

11.3.3 Evidence statements for injections and nerve blocks

Evidence statements	Evidence to recommendations
11.3.3.1 A SR identified a RCT that met the inclusion criteria It showed that facet-joint corticosteroid injections were not associated with any improvement in health outcomes at 1 month, and with improvement in pain at 6 months (however the effect was reduced when concurrent interventions were taken into account). Overall conclusion was that facet-joint injections were of little value.(1+) (Boswell, Mark, V, Colson, James D., Sehgal, Nalini et al , 2007). *11.3.3.2 One systematic review on prolotherapy found no effect on pain, disability or well being for patients with chronic low back pain (1++) (Dagenais, S.,*	The GDG agreed that there was a lack of evidence to recommend the use of these treatments and agreed by consensus that injections were of no benefit for this population.

	Yelland, M. J., Del Mar, C. et al , 2007)	
11.3.3.3	*One RCT did not find any effect of intradiscal corticosteroid injections on the health outcomes of interest, compared to saline injections (1+)(Khot, Abhay, Bowditch, Mark, Powell, John et al , 2004)*	
11.3.3.4	*No cost effectiveness studies were identified for injections or nerve blocks*	

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12 Indications for referral for surgery

12.1 Introduction

The scope of this document specifically precluded recommendation regarding surgery. The GDG took the decision to investigate the evidence to inform practitioners which surgical intervention might be effective if the treatments included in this guideline proved ineffective. The GDG were of the opinion that this would inform who should be referred out of the clinical pathway for a surgical opinion. In doing this a review of the efficacy of commonly used surgical treatments was undertaken.

12.2 Recommendations for referral for surgery

12.2.1 Consider referral for an opinion on spinal fusion for people who have completed a comprehensive package of care including a combined physical and psychological treatment programme and who have persistent severe non-specific low back pain for which the patient would consider surgery.

12.2.2 People who have psychological distress should receive appropriate treatment for this before referral for spinal fusion.

12.2.3 If spinal fusion is being considered, refer the patient to a specialist surgical service.

12.2.4 Due consideration should be given to possible risks of spinal fusion.

12.2.5 Do not refer people for intradiscal electrothermal therapy (IDET), percutaneous intradiscal radiofrequency thermocoagulation (PIRFT) or radiofrequency facet joint denervation.

12.3 Referral for Surgery

Clinical question: what are the indications for referral for surgery based on the effectiveness of surgical treatments compared with non-surgical treatment or no treatment on pain, functional disability or psychological distress?

12.3.1 Clinical evidence

A literature search identified 2228 studies, of which 44 were ordered: one systematic review on intra-discal electrothermal therapy (IDET), 2 systematic reviews on lumbar fusion and three RCTs on radiofrequency facet joint denervation were included.

12.3.1.1 IDET

One systematic review (Freeman-Brian, J. C., 2006) reviewed the evidence of clinical efficacy for IDET (intra-discal electrothermal therapy). The PubMed, Medline and the Cochrane Library databases were searched for RCTs and cohorts published up to January 2006. They specified in the inclusion criteria they were looking for at least one of the four following primary outcomes: pain intensity (VAS), back functional status (Oswestry Disability Index), global measurement of overall improvement, return to work.

Three randomized controlled trials were identified (in addition to cohort studies), two of them being on the effectiveness of IDET (the third one was on a slightly different intervention, namely percutaneous intradiscal radio-frequency thermo-coagulation (PIRFT)). The randomized controlled trials compared IDET to sham and primary outcomes were pain (VAS), the Oswestry Disability Index (ODI), SF-36 General Health Questionnaire, Zung Depression Index.

The study on PIRFT showed no statistically significant differences in outcomes between the two groups. The RCT on IDET, where 64 patients were randomized showed significantly better improvements in VAS in the treatment group than in the sham group (p=0.045). However, only 50% of patients randomized to the intervention group benefited appreciably from IDET. The other RCT on IDET failed to show any statistically significant or clinical important differences in the outcomes between groups.

The authors concluded that the 2 RCTs addressing the effectiveness of IDET provide inconsistent evidence, and that the current published evidence does not provide clear evidence of benefit. The overall conclusion was that the evidence for efficacy of IDET remains weak and has not passed the standard of scientific proof. Since this systematic review was published, Freeman published a more recent one (Freeman, Brian. J. C. and Mehdian, Roshana., 2008), however the same studies were included and no new relevant studies were identified.

This was a well conducted systematic review with a low risk of bias

12.3.1.2 Spinal Fusion

A meta-analysis of RCTs was conducted to compare surgical to non-surgical treatment of chronic low back pain (Ibrahim, T., Tleyjeh, I. M., and Gabbar, O., 2008). A search of 4 bibliographic databases (Medline, Embase, Cinahl, Science Citation index) was conducted to identify RCTs published between the dates 1966-2005. Trials must have reported an Oswestry disability Index (ODI) as an outcome measure to be included and the comparators were physical therapy and cognitive therapy. Four relevant papers (Brox, I. J., Sorensen, R., Friis, A. et al , 2003; Ekman, P., Möller, H., and Hedlund, R., 2005; Fairbank, J., Frost, H., Wilson, MacDonald J. et al , 2005; Fritzell, P., Hägg, O., Wessberg, P. et al , 2001) were found that met the inclusion criteria and a meta-analysis was carried out. Ekman et al (2005) was not included in the meta-analysis as it was regarding isthmic spondylolisthesis. The three studies included in the meta-analysis are also included in the Mirza (2007) systematic review. The interventions were all a type of lumbar fusion surgery (see Mirza, 2007 for more details.)

The meta-analysis showed a non-significant trend for surgery to help ODI (4.13, 95% CI, -0.82 to 9.08, p=0.10). The author's conclusion was that the cumulative evidence does not support routine surgical fusion for treating chronic lower back pain. However a member of the team spotted an inconsistency in the paper and redid the meta-analysis and found a benefit from surgery of 4.87 (95%CI 1.62 to 8.12 p=0.003) as measured on the ODI (erratum to be published).

This was a well conducted RCT with a low risk of bias.

One systematic review reviewed the efficacy of lumber fusion surgery for chronic back pain treatment (Mirza, S. K. and Deyo, R. A., 2007). The MEDLINE database was searched as well as references from a Cochrane Review update for RCTs published to May 2006. The inclusion criteria specified RCTs comparing surgical to nonsurgical treatment for discogenic back pain.

Four randomized controlled trials were found, all of which used lumbar fusion surgery of some type. One study (Fritzell, P., Hägg, O., Wessberg, P. et al , 2001) used one of three techniques: 1) Posterolateral fusion (PLF) using iliac crest autograft without fixation 2) Posterolateral fusion using pedicle screws and iliac crest autography, 3) Anterior Lumbar interbody Fusion (ALIF) or Posterior Lumbar Interbody Fusion (PLIF) using bone blocks cut from the iliac crest. Two studies (Brox, I. J., Sorensen, R., Friis, A. et al , 2003; Brox, Jens, I, Reikerås, Olav, Nygaard, Øystein et al , 2006) used posterolateral fusion using pedical screws and iliac crest autograft. One study (Fairbank, J., Frost, H., Wilson, MacDonald J. et al , 2005) used spinal stabilisation using any technique, devices and graft material chosen by the surgeon. The comparators were non-surgical treatment, such as physical therapies, cognitive interventions and intensive rehabilitation. Outcome measures included: VAS, ODI, Million score and General Function Score, Zung Depression Scale.

Results from one study (Fritzell, P., Hägg, O., Wessberg, P. et al , 2001) found that at 2 years there was a reduction in pain for the surgical group by 33% (64 to 43), compared with 7% (63 to 58) in the nonsurgical group (P=0.0002). Disability and back related issues were also reduced significantly. More people in the surgical group felt better and were able to go back to work. In the other three studies there was no significant difference between groups. (Fairbank, J., Frost, H., Wilson, MacDonald J. et al , 2005) did have significant results for ODI at 2 years but this was found non-significant when missing data were imputed.

The authors concluded surgical procedures may be more efficacious when compared to unstructured nonsurgical care but this is not so when compared to structured cognitive behaviour therapy. However it cannot be firmly concluded as there were methodological problems with the RCTs which were included.

This was a well conducted systematic review with a low risk of bias

12.3.1.3 Radiofrequency Facet Joint Denervation

One randomized controlled trial assessed the efficacy of percutaneous radiofrequency articular facet denervation for low back pain (Leclaire, R., Fortin, L., Lambert, R. et al , 2001). Seventy participants were included in the RCT, other inclusion criteria were: aged from18 to 65 years, with lower back pain for more than 3 months duration with previous significant relief for at least 24 hours during the week after facet joint injection. Participants were excluded if they had sciatic pain with neurologic deficit, lower back pain not relating to a mechanical disorder, had undergone low back surgery. A total of 36 patients were randomised to percutaneous radiofrequency articular facet denervation, and 34 were randomised to the same procedure without the denervation. Outcome measures taken at 4 and 12 weeks included the Roland Morris score (RMDQ), Oswestry and VAS.

Treatment effect results at four weeks were 6.2 (-1.3 to 13.8, P=0.05), 0.6 (-4.5 to 5.7) and 4.2 (-6.9 to 15.4) for the RMDQ, ODI and pain scores respectively. At twelve weeks the treatment effect results were 2.6 (-6.2 to 11.4), (-3.2 to 7) and -7.6 (-20.3 to 5.1) for the RMDQ, ODI and pain scores respectively.

The authors concluded that radiofrequency facet joint denervation is not shown to be of benefit as determined by functional disability at 12 weeks and no effect on pain at 4 or 12 weeks.

This was a well conducted RCT with a low risk of bias

One RCT evaluated the effect of percutaneous radiofrequency zygapophysial joint neurotomy in reducing pain and physical impairment in patients with pain from lumbar zygapophysial joints (Nath, Sherdil, Nath, Christine Ann, and Pettersson, Kurt, 2008). 40 patients were included, n=20 in the active treatment (intervention group) and n=20 in the placebo (control group) and followed up at 6 months. Adult patients were included if they had continuous low back pain for at least 2 years, had not responded to previous treatment and were able to identify at least one component of their pain which could be attributed to one or more lumbar zygapohysial joints, had paravertebral tenderness and obtained at least 80% relief of

pain following controlled, medial branch blocks. Both groups received the same procedure except that the placebo group received no current from electrodes and the tip stayed at room temperature. Lidocaine 1% and bupivacaine 2mL was given to anaesthetise the nerves and denervation was achieved by multiple lesions.

Patients' global assessment of pain showed a significant reduction in pain for the intervention group. VAS generalized pain reduction, back pain reduction and referred leg pain reduction were significantly reduced in the intervention group compared to the control group (p=0.004). Thus the author concluded that RF neurotomy can be used successfully as a compliment to other interventions to reduce pain in carefully selected patients. It should be noted that the groups were significantly different (intervention group had higher pain) at the start of the trial which could have confounded results. The sample size was also very small.

This was an RCT with a high risk of bias

One RCT assess the efficacy of radiofrequency facet joint denervation (RF) compared to sham procedure for treatment of chronic low back pain (van Wijk, Roelof. M. A. W., Geurts, Jos. W. M., Wynne, Herman. J. et al , 2005). Eighty one participants were included in the RCT. The inclusion criteria was aged over 17 years, lower back pain with or without radiating pain into the upper leg for more than 6 months with focal tenderness over facet joints, no radicular symptoms, at least 50% pain relief on a VAS 30 minutes after a diagnostic block. Forty patients were randomised to the RF group and forty one to the sham procedure. Outcome measures taken at 3 months included VAS, physical activities scale, use of analgesics scale, global perceived effect (back pain), SF-36, Zung.

Success in the combined outcome measure showed no significant differences between the groups 27.5% in intervention and 29.3% in control (P=0.86). No differences in VAS back or leg or medication use between two groups. More people in the intervention group reported greater than 50% reduction in pain at 3 months 61.5% vs 39% P= 0.044.

The authors concluded that there were no differences between the two procedures except a significant improvement in VAS scores. The global perceived effect was in favour of radiofrequency.

This was a well conducted RCT with a low risk of bias

12.3.2 Health economics

Literature searching retrieved 211 papers of which 3 were ordered. Only one was included: this was a UK-based cost-effectiveness study of surgical stabilisation of the spine compared with a programme of intensive rehabilitation (Rivero, Arias Oliver, Campbell, Helen, Gray, Alastair et al , 2005)

Methods

An economic evaluation was conducted alongside a pragmatic RCT of surgical stabilisation vs. intensive rehabilitation for chronic low back pain. The study recruited 349 patients aged between 18 and 55 with chronic low back pain of at least one year's duration who were considered candidates for spinal fusion. Patients were eligible for the study if it was uncertain which of the two treatments would be best, in the opinion of both patient and consultant.

The particular technique used for spinal fusion was left to the discretion of the operating surgeon. The intensive rehabilitation programme (IRP) consisted of education and exercise provided by physiotherapists and clinical psychologists, for 5 days per week for three consecutive weeks. Most centres offered 75 hours of intervention with one day of follow-up at one, three, six or 12 months after treatment. Patients were not denied alternative healthcare interventions for their back pain. This meant that some patients in each group had both surgery and IRP during the follow-up period.

Main outcome measures were costs related to back pain and incurred by the NHS and patients up to 24 months after randomisation, as well as patient utility as estimated by using the EuroQol EQ-5D questionnaire at several time points. Utility values were used to calculate quality adjusted life years (QALYs). Cost effectiveness was expressed as an incremental cost per QALY. The costing perspective was that of the UK health service. Healthcare resources included those for: initial treatments, other back pain related hospital inpatient and outpatient visits, primary care contacts, and prescribed items of medication. These resources were costed using published

national averages for England. Costs were reported in pounds sterling at 2002/2003 prices. Costs and benefits were discounted at an annual rate of 3.5%.

Sensitivity analysis examined the impact on incremental cost per QALY of:

- Using the least expensive surgical technique
- Using the most expensive surgical technique
- QALY differences between the two groups being maintained for a further two years
- Assuming that patients in each arm of the study would continue to receive both treatments in years 3,4 and 5 at the rates observed in years 1 and 2.
- Assuming that patients in each arm of the study would continue to receive both treatments in years 3,4 and 5 at half the rates observed in years 1 and 2.

Results (base case)

The mean cost (Standard Deviation) for patients in the surgery arm was £7830 (SD=£5202) and for patients in the IRP it was £4526 (SD=£4155).

The difference of £3304 (£2317 to £4291, $p<0.001$) was in favour of the IRP group. At 24 months mean QALYs for the surgery arm was 1.004 (SD=0.405) and for IRP it was 0.936(SD=0.431). The difference was 0.068 (-0.02 to 0.156). Therefore the incremental cost per QALY of using a policy of immediate surgery was £48,588 (-£279,883 to £372,406). Probablistic sensitivity analysis shows that if decision makers are willing to pay £30,000 for a QALY, at two years, the chance that surgery will be cost effective is less than 20%.

Sensitivity analysis

Five scenarios were chosen for sensitivity analysis.

1. If patients who had surgery had the least expensive technique the cost difference between the two groups would fall to £2403 which would result in a lower incremental cost per QALY of £35,338(-£188,876 to £410,404)

2. If patients who had surgery had the most expensive technique the cost difference would rise and the resulting incremental cost per QALY would rise to £60,765 (-£420,210 to £617,081)

3. If QALY differences between the two groups was maintained for a further two years then the incremental cost per QALY would fall to £25,398 (£13,121 to £75,916).

4. If patients in the study continued to receive both treatments in years three, four and five at the rates observed in years one and two, the incremental cost per QALY would fall to £16,824 (-£156,358 to £138,911)

5. If patients in the study continued to receive both treatments in years three, four and five at half the rates observed in years one and two, the incremental cost per QALY would fall to £31,838 (-£407,056 to £283,783)

This study shows that in the base case analysis the incremental cost per QALY of having a policy of immediate surgery for chronic low back pain is £48,588. And if decision makers are willing to pay £30,000 for a QALY, at two years, the chance that surgery will be cost effective is less than 20%. Cost per QALY would be less than £30,000 if either QALY differences between the two groups was maintained for a further two years, or if patients in the study continued to receive both treatments in years 3,4 and 5 at the rates observed in years one and two.

It should be noted that the inclusion criteria specified that patients who were candidates for surgical stabilisation of the spine were eligible only if the clinician and patient were uncertain which of the study treatment strategies was best.

12.3.3 Evidence statements for referral for surgery

Evidence statements	Evidence to recommendations
12.3.3.1 A systematic review on IDET identified 3 RCTs comparing IDET to sham. Primary outcomes included pain intensity (VAS) and functional status (ODI). One RCT found the advantage of IDET over sham was 1.3 on VAS P=0.045 and seven points on ODI. No significant difference was found in SF-36 bodily pain or physical function. Another RCT found no difference between treatments. 1 RCT on PIRFT found no significant differences in VAS, ODI in either group after 8 weeks. Current evidence does not provide clear evidence of benefit for IDET and no evidence of benefit for PIRFT. (1+) (Freeman-Brian, J. C., 2006)	The GDG estimated that the serious adverse events from surgery was between 1-2%. Less serious effects are calculated within the cost effectiveness. Trial data was not specifically on our population, all had chronic LBP for over 1 year. The Fairbank trial excluded a priori people who may have been judged likely or unlikely to respond well to surgery. The GDG felt that this inclusion criterion may have introduced bias into the analysis. Cost effectiveness analysis shows that the chance that surgery is cost effective at 2 years is less than 20%.
12.3.3.2 One meta-analysis of Spinal Fusion vs. non-surgical treatment found 3 RCTs using ODI as the main outcome measure. This showed overall benefit of surgery when compared to other treatments for those with severe pain lasting longer than 1 year.(1+) (Ibrahim, T., Tleyjeh, I. M., and Gabbar, O., 2008)	The group agreed that spinal fusion should be reserved for a small group of selected individuals who failed to respond to a combined physical and psychological intervention where referral for an opinion on spinal fusion may be appropriate.

12.3.3.3 Three RCTs compared radiofrequency facet joint denervation to a sham procedure. One RCT found no effect on pain at 4 or 12 weeks and short term improvement in function at 4 weeks but not at 12 weeks.(1+) (Leclaire, R., Fortin, L., Lambert, R. et al , 2001). A second small RCT showed significant reductions in VAS generalised pain reduction, back pain reduction and referred leg pain in the intervention group compared to the control group at 6 months. The overall conclusion was that radiofrequency neurotomy could be used successfully as a compliment to other interventions to reduce pain in carefully selected patients. (1-) (Nath, Sherdil, Nath, Christine Ann, and Pettersson, Kurt, 2008). The third RCT showed significant improvement in VAS but no difference between the two groups. (1+) (van Wijk, Roelof. M. A. W., Geurts, Jos. W. M., Wynne, Herman. J. et al , 2005) Cost effectiveness *12.3.3.4 One economic evaluation conducted alongside an RCT of spinal fusion vs intensive*	One small study showed some evidence of benefit for radiofrequency facet joint denervation to reduce pain, whilst two other studies found no evidence of benefit. The GDG concluded further research was required. No evidence of benefit was found for IDET

	rehabilitation showed that in the base case analysis the incremental cost per QALY of having a policy of immediate surgery is £48.588. At £30,000 per QALY the chance that surgery will be cost effective at 2 years is less than 20%.(Rivero, Arias Oliver, Campbell, Helen, Gray, Alastair et al , 2005)	

13 Reference List

(1) Airaksinen O, Brox JI, Cedraschi C, Hildebrandt J et al. Chapter 4. European guidelines for the management of chronic nonspecific low back pain. Eur Spine J. 2006; 15 (Supp 2) :S192-S300.

(2) Alaranta H, Rytokoski U, Rissanen A, Talo S et al. Intensive physical and psychosocial training program for patients with chronic low back pain: a controlled clinical trial. Spine. 1994; 19 (12) :1339-1349.

(3) Andersson GB, Lucente T, Davis AM, Kappler RE et al. A comparison of osteopathic spinal manipulation with standard care for patients with low back pain. N Engl J Med. 1999; 341 (19) :1426-1431.

(4) Andersson HI, Ejlertsson G, Leden I, Rosenberg C. Chronic pain in a geographically defined general population: studies of differences in age, gender, social class, and pain localization. Clin J Pain. 1993; 9 (3) :174-182.

(5) Arthritis Research Campaign. Arthritis the big picture. Arthritis Research Campaign. 2002

(6) Atkinson JH, Slater MA, Wahlgren DR, Williams RA et al. Effects of noradrenergic and serotonergic antidepressants on chronic low back pain intensity. Pain. 1999; 83 (2) :137-145.

(7) Atkinson JH, Slater MA, Williams RA, Zisook S et al. A placebo-controlled randomized clinical trial of nortriptyline for chronic low back pain. Pain. 1998; 76 (3) :287-296.

(8) Basford JR, Sheffield CG, Harmsen WS. Laser therapy: a randomized, controlled trial of the effects of low- intensity Nd:YAG laser irradiation on musculoskeletal back pain. Arch Phys Med Rehabil. 1999; 80 (6) :647-652.

(9) Bendix AE, Bendix T, Haestrup C, Busch E. A prospective, randomized 5-year follow-up study of functional restoration in chronic low back pain patients. Eur Spine J. 1998; 7 (2) :111-119.

(10) Bendix AF, Bendix T, Labriola M, Boekgaard P. Functional restoration for chronic low back pain. Two-year follow-up of two randomized clinical trials. Spine. 1998; 23 (6) :717-725.

(11) Bendix AF, Bendix T, Lund C, Kirkbak S et al. Comparison of three intensive programs for chronic low back pain patients: a prospective, randomized, observer-blinded study with one- year follow-up. Scand J Rehabil Med. 1997; 29 (2) :81-89.

(12) Bendix AF, Bendix T, Ostenfeld S, Bush E et al. Active treatment programs for patients with chronic low back pain: a prospective, randomized, observer-blinded study. Eur Spine J. 1995; 4 (3) :148-152.

(13) Bendix AF, Bendix T, Vaegter K, Lund C et al. Multidisciplinary intensive treatment for chronic low back pain: a randomized, prospective study. Cleve Clin J Med. 1996; 63 (1) :62-69.

(14) Bendix T, Bendix A, Labriola M, Haestrup C et al. Functional restoration versus outpatient physical training in chronic low back pain: a randomized comparative study. Spine. 2000; 25 (19) :2494-2500.

(15) Berry H, Bloom B, Hamilton EB, Swinson DR. Naproxen sodium, diflunisal, and placebo in the treatment of chronic back pain. Ann Rheum Dis. 1982; 41 (2) :129-132.

(16) Beurskens AJ, de Vet HC, Koke AJ, Regtop W et al. Efficacy of traction for nonspecific low back pain. 12-week and 6-month results of a randomized clinical trial. Spine. 1997; 22 (23) :2756-2762.

(17) Birbara CA, Puopolo AD, Munoz DR, Sheldon EA et al. Treatment of chronic low back pain with etoricoxib, a new cyclo-oxygenase-2 selective inhibitor: improvement in pain and disability--a randomized, placebo-controlled, 3-month trial. J Pain. 2003; 4 (6) :307-315.

(18) Borman P, Keskin D, Bodur H. The efficacy of lumbar traction in the management of patients with low back pain. Rheumatol Int. 2003; 23 (2) :82-86.

(19) Boswell M, V, Colson JD, Sehgal N, Dunbar EE et al. A systematic review of therapeutic facet joint interventions in chronic spinal pain. Pain Physician. 2007; 10 (1) :229-253.

(20) Brinkhaus B, Witt CM, Jena S, Linde K et al. Acupuncture in patients with chronic low back pain: a randomized controlled trial. Arch Intern Med. 2006; 166 (4) :450-457.

(21) Brox IJ, Sorensen R, Friis A, Nygaard O et al. Randomized clinical trial of lumbar instrumented fusion and cognitive intervention and exercises in patients with chronic low back pain and disc degeneration. Spine. 2003; 28 (17) :1913-1921.

(22) Brox J, I, Reikerås O, Nygaard Ø, Sørensen R et al. Lumbar instrumented fusion compared with cognitive intervention and exercises in patients with chronic back pain after previous surgery for disc herniation: a prospective randomized controlled study. Pain. 2006; 122 (1-2) :145-155.

(23) Burton AK, Waddell G, Tillotson KM, Summerton N. Information and advice to patients with back pain can have a positive effect. A randomized controlled trial of a novel educational booklet in primary care. Spine. 1999; 24 (23) :2484-2491.

(24) Callaghan MJ. Evaluation of a back rehabilitation group for chronic low back pain in an out-patient setting. Physiotherapy. 1994; 80 (10) :677-681.

(25) Carette S, Marcoux S, Truchon R, Grondin C et al. A controlled trial of corticosteroid injections into facet joints for chronic low back pain. N Engl J Med. 1991; 325 (14) :1002-1007.

(26) Cassidy JD, Boyle E, Cote P, He Y et al. Risk of vertebrobasilar stroke and chiropractic care: results of a population-based case-control and case-crossover study. Spine. 2008; 33 (4 Suppl) :S176-S183.

(27) Cassidy JD, Carroll LJ, Cote P. The Saskatchewan health and back pain survey. The prevalence of low back pain and related disability in Saskatchewan adults. Spine. 1998; 23 (17) :1860-1866.

(28) Cherkin DC, Deyo RA, Battié M, Street J et al. A comparison of physical therapy, chiropractic manipulation, and provision of an educational booklet for the treatment of patients with low back pain. N Engl J Med. 1998; 339 (15) :1021-1029.

(29) Clarke J, van TM, Blomberg S, de VH et al. Traction for low back pain with or without sciatica: an updated systematic review within the framework of the Cochrane collaboration. Spine. 2006; 31 (14) :1591-1599.

(30) Coats TL, Borenstein DG, Nangia NK, Brown MT. Effects of valdecoxib in the treatment of chronic low back pain: results of a randomized, placebo-controlled trial. Clin Ther. 2004; 26 (8) :1249-1260.

(31) Cook C, Cook A, Worrell T. Manual therapy provided by physical therapists in a hospital-based setting: a retrospective analysis. J Manipulative Physiol Ther. 2008; 31 (5) :338-343.

(32) Corey DT, Koepfler LE, Etlin D, Day HI. A limited functional restoration program for injured workers: a randomized trial. J Occup Rehabil. 1996; 6 (4) :239-249.

(33) Coxhead CE, Inskip H, Meade TW, North WR et al. Multicentre trial of physiotherapy in the management of sciatic symptoms. Lancet. 1981; 1 (8229) :1065-1068.

(34) Critchley DJ, Ratcliffe J, Noonan S, Jones RH et al. Effectiveness and cost-effectiveness of three types of physiotherapy used to reduce chronic low back pain disability: a pragmatic randomized trial with economic evaluation. Spine. 2007; 32 (14) :1474-1481.

(35) Croft PR, Macfarlane GJ, Papageorgiou AC, Thomas E et al. Outcome of low back pain in general practice: a prospective study. BMJ. 1998; 316 (7141) :1356-1359.

(36) Dagenais S, Caro J, Haldeman S. A systematic review of low back pain cost of illness studies in the United States and internationally. Spine J. 2008; 8 (1) :8-20.

(37) Dagenais S, Yelland MJ, Del Mar C, Schoene ML. Prolotherapy injections for chronic low-back pain. England.: 2007.

(38) Deyo RA, Walsh NE, Martin DC, Schoenfeld LS et al. A controlled trial of transcutaneous electrical nerve stimulation (TENS) and exercise for chronic low back pain. N Engl J Med. 1990;(23) :1627-1634.

(39) Dickens C, Jayson M, Sutton C, Creed F. The relationship between pain and depression in a trial using paroxetine in sufferers of chronic low back pain. Psychosomatics. 2000; 41 (6) :490-499.

(40) Doran DM, Newell DJ. Manipulation in treatment of low back pain: a multicentre study. BMJ. 1975; 2 (5964) :161-164.

(41) Dvorak J, Loustalot D, Baumgartner H, Antinnes JA. Frequency of complications of manipulation of the spine. A survey among the members of the Swiss Medical Society of Manual Medicine. Eur Spine J. 1993; 2 (3) :136-139.

(42) Ekman P, Möller H, Hedlund R. The long-term effect of posterolateral fusion in adult isthmic spondylolisthesis: A randomized controlled study. Spine J. 2005; 5 (1) :36-44.

(43) Ernst E. Adverse effects of spinal manipulation: a systematic review. J R Soc Med. 2007; 100 (7) :330-338.

(44) Fairbank J, Frost H, Wilson MJ, Yu LM et al. Randomised controlled trial to compare surgical stabilisation of the lumbar spine with an intensive rehabilitation programme for patients with chronic low back pain: The MRC spine stabilisation trial. BMJ. 2005; 330 (7502) :1233-1239.

(45) Freeman BJC, Mehdian R. Intradiscal electrothermal therapy, percutaneous discectomy, and nucleoplasty: what is the current evidence? Curr Pain Headache Rep. 2008; 12 (1) :14-21.

(46) Freeman-Brian JC. IDET: a critical appraisal of the evidence. Eur Spine J. 2006; 15 (Suppl 3) :S448-S457.

(47) Friedrich M, Gittler G, Arendasy M, Friedrich KM. Long-term effect of a combined exercise and motivational program on the level of disability of patients with chronic low back pain. Spine. 2005; 30 (9) :995-1000.

(48) Friedrich M, Gittler G, Halberstadt Y, Cermak T et al. Combined exercise and motivation program: effect on the compliance and level of disability of patients with chronic low back pain: a randomized controlled trial. Arch Phys Med Rehabil. 1998; 79 (5) :475-487.

(49) Fritzell P, Hägg O, Wessberg P, Nordwall A. 2001 Volvo Award Winner in Clinical Studies: Lumbar fusion versus nonsurgical treatment for chronic low back pain: a multicenter randomized controlled trial from the Swedish Lumbar Spine Study Group. Spine. 2001; 26 (23) :2521-2532.

(50) Furlan AD, Brosseau L, Imamura M, Irvin E. Massage for low back pain. Cochrane Database of Systematic Reviews, Issue 4 2007. Chichester: John Wiley & Sons Ltd; 2002.

(51) Furlan AD, Van-Tulder MW, Cherkin DC, Tsukayama H et al. Acupuncture and dry-needling for low back pain. England.: 2005.

(52) Gibson JNA, Ahmed M. The effectiveness of flexible and rigid supports in patients with lumbar backache. J Orthop Med. 2002; 24 :84-89.

(53) Gilbert FJ, Grant AM, Gillan M-GC, Vale L et al. Does early imaging influence management and improve outcome in patients with low back pain? A pragmatic randomised controlled trial. Health Technol Assess. 2004; 8 (17) :1-131.

(54) Glomsrod B, Lonn JH, Soukup MG, Bo K et al. "Active back school", prophylactic management for low back pain: Three-year follow-up of a randomized, controlled trial. J Rehabil Med. 2001; 33 (1) :26-30.

(55) Gobel H. Epidemiology and costs of chronic pain syndromes exemplified by specific and unspecific low back pain. Schmerz. 2001; 15 (2) :92-98.

(56) Goldby LJ, Moore AP, Doust Jo, Trew ME. A randomized controlled trial investigating the efficiency of musculoskeletal physiotherapy on chronic low back disorder. Spine. 2006; 31 (10) :1083-1093.

(57) Goodkin K, Gullion CM, Agras WS. A randomized, double-blind, placebo-controlled trial of trazodone hydrochloride in chronic low back pain syndrome. J Clin Psychopharmacol. 1990; 10 (4) :269-278.

(58) Gur A, Karakoc M, Cevik R, Nas K et al. Efficacy of low power laser therapy and exercise on pain and functions in chronic low back pain. Lasers Surg Med. 2003; 32 :233-238.

(59) Haake M, Müller HH, Schade BC, Basler HD et al. German Acupuncture Trials (GERAC) for Chronic Low Back Pain: Randomized, Multicenter, Blinded, Parallel-Group Trial With 3 Groups. Arch Intern Med. 2007; 167 (17) :1892-1898.

(60) Haldorsen-Ellen MH, Grasdal AL, Skouen JS, Risa AE et al. Is there a right treatment for a particular patient group? Comparison of ordinary treatment, light multidisciplinary treatment, and extensive multidisciplinary treatment for long-term sick-listed employees with musculoskeletal pain. Pain. 2002; 95 (1-2) :49-63.

(61) Hayden JA, van Tulder MW, Malmivaara A, Koes BW. Exercise therapy for treatment of non-specific low back pain. Cochrane Database of Systematic Reviews, Issue 3 2006. Chichester: John Wiley & Sons Ltd; 2005.

(62) Hayden JA, van-Tulder MW, Tomlinson G. Systematic review: Strategies for using exercise therapy to improve outcomes in chronic low back pain. Ann Intern Med. 2005; 142 (9) :776-785.

(63) Hestbaek L, Leboeuf-Yde C, Manniche C. Low back pain: what is the long-term course? A review of studies of general patient populations. Eur Spine J. 2003; 12 (2) :149-165.

(64) Heymans MW, Van-Tulder MW, Esmail R, Bombardier C et al. Back schools for non-specific low-back pain. Cochrane Database of Systematic Reviews, Issue 1 2008. Chichester: John Wiley & Sons Ltd; 2004.

(65) Heymans MW, de-Vet-Henrica CW, Bongers PM, Knol DL et al. The effectiveness of high-intensity versus low-intensity back schools in an occupational setting: a pragmatic randomized controlled trial. Spine. 2006; 31 (10) :1075-1082.

(66) Hickey RF. Chronic low back pain: a comparison of diflunisal with paracetamol. N Z Med J. 1982; 95 (707) :312-314.

(67) Hoffman BM, Papas RK, Chatkoff DK, Kerns RD. Meta-analysis of psychological interventions for chronic low back pain. Health Psychol. 2007; 26 (1) :1-9.

(68) Hollingworth W, Gray DT, Martin B, I, Sullivan SD et al. Rapid magnetic resonance imaging for diagnosing cancer-related low back pain. J Gen Intern Med. 2003; 18 (4) :303-312.

(69) Hsieh CY, Phillips RB, Adams AH, Pope MH. Functional outcomes of low back pain: comparison of four treatment groups in a randomized controlled trial. J Manipulative Physiol Ther. 1992; 15 (1) :4-9.

(70) Hsieh RL, Lee WC. One-shot percutaneous electrical nerve stimulation vs. transcutaneous electrical nerve stimulation for low back pain: comparison of therapeutic effects. Am J Phys Med Rehabil. 2002; 81 (11) :838-843.

(71) Hurwitz EL, Morgenstern H, Harber P, Kominski GF et al. A randomized trial of medical care with and without physical therapy and chiropractic care with and without physical modalities for patients with low back pain: 6-month follow-up outcomes from the UCLA low back pain study. Spine. 2002; 27 (20) :2193-2204.

(72) Hurwitz EL, Morgenstern H, Kominski GF, Yu F et al. A randomized trial of chiropractic and medical care for patients with low back pain: eighteen-month follow-up outcomes from the UCLA low back pain study. Spine. 2006; 31 (6) :611-621.

(73) Ibrahim T, Tleyjeh IM, Gabbar O. Surgical versus non-surgical treatment of chronic low back pain: a meta-analysis of randomised trials. Int Orthop. 2008; 32 (1) :107-113.

(74) Jarvik JG, Hollingworth W, Martin B, Emerson SS et al. Rapid magnetic resonance imaging vs radiographs for patients with low back pain: a randomized controlled trial. JAMA. 2003; 289 (21) :2810-2818.

(75) Jarzem PF, Harvey EJ, Arcaro N, Kaczorowski J. Transcutaneous electrical nerve stimulation (TENS) for chronic low back pain. J Musculoskelet Pain. 2005a; 13 (2) :3-9.

(76) Jarzem PF, Harvey EJ, Arcaro N, Kaczorowski J. Transcutaneous electrical nerve stimulation (TENS) for short-term treatment of low back pain - Randomized double blind crossover study of sham versus conventional TENS. J Musculoskelet Pain. 2005b; 13 (2) :11-17.

(77) Jenkins DG, Ebbutt AF, Evans CD. Tofranil in the treatment of low back pain. J Int Med Res. 1976; 4 (2 Suppl) :28-40.

(78) Johnson RE, Jones GT, Wiles NJ, Chaddock C et al. Active exercise, education, and cognitive behavioral therapy for persistent disabling low back pain: a randomized controlled trial. Spine. 2007; 32 (15) :1578-1585.

(79) Kääpä EH, Frantsi K, Sarna S, Malmivaara A. Multidisciplinary group rehabilitation versus individual physiotherapy for chronic nonspecific low back pain: a randomized trial. Spine. 2006; 31 (4) :371-376.

(80) Katz J, Pennella VJ, Hetzel RD, Kanazi GE et al. A randomized, placebo-controlled trial of bupropion sustained release in chronic low back pain. J Pain. 2005; 6 (10) :656-661.

(81) Katz N, Ju WD, Krupa DA, Sperling RS et al. Efficacy and safety of rofecoxib in patients with chronic low back pain: results from two 4-week, randomized, placebo-controlled, parallel-group, double-blind trials. Spine. 2003; 28 (9) :851-858.

(82) Katz N, Rauck R, Ahdieh H, Ma T et al. A 12-week, randomized, placebo-controlled trial assessing the safety and efficacy of oxymorphone extended release for opioid-naive patients with chronic low back pain. Curr Med Res Opin. 2007; 23 (1) :117-128.

(83) Keller S, Ehrhardt SS, Herda C, Schmid S et al. Multidisciplinary rehabilitation for chronic back pain in an outpatient setting: a controlled randomized trial. Eur J Pain. 1997; 1 (4) :279-292.

(84) Kendrick D, Fielding K, Bentley E, Miller P et al. The role of radiography in primary care patients with low back pain of at least 6 weeks duration: a randomised (unblinded) controlled trial. Health Technol Assess. 2001; 5 (30) :1-69.

(85) Kerry S, Hilton S, Patel S, Dundas D et al. Routine referral for radiography of patients presenting with low back pain: Is patients' outcome influenced by GPs' referral for plain radiography? Health Technol Assess. 2000; 4 (20) :-110.

(86) Khot A, Bowditch M, Powell J, Sharp D. The use of intradiscal steroid therapy for lumbar spinal discogenic pain: a randomized controlled trial. Spine. 2004; 29 (8) :833-836.

(87) Klein RG, Eek BC. Low-energy laser treatment and exercise for chronic low back pain: double-blind controlled trial. Arch Phys Med Rehabil. 1990; 71 (1) :34-37.

(88) Koes B, van Tulder M. Low back pain (acute). Clin Evid. 2006;(15) :1619-1633.

(89) Koes BW, van Tulder MW, Ostelo R, Kim BA et al. Clinical guidelines for the management of low back pain in primary care: an international comparison. Spine. 2001; 26 (22) :2504-2513.

(90) Kuukkanen T, Mälkiä E. Effects of a three-month therapeutic exercise programme on flexibility in subjects with low back pain. Physiother Res Int. 2000; 5 (1) :46-61.

(91) Kuukkanen T, Mälkiä E, Kautiainen H, Pohjolainen T. Effectiveness of a home exercise programme in low back pain: a randomized five-year follow-up study. Physiother Res Int. 2007; 12 (4) :213-224.

(92) Larsson U, Choler U, Lidstrom A, Lind G et al. Auto-traction for treatment of lumbago-sciatica. A multicentre controlled investigation. Acta Orthop Scand. 1980; 51 (5) :791-798.

(93) Leclaire R, Fortin L, Lambert R, Bergeron YM et al. Radiofrequency facet joint denervation in the treatment of low back pain: a placebo-controlled clinical trial to assess efficacy. Spine. 2001; 26 (13) :1411-1416.

(94) Lind G. Auto-traction, treatment of low back pain and sciatica. An electromyographic, radiographic and clinical study (thesis). [Linkoping: University of Linkoping; 1974.

(95) Linton SJ, Andersson T. Can chronic disability be prevented? A randomized trial of a cognitive-behavior intervention and two forms of information for patients with spinal pain. Spine. 2000; 25 (21) :2825-2831.

(96) Little P, Lewith G, Webley F, Evans M et al. Randomised controlled trial of Alexander technique lessons, exercise, and massage (ATEAM) for chronic and recurrent back pain. BMJ. 2008; 337 :a884.

(97) Little P, Roberts L, Blowers H, Garwood J et al. Should we give detailed advice and information booklets to patients with back pain? A randomized controlled factorial trial of a self-management booklet and doctor advice to take exercise for back pain. Spine. 2001; 26 (19) :2065-2072.

(98) Longo L, Tamburini A, Monti A. Treatment with 904 nm and 10600 nm laser of acute lumbago - double blind control-laser. Journal Eur Med Laser Ass. 1991; 3 :16-19.

(99) Lønn JH, Glomsrød B, Soukup MG, Bø K et al. Active back school: prophylactic management for low back pain. A randomized, controlled, 1-year follow-up study. Spine. 1999; 24 (9) :865-871.

(100) Macfarlane GJ, Jones GT, Hannaford PC. Managing low back pain presenting to primary care: where do we go from here? Pain. 2006; 122 (3) :219-222.

(101) Maniadakis N, Gray A. The economic burden of back pain in the UK. Pain. 2000; 84 (1) :95-103.

(102) Mannion AF, Müntener M, Taimela S, Dvorak J. Comparison of three active therapies for chronic low back pain: results of a randomized clinical trial with one-year follow-up. Rheumatology. 2001; 40 (7) :772-778.

(103) Maul I, Läubli T, Oliveri M, Krueger H. Long-term effects of supervised physical training in secondary prevention of low back pain. Eur Spine J. 2005; 14 (6) :599-611.

(104) McCracken LM, Turk DC. Behavioral and cognitive-behavioral treatment for chronic pain: outcome, predictors of outcome, and treatment process. Spine. 2002; 27 (22) :2564-2573.

(105) McIlveen B, Robertson VJ. A randomised controlled study of the outcome of hydrotherapy for subjects with low back or back and leg pain. Physiotherapy. 1998; 84 (1) :17-26.

(106) Mirza SK, Deyo RA. Systematic review of randomized trials comparing lumbar fusion surgery to nonoperative care for treatment of chronic back pain. Spine. 2007; 32 (7) :816-823.

(107) Moore JE, Von Korff M, Cherkin D, Saunders K. A randomized trial of a cognitive-behavioral program for enhancing back pain self care in a primary care setting. Pain. 2000; 88 (2) :145-153.

(108) Nath S, Nath CA, Pettersson K. Percutaneous lumbar zygapophysial (Facet) joint neurotomy using radiofrequency current, in the management of chronic low back pain: a randomized double-blind trial. Spine. 2008; 33 (12) :1291-1297.

(109) National Institute for Health and Clinical Excellence. Four commonly used methods to increase physical activity: brief interventions in primary care, exercise referral schemes, pedometers and community-based exercise programmes for walking and cycling. London: National Institute for Health and Clinical Excellence. 2006

(110) National Institute for Health and Clinical Excellence. Osteoarthritis: the care and management of osteoarthritis in adults. London: National Institute of Health and Clinical Excellence. 2008

(111) Office for National Statistics. All items Retail Price Index (RPI) percentage change over 12 months: Table RP04. 2008. Office for National Statistics website [Accessed 2008 Aug. 14]; Available from: URL:http://www.statistics.gov.uk/default.asp

(112) Ostelo RWJG, van Tulder MW, Vlaeyen JWS, Linton SJ et al. Behavioural treatment for chronic low-back pain. Cochrane Database of Systematic Reviews, Issue 3 2006. Chichester: John Wiley & Sons Ltd; 2005.

(113) Parsons S, Breen A, Foster NE, Letley L et al. Prevalence and comparative troublesomeness by age of musculoskeletal pain in different body locations. Fam Pract. 2007; 24 (4) :308-316.

(114) Pengel LH, Herbert RD, Maher CG, Refshauge KM. Acute low back pain: systematic review of its prognosis. BMJ. 2003; 327 (7410) :323.

(115) Penrose KW, Chook K, Stump JL. Acute and chronic effects of pneumatic lumbar support on muscular strength, flexibility, and functional impairment index. Sports Train Med Rehabil. 1991; 2 :121-129.

(116) Pincus T, Santos R, Breen A, Burton AK et al. A review and proposal for a core set of factors for prospective cohorts in low back pain: a consensus statement. Arthritis Rheum. 2008; 59 (1) :14-24.

(117) Ratcliffe J, Thomas KJ, MacPherson H, Brazier J. A randomised controlled trial of acupuncture care for persistent low back pain: cost effectiveness analysis. BMJ. 2006; 333 (7569) :626.

(118) Rivero AO, Campbell H, Gray A, Fairbank J et al. Surgical stabilisation of the spine compared with a programme of intensive rehabilitation for the management of patients with chronic low back pain: cost utility analysis based on a randomised controlled trial. BMJ. 2005; 330 (7502) :1239.

(119) Roberts L, Little P, Chapman J, Cantrell T et al. The back home trial: general practitioner-supported leaflets may change back pain behavior. Spine. 2002; 27 (17) :1821-1828.

(120) Roelofs PDDM, Deyo RA, Koes BW, Scholten RJPM et al. Non-steroidal anti-inflammatory drugs for low back pain. 2008.

(121) Sherman KJ, Cherkin DC, Erro J, Miglioretti DL et al. Comparing yoga, exercise, and a self-care book for chronic low back pain: a randomized, controlled trial. Ann Intern Med. 2005; 143 (12) :849-856.

(122) Skouen JS, Grasdal AL, Haldorsen EMH, Ursin H. Relative cost-effectiveness of extensive and light multidisciplinary treatment programs versus treatment as usual for patients with chronic low back pain on long-term sick leave: randomized controlled study. Spine. 2002; 27 (9) :901-909.

(123) Smeets RJEM, Vlaeyen JWS, Hidding A, Kester ADM et al. Chronic low back pain: physical training, graded activity with problem solving training, or both? The one-year post-treatment results of a randomized controlled trial. Pain. 2008; 134 (3) :263-276.

(124) Soriano F. Gallium Arsenide laser treatment of chronic low back pain: a prospective, randomized and double blind study. Laser Ther. 1998; 10 (4) :175-180.

(125) Spitzer WO, Leblanc FE. Scientific approach to the assessment and management of activity-related spinal disorders. A monograph for clinicians. Report of the Quebec Task Force on Spinal Disorders. Spine. 1987; 12 (7 Suppl) :S1-59.

(126) Steenstra IA, Anema JR, Bongers PM, de-Vet H-CW et al. The effectiveness of graded activity for low back pain in occupational healthcare. Occup Environ Med. 2006; 63 (11) :718-725.

(127) Stevinson C, Ernst E. Risks associated with spinal manipulation. Am J Med. 2002; 112 (7) :566-571.

(128) Storheim K, Brox J, I, Holm I, Koller AK et al. Intensive group training versus cognitive intervention in sub-acute low back pain: short-term results of a single-blind randomized controlled trial. J Rehabil Med. 2003; 35 (3) :132-140.

(129) Tavafian SS, Jamshidi A, Mohammad K, Montazeri A. Low back pain education and short term quality of life: a randomized trial. BMC Musculoskelet Disord. 2007; 8 (21) .

(130) Thomas KJ, MacPherson H, Ratcliffe J, Thorpe L et al. Longer term clinical and economic benefits of offering acupuncture care to patients with chronic low back pain. Health Technol Assess. 2005; 9 (32) :iii-iiv.

(131) Thomsen AB, Sorensen J, Sjogren P, Eriksen J. Economic evaluation of multidisciplinary pain management in chronic pain patients: a qualitative systematic review. J Pain Symptom Manage. 2001; 22 (2) :688-698.

(132) Toya S, Motegi M, Inomata K, Ohshiro T et al. Report on a computer-randomized double blind clinical trial to determine the effectiveness of the GaAlAs (830 nm) diode laser for pain attenuation in selected pain groups. Laser Ther. 1994; 6 :143-148.

(133) Triano JJ, McGregor M, Hondras MA, Brennan PC. Manipulative therapy versus education programs in chronic low back pain. Spine. 1995; 20 (8) :948-955.

(134) Turk DC. Clinical effectiveness and cost-effectiveness of treatments for patients with chronic pain. Clin J Pain. 2002; 18 (6) :355-365.

(135) Turk DC, Okifuji A. Assessment of patients' reporting of pain: an integrated perspective. Lancet. 1999; 353 (9166) :1784-1788.

(136) UK Back pain exercise and manipulation (UKBEAM) Trial Team. United Kingdom back pain exercise and manipulation (UK BEAM) randomised trial: Cost effectiveness of physical treatments for back pain in primary care. BMJ. 2004; 329 (7479) :1381-1385.

(137) UK Back pain exercise and manipulation (UKBEAM) Trial Team. United Kingdom back pain exercise and manipulation (UK BEAM) randomised trial: effectiveness of physical treatments for back pain in primary care. BMJ. 2004; 329 (7479) :1377-1384.

(138) Urquhart DM, Hoving JL, Assendelft W-WJJ, Roland M et al. Antidepressants for non-specific low back pain. England.: 2008.

(139) Urrútia G, Burton AK, Morral A, Bonfill X et al. Neuroreflexotherapy for non-specific low-back pain. England.: 2004.

(140) Valle-Jones JC, Walsh H, O'Hara J, O'Hara H et al. Controlled trial of a back support ('Lumbotrain') in patients with non-specific low back pain. Curr Med Res Opin. 1992; 12 (9) :604-613.

(141) van der Heijden GJ, Beurskens AJ, Dirx MJ, Bouter LM et al. Efficacy of Lumbar Traction: A randomised clinical trial. Physiotherapy. 1995; 81 (1) :29-35.

(142) van Duijvenbode I, Jellema P, van Poppel MNM, van Tulder MW. Lumbar supports for prevention and treatment of low back pain. 2008.

(143) van Wijk RMAW, Geurts JWM, Wynne HJ, Hammink E et al. Radiofrequency denervation of lumbar facet joints in the treatment of chronic low back pain: a randomized, double-blind, sham lesion- controlled trial. Clin J Pain. 2005; 21 (4) :335-344.

(144) Vetter TR. The application of economic evaluation methods in the chronic pain medicine literature. Anesth Analg. 2007b; 105 (1) :114-118.

(145) Vetter TR. A primer on health-related quality of life in chronic pain medicine. Anesth Analg. 2007a; 104 (3) :703-718.

(146) Vorsanger GJ, Xiang J, Gana TJ, Pascual-Maria LG et al. Extended-release tramadol (tramadol ER) in the treatment of chronic low back pain. J Opioid Man. 2008; 4 (2) :87-97.

(147) Walker BF. The prevalence of low back pain: a systematic review of the literature from 1966 to 1998. J Spinal Disord. 2000; 13 (3) :205-217.

(148) Webster LR, Butera PG, Moran LV, Wu N et al. Oxytrex minimizes physical dependence while providing effective analgesia: a randomized controlled trial in low back pain. J Pain. 2006; 7 (12) :937-946.

(149) Witt CM, Jena S, Selim D, Brinkhaus B et al. Pragmatic randomized trial evaluating the clinical and economic effectiveness of acupuncture for chronic low back pain. Am J Epidemiol. 2006; 164 (5) :487-496.

(150) Yousefi NR, Schonstein E, Heidari K, Rashidian A et al. Low level laser therapy for nonspecific low-back pain. Cochrane Database of Sytematic Reviews , 2007 Issue 2. Wiley & Sons Ltd; 2007.